MICHAEL MCKINLEY received his undergraduate degree from the University of California at Berkeley, and both his M.S. and Ph.D. degrees from Arizona State University. He did his postdoctoral fellowship at the University of California Medical School–San Francisco (UCSF) in the laboratory of Dr. Stanley Prusiner, where he worked for 12 years investigating prions and prion diseases. During this time, he was also a member of the UCSF Medical School anatomy faculty and taught medical histology for 10 years. In 1991, Michael became a member of the biology faculty at Glendale Community College (GCC) in Glendale, Arizona. He taught undergraduate anatomy and physiology, general biology, and genetics at the GCC Main Campus. In 2009, he moved to the GCC North Campus, where he taught anatomy and physiology courses exclusively until he retired in 2012. Between 1991 and 2000, Michael also participated in Alzheimer disease research and served as director of the Brain Donation Program at the Sun Health Research Institute. During this time he also taught developmental biology and genetics at Arizona State University West Campus. He has been an author and co-author of more than 80 scientific papers. Mike’s vast experience in histology, neuroanatomy, and cell biology greatly shaped the related content in the market-leading textbook McKinley/O’Loughlin/Pennefather-O’Brien, Human Anatomy, 5th edition. Mike is an active member of the Human Anatomy and Physiology Society (HAPS). He resides in Tempe, Arizona with his wife Jan.

VALERIE DEAN O’LOUGHLIN received her undergraduate degree from the College of William and Mary, and her M.A. and Ph.D. degrees in biological anthropology from Indiana University. She is a professor of anatomy at Indiana University, where she teaches human gross anatomy to medical students, basic human anatomy to undergraduates, and human anatomy for medical imaging evaluation to undergraduate and graduate students. She also teaches a pedagogical methods course and mentors Ph.D. students pursuing anatomy education research. She is active in the American Association of Anatomists (AAA) and the Society for Ultrasound in Medical Education (SUSME). She is a President Emeritus of the Human Anatomy and Physiology Society (HAPS) and currently serves on the Steering Committee. She received the AAA Basmajian Award for excellence in teaching gross anatomy and outstanding accomplishments in scholarship in education, and recently was selected for the AAA Henry Gray Distinguished Educator award. Valerie is co-author of the market-leading textbook McKinley/O’Loughlin/Pennefather-O’Brien, Human Anatomy, 5th edition.

THERESA STOUTER BIDLE received her undergraduate degree from Rutgers University, her M.S. degree in biomedical science from Hood College in Maryland, and has completed additional graduate coursework in genetics at the National Institutes of Health and in science education at the University of Maryland. She is a professor at Hagerstown Community College, where she teaches anatomy and physiology and nutrition to pre–allied health students. She also mentors new full-time and adjunct faculty who teach anatomy and physiology. Before joining the faculty in 1990, she was the coordinator of the Science Learning Center, where she developed study materials and a tutoring program for students enrolled in science classes. Terri has been a developmental reviewer, has written supplemental materials for both textbooks and lab manuals, and is co-author for Eckel/Ross/Bidle, Anatomy and Physiology Laboratory Manual, 2nd edition.
Dedications

I am indebted to Jan (my wife); Renee, Ryan, and Shaun (my children); and Connor, Eric, Patrick, Keighan, Aydan, and Abbygail (my grandchildren). They are the love of my life and my inspiration always.

—Michael P. McKinley

To my husband Bob and my daughter Erin:
Thank you for always being there for me.

—Valerie Dean O’Loughlin

With love and thanks to my husband Jay and my daughter Stephanie for the many ways that they have supported me during this project.

—Terri Stouter Bidle
# Part I: Organization of the Human Body

<table>
<thead>
<tr>
<th>Chapter</th>
<th>Title</th>
<th>Pages</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>The Sciences of Anatomy and Physiology</td>
<td>1</td>
</tr>
<tr>
<td>2</td>
<td>Atoms, Ions, and Molecules</td>
<td>31</td>
</tr>
<tr>
<td>3</td>
<td>Energy, Chemical Reactions, and Cellular Respiration</td>
<td>72</td>
</tr>
<tr>
<td>4</td>
<td>Biology of the Cell</td>
<td>104</td>
</tr>
<tr>
<td>5</td>
<td>Tissue Organization</td>
<td>153</td>
</tr>
</tbody>
</table>

# Part II: Support and Body Movement

<table>
<thead>
<tr>
<th>Chapter</th>
<th>Title</th>
<th>Pages</th>
</tr>
</thead>
<tbody>
<tr>
<td>6</td>
<td>Integumentary System</td>
<td>187</td>
</tr>
<tr>
<td>7</td>
<td>Skeletal System: Bone Structure and Function</td>
<td>213</td>
</tr>
<tr>
<td>8</td>
<td>Skeletal System: Axial and Appendicular Skeleton</td>
<td>241</td>
</tr>
<tr>
<td>9</td>
<td>Skeletal System: Articulations</td>
<td>299</td>
</tr>
<tr>
<td>10</td>
<td>Muscle Tissue</td>
<td>333</td>
</tr>
<tr>
<td>11</td>
<td>Muscular System: Axial and Appendicular Muscles</td>
<td>374</td>
</tr>
</tbody>
</table>

# Part III: Communication and Control

<table>
<thead>
<tr>
<th>Chapter</th>
<th>Title</th>
<th>Pages</th>
</tr>
</thead>
<tbody>
<tr>
<td>12</td>
<td>Nervous System: Nervous Tissue</td>
<td>438</td>
</tr>
<tr>
<td>13</td>
<td>Nervous System: Brain and Cranial Nerves</td>
<td>485</td>
</tr>
<tr>
<td>14</td>
<td>Nervous System: Spinal Cord and Spinal Nerves</td>
<td>539</td>
</tr>
<tr>
<td>15</td>
<td>Nervous System: Autonomic Nervous System</td>
<td>582</td>
</tr>
<tr>
<td>16</td>
<td>Nervous System: Senses</td>
<td>610</td>
</tr>
<tr>
<td>17</td>
<td>Endocrine System</td>
<td>662</td>
</tr>
</tbody>
</table>

# Part IV: Maintenance and Regulation

<table>
<thead>
<tr>
<th>Chapter</th>
<th>Title</th>
<th>Pages</th>
</tr>
</thead>
<tbody>
<tr>
<td>18</td>
<td>Cardiovascular System: Blood</td>
<td>711</td>
</tr>
<tr>
<td>19</td>
<td>Cardiovascular System: Heart</td>
<td>741</td>
</tr>
<tr>
<td>20</td>
<td>Cardiovascular System: Vessels and Circulation</td>
<td>786</td>
</tr>
<tr>
<td>21</td>
<td>Lymphatic System</td>
<td>843</td>
</tr>
<tr>
<td>22</td>
<td>Immune System and the Body’s Defense</td>
<td>859</td>
</tr>
<tr>
<td>23</td>
<td>Respiratory System</td>
<td>900</td>
</tr>
<tr>
<td>24</td>
<td>Urinary System</td>
<td>954</td>
</tr>
<tr>
<td>25</td>
<td>Fluid and Electrolytes</td>
<td>1000</td>
</tr>
<tr>
<td>26</td>
<td>Digestive System</td>
<td>1034</td>
</tr>
<tr>
<td>27</td>
<td>Nutrition and Metabolism</td>
<td>1082</td>
</tr>
</tbody>
</table>

# Part V: Reproduction

<table>
<thead>
<tr>
<th>Chapter</th>
<th>Title</th>
<th>Pages</th>
</tr>
</thead>
<tbody>
<tr>
<td>28</td>
<td>Reproductive System</td>
<td>1104</td>
</tr>
<tr>
<td>29</td>
<td>Development, Pregnancy, and Heredity</td>
<td>1149</td>
</tr>
</tbody>
</table>
13.9 Cranial Nerves 526

CHAPTER 14
Nervous System: Spinal Cord and Spinal Nerves 539

14.1 Overview of the Spinal Cord and Spinal Nerves 540
14.1a General Functions 540
14.1b Spinal Cord Gross Anatomy 540
14.1c Spinal Nerve Identification and Gross Anatomy 540

14.2 Protection and Support of the Spinal Cord 542
14.3 Sectional Anatomy of the Spinal Cord and Spinal Roots 545
14.3a Distribution of Gray Matter 545
14.3b Distribution of White Matter 546

14.4 Sensory and Motor Pathways 548
14.4a Overview of Conduction Pathways 548
14.4b Sensory Pathways 548
14.4c Motor Pathways 552

INTEGRATE: CONCEPT OVERVIEW
Differences Between Sensory and Motor Pathways 554

14.5 Spinal Nerves 555
14.5a General Distribution of Spinal Nerves 555
14.5b Nerve Plexuses 557
14.5c Intercostal Nerves 557
14.5d Cervical Plexuses 558
14.5e Brachial Plexuses 559
14.5f Lumbar Plexuses 565
14.5g Sacral Plexuses 567

14.6 Reflexes 571
14.6a Characteristics of Reflexes 571
14.6b Components of a Reflex Arc 571
14.6c Classifying Spinal Reflexes 572
14.6d Spinal Reflexes 573
14.6e Reflex Testing in a Clinical Setting 576

14.7 Development of the Spinal Cord 577

CHAPTER 15
Nervous System: Autonomic Nervous System 582

15.1 Comparison of the Somatic and Autonomic Nervous Systems 583
15.1a Functional Organization 583
15.1b Lower Motor Neurons of the Somatic vs Autonomic Nervous System 584
15.1c CNS Control of the Autonomic Nervous System 585

15.2 Divisions of the Autonomic Nervous System 586
15.2a Functional Differences 586
15.2b Anatomic Differences in Lower Motor Neurons 586
15.2c Degree of Response 587

15.3 Parasympathetic Division 588
15.3a Cranial Components 588
15.3b Pelvic Splanchnic Nerves 590

15.4 Sympathetic Division 590
15.4a Organization and Anatomy of the Sympathetic Division 590
15.4b Sympathetic Pathways 594

15.5 Autonomic Plexuses and the Enteric Nervous System 596
15.5a Autonomic Plexuses 596
15.5b Enteric Nervous System 597

15.6 Comparison of Neurotransmitters and Receptors of the Two Divisions 597
15.6a Overview of ANS Neurotransmitters 597
15.6b Cholinergic Receptors 598
15.6c Adrenergic Receptors 599

15.7 Interactions Between the Parasympathetic and Sympathetic Divisions 600
15.7a Autonomic Tone 600

INTEGRATE: CONCEPT OVERVIEW
Comparison of the Parasympathetic and Sympathetic Divisions of the ANS 602
19.7 Cardiac Muscle Cells  765
19.7a Cardiac Muscle Cells at Rest  765
19.7b Electrical and Mechanical Events of Cardiac Muscle Cells  765
19.7c Repolarization and the Refractory Period  767
19.7d The ECG Recording  768

19.8 The Cardiac Cycle  770
19.8a Overview of the Cardiac Cycle  770
19.8b Events of the Cardiac Cycle  772

INTEGRATE: CONCEPT OVERVIEW
Changes Associated with a Cardiac Cycle  774

19.9 Cardiac Output  775
19.9a Introduction to Cardiac Output  775
19.9b Variables That Influence Heart Rate  776
19.9c Variables That Influence Stroke Volume  777
19.9d Variables That Influence Cardiac Output  779

19.10 Development of the Heart  780

CHAPTER 20
Cardiovascular System: Vessels and Circulation  786

20.1 Structure and Function of Blood Vessels  787
20.1a General Structure of Vessels  787
20.1b Arteries  789
20.1c Capillaries  791
20.1d Veins  795
20.1e Pathways of Blood Vessels  795

INTEGRATE: CONCEPT OVERVIEW
How Blood Vessel Form Influences Function  796

20.2 Total Cross-Sectional Area and Blood Flow Velocity  797

20.3 Capillary Exchange  798
20.3a Diffusion and Vesicular Transport  798
20.3b Bulk Flow  798
20.3c Net Filtration Pressure  799
20.3d Role of the Lymphatic System  800

20.4 Local Blood Flow  800
20.4a Degree of Vascularization and Angiogenesis  800
20.4b Myogenic Response  801
20.4c Local, Short-Term Regulation  801
20.4d Relationship of Local and Total Blood Flow  802

20.5 Blood Pressure, Resistance, and Total Blood Flow  803
20.5a Blood Pressure  803
20.5b Resistance  808
20.5c Relationship of Blood Flow to Blood Pressure Gradients and Resistance  809

20.6 Regulation of Blood Pressure and Blood Flow  810
20.6a Neural Regulation of Blood Pressure  810
20.6b Hormonal Regulation of Blood Pressure  812

INTEGRATE: CONCEPT OVERVIEW
Factors That Regulate Blood Pressure  814

20.7 Blood Flow Distribution During Exercise  816

20.8 Pulmonary Circulation  816
20.8a Blood Flow Through the Pulmonary Circulation  816
20.8b Characteristics of the Pulmonary Circulation  817

20.9 Systemic Circulation: Vessels from and to the Heart  818
20.9a General Arterial Flow Out of the Heart  818
20.9b General Venous Return to the Heart  820

20.10 Systemic Circulation: Head and Trunk  820
20.10a Head and Neck  820
20.10b Thoracic and Abdominal Walls  824
20.10c Thoracic Organs  826
20.10d Gastrointestinal Tract  827
20.10e Posterior Abdominal Organs, Pelvis, and Perineum  830

20.11 Systemic Circulation: Upper and Lower Limbs  832
20.11a Upper Limb  832
20.11b Lower Limb  834

20.12 Comparison of Fetal and Postnatal Circulation  837
20.12a Fetal Circulation  837
20.12b Postnatal Changes  837

CHAPTER 21
Lymphatic System  843

21.1 Lymph and Lymph Vessels  845
21.1a Lymph and Lymphatic Capillaries  845
21.1b Lymphatic Vessels, Trunks, and Ducts  846

21.2 Overview of Lymphatic Tissue and Organs  848

21.3 Primary Lymphatic Structures  849
21.3a Red Bone Marrow  849
21.3b Thymus  849

21.4 Secondary Lymphatic Structures  850
21.4a Lymph Nodes  850
21.4b Spleen  852
21.4c Thymus  854
21.4d Lymphatic Nodules and MALT  854

INTEGRATE: CONCEPT OVERVIEW
Relationship of the Lymphatic System to Both the Cardiovascular System and Immune System  855

CHAPTER 22
Immune System and the Body's Defense  859

22.1 Overview of Diseases Caused by Infectious Agents  860

22.2 Overview of the Immune System  861
22.2a Immune Cells and Their Locations  861
22.2b Cytokines  862
22.2c Comparison of Innate Immunity and Adaptive Immunity  863

22.3 Innate Immunity  864
22.3a Preventing Entry  864
22.3b Nonspecific Internal Defenses: Cells  866
22.3c Nonspecific Internal Defenses: Antimicrobial Proteins  867
22.3d Nonspecific Internal Defenses: Inflammation  868
22.3e Nonspecific Internal Defenses: Fever  871

INTEGRATE: CONCEPT OVERVIEW
Innate Immunity  872

22.4 Adaptive Immunity: An Introduction  874
22.4a Antigens  874
22.4b General Structure of Lymphocytes  875
22.4c Antigen-Presenting Cells and MHC Molecules  876
22.4d Overview of Life Events of Lymphocytes  881

22.5 Formation and Selection of T-Lymphocytes in Primary Lymphatic Structures  881
22.5a Formation of T-Lymphocytes  881
22.5b Selection and Differentiation of T-Lymphocytes  882
22.5c Migration of T-Lymphocytes  882

22.6 Activation and Clonal Selection of Lymphocytes  883
22.6a Activation of T-Lymphocytes  883
22.6b Activation of B-Lymphocytes  884
22.6c Lymphocyte Recirculation  884

22.7 Effector Response at Infection Site  885
22.7a Effector Response of T-Lymphocytes  885
22.7b Effector Response of B-Lymphocytes  886

22.8 Immunoglobulins  886
22.8a Structure of Immunoglobulins  887
22.8b Actions of Antibodies  887
22.8c Classes of Immunoglobulins  887

22.9 Immunologic Memory and Immunity  889
22.9a Immunologic Memory  889

INTEGRATE: CONCEPT OVERVIEW
Adaptive Immunity  890
22.9b Measure of Immunologic Memory  892
22.9c Active and Passive Immunity  893
CHAPTER 23
Respiratory System 900

23.1 Introduction to the Respiratory System 901
23.1a General Functions of the Respiratory System 901
23.1b General Organization of the Respiratory System 901
23.1c Respiratory Mucosa 902

23.2 Upper Respiratory Tract 903
23.2a Nasal and Nasal Cavity 903
23.2b Paranasal Sinuses 904
23.2c Pharynx 906

23.3 Lower Respiratory Tract 907
23.3a Larynx 907
23.3b Trachea 909
23.3c Bronchial Tree 910
23.3d Respiratory Zone: Respiratory Bronchioles, Alveolar Ducts, and Alveoli 914
23.3e Respiratory Membrane 917

23.4 Lungs 917
23.4a Gross Anatomy of the Lung 917
23.4b Circulation to and Innervation of the Lungs 919
23.4c Pleural Membranes and Pleural Cavity 921
23.4d How Lungs Remain Inflated 922

23.5 Respiration: Pulmonary Ventilation 922
23.5a Introduction to Pulmonary Ventilation 923
23.5b Mechanics of Breathing 924
23.5c Nervous Control of Breathing 928
23.5d Airflow, Pressure Gradients, and Resistance 932
23.5e Pulmonary and Alveolar Ventilation 933
23.5f Volume and Capacity 933

23.6 Respiration: Alveolar and Systemic Gas Exchange 935
23.6a Chemical Principles of Gas Exchange 935
23.6b Alveolar Gas Exchange (External Respiration) 937
23.6c Systemic Gas Exchange (Internal Respiration) 938

23.7 Respiration: Gas Transport 940
23.7a Oxygen Transport 940
23.7b Carbon Dioxide Transport 940
23.7c Hemoglobin as a Transport Molecule 941

23.8 Breathing Rate and Homeostasis 945
23.8a Effects of Hyperventilation and Hypoventilation on Cardiovascular Function 945

INTEGRATE: CONCEPT OVERVIEW
The Movement of Oxygen and Carbon Dioxide 947
23.8b Breathing and Exercise 948

CHAPTER 24
Urinary System 954

24.1 Introduction to the Urinary System 955

24.2 Gross Anatomy of the Kidney 957
24.2a Location and Support 957
24.2b Sectional Anatomy of the Kidney 958
24.2c Innervation of the Kidney 959

24.3 Functional Anatomy of the Kidney 959
24.3a Nephron 959
24.3b Collecting Tubules and Collecting Ducts 963
24.3c Juxtaglomerular Apparatus 964

24.4 Blood Flow and Filtered Fluid Flow 964
24.4a Blood Flow Through the Kidney 964
24.4b Filtrate, Tubular Fluid, and Urine Flow 966

24.5 Production of Filtrate Within the Renal Corpuscle 967
24.5a Overview of Urine Formation 967
24.5b Filtration Membrane 968
24.5c Formation of Filtrate and Its Composition 969
24.5d Pressures Associated with Glomerular Filtration 969
24.5e Regulation of Glomerular Filtration Rate 970

INTEGRATE: CONCEPT OVERVIEW
Glomerular Filtration and Its Regulation 974

24.6 Reabsorption and Secretion in Tubules and Collecting Ducts 975
24.6a Overview of Transport Processes 975
24.6b Transport Maximum and Renal Threshold 976
24.6c Substances Reabsorbed Completely 976
24.6d Substances with Regulated Reabsorption 977
24.6e Substances Eliminated as Waste Products 982
24.6f Establishing the Concentration Gradient 984

INTEGRATE: CONCEPT OVERVIEW
Tubular Reabsorption and Tubular Secretion 986

24.7 Evaluating Kidney Function 987
24.7a Measuring Glomerular Filtration Rate 987
24.7b Measuring Renal Plasma Clearance 987

24.8 Urine Characteristics, Transport, Storage, and Elimination 988
24.8a Characteristics of Urine 988
24.8b Urinary Tract (Ureters, Urinary Bladder, Urethra) 990
24.8c Micturition 994

CHAPTER 25
Fluid and Electrolytes 1000

25.1 Body Fluids 1001
25.1a Percentage of Body Fluid 1001
25.1b Fluid Compartments 1001

25.2 Fluid Balance 1004
25.2a Fluid Intake and Fluid Output 1004
25.2b Fluid Imbalance 1005
25.2c Regulation of Fluid Balance 1007

25.3 Electrolyte Balance 1008
25.3a Nonelectrolytes and Electrolytes 1008
25.3b Major Electrolytes: Location, Functions, and Regulation 1009

25.4 Hormonal Regulation 1013
25.4a Antidiuretic Hormone 1013
25.4b Aldosterone 1016
25.4c Atrial Natriuretic Peptide 1017

25.5 Acid-Base Balance 1019
25.5a Categories of Acid 1019
25.5b The Kidneys and Regulation of Fixed Acids 1019
25.5c Respiration and Regulation of Volatile Acid 1021
25.5d Chemical Buffers 1022

INTEGRATE: CONCEPT OVERVIEW
Maintaining Acid-Base Balance 1023

25.6 Disturbances to Acid-Base Balance 1024
25.6a Overview of Acid-Base Imbalances 1024
25.6b Respiratory-Induced Acid-Base Disturbances 1025
25.6c Metabolic-Induced Acid-Base Disturbances 1025
25.6d Compensation 1027

CHAPTER 26
Digestive System 1034

26.1 Introduction to the Digestive System 1035
26.1a Organization of the Digestive System 1035
26.1b General Functions of the Digestive System 1036
26.1c Gastrointestinal Tract Wall 1036
26.1d Overview of the Regulation of the Digestive System 1038
26.1e Serous Membranes of the Abdominal Cavity 1038

26.2 Upper Gastrointestinal Tract 1040
26.2a Overview of the Upper Gastrointestinal Tract Organs 1040
26.2b Oral Cavity and Salivary Glands 1040
26.2c Pharynx and Esophagus 1044
26.2d Stomach 1047

26.3 Lower Gastrointestinal Tract 1054
26.3a Overview of the Lower Gastrointestinal Tract Organs 1054
26.3b Small Intestine 1054
26.3c Accessory Digestive Organs and Ducts 1058
26.3d Large Intestine 1064
26.4 Nutrients and Their Digestion 1069
  26.4a Carbohydrate Digestion 1069
  26.4b Protein Digestion 1071
  26.4c Lipid Digestion 1073
  26.4d Nucleic Acid Digestion 1075

INTEGRATE: CONCEPT OVERVIEW
Nutrients and Their Digestion 1076
  26.4e Water, Electrolyte, and Vitamin Absorption 1078

CHAPTER 27
Nutrition and Metabolism 1082

27.1 Introduction to Nutrition 1083

27.2 Macronutrients 1083
  27.2a Carbohydrates 1083
  27.2b Lipids 1084
  27.2c Proteins 1084

27.3 Micronutrients 1085
  27.3a Vitamins 1085
  27.3b Minerals 1086

27.4 Guidelines for Adequate Nutrition 1088

27.5 Regulating Blood Levels of Nutrients 1089
  27.5a Absorptive State 1089
  27.5b Postabsorptive State 1090

27.6 Functions of the Liver 1090
  27.6a Cholesterol Synthesis 1090
  27.6b Transport of Lipids 1092
  27.6c Integration of Liver Structure and Function 1093

INTEGRATE: CONCEPT OVERVIEW
Liver Structure and Function 1094

27.7 Central Role of Cellular Respiration 1096
  27.7a ATP Generation 1096
  27.7b Interconversion of Nutrient Biomolecules and Their Building Blocks 1096

27.8 Energy and Heat 1098
  27.8a Metabolic Rate 1098
  27.8b Temperature Regulation 1098

REPRODUCTION

CHAPTER 28
Reproductive System 1104

28.1 Overview of Female and Male Reproductive Systems 1105
  28.1a Common Elements of the Two Systems 1105
  28.1b Female Maturation 1105
  28.1c Anatomy of the Perineum 1105

28.2 Gametogenesis 1106
  28.2a A Brief Review of Heredity 1106
  28.2b An Overview of Meiosis 1107
  28.2c Meiosis I: Reduction Division 1108
  28.2d Meiosis II: Separation of Sister Chromatids 1110

28.3 Female Reproductive System 1111
  28.3a Ovaries 1112
  28.3b Oogenesis and the Ovarian Cycle 1115
  28.3c Ovary, Tubes, Uterus, and Vagina 1119
  28.3d Ovary (Menstrual) Cycle and Menstruation 1122
  28.3e External Genitalia 1123

INTEGRATE: CONCEPT OVERVIEW
The Interrelationships Between Hormones, the Ovarian Cycle, and the Uterine (Menstrual) Cycle 1124
  28.3f Mammary Glands 1126
  28.3g Female Sexual Response 1127

28.4 Male Reproductive System 1129
  28.4a Scrotum 1129
  28.4b Testes and Spermatogenesis 1131
  28.4c Duct System in the Male Reproductive Tract 1136
  28.4d Accessory Glands and Sperm Production 1138
  28.4e Penis 1139
  28.4f Male Sexual Response 1140

28.5 Development and Aging of the Female and Male Reproductive Systems 1140
  28.5a Genetic Versus Phenotypic Sex 1140
  28.5b Formation of Indifferent Gonads and Genital Ducts 1141
  28.5c Internal Genitalia Development 1142
  28.5d External Genitalia Development 1142
  28.5e Puberty 1144
  28.5f Menopause and Male Climacteric 1144

CHAPTER 29
Development, Pregnancy, and Heredity 1149

29.1 Overview of the Prenatal Period 1150

29.2 Pre-Embryonic Period 1151
  29.2a Fertilization 1152
  29.2b Cleavage 1153
  29.2c Implantation 1155
  29.2d Formation of the Bilaminar Germinal Disc and Extraembryonic Membranes 1156
  29.2e Development of the Placenta 1157

29.3 Embryonic Period 1158
  29.3a Gastrulation and Formation of the Primary Germ Layers 1159
  29.3b Folding of the Embryonic Disc 1160
  29.3c Organogenesis 1163

29.4 Fetal Period 1163

29.5 Effects of Pregnancy on the Mother 1166
  29.5a The Course of Pregnancy 1166
  29.5b Hormonal Changes 1166
  29.5c Uterine and Mammary Gland Changes 1167
  29.5d Digestive System, Nutrient, and Metabolic Changes 1168
  29.5e Cardiovascular and Respiratory System Changes 1169
  29.5f Urinary System Changes 1169

29.6 Labor (Parturition) and Delivery 1170
  29.6a Factors That Lead to Labor 1170
  29.6b False Labor 1170
  29.6c Initiation of True Labor 1171
  29.6d Stages of True Labor 1172

29.7 Postnatal Changes for the Newborn 1174

29.8 Changes in the Mother After Delivery 1174
  29.8a Hormonal Changes 1174
  29.8b Blood Volume and Fluid Changes 1175
  29.8c Lactation 1175
  29.8d Uterine Changes 1177

29.9 Heredity 1177
  29.9a Overview of Human Genetics 1177

INTEGRATE: CONCEPT OVERVIEW
Anatomic and Physiologic Changes That Occur in the M other 1178
  29.9b Patterns of Inheritance 1180
  29.9c Sex-Linked Inheritance 1181
  29.9d Penetration and Environmental Influences on Heredity 1182

Appendix A A-1
Appendix B B-1
Glossary G-1
Index I-1
Human anatomy and physiology is a fascinating subject. However, students can be overwhelmed by the complexity, the interrelatedness of concepts from different chapters, and the massive amount of material in the course. Our goal was to create a textbook to guide students on a clearly written and expertly illustrated beginner’s path through the human body.

An Integrative Approach

One of the most daunting challenges that students face in mastering concepts in an anatomy and physiology course is integrating related content from numerous chapters. Understanding a topic like blood pressure, for example, requires knowledge from the chapters on the heart, blood vessels, kidneys, and how these structures are regulated by the nervous and endocrine systems. The usefulness of a human anatomy and physiology text is dependent in part on how successfully it helps students integrate these related concepts. Without this, students are only acquiring what seems like unrelated facts without seeing how they fit into the whole.

To adequately explain such complex concepts to beginning students in our own classrooms, we as teachers present multiple topics over the course of many class periods, all the while balancing these detailed explanations with refreshers of content previously covered and intermittent glimpses of the big picture. Doing so ensures that students learn not only the individual pieces, but also how the pieces ultimately fit together. This book represents our best effort to replicate this teaching process. In fact, it is the effective integration of concepts throughout the text that makes this book truly unique from other undergraduate anatomy and physiology texts.

Our goal of emphasizing the interrelatedness of body systems and the connections between form and function necessitates a well-thought-out pedagogical platform to deliver the content. First and foremost, we have written a very user-friendly text with concise, accurate descriptions that are thorough, but don’t overwhelm readers with nonessential details. The text narrative is deeply integrated with corresponding illustrations drawn specifically to match the textual explanations. In addition, we have included a set of “Integrate” features that support our theme and work together to give the student a well-rounded introduction to anatomy and physiology. Integrate: Concept Overview figures are one- or two-page visual summaries that aggregate related concepts in a big-picture view. These comprehensive figures link multiple sections of a chapter together in a cohesive snapshot ideal for study and review. Integrate: Concept Connections boxes provide glimpses of how concepts at hand will play out in upcoming chapters, and also pull vital information from earlier chapters back into the discussion at crucial points when relevant to a new topic. Integrate: Clinical View discussions apply concepts from the surrounding narrative to practical or clinical contexts, providing examples of what can go wrong in the human body to help crystallize understanding of the “norm.” Integrate: Learning Strategy boxes infuse each chapter with practical study tips to understand and remember information. Learning strategies include mnemonics, analogies, and kinesthetic activities that students can perform to relate the anatomy and physiology to their own bodies. Finally, the digital assets that accompany our book are tied to each section’s learning objectives and previewed in the Integrate: Online Study Tools boxes at the end of each chapter.

Chapter Organization

In order to successfully execute an integrative approach, foundational topics must be presented at the point when it matters most for understanding. This provides students with a baseline of knowledge about a given concept before it comes time to apply that information in a more complex situation. Topics are thus subdivided and covered in this sequence:

- **Chapter 2: Atoms, Ions, and Molecules**  Most students taking an A&P course have limited or no chemistry background, which requires a textbook to provide a detailed, organized treatment of atomic and molecular structure, bonding, water, and biological macromolecules as a basis to understanding physiological processes.

- **Chapter 3: Energy, Chemical Reactions, and Cellular Respiration**  ATP is essential to all life processes. A solid understanding of ATP furthers student comprehension of movement of materials across a membrane, muscle contractions, production of needed replacement molecules and structures in cells, action potentials in nerves, pumping of the heart, and removal of waste materials in the kidneys. This textbook elevates the importance of the key concept of ATP by teaching it early. We then utilize this knowledge in later chapters as needed, expanding on what has already been introduced rather than re-teaching it entirely.

- **Chapter 13: Nervous System: Brain and Cranial Nerves** and **Chapter 14: Nervous System: Spinal Cord and Spinal Nerves**  Instead of subdividing the nervous system discussion into separate central nervous system (CNS) and peripheral nervous system (PNS) chapters, nervous system structures are grouped by region. Thus, students can integrate the cranial nerves with their respective nuclei in the brain, and they can integrate the spinal cord regions with the specific spinal nerves that originate from these regions.

- **Chapter 17: Endocrine System**  We have organized both the endocrine system chapter and the specific coverage of the many hormones released from endocrine glands to most effectively and efficiently guide students in understanding how this system of control functions in maintaining homeostasis. Within the chapter on the endocrine system, we provide an introduction and general discussion of the endocrine system’s central concepts and describe selected representative hormones that maintain body homeostasis. Details of the actions of most other hormones—which require an understanding of specific anatomic structures covered in other chapters—are described in those chapters; for example, sex hormones are discussed in Chapter 28: Reproductive System. Learning the various hormones is facilitated by the inclusion of a “template” figure for each major hormone; each visual template includes the same components (stimulus,
receptor, control center, and effectors) organized in a similar layout. In addition, information on each major hormone described in this text can be quickly accessed in the summary tables following chapter 17.

- **Chapter 21: Lymphatic System and Chapter 22: Immune System and the Body’s Defense** A single chapter that discusses both the lymphatic system and immune system is overwhelming for most students. Thus, we separated the discussion into two separate chapters. The lymphatic system chapter focuses on the anatomic structures that compose the system, and provides a brief functional overview of each structure. This allows us to provide a thorough discussion and overview of the immune system in a separate chapter, where we frequently reference and integrate material from the earlier chapter.

- **Chapter 29: Development, Pregnancy, and Heredity** Coverage of heredity is included in the chapter on pregnancy and human development as a natural extension of Chapter 28: Reproductive System. This introduction will serve well as a precursor for students who follow their A&P course with a genetics course.

### Changes to the Third Edition

Real student data points derived from thousands of SmartBook users have guided the revision process for this edition. In addition, this revision has been informed by dozens of chapter reviews by A&P instructors. The following global changes have been implemented throughout all chapters:

- Additional references were added to concepts previously covered, as well as to related material in upcoming sections and chapters, to further connect concepts.
- Terminology has been updated and definitions are added throughout.
- New “What Do You Think?” and “What Did You Learn?” questions were added throughout the text.

**Chapter 1**

- New section added about how best to study A&P
- Revised: figure 1.8, figure 1.9, figure 1.13
- Clinical View 1.1: Etiology (Causes) and Pathogenesis (Development) of Disease updated to include more detail on sonography and imaging; added new photos and labeling to images

**Chapter 2**

- Moved description of inorganic and organic molecules from section 2.7: Biological Molecules to beginning of section 2.4: Molecular Structure of Water and the Properties of Water
- Revised: figure 2.1b, figure 2.9, figure 2.10, figure 2.13, figure 2.17, figure 2.19, figure 2.20, figure 2.21, figure 2.22, figure 2.24, figures within table 2.4

**Chapter 3**

- Revised: figure 3.1, figure 3.3, figure 3.6, figure 3.7, figure 3.10, figure 3.13, figure 3.14, figure 3.16, figure 3.18, figure 3.19
- Revised coverage of ATP cycling in section 3.2b: Classification of Chemical Reactions

**Chapter 4**

- Revised: figure 4.4, figure 4.5, figure 4.6, figure 4.7, figure 4.9, figure 4.10, figure 4.11, figure 4.14, figure 4.15, figure 4.17, figure 4.18, figure 4.19, figure 4.20, figure 4.21, figure 4.23, figure 4.27, figure 4.28, figure 4.30, figure 4.32, figure 4.39, figure 4.42 (several new photos)
- New figure 4.38 on genetic code
- Modified section 4.1a: How Cells Are Studied
- Updated section 4.2b: Membrane Proteins
- Revised section 4.3: Membrane Transport
- Revised and reorganized section 4.6b: Non-Membrane-Bound Organelles

**Chapter 5**

- Updated art in tables 5.2, 5.3
- Revised: figure 5.4, figure 5.8, figure 5.10, figure 5.11, figure 5.12
- Modified section 5.2b: Functions of Connective Tissue
- Updated text in tables 5.6, 5.10
- Removed coverage of perichondrium (covered in Chapter 7)
- Modified section 5.5b: Body Membranes
- Updated Clinical View 5.4: Stem Cells
- Revised Clinical View 5.5: Gangrene
- Updated Chapter Summary to include lymph in discussion of fluid connective tissue

**Chapter 6**

- Updated terminology to use “keratinocyte” instead of “cell” where appropriate
- Updated section on stratum corneum to include coverage of dermidicin
- Removed reference to human pheromones

**Chapter 7**

- In section 7.2, added information on the appearance of living bone
- Revised: figure 7.4, figure 7.11, figure 7.15
- Revised discussion of exercise in space
- Clinical View 7.7: Osteoporosis—added information on DEXA scans

**Chapter 8**

- Table 8.1 revised to include parietal foramina
- Revised: figure 8.5, figure 8.7a, figure 8.11, figure 8.12a, figure 8.14, figure 8.22a, figure 8.31, figure 8.34b
- In section 8.2b: Views of the Skull and Landmark Features, revised sella turcica information to include hypophyseal fossa
- Table 8.2 and table 8.3 figures were revised to improve clarity and accuracy
- Revised Clinical View 8.2: Craniosynostosis and Plagiocephaly
- In section 8.3: Bones Associated with the Skull, revised information on functions of the hyoid bone’s cornua and body
- Revised figure in Clinical View 8.4: Herniated Discs
- Table 8.6 text and figures updated regarding width of pelvis and ilia
Chapter 9
- Reversed order of sections 9.5 and 9.6, so Movements of Synovial Joints are discussed prior to Synovial Joints and Levers
- Table 9.1 simplified
- Revised: figure 9.2, figure 9.3, figure 9.6, figure 9.14
- Modified description of synovial membrane

Chapter 10
- Updated section 10.1a: Functions of Skeletal Muscle and section 10.1b: Characteristics of Skeletal Muscle Cells
- Revised section 10.2a: Gross Anatomy of Skeletal Muscle
- Revised section 10.2b: Microscopic Anatomy of Skeletal Muscle to add details of triad
- Revised: figure 10.6, figure 10.10, figure 10.11, figure 10.12, figure 10.14, figure 10.15, figure 10.16, figure 10.17, figure 10.20, figure 10.21, figure 10.22, figure 10.30
- Revised: table 10.3, table 10.8, table 10.18
- New photo in Clinical View 12.1: Pathogenic Agents and Fast Axonal Transport figure of axonal transport for how pathogenic organisms move to cell body
- New illustration of battery for text discussion on Ohm’s Law (pg. 457)
- New: figure 12.13: Neuron’s and Ohm’s Law
- New photo in figure 12.17

Chapter 11
- Replaced the terms origin and insertion with superior attachment and inferior attachment where appropriate
- Revised Clinical View 11.2: Idiopathic Facial Nerve Paralysis (Bell Palsy) to include information on Lyme disease effects
- New photo in Clinical View 11.2: Idiopathic Facial Nerve Paralysis (Bell Palsy)
- Revised: figure 11.3, table 11.8, table 11.18
- Revised: figure 11.17, figure 11.19, figure 11.21b, figure 11.22
- New photo in Clinical View 11.7: Lateral Epicondylitis (“Tennis Elbow”)
- Revised figure in Clinical View 11.8: Carpal Tunnel Syndrome

Chapter 12
- Revised section 12.2b: Neuron Structure
- Added section 12.1c: Nerves and Ganglia
- New Concept Connection on bundling by connective tissue
- New Learning Strategy on glial cells
- Clinical View 12.3: Nervous System Disorders Affecting Myelin now includes Zika virus as it relates to Guillain-Barré syndrome
- New Learning Strategy on states of voltage-gated Na⁺ channels
- Revised Clinical View 12.6: Altered Acetylcholine Function and Changes in Breathing
- Revised section 12.1c: Nerves and Ganglia was previously section 12.2e (moved forward in the chapter)
- Revised: figure 12.3, figure 12.5, figure 12.6, figure 12.7, figure 12.9b, figure 12.10, figure 12.11, figure 12.14, figure 12.16, figure 12.17, figure 12.18, figure 12.21, figure 12.22, figure 12.23, figure 12.24, figure 12.25
- New Clinical View 12.1: Pathogenic Agents and Fast Axonal Transport
- New: figure 12.13 on ATP for muscle metabolism; figure 12.21 on recruitment; figure 10.24 comparing isometric and isotonic contractions; figure 10.26 on maximizing force of contractions

Chapter 13
- Revised section 13.1: Brain Organization and Development
- Revised Clinical View 13.1: Traumatic Brain Injuries: Concussion and Contusion
- Revised: figure 13.1, figure 13.4, figure 13.5, figure 13.9, figure 13.12, figure 13.14, figure 13.21, figure 13.23b, figure 13.24a, figure 13.25, figure 13.30, figure 13.31
- Revised: table 13.2, table 13.4, table 13.5
- Updated Clinical View 13.3: Meningitis and Encephalitis
- Revised Clinical View 13.6: Mapping Functional Brain Regions
- New Learning Strategy on functions of the hypothalamus
- Revised coverage of medulla autonomic centers

Chapter 14
- Revised section 14.1: Overview of the Spinal Cord and Spinal Nerves reorganized to provide an overview of the chapter content; section 14.1c: Spinal Nerve Identification and Gross Anatomy now contains content on spinal roots that was moved from section 14.5a
- Section 14.2: Protection and Support of the Spinal Column revised to include more explanation on vertebral column
- Section 14.3: Sectional Anatomy of the Spinal Cord and Spinal Roots provides more information on functional relationship between gray matter and spinal nerve roots, sensory receptors, and effectors.
- Section 14.5a: General Distribution of Spinal Nerves
- Revised: figure 14.1, figure 14.2, figure 14.4, figure 14.5, figure 14.6, figure 14.10, figure 14.14, figure 14.18c

Chapter 15
- Section 15.3b: Pelvic Splanchnic Nerves rearranged to discuss parasympathetic cranial nerve physiology first, followed by anatomy
- Section 15.5: Autonomic Plexuses and the Enteric Nervous System moved forward to appear after discussion of sympathetic and parasympathetic systems
- New section 15.5b: Enteric Nervous System
- New Learning Strategy on parasympathetic division
• Updated Clinical View 15.3: Raynaud Syndrome, with photo added
• Revised: figure 15.4, figure 15.6, figure 15.7b, figure 15.10, figure 15.11

Chapter 16
• New Clinical View 16.2: Eye Infections
• Revised: figure 16.2, figure 16.3, figure 16.5, figure 16.7, figure 16.8, figure 16.10, figure 16.15, figure 16.18, figure 16.22, figure 16.26, figure 16.27, figure 16.28

Chapter 17
• Section 17.1a: Overview of Endocrine System rewritten and expanded
• Revised: Section 17.1b: Comparison of the Two Control Systems
• Section 17.1c: General Functions of the Endocrine System contains added examples for each function of the endocrine system
• Section 17.3b: Local Hormones rewritten, now includes new Concept Connection on local hormones that act as vasoactive substances; new Clinical View 17.1: Synthesis of Eicosanoids
• Section 17.7b: Interactions Between the Hypothalamus and the Posterior Pituitary Gland contains expanded description of ADH and oxytocin
• Section 17.7c: Interactions Between the Hypothalamus and the Anterior Pituitary Gland reorganized and updated to add explanation for figure 17.12
• Revised: figure 17.1, figure 17.5, figure 17.7, figure 17.8, figure 17.10, figure 17.11, figure 17.12, figure 17.14, figure 17.16, figure 17.17, figure 17.18, figure 17.19, figure 17.20, figure 17.22, figure 17.23

Chapter 18
• Clinical View 18.3: Transfusions updated to include information on donor wait times between transfusions
• New Clinical View 18.4: Whole Blood Versus Plasma Donations: What’s the Difference?
• New Clinical View 18.5: Fetal Hemoglobin and Physiologic Jaundice
• New Learning Strategy on Blood Types
• Revised: figure 18.5a, 18.7, figure 18.8, figure 18.11 (colorized micrograph of blood clotting), figure 18.12

Chapter 19
• Section 19.1a: General Function contains expanded content of the function of the cardiovascular system in transporting blood, including a new Concept Connection that provides examples of body systems dependent on blood transport
• Section 19.1b: Overview of Components revised to further describe circulation routes through the right and left sides of the heart
• New Clinical View 19.1: Congestive Heart Failure
• Section 19.2b: The Pericardium contains added description of pericardial sac
• Section 19.3a: Superficial Features of the Heart contains added explanation to align with figure 19.7
• Revised Clinical View 19.5: Coronary Heart Disease, Angina Pectoris, and Myocardial Infarction to add content on coronary heart disease

Chapter 20
• Revised: figure 20.1, figure 20.3, figure 20.4, figure 20.5, figure 20.7, figure 20.14, figure 20.18, figure 20.19, figure 20.20, figure 20.22, figure 20.26, figure 20.27

Chapter 21
• Revised Learning Strategy on lymphocytes to describe origin of name for B-lymphocytes
• Revised: figure 21.1, figure 21.6, figure 21.9

Chapter 22
• New Table 22.5: Actions of Antibodies Following Antigen Binding
• Section 22.1: Overview of Diseases Caused by Infectious Agents revised to update definition of bacteria
• New Learning Strategy on the study of the immune system
• Revised Section 22.3a: Preventing Entry
• New Learning Strategy on CD4/CD8 with MHC Class I/II
• Section 22.5b: Selection and Differentiation of T-Lymphocytes rearranged for better alignment of illustration and text
• Revised: figure 22.1, figure 22.2, figure 22.3, figure 22.4, figure 22.7, figure 22.8, figure 22.10, figure 22.12, figure 22.13, figure 22.14, figure 22.15, figure 22.16, figure 22.17, figure 22.19, figure 22.20

Chapter 23
• New Learning Strategy on structural and functional organization of the respiratory system
• Revised Section 23.3b: Trachea
• New Clinical View 23.4: Tracheotomy
• Clinical View 23.5: Bronchitis now includes coverage on exercise-induced asthma
• Revised Section 23.3c: Bronchial Tree
• Revised Section 23.3d: Respiratory Zone: Respiratory Bronchioles, Alveolar Ducts, and Alveoli
• New Clinical View 23.7: Pneumonia
• New photos of lungs in Clinical View 23.8: Smoking
• Revised: figure 23.3, figure 23.5, figure 23.6, figure 23.8, figure 23.9, figure 23.10, figure 23.11, figure 23.14, figure 23.19, figure 23.14, figure 23.16, figure 23.19, figure 23.21, figure 23.23, figure 23.25, figure 23.26, figure 23.31
• New figure 23.27: Changes in Respiratory Gas Partial Pressures Within the Blood
Chapter 24
- New figure in Clinical View 24.1: Renal Ptosis and Hydrenephrosis
- Section 24.3c: Juxtaglomerular Apparatus revised to expand coverage of mesangial cells
- Concept Connection on blood pressure expanded
- Revised: figure 24.2, figure 24.3, figure 24.4, figure 24.5, figure 24.6, figure 24.7, figure 24.9, figure 24.11, figure 24.13, figure 24.14, figure 24.15, figure 24.16, figure 24.18, figure 24.19, figure 24.22, figure 24.23, figure 24.24, figure 24.26, figure 24.27, figure 24.28

Chapter 25
- Section 25.1: Body Fluids introduction revised to emphasize the main points of the chapter
- Figure 25.2: Percentages of Solute in Body Fluids is new and contains the information from previous edition’s Table 25.1
- New Clinical View 25.2: Hemorrhaging
- New Clinical View 25.4: Angiotensin-Converting Enzyme (ACE) Inhibitors
- Section 25.3b: Major Electrolytes: Location, Functions, and Regulation revised to integrate concepts of acid-base balance and hyperkalemia and hypokalemia
- Section 25.5: Acid-Base Balance revised for increased readability
- Section 25.5c: Respiration and Regulation of Volatile Acid has tighter integration with concepts in Chapter 23: Respiratory System
- New Learning Strategy on Type A and Type B Intercalated Cells
- Section 25.6: Disturbances to Acid-Base Balance is revised for increased readability and tighter integration with Clinical View 25.8: Arterial Blood Gas (ABG) and Diagnosing Different Types of Acid-Base Disturbances
- Section 25.6b: Respiratory-Induced Acid-Base Disturbances includes normal values for arterial blood gas
- New: figure 25.2, figure 25.12, figure 25.16
- Revised: figure 25.1, figure 25.4, figure 25.5, figure 25.6, figure 25.7, figure 25.8, figure 25.9, figure 25.10, figure 25.11, figure 25.12, figure 25.13, figure 25.14, figure 25.15

Chapter 26
- Sections 26.1b, 26.1c, 26.1d, and 26.1e revised for readability
- New Learning Strategy for layers of muscularis in GI tract wall
- New Clinical View 26.3: Achalasia
- New Learning Strategy on gastric gland secretions for parietal cells and chief cells
- Sections 26.3b: Small Intestine and 26.3c: Accessory Digestive Organs and Ducts revised
- New Clinical View 26.10: Pancreatic Cancer
- New Clinical View 26.13: Fecal Transplant
- New Learning Strategy on lipid digestion and absorption
- New Clinical View 26.17: Cystic Fibrosis and the Pancreas
- New Section 26.4e: Water, Electrolyte, and Vitamin Absorption
- Revised: figure 26.2c, figure 26.6, figure 26.8, figure 26.13, figure 26.14, figure 26.15, figure 26.16, figure 26.18, figure 26.20, figure 26.22, figure 26.29

Chapter 27
- New Clinical View 27.3: Obesity
- New Clinical View 27.5: Heat Related Illnesses
- Expanded Clinical View 27.6: Hypothermia, Frostbite, and Dry Gangrene

Chapter 28
- Sections 28.3a: Ovaries and 28.3b: Oogenesis and the Ovarian Cycle discussion on primary and secondary follicles revised, and discussion on antral follicles expanded
- Revised information on ovarian ligaments
- Revised Clinical View 28.2: Ovarian Cancer with current statistics
- Revised Clinical View 28.5: Cervical Cancer to include information on recommendations for vaccination
- Updated Clinical View 28.6: Breast Cancer
- Revised: figure 28.4, figure 28.5, figure 28.6, figure 28.7, figure 28.9, figure 28.11, figure 28.12, figure 28.15, figure 28.16, figure 28.18, figure 28.19d

Chapter 29
- Revised Clinical View 29.2: Infertility and Infertility Treatments
- Revised Clinical View 29.3: Gestational Diabetes
- Revised: figure 29.1, figure 29.3, figure 29.4, figure 29.7, figure 29.16

We Welcome Your Input!
We hope you enjoy reading this textbook, and that it becomes central to mastering the concepts in your anatomy and physiology course. This text is a product that represents over 75 years of combined teaching experience in anatomy and physiology. We are active classroom instructors, and are well aware of the challenges that current students face in mastering these subjects. We have taken what we have learned in the classroom and have created a textbook truly written for students.

Please let us know what you think about this text. We welcome your thoughts and suggestions for improvement, and look forward to your feedback!

Michael P. McKinley
Glendale Community College, retired
mpmckinley@hotmail.com

Valerie Dean O’Loughlin
Medical Sciences
Indiana University
vdean@indiana.edu

Terri Stouter Bidle
Science Division
Hagerstown Community College
tsbidle@hagerstowncc.edu
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Finally, we could not have performed this effort were it not for the love and support of our families. Jan, Renee, Ryan, and Shaun McKinley; Bob and Erin O’Loughlin; and Jay and Stephanie Bidle—thank you and we love you! We are blessed to have you all.

Many instructors and students across the country have positively affected this text through their careful reviews of manuscript drafts, art proofs, and page proofs, as well as through class tests and through their attendance at focus groups and symposia. We gratefully acknowledge their contributions to this text.

Reviewers
Tim Ballard  
University of North Carolina—Wilmington

Charles Benton  
Madison College

Lindsay Biga  
Oregon State University

Jeff Bolles  
University of North Carolina—Pembroke

Chester Brown  
University of Illinois—Urbana-Champaign

Susan C. Burgoon  
Amarillo College

Dennis Burke  
Quincy College—Plymouth

Charles Cahill  
West Kentucky Community and Technical College

Melody Candler-Catt  
Vincennes University

Ronald A. Canterbury  
University of Cincinnati

Rajeev Chandra  
Norfolk State University

Cathleen Ciesielski  
Gardner-Webb University

Jordan Clark  
Sam Houston State University

Beth Collins  
Iowa Central Community College

Andrew Corless  
Vincennes University

Smruti Desai  
Lone Star College—CyFair

Cynthia Doffitt  
Northwestern State University

Bruce Evans  
Huntington University

David Evans  
Penn College

Colin Everhart  
St. Petersburg College

John Fishback  
Ozarks Technical Community College

Margaret Fleming  
Austin Community College

Caroline Garrison  
Carroll Community College

Nola Kelly-Gondek  
Hudson Valley Community College

Elizabeth Granier  
St. Louis Community College

Siabhon M. Harris  
Tidewater Community College

Cynthia A. Herbrandson  
Kellogg Community College

Lisa Hight  
Baptist College of Health Sciences

Kendricks D. Hooker  
Baptist College of Health Sciences

Shahdi Jalilvand  
Tarrant County College—Southeast

Kurt E. Kwast  
University of Illinois—Urbana-Champaign

Marta Klesath  
North Carolina State University

Kristine N. Kraft  
University of Akron

Paul Luyster  
Tarrant County College—South

Benjamin Navia  
Andrews University

Raffaella Pernice  
Hudson County Community College

Julie L. Posey  
Columbus State Community College

Laura H. Ritt  
Rowan College—Burlington County

Corinna Ross  
Texas A&M San Antonio

Merideth Sellars  
Columbus State Community College

Michael A. Silva  
El Paso Community College

William G. Sproat, Jr.  
Walters State Community College

Michael Thompson  
Jefferson Community and Technical College

Emmanuel Vrotsos  
Broward College

Chad Wayne  
University of Houston

Robinlyn Wright  
Houston Community College
Fully Integrated Content and Pedagogy

Anatomy and Physiology: An Integrative Approach is structured around a tightly integrated learning system that combines illustrations and photos with textual descriptions; focused discussions with big-picture summaries; previously learned material with new content; factual explanations with practical and clinical examples; and bite-sized topical sections with multi-tiered assessment.

Unparalleled Art Program

In a visually oriented subject like A&P, quality illustrations are crucial to understanding and retention. The brilliant illustrations in Anatomy and Physiology: An Integrative Approach have been carefully rendered to convey realistic, three-dimensional detail while incorporating pedagogical conventions that help deliver a clear message. Each figure has been meticulously reviewed for accuracy and consistency, and precisely labeled to coordinate with the text discussions.

Rich Detail

Vibrant colors and three-dimensional shading make it easy to envision body structures and processes.

Photographs

Atlas-quality micrographs and cadaver images are frequently paired with illustrations to expose students to the appearance of real anatomic structures.
### Synovial Joints

Example(s) Functional Classification

**Uniaxial**
- **Plane joint**: Flattened or slightly curved faces slide across one another.
- **Hinge joint**: Convex feature of one bone fits into concave depression of another bone.
- **Pivot joint**: Bone with a rounded surface fits into a ring formed by a ligament and another bone.

**Plane joint**: Intercarpal joints, intertarsal joints
**Hinge joint**: Elbow joint, knee joint, IP (interphalangeal) joints
**Pivot joint**: Atlantoaxial joint

**Biaxial**
- **Condylar joint**: Oval articular surface on one bone closely interfaces with a depressed oval surface on another bone.
- **Saddle joint**: Saddle-shaped articular surface on one bone closely interfaces with a saddle-shaped surface on another bone.

**Condylar joint**: MP (metacarpophalangeal or metatarsophalangeal) joints
**Saddle joint**: Articulation between a carpal bone (the trapezium) and first metacarpal

**Diarthrosis (freely mobile)**

**Multiaxial**
- **Ball-and-socket joint**: Round head of one bone rests within cup-shaped depression in another bone.

**Ball-and-socket joint**: Glenohumeral (shoulder) joint, hip joint

**Diarthrosis (freely mobile)**

---

**INTEGRATE CONCEPT OVERVIEW**

Figure 9.6 **Synovial Joints.** Synovial joints contain a joint cavity within an articular capsule lined by a synovial membrane. All synovial joints are diarthroses. The six types of synovial joints and examples of their locations in the body are shown.

**Multilevel Perspective**
Microscopic structures are connected to macroscopic views to show changes in perspective between increasingly detailed drawings.

**Color Coding**
Many figures use color coding to organize information and clarify concepts for visual learners.

**Real-Life Context**
Illustrations include depictions of realistic people and situations to make figures more relevant and memorable.
Antimicrobial Proteins and Chemicals

What are the two means by which the kidney helps to regulate blood by binding through α/β?

Integrative Visual Summaries

The groundbreaking Integrative: Concept Overview figures combine multiple concepts into one big-picture summary. These striking, visually dynamic presentations offer a review of previously covered material in a creatively designed environment to emphasize how individual parts fit together in the understanding of a larger mechanism or concept.

Integrate: Concept Overview Figures
Multifaceted concepts are brought together in captivating one- or two-page visual presentations.

Practical and Clinical Applications

Integrating familiar contexts into the study of A&P makes seemingly abstract concepts more relevant and memorable. Integrative: Learning Strategy boxes provide simple, practical advice for learning the material. Integrative: Clinical View readings offer insight on how complex physiologic processes or anatomic relationships affect body functioning.

Learning Strategies

Classroom tried-and-tested learning strategies offer everyday analogies, mnemonics, and useful tips to aid understanding and memory.

LEARNING STRATEGY

To understand the retroperitoneal position of the kidneys, imagine placing an eraser against a blackboard, which represents the posterior abdominal wall. Then hang a cloth that represents the parietal peritoneum so that the eraser is between the blackboard and the sheet. The eraser, which is located posterior to the sheet (the parietal peritoneum), is in a region called retroperitoneal. Structures that would be in front of (and enclosed by) the sheet are described as being intraperitoneal.
Clinical View
Interesting clinical sidebars reinforce or expand upon the facts discussed within the narrative. The clinical views are adjacent to the facts in the narrative (rather than placed at the end of the chapter) so students may immediately make connections between the narrative and real-life applications.

Concept Integration
Both backward and forward references are supplied throughout the text to remind the reader of the significance of previously covered material, and to foreshadow how knowledge of a topic at hand will come into play in a later discussion. Simple references appear in the flow of the text, while more detailed refreshers are presented in Integrate: Concept Connection boxes.
CHALLENGE YOURSELF

4. Limited ground substance yet abundant collagen fibers that are packed connective tissue, dense irregular connective tissue, and elastic connective tissue? Because collagen fibers usually are the dominant fiber type.

What Did You Learn?

These mini self-tests at the end of each section help students determine whether they have a sufficient grasp of the information before moving on to the next section.

12. Compare loose connective tissue to dense connective tissue with respect to fiber density, fiber distribution, and the amount of ground substance.
13. Describe the composition and location of fibrocartilage.
14. Why is blood considered a connective tissue?

What Did You Think?

These critical-thinking questions engage students in application or analysis and encourage them to think more globally about the content.

WHAT DO YOU THINK?

3. What type of connective tissue have you damaged when you sprain your ankle?

Do You Know the Basics?

1. Which tissue contains a calcified ground substance and is specialized for structural support?
   a. muscle tissue
   b. dense regular connective tissue
   c. areolar connective tissue
   d. bone connective tissue

Challenge Yourself

Assessments at the end of each chapter are correlated with Bloom’s Taxonomy and progress through knowledge-, application-, and synthesis-level questions. The “Can You Apply …” and “Can You Synthesize …” question sets are clinically oriented to encourage concept application, and expose students who may be pursuing health-related careers to problem solving in clinical contexts.

Can You Apply What You’ve Learned?

1. John is a 53-year-old construction worker who has come into your office complaining of a sore knee joint. You see a buildup of fluid close to the patella (kneecap) but deep to the skin and suspect the soreness is due to bursitis, an inflammation of membranes that surround some joints. Which type of body membrane is inflamed?
   a. cutaneous membrane
   b. serous membrane
   c. synovial membrane
   d. mucous membrane

Can You Synthesize What You’ve Learned?

1. During a microscopy exercise in the anatomy laboratory, a student makes the following observations about a tissue section: (a) The section contains some different types of scattered protein fibers—that is, they exhibit different widths, some are branched, and some are long and unbranched. (b) The observed section has some “open spaces”—that is, places between both cells and the fibers that appear clear with no recognizable features. (c) Several connective tissue cell types are scattered throughout the section, but these cells are not grouped tightly...
**Concept Overviews into Digital Learning**

Selected **Concept Overview Figures** from the textbook have been transformed into interactive study modules. This digital transformation process was guided by anatomy and physiology professors who reviewed the modules throughout the development process. Interactive Concept Overview Figures also have assessable, autograded learning activities in Connect®, and are also provided separately to instructors as classroom presentation tools.

Concept Overview Interactives are available for the following topics:
- Membrane Transport
- Muscle Contraction
- Neuron Physiology
- Endocrine System (New)
- Cardiac Cycle
- Blood Pressure (New)
- Innate Immunity (New)
- Adaptive Immunity (New)
- Respiration
- Glomerular Filtration
- Tubular Resorption/Secretion

![Interactive Presentation Study Tool](Image)

**Assessable Autograded Activity in Connect**
Lab Manual Options to Fit Your Course

**Anatomy & Physiology Laboratory Manual** by Christine Eckel, Kyla Ross, and Theresa Bidle is a laboratory manual specifically developed for the McKinley/O’Loughlin/Bidle Anatomy and Physiology: An Integrative Approach text:

- Three versions are available including main, cat, and fetal pig.
- Each chapter opens with a set of learning objectives that are keyed to the post-laboratory worksheet to ensure student understanding of each chapter’s objectives.
- The manual includes the highest-quality photographs and illustrations of any laboratory manual in the market.
- Laboratory exercises are “how-to” guides that involve touch, dissection, observation, experimentation, and critical-thinking exercises.
- In-chapter learning activities offer a mixture of labeling exercises, sketching activities, table completion exercises, data recording, palpation of surface anatomy, and other sources of learning.
- Numerous exercises throughout the manual utilize Physiology Interactive Lab Simulations (Ph.I.L.S.) 4.0 Online to provide additional student understanding of physiology.
- Pre-Laboratory Worksheet questions and Post-Laboratory Worksheet questions from each chapter are assignable in Connect.
- Ph.I.L.S. 4.0 is included with each new laboratory manual.

**Laboratory Manual for Human Anatomy & Physiology** by Terry Martin is written to coincide with any A&P textbook:

- Three versions available, including main, cat, and fetal pig
- Includes Ph.I.L.S. 4.0 Online
- Outcomes and assessments format
- Clear, concise writing style

### Student Supplements

McGraw-Hill offers various tools and technology products to support the textbook. Students can order supplemental study materials by contacting their campus bookstore or online at https://create.mheducation.com/shop/

### Instructor Supplements

Instructors can obtain teaching aids by calling the McGraw-Hill Customer Service Department at 1-800-338-3987, visiting our online catalog at https://create.mheducation.com/shop/, or by contacting their local McGraw-Hill sales representative.
Top 10 Tips to Thrive in Your Anatomy & Physiology Course

1. **Preview**
   Preview assigned material before lecture. Lecture will make much more sense if you’ve previewed what will be discussed.

2. **Look**
   Look at the images to be covered in lecture. Anatomy and Physiology is a very visual course.

3. **Review**
   Review the prior lecture’s material by re-writing your notes or making summary tables/flow charts.

4. **Visuals and Notes**
   Always study your notes along with related visuals. You need to be able to combine visual images with black and white text.

5. **Avoid Cramming**
   Study anatomy and physiology every day or at least every other day. More frequent studying is preferable to studying only two or three days per week. Set a schedule where you spend some time every day either previewing or reviewing anatomy and physiology information.

6. **Organize**
   Organize the course material in a manner that makes the most sense to you. You can create notecards that summarize similar information, design a flow chart, draw simple line diagrams, create mnemonics, or create a table or chart of information.

7. **Quiz Yourself**
   Make your own exam questions. This is a great technique to utilize once you have done a fair amount of studying. Ensure you don’t shy away from quizzing yourself on topics you’re not confident about.

8. **Explain**
   You master a concept best when you are able to explain it. Practice explaining what you’ve learned—a process or concept—to someone who knows nothing about anatomy and physiology, or to a fellow classmate.

9. **Study Group**
   Meet weekly or before every exam with several other students to learn the material. Assign each member different challenging topics and have that person teach it to the others in the group. You could also create a few questions on certain topics and then meet and share them with your group. Through the process of creating the questions you will become an “expert” in those topics and could better explain/clarify this information to each other.

10. **Office Hours**
    Make appointments to meet with your instructor to clarify information.
Homework and Adaptive Learning

- Connect’s assignments help students contextualize what they’ve learned through application, so they can better understand the material and think critically.
- Connect will create a personalized study path customized to individual student needs through SmartBook®.
- SmartBook helps students study more efficiently by delivering an interactive reading experience through adaptive highlighting and review.

Over 7 billion questions have been answered, making McGraw-Hill Education products more intelligent, reliable, and precise.

Quality Content and Learning Resources

- Connect content is authored by the world’s best subject matter experts, and is available to your class through a simple and intuitive interface.
- The Connect eBook makes it easy for students to access their reading material on smartphones and tablets. They can study on the go and don’t need internet access to use the eBook as a reference, with full functionality.
- Multimedia content such as videos, simulations, and games drive student engagement and critical thinking skills.

Connect’s Impact on Retention Rates, Pass Rates, and Average Exam Scores

Using Connect improves retention rates by 19.8%, passing rates by 12.7%, and exam scores by 9.1%.

73% of instructors who use Connect require it; instructor satisfaction increases by 28% when Connect is required.
Robust Analytics and Reporting

- Connect Insight® generates easy-to-read reports on individual students, the class as a whole, and on specific assignments.
- The Connect Insight dashboard delivers data on performance, study behavior, and effort. Instructors can quickly identify students who struggle and focus on material that the class has yet to master.
- Connect automatically grades assignments and quizzes, providing easy-to-read reports on individual and class performance.

### Impact on Final Course Grade Distribution

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<thead>
<tr>
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<th>With Connect</th>
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<tr>
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<td>27.4%</td>
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More students earn As and Bs when they use Connect.

Trusted Service and Support

- Connect integrates with your LMS to provide single sign-on and automatic syncing of grades. Integration with Blackboard®, D2L®, and Canvas also provides automatic syncing of the course calendar and assignment-level linking.
- Connect offers comprehensive service, support, and training throughout every phase of your implementation.
- If you’re looking for some guidance on how to use Connect, or want to learn tips and tricks from super users, you can find tutorials as you work. Our Digital Faculty Consultants and Student Ambassadors offer insight into how to achieve the results you want with Connect.
50% of the country’s students are not ready for A&P

LearnSmart® Prep can help!

Improve preparation for the course and increase student success with the only adaptive Prep tool available for students today. Areas of individual weaknesses are identified in order to help students improve their understanding of core course areas needed to succeed.

Students seek lab time that fits their busy schedules. Anatomy & Physiology REVEALED 3.2, our Virtual Dissection tool, allows them practice anytime, anywhere. Now featuring enhanced physiology with Concept Overview Interactives (COVI’s) and 3D animations!

Bringing to life complex processes is a challenge. Ph.I.L.S. 4.0 is the perfect way to reinforce key physiology concepts with powerful lab experiments. Tools like Concept Overview Interactives, Ph.I.L.S., and world-class animations make it easier than ever.

Since 2009, our adaptive programs in A&P have hosted 900,000 unique users who have answered more than 800 million probes, giving us the only data-driven solutions to help your students get from their first college-level course to program readiness.
You are about to embark on an adventure into the amazing world of human anatomy and physiology. Both fields explore the incredible workings of the human body. Anatomy studies the form and structure of the body, whereas physiology examines how the body functions. In this book, you will learn that structure and function are inseparable. Together, these applied sciences provide the basis for understanding health and human performance.

We introduce you to a number of concepts in this chapter that will be used throughout the text and will prove central to your study of anatomy and physiology. These diverse topics include: (1) a comparison of the disciplines of anatomy and physiology; (2) study tips for how to most effectively study for this course; (3) the body’s levels of organization; (4) the basic vocabulary of anatomy and physiology that is derived from both Greek and Latin; (5) the core features of homeostasis, which is the general regulatory process for maintaining a healthy body; as well as (6) the general relationship between homeostasis, health, and disease. We welcome you to the exciting and challenging study of human anatomy and physiology!
1.1 Anatomy and Physiology Compared

In this section, we compare anatomy and physiology and present the general subdivisions of these sciences.

Anatomy is the study of structure and form. The word *anatomy* is derived from the Greek word *anatomoe*, which means to cut apart or dissect. Anatomists are scientists who study the form and structure of organisms. Specifically, they examine the relationships among parts of the body as well as the structure of individual organs. Physiology is the study of function of the body parts. Physiologists are scientists who examine how organs and body systems function under normal circumstances, as well as how the functioning of these organs may be altered via medication or disease. For example, when studying blood capillaries (the smallest of blood vessels), an anatomist may describe the composition of the thin wall. In contrast, a physiologist will explain how the thin wall promotes gas and nutrient exchange between the blood within the capillary and the tissue cells external to the capillary.

Anatomists and physiologists are professionals who use the scientific method to explain and understand the workings of the body. The scientific method is a systematic and rigorous process by which scientists:

- Examine natural events (or phenomena) through observation
- Develop a hypothesis (possible explanation) for explaining these phenomena
- Experiment and test the hypothesis through the collection of data
- Determine if the data support the hypothesis, or if the hypothesis needs to be rejected or modified

For example, early anatomists and physiologists used the scientific method to explain how blood circulates through the body. Today, we continue to use the scientific method for a variety of topics, such as to understand how the brain stores memories or explain how cancer may spread throughout the body.

Throughout this text, we have attempted to integrate the study of both anatomy and physiology, showing how form and function are interrelated.

1.1a Anatomy: Details of Structure and Form

LEARNING OBJECTIVES

1. Describe the science of anatomy.
2. List the subdivisions in both microscopic and gross anatomy.

The discipline of anatomy is extremely broad and can be divided into several more specific fields. Microscopic anatomy examines structures that cannot be seen by the unaided eye. For most of these studies, scientists prepare individual cells or thin slices of body structures and examine these specimens under the microscope. Microscopic anatomy has several subdivisions with two main divisions:

- **Cytology** (si-tol’o-jē; kytos = a hollow cell, logos = study), or cellular anatomy, is the study of body cells and their internal structure.
- **Histology** (his-tol’o-jē; histos = web, tissue) is the study of body tissues.

Gross anatomy, also called *macroscopic anatomy*, investigates the structure and relationships of body parts that are visible to the unaided eye, such as the intestines, stomach, brain, heart, and kidneys. In these macroscopic investigations, specimens or their parts are often dissected (cut open) for examination. Gross anatomy may be approached in several ways:

- **Systemic anatomy** studies the anatomy of each functional body system. For example, studying the urinary system would involve examining the kidneys (where urine is formed) and the organs of urine transport (ureters and urethra) and storage (urinary bladder). Most undergraduate anatomy and physiology classes use this systemic approach.
- **Regional anatomy** examines all of the structures in a particular region of the body as a complete unit. For example, one may study the axillary (armpit) region of the body, and in so doing examine the blood vessels (axillary artery and vein), nerves (branches of the brachial plexus), lymph nodes (axillary lymph nodes), musculature, connective tissue, and skin. Most medical school gross anatomy courses are taught using a regional anatomy approach.
- **Surface anatomy** focuses on both superficial anatomic markings and the internal body structures that relate to the skin covering them. Health-care providers use surface features to identify and locate important landmarks, such as pulse locations or the proper body region on which to perform cardiopulmonary resuscitation (CPR). Most anatomy and physiology classes also instruct students on important surface anatomy locations.
- **Comparative anatomy** examines the similarities and differences in the anatomy of different species. For example, a comparative anatomy class may examine limb structure in humans, chimps, dogs, and cats.
- **Embryology** (em’brē-ol’o-jē; embryon = young one) is the discipline concerned with developmental changes occurring from conception to birth.

Several specialized branches of anatomy focus on the diagnosis of medical conditions or the advancement of basic scientific research. Pathologic (path-ō-loj’ik; pathos = disease) anatomy examines all anatomic changes resulting from disease. Both gross-anatomic changes and microscopic structures are examined. Radiographic anatomy investigates the relationships among internal structures that may be visualized by specific scanning procedures, such as sonography, magnetic resonance imaging (MRI), or x-ray. (See Clinical View 1.4: “Medical Imaging.”)

It may seem as though nothing new can be learned about anatomy—after all, the body has been much the same for thousands of years. Yet in fact, new information is being learned from ongoing anatomic studies, some of which displace the traditional thinking about the workings of various organs. Never forget that anatomy is a dynamic, changing science, not a static, unchanging one.

WHAT DID YOU LEARN?

1. How might knowledge of surface anatomy be important for a health-care worker during a CPR emergency?
Physiologists examine the function of various organ systems, and they typically focus on the molecular or cellular level. Thus, a basic knowledge of both chemistry and cells is essential in understanding physiology, and that’s why we’ve included several early chapters on these topics. Mastery of these early chapters on chemistry and cells is critical to understanding the physiologic concepts that are covered throughout the text.

The discipline of physiology parallels anatomy because it also is very broad and may be subdivided into smaller groups. Many specific physiology subdisciplines focus their studies on a particular body system. For example, cardiovascular physiology examines the functioning of the heart, blood vessels, and blood. Cardiovascular physiologists examine how the heart pumps the blood, what are the parameters for healthy blood pressure, and details of the cellular exchange mechanisms by which respiratory gases, nutrients, and wastes move between blood and body structures. Other examples include neurophysiology (which examines how nerve impulses are propagated throughout the nervous system), respiratory physiology (which studies how respiratory gases are transferred by gas exchange between the lungs and the blood vessels), and reproductive physiology (which explores how the regulation of reproductive hormones can drive the reproductive cycle and influence sex cell production and maturation).

Pathophysiology investigates the relationship between the functioning of an organ system and disease or injury to that organ system. For example, a pathophysiologist would examine how blood pressure, contractile force of the heart, and both gas and nutrient exchange may be affected in an individual afflicted with heart disease.

**WHAT DID YOU LEARN?**

2. What is the relationship between anatomy and physiology?

3. ________ physiology examines how the heart, blood vessels, and blood function.

**INTEGRATE**

**CLINICAL VIEW 1.1**

**Etiology (Causes) and Pathogenesis (Development) of Disease**

All health-care professionals must understand both how body structures function normally and how disease or injury can affect them. Throughout the chapters in this book, Clinical View boxes (which are always enclosed in the color blue) provide you with selected pathologies and how these pathologies affect the anatomy and physiology of those structures.

**1.2 Anatomy and Physiology Integrated**

**LEARNING OBJECTIVE**

5. Explain how the studies of form and function are interrelated.

The sciences of anatomy and physiology are intertwined; one must have some understanding of anatomic form to study physiologic function of a structure. Likewise, one cannot adequately describe and understand the anatomic form of an organ without learning that organ’s function. This interdependence of the study of anatomy and physiology reflects the inherent and important interrelationship of how the structure and form of a component of the body determine how it functions. This concept is central to mastering the study of anatomy and physiology.

Integrating the disciplines of anatomy and physiology, rather than trying to separate discussion of form and function, is the most effective way to learn about both fields. Anatomists and physiologists may be describing the organs slightly differently, but both disciplines must use information from the other field for a full understanding of the organ system. You cannot fully understand how the small intestine propels food and digests or absorbs nutrients unless you also know about the structure of the small intestine wall. **Figure 1.1** visually compares how anatomists and physiologists examine the human body, using the small intestine as an example. Note that anatomists (left side of the figure) tend to focus on the form and structure, whereas physiologists (right side of figure) focus on the mechanisms and functions of these structures. However, both anatomists and physiologists understand that the form and function of structures are interrelated. Throughout this text, we integrate these disciplines so you can more easily see that anatomic form and physiologic function are inseparable.

Note that figure 1.1 is an example of a central feature of this text called Concept Overview (COV) figures. These specialized illustrations are included in each chapter (e.g., figures 4.19 and 23.31) and are designed to help you to visually connect and integrate content that has been previously discussed within the chapter.

**WHAT DID YOU LEARN?**

4. Compare and contrast how anatomists and physiologists specifically describe the small intestine.

**1.3 How to Study Anatomy and Physiology Effectively**

**LEARNING OBJECTIVE**

6. Describe best practices for studying anatomy and physiology effectively.

Anatomy and Physiology (A&P) is a content dense course that sometimes may overwhelm learners new to the subject. Success in the course requires careful time management and appropriate study skills for comprehending the material. When we teach our courses, we often encounter students who simply need to adopt more effective study strategies to perform well. In this section, we discuss some of these strategies.
Figure 1.1 Comparing How Anatomists and Physiologists Examine the Human Body.

(a) Anatomists typically focus on the form and structure of an organ, such as the small intestine. (b) Physiologists tend to focus on the function of an organ or a system. However, both anatomists and physiologists recognize that form and function are interrelated.

(top left organelle) ©Dennis Kunkel Microscopy, Inc./Medical Images; (top right organelle) ©Keith R. Porter/Science Source; (bottom left organelle) ©Don W. Fawcett/Science Source; (bottom right organelle) ©EM Research Services, Newcastle University
(b) Physiologists
Focus on the function of the small intestine

PHYSIOLOGISTS
Examine how the muscles of the small intestine propel food through the digestive tract

Anatomists and Physiologists
Know form and function of the small intestine are interrelated

PHYSIOLOGISTS
Describe the mechanisms by which different nutrients are broken down

PHYSIOLOGISTS
Study the mechanisms by which different nutrients are absorbed

Peristalsis
Wave of contraction
Relaxation
Propulsion of bolus forward

Focus on the form and structure of the small intestine
(a) Anatomists
Study the tissues of the small intestine and the cells that compose them

Small intestine
Peristalsis
Relaxation
Bolus

Blood capillary
Lymphatic capillary
Epithelial cell of intestinal villus

Carbohydrate
Protein
Amino acids
Monosaccharides
Monoglycerides
Fat globules
Bile salts

Liver
Stomach
Small intestine
Large intestine
Esophagus
Chapter One

How NOT to Study for A&P

1. Wait until the last minute to study. As previously mentioned, A&P is content rich and requires the learner to be able to understand many complex processes. Beginning your studying a few days before an exam is simply not enough time for you to understand the material and truly learn it.

2. Study for long periods of time without breaks. Your brain works best if you study for shorter periods of time (½ hour or less) and then take a short break before studying again. A 4-hour marathon study session will just leave you feeling overwhelmed, and you likely will not remember anything you studied.

3. Study with multiple distractions. Do you try to study with the TV on, your phone available to answer texts, and your computer open to your social media account? If so, the time you think you are spending studying is not effective. For each time you take a break to answer a text, check email, or listen to TV, you are not focusing on the material. Multitasking is a myth—in reality, you are quickly switching from one task to another without staying focused on any one thing. This type of study method is disjointed and will prevent you from engaging in the material.

4. Simply passively read over your notes. Don't simply read over your notes multiple times as a form of studying. This study method is referred to as passive learning—it is called passive because the person doesn't have to do much in the process! Although you may think you are learning the material, in fact, you are only acquiring a superficial recognition of the material. Unless you practice quizzing yourself over the material to repeatedly retrieve the material from your memory and do other active learning methods, your brain will not be able to quickly access what you've learned for an exam. Students who rely solely on re-reading their notes often will say, “I recognized the material on the exam, but I wasn’t sure of what answer to choose.”

5. Study by yourself only. When you study by yourself only, you can't accurately gauge if you know the material well and can explain it to others. You also are more likely to reinforce a misconception if you don't have a study partner who can help you work through some of the more difficult concepts.

So now that we’ve discussed some of the big mistakes in studying A&P, what are more effective ways of studying? The following is a list of best practices for studying.

Best Practices for Studying A&P

1. Schedule regular daily study sessions well before the upcoming exam. Your studying should begin the first week of class and should be a part of a daily or every-other-day schedule. Do not wait until the week prior to an exam to first become acquainted with the material! The night after a lecture or lab, review the material you’ve learned with some of the methods outlined in this list. Connect the material you are learning with A&P material previously covered. If you follow this plan, then you may spend the week prior to the exam reviewing material you’ve already studied, rather than starting your study process.

2. Study for multiple, short periods of time. During these daily (or every-other-day) study periods, set a timer for ½ hour or a little less and promise yourself you will focus just on the A&P material at hand. Select a study topic that you can review effectively in that ½ hour. For example, you could compare and contrast the epidermis and the dermis of the skin during that time. After ½ hour has passed, reward yourself with a short (~5-minute) break, and then reset the timer to study again. After three of these short periods, reward yourself with a longer break. You will be able to review more material, and remember the material you’ve reviewed, better than if you tried to study in one long 4-hour block.

3. Minimize your distractions. Put away the phone, turn off the TV, and shut down your email. Research has shown that people don’t multitask—rather, the brain jumps from one task to another quickly, so the activity for each task is disjointed and may not be well organized. You will be amazed at how much more efficient your studying becomes when you minimize the distractions and focus on the material. If you use the timer technique mentioned previously (study for ½ hour with no distractions), you can reward yourself during those short breaks by looking at your texts or social media.

4. Utilize active learning methods when you study. Active learning is defined as a process by which you are engaged in the material, problem solving, and applying what you’ve learned to previous knowledge. It is the opposite of passive learning. Examples of active learning include:

a. Make your own tables to organize material. Take your lecture notes and reorganize them into tabular form. For example, you can group muscles of similar functions. The act of writing out the muscles and reorganizing the information in tabular form will help you remember the material better than if you just read over your notes.

b. Draw and label anatomic structures. Make your own sketches of organs and tissues, and label the key features. When you draw, you are integrating multiple pieces of information into one diagram. You don’t have to be an artist and the drawing doesn’t have to be pretty—rather, it simply has to make sense to you.

c. Make flowcharts of physiological processes. Map out the pathway that filtrate becomes urine in the kidney. Create a flowchart to illustrate how blood travels from the heart to the lungs, and back to the heart.

d. Quiz yourself repeatedly on the material. Educational research has shown that long-term learning is most likely to occur when an individual practices and retrieves that material on multiple occasions. Your textbook has multiple opportunities to quiz yourself—you can use the end-of-chapter questions, LearnSmart modules associated with the e-text, and the quizzing feature in the Anatomy and Physiology | Revealed program associated with the McGraw-Hill Connect site. If you are studying with a partner, take turns quizzing each other. When you can retrieve the information accurately, you know the material. You do not want to wait until you are taking the exam to determine if you can do this.
6. INTEGRATE dioxide) by the blood throughout the body. System work together in the transport of respiratory gases (oxygen and carbon overlapping functions. For example, the cardiovascular system and respiratory systems do not work in isolation, but rather are interconnected to carry out throughout future chapters, Concept Connection boxes like this one (which are always enclosed in the color orange) will highlight how various organ systems do not work in isolation, but rather are interconnected to carry out overlapping functions. For example, the cardiovascular system and respiratory system work together in the transport of respiratory gases (oxygen and carbon dioxide) by the blood throughout the body.

5. Study with a partner or group. A lot of the active study methods mentioned work best when you are studying with a partner. It is difficult to quiz yourself and know for sure if you truly understand a concept. You and your study partner can each help determine where gaps in knowledge are, keep study sessions focused and on track, and serve as a “sounding board” when trying to explain a concept.

6. Utilize all of the resources your textbook has to offer. Your textbook and its accompanying digital platform contain numerous resources to help you learn anatomy and physiology more efficiently. So don’t just read the text—use the following aids provided in each chapter of the text:

   a. Integrate: Learning Strategy boxes. These boxes provide analogies, mnemonics, and study tips to help you learn the material.

   b. Integrate: Concept Connection boxes. These boxes provide summaries of topics that may be discussed and presented across multiple chapters, such as acid-base balance or hormonal regulation of growth. Read these boxes to help you connect material among different chapters.

   c. Integrate: Concept Overview figures. Each chapter has one or more of these figures, designed to provide a big-picture summary of a major concept in that chapter. For example, Figure 1.1 provides a comparison of how anatomists and physiologists study the body. Let these figures guide your explanation of a concept to a study partner.

   d. Integrated, multiple assessments in each chapter. As you read, write out your answers for the What Did You Learn? questions at the end of each section of text. When you are done reading a chapter, use the end-of-chapter questions to test your knowledge.

   e. LearnSmart. Each chapter is associated with an interactive e-module that allows you to test yourself on concepts you have read. The program will highlight topics you have not yet mastered and create a study plan for you about these topics.

   f. Anatomy and Physiology | REVEALED (APR). APR is an interactive cadaver dissection tool that allows you to highlight anatomic features and review lab and lecture concepts. You can view both gross anatomy and histology concepts, watch animations about particular physiologic processes, and test yourself with the lab quiz tool.

This list of best practices is not exhaustive; you may have some additional study strategies that are equally effective. Although we cannot guarantee you will earn an A, we can be reasonably certain that your understanding of anatomy and physiology will greatly increase if you adopt the best practices outlined here. We encourage you to use these best practices for your other courses as well.

1.4 The Body’s Levels of Organization

Scientists group the body’s components into an organizational hierarchy of form and function. In thinking about these levels, it is helpful to know the characteristics common to living things and how each organizational level supports these characteristics. For example, the organ system concept allows functions to be considered as an interaction between many organs.

1.4a Characteristics That Describe Living Things

LEARNING OBJECTIVE

7. List the characteristics common to all living things.

Several distinctive properties are common to all organisms, including humans:

- Organization. All organisms exhibit a complex structure and order. In section 1.4b, we describe the increasingly complex levels of organization of the human body.

- Metabolism. All organisms engage in metabolism (mē-tab′o-lizm; metabolize = change), which is defined as the sum of all of the chemical reactions that occur within the body. Metabolism consists of both anabolism (ā-nab′o-lizm; anabole = a raising up), in which small molecules are joined to form larger molecules, and catabolism (kā-tab′o-lizm; katabole = a casting down), in which large molecules are broken down into smaller molecules. An example of a metabolic reaction is the use of cellular energy (called ATP; see section 2.7d) for muscle contraction (see section 10.3). The concepts of chemical reactions and metabolism are discussed in sections 3.2a and 3.2b, respectively.

WHAT DO YOU THINK?

1. When you digest a meal, what type of metabolic reactions do you think you are utilizing primarily: anabolic or catabolic chemical reactions? Why?

- Growth and development During their lifetime, organisms assimilate materials from their environment and often exhibit increased size (growth) and increased specialization as related to form and function (development). As the human body grows and develops, structures such as the brain become more complex and elaborately integrated.
The organ level is composed of organs. An organ contains two or more tissue types that work together to perform specific, complex functions. The small intestine is an example of an organ that is composed of all four tissue types, which work together to process and absorb digested nutrients. The general features of body tissues and their organization within organs are covered in chapter 5.

The organ system level contains multiple related organs that work together to coordinate activities and achieve a common function. For example, the organs of the digestive system (e.g., oral cavity, stomach, small and large intestine, and liver) work together to digest food particles, absorb nutrients, and expel the waste products. The 11 organ systems are introduced in section 1.4c.

Anatomists and physiologists recognize several levels of increasingly complex organization in humans, as illustrated in figure 1.2. These levels, from simplest to most complex, are the chemical level, cellular level, tissue level, organ level, organ system level, and organismal level.

The chemical level is the simplest level, and it involves atoms and molecules. Atoms are the smallest units of matter that exhibit the characteristics of an element, such as carbon and hydrogen. When two or more atoms combine, they form a molecule. Examples of molecules include a sugar, a water molecule, or a vitamin. More complex molecules are called macromolecules and include some proteins and the deoxyribonucleic acid (DNA) molecules. Macromolecules form specialized microscopic subunits in cells, called organelles. Chemical structures are described in chapter 2.

The cellular level consists of cells, which are the smallest living structures and serve as the basic units of structure and function in organisms. Cells and their components are formed from the atoms and molecules from the chemical level. The structures of cells vary widely, reflecting the specializations needed for their different functions. For example, a skeletal muscle cell may be very long and contain numerous organized protein filaments that aid in muscle contraction, whereas a red blood cell is small and has a flattened disc shape that facilitates the quick and effective ex-change of respiratory gases. Cells and cellular organelles are discussed in chapter 4.

The tissue level consists of tissues, which are groups of similar cells that perform common functions. There are four major types of tissues. Epithelial tissue covers exposed surfaces and lines body cavities. Connective tissue protects, supports, and binds structures and organs. Muscle tissue produces movement. Finally, nervous tissue conducts nerve impulses for communication.

The highest level of structural organization in the body is the organismal level. All body systems function interdependently in an organism, which is the living person.

1.4b The View from Simplest to Most Complex

LEARNING OBJECTIVE
8. Describe the levels of organization in the human body.

WHAT DID YOU LEARN?
6. What does it mean if an organism is “responsive,” and how does this characteristic relate to the survival of this organism?

1.4c Introduction to Organ Systems

LEARNING OBJECTIVE
9. Compare the organ systems of the human body.

WHAT DID YOU LEARN?
7. Does a higher level of organization contain all the levels beneath it? Explain.

8. Which organ system is responsible for filtering the blood and removing the waste products of the blood in the form of urine?
1.5 The Precise Language of Anatomy and Physiology

Clinicians and researchers in anatomy and physiology require a precise language to ensure that they are all discussing the same features and functions. A technical terminology has been developed that describes body position, direction, regions, and body cavities. These technical terms are different from those used in everyday conversation, because the more conversational terms often do not accurately describe location and position or identify structures. For example, the term arm in everyday conversation refers to the entire upper limb, but in anatomy the specific portions of the upper limb are named, and the term arm or brachium refers only to that part of the upper limb between the shoulder and the elbow.

Most anatomic and physiologic terms are derived from Greek or Latin, and we frequently provide word origins, pronunciations, and definitions of terms where appropriate throughout this text. We’ve used Stedman’s Medical Dictionary (which defines all medical terms) and Terminologia Anatomica (which lists and categorizes the modern, proper anatomic terms) as references. If you actively practice the vocabulary and descriptive terminology presented here, your understanding and appreciation of body structure and function will be enhanced significantly.

Figure 1.2 Levels of Organization in the Human Body. The most simple level is the chemical level, followed by increasingly more complex levels of organization.

INTEGRATE

LEARNING STRATEGY

Breaking a word into smaller parts can help you understand and remember its meaning. In this book, we provide word derivations for new terms following their pronunciations. For example, in the case of histology, the study of tissues, we provide the following: (histos = web, tissue, logos = study).

Many biological terms share some of the same prefixes, suffixes, and word roots, so learning the meanings of these common terms can help you figure out the meanings of unfamiliar terms.
Chapter One
The Sciences of Anatomy and Physiology

**Integumentary System** (Chapter 6)
Provides protection, regulates body temperature, site of cutaneous receptors and some glands, synthesizes vitamin D, prevents water loss.

**Muscular System** (Chapters 10–11)
Produces body movement, generates heat when muscles contract.

**Skeletal System** (Chapters 7–9)
Provides support and protection, site of hemopoiesis (blood cell production), stores calcium and phosphorus, provides sites for ligament and muscle attachments.

**Nervous System** (Chapters 12–16)
A regulatory system that controls muscles and some glands, responds to sensory stimuli, and helps control all other systems of the body. Also responsible for consciousness, intelligence, memory.

Figure 1.3 Organ Systems. Major components and characteristics of the 11 organ systems of the human body are presented.
Endocrine System (Chapter 17)
Consists of glands and cell clusters that secrete hormones, (some of which regulate development, growth and metabolism); maintain homeostasis of blood composition and volume, control digestive processes, and control reproductive functions.

Cardiovascular System (Chapters 18–20)
Consists of the heart (a pump) and blood vessels; the heart moves blood through blood vessels in order to distribute hormones, nutrients, gases, and pick up waste products.

Lymphatic System (Chapters 21–22)
Transports and filters lymph (interstitial fluid that is collected in and transported through lymph vessels) and may participate in an immune response.

Respiratory System (Chapter 23)
Responsible for exchange of gases (oxygen and carbon dioxide) between blood and the air in the lungs.
Chapter One
The Sciences of Anatomy and Physiology

Salivary gland

Digestive System (Chapters 26–27)
Mechanically and chemically digests food, absorbs nutrients, and expels waste products.

Pharynx (throat)
Oral cavity (mouth)

Esophagus
Liver
Stomach
Large intestine
Small intestine

Urinary System (Chapters 24–25)
Filters the blood to remove waste products and biologically active molecules, concentrates waste products in the form of urine, and expels urine from the body.

Urine
Kidney
Ureter
Urinary bladder
Urethra

Seminal vesicle
Prostate gland
Ductus deferens
Epididymis
Testis
Penis
Scrotum

Mammary glands
Ovary
Uterine tube
Uterus
Vagina
External genitalia (clitoris, labia)

Male Reproductive System (Chapter 28)
Produces male sex cells (sperm) and male hormones (e.g., testosterone), transfers sperm to the female.

Female Reproductive System (Chapters 28–29)
Produces female sex cells (oocytes) and female hormones (e.g., estrogen and progesterone), receives sperm from male, site of fertilization of oocyte, site of growth and development of embryo and fetus, produces and secretes breast milk for nourishment of newborn.

Figure 1.3 Organ Systems. (continued)
describe the position of one body part relative to another. The term section implies an actual cut or slice to expose the internal anatomy, whereas the word plane implies an imaginary flat surface passing through the body. The three major anatomic planes are the coronal, transverse, and midsagittal planes (figure 1.4).

A coronal (kö'ra-nəl; korone = crown) plane, also called a frontal plane, is a vertical plane that divides the body or organ into anterior (front) and posterior (back) parts. When a coronal plane is taken through the trunk, the anterior portion contains the chest and the posterior portion contains the back and buttocks.

A transverse plane, also called a horizontal plane or cross-sectional plane, divides the body or organ into superior (top) and inferior (bottom) parts. If a transverse plane is taken through the middle of the trunk, the superior portion contains the chest and the inferior portion contains the abdomen.

A midsagittal (mid-saj′-tāl; sagitta = arrow) plane, or median plane, is a vertical plane and divides the body or organ into equal left and right halves. A midsagittal plane through the head will split it into a left half and a right half (each containing one eye, one ear, and half of the nose and mouth). A plane that is parallel to the midsagittal plane, but either to the left or right of the midsagittal plane, is termed a sagittal plane. A sagittal plane divides a structure into left and right portions that are not equal. Although there is only one midsagittal plane, an infinite number of sagittal planes are possible.

In addition to these major planes, there are numerous minor planes called oblique (ob-lēk′) planes that pass through a structure at an angle (figure 1.5).

Interpreting body sections has become increasingly important for health-care professionals. Technical advances in medical imaging have produced sectional images of internal body structures (figures 1.4a-b-d). To determine the shape of any object within a section, we must be able to reconstruct its three-dimensional shape by observing many serial sections.
Sectioning the body or an organ along different planes often results in very different views of that organ or region. For example, different sections through the abdominal cavity exhibit multiple profiles of the long, twisted tube that is the small intestine. These sections may appear as circles, ovals, a figure eight, or maybe a long tube with parallel sides, depending on where the section was taken (figure 1.5). Being able to convert and interpret two-dimensional images into three-dimensional structures is especially important when comparing and understanding histologic and gross anatomic views of the same organ.

### 1.5c Anatomic Directions

**LEARNING OBJECTIVE**

12. Define the different anatomic directional terms.

When the body is in the anatomic position, we can precisely describe the relative positions of structures by using specific directional terms. These directional terms are precise and usually presented in opposing pairs. Examples include anterior (in front of) and posterior (in back of), and proximal (nearer to the trunk) and distal (farther from the trunk). Table 1.1 and figure 1.6 describe some commonly used directional terms. Studying the table and figure together, and referring back to them as needed, will maximize your understanding of anatomic directions and aid your study of anatomy throughout the rest of this book.

**WHAT DID YOU LEARN?**

9. What type of plane would separate the nose and mouth into superior and inferior structures?

10. Which directional term would be most appropriate in the sentence “The elbow is ________ to the wrist”?

### 1.5d Regional Anatomy

**LEARNING OBJECTIVE**

13. Identify the major regions of the body, using proper anatomic terminology.

The human body is partitioned into two main regions, the axial and appendicular regions. The axial (akˈsē-əl) region includes the head, neck, and trunk; it forms the main vertical axis of the body. The appendicular (apˈen-dikˈə-lər) region is composed of the upper and lower limbs, which attach to the axial region. Several more specific regions are located within these two main ones, and they are identified by proper anatomic terminology. Figure 1.7 and table 1.2 identify the major regional terms and some additional minor ones. Not all regions are shown in figure 1.7.

**WHAT DID YOU LEARN?**

11. The term antebrachial refers to which body region?

### 1.5e Body Cavities and Membranes

**LEARNING OBJECTIVES**

14. Describe the body cavities and their subdivisions.

15. Explain the role of serous membranes in the ventral cavities.

Internal organs and organ systems are housed within enclosed spaces, or cavities. These body cavities are named according to either the bones that surround them or the organs they contain. For purposes of discussion, these body cavities are grouped into a posterior aspect and a ventral cavity.

**Posterior Aspect**

The posterior aspect of the body is different from the ventral cavity, in that the posterior aspect contains cavities that are completely encased in bone and are physically and developmentally different

<table>
<thead>
<tr>
<th>Table 1.1</th>
<th>Anatomic Directional Terms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Direction</td>
<td>Term</td>
</tr>
<tr>
<td>Relative to front (belly side) or back of the body</td>
<td>Anterior</td>
</tr>
<tr>
<td>Posterior</td>
<td>In back of; toward the back surface</td>
</tr>
<tr>
<td>Dorsal</td>
<td>Toward the back side of the human body</td>
</tr>
<tr>
<td>Ventral</td>
<td>Toward the belly side of the human body</td>
</tr>
<tr>
<td>Relative to the head or bottom of the body</td>
<td>Superior</td>
</tr>
<tr>
<td>Inferior</td>
<td>Closer to the feet</td>
</tr>
<tr>
<td>Cranial (cephalic)</td>
<td>Toward the head end</td>
</tr>
<tr>
<td>Caudal</td>
<td>Toward the rear or tail end</td>
</tr>
<tr>
<td>Rostral</td>
<td>Toward the nose or mouth</td>
</tr>
<tr>
<td>Relative to the midline or center of the body</td>
<td>Medial</td>
</tr>
<tr>
<td>Lateral</td>
<td>Away from the midline of the body</td>
</tr>
<tr>
<td>Ipsilateral</td>
<td>On the same side</td>
</tr>
<tr>
<td>Contralateral</td>
<td>On the opposite side</td>
</tr>
<tr>
<td>Deep</td>
<td>Closer to the inside, internal to another structure</td>
</tr>
<tr>
<td>Superficial</td>
<td>Closer to the outside, external to another structure</td>
</tr>
<tr>
<td>Relative to point of attachment of appendage</td>
<td>Proximal</td>
</tr>
<tr>
<td>Distal</td>
<td>Farther away from point of attachment to trunk</td>
</tr>
</tbody>
</table>
from the ventral cavity. The term *dorsal body cavity* has been used by others to describe this posterior aspect but is not used here because of these differences between the ventral cavity and posterior aspect.

The posterior aspect is subdivided into two enclosed cavities (figure 1.8a). A *cranial cavity* is formed by the bones of the cranium, and so it also goes by the name *endocranium*. The cranial cavity houses the brain. The second cavity is the *vertebral* (ver′te-brăl) *canal*, which is formed by the bones of the vertebral column. The vertebral canal houses the spinal cord.

**Figure 1.6** Directional Terms in Anatomy. Directional terms precisely describe the location and relative relationships of body parts. (See also table 1.1.)

**Figure 1.7** Regional Terms. (a) Anterior and (b) posterior views show key regions of the body. Their common names appear in parentheses.

**Ventral Cavity**

The *ventral cavity* is the larger, anteriorly placed cavity in the body (figure 1.8). Unlike the posterior aspect, the ventral cavity and its subdivisions do not completely encase their organs in bone. The ventral cavity is partitioned by the *thoracic diaphragm* into a superior *thoracic* (thō-ras′ik) *cavity* and an inferior *abdominopelvic* (ab-dom′i-nō-pēl′vik) *cavity*.

Another significant difference between the posterior aspect and the ventral cavity is that the subdivisions of the ventral cavity are...
### Table 1.2 Human Body Regions

<table>
<thead>
<tr>
<th>Region Name</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abdominal</td>
<td>Region inferior to the thorax (chest) and superior to the pelvic brim of the hip bones</td>
</tr>
<tr>
<td>Antebrachial</td>
<td>Forearm (the portion of the upper limb between the elbow and the wrist)</td>
</tr>
<tr>
<td>Antecubital</td>
<td>Region anterior to the elbow; also known as the cubital region</td>
</tr>
<tr>
<td>Auricular</td>
<td>Visible surface structures of the ear</td>
</tr>
<tr>
<td>Axillary</td>
<td>Armpit</td>
</tr>
<tr>
<td>Brachial</td>
<td>Arm (the portion of the upper limb between the shoulder and the elbow)</td>
</tr>
<tr>
<td>Buccal</td>
<td>Cheek</td>
</tr>
<tr>
<td>Calcaneal</td>
<td>Heel of the foot</td>
</tr>
<tr>
<td>Carpal</td>
<td>Wrist</td>
</tr>
<tr>
<td>Cephalic</td>
<td>Head</td>
</tr>
<tr>
<td>Cervical</td>
<td>Neck</td>
</tr>
<tr>
<td>Coxal</td>
<td>Hip</td>
</tr>
<tr>
<td>Cranial</td>
<td>Skull</td>
</tr>
<tr>
<td>Crural</td>
<td>Leg (the portion of the lower limb between the knee and the ankle)</td>
</tr>
<tr>
<td>Deltoid</td>
<td>Shoulder</td>
</tr>
<tr>
<td>Digital</td>
<td>Fingers or toes (also called phalangeal)</td>
</tr>
<tr>
<td>Dorsal/ Dorsum</td>
<td>Back</td>
</tr>
<tr>
<td>Facial</td>
<td>Face</td>
</tr>
<tr>
<td>Femoral</td>
<td>Thigh</td>
</tr>
<tr>
<td>Fibular</td>
<td>Lateral aspect of the leg</td>
</tr>
<tr>
<td>Frontal</td>
<td>Forehead</td>
</tr>
<tr>
<td>Gluteal</td>
<td>Buttock</td>
</tr>
<tr>
<td>Hallux</td>
<td>Great toe</td>
</tr>
<tr>
<td>Inguinal</td>
<td>Groin (sometimes used to indicate the crease or junction of the thigh with the trunk)</td>
</tr>
<tr>
<td>Lumbar</td>
<td>The “small of the back”; the inferior part of the back between the ribs and the pelvis</td>
</tr>
<tr>
<td>Mammary</td>
<td>Breast</td>
</tr>
<tr>
<td>Manus</td>
<td>Hand</td>
</tr>
<tr>
<td>Mental</td>
<td>Chin</td>
</tr>
<tr>
<td>Nasal</td>
<td>Nose</td>
</tr>
<tr>
<td>Occipital</td>
<td>Posterior aspect of the head</td>
</tr>
<tr>
<td>Olecranal</td>
<td>Posterior aspect of the elbow</td>
</tr>
<tr>
<td>Oral</td>
<td>Mouth</td>
</tr>
<tr>
<td>Orbital</td>
<td>Eye</td>
</tr>
<tr>
<td>Palmar</td>
<td>Palm (anterior surface) of the hand</td>
</tr>
<tr>
<td>Patellar</td>
<td>Kneecap</td>
</tr>
<tr>
<td>Pectoral</td>
<td>Chest, includes mammary region</td>
</tr>
<tr>
<td>Pelvic</td>
<td>Pelvis; region inferior to the pelvic brim of the hip bones</td>
</tr>
<tr>
<td>Perineal</td>
<td>Diamond-shaped region between the thighs that contains the anus and external reproductive organs</td>
</tr>
<tr>
<td>Pes</td>
<td>Foot</td>
</tr>
<tr>
<td>Plantar</td>
<td>Sole of the foot</td>
</tr>
<tr>
<td>Pollex</td>
<td>Thumb</td>
</tr>
<tr>
<td>Popliteal</td>
<td>Area posterior to the knee</td>
</tr>
<tr>
<td>Pubic</td>
<td>Anterior region of the pelvis</td>
</tr>
<tr>
<td>Radial</td>
<td>Lateral aspect (thumb side) of forearm</td>
</tr>
<tr>
<td>Sacral</td>
<td>Posterior region between the hip bones</td>
</tr>
<tr>
<td>Scapular</td>
<td>Shoulder blade</td>
</tr>
<tr>
<td>Sternal</td>
<td>Anterior middle region of the thorax</td>
</tr>
<tr>
<td>Sural</td>
<td>Calf (posterior part of the leg)</td>
</tr>
<tr>
<td>Tarsal</td>
<td>Proximal part of the foot and ankle</td>
</tr>
<tr>
<td>Thoracic</td>
<td>Part of torso superior to thoracic diaphragm; contains the pectoral, axillary, and sternal regions</td>
</tr>
<tr>
<td>Tibial</td>
<td>Medial aspect of leg</td>
</tr>
<tr>
<td>Ulnar</td>
<td>Medial aspect (pinky side) of the forearm</td>
</tr>
<tr>
<td>Umbilical</td>
<td>Navel</td>
</tr>
<tr>
<td>Vertebral</td>
<td>Spinal column</td>
</tr>
</tbody>
</table>

1. The word *region* should follow each region name listed in the table (e.g., femoral region).

Lined with thin serous membranes. (Posterior aspect cavities have no serous membranes.) In this usage, a membrane is a continuous layer of cells, as compared to the plasma membrane that surrounds a single cell (see section 4.1c). Serous membranes form two layers: (1) a parietal (pā-rē’t-l) layer that typically lines the internal surface of the body wall and (2) a visceral (vis′er-ăl) layer that covers the external surface of the organs (viscera) within that cavity. Between the parietal and visceral serous membrane layers is a potential space called the serous cavity. (Note: A potential space is capable of becoming a larger opening under certain physiological or pathological conditions.) Serous membranes secrete a liquid called serous fluid within a serous cavity. Serous fluid has the consistency of oil and serves as a lubricant. In a living person, organs (e.g., heart, lungs, intestines) move and rub against each other and the body wall. Friction caused by this movement is reduced by the serous fluid.*
fluid so the organs move more smoothly against one another and the body walls. Serous membranes will be discussed again in section 5.5b.

**WHAT DO YOU THINK?**

What do you think would happen to your body organs if there were no serous fluid between the parietal and visceral layers?

Figure 1.9a provides a helpful analogy for visualizing the serous membrane layers. The closed fist is comparable to an organ, and the balloon is comparable to a serous membrane. When a fist is pushed against the wall of the balloon, the inner balloon wall that surrounds the fist is comparable to the visceral layer of the serous membrane. The outer balloon wall is comparable to the parietal layer of the serous membrane. The thin, air-filled space within the balloon, between the two “walls,” is comparable to the serous cavity. Note that the organ is not inside the serous cavity; it is actually outside the cavity and merely covered by the serous membrane.

**Thoracic Cavity** Within the thoracic cavity, the median space between the lungs is called the mediastinum (mē-dē-as-tiˈnəm; mediōs = middle) (figure 1.8b). It contains the heart, thymus, esophagus, trachea, and major blood vessels that connect to the heart.

Within the mediastinum, the heart is enclosed by a two-layered serous membrane called the pericardium (per-i-kar′dē-əm; peri = around, kardia = heart). The parietal pericardium is the outermost layer of the serous membrane and forms the sac around the heart, whereas the visceral pericardium forms the heart’s external surface (figure 1.9b). The pericardial cavity is the serous cavity between the parietal and visceral layers of the pericardium, and it contains serous fluid. (see section 19.2b).

The right and left sides of the thoracic cavity house the lungs, which are associated with a two-layered serous membrane called the pleura (plur′ě; a rib) (figure 1.9c).
The parietal pleura is the outer layer of the serous membrane and lines the internal surface of the thoracic wall. The inner layer is the visceral pleura, which covers the external surface of each lung. The pleural cavity is the serous cavity between these parietal and visceral layers, and it contains serous fluid. (see section 23.4c)

Abdominopelvic Cavity The abdominopelvic cavity consists of an abdominal cavity, which is superior to the pelvic brim of the hip bones (see section 8.10b), and a pelvic cavity, which is inferior to the pelvic brim. The abdominal cavity contains most of the digestive system organs, as well as the kidneys and most of the ureters. The pelvic cavity contains the distal part of the large intestine, the remainder of the ureters and the urinary bladder, and the internal reproductive organs.

The peritoneum (per′i-tō-nē′um; periteino = to stretch over) is the two-layered serous membrane that lines the abdominopelvic cavity (figure 1.9d). The parietal peritoneum, the outer layer of this serous membrane, lines the internal walls of the abdominopelvic cavity. The visceral peritoneum is the inner layer of this serous membrane, and it covers the external surfaces of most abdominal and pelvic organs. The serous cavity between these serous membrane layers is the peritoneal cavity, which contains and is lubricated by serous fluid.

**WHAT DID YOU LEARN?**

12 Which body cavity is associated with the lungs, and what are the names of its serous membranes?

### 1.5f Abdominopelvic Regions and Quadrants

**LEARNING OBJECTIVE**

16. Compare the terms used to subdivide the abdominopelvic region into nine regions or four quadrants.

To more accurately describe organ location, anatomists and healthcare professionals commonly partition the large abdominopelvic cavity into smaller compartments. Nine compartments, called abdominopelvic regions, are delineated by using two transverse planes and two sagittal planes.

These nine regions are shown in figure 1.10a and summarized here:

- The umbilical (ūm-bil′i-kāl; navel) region is the middle region and is named for the umbilicus, or navel (belly button) that lies in its center.
- The epigastric (ep-i-gas′tri-k; epi = above, gaster = belly) region is superior to the umbilical region.
The hypogastric (hī-pō-gas′trik; hypo = under) region lies inferior to the umbilical region.

The right and left hypochondriac (hī-pō-kon′drē-ak; chondr = cartilage) regions are inferior to the costal cartilages (cartilage attached to the ribs) and lateral to the epigastric region.

The right and left lumbar regions are lateral to the umbilical region.

The right and left iliac (il′ē-ak; eileo = to twist) regions are lateral to the hypogastric region.

Some health-care professionals prefer to partition the abdomen more simply into four quadrants, using the umbilicus as the central point and having imaginary transverse and midsagittal planes pass through the umbilicus (figure 1.10b). The quadrants are named right upper quadrant (RUQ), left upper quadrant (LUQ), right lower quadrant (RLQ), and left lower quadrant (LLQ). These quadrants, like the abdominopelvic regions, are used to accurately locate and describe various aches, pains, injuries, or other abnormalities.

**WHAT DID YOU LEARN?**

If a physician makes an incision into the abdomen along the midsagittal plane, superior to the umbilicus and just inferior to the thoracic diaphragm, then the skin of the abdominopelvic region has been incised.

### 1.6a Components of Homeostatic Systems

**LEARNING OBJECTIVES**

17. Define the components of a homeostatic system.

18. Be able to recognize each of the components in representative systems.

The body maintains homeostasis by utilizing homeostatic control systems. Three components are associated with each homeostatic system: receptor, control center, and effector (figure 1.11).

**Receptor**

The receptor is the body structure that detects changes in a variable, which is a substance or process that is regulated. A receptor
typically consists of sensory neurons (nerve cells). These neurons may be in the skin, internal organs of the body, or specialized organs such as the eye, ear, tongue, or nose. A stimulus is a change in the variable (a physical or chemical factor), such as a change in light, temperature, chemicals (e.g., glucose or oxygen levels), or stretch in muscle. Thus, a receptor is the structure that detects a stimulus. For example, the retina of the eye (receptor) detects a change in light (stimulus) entering the eye.

Control Center
The control center is the structure that both interprets input from the receptor and initiates changes through the effector. You can think of it as the “go between” for the other two components of a homeostatic system. The control center is generally a portion of the nervous system (brain or spinal cord) or an organ of the endocrine system (e.g., the thyroid gland). A homeostatic system involving the nervous system provides a relatively quick means of responding to change. An example is regulating blood pressure when you rise from bed in the morning. In contrast, the endocrine system usually provides a means of a more sustained response over several hours or days through the release of hormones. An example is when the parathyroid hormone continuously regulates blood calcium levels, a process that is essential for the normal function of both muscles and nerves (see section 17.10b). Note that the control center is sometimes the same structure as the receptor because it both detects the stimulus and causes a response to regulate it. For example, the pancreas acts as a receptor because it detects an increase in blood glucose and acts as a control center because it releases the hormone insulin in response (see section 17.9b).

Effectors
The effector is the structure that brings about the change to alter the stimulus (i.e., the effector causes an “effect”). Most body structures can serve as effectors, although muscles and exocrine glands (see section 5.1d) are often the effectors. For example, smooth muscle in the walls of air passageways (bronchioles) regulates airflow into and out of the lungs. Salivary glands increase their release of saliva to moisten the mouth.

As you view figure 1.11, notice that the response of a homeostatic system occurs through a feedback loop that includes the following:

- A stimulus, which is the change in the variable
- A receptor that detects the stimulus
- The control center, which both integrates input information from the receptor and initiates output to the effectors
- The effectors that cause the change (or effect)
- Homeostasis restored as a result of the changes from the effectors

![Figure 1.11 Components of a Homeostatic Control Mechanism.](image-url)
Homeostatic control systems are separated into two broad categories based on whether the system maintains the variable within a normal range by moving the stimulus in the opposite direction, or amplifies the stimulus in the same direction. These two types of feedback control are called negative feedback and positive feedback, respectively.

**1.6b Homeostatic Systems Regulated by Negative Feedback**

**LEARNING OBJECTIVES**

19. Define negative feedback.

20. Explain how homeostatic mechanisms regulated by negative feedback detect and respond to environmental changes.

Most processes in the body are controlled by negative feedback. If a homeostatic system is controlled by negative feedback, the resulting action will always be in the opposite direction of the stimulus. In this way, the variable is maintained within a normal level, or what is called its set point.

How a variable that is regulated by negative feedback fluctuates over time can be viewed in **figure 1.12**. Notice that the variable does not remain constant over time but instead fluctuates, and its fluctuation occurs around the set point. If the stimulus increases, the homeostatic system is activated to cause a decrease in the stimulus until it returns to the set point. In contrast, if the stimulus decreases, the homeostatic system causes an increase in the stimulus until it returns to normal. This idea is generally better understood by describing a specific example, such as temperature regulation.

**Temperature Regulation**

We begin by first explaining how a negative feedback mechanism works to maintain the temperature of your home at a set point of 70°F. On a very cold day, the indoor temperature drops. This drop in temperature is detected by the thermostat. The drop in temperature is relayed through the electrical wiring of your home to the heat pump, which then turns on. The heat pump continues to heat your home until the thermostat reaches 70°F. An electrical signal is then sent from the thermostat to shut off the heat pump.

Body temperature is regulated in an analogous way to how the temperature of your home is regulated (figure 1.13a). If you venture outside on a cold day, body temperature may begin to drop. This decrease in body temperature is detected by the sensory receptors of the skin, which send nerve impulses to the hypothalamus (a component of the brain; see section 13.4c). (The hypothalamus can also directly detect changes in body temperature by monitoring blood temperature as it passes through this region of the brain.) The hypothalamus compares sensory input to body temperature set point (e.g., 37°C or 98.6°F), and initiates motor output to blood vessels in the skin to decrease the diameter of the inside opening (lumen) of the vessels, thus decreasing the amount of blood circulating to the surface of the body. As a result, less heat is released through the skin. Nerve impulses are also sent to skeletal muscles, which cause shivering, and perhaps to smooth muscle associated with hair follicles of the skin, causing “goose bumps.”

In contrast, on a very hot day (figure 1.13b), or when you are engaging in strenuous exercise, an increase in body temperature is detected by the sensory receptors of the skin or hypothalamus. The hypothalamus detects the difference between the increased body temperature and the original temperature set point, and initiates motor output to the blood vessels of the skin. This change increases the lumen diameters of blood vessels so that additional blood is brought near the surface of the body for the release of heat through the skin. Nerve impulses are also sent from the hypothalamus to the sweat glands to initiate sweating. Both responses help cool the body by the loss of heat from its surface. In these examples, regulation occurs through the nervous system.

Other examples of homeostatic regulation through the nervous system include the withdrawal reflex in response to injury from stepping on glass or burning your hand (see section 14.6), regulating heart rate and blood pressure when you exercise (see section 20.6a), or changing breathing rate in response to an increase in carbon dioxide levels (see section 23.5).

Recall that the control center may also be an organ of the endocrine system. Examples of homeostatic systems that regulate through the endocrine system include the parathyroid gland release of parathyroid hormone in response to a decrease in blood calcium (see section 7.6b) or pancreas release of insulin in response to an increase in blood glucose (see section 17.9b).
Figure 1.13 Negative Feedback Mechanisms for Regulating Body Temperature.

Feedback mechanisms initiated when body temperature (a) falls below normal or (b) rises above normal are compared.

(a) Body Temperature Falls Below Normal

A decrease in body temperature stimulates a negative feedback mechanism.

STIMULUS
Cold environmental temperatures lower body temperature to below normal.

RECEPTORS
Sensory receptors in skin detect cold.

CONTROL CENTER
Hypothalamus of brain compares sensory input regarding temperature decrease to normal set point of 37°C.

EFFECTORS
Blood vessels in skin constrict; sweat glands become inactive; skeletal muscles shiver to generate heat.

HOMEOSTASIS
Body temperature returns to normal.

Heat is conserved.
Vigorous exercise or hot environmental temperatures raise body temperature to above normal. 

**CONTROL CENTER**

Hypothalamus of brain compares sensory input regarding temperature increase to normal set point of 37°C.

**RECEPTORS**

Sensory receptors in skin and other organs detect heat.

**EFFECTORS**

Blood vessels in skin dilate; sweat glands secrete sweat, which, if evaporated, will cool the skin’s surface.

**STIMULUS**

Heat is given off.

**HOMEOSTASIS**

Body temperature returns to normal.
LEARNING OBJECTIVES

21. Define positive feedback.
22. Describe the actions of a positive feedback loop.

A homeostatic system may also be controlled by positive feedback. The stimulus here is reinforced to continue in the same direction until a climactic event occurs (figure 1.14). Following the climactic event, the body again returns to homeostasis. Because their end result is to increase the activity (instead of initially returning the body to homeostasis), positive feedback mechanisms occur much less frequently than negative feedback mechanisms.

Figure 1.15 illustrates one example of a positive feedback mechanism in the human body, when a mother breastfeeds her baby. The baby sucking at the breast is the initial stimulus detected by sensory receptors in the skin of the nipple region. The receptors transmit this input to the control center, which is the hypothalamus of the brain. The hypothalamus signals the posterior pituitary (an endocrine gland) to release the hormone oxytocin into the blood. Oxytocin is the “output” that is sent to the effector, which is the glandular tissue of the breast. Oxytocin stimulates the mammary gland to eject the breast milk. The baby feeds and the cycle repeats as long as the baby suckles. Once the baby stops suckling (and thus the initial stimulus is removed), then the cycle will stop.

Other examples of positive feedback mechanisms include the blood clotting cascade (see section 18.4c) and uterine contractions involved in labor and childbirth (see section 29.6c).

WHAT DID YOU LEARN?

16. What is the main difference between a homeostatic system regulated by negative feedback and one regulated by positive feedback?

Figure 1.14 Positive Feedback. Positive feedback results in the stimulus being reinforced until a climactic event occurs, and then the body returns to homeostasis.

Figure 1.15 Positive Feedback. Positive feedback mechanisms often work in loops, where the initial step in the pathway is the stimulus, and the end product of the pathway is to stimulate (not turn off) the pathway activity. In this example of a mother breastfeeding her child, the stimulus of the baby sucking initiates nerve impulses to the brain to cause release of hormones that stimulate the breast to secrete more breast milk.
1.7 Homeostasis, Health, and Disease

LEARNING OBJECTIVE

23. Explain the general relationship of maintaining homeostasis to health and disease.

In summary, homeostasis is a term that describes the many physiologic processes to maintain the health of the body. These characteristics are noted about homeostatic systems:

- They are dynamic.
- The control center is generally the nervous system or the endocrine system.
- There are three components: receptor, control center, and effector.
- They are typically regulated through negative feedback to maintain a normal value or set point.
- It is when these systems fail that a homeostatic imbalance or disease potentially results and ultimately may threaten an individual’s survival.

Diabetes is an example of a homeostatic imbalance. Diabetes occurs when the homeostatic mechanisms for regulating blood glucose are not functioning normally, and blood glucose fluctuates out of the normal range, sometimes resulting in extremely high blood glucose readings. High blood glucose results in damage to anatomic structures throughout the body. Patients with diabetes must rely on other methods, such as diet restriction, exercise, and perhaps a medication, to lower blood glucose.

Sometimes a homeostatic imbalance results when critical changes from aging or disease cause a variable that is normally controlled by negative feedback to be abnormally controlled by positive feedback. An example is when there is extensive damage to the heart, perhaps from a heart attack. This heart is less able to pump blood to the structures of the body, including the heart itself. Consequently, the heart receives reduced amounts of nutrients and oxygen. The heart becomes progressively weaker, and even less able to pump blood to the body’s structure. Ultimately, the heart becomes so weak that the heart stops beating.

Treating patients generally involves determining a diagnosis, or a specific cause of the homeostatic imbalance. Once diagnosed, the patient is treated through the administration of medications or through other therapeutic avenues to facilitate the body in maintaining homeostasis.

Health-care practitioners also need to understand how the drugs patients are taking may affect the normal homeostatic control mechanisms. For example, one type of medication for the treatment of depression is an SSRI, which stands for selective serotonin reuptake inhibitor. Paroxetine (Paxil), fluoxetine (Prozac), and sertraline (Zoloft) are examples of SSRIs. Serotonin is a type of neurotransmitter. Normally, a neurotransmitter is released from one nerve cell in response to a stimulation (nerve impulse). The neurotransmitter accomplishes its communication task, and then is taken up again by the nerve cell for future use. Some depressed individuals may have lower levels of serotonin, so an SSRI blocks the reuptake of serotonin into the nerve cell. Therefore, serotonin stays outside the nerve cell for a longer period of time and its effects are prolonged, which may elevate the mood of the patient taking the SSRI.

However, like all drugs, SSRIs come with some undesirable side effects. Some SSRI side effects include digestive system distress, such as nausea, upset stomach, diarrhea, or combinations of all three. As it turns out, serotonin is also used in the nerve cells of the digestive system. By tinkering with the serotonin reuptake in the brain, the drug also affects serotonin reuptake in the digestive system. Essentially, the digestive system becomes more excitable due to the intake of the SSRI drug, with the symptoms just described.

Virtually all medications have some benefits and some side effects, many of which can be explained by examining the homeostatic control mechanisms with which they interact. Thus, an understanding of these mechanisms is a must for anatomists, physiologists, and health-care practitioners.

WHAT DID YOU LEARN?

17 What is an example of a disease process by which homeostasis is disrupted?
Clinical View 1.4  
Medical Imaging

Health-care professionals have taken advantage of sophisticated medical imaging techniques to extend their ability to visualize internal body structures noninvasively (i.e., without inserting an instrument into the body). Some of the most common techniques are radiography, sonography, computed tomography, digital subtraction angiography, dynamic spatial reconstruction, magnetic resonance imaging, and positron emission tomography.

Radiography
Radiography (rā-dē-og’-ra-fē; radius = ray, grapho = to write) is the primary method of obtaining an image of a body part for diagnostic purposes. A beam of x-rays, which are a form of high-energy radiation, penetrates solid structures within the body. X-rays can pass through soft tissues but they are absorbed by dense tissues, including bone, teeth, and tumors. Film images produced by x-rays passing through soft tissues leave the film lighter in the areas where x-rays are absorbed. Hollow organs can be visualized if they are filled with a radiopaque (rā-di-ō-pāk; opacus = shady) substance that absorbs x-rays.

The term x-ray also applies to the photograph (radiograph) made by this technique. Originally, x-rays got their name because they were an unknown type of radiation, but they are also called roentgen rays in honor of Wilhelm Roentgen, the German physicist who accidentally discovered them. Radiography is commonly used in dentistry, mammography, diagnosis of fractures, and chest examination. Disadvantages of x-rays are that they are difficult to interpret when organs overlap in the images, and they are unable to reveal slight differences in tissue density. In addition, the radiation of an x-ray is not without risk.

Sonography
The second most widely used imaging method is sonography (so-nog’-ra-fē; sonus = sound), also known as ultrasound. A technician slowly moves a small,

1. CT and MRI films taken in the transverse plane are usually, but not always, read from an inferior view. So the right side of the body is on the left side of the image, and the left side of the body is on the right side of the image. Thus, when reading a CT or MRI scan in transverse section, check the orientation of the image. There should be L and R letters to let you know which side of the film corresponds to the left or right side of the patient.
Dynamic Spatial Reconstruction (DSR)
Using modified CT scanners, a special technique called dynamic spatial reconstruction (DSR) provides two important pieces of medical information: (1) three-dimensional images of body organs, and (2) information about the normal organ movement as well as changes in its internal volume. Unlike traditional static CT scans, DSR allows the physician to see the movement of an organ. This type of observation, at slow speed or halted in time completely, has been invaluable in observations of the heart and the flow of blood through blood vessels.

Magnetic Resonance Imaging (MRI)
Magnetic resonance imaging (MRI), previously called nuclear magnetic resonance (NMR) imaging, was developed as a noninvasive technique to visualize soft tissues. The patient is placed in a supine position within a cylindrical chamber that is surrounded by a large electromagnet. The magnet generates a strong magnetic field that causes protons in the nuclei of hydrogen atoms in the tissues to align. Thereafter, upon exposure to radio waves, the protons absorb additional energy and align in a different direction. The hydrogen atoms then abruptly realign themselves to the magnetic field immediately after the radio waves are turned off. This results in the release of the atoms’ excess energy at different rates, depending on the type of tissue. A computer analyzes the emitted energy to produce an image of the body. MRI is better than CT for distinguishing between soft tissues, such as the white and gray matter of the nervous system. However, dense structures (e.g., bone) do not show up well in MRI. Formerly, another disadvantage of MRI was that patients felt claustrophobic while isolated in the closed cylinder. However, newer MRI technology has improved the hardware and lessened this effect.

A specific type of MRI, called functional MRI (fMRI), maps brain function based on local oxygen concentration differences in blood flow. Increased blood flow relates to increased brain activity and is detected by a decrease in deoxyhemoglobin (the form of hemoglobin lacking oxygen) in the blood.

Positron Emission Tomography (PET)
The positron emission tomography (PET) scan is used both to analyze the metabolic state of a tissue at a given moment in time and to determine which tissues are most active. The procedure begins with an injection of radioactively labeled glucose (sugar), which emits particles called positrons (like electrons, but with a positive charge). Collisions between positrons and electrons cause the release of gamma rays that can be detected by sensors and analyzed by computer. The result is a brilliant color image that shows which tissues were using the most glucose at that moment. In cardiology, the image can reveal the extent of damaged heart tissue—because damaged heart tissue consumes little or no glucose, the damaged tissue will appear dark. PET scans have been used to illustrate activity levels in the brain and, in so doing, have been useful in examining the effects of neurologic ailments (e.g., schizophrenia, Alzheimer disease). They also may detect whether certain cancers have metastasized throughout the body, because cancerous cells will take up more glucose and show up as a hot spot on the scan. The PET scan is an example of nuclear medicine, which uses radioisotopes (see section 2.1b) to form anatomic images of the body.
# Chapter Summary

## 1.1 Anatomy and Physiology Compared

1.1a Anatomy: Details of Structure and Form
- Anatomy may be subdivided into microscopic anatomy (anatomic study of materials using the microscope) and gross anatomy (the study of structures visible to the unaided eye).

1.1b Physiology: Details of Function
- Physiologists may examine the function of specific body systems (e.g., cardiovascular physiology) and may focus on problems or pathologies of such systems (pathophysiology).

## 1.2 Anatomy and Physiology Integrated

- Form and function are interrelated. Anatomists cannot gain a full appreciation of anatomic form without first understanding the structure’s function. Likewise, physiologists cannot fully appreciate body functions without learning about the structure’s form.
- It is effective to learn anatomy and physiology by integrating the two disciplines, rather than trying to separate the study of form from the study of function.

## 1.3 How to Study Anatomy and Physiology Effectively
- Utilize active learning techniques, draw out structures, make tables, and work with a partner to learn the material. If you can accurately explain a concept to your partner, then you truly understand the concept.

## 1.4 The Body’s Levels of Organization

1.4a Characteristics That Describe Living Things
- All living organisms exhibit several common properties: organization, metabolism, growth and development, responsiveness, adaptation, and reproduction.

1.4b The View from Simplest to Most Complex
- Anatomic structure is organized in an increasingly complex series of levels: the chemical level, cellular level, tissue level, organ level, organ system level, and organismal level.

1.4c Introduction to Organ Systems
- The human body contains 11 organ systems: integumentary, skeletal, muscular, nervous, endocrine, cardiovascular, lymphatic, respiratory, urinary, digestive, and reproductive.

## 1.5 The Precise Language of Anatomy and Physiology

1.5a Anatomic Position
- The anatomic position is used as a standard reference point for the human body.

1.5b Sections and Planes
- Three planes section the body and help describe relationships among the parts of the three-dimensional human body: the coronal plane, the transverse plane, and the midsagittal plane.

1.5c Anatomic Directions
- Specific directional terms indicate body structure locations.

1.5d Regional Anatomy
- Specific anatomic terms identify body regions.

1.5e Body Cavities and Membranes
- Body cavities are spaces that enclose organs and organ systems.
- The posterior aspect of the body contains the cranial cavity and the vertebral canal.
- The ventral cavity is subdivided into a thoracic cavity and an abdominopelvic cavity (which is partitioned into an abdominal cavity and a pelvic cavity).
- The ventral cavity is lined by thin serous membranes. A parietal layer lines the internal body wall surface, and a visceral layer covers the organs.

1.5f Abdominopelvic Regions and Quadrants
- Regions and quadrants are two aids for describing locations of the abdominopelvic viscera.
- There are nine abdominopelvic regions and four abdominopelvic quadrants.

## 1.6 Homeostasis: Keeping Internal Conditions Stable

1.6a Components of Homeostatic Systems
- The three components are the receptor (detects a stimulus), control center (interprets input from the receptor and initiates changes through the effector), and effector (the structure that brings about a change to the stimulus).

1.6b Homeostatic Systems Regulated by Negative Feedback
- Negative feedback mechanisms or loops are initiated by either an increase or a decrease in the stimulus, and the end result is to return the stimulus to within its normal range or set point. Most feedback mechanisms in the human body work by negative feedback.

1.6c Homeostatic Systems Regulated by Positive Feedback
- Positive feedback mechanisms are initiated by a stimulus, and they maintain or increase the activity of the original stimulus until a climatic event.

## 1.7 Homeostasis, Health, and Disease
- An understanding of the concept of homeostasis is essential when understanding the structure and function of a normal, healthy body, the mechanisms of disease, and how the body reacts to pharmaceutical agents.
1. Examining the superficial anatomic markings and internal body structures as they relate to the covering skin is called
   a. regional anatomy.
   b. surface anatomy.
   c. pathologic anatomy.
   d. comparative anatomy.

2. The ___________ level of organization is composed of two or more tissue types that work together to perform a common function.
   a. cellular
   b. molecular
   c. organ
   d. organismal

3. The term ___________ refers to the sum of all chemical reactions in the body.
   a. metabolism
   b. responsiveness
   c. stimulus
   d. reproduction

4. A midsagittal plane separates the body into
   a. anterior and posterior portions.
   b. superior and inferior portions.
   c. right and left halves.
   d. unequal right and left portions.

5. The term used to describe an appendage structure that is closest to its point of attachment to the trunk is
   a. distal.
   b. lateral.
   c. superior.
   d. proximal.

6. The ___________ region is the anterior part of the knee.
   a. patellar
   b. popliteal
   c. pes
   d. inguinal

7. Which body cavity is located inferior to the thoracic diaphragm and superior to the pelvic brim of the hip bones?
   a. abdominal cavity
   b. pelvic cavity
   c. pleural cavity
   d. pericardial cavity

8. The ___________ is the serous membrane layer that covers the surface of the lungs.
   a. parietal pleura
   b. visceral pericardium
   c. visceral peritoneum
   d. visceral pleura

9. The state of maintaining a constant internal environment within an organism is called
   a. reproduction.
   b. homeostasis.
   c. imbalance.
   d. life.

10. In a negative feedback mechanism, which of the following events does not occur?
    a. A stimulus (i.e., a change in some variable) occurs.
    b. A receptor perceives a stimulus.
    c. The control center sends output to an effector.
    d. The effector stimulates or increases the stimulus, so the cycle continues.

11. What are the similarities and differences between anatomy and physiology?

12. List the levels of organization in a human, starting at the simplest level and proceeding to the most complex. Give an example of a body structure in each level.

13. What properties are common to all living things?

14. Name the eleven organ systems in the human body.

15. Describe the body in the anatomic position. Why is the anatomic position used?

16. List the anatomic terms that describe the following regions: forearm, wrist, chest, armpit, thigh, and foot.

17. What are the two body cavities within the posterior aspect, and what does each cavity contain?

18. Describe the structure and function of serous membranes in the body.

19. What are the main components in a homeostatic control system?

20. Compare and contrast negative and positive feedback mechanisms.

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**Can You Apply What You’ve Learned?**

*Use the following paragraph to answer questions 1–3.*

Your friend Eric complains of some pain in his “belly area.” You ask him to point to the precise location of the pain. He points to a region that is below his umbilicus, on the lower right side of his abdomen, and just medial to his hip bones.

1. Which abdominal quadrant contains Eric’s pain?
   a. right upper quadrant
   b. right lower quadrant
   c. left upper quadrant
   d. left lower quadrant

2. You also could describe the pain as being in the ___________ abdominopelvic region.
   a. right lumbar
   b. right hypochondriac
   c. right umbilical
   d. right iliac
3. Eric goes to the doctor to determine the cause and source of the pain. The physician orders a CT scan, which shows that Eric has an enlarged and inflamed appendix (an organ associated with the digestive system). Eric asks the physician why she didn’t just take an x-ray of his belly region. She explains an x-ray would not be the best diagnostic imaging tool in this case because
   a. x-ray images are more expensive to produce than CT scans.
   b. soft-tissue structures don’t show up well on basic x-rays.
   c. the x-rays could inflame the appendix further and cause it to burst.
   d. x-rays now are used primarily for bone injuries only.

4. When you are outside on a hot, humid day, what body changes occur to help your body temperature return to normal?
   a. The blood vessels in your skin constrict.
   b. The sweat glands release sweat.
   c. Nerve impulses are sent to muscles to cause shivering.
   d. The smooth muscle associated with hair follicles contracts, causing goose bumps.

5. A friend just started taking Zoloft (an SSRI) and is experiencing an upset stomach and diarrhea. Your friend asks if the drug is causing her symptoms and you respond:
   a. Yes, because the drug is irritating her stomach lining and that explains her symptoms.
   b. Yes, because serotonin is located in both the brain and the digestive tract, so the drug is altering digestive system functioning.
   c. No, because the drug is supposed to elevate mood and affect brain function, and it shouldn’t have any effect on the digestive system.
   d. No, because the drug is quickly absorbed from the digestive tract and does not remain in the digestive system long enough to have any effect there.

Can You Synthesize What You’ve Learned?

1. Lynn was knocked off her bicycle during a race. She broke some bones in her right antebrachial region, suffered an abrasion on her mental region, and had severe bruising on her right gluteal and femoral regions. Explain where each of these injuries is located.

2. Carly was stung by a bee and was taken to the emergency room because she was undergoing anaphylactic shock (e.g., her breathing became more rapid and more difficult, her heartbeat increased). She was given a shot of epinephrine, which reduced her allergic reactions and brought her breathing and heartbeat back to normal. Did the dose of epinephrine result in a negative feedback mechanism occurring, or a positive feedback mechanism occurring? Explain your answer.

3. Your grandmother is being seen by a radiologist to diagnose a possible tumor in her small intestine. Explain to your grandmother what imaging techniques would best determine whether a tumor exists, and which techniques would be inadequate for determining the placement of the tumor.
In later chapters we describe many fascinating physiologic processes that occur within the human body, including: the transmission of an impulse along a nerve cell, the transport of oxygen within the blood, and nutrient digestion in the gastrointestinal tract. By reading and comprehending the material in this chapter on atoms, ions, and molecules—and information on energy, enzymes, and metabolism in chapter 3—you will develop a working knowledge of the basic chemical concepts needed to understand these concepts and other important physiologic processes. We have also included some of the common medical diagnostic tests (e.g., complete blood cell counts and urinalysis tests) in later chapters. Interpreting these tests requires an understanding of these same chemical concepts. We will refer back to the content within this chapter throughout the rest of the text, so that you will more easily see the connections between chemistry and concepts presented in later chapters.

Our coverage of chemistry is not comprehensive. Rather, our discussion is tailored to focus primarily on chemical structures relevant to the study of anatomy and physiology, and we have included examples of their application in the human body. The general characteristics of atoms, ions, and molecules are presented in the earlier sections of this chapter. Then we describe specific molecules, including water and water mixtures, and the four major biological macromolecules: lipids, carbohydrates, nucleic acids, and proteins. The chapter concludes with a section devoted to proteins, the most versatile biological macromolecules of living systems. Now, let’s embark upon an adventure to explore the body’s simplest constituents: atoms and molecules.
2.1 Atomic Structure

The human body at its simplest level of organization is composed of chemical structures that include atoms, ions, and molecules. We begin our discussion on the human body’s chemical composition by describing matter, atoms, elements, and the position of each element in the periodic table. This information allows us to make certain predictions regarding the chemical properties of each element, including whether and how the element forms ions and molecules.

2.1a Matter, Atoms, Elements, and the Periodic Table

LEARNING OBJECTIVES

1. Define matter, and list its three forms.
2. Describe and differentiate among the subatomic particles that compose atoms.
3. Explain the arrangement of elements in the periodic table based on atomic number.
4. Diagram the structure of an atom.

The human body is composed of matter, which is generally defined as a substance that has mass and occupies space. Matter is present in the body in three forms: solid, liquid, and gas. For example, bone is a solid, blood is a liquid, and oxygen (O₂) and carbon dioxide (CO₂) are gases.

All matter is composed of atoms. An atom is the smallest particle that exhibits the chemical properties of an element. There are 92 naturally occurring elements. Hydrogen is the smallest and lightest element; uranium is the largest and heaviest element. Technical advances in both chemistry and physics have resulted in the ability to produce “ultraheavy” elements that are larger than uranium. All elements, including the scientifically manufactured elements, are organized into a chart called the periodic table of elements (figure 2.1a).

Elements are grouped into major, minor, and trace elements based on the percentage each composes by weight in the human body. Major elements make up almost 99% of our body weight and minor elements less than 1% (figure 2.1b). In comparison, trace elements appear in the body in only limited amounts (less than 0.01%). Only 12 elements occur in living organisms in greater than 0.1% (figure 2.1c). In comparison, trace elements appear in the body in only limited amounts (less than 0.01%). Only 12 elements occur in living organisms in greater than 0.1%. Six are major elements, which include oxygen, carbon, hydrogen, nitrogen, calcium, phosphorus and six are minor elements, which include sulfur, potassium, sodium, chlorine, magnesium, and iron.

Note in figure 2.1a that the 12 major and minor elements are elevated above the other elements. Each element is color-coded, and these color-codes are used throughout the text.

The Components of an Atom

Atoms are composed of three subatomic particles: protons, neutrons, and electrons (figure 2.2). Two major criteria differentiate subatomic particles—namely, mass and charge. The mass of an atom is expressed as the atomic mass unit (amu), or dalton. (An atomic mass unit is very small: consider that 1 amu is equal to $1.66 \times 10^{-27}$ kilograms.)

Protons and neutrons each have a mass of 1 amu. A proton has a positive charge of one (+1), whereas a neutron is uncharged (meaning it is neutral). Protons and neutrons compose almost the entire mass of an atom and are located at the center, or core, of the atom, called the nucleus. The nucleus contains mass because it has both protons and neutrons, and it is positively charged because of the protons.

The electron is the third component of an atom. An electron has a very small mass—only about 1/1800th of the mass of a proton or neutron—and makes a negligible (very small) contribution to the total mass of the atom. Each electron has a negative charge of one (−1). Electrons are located at varying distances from the nucleus in regions called orbitals, often depicted either as an electron cloud (in a cloud model) or as discrete energy shells (in a shell model). Both the cloud model and shell model indicate where the electrons are most likely found, as depicted in figure 2.2. For simplicity, we diagram atoms with the shell model in this text.

Elements and the Periodic Table

Elements differ in the number of subatomic particles. The periodic table may be used to obtain the number of subatomic particles in an atom of a specific element. Several important features for each element appear in the periodic table, including the element’s chemical symbol, atomic number, and average atomic mass.

A unique chemical symbol has been assigned to each element. An element is usually identified either by its first letter or by its first letter plus an additional letter of its English name. For example, H is for hydrogen, C is for carbon, and O is for oxygen. A second letter, which is always lowercase, distinguishes elements that begin with the same letter (e.g., Ca for calcium and Cl for chlorine). The symbol of some elements is derived from their Latin name. For instance, the symbol for sodium is Na from the Latin natrium and potassium is K from the Latin kalium.

The atomic number of an element indicates the number of protons in an atom of that element and is located above its symbol in the periodic table. Note that elements are arranged by the atomic number in consecutive order within rows (figure 2.1a). The atomic number is designated as a subscript at the left of the chemical symbol when it is written. For example, H shows that the nucleus of a hydrogen atom has one proton, and 6C indicates that the carbon nucleus has six protons.

The atomic mass indicates the mass of both protons and neutrons in the atomic nucleus, and it reflects the “heaviness” of an element’s atoms relative to other atoms. (The electrons are not included because of their relatively small mass.) It is shown below the element’s symbol on the periodic table. The average atomic mass (described in section 2.1b) is rounded to the nearest whole number, and it is designated by a superscript to the left of the chemical symbol when it is written. For example, a sodium atom, with an atomic number of 11 and an average atomic mass of 22.99, is designated as $^{23}$Na.

WHAT DO YOU THINK?

How would the chemical shorthand for oxygen be written?

Determining the Number of Subatomic Particles

The number of each type of subatomic particle is determined as follows:

- The number of protons is the atomic number—thus, carbon has six protons and oxygen has eight protons.
- The number of neutrons can be determined by subtracting the atomic number (number of protons) from the atomic mass.
given energy level. Each shell can hold only a limited number of electrons within it. The electrons within a shell have a specific energy level.

The shell model represents the atom as having shells of electrons that surround the atomic nucleus. The electrons within a shell have a specific energy level.

### Diagramming Atomic Structures

The shell model represents the atom as having shells of electrons that surround the atomic nucleus. The electrons within a shell have a given energy level. Each shell can hold only a limited number of electrons. The innermost shell, or first shell, may hold up to two electrons.

### Figure 2.1 Periodic Table of Elements

(a) The periodic table includes all of the elements arranged in chart form. The grayed-out boxes at the bottom of the table are for proposed elements that as of yet do not have sufficient evidence to support their official inclusion as elements. 

(b) Twelve of the elements that compose the human body are present in greater than trace amounts. These 12 elements are color-coded in both (a) and (b), and this color scheme is used throughout the book to represent these elements.

### Figure 2.2 General Atomic Structure

Oxygen atoms are depicted with protons and neutrons in the nucleus. Electrons are shown in both a cloud model (a) and an energy shell model (b). 

### Table of Elements

<table>
<thead>
<tr>
<th>Symbol</th>
<th>Major elements (collectively compose almost 99% of body weight)</th>
<th>Minor elements (collectively compose less than 1% of body weight)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Oxygen</td>
<td>65.0</td>
</tr>
<tr>
<td></td>
<td>Carbon</td>
<td>18.5</td>
</tr>
<tr>
<td></td>
<td>Hydrogen</td>
<td>9.5</td>
</tr>
<tr>
<td></td>
<td>Nitrogen</td>
<td>3.0</td>
</tr>
<tr>
<td></td>
<td>Calcium</td>
<td>1.5</td>
</tr>
<tr>
<td></td>
<td>Phosphorus</td>
<td>1.0</td>
</tr>
</tbody>
</table>

(protons and neutrons). For example, to calculate the number of neutrons in sodium (\( \text{Na} \)), you would take the total of 23 protons and neutrons, and subtract the number of protons = 11; thus, sodium has 12 neutrons (23 – 11 = 12).

- The **number of electrons** in an atom is also determined by the atomic number. This is possible because all atoms are neutral. The number of negatively charged electrons must equal the number of positively charged protons for an atom to be neutral. Each electron has a charge of \(-1\) and counters the \(+1\) charge of a proton in the nucleus—therefore, the atom has zero charge, meaning it has no net charge.
electrons and the second shell up to eight electrons. All subsequent shells have a capacity of at least eight electrons. The electron shells closest to the nucleus must be filled prior to filling any potential shells at some greater distance from the nucleus when diagramming an atom. (Note: This is a general rule for elements with an atomic number of 18 or less.) Figure 2.2 shows the placement of protons and neutrons within the nucleus and electrons in specific shells for the atomic structure of oxygen.

### WHAT DID YOU LEARN?
1. What subatomic particles determine the mass of an atom? What subatomic particles determine the charge of an atom?
2. Diagram the atomic structure of chlorine—the atomic number is 17 and the mass number is 35.

#### 2.1b Isotopes

**LEARNING OBJECTIVES**

5. Describe an isotope.
6. Explain how radioisotopes differ from other types of isotopes.

Elements in nature usually occur as a mixture of isotopes. Isotopes (i’t-o-top; iso = same) are atoms of the same element that have the same number of protons and electrons but differ in the number of neutrons. Isotopes of an element exhibit essentially identical chemical characteristics but have different atomic masses.

For example, carbon exists in three isotopes: carbon-12, carbon-13, and carbon-14 (figure 2.3). All isotopes of carbon have six protons in their nuclei and six electrons in their atomic shells. However, carbon-12 has six neutrons, carbon-13 has seven neutrons, and carbon-14 has eight neutrons. Generally, one isotope is usually more common than the others. Carbon-12 is the most common isotope for carbon.

The weighted average of the atomic mass for all isotopes of an element is the average atomic mass (or atomic weight). This value is included below each element on the periodic table, as described in section 2.1a. The average atomic mass of carbon, for example, is 12.01 amu.

Some isotopes are referred to as radioisotopes. Radioisotopes are generally unstable because their nuclei contain an excess number of neutrons. For example, carbon-14 has eight neutrons in its nucleus and is unstable and radioactive, whereas carbon-12 has six neutrons in its nucleus and is stable and not radioactive. Radioisotopes usually lose nuclear components in the form of high-energy radiation that includes alpha particles, beta particles, or gamma rays as they decay or break down into a more stable isotope. The time it takes for 50% of the radioisotope to become stable is its physical half-life. This time may vary from a few hours to thousands of years. Radioisotopes produced in a nuclear power plant, for example, have a half-life of at least 10,000 years.

### WHAT DID YOU LEARN?
3. Do isotopes represent the same element? Do they have the same number of protons, neutrons, or electrons? Describe a radioisotope.

#### 2.1c Chemical Stability and the Octet Rule

**LEARNING OBJECTIVES**

7. Describe how elements are organized in the periodic table based on the valence electron number.
8. State the octet rule.

Recall that the periodic table is organized into rows based on atomic number. It is also organized into columns based on the number of electrons in the outer shell, or what is referred to as the valence shell. This organization is presented in figure 2.4, showing the atomic structure of elements 1 to 20 arranged as they appear in a periodic table. Column IA shows hydrogen, lithium, sodium, and potassium: All the atomic structures of these elements contain one electron in their outer shell. Each consecutive column thereafter (columns IIA–VIIIA) has one additional electron in its outer shell for each element in that column. This organization allows us to make predictions about the chemical characteristics of a given element simply by its location in the periodic table.

Notice that the elements in column VIIIA each have a valence shell that is full or complete. These elements (only helium, neon, and argon are shown in figure 2.4) have an outermost shell housing eight electrons, except for helium, which has only two electrons. A complete outer shell results in chemical stability. These stable atoms are relatively chemically inert and exhibit low reactivity; thus, these elements do not usually combine with other elements. The atoms in column VIIIA are referred to as noble gases because they do not typically react with the “common” elements in other columns of the periodic table.
Examine the atomic structure of the other elements in figure 2.4 (i.e., those that are not noble gases) and note that they lack a full outer shell with eight electrons. As we will see, these elements tend to lose, gain, or share electrons to obtain a complete outer shell. Chemists call this tendency the octet rule: Atoms obtain an outer shell with eight electrons and gain chemical stability through the loss, gain, or sharing of electrons. Not all elements follow the octet rule, but it is accurate for our purposes here. An ion is formed from an atom with either the loss or the gain of electrons, whereas a covalent bond is formed by the sharing of electrons between two atoms. We describe the formation of ions and covalent bonds in the next two sections.

**WHAT DID YOU LEARN?**

4. What is the relationship of the octet rule and chemical stability?
### 2.2 Ions and Ionic Compounds

The body consists mostly of chemical compounds. **Chemical compounds** are stable associations between two or more elements combined in a fixed ratio. These associations are classified as either ionic compounds or molecular compounds. Here we describe ionic compounds, which are structures composed of ions that are held together in a lattice by electrostatic interactions called ionic bonds. We first define ions and list some common ions of the human body, then explain how ions are formed and their charge determined, and finally we describe the electrostatic interaction between ions within an ionic compound. Molecular compounds are described in section 2.3.

#### 2.2a Ions

**LEARNING OBJECTIVES**

1. Define an ion.
2. List some common ions in the body.
3. Differentiate between cations and anions.
4. Describe how charges are assigned to ions.

**Ions** are either individual atoms or groups of atoms that have a positive or negative charge. An ion can have either a positive charge from the loss of one or more electrons or a negative charge from the gain of one or more electrons. Examples of ions include sodium ion (Na⁺), chloride ion (Cl⁻), and bicarbonate ion (HCO₃⁻). Table 2.1 lists the most common ions in the human body along with their significant physiologic functions—notice the diversity of body structures (e.g., nerves, muscles, liver, stomach) that require specific ions to function normally.

#### Losing Electrons and the Formation of Cations

A sodium atom, found in column IA of the periodic table (figure 2.4), is a good example of an element that can reach stability by losing an electron. The atomic structure of sodium has one electron in its outer shell. By giving up or donating that electron, sodium now satisfies the octet rule and becomes stable (figure 2.5a). But is the structure still neutral? Recall that neutral means that the number of positively charged protons is equal to the number of negatively charged electrons. Because an electron has been donated by the sodium atom, the newly formed sodium ion has 11 protons but only 10 electrons, and

<table>
<thead>
<tr>
<th>Table 2.1</th>
<th>Common Ions in the Human Body and Their Physiologic Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>COMMON CATIONS (POSITIVELY CHARGED IONS)</strong></td>
<td></td>
</tr>
<tr>
<td>Cation</td>
<td>Structure</td>
</tr>
<tr>
<td>Sodium ion</td>
<td>Na⁺</td>
</tr>
<tr>
<td></td>
<td></td>
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<td></td>
<td></td>
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<tr>
<td></td>
<td></td>
</tr>
<tr>
<td>Potassium ion</td>
<td>K⁺</td>
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<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td>Calcium ion</td>
<td>Ca²⁺</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td>Magnesium ion</td>
<td>Mg²⁺</td>
</tr>
<tr>
<td>Hydrogen ion</td>
<td>H⁺</td>
</tr>
</tbody>
</table>

| **COMMON ANIONS (NEGATIVELY CHARGED IONS)** |  |
| Anion | Structure | Physiologic Significance |
| Chloride ion | Cl⁻ | • Alters nerve cell responsiveness to stimulation |
| | | • Component of stomach acid (HCl) |
| | | • Chloride shift in erythrocytes |
| Bicarbonate ion | HCO₃⁻ | • Conversion of CO₂ gas to HCO₃⁻, which is transported in the blood |
| | | • Buffering of pH in blood |
| Phosphate ion | PO₄³⁻ | • As Ca₃(PO₄)₂, it hardens bone and teeth |
| | | • Component of phospholipids (membranes) |
| | | • Component of nucleotides, including ATP and nucleic acids (DNA and RNA) |
| | | • Most common intracellular anion |
| | | • Intracellular buffer |
the charge is calculated as follows: $11(+)$ and $10(-) = +1$. Ions with a positive charge are called cations. Thus, sodium ion is a cation with a $+1$ charge and is designated as Na$^{+}$. Other examples of common cations, as listed in table 2.1, include K$^{+}$, Ca$^{2+}$, Mg$^{2+}$, and H$^{+}$.

### Gaining Electrons and the Formation of Anions

A chlorine atom, found in column VIIA of the periodic table (figure 2.4), is a good example of an element that can reach stability by gaining an electron. The atomic structure of chlorine contains seven electrons in its outer shell, and by gaining one electron, stability is reached (figure 2.5a). The structure formed is referred to as a chloride ion. Because an electron has been gained, the chloride ion has 17 protons and now has 18 electrons, and the charge is calculated as follows: $17(+)$ and $18(-) = -1$, written as Cl$^{-}$. Negatively charged ions are called anions. Common anions are listed in table 2.1.

Two of the common anions included in table 2.1, bicarbonate ion (HCO$_3^-$) and phosphate ion (PO$_4^{3-}$), are composed of more than one atom and are referred to as polyatomic (pol‘ë-ät-om‘ik; poly = many) ions. Bicarbonate ion contains one oxygen atom that has gained an electron, whereas phosphate ion contains three oxygen atoms that have each gained an electron.

### General Rules for Assigning Charges

A general rule helps you determine which atoms gain or lose electrons and the charge that they develop (figure 2.4). Atoms with one, two, or three electrons in the outer shell generally donate electrons and become positively charged cations. The amount of charge depends upon the number of electrons donated—namely, one, two, or three. For example, because calcium has two electrons in its outer shell, it reaches stability by losing two negatively charged electrons, develops a charge of $+2$, and in ionic form is written as Ca$^{2+}$.

In comparison, atoms with five, six, or seven electrons in the outer shell tend to gain electrons and become negatively charged anions. The amount of charge depends upon the number of electrons gained to meet the octet rule criterion—namely, three, two, or one. An atom with seven electrons in the outer shell, such as chlorine, reaches stability and becomes chloride (Cl$^{-}$) when it gains one electron and develops a $-1$ charge.

### Using the Periodic Table to Assign Charges

The periodic table (see figure 2.1a) may be used to quickly assess whether an atom will become a cation or anion and the amount of its specific charge. Usually, elements on the left side of the periodic table, and in column IIIA, tend to lose electrons. The specific positive charge is dependent upon the position of the element in the periodic table: Group IIA = +2, group VA = +3, and group VA = +5. In contrast, elements on the right side of the periodic table (columns VA–VIIA) tend to gain electrons. The specific amount of negative charge is as follows: Group VA = $-3$, group VIA = $-2$, and group VIIA = $-1$. Sometimes there are anomalies, such as iron (Fe), which is the metal in the hemoglobin molecule within red blood cells (erythrocytes). It can form more than one type of ion, either a ferrous (Fe$^{2+}$) or a ferric (Fe$^{3+}$) ion.

### WHAT DID YOU LEARN?

5. List the common cations and anions of the human body, including their name and symbol.
6. On the periodic table (see figure 2.1), highlight the elements that form the common ions of the human body (do not include the polyatomic ions).
7. Explain how and why ions form based on the octet rule.

### 2.2b Ionic Bonds

**LEARNING OBJECTIVES**

14. Describe an ionic compound of NaCl.
15. List other examples of ionic compounds.

Positively charged cations and negatively charged anions may bind together by electrostatic interactions called ionic bonds. The structure formed is typically a salt. A classic example involves the formation of common table salt from atoms of sodium and atoms of chlorine. Each sodium atom loses one outer shell electron to a chlorine atom. The sodium atom then becomes a sodium ion (Na$^{+}$), and the chlorine atom becomes a chloride ion (Cl$^{-}$). The oppositely charged Na$^{+}$ and Cl$^{-}$ ions are held together by ionic bonds in a precise, lattice crystal structure composing an ionic compound (figure 2.5d). NaCl is the smallest repeating structure of this ionic compound and represents its chemical formula (the chemical constituents in a compound and their ratios).

Consider also the ionic compound magnesium chloride (MgCl$_2$). Notice that the chemical formula contains one magnesium and two chloride ions. This is because magnesium, which is in column IIA on...
the periodic table, has two electrons in its outer shell. It becomes stable by losing one electron to each of the two chlorine atoms.

Other examples of ionic compounds include those involving polyatomic anions, sodium bicarbonate (NaHCO₃), and the most common ionic compound in the body, calcium phosphate, Ca₃(PO₄)₂, which helps harden bones and teeth. Notice that each of these examples is a combination of a common cation and common anion (table 2.1).

**WHAT DID YOU LEARN?**

Could an ionic bond form between two cations or between two anions? Explain.

### 2.3 Covalent Bonding, Molecules, and Molecular Compounds

Instead of losing or gaining electrons to form ionic compounds that are arranged in a lattice, atoms also can reach chemical stability by sharing electrons. The sharing of electrons between two atoms results in a covalent bond. The resulting structure of the covalently bonded atoms is a molecule. Molecules composed of two or more different elements are more specifically called molecular compounds. Thus, molecules of carbon dioxide (CO₂) and water (H₂O) are molecular compounds. However, molecules composed of only one element are not, such as molecular oxygen (O₂) and molecular hydrogen (H₂).

Here we describe covalent bonds, the different types of covalently bonded molecules, and interactions between covalently bonded molecules, after first discussing how molecules are represented with molecular and structural formulas.

#### 2.3a Chemical Formulas: Molecular and Structural

**LEARNING OBJECTIVES**


17. Describe a structural formula, and explain its use in differentiating isomers.

### Molecular Formula

The molecular formula is the number and types of atoms composing a molecule. An example of a molecular formula would be H₂CO₃ representing carbonic acid, where the molecule contains two hydrogen atoms, one carbon atom, and three oxygen atoms.

### Structural Formula

The structural formula of a molecule is complementary to its molecular formula and exhibits not only the numbers and types of atoms but also their spatial arrangements within the molecule. Atoms are always arranged in a defined manner within each molecule. The molecular formula for carbon dioxide (CO₂) thus is complemented by its structural formula (O= C= O).

Structural formulas provide a means for differentiating isomers, which are molecules composed of the same number and types of elements but arranged differently in space. Two important isomers in humans are glucose and galactose (figure 2.6). These sugar molecules both have a molecular formula of C₆H₁₂O₆, indicating that each molecule has 6 carbon, 12 hydrogen, and 6 oxygen atoms. However, the atoms are arranged differently in space, as shown in their structural formulas. Notice the different arrangement of atoms on carbon four in the six-sided ring structure of glucose and galactose. These sugars in a ring-structure have carbon atoms that are numbered beginning with the carbon to the right of the oxygen as carbon one, and then are numbered consecutively clockwise around the ring.) Although fructose is a five-sided ring, it is also an isomer of glucose and galactose because it has the same molecular formula (C₆H₁₂O₆), but it has a different structural arrangement.

Isomers may have very different properties from one another—therefore, structural formulas are an important piece of chemical information.

**WHAT DID YOU LEARN?**

9. What information about a molecule is gained by a structural formula? How does a structural formula differ from a molecular formula?

10. What is an isomer?
2.3b Covalent Bonds

LEARNING OBJECTIVES

18. Describe a covalent bond, and explain its formation based on the octet rule.
19. List the four most common elements in the human body.
20. Distinguish between single, double, and triple covalent bonds.
21. Explain polar and nonpolar covalent bonds.

The bond that is formed when atoms share electrons is a covalent bond. A covalent bond forms when both atoms require electrons to become stable. This takes place when the participating atoms that form the chemical bond have four, five, six, or seven electrons in the outer shell. View figure 2.4 and note that this applies to the elements on the right side of the periodic table. (The exception is hydrogen because only two electrons are needed to complete its outermost electron shell.)

The four most common elements of the human body that form covalent bonds are hydrogen (H), oxygen (O), nitrogen (N), and carbon (C). These four elements account for over 96% of the body’s weight. The simplest example of covalent bond formation occurs when hydrogen gas is formed from two hydrogen atoms. The covalent bond formation between two hydrogen atoms fills the outer shell of each atom because each hydrogen atom shares its single electron (and only two electrons are required for the first shell to be complete).

The Number of Bonds an Atom Can Form

Although hydrogen can share only one pair of electrons and thus produce one covalent bond to become stable, some elements are able to share more than one pair. The number of covalent bonds formed by an atom may be determined by examining the number of electrons needed to complete the outer shell (see figure 2.4). The atomic structure of the four most common elements that compose molecules shows that hydrogen needs one electron, oxygen needs two electrons, nitrogen needs three electrons, and carbon needs four electrons. Thus, hydrogen can form one covalent bond, oxygen two, nitrogen three, and carbon four.

INTEGRATE

LEARNING STRATEGY

The interaction between elements on the right side of the periodic table (e.g., carbon, oxygen, nitrogen), or between these elements and a hydrogen atom, typically forms a covalent bond. The resulting structure, composed of elements that are covalently bonded, is a molecule.

INTEGRATE

LEARNING STRATEGY

The number of bonds formed by the four most common elements can be remembered with the acronym HONC: hydrogen = 1, oxygen = 2, nitrogen = 3, and carbon = 4.

Single, Double, and Triple Covalent Bonds

Atoms of elements that can form more than one covalent bond may do so through combinations of single, double, or triple covalent bonds (figure 2.7). A single covalent bond is one pair of electrons shared between two atoms. The bond just described between two hydrogen atoms is a single covalent bond. A double covalent bond involves the sharing of two pairs of electrons between two atoms. An example is the double covalent bond between two oxygen atoms. The sharing of two pairs of electrons between oxygen atoms is necessary to achieve stability because each oxygen atom has only six electrons in its outer shell but needs eight electrons to satisfy the octet rule. Three pairs of electrons are shared between atoms in some molecules, forming a triple covalent bond. A prime example is the triple covalent bond between two nitrogen atoms. The order of stability (i.e., the more energy required to break the bonds) is from least to greatest: single covalent bond, double covalent bond, triple covalent bond.

An atom of a specific element might share electrons in a variety of ways to satisfy the octet rule. For example, a carbon atom contains four electrons in the outer electron shell and thus needs four electrons to satisfy the octet rule. These four electrons can be obtained in a number of ways to form different types of molecules (figure 2.8).

Carbon Skeleton Formation

In later sections of this chapter and in subsequent chapters we will see examples of molecules that have numerous carbon atoms bonded together within their chemical structure. The arrangement of these carbon atoms is referred to as the molecule’s carbon skeleton. The carbon skeleton can be thought of as the molecule’s “backbone.” Three common carbon skeleton arrangements are: a straight chain, a branched chain, and a ring (figure 2.9). Notice that in a structural formula of a carbon chain or ring skeleton, the letter C is often not included with the understanding that a carbon atom lies where lines meet at an angle. In addition, if a carbon atom does not have its
required four bonds shown in the structural formula, each bond that is not shown is a bond between the carbon and a hydrogen atom.

Nonpolar and Polar Covalent Bonds
Atoms share electrons in a covalent bond either equally or unequally between the atoms. How they share is determined by the relative attraction each atom has for electrons, a concept referred to as electronegativity. Because two atoms of the same element, such as two hydrogen atoms, two oxygen atoms, or two carbon atoms, have equal attraction for electrons, they share the electrons equally. The resultant bond is a nonpolar covalent bond.

Different types of atoms have varying degrees of electronegativity, or attraction for electrons, and thus may share the electrons unequally. The resultant bond is a polar covalent bond (an important exception will be described at the end of this section). As a general rule, electronegativity increases both from left to right across a row of the periodic table and from bottom to top in a column (see figure 2.1a). These trends reflect that, for elements across a specific row, a greater number of protons in the nucleus of the atom are “pulling” on the electrons. For elements in a column, the elements closer to the top of the periodic table have electrons in shells closer to the nucleus (see figure 2.4). Thus, electronegativity is determined both by the number of protons in the nucleus and by the proximity of the valence electron shells to the nucleus.

Consequently, for the four most common elements composing living organisms, the order of electronegativity from least to greatest is as follows: hydrogen < carbon < nitrogen < oxygen. Therefore, of these four elements, hydrogen has the least attraction for electrons and oxygen has the greatest. The electrons being shared in a covalent bond spend a greater amount of time orbiting the nucleus of the more electronegative atom.

Because electrons have a negative charge, the more electronegative atom develops a partial negative charge, and the less electronegative atom develops a partial positive charge. Partial charges are written using the Greek letter delta (δ) followed by a superscript + or − to designate the relative charge. For example, a polar covalent bond formed between oxygen and hydrogen would be assigned and written as $\delta^–O–\delta^+H$. Note that the term polar (or dipole) refers to the “poles” of partial electrical charges, which are analogous to poles of a magnet.
Polar bonds have varying degrees of unequal sharing of electrons. Thus, polar bonds are along a continuum with ionic bonds (which involve a complete donation of electrons) on one end and nonpolar bonds (with equal sharing of electrons) on the other.

One important exception exists to the rule that a polar bond generally forms between two different atoms. The exception is carbon bonding with hydrogen. Because the electronegativity difference between carbon and hydrogen is relatively small, a covalent bond produced between carbon and hydrogen (C—H) has approximately equal sharing of electrons, and an essentially nonpolar covalent bond forms between them.

**WHAT DID YOU LEARN?**

11. Explain covalent bond formation in terms of chemical stability.
12. Assign the partial charges between nitrogen and hydrogen (N—H) in a polar covalent bond.
13. Why are some covalent bonds nonpolar and others polar? Identify the exception to the rule that polar covalent bonds are formed between two different types of atoms.

### Nonpolar Molecules

<table>
<thead>
<tr>
<th>Oxygen</th>
<th>Carbon dioxide</th>
<th>Triglyceride</th>
</tr>
</thead>
<tbody>
<tr>
<td>O=O</td>
<td>O=C=O</td>
<td></td>
</tr>
</tbody>
</table>

### Polar Molecules

<table>
<thead>
<tr>
<th>Water</th>
<th>Glucose</th>
</tr>
</thead>
<tbody>
<tr>
<td>H2O</td>
<td></td>
</tr>
</tbody>
</table>

### Amphipathic Molecule

<table>
<thead>
<tr>
<th>Polar region (attracted to water)</th>
<th>Nonpolar region (attracted to other fatty molecules)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phosphate</td>
<td>Fatty acids (two)</td>
</tr>
<tr>
<td>Glycerol</td>
<td></td>
</tr>
</tbody>
</table>

**Figure 2.10 Nonpolar, Polar, and Amphiphatic Molecules.** (a) Oxygen, carbon dioxide, and a triglyceride are examples of nonpolar molecules. (b) Water and glucose are examples of polar molecules. (c) A phospholipid is an example of an amphiphatic molecule.

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**LEARNING OBJECTIVES**

22. Describe the difference between a nonpolar molecule and a polar molecule.
23. Define an amphiphatic molecule.

Covalent bonds may be nonpolar or polar. To determine whether an entire molecule is nonpolar or polar, the molecule as a whole is evaluated to determine the prevalence (and relative strength) of its nonpolar and polar bonds. The most important concept to remember is that nonpolar molecules contain primarily nonpolar covalent bonds between the atoms within the molecule. As previously described, nonpolar covalent bonds are bonds formed between the same elements (e.g., C—C, O—O), by C—H bonds, or both. Oxygen (O₂) and triglyceride (fat) molecules are examples of nonpolar molecules *(figure 2.10a)*.

In comparison, polar molecules contain relatively more polar covalent bonds between the atoms within the molecule. Recall from
The two respiratory gases, O₂ and CO₂, are both nonpolar molecules. This chemical characteristic—and the fact that they are small in size—permits both to easily cross cell membranes. The diffusion of respiratory gases is discussed in other chapters of the text, including section 4.3a on membrane transport and section 23.6 on the exchange of O₂ and CO₂ between the blood and alveoli (air sacs) and between the blood and systemic cells.

The previous section that polar covalent bonds are between different elements, such as O—H, C—O, N—H, and N—O. Water (H₂O) and glucose (C₆H₁₂O₆) are both polar molecules (figure 2.10b). Notice that oxygen is bonded to two hydrogen atoms in a water molecule, and several C—O and O—H bonds are within a glucose molecule. One exception to this general pattern exists: A molecule containing polar covalent bonds that extend in opposite directions can be nonpolar because the partial charges cancel each other. Carbon dioxide (O=O=C=O) is an example.

Sometimes a molecule is large enough that it can have one major part that is nonpolar and another part that is polar. Molecules that contain both nonpolar and polar components are called amphipathic (amphi = both, patheia = feeling) molecules. A phospholipid molecule is an example of an amphipathic molecule (figure 2.10c).

WHAT DO YOU THINK?
3. Is the fatty acid portion of a triglyceride (figure 2.10a) nonpolar or polar molecule? Explain your answer. Would you predict that it will or will not dissolve in water?

WHAT DID YOU LEARN?
14. Are O₂ and CO₂ nonpolar or polar molecules?

2.3d Intermolecular Attractions

LEARNING OBJECTIVES
24. Describe hydrogen bonding between polar molecules.
25. List and define the intermolecular attractions between nonpolar molecules.

Molecules sometimes have weak chemical attractions to other molecules called intermolecular (inter = between) attractions. One important intermolecular attraction is called a hydrogen bond. A hydrogen bond forms between polar molecules. It is a weak attraction between a partially positive (δ+) hydrogen atom within a polar molecule and a partially negative (δ⁻) atom within a polar molecule. The partially negative atom is usually oxygen, but sometimes nitrogen. A hydrogen bond is designated in this text with a dotted or broken line. Several hydrogen bonds are shown in figure 2.11. Although an individual hydrogen bond is a weak bond or attraction (approximately 5–10% the strength of a covalent bond), hydrogen bonds are strong collectively.

Figure 2.11 Hydrogen Bonding.
Several hydrogen bonds between glucose and water are shown. Each is formed between a partially positive charged hydrogen atom of a glucose molecule and the partially negative charged oxygen atom of a water molecule.

Another type of intermolecular attraction involves nonpolar molecules. These occur when electrons orbiting the nucleus of an atom of a nonpolar molecule are distributed unequally for a brief instant. One portion of the atom is slightly negative and another portion is slightly positive. This momentary unequal distribution of charge in the atom induces an unequal distribution of electrons in an adjacent atom of another nonpolar molecule. This temporary unequal distribution of the electrons allows the atoms within the nonpolar molecules to form a brief attraction. Although these intermolecular forces between nonpolar molecules are weak (about 1% of the strength of a covalent bond), they also are strong collectively.

A third type of interaction is called hydrophobic interaction, which results when nonpolar molecules are placed in water or another polar substance. (Hydrophobic interactions are described in section 2.4c.) Note that all of these intermolecular attractions may also occur between different portions of a large molecule. In this case, they are more appropriately called intramolecular (intra = within) attractions.

Intermolecular (and intramolecular) attractions are important in establishing and maintaining the three-dimensional shape of complex molecules such as DNA (see section 2.7d) and proteins (see sections 2.7e and 2.8), as well as the temporary binding of molecular structures to one another, such as the binding of a hormone to a protein receptor. Hydrogen bonds also form between water molecules and have significant influence in how water molecules behave, as described in section 2.4.

WHAT DID YOU LEARN?
15. What is the name of the intermolecular attraction between a partially charged hydrogen of one polar molecule and a partially negative atom of another polar molecule?
2.4 Molecular Structure and Properties of Water

Chemists classify molecules into two broad categories—organic molecules and inorganic molecules. Organic molecules are defined as molecules that contain carbon, which are (or have been) components of living organisms (e.g., glucose, protein, triglycerides). All other types of molecules are inorganic molecules. Examples of inorganic molecules include water, salts (e.g., sodium chloride), acids (e.g., hydrochloric acid), and bases (e.g., sodium hydroxide). The remaining portions of this chapter discuss in detail specific types of molecules—including water, acids, bases, and the four primary organic biological macromolecules (lipids, carbohydrates, nucleic acids, and proteins).

Water is the first molecule that we examine in detail. It is appropriate to begin with water because it is the substance that composes approximately two-thirds of the human body by weight. We first look closely at the molecular structure of water molecules and then describe several important water properties. The relevance to normal body activities is included for each property.

2.4a Molecular Structure of Water

LEARNING OBJECTIVE

26. Describe the molecular structure of water and how each water molecule can form four hydrogen bonds.

Water is a polar molecule composed of one oxygen atom bonded to two hydrogen atoms. It exhibits polarity because there is an unequal sharing of electrons between the oxygen atom and each of the two hydrogen atoms (figure 2.12a). The oxygen atom is more electronegative, and it has two partial negative charges. In contrast, each hydrogen atom exhibits a single partial positive charge.

Every water molecule has the ability to form four hydrogen bonds with adjacent water molecules. This is because each of the two hydrogen atoms forms one hydrogen bond, and each oxygen atom forms two hydrogen bonds (figure 2.12b). Recall from our earlier discussion of hydrogen bonds that these intermolecular attractions are individually weak but collectively very strong. Thus, hydrogen bonding between water molecules is central to the properties exhibited by water.

WHAT DID YOU LEARN?

16. What is the intermolecular bond that is significant in determining the properties of water?

Figure 2.12 Water Molecule. (a) A water molecule is a polar molecule due to the unequal sharing of electrons between the oxygen atom and each of the two hydrogen atoms. Partial charges are shown. (b) Hydrogen bonds form between the partial positive (δ⁺) hydrogen atom of one water molecule and the partial negative (δ⁻) oxygen atom of a different water molecule.
2.4b Properties of Water

LEARNING OBJECTIVE

27. List the different properties of water, and provide an example of the importance of each property within the body.

Phases of Water

Water is present in three phases, depending upon the temperature: a gas (water vapor), a liquid (water), and a solid (ice). Substances that have a low molecular mass (described in section 2.6b) such as water generally are present in the gaseous phase at room temperature. However, water is liquid at room temperature because hydrogen bonds hold the water molecules in the liquid phase and limit their escape into the gaseous phase. Almost all water within the human body occurs within the liquid phase, although small amounts of water are present as water vapor within the air passageways. As a liquid, water serves the following functions:

- **Transports.** Substances are dissolved in water and moved throughout the body in water-based fluids (e.g., blood [see section 18.1b] and lymph [see section 21.1a]).
- **Lubricates.** Water-based fluids located between body structures decrease friction (e.g., serous fluid between the heart and its sac [see sections 1.5e and 19.2b], synovial fluid within joints [see section 9.4a]).
- **Cushions.** The force of sudden body movements is absorbed by water-based fluids (e.g., cerebrospinal fluid surrounding the brain and spinal cord [see section 13.2c]).
- **Excretes wastes.** Unwanted substances are eliminated in the body dissolved in water (e.g., urine [see section 24.8a]).

Cohesion, Surface Tension, and Adhesion

**Cohesion** is the attraction between water molecules. They are inclined to “stick together” because hydrogen bonds form between these molecules. **Surface tension** is the inward force of cohesive forces at the surface of water. This inward attraction occurs because water molecules at the surface are pulled by hydrogen bonds in only three directions, whereas water molecules that are internal in the liquid are pulled by hydrogen bonds in four directions. **Adhesion** is the attraction between water molecules and a substance other than water. This occurs when hydrogen bonds form between water molecules and the molecules that compose those other substances.

Surface tension can be demonstrated readily. Try this experiment: First, stack two flat plates of glass, such as two clean microscope slides, and then lift them apart. Note that they are easily separated. Then repeat this experiment, but first place one or two drops of water between the slides before they are stacked. Note it is much more difficult, if not impossible, to separate the plates of glass without first wedging them apart. This is because water causes increased surface tension between the surfaces.

### INTEGRATE

#### CLINICAL VIEW 2.2

**Surface Tension and Surfactant**

Surface tension can be exhibited within the walls of the alveoli (air sacs) because opposing alveolar walls are moist and if collapsed will stick together. However, we produce a mixture of lipids and proteins called pulmonary surfactant (see section 23.3d) that prevents the alveoli from collapsing when we breathe out. Without surfactant (a risk of some premature infants), alveoli collapse with each breath out, and the two moist sides of the alveoli adhere to one another. The next breath in requires breaking of the surface tension within alveoli and their re-inflation—a situation that requires much greater effort.

High Specific Heat and High Heat of Vaporization

**Temperature** is a measure of the kinetic energy, or random movement, of atoms or molecules within a substance. The relationship between temperature and kinetic energy is direct—the temperature is higher when there is a greater amount of kinetic energy in an object. Two properties of water influence water temperature: its specific heat and the heat of vaporization.

**Specific heat** is the amount of energy (measured in calories) required to increase the temperature of 1 gram of a substance by 1 degree Celsius (C). The specific heat of water has one of the highest values of any substance (1 calorie/gram°C). This is because most of the energy imparted into water during heating is first used to break hydrogen bonds. Thereafter, the energy from heating increases the kinetic energy of water molecules. As we change between cool and warm environments, or generate large amounts of heat during physical exertion, much of this heat (energy) is used to break hydrogen bonds and not increase the random movement of molecules (kinetic energy) within the body. Thus, body temperature remains relatively constant.

**Heat of vaporization** is the energy required for the release of molecules from a liquid phase into the gaseous phase for 1 gram of a substance. Water has a high heat of vaporization because the hydrogen bonds between individual water molecules must first be broken before these molecules can be released from the liquid phase into the gaseous phase. This is the reason sweating is an effective measure in helping to cool the body. As water molecules evaporate from the surface of the skin, excess heat is dissipated from the body as liquid water is changed to a gas.

**WHAT DID YOU LEARN?**

17. Which property of water contributes to the need to produce surfactant and prevent collapse of the alveoli? Which property contributes to body temperature regulation through sweating? Why is sweating less effective in cooling the body on a humid day?

### 2.4c Water as the Universal Solvent

LEARNING OBJECTIVES

28. Compare substances that dissolve in water with those that both dissolve and dissociate in water. Distinguish between electrolytes and nonelectrolytes.

29. Describe the chemical interactions of nonpolar substances and water.

30. Explain how amphipathic molecules interact in water to form chemical barriers.

Water is the solvent of the body, and substances that dissolve in water are called solutes. Water is called the universal solvent because most substances dissolve in it. However, not all substances dissolve completely or at all in water. The chemical properties of a substance (whether it is a charged ion, a nonpolar molecule, a polar molecule, or an amphipathic molecule) determine how the substance interacts with water molecules. Here we examine (1) the substances that dissolve in water (polar molecules and ions), (2) those that do not dissolve in water (nonpolar molecules), and (3) those that partially dissolve in water (amphipathic molecules).

**Substances That Dissolve in Water**

(Polar Molecules and Ions)

Both polar molecules (e.g., glucose) and ions (e.g., Na\(^+\), HCO\(_3\)\(^-\)) favorably interact with water molecules to disperse or dissolve within water. For this reason they are appropriately called hydrophilic (meaning water-loving).

---

**Atoms, Ions, and Molecules**

44 Chapter Two
Polar molecules such as glucose dissolve in water as a result of the hydrogen bonds that form between those molecules and water molecules. Observe in figure 2.13a how water molecules surround each polar molecule and form a hydration shell around each molecule. Electrolytes, which include salts, acids, and bases, dissolve and dissociate in water to a certain extent as water molecules form hydration shells around each ion. (b) Hydrophobic molecules are nonpolar and do not dissolve in water; rather, the nonpolar molecules are “pushed” out of the water by hydrophobic exclusion. (c) Amphipathic molecules are unique in that the polar portion dissolves in water and the nonpolar portion does not. Membranes (e.g., plasma membrane, nuclear envelope) formed from phospholipid molecules and micelles formed from bile salts are two common arrangements formed within the body by amphipathic molecules.

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Figure 2.13 Substance Interaction with Water. Chemical properties of the substance combined with water will determine their interaction. (a) Hydrophilic substances dissolve in water. Nonelectrolytes, which include polar molecules, dissolve and remain intact within water as water molecules form a hydration shell around each molecule. Electrolytes, which include salts, acids, and bases, dissolve and dissociate in water to a certain extent as water molecules form hydration shells around each ion. (b) Hydrophobic molecules are nonpolar and do not dissolve in water; rather, the nonpolar molecules are “pushed” out of the water by hydrophobic exclusion. (c) Amphipathic molecules are unique in that the polar portion dissolves in water and the nonpolar portion does not. Membranes (e.g., plasma membrane, nuclear envelope) formed from phospholipid molecules and micelles formed from bile salts are two common arrangements formed within the body by amphipathic molecules.

Sodium bicarbonate dissociates to form both Na⁺ and HCO₃⁻ ions. Acids and bases are described in detail in section 2.5.

Substances that both dissolve and dissociate in water, such as salts, acids, and bases, can readily conduct an electric current. For this reason, they are called electrolytes. In contrast, substances that remain intact when introduced into water, such as glucose, do not conduct an electric current and are called nonelectrolytes. Maintaining normal levels of electrolytes including salts, acids, and bases is discussed in section 25.3a.

Substances that do not dissolve in water (nonpolar molecules)

Nonpolar molecules do not dissolve in water, and they are called hydrophobic (meaning water-fearing). The hydrogen bonds between water molecules cause the water molecules to be cohesive and attract each other; at the same time, they exclude, or “force out,” the
nonpolar molecules by a process called hydrophobic exclusion (figure 2.13b). The interaction between the molecules of the excluded nonpolar substance is termed hydrophobic interaction because it appears that these molecules are avoiding water. In this case, contact between the polar water molecules and the nonpolar substance is minimized. You can observe hydrophobic exclusion by placing a few drops of oil into water; the oil forms small, spherical drops on the water’s surface.

Hydrophobic substances, such as triglycerides (fats) and cholesterol, require carrier proteins to be transported within the blood because of their inability to dissolve within water. The nonpolar molecules are enclosed within the confines of the protein molecule to limit its contact with the water in the blood (see section 18.2a).

**Substances That Partially Dissolve in Water (Amphipathic Molecules)**

Amphipathic molecules have both polar and nonpolar regions. They do not completely dissolve, nor are they completely excluded when placed into water. Instead, the polar portion dissolves in water (i.e., it is hydrophilic), and the nonpolar portion is repelled by water (i.e., it is hydrophobic). Through hydrophobic exclusion, nonpolar portions become positioned in close proximity (figure 2.13c).

Recall from section 2.3c that phospholipid molecules are amphipathic molecules. The polar heads of these molecules are hydrophilic and have contact with water, but their nonpolar tails are hydrophobic and group together, limiting their contact with water. This results in bilayers (two layers) of phospholipids that form chemical barriers within the body. A bilayer of phospholipid molecules composes membranes of a cell (e.g., the plasma membrane, which forms the outside barrier of a cell; see section 4.2a). Other amphipathic molecules (e.g., bile salts) form a spherical structure called a micelle, in which the nonpolar tails extend inward. This is a special structure within the digestive tract that is associated with the breakdown and absorption of nonpolar molecules, including triglycerides (see section 26.4c).

The many functions of water in the human body are summarized in figure 2.14. Note that the property of water as a neutral solvent (included in this figure) is described in section 2.5.

### WHAT DID YOU LEARN?

18. How does the interaction of a nonelectrolyte and water differ from the interaction of an electrolyte and water? Give examples of each.

19. How do phospholipid molecules interact with water to form a membrane?

### 2.5 Acidic and Basic Solutions, pH, and Buffers

Acidic and basic solutions occur specifically when an acid or base is added to water. Here we describe why water is neutral; define an acid and a base; and explain pH, neutralization, and the action of buffers.

#### 2.5a Water: A Neutral Solvent

**LEARNING OBJECTIVE**

31. Describe what is formed when water molecules dissociate.

Another property of water is that water molecules spontaneously dissociate to form ions. The covalent chemical bond between oxygen and either of the two hydrogen atoms in a water molecule spontaneously breaks apart at a low rate (about two dissociations occur per billion water molecules). This number is about \(10^{-7}\) ions (or 1/10,000,000 ions) per liter.

A hydrogen ion (\(H^+\)) transfers to a second water molecule during dissociation. The water molecule that picked up the extra hydrogen ion is called a hydronium ion, and it is represented as \(H_3O^+\). The electron of this “transferred” hydrogen remains associated with the original water molecule, which now is deficient in one hydrogen ion but still has the original electron. This molecule is called a hydroxide ion (\(OH^-\)). This dissociation reaction is written as

\[
H_2O + H_2O \rightarrow H_3O^+ + OH^-
\]

simplified to

\[
H_2O \rightarrow H^+ + OH^-
\]
Hydrophobic molecules

Water molecules exclude (or force out) nonpolar molecules; thus, proteins are required for their transport within the body.

Amphipathic molecules

Polar portion dissolves, nonpolar portion excluded.
Amphipathic molecules form chemical barriers (e.g., cell membranes, micelles).

CONCEPT OVERVIEW

Figure 2.14 Water’s Roles in the Body.
Water serves several critical functions within the body. It helps regulate body temperature, serves as the universal solvent, cushions, transports, lubricates, and produces high surface tension that allows body structures to cling to each other. The neutral pH of water is changed by the addition of acid or base.

REGULATES BODY TEMPERATURE

Water helps regulate body temperature due to its high specific heat and high heat of vaporization.

Hydrophilic substance

Non-electrolytes dissolve and remain intact.

Electrolytes dissolve and dissociate.

Hydrophobic molecules

Water molecules exclude (or force out) nonpolar molecules; thus, proteins are required for their transport within the body.

Amphipathic molecules

Polar portion dissolves, nonpolar portion excluded.
Amphipathic molecules form chemical barriers (e.g., cell membranes, micelles).

UNIVERSAL SOLVENT

Hydrophilic substance

Non-electrolytes dissolve and remain intact.

Electrolytes dissolve and dissociate.

UNIVERSAL SOLVENT

Electrolytes dissolve and dissociate.

CUSHIONS

Cerebrospinal fluid

Fluid cushions against sudden movements.

LUBRICATES

Fluid serves as a lubricant to decrease friction.

HIGH SURFACE TENSION

Water’s high surface tension causes structures to adhere. The moist alveoli in the lungs are prevented from collapsing and adhering by surfactant.

NEUTRAL pH

Water has a neutral pH. Body fluids are altered in pH with the addition of either an acid (e.g., within stomach) or a base (e.g., within small intestine).
Equal numbers of positively charged hydrogen ions (H\(^+\)) and negatively charged hydroxide ions (OH\(^-\)) are produced from the dissociation of water. Consequently, water has no net charge and is neutral.

### 2.5b Acids and Bases

**LEARNING OBJECTIVE**

32. Explain the difference between an acid and a base.

An acid is a substance that dissociates in water to produce both an H\(^+\) and an anion. An acid increases the concentration of H\(^+\) (written as [H\(^+\)]) that is free in solution (figure 2.15). Because H\(^+\) is a proton, an acid is also called a proton donor. The equation is as follows:

Substance A (an acid in water) → H\(^+\) + Anion

Strong acids dissociate to a greater extent and produce more H\(^+\). Hydrochloric acid (HCl), secreted by cells lining the stomach, is a good example of a strong acid. Weak acids, such as carbonic acid (H\(_2\)CO\(_3\)), within the blood, dissociate to a lesser extent, producing fewer H\(^+\) ions.

In contrast, a base accepts H\(^+\) when added to a solution. Therefore, a base is also called a proton acceptor. A base decreases the concentration of H\(^+\) free in solution. Thus,

Substance B (a base in water) + H\(^+\) → B—H

Stronger bases dissociate to a greater extent and bind more H\(^+\) than do weak bases, leaving less H\(^+\) in solution. Sodium hydroxide (NaOH) is an example of a strong base. Weak bases bind less H\(^+\), leaving more H\(^+\) in solution. Bicarbonate (HCO\(_3\)) is one of the most important weak bases in the body; it is both transported in the blood and released into secretions from the liver and pancreas that enter the small intestine.

**WHAT DID YOU LEARN?**

21. Which type of substance releases H\(^+\) when added to water?

---

**Figure 2.15 pH.** pH scale is a measure of the relative concentrations of H\(^+\) and OH\(^-\). A neutral solution has equal amounts of H\(^+\) and OH\(^-\), acidic solutions contain greater amounts of H\(^+\) than OH\(^-\), and basic solutions contain lesser amounts of H\(^+\) than OH\(^-\). Examples of common solutions that exhibit a specific pH are shown.

### 2.5c pH, Neutralization, and the Action of Buffers

**LEARNING OBJECTIVES**

33. Define pH, and explain the relative pH values of both acids and bases.

34. Explain neutralization, and describe how the neutralization of both an acid and a base occurs.

35. Describe the action of a buffer.

The pH of a solution is a measure of the relative amounts of H\(^+\) it contains; it is expressed as a number between 0 and 14. (The term pH is an abbreviation of the phrase potential of hydrogen. The unit of measurement for the pH scale is moles/liter.) pH is the inverse relationship of the logarithmic values for a given hydrogen ion concentration [H\(^+\)]:

\[
\text{Negative log of } [\text{H}^+] = \frac{1}{\log [\text{H}^+]} 
\]

Recall that water readily dissociates to produce 10\(^{-7}\) H\(^+\) and OH\(^-\) ions (or 1/10,000,000 ions) per liter. If this concentration of H\(^+\) is placed into the formula just given for pH, then the value for the pH of water is calculated to be equal to 7. In other words:

\[
[H^+] = 1 \times 10^{-7} \\
[H^+] = 0.0000001 \\
pH = 7 
\]

Notice that as [H\(^+\)] changes, pH changes. For example, if the [H\(^+\)] increases so that \([H^+] = 1 \times 10^{-5}, [H^+] = 0.0001,\) then the pH decreases to 4. Conversely, if the [H\(^+\)] decreases so that \([H^+] = 1 \times 10^{-9}, [H^+] = 0.000000001,\) then the pH increases to 9. Thus, [H\(^+\)] and pH value are inversely related. The inverse relationship between [H\(^+\)] and pH is an extremely important concept. Remember, as [H\(^+\)] increases, pH decreases, and as [H\(^+\)] decreases, pH increases.

**Interpreting the pH Scale**

Pure water and other solutions that have equal concentrations of H\(^+\) and OH\(^-\) are neutral and have a pH of 7. Solutions with a pH below 7 are acidic, and solutions with a pH above 7 are basic, or alkaline.

Moving from one increment to another (e.g., 7 to 6) represents a 10-fold change in [H\(^+\)]. Therefore, a pH 6 solution has a [H\(^+\)] that is...
10 times greater than pure water. Changing by two units (e.g., 7 to 5) is a 100-fold increase in [H\(^+\)]. This relationship is accurate for changes above 7 as well, except that each increment is a 10-fold decrease in [H\(^+\)].

**WHAT DO YOU THINK?**

If stomach acid has a pH of 2, how much more acidic is stomach acid than water (pH 7)? Predict what would happen to the stomach if it were not protected from the effects of hydrochloric acid.

**Neutralization**

Neutralization occurs when a solution that is either acidic or basic becomes neutral (i.e., has a pH of 7). The neutralization of an acidic solution is accomplished by adding a base, whereas a basic solution is neutralized by adding an acid. Thus, over-the-counter antacids must contain a base to neutralize stomach acid.

**Buffers**

A buffer is either a single type of molecule or two or more different types of molecules that helps prevent pH changes if either acid or base is added. A buffer acts either to accept H\(^+\) from added acid or to donate H\(^+\) to neutralize added base. Both bicarbonate (HCO\(_3\)\(^−\)) and carbonic acid (H\(_2\)CO\(_3\)), for example, are present within the blood and serve as buffers. Bicarbonate (HCO\(_3\)\(^−\)) accepts H\(^+\) as acid is added to the blood and carbonic acid (H\(_2\)CO\(_3\)) releases H\(^+\) as base is added to the blood to maintain the pH of the blood within the normal range of 7.35 to 7.45 (see section 18.1b). It is critical to maintain acid-base balance in the body because even small changes in pH (called an acid-base disturbance or imbalance) can be fatal. Acid-base balance and disturbances to acid-base balance are described in detail in sections 25.5 and 25.6, respectively.

**WHAT DID YOU LEARN?**

22. What is the general relationship of [H\(^+\)] and pH?
23. Why are buffers important, and how do they function to help maintain pH?

---

**2.6 Water Mixtures**

Mixtures are formed from the combining or mixing of two or more substances. Several types of mixtures have already been described, including sugar water, salt water, acidic solutions, and basic solutions. Two defining features of mixtures are (1) the substances that are mixed are not chemically changed and (2) the substances in the mixture can be separated by physical means, such as by evaporation or by filtering. Our emphasis here is on water mixtures. We describe how water mixtures are categorized into three types and explain how solution concentration is expressed.

**2.6a Categories of Water Mixtures**

**LEARNING OBJECTIVES**

36. Compare and contrast the three different types of water mixtures.
37. Explain how an emulsion differs from other types of mixtures.

Water mixtures are placed into three categories based on the relative size of the substance mixed with water and include suspensions, colloids, and solutions (figure 2.16).

- **Suspension.** A suspension is a mixture composed of particles that are relatively large (e.g., greater in size than 1 millimeter). These types of mixtures do not remain mixed together unless the mixture is in motion. The large solutes or cells settle out...
of a suspension when it is not in motion. A suspension appears cloudy or opaque and scatters light until the particles drop out of the liquid. Sand in water is an example of a suspension. Blood cells within the plasma (the liquid portion) of blood form a suspension.

- **Colloid.** A colloid is a mixture composed of smaller particles than those in a suspension (but larger than those in a solution). A colloid may appear either opaque or milky and scatters light like a suspension—but, unlike a suspension, remains mixed when not in motion. Some colloids, including gelatin and agar media (used in the microbiology laboratory), display an interesting feature—namely, they contain protein and become liquid when heated but change to a gel-like state when left standing and cooled. Colloids within the body include fluid within a cell (cytosol) and fluid within the blood (plasma).

- **Solution.** A solution is a homogeneous mixture in which the dissolved substance is very small (less than 1 nanometer in diameter). The water is the solvent, and the dissolved substance is the solute. Both salt water and sugar water are examples of solutions. The small size of the solutes in a solution results in a mixture with these characteristics: The solutes are not visible, do not scatter light, and do not settle if the solution is not in motion. Blood plasma is an example of a body solution, with salts, glucose, HCO$_3^-$, and other dissolved nonprotein substances.

### Table 2.2: Expressing Solution Concentrations

<table>
<thead>
<tr>
<th>Solution Concentration</th>
<th>Expressed As</th>
<th>Unit of Measurement</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mass/volume</td>
<td>Mass of solute per volume of solution</td>
<td>$\mu$g solute/dL solution</td>
<td>Normal blood concentration of iron is within the range of 40 to 150 $\mu$g/dL. Normal blood concentration of glucose is between 70 and 110 mg/dL.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>mg solute/dL solution</td>
<td></td>
</tr>
<tr>
<td>Mass/volume percent</td>
<td>Mass of solute per 100 milliliters (mL) of solution</td>
<td>grams/100 mL</td>
<td>5% dextrose intravenous (IV) solution (D5W) has a concentration of 5 grams of dextrose (glucose) per 100 mL of solution. Physiologic saline (0.9% NaCl) has 0.9 gram of NaCl per 100 mL of solution.</td>
</tr>
<tr>
<td>Molarity</td>
<td>Moles of solute per liter of solution</td>
<td>moles solute/L solution</td>
<td>0.164 mol/L solution</td>
</tr>
<tr>
<td>Molality</td>
<td>Moles of solute per kilogram of solvent</td>
<td>moles solute/kg solvent</td>
<td>0.164 mol/kg solvent</td>
</tr>
</tbody>
</table>

---

**WHAT DID YOU LEARN?**

24. When left standing, erythrocytes (red blood cells) settle to the bottom of a tube of blood. Based on this characteristic alone, blood would be characterized as a (a) suspension, (b) colloid, or (c) solution?

25. Why is blood also considered the other two types of water mixtures?

---

**LEARNING OBJECTIVE**

38. Explain the different ways to express the concentration of solute in a solution.

The amount of solute dissolved in a solution determines the concentration of a solution. Concentration of a solution may be expressed in several ways, including mass/volume, mass/volume percent, molarity, and molality. The units for expressing concentration are summarized in Table 2.2, which includes a description, units of measurement, and an example for each.

- **Mass/volume** is mass of solute per volume of solution. Results from a blood test are often expressed in mass/volume. **Mass/volume percent** is grams of solute per 100 milliliters of solution. For example, mass/volume percent is the unit of measurement for intravenous (IV) solutions.

- **Molarity** is a measure of number of moles per liter of solution. A molar solution of glucose is made by placing 180.10 grams (its molecular mass) of glucose into a container and adding enough water until it measures 1 liter. (Both moles and molecular mass are described shortly.) **Molality** is the moles per kilogram of solvent. A solution of one molality is made by placing 180.10 grams of glucose into a container and adding 1 kilogram of water. Molarity and molality may be used interchangeably, subject to this caveat: The two values are the closest when the measurements are taken at 4°C. At this temperature, 1 liter of water is at its most dense, and its mass is exactly equal to 1 kilogram of water.

---

**INTEGRATE**

**CONCEPT CONNECTION**

Blood exhibits all three types of mixtures: suspension, colloid, and solution. Blood is a suspension of formed elements that includes erythrocytes (red blood cells), leukocytes (white blood cells), and platelets within plasma (see section 18.1c). If blood is withdrawn from the body, the formed elements (red blood cells), leukocytes (white blood cells), and platelets within plasma of formed elements that includes erythrocytes (red blood cells), leukocytes (white blood cells), and platelets within plasma form a suspension.

Breast milk is an example of an emulsion in the body. Emulsions are classified as a specific type of colloid.
Molarity alters with changes in temperature (and to a limited degree with changes in pressure). When water temperature increases above 4°C, the solution expands, and molarity (moles per liter of solution) decreases slightly because it is based on volume (liter) of solution. In contrast, molality (moles per kilogram of solvent) does not alter with changes in temperature because it is based on mass (kilograms) of solvent. Consequently, molality is the more accurate of the two values. However, molality is more difficult to measure in the human body; thus, molarity—the slightly less accurate unit of concentration—is more often used.

**Osmoles, Osmolarity, and Osmolality**

Another means of expressing concentration is with osmoles (osm), which reflect whether a substance either dissolves, or dissolves and dissociates, when placed into a solution (i.e., whether it is a nonelectrolyte or an electrolyte). It is the unit of measurement for the number of particles in solution. The term osmole generally is used to reflect the extent a solution is able to alter water movement through osmosis (a concept described in section 4.3b). If a solute dissolves but does not dissociate, as occurs when glucose, amino acids, or proteins are placed in water, then the osmolarity = 1 osmole (osm). However, if the solute both dissolves and dissociates, as occurs with both NaCl and CaCl₂, then there is a change in the number of particles after the solute is in solution. A 1-molar (1 M) solution of NaCl dissociates in solution to form both 1 M Na⁺ and 1 M Cl⁻. The osmoles of 1 M of NaCl solution = 2 osm. What would you predict for the osmoles of CaCl₂? Each molecule of CaCl₂ dissolves into three particles: 1 Ca²⁺ and 2 Cl⁻; thus, 1 M CaCl₂ = 3 osm.

Osmoles can be expressed as either osmolarity or osmolality. **Osmolarity** is the number of particles in a 1-liter solution, whereas **osmolality** is the number of particles in 1 kilogram of water. Osmolality more accurately reflects the osmotic movement of water (see section 4.3b) in the body, but it is difficult to measure. Osmolarity is a close approximation to osmolality. Although osmolality is less accurate, it is often the preferred unit of measurement for the same reason that molarity is used over molality.

The range of values associated with the body is generally much smaller than osmoles and given as milliosmoles (mOsm). Note that 1 osm = 1000 mOsm. Thus, normal blood serum may be expressed as either 275 to 295 mOsm per liter or 275 to 295 mOsm per kilogram.

**Moles and Molecular Mass**

Notice in table 2.2 that molarity and molality are based on the number of particles in units called a mole. The specific value of 1 mole is 6.022 × 10²³ atoms, ions, or molecules. The number of particles may seem huge, but the particles themselves are minuscule.

A mole is the mass in grams that is equal to either the average atomic mass of an element or the molecular mass of a compound. For example, a mole of carbon is equal to 12.01 grams. Molecular mass is determined using the molecular formula and the average atomic mass for each element. To find a compound’s molecular mass, multiply the number of units of each element by its average atomic mass and add together the totals. The molecular mass of glucose (C₆H₁₂O₆), for example, is determined as follows:

- 6 carbon atoms × 12.01 amu = 72.06 amu
- 12 hydrogen atoms × 1.008 amu = 12.10 amu
- 6 oxygen atoms × 15.99 amu = 95.94 amu

Molecular mass = 180.10 amu

Thus, 1 mole of glucose (C₆H₁₂O₆) would be equal to 180.10 grams (with some variation due to isotopes).

**LEARNING STRATEGY**

You can use the acronym CHON P.S. to remember the four major classes of macromolecules—Carbohydrates, Lipids, Proteins, and Nucleic acids.

**2.7a General Characteristics**

**LEARNING OBJECTIVES**

39. Identify the six chemical elements that generally compose biological macromolecules.
40. Describe a hydrocarbon and its chemical properties, and explain and give examples of functional groups and their chemical properties.
41. Define the terms monomer, dimer, and polymer.
42. Describe the role of water in both dehydration and hydrolysis reactions in altering biological macromolecules.

**Biological macromolecules** are large organic molecules (see section 2.4) that are synthesized by the human body. These molecules always contain the elements carbon, hydrogen, and oxygen. Some biological macromolecules may also have one or more of the following: nitrogen (N), phosphorus (P), or sulfur (S). Notice that all of these elements (except hydrogen) are clustered on the right side of the periodic table (see figure 2.1a). (You can remember the six elements that compose biological macromolecules with the acronym CHON P.S.)

The carbon component of biological macromolecules may simply be an individual carbon atom or numerous carbon atoms arranged in a carbon skeleton as a chain, branch, or ring (see section 2.3b).

A single carbon atom or a carbon skeleton can have only hydrogen atoms attached. These molecules are more specifically called hydrocarbons. They are nonpolar molecules because they contain only C—C and C—H bonds (see section 2.3c). Consequently, hydrocarbons are hydrophobic and not soluble in water (see section 2.4c). Methane gas (CH₄) is an example of a hydrocarbon (see figure 2.8a).

Biological macromolecules are not simply hydrocarbons because these molecules also contain what are called functional groups. A functional group is two or more atoms that when present together on a molecule always exhibit the same specific chemical characteristics. Functional groups include hydroxyl (—OH), carboxyl or carboxylic acid (—COOH), amine (—NH₂), and phosphate (PO₄³⁻). Each of these functional groups is polar and able to form hydrogen bonds (see section 2.3d), increasing the molecule’s solubility in water (see section 2.4c). In addition, some functional groups may act as an acid and release H⁺, such as a carboxyl group, whereas others may act as a base.
by binding $H^+$, such as an amine group. Biological macromolecules typically have more than one functional group within them. These four important functional groups, their chemical properties, and the biological macromolecules that contain them are presented in table 2.3.

### Polymers
Many important biological macromolecules are polymers. Polymers are molecules that are made up of repeating subunits called monomers, and each monomer is either identical or similar in its chemical structure. Some important carbohydrates (e.g., glycogen, starch), nucleic acids, and proteins are polymers, whereas lipids are not. Carbohydrate polymers contain sugar monomers, nucleic acids have nucleotide monomers, and proteins are composed of amino acid monomers. Note that two monomers bonded together are called a dimer.

### Process of Dehydration Synthesis and Hydrolysis
Two processes are associated with both the synthesis and the breakdown of complex biological macromolecules: dehydration synthesis and hydrolysis, respectively. During the synthesis of complex molecules from simpler subunits, one specific subunit loses an $–H$, and the other subunit loses an $–OH$, to form a water molecule (which is released) as a new covalent bond is formed. A polymer is like a necklace. This necklace might be a pearl necklace, where every subunit is identical, or it might be a charm necklace, where every unit is slightly different. However, like the individual pieces in a necklace, the chemical subunits combine to produce the polymer that is the finished product.

### Table 2.3
**Functional Groups and Their Chemical Properties**

<table>
<thead>
<tr>
<th>Functional Group</th>
<th>Structural Formula</th>
<th>Properties</th>
<th>Representative Molecules</th>
<th>Structural Diagram of Example Molecule</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hydroxyl</td>
<td>$–OH$</td>
<td>• Polar</td>
<td>• Carbohydrates</td>
<td><img src="image" alt="Glucose" /></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Forms hydrogen bonds</td>
<td>• Proteins</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Increases molecules’ solubility in water</td>
<td>• Nucleic acids</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Acts as a base</td>
<td>• Lipids</td>
<td></td>
</tr>
<tr>
<td>Carboxyl (carboxylic acid)</td>
<td>$–COOH$</td>
<td>• Polar</td>
<td>• Proteins</td>
<td><img src="image" alt="Fatty acid" /></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Forms hydrogen bonds</td>
<td>• Lipids</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Increases molecules’ solubility in water</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Acts as an acid</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Amine</td>
<td>$–NH_2$</td>
<td>• Polar</td>
<td>• Proteins</td>
<td><img src="image" alt="Alanine" /></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Forms hydrogen bonds</td>
<td>• Nucleic acids</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Increases molecules’ solubility in water</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Acts as a base</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Phosphate</td>
<td>$–PO_4$</td>
<td>• Polar</td>
<td>• Nucleic acids</td>
<td><img src="image" alt="Adenosine triphosphate" /></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Forms phosphodiester bonds</td>
<td>• Phospholipids</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Acts as an acid (shown here with hydrogens released)</td>
<td>• ATP</td>
<td></td>
</tr>
</tbody>
</table>
produced. This type of reaction is called dehydration (de = away, hydro = water) synthesis or condensation because the equivalent of a water molecule is “lost” from the original structures (figure 2.17).

During the breakdown of complex molecules, \( \text{H}_2\text{O} \) molecules are split. An \(-\text{H}\) is added to one subunit, and an \(-\text{OH}\) is added to another subunit in the complex molecule, and the chemical bond is broken between them. Because the equivalent of water is added to break a bond within the molecule, this process is referred to as hydrolysis (hi-drol’i-sis; lysis = destruction) or a hydrolysis reaction. We will see examples of both of these types of reactions in the following sections on the specific classes of biological macromolecules.

**Figure 2.17 Dehydration Synthesis and Hydrolysis.** (a) Dehydration synthesis involves the loss of a water molecule from simpler components as they are formed into a complex molecule. (b) Hydrolysis occurs with the addition of a water molecule to a complex molecule as it is digested into simpler components.

**WHAT DID YOU LEARN?**

27 Using a different color than you did for highlighting the common ions on the periodic table, highlight the six common elements that form biological macromolecules. Which element both (a) forms a common ion and (b) is a common element in biological macromolecules?

28 What functional groups may act as an acid?

29 What defines a polymer? List the three biological macromolecules that are polymers and the monomers that compose them.

### 2.7b Lipids

**LEARNING OBJECTIVES**

43. Describe the general characteristics of a lipid.

44. Identify the four types of lipids and their physiologic roles.

Lipids are a very diverse group of fatty, water-insoluble (hydrophobic) molecules that function as stored energy, components of cellular membranes, and hormones. Triglycerides (neutral fats), phospholipids, steroids, and eicosanoids are the four primary classes of lipids. They are the only category of biological macromolecules that are not polymers because they are not formed from repeating monomers. Lipids are summarized in table 2.4.

**Triglycerides: Energy Storage**

Triglycerides (tri-glis’ér-idz; tri = three), or triacylglycerols, are the most common form of lipids in living things. They are used for long-term energy storage in adipose connective tissue (see section 5.2) and for structural support, cushioning, and insulation of the body. Adipose connective tissue deep to the skin in the abdomen, for example, serves as long-term energy storage and insulates the abdomen against heat loss. Adipose connective tissue posterior to the eye cushions the eye within the eye’s bony orbit (see section 16.4a).
Triglycerides are formed from a glycerol molecule and three fatty acids. Glycerol is a three-carbon molecule with a hydroxyl functional group attached to each carbon. A fatty acid is composed of a long chain of hydrocarbons with a carboxylic acid functional group on one end. Triglyceride molecules form by the process of dehydration synthesis, during which the equivalent of a water molecule is lost for each fatty acid added to the glycerol: an —H from the glycerol and an —OH from the fatty acid (figure 2.18).

Fatty acids may vary in length—commonly ranging in even numbers from 14 to 20 carbons—and may differ in the number and position of double bonds between the carbons in the chain. The fatty acid is saturated if it lacks double bonds—that is, every carbon has the maximum number of hydrogen atoms bound to it. An unsaturated fatty acid has one double bond, and a polyunsaturated fatty acid has two or more double bonds.

Adipose connective tissue is used to store triglycerides. When conditions of excess nutrients exist, adipose connective tissue binds fatty acids to glycerol to form triglycerides in a dehydration synthesis process called lipogenesis (li-p'o-jen'e-sis; lipos = fat, genesis = production). Adipose connective tissue breaks down triglycerides and releases the products into the blood when nutrients are needed. This process is a hydrolysis reaction called lipolysis (li-pol'i-sis).

Table 2.4 Major Classes of Lipids

<table>
<thead>
<tr>
<th>Class</th>
<th>Structure</th>
<th>Description</th>
<th>Function</th>
</tr>
</thead>
<tbody>
<tr>
<td>Triglycerides</td>
<td><img src="image" alt="Glycerol and Fatty Acids" /></td>
<td>Composed of glycerol and three fatty acids</td>
<td>Long-term energy storage in adipose connective tissue</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Fatty acids may be saturated or unsaturated</td>
<td>Structural support, cushioning, and insulation of the body</td>
</tr>
<tr>
<td>Phospholipids</td>
<td><img src="image" alt="Phospholipid Structure" /></td>
<td>Composed of glycerol, two fatty acids, a phosphate, and various organic groups</td>
<td>Major component of membranes, including the plasma membrane, which forms the chemical barrier between the inside and outside of a cell</td>
</tr>
<tr>
<td>Steroids (include cholesterol, steroid hormones, and bile salts)</td>
<td><img src="image" alt="Steroid Molecule" /></td>
<td>Four rings composed predominantly of hydrocarbons that differ in the side chains extending from the rings</td>
<td>Cholesterol is a component of plasma membranes and is the precursor molecule for synthesis of other steroids. Steroid hormones are regulatory molecules released by certain endocrine glands. Bile salts facilitate micelle formation in the digestive tract.</td>
</tr>
<tr>
<td>Eicosanoids (include prostaglandins, prostacyclins, thromboxanes, and leukotrienes)</td>
<td><img src="image" alt="Eicosanoid Molecule" /></td>
<td>Modified 20-carbon fatty acids</td>
<td>Locally acting signaling molecules associated with all body systems; have primary functions in both the inflammatory response of the immune system and communication within the nervous system</td>
</tr>
</tbody>
</table>

1. Glycolipids and fat-soluble vitamins are also types of lipids (not shown here).
were previously described as amphipathic molecules that form chemical barriers of cell membranes, including plasma membranes that form the outer barrier of a cell (see figure 2.13c). The chemical structure of a phospholipid is similar to a triglyceride, except that one end of the glycerol has a polar phosphate group with various organic groups (choline, ethanolamine, or the amino acid serine) attached to it instead of a fatty acid (table 2.4). The glycerol, phosphate, and organic groups are polar and form the water-soluble hydrophilic part of the molecule referred to as the hydrophilic (polar) head. The two fatty acid molecules attached to the glycerol form a water-insoluble hydrophobic end called the hydrophobic (nonpolar) tails. Phospholipid molecules within a plasma membrane are conventionally depicted with an icon of what appears like a balloon with two tails (see figure 2.13c).

**Figure 2.18 Triglycerides.** (a) A glycerol and three fatty acid molecules. The middle fatty acid is a saturated fatty acid, whereas the other two are unsaturated fatty acids. (b) A triglyceride molecule. Lipogenesis occurs through a dehydration synthesis reaction that involves the removal of a water molecule between each fatty acid and a glycerol. Lipolysis is a hydrolysis reaction that splits the glycerol and three fatty acids by the addition of water at each of the fatty acids.

**Phospholipids: Form Cell Membranes**

Phospholipids were previously described as amphipathic molecules that form chemical barriers of cell membranes, including plasma membranes that form the outer barrier of a cell (see figure 2.13c). The chemical structure of a phospholipid is similar to a triglyceride, except that one end of the glycerol has a polar phosphate group with various organic groups (choline, ethanolamine, or the amino acid serine) attached to it instead of a fatty acid (table 2.4). The glycerol, phosphate, and organic groups are polar and form the water-soluble hydrophilic part of the molecule referred to as the hydrophilic (polar) head. The two fatty acid molecules attached to the glycerol form a water-insoluble hydrophobic end called the hydrophobic (nonpolar) tails. Phospholipid molecules within a plasma membrane are conventionally depicted with an icon of what appears like a balloon with two tails (see figure 2.13c).

**Steroids: Ringed Structures, Including Some Hormones**

Steroids are composed predominantly of hydrocarbons arranged in a distinct multiringed structure. A steroid has four attached carbon rings; three rings have six carbon atoms and one ring has five carbon atoms. Steroids differ in the side chains extending from their rings. Steroids include cholesterol, steroid hormones (e.g., testosterone, estrogen), and bile salts. Cholesterol is a component of animal plasma membranes as well as the precursor used to synthesize other steroids. Cholesterol is synthesized in the liver from fatty acids and may be obtained from eating animal products such as meat, eggs, and milk.

Chapter Two  
Atoms, Ions, and Molecules  
55
Glycogen is formed from glucose molecules through glycogenesis, whereas glycogen is digested into glucose through glycogenolysis.

**Glucose and Glycogen**

Glucose is a six-carbon (hexose) carbohydrate that is the most common monosaccharide. It is shown here (and throughout the text) in the ring form (figure 2.19). Glucose is crucial to life processes because it is the primary nutrient supplying energy to cells. In fact, the brain and other nervous tissue use glucose almost exclusively as their nutrient fuel molecule. The concentration of blood glucose must be carefully maintained by homeostasis (see section 1.6) to ensure a continual, adequate energy supply for cellular activities. One way the body ensures its supply is to store excess glucose immediately following a meal. Liver and skeletal muscle tissue absorb the excess glucose—and then bind the glucose monomers together to form a polysaccharide called glycogen by a process called **glycogenesis** (gliˈkō-jenˈĕ-sis). The glycogen polymer is shown in figure 2.19b—although only several glucose molecules are shown, glycogen may contain thousands of glucose monomers.

When blood glucose levels drop between meals, the liver hydrolyzes some of the glycogen into glucose and releases it into the blood. This process is called **glycogenolysis** (gliˈkō-jĕ-nolˈĭ-sis). Thus, the liver serves the role of a “glucose bank” by storing glycogen, then breaking down glycogen as needed to release glucose (see section 17.10b). Nutrient storage and release are important in the endocrine regulation of nutrient blood levels of both triglycerides and glucose. Note: The liver can also form glucose from noncarbohydrate sources (e.g., fats, proteins) through a process called **gluconeogenesis**. See Clinical View 17.7: “The Stress Response (General Adaptation Syndrome).”

**Eicosanoids: Locally Acting Hormones**

Eicosanoids (iˈkō-sā-nōdz; eicosa = 20, eido = form) are modified 20-carbon fatty acids that are obtained from the phospholipids of plasma membranes, which form the barrier of cells. Four classes of eicosanoids are produced and include prostaglandins, prostaoyclins, thromboxanes, and leukotrienes. These are signaling molecules that act locally and are associated with all body systems: They have primary functions in the inflammatory response of the immune system and communication within the nervous system. The synthesis of eicosanoids is described in section 17.3b.

**Other Lipids**

Glycolipids are lipid molecules with an attached carbohydrate. These molecules are associated with plasma membranes and serve several roles, including cellular recognition to form tissues (see section 4.5a). Fat-soluble vitamins such as vitamins A, E, and K (see section 27.3a) are also lipids.

**2.7c Carbohydrates**

**LEARNING OBJECTIVES**

45. Describe the distinguishing characteristics of carbohydrates.
46. Explain the relationship between glucose and glycogen.
47. Name some other carbohydrates found in living systems.

The term carbohydrate means hydrated carbon. Nearly every carbon is hydrated with the equivalent of a water molecule—that is, both an —H and an —OH are usually attached to every carbon. The general chemical formula for carbohydrates is (CH₂O)n, where n indicates the number of carbon atoms that are in a molecule. The number of carbon atoms typically ranges from three to seven. The least complex carbohydrates are simple sugar monomers called monosaccharides. All monosaccharides have between three and seven carbon atoms. Carbohydrates that are dimers formed from two monosaccharides are disaccharides, and those with many monosaccharides are polysaccharides.
Other Types of Carbohydrates

Other hexose monosaccharides include galactose and fructose, which are glucose isomers, as described in section 2.3a (figure 2.20a). Some monosaccharides, such as ribose and deoxyribose, are composed of five carbons. These five-carbon monosaccharides are called pentose sugars. The pentose sugars ribose and deoxyribose are structural components of nucleic acids, which are discussed in the section 2.7d. The only structural difference between these pentose sugars is the lack of an oxygen atom on carbon two of the deoxyribose sugar.

Disaccharides (which you will recall are dimers composed of two monosaccharides bonded together) include: sucrose (table sugar), lactose (milk sugar), and maltose (malt sugar, which is found in sprouting grains). All three disaccharides contain a glucose monosaccharide bonded to a second hexose monosaccharide (figure 2.20b).

Polysaccharides (which you will recall are composed of three or more monosaccharides) include glycogen (figure 2.19b), which is the storage form of glucose within liver and muscle cells of animals. Polysaccharides in plants include starch and cellulose, which are also composed of repeating glucose monomers. Plant starch is a major nutritional source of glucose for humans. It is found in potatoes, grains, and many other plant foods. Glucose released from the breakdown of starch within the digestive tract is absorbed into the blood. Cellulose, a structural polysaccharide of plant cell walls, however, is a source of fiber (nondigestible substances). Humans cannot digest cellulose because of the unique chemical bonds between the glucose molecules. The breakdown of both disaccharides and polysaccharides is described in section 26.4a.

**WHAT DID YOU LEARN?**

32. What is the repeating monomer of glycogen? Where is glycogen stored in the body?
33. For each of the following, indicate if it is a monosaccharide, disaccharide, or polysaccharide: fructose, galactose, glucose, glycogen, lactose, maltose, starch, and sucrose.

**2.7d Nucleic Acids**

**LEARNING OBJECTIVES**

48. Describe the general structure of a nucleic acid.
49. Describe the structure of a nucleotide monomer.
50. Distinguish between DNA and RNA.
51. Name other important nucleotides.

Nucleic acids (figure 2.21c, d) are biological macromolecules within cells that store and transfer genetic, or hereditary, information. Originally discovered within the cell nucleus.
Figure 2.21 Nucleic Acids. (a) A general representation of a nucleotide monomer, which is composed of a pentose sugar (ribose or deoxyribose), a phosphate functional group, and a nitrogenous base. Nucleotides that contain ribose are ribonucleotides, and nucleotides that contain deoxyribose are deoxyribonucleotides. Note the numbering of the carbon atoms in the ribose/deoxyribose of a nucleotide monomer. (b) The five nitrogenous bases. (c) RNA is a single-stranded nucleic acid formed from repeating units of ribonucleotides linked together by phosphodiester bonds. Each ribonucleotide contains one of the nitrogenous bases uracil, guanine, adenine, or cytosine. (d) DNA is a double-stranded nucleic acid with each strand composed of repeating units of deoxyribonucleotides linked together by phosphodiester bonds. Each deoxyribonucleotide contains one of the nitrogenous bases thymine, guanine, adenine, or cytosine. Hydrogen bonds between complementary bases (T:A and C:G) hold the two strands together. Both RNA and DNA participate in protein formation.
(see section 4.7), nucleic acids ultimately determine the types of proteins synthesized within cells—a process described in detail in section 4.8.

The two classes of nucleic acid are deoxyribonucleic acid (DNA) and ribonucleic acid (RNA). Both DNA and RNA are polymers composed of nucleotide monomers. These monomers are linked together through covalent bonds between one nucleotide monomer and an adjacent nucleotide monomer. This covalent bond between the phosphate of one nucleotide and the sugar of the adjacent nucleotide is called a phosphodiester bond.

Nucleotide
A nucleotide has three components: a sugar, a phosphate functional group, and a nitrogenous base (figure 2.21a). The sugar is a five-carbon pentose sugar (deoxyribose for DNA and ribose for RNA). A phosphate functional group is attached at carbon number five; a nitrogenous base is attached to the same sugar but at carbon number one. A nitrogenous base has either a single-ring or a double-ring structure that contains both carbon and nitrogen within the ring.

Five different nitrogenous bases commonly occur in nucleic acids (figure 2.21b). Single-ring nitrogenous bases are called pyrimidines, and they include cytosine (C), uracil (U), and thymine (T). (You can remember these bases with the acronym CUT.) Double-ring nitrogenous bases are called purines, which include adenine (A) and guanine (G). The nitrogenous bases within either group—pyrimidines or purines—differ in the functional groups attached to the ring.

Deoxyribonucleic Acid (DNA)
Deoxyribonucleic acid (DNA) is a double-stranded nucleic acid (figure 2.21d); it can be found as a component of chromosomes within the nucleus (see section 4.7). A small, circular strand of DNA is also within mitochondria (see sections 3.4c and 4.6a). The nucleotides that form DNA have a deoxyribose sugar, a phosphate, and one of four nitrogenous bases: adenine, guanine, cytosine, or thymine. Notice that DNA does not contain uracil. The double strands of nucleic acid are held together by hydrogen bonds formed between complementary nitrogenous bases: thymine with adenine and guanine with cytosine.

Ribonucleic Acid (RNA)
Ribonucleic acid (RNA) is a single-stranded nucleic acid located both within the cell nucleus and within the cytoplasm (section 4.1c) of the cell (figure 2.21c). The nucleotides that are part of RNA molecules are composed of the sugar ribose, a phosphate, and one of four nitrogenous bases: adenine, guanine, cytosine, or uracil. RNA does not contain thymine. Table 2.5 compares the chemical structural differences between RNA and DNA.

<table>
<thead>
<tr>
<th>Table 2.5 Differences Between RNA and DNA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Characteristic</td>
</tr>
<tr>
<td>Number of strands</td>
</tr>
<tr>
<td>Sugar</td>
</tr>
<tr>
<td>Nitrogenous base</td>
</tr>
</tbody>
</table>

Figure 2.22 ATP. Adenosine triphosphate (ATP) is composed of the sugar ribose and the nitrogenous base adenine, which together are referred to as adenosine. Three phosphates attached to adenosine form adenosine triphosphate.

Other Important Nucleotides and Nucleotide-Containing Molecules
An important nucleotide is adenosine triphosphate (a-den’o-sên tri-fos’ät), or ATP. It is composed of the nitrogenous base adenine, a ribose sugar, and three phosphate groups covalently linked (figure 2.22). ATP is the central molecule in the transfer of chemical energy within cells. Biologists often refer to this molecule as the “energy currency” of a cell. The covalent phosphate bond linkages between the last two phosphate groups are unique, energy-rich bonds. ATP is produced continuously and only stored in limited amounts within cells (e.g., muscle cell ATP stores last for approximately 4–6 seconds during high intensity exercise). When ATP molecules are split into adenosine diphosphate (ADP) and phosphate, energy is released. This energy is then used by the cell (e.g., muscle contraction).

Two important nucleotide-containing molecules are nicotinamide adenine dinucleotide (NAD⁺) and flavin adenine dinucleotide (FAD). Both molecules participate in the production of ATP that occurs in cellular mitochondria. (ATP, NAD⁺, and FAD are discussed in more detail in chapter 3.)

WHAT DID YOU LEARN?

33. What is the general function of nucleic acids?
36. What are the structural differences between RNA and DNA?

2.7e Proteins

LEARNING OBJECTIVES

52. List the general functions of proteins.
53. Describe the general structure of amino acids and proteins.

Scientists estimate that approximately 50,000 different proteins are synthesized (produced) by cells, and that proteins account for about one-fifth of the human body by weight. Following their synthesis, proteins may function within a cell, a plasma membrane, or blood plasma and other body fluids. Proteins serve a vast array of functions. For example, proteins

- Serve as catalysts (enzymes) in most metabolic reactions of the body (see section 3.3)
• Act in defense, which occurs, for example, when immunoglobulins (antibodies) attach to foreign substances for their elimination (see section 22.8)
• Aid in transport, as when hemoglobin molecules transport respiratory gases within the blood (see section 18.3b)
• Contribute to structural support, such as collagen, a major component of ligaments and tendons (see section 5.2d)
• Cause movement, when myosin and actin proteins interact during contraction of muscle tissue (see section 10.2b)
• Perform regulation, as occurs when insulin helps control blood glucose levels (see section 17.10.b)
• Provide storage, such as ferritin, which stores iron in liver cells (see section 18.3b)

Table 2.6 organizes the functions of proteins into several categories providing the general function, class of protein, and examples for each.

### General Protein Structure

Proteins are polymers composed of one or more linear strands of amino acid monomers that may number in the thousands (figure 2.23). Twenty standard amino acids are normally found in the proteins of living organisms. Each amino acid has both an amine (—NH₂)
functional group and a carboxylic acid (—COOH) functional group (see table 2.3). Both functional groups are covalently linked to the same carbon atom, which accounts for the general name “amino acid” for these monomers. The other two covalent bonds to this carbon are a hydrogen (—H) and different side-chain structures that are simply referred to as the R (Remainder) group. The R groups distinguish different amino acids from one another. Properties of the R groups form the basis for classifying amino acids (described in section 2.8a).

Amino acids are linked covalently by peptide bonds that form during dehydration synthesis reactions between the amine functional group of one amino acid and the carboxylic acid functional group of a second amino acid. An —H is lost from the amine group and an —OH from the carboxylic acid of another amino acid. The ends of a protein are distinguished as the N-terminal end, which has a free amine group, and the C-terminal end, which has a free carboxyl group.

A strand of amino acids that includes between 3 and 20 amino acids is termed an oligopeptide, whereas a polypeptide has a strand composed of between 21 and 199 amino acids. If more than 200 amino acids are linked, the structure is called a protein. (Note that the specific numbers of amino acids for each category of protein are debated by protein chemist experts.) In this text, we use the general term protein to apply to all three types of these structures.

Proteins with carbohydrate attached are called glycoproteins. ABO blood groups are based on structural differences in glycoproteins within the plasma membrane of erythrocytes (see section 18.3b). The glyocalyx of cells (see section 4.2b), which is composed of both glycoproteins and glycolipids, is used to identify the cell as self (see section 22.4a).

Lipids, carbohydrates, nucleic acids, and proteins are four major classes of biological macromolecules that compose the human body. They are summarized in figure 2.24.

Figure 2.23 Proteins. (a) Amino acids are the monomers of proteins. (b) Dehydration synthesis reaction occurs as a hydroxyl functional group is removed from the carboxylic acid of one amino acid and a hydrogen atom is removed from the amine group of another amino acid to form a peptide bond between two amino acids. A molecule of water is released during the process. (c) The polymer protein is composed of repeating amino acid monomers that are held together by peptide bonds.

INTEGRATE

CONCEPT CONNECTION

The amine group of an amino acid can be removed from the amino acid by a process known as deamination. Nitrogen in the amine group is converted into urea, one form of nitrogenous waste, through a metabolic process called the urea cycle. Other types of nitrogenous wastes include uric acid, a waste product of the breakdown of nucleic acid, and creatinine, a waste product of muscle tissue breakdown. Nitrogenous waste is eliminated from the body by the urinary system (see section 24.6e).

WHAT DID YOU LEARN?

36 What are the monomers of proteins and the name of the bond between them?

37 What are the names of structures that contain 2 amino acids, 3 to 20 amino acids, 21 to 199 amino acids, and 200 or more amino acids? What general term is used to refer to any of these structures, except a structure composed of 2 amino acids?
**Figure 2.24 Biological Macromolecules.**
The four primary biological macromolecules include (a) lipids, (b) carbohydrates, (c) nucleic acids, and (d) proteins.
The liver stores glucose as glycogen and breaks down glycogen to glucose as needed.

ATP is a nucleotide that is the central molecule in the transfer of chemical energy within cells. It is often referred to as the "energy currency" of a cell.

Proteins are macromolecules made of one or more linear strands of amino acid monomers. Proteins, once synthesized, function within the cell, plasma membrane, blood plasma, and in other body fluids.

Amino acids are the building blocks that form proteins. There are 20 standard amino acids: they differ at their R groups.
2.8 Protein Structure

Here we describe protein structure in more depth, including categories of amino acids, amino acid sequence, and three-dimensional protein shape. We also discuss how a protein can lose its three-dimensional shape and the consequences of this occurrence.

2.8a Categories of Amino Acids

LEARNING OBJECTIVES

54. Name the categories of amino acids.
55. Distinguish between nonpolar, polar, and charged amino acids.
56. Give examples of amino acids with special characteristics.

Amino acids are organized into groups based on the chemical characteristics of their R group (see section 2.7e). Each amino acid is categorized as nonpolar, polar, charged, and those having special functions (figure 2.25).

- **Nonpolar amino acids** contain R groups with either hydrogen (glycine) or hydrocarbons (alanine, valine, isoleucine, leucine, phenylalanine, and tryptophan). They tend to group with other nonpolar amino acids by hydrophobic interactions within the body’s aqueous environment (see section 2.3c).

- **Polar amino acids** contain R groups with elements in addition to carbon and hydrogen (i.e., O, N, S) (serine, threonine, asparagine, glutamine, and tyrosine). They form interactions with other polar amino acids and with water molecules.

- **Charged amino acids** can have either a negative charge or a positive charge. Those with a negatively charged R group include glutamate and aspartate, and those with a positively charged R group include histidine, lysine, and arginine. An ionic bond (electrostatic interaction) can form between an R group with a negative charge and an R group with a positive charge. Groups of amino acids that are either polar or charged are hydrophilic, and their presence increases the solubility of the protein in water.

- **Amino acids with special functions**—three amino acids have unique characteristics. The R group in proline attaches to the amine group, forming a ring. Proline amino acids cause a bend in the protein chain. The sulfhydryl (—S—H) functional groups of two cysteine amino acids form disulfide bonds. These covalent bonds are significant in stabilizing the folding of a protein (described in section 2.8b). Methionine is always the first amino acid positioned when a protein is synthesized (see section 4.8b), and it may or may not be removed later.

WHAT DID YOU LEARN?

38 Why is the amino acid leucine (figure 2.25) classified as a nonpolar amino acid?

INTEGRATE

LEARNING STRATEGY

The formation of proteins from amino acids is similar to the building of words from the letters of an alphabet. Just as English, Spanish, and many other languages are built upon words formed by stringing letters together, the “language of proteins” is built upon the stringing of amino acids together.
### Amino Acids

Amino acids are categorized based on the chemical properties of the R groups. The categories include nonpolar, polar, charged, and those with special functions.

#### Nonpolar
- **Glycine (Gly)**
- **Valine (Val)**
- **Isoleucine (Ile)**
- **Leucine (Leu)**
- **Phenylalanine (Phe)**
- **Tryptophan (Trp)**

#### Polar
- **Serine (Ser)**
- **Threonine (Thr)**
- **Asparagine (Asn)**
- **Glutamine (Gln)**
- **Tyrosine (Tyr)**

#### Charged
- **Glutamate (Glu)**
- **Aspartate (Asp)**
- **Histidine (His)**
- **Lysine (Lys)**
- **Arginine (Arg)**

#### Special Functions
- **Proline (Pro)**: Allows bends in protein chain
- **Cysteine (Cys)**: Forms disulfide bond
- **Methionine (Met)**: Always the first amino acid in a protein sequence (may be removed following synthesis of protein)

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**Figure 2.25 Amino Acids.** Amino acids are categorized based on the chemical properties of the R groups. The categories include nonpolar, polar, charged, and those with special functions.
We describe a protein as being composed of a linear sequence of amino acids that are bonded together through covalent peptide bonds. This sequence is called its primary structure (Figure 2.26a). The protein then folds to form into its three-dimensional shape, or conformation. Protein conformation is crucial for its proper function.

The conformational structure of proteins has increasingly complex hierarchies, or levels, of organization beyond a protein’s primary structure, including secondary, tertiary, and perhaps quaternary structural levels. These more complex structural organizations are dependent upon intramolecular attractions between the amino acids in the linear sequence for the proper folding and maintaining of a protein’s conformation. The process of protein folding is assisted by specialized proteins called chaperones that “direct” the folding process.

The intramolecular interactions that contribute to the final conformation of a protein are as follows:

- The primary structure of a protein is forced into its initial shape as hydrophobic exclusion “tucks” amino acids with nonpolar R groups into a more central location, limiting their contact with water.
Hydrogen bonds form between polar R groups, and between the amine and carboxylic acid functional groups of closely positioned amino acids.

- Electrostatic interactions (ionic bonds) form between negatively charged and positively charged R groups.
- Disulfide bonds form between the sulfhydryl (—S—H) groups of two cysteine amino acids.

Higher levels of protein organization result from folding. The secondary structure is a pattern within a protein that may repeat several times. The two distinctive secondary structures are a spiral coil, called an alpha helix, and a planar pleat arrangement, called a beta sheet. These secondary structures confer unique characteristics on the regions of the protein where they occur. Alpha helix gives some elasticity to fibrous proteins that are located, for example, in skin or hair. In contrast, beta sheets give some degree of flexibility to many globular proteins (e.g., enzymes).

Tertiary structure is the final three-dimensional shape exhibited by one completed protein chain. Two categories of proteins—either globular or fibrous—are distinguished by their molecular shape. Globular proteins fold into a compact, often nearly spherical shape such as enzymes (see figure 3.9), antibodies (see figure 22.18), and some hormones. In comparison, fibrous proteins are extended linear molecules that are constituents of ligaments and tendons (see figure in table 5.6) and contractile proteins within muscle cells (see figure in table 5.10).

The quaternary structure of a protein is present only in those proteins with two or more protein strands. The protein hemoglobin is an example because it is composed of four protein chains (see section 18.3b). Each of these chains has its own primary, secondary, and tertiary structures. Only when the four separate strands associate through intermolecular attractions to form the quaternary structure does the biological molecule of hemoglobin become active. Therefore, hemoglobin is functional only when all four polypeptide chains are present in the correct association.

The normal function of a protein may also require a prosthetic group. This is a nonprotein structure covalently bonded to the protein. The lipid heme group in the hemoglobin protein is an example of a prosthetic group (see figure 18.6).

Figure 2.27 Denaturation. Proteins denature in response to (a) increased H⁺ (decrease in pH) as H⁺ is added to the negatively charged R group or (b) decreased H⁺ (increase in pH) as H⁺ is removed from the positively charged R group.

WHAT DO YOU THINK?

5. Why might proteins be rendered nonfunctional by exposure to high temperatures?

The biological activity of a protein is usually disturbed or terminated when its conformation (or structure) is changed. This change in protein conformation is called denaturation (dé-na’tyu-ra’shun). The tertiary structure of the protein is disrupted if the protein is heated or chemically altered. Usually, the loss of biological activity cannot be reversed. Denaturation may occur as a consequence of increased temperature because this increase weakens the intramolecular interactions that hold the protein in its three-dimensional shape. The risks of an elevated body temperature and denaturation are discussed in the section on the risks of a high fever (see section 22.3e).

Alternatively, denaturation may take place in response to changes in pH. Changes in pH can denature proteins because the alteration of hydrogen ion concentration [H⁺] interferes with electrostatic interactions (and other intramolecular bonds) that hold the protein in its three-dimensional shape. If pH decreases as a consequence of an increase in [H⁺], the excess H⁺ binds to negatively charged R groups, as shown in figure 2.27a. The electrostatic interaction is disrupted because an H⁺ attaches to the negatively charged R group, with an accompanying loss of the negative charge on the R group that previously participated in the electrostatic interaction. If pH increases, reflecting a decrease in [H⁺], the electrostatic interaction is disrupted because the H⁺ that previously participated in the electrostatic interaction has been removed, as shown in figure 2.27b. Changes in blood pH out of the normal homeostatic range can be lethal because of the potential disruption of protein structure and function (acid-base balance is described in section 25.5). Proteins are essential in the normal processes of the body, and the structure and function of many different proteins will be discussed throughout this text.

WHAT DID YOU LEARN?

38. What distinguishes the tertiary and quaternary levels of organization of a protein?

39. What happens to a protein when it denatures? How does a protein denature when it is exposed to higher than normal H⁺ concentration?
## CHAPTER SUMMARY

- Atoms, ions, and molecules form the human body at its simplest level.

### 2.1 Atomic Structure

- Diagramming atomic structure from the periodic table provides the foundation to understand isotopes, ions, and molecules.

#### 2.1a Matter, Atoms, Elements, and the Periodic Table

- An atom is the smallest particle that exhibits the chemical properties of an element.
- Atomic structure—composed of protons, neutrons, and electrons—can be drawn from the information obtained from the periodic table.

#### 2.1b Isotopes

- Atoms having the same number of protons and electrons—but differing in the number of neutrons and thus atomic mass—are called isotopes.
- Unstable isotopes resulting from an excess number of neutrons are called radioisotopes.

#### 2.1c Chemical Stability and the Octet Rule

- Atoms with a complete outer shell of eight electrons are chemically stable. Atoms bond to reach chemical stability.

### 2.2 Ions and Ionic Compounds

- Chemical compounds, which include ionic compounds and molecular compounds, are stable associations between two or more elements combined in a fixed ratio.

#### 2.2a Ions

- An ion is a charged atom that is either positively charged or negatively charged as a result of having lost or gained electrons, respectively.
- Common ions of the human body include sodium (Na⁺), potassium (K⁺), calcium (Ca²⁺), magnesium (Mg²⁺), hydrogen (H⁺), chloride (Cl⁻), bicarbonate (HCO₃⁻), and phosphate (PO₄³⁻).
- Cations are positively charged ions that are formed by the loss of electron(s) from atoms with one, two, or three electrons in their outer shell, or elements in columns IA, IIA, or IIIA in the periodic table, respectively.
- Anions are negatively charged ions that are formed by the gain of electron(s) by atoms typically with five, six, or seven electrons in the outer shell, or elements in columns VA, VIA, or VIIA in the periodic table, respectively.

#### 2.2b Ionic Bonds

- Ionic bonds are electrostatic attractions between positively charged cations and negatively charged anions that hold the ions in a lattice crystal (or salt).

### 2.3 Covalent Bonding, Molecules, and Molecular Compounds

- Molecules formed with two or more atoms of the same or different elements are covalently bonded together.
- Molecular compounds are formed by two different elements covalently bonded together.

#### 2.3a Chemical Formulas: Molecular and Structural

- The molecular formula is the number and kinds of atoms within a molecule.
- The structural formula demonstrates both the number and kind of atoms within a molecule and their arrangement within the molecule—and can be used to distinguish isomers.
- Isomers have the same number and kind of atoms, or molecular formula, but differ in their arrangement in space.

#### 2.3b Covalent Bonds

- Covalent bonds are formed between two atoms in which both atoms have four, five, six, or seven electrons in their outer shell (as well as hydrogen atoms, which require only two electrons to have a complete valence shell).
- A single covalent bond is the typical covalent bond and involves the sharing of a pair of electrons. A double or triple covalent bond can be formed if both atoms, respectively, need at least two or three electrons to become stable.
- Nonpolar covalent bonds occur when the two atoms share electrons equally, as occurs between atoms of the same element, or almost equally, as occurs when hydrogen bonds to carbon. Polar covalent bonds occur between atoms of different elements that share electrons unequally.

#### 2.3c Nonpolar, Polar, and Amphipathic Molecules

- Nonpolar molecules generally include those molecules composed predominantly of nonpolar bonds between the atoms.
- Polar molecules generally include those molecules composed of relatively more polar bonds between the atoms.
- Amphipathic molecules are large molecules that have both nonpolar and polar regions.

#### 2.3d Intermolecular Attractions

- Intermolecular attractions occur between molecules, and intramolecular attractions occur between regions within large molecules.
- Hydrogen bonds occur between a partially positively charged hydrogen atom and a partially negatively charged atom of polar molecules.
- Intermolecular attractions between nonpolar molecules occur with a temporary unequal distribution of electrons. Hydrophobic interactions occur when nonpolar molecules are placed in water.

### 2.4 Molecular Structure and Properties of Water

- Water makes up on average about two-thirds of the human body by weight.

#### 2.4a Molecular Structure of Water

- Water is a polar molecule that can form four hydrogen bonds with other water molecules.

#### 2.4b Properties of Water

- Water is present in three phases (water vapor, liquid, and ice), depending upon the temperature.
- Cohesion is attraction between water molecules, surface tension is the inward pull of water molecules at the surface, and adhesion is the attraction of water molecules for substances other than water.
- Water’s high specific heat and high heat of vaporization help maintain a normal body temperature.
### 2.4c Water as the Universal Solvent
- Polar organic molecules, such as glucose, dissolve and remain intact within water and are nonelectrolytes.
- Salts, acids, and bases dissolve and dissociate in water and are electrolytes.
- Nonpolar substances do not form hydrogen bonds with water and are separated from water molecules by hydrophobic exclusion.
- The polar portion of an amphipathic molecule dissolves in water, and the nonpolar portion does not. Amphipathic molecules form chemical barriers within the body, including membranes and micelles.

### 2.5a Water: A Neutral Solvent
- Water has a neutral pH, and its pH is changed by the addition of either an acid or a base.

### 2.5b Acids and Bases
- Acids increase and bases decrease the hydrogen ion concentration in solution.

### 2.5c pH, Neutralization, and the Action of Buffers
- pH is a measure of hydrogen ion concentration in solution. pH values are inversely related to hydrogen ion concentration.
- Neutralization is the changing of an acidic or basic solution to neutral.
- A buffer helps prevent pH changes by "absorbing" and "releasing" hydrogen ions.

### 2.6 Water Mixtures
- Mixtures are formed from the mixing of two or more substances.
- Mixtures are not chemically changed, and the components can be separated by physical means.

### 2.6a Categories of Water Mixtures
- Types of water mixtures include suspensions, colloids, and solutions.
- Emulsions are a type of colloid formed by water and a liquid nonpolar substance when it is agitated.

### 2.6b Expressions of Solution Concentration
- The concentration of solutions can be expressed in several ways, including mass/volume, mass/volume percent, molarity, and molality.
- Osmoles, osmolarity, and osmolality reflect number of particles in solution and are relevant in the movement of water by osmosis.

### 2.7 Biological Macromolecules
- The four major classes of organic biological macromolecules are lipids, carbohydrates, nucleic acids, and proteins.

### 2.7a General Characteristics
- Biological macromolecules have diverse carbon skeletons with varying amounts of hydrogen and functional groups attached to them.
- Three of the four major classes of biological macromolecules—including complex carbohydrates, nucleic acids, and proteins—exist as polymers, chemical structures that are composed of repeating identical or similar monomers. Lipids are not polymers.
- All of the classes of biological macromolecules are formed by dehydration synthesis reactions and digested through hydrolysis.

### 2.7b Lipids
- Lipids are a very diverse group of fattylike, water-insoluble molecules that include triglycerides, phospholipids, steroids, and eicosanoids.
- Triglycerides are composed of glycerol and three fatty acids and are generally used for long-term energy storage.
- Phospholipids are made up of glycerol, two fatty acids, and a phosphate functional group with various organic groups attached to it. Phospholipids are amphipathic molecules containing a polar head and two nonpolar tails that form membranes.
- Steroids are distinct multiringed structures formed predominantly of hydrocarbons and include cholesterol, steroid hormones, and bile salts.
- Eicosanoids are modified 20-carbon fatty acids that are synthesized as needed from arachidonic acid, a common component of plasma membranes. Eicosanoids act locally.
- Other lipids include glycolipids and fat-soluble vitamins.

### 2.7c Carbohydrates
- Carbohydrates are molecules with the following chemical formula: (CH₂O)n. Carbohydrates exist in increasing levels of complexity that include monosaccharides, disaccharides, and polysaccharides.
- Glucose is the most common monosaccharide in the human body and is used for energy. When in excess, glucose is stored as the polysaccharide called glycogen in liver and skeletal muscle tissue.
- Other types of carbohydrates include the monosaccharides galactose, fructose, ribose, and deoxyribose; the disaccharides sucrose, lactose, and maltose; and the polysaccharides starch and cellulose.

### 2.7d Nucleic Acids
- Nucleic acids include deoxyribonucleic acid (DNA) and ribonucleic acid (RNA), polymers formed from nucleotide monomers. These molecules ultimately determine the type of proteins synthesized by cells.
- Adenosine triphosphate (ATP) is a nucleotide that serves as the energy currency molecule of a cell.

### 2.7e Proteins
- Proteins serve many different functions in the body.
- Proteins are polymers that differ in the number and sequence of 20 different amino acid monomers arranged in a unique linear sequence.

(continued on next page)
2.8 Protein Structure
- The three-dimensional structure of proteins is dependent upon the linear sequence of its amino acids.

2.8a Categories of Amino Acids
- The 20 amino acids can be categorized based on the chemical composition of their R group as nonpolar, polar, charged, and those with special functions.

2.8b Amino Acid Sequence and Protein Conformation
- Protein organization includes the primary, secondary, and tertiary structures—as well as a quaternary structure if there are two or more protein chains. These levels of organization ultimately determine the structure and function of a protein.
- Denaturation usually results in the loss of biological activity of a protein in response to the change in its three-dimensional shape that may have occurred through an increase in temperature or a change in pH.

CHALLENGE YOURSELF

Do You Know the Basics?

1. Atoms composed of the same numbers of protons and electrons, but different numbers of neutrons, are called
   a. isomers.  
   b. ions.  
   c. isotopes.  
   d. organic atoms.
2. Substances that dissolve in water include all of the following except
   a. lipids.  
   b. glucose.  
   c. proteins.  
   d. salts.
3. Temperature stabilization is dependent upon which properties of water?
   a. cohesion and adhesion  
   b. capillary action and adhesion  
   c. specific heat and heat of vaporization  
   d. cohesion and specific heat
4. All of the following are accurate about H\(^+\) concentration and pH except
   a. acids contain more H\(^+\) than water.  
   b. H\(^+\) concentration and pH are inversely related.  
   c. neutralizing an acidic solution requires that base is added.  
   d. a pH of 6 is basic, or alkaline.
5. Blood is a mixture that is more specifically described as a
   a. suspension.  
   b. colloid.  
   c. solution.  
   d. All of these are correct.
6. Which biological macromolecule is not a polymer?
   a. triglyceride  
   b. protein  
   c. glycogen  
   d. DNA
7. Glucose is stored as which molecule within the liver and skeletal muscle tissue?
   a. starch  
   b. phospholipid  
   c. glycogen  
   d. glucagon
8. All of the following are common ions of the human body except
   a. Na\(^+\).  
   b. P\(^+\).  
   c. Ca\(^{2+}\).  
   d. Cl\(^-\).
9. Intermolecular attractions between polar molecules are
   a. hydrophobic interactions.  
   b. hydrogen bonds.  
   c. van der Waals forces.  
   d. ionic bonds.
10. When a protein permanently unfolds, it has been
    a. polymerized.  
    b. denatured.  
    c. converted to nucleic acids.  
    d. made more efficient.
11. List the common ions of the human body by name, symbol, and charge.
12. Describe a polar bond and a polar molecule.
13. Diagram two water molecules, and label the polar covalent bonds and a hydrogen bond.
14. Compare and contrast what occurs when a substance dissolves in water with a substance that dissolves and dissociates in water. Include examples of specific substances.
15. Define the terms acid, base, pH, and buffers.
16. Explain the units for expressing a concentration that are included in this chapter.
17. List the four biological macromolecules and the building blocks that compose them.
18. Which two biological macromolecules contain nitrogen atoms and contribute to the formation of nitrogenous waste that must be eliminated by the urinary system?
19. Describe how phospholipid molecules form the plasma membrane of a cell.
20. Explain protein denaturation, including how it occurs and the consequences in response to an increase in temperature and a change in pH.
Can You Apply What You’ve Learned?

1. Which property of water is significant in children born prematurely because it causes the air sacs to collapse in the lungs, making breathing difficult?
   a. specific heat  
   b. water reactivity  
   c. surface tension  
   d. capillary action

2. A young boy playing outside on a very hot day has become dehydrated. When he enters the house, he appears lethargic. The mother is a nurse and becomes concerned that he may be experiencing a fluid and electrolyte imbalance. Electrolytes include all of the following except
   a. sodium ion.  
   b. glucose.  
   c. potassium ion.  
   d. chloride ion.

3. A young woman has noticed that her thyroid gland appears enlarged. One of the diagnostic procedures used to produce an image of her thyroid gland requires this type of substance, which emits high-energy radiation.
   a. ions  
   b. radioisotopes  
   c. radioisomers  
   d. isomers

4. The condition of rickets involves bones that have insufficient amounts of this common ion, resulting in the bones bending under a child’s weight.
   a. Na⁺  
   b. K⁺  
   c. Cl⁻  
   d. Ca²⁺

5. The hormone insulin is a ___________ composed of repeating units of amino acids and cannot be administered orally because the enzymes within the gastrointestinal tract will break the peptide bond through the process of hydrolysis, releasing individual amino acids.
   a. nucleic acid  
   b. glycogen  
   c. protein  
   d. steroid

Can You Synthesize What You’ve Learned?

1. An individual is exposed to high-energy radiation. Which biological macromolecule that regulates the process of protein synthesis may have been mutated?

2. The lab results from a diabetic patient show a lower than normal pH (a condition referred to as acidosis). Explain the change in H⁺ concentration in the blood, and describe how this change may affect the folding of proteins in the blood plasma (and elsewhere).

3. A patient is given a new drug that decreases blood sugar levels. This drug is regulating which specific molecule?

INTEGRATE

ONLINE STUDY TOOLS

The following study aids may be accessed through Connect.

Clinical Case Study: A True Story of Killing Patients with Potassium Chloride

Interactive Questions: This chapter’s content is served up in a number of multimedia question formats for student study

SmartBook: Topics and terminology include atomic structure; ions and ionic compounds; covalent bonding, molecules, and molecular compounds; molecular structure of water and the properties of water, acidic and basic solutions, pH, and buffers; water mixtures; biological macromolecules; and protein structure

Anatomy & Physiology Revealed: Topics include atomic structure, bonds

Animations: Topics include ionic solutions; ionic bond; solutions; making solutions; buffers

Energy, Chemical Reactions, and Cellular Respiration

3.1 Energy
3.1a Classes of Energy
3.1b Forms of Energy
3.1c Laws of Thermodynamics

INTEGRATE: CONCEPT OVERVIEW
Energy as It Relates to Human Body Function

3.2 Chemical Reactions
3.2a Chemical Equations
3.2b Classification of Chemical Reactions
3.2c Reaction Rates and Activation Energy

3.3 Enzymes
3.3a Function of Enzymes
3.3b Enzyme Structure and Location
3.3c Mechanism of Enzyme Action
3.3d Classification and Naming of Enzymes
3.3e Enzymes and Reaction Rates
3.3f Controlling Enzymes
3.3g Metabolic Pathways and Multienzyme Complexes

3.4 Cellular Respiration
3.4a Overview of Glucose Oxidation
INTEGRATE: CONCEPT OVERVIEW
How Enzymes Work
3.4b Glycolysis
3.4c Intermediate Stage
3.4d Citric Acid Cycle
3.4e The Electron Transport System
3.4f ATP Production
3.4g The Fate of Pyruvate with Insufficient Oxygen
3.4h Other Fuel Molecules That Are Oxidized in Cellular Respiration

All living organisms require energy. In humans, energy is needed to power muscle contractions when walking, pump blood through the body, absorb nutrients from the gastrointestinal tract, and exchange respiratory gases. Energy is also required both to synthesize (produce) new molecules for maintenance, growth, and repair and to establish ion concentrations in cells. Here we discuss the chemical principles of energy, chemical reactions, enzymes, and metabolic pathways. Many of these concepts are then integrated to describe the metabolic pathway that breaks down glucose molecules. It is during the breakdown of glucose (and other fuel molecules) that energy is released to synthesize adenosine triphosphate (ATP). ATP is the molecule that serves as the “energy currency” of a cell for all energy-requiring cellular processes.

CAREER PATH

Biochemists

Biochemists study the chemical composition and physical principles of living cells and organisms, including those associated with cell metabolism, development, growth, reproduction, and heredity. Their work may involve determining the effects of substances (e.g., foods, vitamins, enzymes, hormones, allergens) on living organisms or studying the effects of mutations that lead to cancer.
**3.1 Energy**

Energy is defined as the capacity to do work. Energy differs from matter in that it has no mass and does not take up space. It is invisible, but its effects on matter may be observed. This section describes the two major classes of energy, the various forms of energy, and physical laws that govern energy.

### 3.1a Classes of Energy

**LEARNING OBJECTIVE**

1. Describe the two classes of energy.

Two classes of energy exist: potential energy and kinetic energy. Potential energy is the energy of position or stored energy. Kinetic energy is the energy of motion. Potential energy can be converted, or changed, to kinetic energy, and vice versa. For example, water behind a dam has potential energy because of its position; when the water falls over the dam it now has kinetic energy because of its motion. The kinetic energy of falling water can be harnessed to do work if it drives a water wheel at the bottom of the dam.

A bow and arrow also provides an example of an energy conversion from potential energy to kinetic energy. When the arrow is pulled back in the bow, it has potential energy because of the tension in the bowstring. This potential energy is converted to kinetic energy as the string is released and the arrow flies. The kinetic energy of the flying arrow can do work when it knocks an apple from a tree.

Potential energy is exhibited in cells of living organisms when a concentration gradient (i.e., a difference in the amount of a substance in two areas) exists across the plasma membrane, which is the boundary between the inside and outside of a cell (figure 3.1a). Sodium ion (Na\(^+\)) concentration typically is greater outside the cell than inside. This difference in Na\(^+\) concentration across the membrane is analogous to the water at the top of a dam because it represents potential energy. The movement of Na\(^+\) from a high concentration outside the cell to a low concentration inside the cell is an example of kinetic energy. Like water falling over a dam, the kinetic energy of Na\(^+\) movement may be harnessed to do work. You will see applications of this principle both in this chapter and in later chapters (see section 24.6c).

Potential energy is also exhibited by the position of electrons in electron shells relative to an atom’s nucleus (figure 3.1b). Electrons can move from a higher-energy shell to a lower-energy shell. Note that when electrons move during a chemical reaction, they may do so either within the same chemical structure or from one chemical structure to another (e.g., in the electron transport chain of a mitochondrion [see figure 3.19], a cell organelle that synthesizes ATP). The kinetic energy of electron movement can be harnessed to do work—movement of electrons is critical to the formation of ATP molecules.

Note that potential energy has the ability, or potential, to do work because of its position. Potential energy must be converted to kinetic energy to be actively engaged in doing work.

**WHAT DID YOU LEARN?**

1. Both the movement of Na\(^+\) from an area of higher concentration to an area of lower concentration and the movement of an electron from a higher energy to a lower energy state are examples of (a) potential energy or (b) kinetic energy?

### 3.1b Forms of Energy

**LEARNING OBJECTIVES**

2. Describe chemical energy (one form of potential energy) and the various forms of kinetic energy.
3. List the three important molecules within the body that function primarily in chemical energy.

Potential and kinetic energy exist in several forms. We first describe chemical energy, which is one form of potential energy, and then describe several forms of kinetic energy.

**Figure 3.31 Conversion of Potential Energy to Kinetic Energy.** Potential energy that is converted to kinetic energy may be harnessed to do work. (a) The Na\(^+\) gradient across the plasma membrane has potential energy that changes to kinetic energy when Na\(^+\) ions move from where they are in high concentration outside the cell to where they are in low concentration inside the cell. (b) A high-energy electron has potential energy and may be converted to kinetic energy in the same atom or be transferred to different molecules as the electron “falls” from high-energy shells to low-energy shells.
Chemical Energy (a Form of Potential Energy)

Chemical energy is one form of potential energy. Chemical energy is the energy stored in a molecule’s chemical bonds, and is the most important form of energy in the human body. It specifically is used for the energy-requiring processes of movement, synthesis of molecules, and establishment of concentration gradients. The chemical bonds of all molecules have chemical energy. This energy is released when bonds are broken during chemical reactions.

Three important molecules in the human body function primarily in chemical energy storage: triglycerides, glucose, and adenosine triphosphate (ATP). These molecules differ in their chemical structure, where they are stored, and the length of time each generally stores energy. Recall the following from chapter 2:

- Triglycerides are involved in long-term energy storage in adipose connective tissue (see section 2.7b).
- Glucose is stored in the liver and muscle tissue in the form of the polymer glycogen (see section 2.7c).
- ATP is stored in all cells in limited amounts and is produced continuously and used immediately for cells’ energy-requiring processes (see section 2.7d).

Note that protein also stores chemical energy and can be used as a fuel molecule. However, as described in section 2.7e, proteins are primarily important as the structural and functional components of the body.

Kinetic Energy Forms

Other forms of energy—electrical, mechanical, sound, radiant, and heat—exist as kinetic energy. Electrical energy is the movement of charged particles. Examples of electrical energy include electricity, which is the movement of electrons along a wire, and the propagation of a nerve signal (an impulse) due to the movement of ions across the plasma membrane of a neuron (nerve cell; see section 12.2a).

Mechanical energy is exhibited by an object in motion due to an applied force. Examples of mechanical energy include muscle contraction for walking and the pumping action of the heart to circulate blood.

Sound energy occurs when the compression of molecules that move in a solid, liquid, or gas is caused by a vibrating object, such as the head of a drum or the vibration of the vocal cords. The sense of hearing is initiated when sound waves cause vibration of the tympanic membrane (eardrum) in the ear (see section 16.5a).

Radiant energy is the energy of electromagnetic waves traveling in the universe. Radiant energy consists of a spectrum of different energy forms that vary in wavelength and frequency (figure 3.2). The higher the frequency in the spectrum, the greater the...
amount of radiant energy associated with it. Gamma rays have the highest amount of radiant energy, whereas radio waves have the lowest. All forms of radiant energy with a frequency higher than visible light (gamma rays, x-rays, and ultraviolet [UV] light) have sufficient energy to penetrate the body and mutate (change) the DNA of living organisms. Cells of the skin normally protect themselves from everyday UV light exposure by producing the pigment melanin (see section 6.1a). This process commonly darkens skin color and is referred to as tanning. Visible light is a lower-frequency radiant energy that is detected by retinal cells of the eye. This visual input is then relayed along the optic nerve to the brain for interpretation.

Heat is the kinetic energy associated with random motion of atoms, ions, or molecules. It is usually considered an unusable form of energy, or a waste product that accompanies all changes in energy form because heat is the only type of energy that is not available to do work. Heat is measured as the temperature of a substance.

What did you learn?

Muscle contraction is an example of what form of energy?

3.1c Laws of Thermodynamics

Learning objectives

4. State the first law and second law of thermodynamics.

5. Explain why energy conversion is always less than 100%.

Energy can be converted from one form to another. For example:

- When a candle is burned, chemical energy in the burning wax is converted to both light and heat.
- Light energy from the sun is converted by the retinal cells into electrical energy associated with nerve signals involved in sight (see section 16.4d).
- Chemical energy in the food we eat is first converted into another chemical form (ATP), which is then converted in our cells into mechanical energy used to power muscle contraction (see section 10.4a).

In these examples, energy is simply changing from one form to another. The study of energy transformations is called thermodynamics (ther′mo-dī-nam′iks; thermo = heat, dynamis = force).

Two laws of thermodynamics describe energy transformations. The first law of thermodynamics states that energy can neither be created nor destroyed—it can only be transformed, or converted, from one form to another.

The second law of thermodynamics states that every time energy is transformed from one form to another, some of that energy is converted to heat. That means there is never 100% conversion of one form of usable energy to another. Energy conversions have a price, and that price always appears as heat. Because heat is not available to do work, the usable amount of energy is decreased each time an energy conversion occurs. For example, the conversion of the chemical energy in gasoline to the mechanical energy (movement) of a car is approximately 25%. This means that approximately 75% of gasoline’s chemical energy is converted to sound and heat.

Heat is produced when the chemical energy stored in the foods we eat is used to power our muscle contractions. One of the functions of muscle tissue is to produce heat that keeps the body warm (see section 10.1a). When the environmental temperature drops, and we begin to move around in the hope of generating enough heat to keep ourselves warm, we are applying the second law of thermodynamics.

Figure 3.3 summarizes the two major classes of energy, the various forms of energy as they relate to the body, and the laws of energy.

What did you learn?

Energy can neither be created nor destroyed. However, according to the first and second laws of thermodynamics, what can happen to it, and what is always generated?
Energy as It Relates to Human Body Function.

(a) Potential and kinetic energy are the two classes of energy. (b) Forms of usable energy include chemical energy and various forms of kinetic energy. (c) Laws of energy describe how energy can be converted from one form to another and that heat is always produced during the process.

(a) Potential and Kinetic Energy

Potential Energy: The energy of position
Na\(^+\) ions have potential energy due to the concentration gradient difference between the outside and inside of the cell.

Kinetic Energy: The energy of motion
Na\(^+\) ions exhibit kinetic energy as they move down their concentration gradient.

(b) Forms of Usable Energy Available to Do Work

Potential Energy

Chemical Energy: Energy stored in chemical bonds of molecules

Example: Glucose, a high-energy molecule, can be stored as glycogen within liver and muscle cells for later use.

Electrical Energy: Movement of charged particles

Example: The propagation of a nerve signal in a neuron is due to the movement of charged ions across its plasma membrane.
Energy is being converted constantly from one form to another in order to perform the tasks that keep the human body alive and active.

### (c) Laws of Energy

#### First Law of Thermodynamics
Energy cannot be created or destroyed; it can only be converted from one form to another.

#### Second Law of Thermodynamics
Every time energy is transformed from one form to another, some of that energy is converted to heat.

### Kinetic Energy

- **Mechanical Energy:** Movement of a structure or a substance due to an applied force
  - Example: The pumping action of the heart to circulate blood is a form of mechanical energy.

- **Sound Energy:** Movement of compressed molecules through a medium initiated by a vibrating object
  - Example: Sound waves vibrating the tympanic membrane of the ear stimulate sensory receptors for hearing.

- **Radiant Energy:** Movement of electromagnetic waves that travel in the universe and vary in wavelength and frequency
  - Example: Visible light, a form of radiant energy, is focused on the retina of the eye for vision.
Chapter Three
Energy, Chemical Reactions, and Cellular Respiration

3.2 Chemical Reactions

Millions of chemical reactions are occurring in living organisms at any given time. Metabolism is the collective term for all biochemical reactions in living organisms. A chemical reaction occurs when chemical bonds in an existing molecular structure are broken and new ones formed to produce a different structure.

3.2a Chemical Equations

**LEARNING OBJECTIVES**

6. Explain what occurs in a chemical reaction.
7. Distinguish between reactants and products.

When chemical reactions occur (and thus molecular structures are changed), a summary of their changes is written as a chemical equation. The components of a chemical equation are called reactants and products. Reactants are the substrates, or substances, that are present prior to the start of the chemical reaction; they are usually written on the left side of the equation. Products are substances that are formed from the reactants by the subsequent chemical reaction. The products are generally written on the right side of the equation. For example, a generic chemical reaction is written

\[ \text{A + B} \rightarrow \text{C} \]

A and B are reactants in this reaction and C is the product. An arrow is used to indicate the reaction direction. A chemical reaction typically has the arrow drawn to the right, indicating a net change of reactants to products.

The number of elements on one side of the reaction is equal to the number of elements on the other side in a balanced chemical equation. For example:

\[ \text{Ca}^{2+} + 2 \text{Cl}^{-} \rightarrow \text{CaCl}_2 \]

which indicates that one calcium ion combines with two chloride ions to form calcium chloride.

**WHAT DID YOU LEARN?**

4. What are the differences between reactants and products in a chemical equation?

3.2b Classification of Chemical Reactions

**LEARNING OBJECTIVES**

8. Describe the three classifications of chemical reactions.
9. Distinguish between catabolism and anabolism.
10. Discuss the exchange that takes place in an oxidation-reduction reaction.
11. Explain ATP cycling.

Chemical reactions are classified based upon three different criteria: (1) changes in chemical structure, (2) changes in chemical energy, and (3) whether the reaction is irreversible or reversible.

**Classifying Changes in Chemical Structure**

The categories of chemical reactions based on changes in chemical structure include decomposition, synthesis, and exchange reactions (figure 3.4). The first category is referred to as a decomposition (dē′kəm-pō-zhĭ-ăn) reaction because the initial large molecule is digested or broken down into smaller structures. A simplified equation for a decomposition reaction is

\[ \text{AB} \rightarrow \text{A} + \text{B} \]

An example of a decomposition reaction is the hydrolysis reaction (see section 2.7a) of sucrose into glucose and fructose molecules in the digestive tract (figure 3.4a). All of the
decomposition reactions in the body are collectively referred to as either catabolism (kā-tab′-ŏ-lizm; katabole = a casting down) or catabolic reactions.

A synthesis (sin′thĕ-sis; syn = together, thesis = arranging) reaction occurs when two or more atoms, ions, or molecules are combined to form a larger chemical structure as existing bonds are broken and new bonds are formed. A simplified equation for a synthesis reaction is

\[ A + B \rightarrow AB \]

An example of a synthesis reaction is the dehydration synthesis reaction (see section 2.7a) that occurs during the formation of a dipeptide from two amino acids (figure 3.4b). Anabolism (ă-nab′-ŏ-lizm; ana = up) is the collective term for all synthesis reactions in the body. These are also called anabolic reactions.

The third category of reactions based upon changes in chemical structure is the exchange reaction, in which atoms, molecules, ions, or electrons are exchanged between two chemical structures. An exchange reaction has both decomposition and synthesis components and is the most prevalent type of reaction in the human body. A simplified equation for an exchange reaction is

\[ AB + C \rightarrow A + BC \]

The production of adenosine triphosphate (ATP) in muscle tissue is an example of an exchange reaction:

\[ \text{Creatine phosphate} + \text{Adenosine diphosphate (ADP)} \rightarrow \text{Creatine} + \text{ATP} \]

The bond between phosphate and creatine is broken in this reaction. The creatine becomes a free molecule, while the phosphate is transferred and bonded to ADP to form ATP (figure 3.4c).

Oxidation-Reduction Reactions An oxidation-reduction reaction (also termed a redox reaction) is a specific type of exchange reaction that involves the movement of electrons from

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INTEGRATE LEARNING STRATEGY

- **Catabolism** involves complex molecules being broken down, or digested, into simpler molecules. We can remember catabolism by thinking of a “cat” eating from a “bowl,” which leads to food molecules being digested.
- **Anabolism** is the reverse reaction, namely synthesis or the building of complex molecules from simple molecules. For example, some athletes illegally use anabolic steroids to stimulate synthesis of contractile proteins within muscle tissue.
- **Metabolism** is the collective term for all biochemical reactions that occur within the human body; these include the processes of both catabolism and anabolism.
Oxidation, 11/11/17 5:13 pm

C NH NH
Reduction + +
This cycling involves both (1) -less i i
while NAD as glucose, is oxidized because it has given up two hydrogen atoms, a hydrogen ion that together are shown as a hydrogen atom, H). (e
panied by a hydrogen ion (H
the electrons in oxidation-reduction reactions represent energy
local environment during this reaction.)

80

Electron transfer occurs when NAD
molecule, which is a
energy-rich molecule, such as glucose, is oxidized because it has given up two hydrogen atoms, while NAD
has gained both a hydrogen ion (H
) and two electrons (e
) and is reduced. (Note that one H
is released into the surrounding local environment during this reaction.)
The movement of electrons can be harnessed to do work. Thus, the electrons in oxidation-reduction reactions represent energy transfer. Consequently, when we say that glucose is oxidized, we indicate that the glucose is losing its electrons and releasing its chemical energy. Other molecules are reduced and gain both electrons and energy (e.g., such as NAD
becoming NADH).

Classifying Changes in Chemical Energy
Chemical reactions are also classified by the relative amounts of chemical energy associated with the reactants and products. These two categories are based upon energy change and are termed exergonic reactions and endergonic reactions.

Exergonic (ek'sêr-gon'ik; exo = outside, ergon = work) reactions involve reactants at the start of a reaction that have more potential energy within their chemical bonds than do the products that are formed (figure 3.6a). Exergonic means that energy “goes out,” or is released during the course of breakdown reactions. Decomposition reactions, such as the decomposition of glucose to carbon dioxide and water, are normally exergonic reactions.

Endergonic (en'der-gon'ik; endo = within) reactions involve reactants that have less energy within their chemical bonds than do the products. Endergonic means that energy must be “put in,” or supplied, to proceed (figure 3.6b). Endergonic reactions yield products that have a net increase in chemical energy as compared to what was present in the reactants. Synthesis reactions, such as the formation of a dipeptide from two amino acids, are endergonic reactions.

ATP Cycling ATP cycling is the continuous formation and breakdown of ATP (figure 3.7). This cycling involves both (1) ATP formation from ADP and P;
, which is an energy-requiring (endergonic) reaction, and (2) ATP splitting into ADP and P,
, which is an energy-releasing (exergonic) reaction.

An example of an oxidation-reduction reaction in the cells involves the nicotinamide adenine dinucleotide (NAD
) molecule, which is a modified dinucleotide that is linked at the phosphates and contains nicotinamide (a nitrogenous base, which is not found in DNA or RNA; see section 2.7d) and adenine. NAD
is important in ATP synthesis. Figure 3.5 shows an example in which an energy-rich molecule, such as glucose, is oxidized because it has given up two hydrogen atoms, while NAD
has gained both a hydrogen ion (H
) and two electrons (e
) and is reduced. (Note that one H
is released into the surrounding local environment during this reaction.)

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The energy required for ATP formation is supplied from the breakdown of glucose or other fuel molecules from the foods we eat. These molecules undergo oxidation, and energy stored within their chemical bonds is transferred to ADP and P;
, to form ATP. In turn, ATP splitting releases the stored energy, which is used for energy-requiring cellular processes. Thus, ATP cycling involves ATP as the “intermediary” between fuel molecules that release energy (e.g., glucose) and cellular processes that require energy input.

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, to form ATP. In turn, ATP splitting releases the stored energy, which is used for energy-requiring cellular processes. Thus, ATP cycling involves ATP as the “intermediary” between fuel molecules that release energy (e.g., glucose) and cellular processes that require energy input.
A cell cannot stockpile ATP, so typically only a few seconds’ worth of ATP is present. Instead, the breakdown of glucose (and other fuel molecules) and the formation of new ATP molecules must occur continuously.

Classifying Reactions as Irreversible or Reversible

A third way of classifying chemical reactions is based upon whether they are irreversible or reversible. An **irreversible reaction** involves reactants converted to product at a rate that yields a net loss of reactants and a net gain in product. Many reactions are irreversible and are written with the arrow to the right:

\[ A + B \rightarrow AB \] or \[ AB \rightarrow A + B \]

A **reversible reaction** differs from an irreversible reaction because it does not proceed only to the right with reactants becoming products over time, but instead reactants become products at a rate equal to products becoming reactants (once equilibrium is reached). Consequently, there is no net change in concentration in either reactants or products, and the reaction is in a state of equilibrium. The relationship of the reactants and products in a reversible reaction is shown with arrows in both directions:

\[ A + B \rightleftharpoons AB \]

A reversible reaction remains in equilibrium if left undisturbed. However, the equilibrium can be disturbed in a reversible reaction if a change in either the amount of reactant or the amount of product occurs. For example, either an increase in reactants or a decrease in products drives the equation to the right, which contributes to the formation of additional product until a new equilibrium is reached. In contrast, a decrease in reactants or an increase in product drives the equation to the left, which contributes to the formation of additional reactants until a new equilibrium is reached.

An important example of a reversible reaction in the human body is the **carbonic acid reaction**. This reaction occurs when carbon dioxide (CO₂) and water (H₂O) combine to form carbonic acid (H₃CO₃). The reaction is

\[ CO_2 + H_2O \rightleftharpoons H_2CO_3 \]

**Figure 3.6 Exergonic and Endergonic Reactions.** Chemical reactions are classified based on the change in chemical energy of the reactants and products. (a) The reactants have more energy than the products, and energy is released, during an exergonic reaction. (b) The reactants have less energy than the products, and energy must be supplied, in an endergonic reaction.

**Figure 3.7 ATP Cycling.** (a) The high-energy chemical bond of ATP is formed between ADP and Pᵢ. Energy is required and is supplied by the energy-releasing oxidation of fuel molecules. (b) The high-energy chemical bond of ATP is split to form ADP and Pᵢ. Energy released is used in energy-requiring cellular processes.
The newly formed carbonic acid is unstable, and it dissociates to yield both hydrogen ion (H\(^+\)) and bicarbonate ion (HCO\(_3\)\(^-\)). The equation for the complete chemical reaction is

\[
\text{CO}_2 + \text{H}_2\text{O} \rightleftharpoons \text{H}_2\text{CO}_3 \rightleftharpoons \text{H}^+ + \text{HCO}_3^- 
\]

This reversible reaction occurs in different locations within the human body and is important in several critical physiologic processes, including blood transport of carbon dioxide (see section 23.7b) and maintaining acid-base balance (see section 25.5).

**Table 3.1** summarizes the three major ways chemical reactions are classified.

### WHAT DID YOU LEARN?

1. For a biochemical reaction that involves simple chemical structures bonded together into a more complex molecule, choose the more accurate term in each pair that best describes this type of chemical reaction: (a) synthesis or decomposition reaction; (b) exergonic or endergonic reaction; (c) collective term for this type of reaction (catabolism or anabolism).

2. What molecule is formed from glucose oxidation and used as the energy currency for energy-requiring processes within the cell?

3. Explain what occurs when the equilibrium is disturbed in reversible reactions by changes in reactants and products.

### 3.2c Reaction Rates and Activation Energy

**LEARNING OBJECTIVES**

12. Define chemical reaction rate.

13. Define activation energy.

**Reaction rate** is the measure of how quickly a chemical reaction takes place; this rate determines the amount of product formed per unit of time. A primary factor that influences the reaction rate is the energy required to break the chemical bonds in a molecule so that new bonds can form the product. The energy required to break existing chemical bonds for the chemical reaction to proceed is called the **activation energy**, or \( E_a \). A chemical reaction occurs when sufficient energy is supplied to overcome the \( E_a \).

In the laboratory setting, merely heating a mixture of reactants often overcomes the \( E_a \). An elevation in temperature increases the kinetic energy of the molecules, providing enough energy to break chemical bonds. However, this approach is not feasible in a living cell. The consequence of an increase in temperature within the cell would denature all of its proteins.
and cause the cell’s death (see section 2.8b). Cells have solved their $E_a$ problem through the use of biologically active protein catalysts called enzymes, the topic of section 3.3.

**WHAT DID YOU LEARN?**

Explain the effect a fever would have on chemical reaction rates within the body. What is the risk to protein structure with a high fever?

### 3.3 Enzymes

Chemical reactions must proceed at a rate that is sufficient to sustain life. Catalysts are substances that accelerate or promote chemical reactions. Enzymes are the biologically active catalysts that facilitate chemical changes in the human body by decreasing the activation energy ($E_a$) of millions of chemical changes that occur every second. Their importance cannot be overstated.

#### 3.3a Function of Enzymes

**LEARNING OBJECTIVE**

14. Describe the general function of enzymes.

Enzymes function to accelerate normal physiologic activities by decreasing the activation energy ($E_a$) of chemical reactions. Figure 3.8 shows the difference in $E_a$ of an uncatalyzed reaction (chemical reaction without an enzyme) and a catalyzed reaction (chemical reaction with an enzyme) of sucrose decomposition to yield glucose and fructose. Notice the following:

- The reaction is exergonic because the reactant, sucrose, has higher potential energy than the combined potential energy of the products glucose and fructose.
- Activation energy is required to initiate the reaction to occur even though it is exergonic.
- The presence of an enzyme lowers the required $E_a$.

More glucose and fructose are formed in a given period of time in the presence of an enzyme than would be formed without the enzyme.

Note that enzymes only facilitate chemical reactions to proceed that would already occur; their presence increases the rate of product formation by lowering the $E_a$. For example, let’s compare the uncatalyzed and catalyzed rate of production for the reversible carbonic acid reaction:

$$\text{CO}_2 + \text{H}_2\text{O} \rightleftharpoons \text{H}_2\text{CO}_3 \rightleftharpoons \text{H}^+ + \text{HCO}_3^-$$

This reaction is catalyzed by the enzyme carbonic anhydrase. The chemical reaction still proceeds when carbonic anhydrase is absent; however, only about 100 $\text{H}_2\text{CO}_3$ molecules are formed per hour. In contrast, when the enzyme carbonic anhydrase is present, up to 2.16 billion $\text{H}_2\text{CO}_3$ molecules may be formed per hour—a tremendously greater rate.

**WHAT DID YOU LEARN?**

What is the relationship of enzymes and activation energy?

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**Figure 3.8 Activation Energy ($E_a$).** The energy barrier that must be overcome for a reaction to proceed is the activation energy ($E_a$). Comparison of the $E_a$ of an uncatalyzed reaction and a catalyzed reaction.
Enzymes may bind to a specific active site forming the enzyme-substrate complex. The active site accommodates the substrate(s) of a reaction to temporarily form an enzyme-substrate complex (figure 3.9). The specificity in the shape of the active site permits only a single substrate, or type of substrate, to bind to the active site, and thus the enzyme is capable of catalyzing only one specific reaction.

Enzymes are produced by protein synthesis processes within cells (see section 4.8). Once formed, the location of the enzyme varies. Enzymes may

- Remain within the cell; an example is RNA polymerase, which helps form RNA from DNA (see section 4.8a).
- Become embedded within the plasma membrane (the outer boundary of a cell); an example is lactase, which digests the milk sugar lactose and is found in plasma membranes of cells that line the small intestine (see Clinical View 3.2: “Lactose Intolerance”).
- Be secreted from the cell; an example is pancreatic amylase released from the pancreas into the small intestine (see Clinical View 3.2: “Lactose Intolerance”).

Cofactors

Enzymes often require cofactors that are “helper” ions or molecules to ensure that a reaction occurs. A cofactor is a nonprotein structure that may be either an inorganic or organic substance (see section 2.4) associated with a particular enzyme or enzymatic reaction.

Inorganic cofactors are attached to the enzyme and are required for their normal function. For example, zinc ion is bound to carbonic anhydrase enzyme; without zinc, carbonic anhydrase is unable to function.

Organic cofactors are not attached to enzymes and have specific functions in assisting enzymes. Many vitamins (e.g., B₆ and B₁₂), derivatives of vitamins, or modified nucleotides such as NAD⁺ may serve as organic cofactors. For example, the NAD⁺ coenzyme accepts hydrogen during chemical reactions to become NADH. Organic cofactors are more specifically referred to as coenzymes in some sources, and this term is also used in this text.

WHAT DID YOU LEARN?

10. What is the active site of an enzyme, and how does it relate to a substrate?

11. What is the mechanism of enzyme action, including the role of cofactors?

### Table 3.2

<table>
<thead>
<tr>
<th>Subclass</th>
<th>General Functions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oxidoreductase</td>
<td>Oxidation-reduction reactions</td>
</tr>
<tr>
<td>Transferase</td>
<td>Transfer of functional groups</td>
</tr>
<tr>
<td>Hydrolase</td>
<td>Hydrolysis reactions</td>
</tr>
<tr>
<td>Isomerase</td>
<td>Interconversion of isomers</td>
</tr>
<tr>
<td>Ligase</td>
<td>Ligation reactions</td>
</tr>
<tr>
<td>Lyase</td>
<td>Cyclization and deamination reactions</td>
</tr>
</tbody>
</table>

There are thousands of different enzymes. To help make sense of the many different types of enzymes, biochemists organize them into six major functional classes, with subclasses within each category. Table 3.2 briefly describes the six major classes of enzymes, including oxidoreductase, transferase, hydrolase, isomerase, ligase, and lyase.
Substrate: Lactose

Enzyme: Lactase

Decomposition reaction: Lactose digested to glucose and galactose

1. The substrate lactose binds to the enzyme, forming an enzyme-substrate complex.
2. The enzyme changes shape, resulting in an induced fit between substrate and enzyme.
3. The bond is broken between glucose and galactose.
4. Products: Glucose and galactose are released, and the enzyme is free to bind other substrates.

Substrate: Glucose

Enzyme: Glycogen synthetase

Synthesis reaction: Glucose molecules synthesized into a glycogen molecule

1. The glucose substrate binds to the enzyme, forming an enzyme-substrate complex.
2. The enzyme changes shape, resulting in an induced fit between substrate and enzyme.
3. A bond is formed between the new glucose molecule and the growing glycogen molecule.
4. Product: Glycogen is released, and the enzyme is free to bind other substrates.

Figure 3.10 Mechanism of Action for Enzymes in Decomposition and Synthesis Reactions. (a) Enzymes may decompose larger complex molecules into simpler chemical structures, such as when lactose is broken down into glucose and galactose. (b) Enzymes may synthesize simple chemical structures into larger complex structures, such as when glucose molecules are bonded together to form glycogen.

<table>
<thead>
<tr>
<th>Table 3.2 Major Classes of Enzymes</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Enzyme Class</strong></td>
</tr>
<tr>
<td>------------------</td>
</tr>
<tr>
<td>Oxidoreductase</td>
</tr>
<tr>
<td>Transferase</td>
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<tr>
<td>Hydrolase</td>
</tr>
<tr>
<td>Isomerase</td>
</tr>
<tr>
<td>Ligase</td>
</tr>
<tr>
<td>Lyase</td>
</tr>
</tbody>
</table>
Enzymes in the oxidoreductase class, for example, participate in oxidation-reduction reactions. **Dehydrogenase** (dē-hō′drō-jen-ās; de = from) enzymes are a subcategory of enzymes within the oxidoreductase class. These enzymes participate in oxidation-reduction reactions by moving hydrogen from one molecule to a different molecule.

Another example of a class of enzymes is the transferase class. All enzymes in this class transfer atoms or molecules between chemical structures. **Kinase** (kīnās) enzymes belong to this class because they specifically transfer a phosphate functional group, usually from ATP to another molecule. You will learn about specific examples of both dehydrogenase and kinase enzymes in section 3.4.

### WHAT DO YOU THINK?

2. Given what you already know about isomers (see section 2.3a), what can you predict that an enzyme in the isomerase class would do?

The name of a given enzyme is generally based upon the name of the substrate or product involved in the chemical reaction, sometimes the name of the subclass, and the suffix -ase, added to the final word of the name. Here are three examples:

- **Pyruvate dehydrogenase** is an enzyme that transfers a hydrogen, specifically from a pyruvate molecule (see section 3.4c).
- **DNA polymerase** is central to the formation of the polymer DNA from deoxyribonucleotides (see section 4.9b).
- **Lactase** digests the disaccharide lactose. (see section 26.4a).

Although the name of an enzyme generally contains an -ase suffix and the rest of the name reflects its function, there are exceptions. For example, pepsin, trypsin, and chymotrypsin (see section 26.4b) are all protein-digesting enzymes with names that do not provide clear clues to these molecules’ enzymatic nature or specific activity.

### WHAT DID YOU LEARN?

12. Explain how enzymes are generally named.

### 3.3e Enzymes and Reaction Rates

**LEARNING OBJECTIVES**

21. Define how enzyme and substrate concentration affect reaction rates.
22. Explain the effect of temperature on enzymes.
23. Describe how pH changes affect enzymes.

Several conditions influence the reaction rates catalyzed by enzymes. The most significant factors are enzyme and substrate concentration, temperature, and pH.

#### Effect of Enzyme and Substrate Concentration

The rate of a chemical reaction may be accelerated by either an increase in enzyme concentration or an increase in substrate concentration. An increase in substrate concentration, however, increases the rate of reaction only up to the point of saturation of the enzyme (figure 3.11a). **Saturation** occurs when so much substrate is present that all enzyme molecules are actively engaged in the chemical reaction, resulting in no further (notable) increase in reaction rate.

#### Effect of Temperature

Enzymes typically are proteins, and their three-dimensional shape is dependent upon environmental variables, including temperature and pH, as described in section 2.8b. Each enzyme has a specific environment in which it can most effectively participate in a chemical reaction. Human enzymes function efficiently at normal body temperature, which, for most individuals is around 37°C (98.6°F) (figure 3.11b). The activity of human enzymes increases with a rise in body temperature (within several degrees) and continues to increase until the **optimal temperature** is reached. This is generally around 40°C (104°F) for enzymes within the human body. These increases in body...
temperature, as observed with a low fever, facilitate the eliminating of infectious agents (e.g., bacteria, viruses) (see section 22.3e).

However, more severe increases in temperature—meaning temperatures greater than 40°C (104°F) in humans—weaken the intramolecular bonds that hold an enzyme’s protein structure in its three-dimensional shape. The enzyme subsequently denatures, permanently losing function. The greater the increase in temperature, the more likely this is to occur. Observe in figure 3.11b the severe decrease in the rate of reaction with temperatures greater than 40°C (104°F).

**Effect of pH**

Enzymes function most efficiently at their optimal pH. Optimal pH for most human enzymes is between pH 6 and 8, and changes in pH can affect the enzyme (figure 3.11c). An increase in H⁺ (which causes a decrease in pH) results in additional H⁺ binding to the enzyme. In contrast, a decrease in H⁺ (which causes an increase in pH) results in the release of H⁺ from an enzyme. In either case, the change in amount of H⁺ attached to the enzyme disrupts the electrostatic interactions that hold the enzyme protein in its shape. A significant disruption results in denaturation of the enzyme (see section 2.8b).

Not all enzymes have an optimal pH between 6 and 8. The pH in the stomach, for example, is between 2 and 4; thus, the optimal pH for the stomach enzyme pepsin corresponds to this pH range. In comparison, the pH in the small intestine is between 6 and 9. Thus, when stomach contents are moved into the small intestine, the stomach enzyme pepsin is inactivated (see section 26.4b).

**WHAT DID YOU LEARN?**

13. How do changes in substrate concentration, temperature, and pH affect the reaction rate of enzyme-catalyzed chemical reactions?

**3.3f Controlling Enzymes**

**LEARNING OBJECTIVE**

24. Describe how competitive and noncompetitive inhibitors control enzyme action.

An enzyme continues to facilitate the conversion of its substrate(s) to product as long as ample substrate is present and environmental conditions are close to normal. However, uncontrolled enzymes would result in depleted substrate levels and concentration of products that exceeds what is needed. Thus, enzymes must be temporarily “turned off” to prevent overproduction of the product. Control of enzymes occurs through inhibitors, which are substances that bind to an enzyme and turn it off, thus preventing it from catalyzing the reaction (figure 3.12). Later, the release of the inhibitor from the enzyme allows it to function and continue catalyzing the reaction. This switching occurs in different ways, depending upon whether the inhibitor is competitive or noncompetitive.

A competitive inhibitor resembles the substrate and binds to the active site of the enzyme. Consequently, the substrate and the regulatory compound compete with each other for occupation of the enzyme’s active site (figure 3.12b). The amount of substrate relative to the amount of competitive inhibitor determines the degree of inhibition. The greater the concentration of the substrate, the less likely the competitive inhibitor will occupy the enzyme’s active site. In contrast, if substrate concentration decreases, the competitive inhibitor is more likely to occupy the enzyme’s active site, and lower amounts of product are formed.

Noncompetitive inhibitors do not resemble the substrate, but rather function to inhibit an enzyme by binding to a site on the enzyme other than the active site. This type of inhibition is not influenced by the concentration of substrate. Rather, it is simply dependent upon the amount of inhibitor. The greater the amount of inhibitor, the greater the degree of inhibition. In contrast, the lesser the amount of inhibitor, the lesser the degree of inhibition. Most noncompetitive enzymes bind to a specific part of an enzyme termed the allosteric (al′o-ster′ik; allo = other, stereo = three-dimensionality) site. Binding of a noncompetitive inhibitor to the allosteric site induces a conformational change in the enzyme with an accompanying change in the shape of the enzyme’s active site (figure 3.12c). This type of noncompetitive inhibitor is more specifically called an allosteric inhibitor.

**WHAT DID YOU LEARN?**

14. How are enzymes regulated through competitive and noncompetitive inhibitors?

**3.3g Metabolic Pathways and Multienzyme Complexes**

**LEARNING OBJECTIVES**

25. Distinguish between a metabolic pathway and a multienzyme complex.

26. Explain the role of negative feedback in enzyme regulation.

27. Identify and explain the processes involving phosphate that commonly are used to regulate enzymes.

Usually, multiple enzymes are required to convert an initial substrate to a final product. Depending upon both the substrate and sequence of conversion, these multiple enzymes are arranged either in a metabolic pathway or as a multienzyme complex.

---

**Figure 3.12 Enzyme Inhibition.** (a) The substrate binds to the active site of the enzyme with no inhibitor present. A substrate can be prevented from binding to an active site by (b) a competitive inhibitor that enters the active site or (c) a noncompetitive inhibitor (functioning as an allosteric inhibitor) binds to an allosteric site to induce a conformational change in the enzyme with an accompanying change in its active site.
A metabolic pathway is formed by numerous enzymes (figure 3.13). Each enzyme catalyzes one progressive change to its specific substrate molecule and then releases the product. In turn, the product of one enzyme becomes the substrate of the next enzyme. For example, there are numerous enzymes involved in the chemical breakdown of glucose to produce carbon dioxide and water during the production of ATP (see figures 3.16 and 3.18).

A multienzyme complex is a group of enzymes that are physically attached to each other through noncovalent bonds to form the complex. These attached enzymes work in a sequence of reactions. Pyruvate dehydrogenase, the multienzyme complex involved in breakdown of glucose, is an example, as shown in figure 3.17.

A multienzyme complex has two major advantages. First, the product from one chemical reaction is formed and less likely that the substance will diffuse away and come into contact with an enzyme from a different biochemical pathway. Second, the enzymatic pathway can be regulated by controlling the single complex rather than multiple individual enzymes.

Metabolic pathways and multienzyme complexes must be regulated to prevent overproduction of an unneeded product and exhaustion of substrates that could be used elsewhere. This regulation occurs through the process of negative feedback. Here, the product from a metabolic pathway acts as an allosteric inhibitor to turn off an enzyme early in the metabolic pathway. As the product accumulates, it is more likely to become bound to the enzyme and inhibit the metabolic pathway, with progressively less and less product being formed. Over time, as the amount of product decreases, the amount of the allosteric inhibitor bound to the enzyme decreases, and activity of that enzymatic pathway increases once again. In this way, a steady state of product is produced.

One specific mechanism for regulating enzymes is by either phosphorylation or dephosphorylation of the enzyme. Phosphorylation (fos′fo ˉr-i-la ˉ′shu ˘n) is the addition of a phosphate group, whereas dephosphorylation is the removal of a phosphate group. Note that phosphorylation may turn on some enzymes but turn off other enzymes. Equally, dephosphorylation may cause opposite effects in activity by different types of enzymes. The enzymes that add phosphate are generally called either phosphorlyases or kinases.

Figure 3.13 Metabolic Pathway. A metabolic pathway is composed of numerous enzymes to convert a specific substrate to the final product. The product of one enzyme is the substrate for the next enzyme in the pathway. Metabolic pathways can be regulated by negative feedback that involves a product that serves as an allosteric inhibitor binding to an enzyme early in the pathway.
whereas enzymes that remove the phosphates are called phosphatases (see figure 4.21 in section 4.5b). This concept is described in more detail in section 17.5b in discussion of the endocrine system.

**Figure 3.14** summarizes some important concepts and features of enzymes, including their function, structure and location, mechanism of action, and other features.

### WHAT DID YOU LEARN?

15. What is a metabolic pathway? Explain the role of negative feedback in enzyme regulation.

16. What two processes involve phosphate and are commonly used to regulate enzymes in a metabolic pathway or a multienzyme complex?

### 3.4 Cellular Respiration

**Cellular respiration** is a multistep metabolic pathway whereby organic molecules (e.g., glucose, fatty acids, amino acids) are disassembled (broken down) in a controlled manner by a series of enzymes. During this disassembly, potential energy stored in the molecule’s chemical bonds is released; the energy is then used to make new bonds between ADP and P_i (free phosphate) to form ATP (see figure 3.7). It is important to note the following about the processes of cellular respiration:

- These processes are exergonic, or energy-releasing.
- The organic molecule that has given up its energy has done so by releasing high-energy electrons; thus, the molecule is said to be oxidized.
- The energy released is used to synthesize ATP, which is an endergonic, or energy-requiring, process.
- Oxygen is required for maximum ATP production.

Although different types of organic molecules may be chemically digested during the collective processes of cellular respiration, our discussion here focuses on the oxidation of glucose.

### 3.4a Overview of Glucose Oxidation

**LEARNING OBJECTIVES**

28. Write the overall formula for glucose oxidation.

29. Name the two pathways that generate ATP.

30. List the four stages of glucose oxidation and where each stage occurs within a cell.

**Glucose oxidation** occurs within cells and is a step-by-step enzymatic breakdown of glucose with the accompanying release of energy to synthesize ATP. If oxygen is available, glucose is completely broken down and carbon dioxide and water are formed. Here we describe several significant features of glucose oxidation.

**Overall Chemical Reaction** Glucose has the molecular formula C_6H_{12}O_6. It is an energy-rich molecule because of its many C—C, C—H, and C—O chemical bonds as can be viewed in its structural formula (see figure 2.19a). When enzymes completely disassemble glucose, the net chemical reaction for the process is

\[
C_6H_{12}O_6 + 6 O_2 \rightarrow 6 CO_2 + 6 H_2O
\]

**Pathways for ATP Production** Glucose oxidation is an exergonic reaction (see section 3.2b). During the many enzymatic reaction steps that accomplish the breakdown of glucose, some of the energy of the broken bonds is captured to attach P_i to ADP to synthesize ATP. The energy transfer from bonds in the glucose molecule can be used either directly (least common way) or indirectly (most common way) to form ATP. The direct method of synthesizing ATP is called **substrate-level phosphorylation**. The indirect method—in which the energy is first released to coenzymes (i.e., NAD^+, FAD), which then transfer the energy to form ATP—is called **oxidative phosphorylation**.
Competitive inhibitors interfere with active site directly. Noncompetitive inhibitors are allosteric inhibitors that change the shape of an enzyme so the substrate cannot bind to the active site.

**Figure 3.14 How Enzymes Work.** Characteristics of enzymes include:

- **(a) Enzyme function**
  - Enzymes decrease the activation energy ($E_a$) so reaction rate increases and more product is formed in a given time period.

- **(b) Structure and location**
  - Most enzymes are globular proteins with a unique active site.

- **(c) Naming of enzymes**
  - The enzyme name typically includes the name of the substrate or product, or sometimes the name of the class or subclass involved in the chemical reaction with an -ase ending.
  - Example: Lactose + -ase = Lactase

- **(d) Mechanism of action**
  - Enzymes participate in either decomposition or synthesis reactions.

- **(e) Reaction rate (speed of a chemical reaction)**
  - Reaction rate is influenced by substrate or enzyme concentration, temperature, and pH.

**INTEGRATE**

**CONCEPT OVERVIEW**
**Competitive inhibitors** interfere with active site directly. **Noncompetitive inhibitors** are allosteric inhibitors that change the shape of an enzyme so the substrate cannot bind to the active site.

**Metabolic pathway and multienzyme complex**

<table>
<thead>
<tr>
<th>Metabolic pathway: Series of enzymes</th>
<th>Multienzyme complex: Physically linked enzymes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Many metabolic pathways are regulated by negative feedback by a product.</td>
<td>The product of one enzyme becomes the substrate of a different enzyme in the complex.</td>
</tr>
<tr>
<td><img src="image1" alt="Diagram of metabolic pathway with substrate, enzyme, and product" /></td>
<td><img src="image2" alt="Diagram of multienzyme complex with substrates and enzymes" /></td>
</tr>
<tr>
<td><img src="image3" alt="Diagram of allosteric site" /></td>
<td><img src="image4" alt="Diagram of active site shape change" /></td>
</tr>
<tr>
<td><img src="image5" alt="Diagram of competitive inhibitor" /></td>
<td>Products of each enzyme in the complex are less likely to diffuse away to participate in other chemical reactions.</td>
</tr>
</tbody>
</table>

**Controlling enzymes**

<table>
<thead>
<tr>
<th>Competitive inhibitor</th>
<th>Noncompetitive inhibitor</th>
</tr>
</thead>
<tbody>
<tr>
<td>Competitive inhibitors interfere with active site directly.</td>
<td>Noncompetitive inhibitors are allosteric inhibitors that change the shape of an enzyme so the substrate cannot bind to the active site.</td>
</tr>
<tr>
<td><img src="image6" alt="Diagram of competitive inhibitor" /></td>
<td><img src="image7" alt="Diagram of noncompetitive inhibitor" /></td>
</tr>
<tr>
<td><img src="image8" alt="Diagram of substrate access blocked" /></td>
<td><img src="image9" alt="Diagram of active site shape change" /></td>
</tr>
</tbody>
</table>

**INTEGRATE**

**CLINICAL VIEW 3.2 Lactose Intolerance**

Lactase is an enzyme required to break the bond in the disaccharide lactose (milk sugar) into glucose and galactose for its absorption from the digestive tract into the blood. **Lactose intolerance** (the inability to break down lactose) is caused by either a deficiency in the enzyme lactase or an abnormal (low-functioning) lactase enzyme. Differences in lactase enzyme function are due to genetic variation within the population. For example, individuals of northern European descent have a low incidence of lactose intolerance. Lactose intolerance is also more common in older adults because they produce less lactase over time. Abdominal upset including nausea, diarrhea, bloating, and gas are the most common symptoms. Avoidance of foods containing milk, drinking milk with lactose removed (lactose-free milk), or the oral administration of products containing lactase enzymes are recommended to avoid symptoms of lactose intolerance.

Lactase is embedded in the plasma membrane of cells lining the small intestine.
 Components of the cell associated with glucose oxidation include the cytosol, where the enzymes for glycolysis are located, and mitochondria, where the enzymes for aerobic cellular respiration (intermediate stage, citric acid cycle, and electron transport system) are housed.

**Cellular Location** The complete oxidation of glucose requires at least 20 different enzymes that are located in both the cell’s cytosol and its mitochondria (Figure 3.15). Cytosol is the semifluid contents of the cell. Mitochondria (sing., mitochondrion) are small organelles within the cell, described in section 3.4c.

**Four Stages of Cellular Respiration** We separate the processes of glucose oxidation into four stages: glycolysis, intermediate stage, citric acid cycle, and electron transport system. Glycolysis occurs in the cytosol and does not require oxygen; thus, glycolysis can occur either in the presence of oxygen or in the absence of oxygen. The other three stages occur in the mitochondria and require oxygen to proceed.

---

**LEARNING STRATEGY**

Keep in mind the following questions as you read through each of the first three stages of cellular respiration (the stages required for completely oxidizing (disassembling) glucose):

1. Does it occur in the cytosol or mitochondria of a cell?
2. Does it require oxygen (i.e., is it aerobic)?
3. What are the initial substrate and the final product?
4. Is energy released to produce ATP directly (substrate-level phosphorylation), transferred to a coenzyme that serves as a “temporary holder” that will participate in oxidative phosphorylation, or both?

---

**WHAT DID YOU LEARN?**

17. Write the overall chemical reaction for glucose oxidation, and explain the general process of what is occurring.
18. What are the four stages of cellular respiration for glucose oxidation, and where does each occur in the cell?
**3.4b Glycolysis**

**LEARNING OBJECTIVE**

31. Summarize the metabolic pathway of glycolysis, including (a) where it occurs in a cell, (b) if it requires oxygen, (c) the initial substrate and final product, and (d) the molecules formed during energy transfer.

**Glycolysis** (glk-kol′i-sis; glykys = sweet, lysis = loosening) does not require oxygen. Ten enzymes within the cytosol of a cell participate in the metabolic pathway of glycolysis. Glucose is broken down in this pathway into two pyruvate molecules with an accompanying energy transfer to form a net production of 2 ATP molecules and 2 NADH molecules.

**Steps of Glycolysis**

The 10 enzymatically regulated chemical reactions of glycolysis are shown in figure 3.16; both an overview figure (figure a) and the detailed steps (figure b) are included. Note that steps 1 through 5 occur once per glucose, and steps 6 through 10 occur twice per glucose because glucose is split into two three-carbon molecules.

1–5 Steps 1 through 5 of glycolysis involve splitting glucose into two molecules of glyceraldehyde 3-phosphate (G3P) through the action of the first five enzymes. ATP is “invested” when kinase enzymes transfer P_i from ATP to glucose and the breakdown products of glucose (steps 1 and 3). Thus, an investment of 2 ATP molecules occurs at these two steps.

6–7 Steps 6 and 7 of glycolysis occur twice in oxidation of a glucose molecule. Step 6 involves transferring an unattached P_i to the substrate (so this molecule now has two phosphates), and two hydrogen atoms are released to NAD^+ to form an NADH (and H^+). This transfer of hydrogen is catalyzed by a hydride enzyme. In step 7, the original P_i is transferred to ADP to form ATP through substrate-level phosphorylation by a kinase enzyme. Steps 8 through 10 of glycolysis also occur twice in oxidation of a glucose molecule. These steps involve converting the molecule produced in step 7 to an isomer (step 8) and then the loss of a water molecule (step 9). The remaining P_i is transferred to ADP to form ATP through substrate-level phosphorylation by a kinase enzyme (step 10), forming the final product of pyruvate.

**WHAT DO YOU THINK?**

3 What is the net energy transfer during glycolysis?

**Summary of Glycolysis**

Glycolysis is a metabolic process that occurs in the cytosol without the requirement of oxygen. Glucose is the initial substrate and pyruvate is the final product. The net transfer of energy is used in the formation of 2 ATP and 2 NADH molecules.

- **Formation of ATP.** Two ATP molecules are invested early in glycolysis (steps 1 and 3). Four ATP molecules are formed during glycolysis (steps 7 and 10, which occur twice per the original glucose molecule). Thus, there is a net of 2 ATP molecules formed during glycolysis (2 ATP invested, 4 ATP formed).
- **Formation of NADH.** Two NADH molecules are formed from glucose breakdown during glycolysis (step 6, which occurs twice per the original glucose molecule).
Regulation of Glycolysis

Glycolysis is regulated through negative feedback, like many metabolic pathways. ATP acts as an allosteric inhibitor to “turn off” phosphofructokinase (PFK) (step 3).

As ATP levels increase in the cell cytosol, ATP binding inhibits PFK, and the glycolytic pathway is progressively shut down. In contrast, as ATP decreases, glycolysis increases. Phosphofructokinase is also regulated in a similar way by other substances that indicate the “energy status” of the cell, including NADH, citrate (an intermediate in the citric acid cycle), fatty acids, and other fuel molecules. Increased levels of these substances result in a decrease in the processes of glycolysis.

The Fate of Pyruvate

Pyruvate is the final product of glycolysis. What chemical changes are then made to pyruvate depend upon the availability of oxygen. If sufficient oxygen is available, pyruvate enters a mitochondrion to complete its aerobic breakdown yielding carbon dioxide and water (described next). In contrast, if sufficient oxygen is not available, pyruvate is converted to lactate (described in section 3.4g).

WHAT DID YOU LEARN?

19. Describe glycolysis—where it occurs, if the process requires oxygen (i.e., is aerobic), the net chemical reaction, and the net energy transfer.

20. What are the two general fates of pyruvate, and what is the criterion that determines its fate?

3.4c Intermediate Stage

LEARNING OBJECTIVES

32. Explain the enzymatic reaction of the intermediate stage, including (a) where it occurs in a cell, (b) if it requires oxygen, (c) the initial substrate and final product, and (d) the molecules formed during energy transfer.

33. Define decarboxylation.

The remaining stages of cellular respiration, including the intermediate stage, citric acid cycle, and electron transport system, are aerobic processes that occur within mitochondria.

Mitochondrion Structure

A mitochondrion is a double-membrane organelle, composed of an outer membrane and an inner membrane that has inward folds called cristae (figure 3.17a). The fluid-filled space between the two membranes is the outer compartment. The innermost space in a mitochondrion is called the matrix. Both the multienzyme complex of the intermediate stage and the enzymes of the citric acid cycle metabolic pathway reside in the matrix. The significant molecules that participate in the electron transport system are embedded in the cristae.

Intermediate Stage and Pyruvate Dehydrogenase

The intermediate stage (figure 3.17b) is the “link” between the multistep metabolic processes of glycolysis (first stage) and the multistep metabolic processes that occur in the citric acid cycle (third stage). The intermediate stage is catalyzed by a multienzyme complex called pyruvate dehydrogenase.

During the intermediate stage, pyruvate dehydrogenase brings together pyruvate and a molecule of coenzyme A (CoA) that is already present within the matrix to form acetyl CoA (a two-carbon molecule with CoA attached). Concurrently, a carboxyl group, consisting of one carbon atom and two oxygen atoms, is released from the pyruvate as CO₂. This process is termed decarboxylation (dé’kar-bok’si-lā’shūn; de = away). Energy is released during decarboxylation as two hydrogen atoms (two electrons plus two hydrogen ions) are transferred to the coenzyme NAD⁺ to form NADH (and H⁺) during this process. The acetyl CoA then enters the third stage of glucose oxidation, termed the citric acid cycle.

Note that the intermediate stage must occur twice for the complete digestion of the original glucose molecule because two pyruvate molecules were produced from each glucose that went through glycolysis. Thus, two NADH are produced from the original glucose molecule.

WHAT DID YOU LEARN?

21. Explain the enzymatic reaction involving pyruvate dehydrogenase in the intermediate stage—where it occurs, if the process requires oxygen, the net chemical reaction, and the net energy transfer.

3.4d Citric Acid Cycle

LEARNING OBJECTIVE

34. Summarize the metabolic pathway of the citric acid cycle, including (a) where it occurs in a cell, (b) if it requires oxygen, (c) the initial substrate and final product, and (d) the molecules formed during energy transfer.

The citric acid cycle (also known as the Krebs cycle) is a cyclic metabolic pathway that occurs through the activity of nine enzymes located within the matrix of mitochondria. During the citric acid cycle, the acetyl CoA produced in the intermediate stage is converted...
to two CO₂ molecules and a CoA molecule is released. Energy is transferred to form 1 ATP molecule, 3 NADH molecules, and 1 FADH₂ molecule during one “turn” of the citric acid cycle.

**Steps of the Citric Acid Cycle**

The nine enzymatic steps of the citric acid cycle are shown in figure 3.18; both an overview figure and the detailed steps are included.

1. Step 1 of the citric acid cycle uses the first enzyme to combine an acetyl CoA molecule produced in the intermediate stage with a molecule of oxaloacetate (ok′s-ă-lo-ă-sē′tät) to form citrate. (Note that the addition of a hydrogen ion to citrate forms citric acid.) The first step of this cycle gives this enzymatic pathway its name.

---

**Figure 3.18 Citric Acid Cycle.** The citric acid cycle is the metabolic pathway that occurs within the matrix of mitochondria for the chemical breakdown of acetyl CoA with the net transfer of energy to form 1 ATP, 3 NADH, and 1 FADH₂ molecules. (a) An overview of the citric acid cycle. (b) The detailed pathway of the citric acid cycle.
Steps 2 and 3 of the citric acid cycle form an isomer by removing a water molecule from citrate and then reattaching it to a different location on the molecule.

Steps 4 and 5 of the citric acid cycle occur through two different dehydrogenase enzymes that participate in the transfer of hydrogen to NAD⁺ to form NADH. CoA is also attached during step 5.

Step 6 of the citric acid cycle involves the removal of CoA and the formation of ATP through substrate-level phosphorylation.

Step 7 of the citric acid cycle occurs through the action of a dehydrogenase that transfers hydrogens to FAD to form FADH₂.

Step 8 of the citric acid cycle is the removal of water.

Step 9 of the citric acid cycle is catalyzed by a dehydrogenase that transfers hydrogen to NAD⁺ to form NADH. Oxaloacetate (OAA) is regenerated in this final step.

**Summary of the Citric Acid Cycle**

The citric acid cycle is a metabolic process that occurs in mitochondria and requires oxygen. Acetyl CoA is the initial substrate and 2 CO₂ molecules and 1 CoA molecule are the products. The net transfer of energy produced in this cycle is used to form 1 ATP molecule, 3 NADH molecules, and 1 FADH₂ molecule.

- **Formation of ATP.** One ATP molecule is formed during the citric acid cycle (step 6) through substrate-level phosphorylation.
- **Formation of NADH.** Three NADH molecules are formed during the citric acid cycle (steps 4, 5, and 9).
- **Formation of FADH₂.** One FADH₂ molecule is formed during the citric acid cycle (step 7).

**WHAT DO YOU THINK?**

Why is the enzymatic pathway of the citric acid cycle considered to be a “cycle”?

This enzymatic pathway is called a “cycle” because oxaloacetate is involved in the first step and is regenerated in the last step. Note that two “turns” of the citric acid cycle must also occur for the complete breakdown of the original glucose molecule (one per each acetyl CoA generated from the original glucose molecule). Consequently, the number of high-energy molecules produced within the citric acid cycle from 1 glucose molecule is 2 ATP molecules, 6 NADH molecules, and 2 FADH₂ molecules.

**Regulation of the Citric Acid Cycle**

Regulation of the citric acid cycle occurs primarily at the enzyme in the first step of the citric acid cycle (citrate synthetase). The levels of NADH, ATP, and pathway intermediates are the primary regulators of citrate synthetase activity. A low level of NADH, ATP, and pathway intermediates indicates that cellular energy demands are high. This results in increased activity of citrate synthetase and the citric acid cycle. In contrast, a high level of NADH, ATP, and pathway intermediates indicates that cellular energy demands are low. This results in decreased activity of citrate synthetase and the citric acid cycle. These physiologic adjustments help maintain homeostatic levels of ATP molecules.

**Completion of Glucose Digestion**

Following glycolysis and two “turns” through both the intermediate stage (which generates 2 CO₂ molecules) and the citric acid cycle (which produces 4 CO₂ molecules), glucose has been completely digested and the 6 carbon atoms of glucose (C₆H₁₂O₆) have been released as 6 CO₂ molecules. Notice that the carbon atoms in the glucose (and other fuel molecules) that you eat are converted to carbon dioxide within the mitochondria of your cells.

**Summary of the Chemical Breakdown of Glucose**

Table 3.3 provides a summary of each of the first three stages of glucose oxidation that result in the chemical breakdown of glucose into carbon dioxide. The critical aspects of this process include:

- **Glycolysis.** Glycolysis occurs in the cytosol and does not require oxygen. Energy is transferred to form 2 ATP molecules (net) and 2 NADH molecules. If sufficient oxygen is available, the pyruvate formed enters a mitochondrion and is further metabolized in the intermediate stage and the citric acid cycle.

- **The intermediate stage.** The intermediate stage occurs in a mitochondrion and requires oxygen. It involves a multienzyme complex that converts pyruvate to acetyl CoA and 1 CO₂ molecule. Energy is transferred to form 1 NADH molecule. Remember, 1 NADH molecule is formed per pyruvate entering the intermediate stage. Recall that 2 pyruvates are produced from 1 glucose molecule. Thus, the intermediate stage must occur twice—so a total of 2 NADH molecules are formed from the original glucose molecule.

- **The citric acid cycle.** The citric acid cycle also occurs in a mitochondrion, requires oxygen, and completes the breakdown of glucose. Two CO₂ molecules are produced per turn of the cycle. Energy is transferred during this process to form 1 ATP, 3 NADH, and 1 FADH₂. Remember, this reflects the energy transferred per each acetyl CoA entering the citric acid cycle. Two acetyl CoA molecules are produced from 1 glucose molecule. Thus, the citric acid cycle must occur twice—so a total of 2 ATP, 6 NADH, and 2 FADH₂ are formed from the original glucose molecule.

Thus, through glycolysis and two turns of both the intermediate stage and the citric acid cycle, the 6 carbons in the original glucose have
been released as 6 CO₂ molecules and the energy has been transferred to form

| Glycolysis | → 2 ATP  | 2 NADH |
| Intermediate stage | → 2 NADH |
| Citric acid cycle | → 2 ATP  | 6 NADH  | 2 FADH₂ |

### WHAT DID YOU LEARN?

22. Summarize the metabolic pathway of the citric acid cycle—where it occurs, if the process requires oxygen, the net chemical reaction, and the net energy transfer.

23. What energy molecules are produced from the chemical breakdown of glucose during each of the three steps of cellular respiration?

### 3.4e The Electron Transport System

#### LEARNING OBJECTIVES

35. Describe the importance of NADH and FADH₂ in energy transfer.

36. Explain the actions that take place in the electron transport system.

Given that the breakdown of glucose is completed by the end of the citric acid cycle, what is the function of the electron transport system, the final stage of cellular respiration? The electron transport system involves the transfer of electrons (energy) from the coenzymes NADH and FADH₂; that are produced during the first three stages of cellular respiration. The energy released from these coenzymes is used to form ATP. This is a critical stage in cellular respiration because most of the energy captured in glucose oxidation is initially transferred to form NADH from NAD⁺, as well as the smaller amounts of energy to form FADH₂ from FAD. Thus, it is through the electron transport system that the majority of chemical energy that was originally in the glucose molecule and transferred to the coenzymes (in the previous three stages of cellular respiration) is now released from the coenzymes and transferred to form the high energy bond between ADP and Pᵢ as ATP is synthesized. The electron transport system involves structures located in the inner folded membrane (or cristae) of mitochondria.

#### Structures of the Electron Transport System

Several significant types of molecules are embedded within the cristae of the mitochondria: H⁺ pumps, electron carriers, and ATP synthase enzymes (figure 3.19). H⁺ pumps are proteins that transport H⁺ from the matrix to the outer membrane compartment. This maintains a H⁺ gradient between the outer compartment and the matrix within a mitochondrion, with more H⁺ in the outer compartment than in the matrix. H⁺ pumps also bind and release electrons (e⁻).

Electron carriers ubiquinone (Q) and cytochrome c (C) are located between proteins serving as H⁺ pumps. Electron carriers transport electrons (e⁻) between the H⁺ pumps. You may be familiar with these electron carriers because they are purchased as antioxidant supplements by cyclists, bodybuilders, and other athletes (e.g., CoQ10 as a ubiquinone supplement).

This series of H⁺ pumps and electron carriers is collectively called the electron transport chain. ATP synthase allows for the passage of H⁺ from the outer compartment back into the matrix. During this process, the kinetic energy from the flow of H⁺ down its concentration gradient is harnessed to bond Pᵢ to ADP to form ATP.

#### Steps of the Electron Transport System

The processes of the electron transport system are organized into three major steps (figure 3.19):

1. **Electrons are transferred from coenzymes to O₂.** The coenzyme, either NADH or FADH₂, releases hydrogen (e⁻ and H⁺) and it is oxidized. The released electrons are...
passed through the electron transport chain to O$_2$, which serves as the final electron acceptor. O$_2$ combines with $4 \text{e}^- + 4 \text{H}^+$ to produce two molecules of H$_2$O. Thus, oxygen is a reactant in cellular respiration, and it becomes part of the water that is produced. Notice that the oxygen you breathe is converted to water within the mitochondria of your cells!

**Proton gradient is established.** As electrons are “falling” and passed through the electron transport chain, their kinetic energy is harnessed by H$^+$ pumps to move H$^+$ from the mitochondrial matrix into the outer compartment, maintaining a proton gradient.

**Proton gradient is harnessed to form ATP.** H$^+$ moves down its concentration gradient as it is transported across the inner membrane by ATP synthase. It moves from the outer compartment into the matrix. (Note that H$^+$ moves back into the area of the mitochondrion from which it was just pumped.) This process is analogous to water falling over a dam and turning a water wheel. The kinetic energy of the falling H$^+$ is harnessed by ATP synthase to form a new bond between ADP and P$_i$, producing an ATP.

The process of forming ATP is referred to as **oxidative phosphorylation** because it involves oxygen as the final electron acceptor, and ATP is formed from the phosphorylation of ADP. This process is distinguished from substrate-level phosphorylation, which forms ATP from energy directly released from a substrate, as occurs in specific steps of glycolysis (see figure 3.16, steps 7 and 10) and the citric acid cycle (see figure 3.18, step 6). The steps of cellular respiration are summarized in **figure 3.20**.

**WHAT DID YOU LEARN?**

**24** What is the importance of NADH and FADH$_2$ in energy transfer?

**25** What are the three primary steps that take place in the electron transport system?
3.4f ATP Production

**LEARNING OBJECTIVE**

37. Calculate the number of ATP molecules produced in cellular respiration if oxygen is not available and if oxygen is available.

The number of ATP molecules generated when electrons are released from coenzymes is dependent upon the entry point of the electrons into the electron transport chain (figure 3.19). The electrons from NADH enter at the top of the electron transport chain and are passed through three \( \text{H}^+ \) pumps, which results in enough energy being released to generate 3 ATP molecules. In contrast, the electrons from \( \text{FADH}_2 \) enter at the second \( \text{H}^+ \) pump; this results in the generation of 2 ATP molecules. Consequently, each NADH generates 3 ATP and each \( \text{FADH}_2 \) generates 2 ATP.

**WHAT DO YOU THINK?**

3. Given that energy from each NADH produces 3 ATP molecules and each \( \text{FADH}_2 \) produces 2 ATP molecules, calculate the number of ATP molecules generated from glucose during cellular respiration.

We are able to calculate the specific number of ATP molecules produced in breakdown of a glucose molecule by knowing the following: (1) the specific number of energy molecules (i.e., ATP, NADH, and \( \text{FADH}_2 \)) that are generated from glucose breakdown in each of the first three stages of cellular respiration and (2) the specific number of ATP generated by the oxidation of each type of coenzyme in the electron transport system (NADH = 3 ATP molecules and \( \text{FADH}_2 \) = 2 ATP molecules).

The following is a summary of the number of ATP molecules produced by substrate-level phosphorylation and the number of ATP produced by oxidative phosphorylation from glucose oxidation.

<table>
<thead>
<tr>
<th>Stage/Total</th>
<th>Substrate-Level Phosphorylation</th>
<th>Oxidative Phosphorylation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glycolysis</td>
<td>2 ATP</td>
<td>2 NADH \rightarrow 6 ATP</td>
</tr>
<tr>
<td>Intermediate stage</td>
<td>—</td>
<td>2 NADH \rightarrow 6 ATP</td>
</tr>
<tr>
<td>Citric acid cycle</td>
<td>2 ATP</td>
<td>6 NADH \rightarrow 18 ATP</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2 ( \text{FADH}_2 ) \rightarrow 4 ATP</td>
</tr>
<tr>
<td>Total Number of ATP/</td>
<td>4 ATP</td>
<td>34 ATP</td>
</tr>
<tr>
<td>Based on Method of</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Formation</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

In theory, the total ATP produced from 1 glucose molecule is 38 ATP. However—and this is very important for energy totals—the actual net yield is lower. There are several energy-requiring steps for transporting molecules during cellular respiration that decrease the actual net ATP produced. These energy-requiring processes include moving (1) pyruvate from the cytosol into mitochondria, (2) phosphate and ADP into mitochondria for its use in ATP synthesis, and (3) NADH produced during glycolysis into mitochondria for oxidative phosphorylation in the electron transport system. Note: The net ATP produced from a glucose molecule is 30 ATP.

**WHAT DID YOU LEARN?**

26. How many net ATP molecules are generated through glycolysis (i.e., without participation of mitochondrial)? How many net ATP molecules are formed through the combined processes that occur in the cytosol and those that occur within mitochondria?

3.4g The Fate of Pyruvate with Insufficient Oxygen

**LEARNING OBJECTIVES**

38. Explain the fate of pyruvate when oxygen is in short supply.

39. Describe the impact on ATP production if there is insufficient oxygen.

We followed pyruvate in the previous discussion assuming that sufficient oxygen was present for oxidative phosphorylation to occur within mitochondria. If sufficient oxygen is not available, we must consider the following:

1. Cellular respiration processes requiring oxygen (i.e., aerobic cellular respiration) decrease, including the activity of the electron transport chain. Electrons remain with the NADH and \( \text{FADH}_2 \) molecules and NADH and \( \text{FADH}_2 \) accumulate. This is accompanied by decreased levels of \( \text{NAD}^+ \) and FAD.
2. The cell becomes increasingly dependent upon glycolysis, a metabolic pathway that requires \( \text{NAD}^+ \) to continue.
3. Extended low-oxygen conditions would ultimately result in the complete shutdown of glycolysis within the cell because of the lack of \( \text{NAD}^+ \).
4. \( \text{NAD}^+ \) must be regenerated if glycolysis is to continue.

Regenerating \( \text{NAD}^+ \) involves the transfer of hydrogen from NADH. Two electrons and hydrogen are transferred from NADH to pyruvate, which is converted to lactate. (Note that the addition of a hydrogen ion to lactate forms lactic acid.) This enzymatic reaction is catalyzed by lactate dehydrogenase (figure 3.21).

Although this process is an effective means to permit glycolysis to continue (because it makes \( \text{NAD}^+ \) available), we must keep in mind that without the availability and use of mitochondria, only 2 ATP are produced per glucose. Compared to the net 30 ATP produced with sufficient oxygen, there is significantly less ATP generated (2 ATP.

**Figure 3.21 Conversion of Pyruvate to Lactate.** Lactate dehydrogenase converts pyruvate to lactate to regenerate \( \text{NAD}^+ \) molecules.
versus 30 ATP). This is a 15-fold difference! Remember this important association: Low O₂ equals low energy. So, in clinical practice when you work with individuals with decreased ability to deliver oxygen to cells (e.g., those with impaired respiratory or cardiovascular function), keep in mind that they will have less available ATP to meet the body’s energy needs.

**WHAT DID YOU LEARN?**

27. Pyruvate is converted to what molecule if there is insufficient oxygen? Explain why this occurs.

### 3.4h Other Fuel Molecules That Are Oxidized in Cellular Respiration

**LEARNING OBJECTIVE**

40. Describe the entry point in the metabolic pathway of cellular respiration for both fatty acids and amino acids.

There are other fuel molecules, such as fatty acids and amino acids that may be oxidized to generate ATP (see figure 27.6).

Fatty acids are enzymatically changed two carbon units at a time to form acetyl CoA. This process is called beta-oxidation. Acetyl CoA then enters the cell respiration metabolic pathway at the citric acid cycle. Because fatty acids enter this metabolic pathway in the mitochondria, they can only be oxidized aerobically. (Note that a by-product of fatty acid metabolism is the production of ketoacids, with significant amounts produced in individuals with uncontrolled diabetes mellitus; see Clinical View 25.7: “Lactic Acidosis and Ketoacidosis”).

A different pathway is employed if protein is used for fuel. The point of entry of deaminated amino acids (amino acids with the amine group [–NH₂] removed) is dependent upon the specific type of amino acids. Different amino acids enter the metabolic pathway at glycolysis, the intermediate stage, or the citric acid cycle. The amine group is a waste product that is converted to urea and excreted by the kidneys.

**WHAT DID YOU LEARN?**

28. Why is oxygen required to burn fatty acids?

### INTEGRATE

**CONCEPT CONNECTION**

What happens to the increased levels of lactate produced by skeletal muscle tissue? Lactate is either absorbed by surrounding muscle tissue or transported by the blood to the liver. Muscle cells may use lactate immediately for ATP synthesis by either converting it back to pyruvate or converting it to glucose and storing it as glycogen. Liver cells convert lactate into glucose. Glucose formed in the liver is either stored as glycogen in the liver or released back into the blood (for muscles or other cells to take up). This cycling of lactate from muscles to the liver, the conversion of lactate to glucose, and the subsequent transport of glucose from the liver to muscle is called the Cori cycle.

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### CHAPTER SUMMARY

- The concepts discussed are energy, chemical reactions, enzymes, metabolic pathways, and the production of ATP through cellular respiration.

### 3.1 Energy

- **Energy** is the capacity to do work.

#### 3.1a Classes of Energy

- Energy exists in two classes: energy based upon position, called potential energy, and energy of motion, called kinetic energy.
- Energy can be converted from potential energy to kinetic energy (or vice versa). Examples are the movement of a substance down its concentration gradient and the movement of electrons from a higher-energy state to a lower-energy state.

#### 3.1b Forms of Energy

- Energy exists in different forms, including chemical, electrical, mechanical, sound, radiant, and heat.

#### 3.1c Laws of Thermodynamics

- The first law of thermodynamics states that energy cannot be created or destroyed, only converted from one form to another.
- The second law of thermodynamics states that some energy is lost as heat with every energy conversion.

### 3.2 Chemical Reactions

- Chemical reactions are expressed in chemical equations and are classified using various criteria.

#### 3.2a Chemical Equations

- **Metabolism** is the collective term for all biochemical reactions that occur within the body.
- Reactants become products in a chemical reaction, and an arrow indicates the direction of change.

#### 3.2b Classification of Chemical Reactions

- Chemical reactions can be classified using different criteria: change in chemical structure, change in chemical energy, and if the reaction is irreversible or reversible.

#### 3.2c Reaction Rates and Activation Energy

- Reaction rate is the measure of how quickly a chemical reaction takes place; this determines the amount of product formed per unit of time.
- Activation energy is the energy required to break existing chemical bonds for the chemical reaction to proceed.
3.3 Enzymes

3.3a Function of Enzymes
- Enzymes facilitate chemical reactions.

3.3b Enzyme Structure and Location
- Generally, enzymes are globular proteins with an active site that bind a specific substrate. Enzymes can be located within cells, embedded in the plasma membrane, or present in fluid outside of cells.

3.3c Mechanism of Enzyme Action
- Enzymes are catalysts that participate in both decomposition and synthesis reactions.

3.3d Classification and Naming of Enzymes
- Enzymes are usually named based upon the name of the substrate, product, or type of chemical reaction (as indicated by the enzyme class or subclass) and contain the -ase suffix.

3.3e Enzymes and Reaction Rates
- The reaction rate is dependent upon the concentrations of both the enzyme and substrate, temperature, and pH.

3.3f Controlling Enzymes
- Enzymes can be controlled by either competitive inhibitors or noncompetitive inhibitors.

3.3g Metabolic Pathways and Multienzyme Complexes
- A metabolic pathway involves numerous enzymes that subsequently convert a substrate to a final product. Metabolic pathways are regulated by negative feedback to maintain the needed amount of the final product.
- A multienzyme complex is a structure composed of enzymes physically linked to convert a substrate to a final product.
- Phosphorylation is the addition of a phosphate group, and dephosphorylation is the removal of a phosphate group. This is a common means of regulating enzymes.

3.4 Cellular Respiration

3.4a Overview of Glucose Oxidation
- The net chemical reaction for glucose oxidation is \( C_6H_{12}O_6 + 6 \ O_2 \rightarrow 6 \ CO_2 + 6 \ H_2O \).
- ATP is produced directly through substrate-level phosphorylation and indirectly by oxidative phosphorylation.
- Glucose oxidation occurs within a cell: glycolysis within the cytosol and aerobic cellular respiration (the intermediate stage, the citric acid cycle, and the electron transport system) within mitochondria.

3.4b Glycolysis
- Glycolysis, which occurs within the cytosol, is a metabolic pathway that uses 10 enzymes and does not require oxygen. Glucose is converted to 2 pyruvate molecules, producing 2 net ATP and 2 NADH per glucose.
- The fate of pyruvate is dependent upon the availability of oxygen.

3.4c Intermediate Stage
- In the intermediate stage, which occurs within mitochondria, the multienzyme complex pyruvate dehydrogenase converts pyruvate to acetyl CoA and releases 1 CO\(_2\) (by decarboxylation). One NADH is produced per pyruvate.
- The intermediate stage occurs twice per the original glucose.

3.4d Citric Acid Cycle
- The citric acid cycle, which also occurs within mitochondria, is a metabolic pathway that breaks down acetyl CoA with 2 CO\(_2\) and CoA released. One ATP molecule, 3 NADH molecules, and 1 FADH\(_2\) molecule are produced per acetyl CoA.
- The citric acid cycle occurs twice per the original glucose and completes the digestion of glucose.

3.4e The Electron Transport System
- The electron transport system involves several significant structures that are embedded in the cristae membrane of a mitochondrion, including H\(^+\) pumps, electron carriers, and the enzyme ATP synthase.
- Electrons from NADH and FADH\(_2\) are transferred to electron carriers in the electron transport chain of a mitochondrion, and ultimately to O\(_2\). The electrons, oxygen, and hydrogen ions form H\(_2\)O.
- A H\(^+\) ion gradient is formed; H\(^+\) ions then flow down this gradient and the energy is harnessed by ATP synthase to produce ATP through oxidative phosphorylation.

3.4f ATP Production
- Glucose oxidation produces a net of 2 ATP in glycolysis and 30 ATP in the complete breakdown of glucose.

3.4g The Fate of Pyruvate with Insufficient Oxygen
- If insufficient oxygen is available, pyruvate will be converted by lactate dehydrogenase to lactate to regenerate NAD\(^+\) so glycolysis can continue.

3.4h Other Fuel Molecules That Are Oxidized in Cellular Respiration
- The digestion of other fuel molecules, such as fatty acids and amino acids, can also be oxidized to generate ATP.
1. Energy in ATP is used to power skeletal muscle contraction. This is an example of what type of energy conversion?
   a. chemical energy to mechanical energy
   b. light energy to mechanical energy
   c. chemical energy to light energy
   d. electrical energy to chemical energy

2. Oxidation-reduction can be best classified as a(n) ______ reaction.
   a. exchange
   b. endergonic
   c. synthesis
   d. reversible

3. All of the following increase enzymatic activity except
   a. an increase in temperature.
   b. an increase in pH.
   c. an increase in concentration of the substrate.
   d. an increase in concentration of the enzyme that catalyzes the reaction.

4. ATP inhibits phosphofructokinase by binding to an allosteric site in glycolysis. ATP is functioning as a
   a. competitive inhibitor.
   b. competitive activator.
   c. noncompetitive inhibitor.
   d. noncompetitive activator.

5. All of the following are accurate about enzymes except
   a. enzymes are typically globular proteins with an active site.
   b. enzymes decrease activation energy.
   c. enzymes can be used over and over to catalyze a substrate to a product.
   d. enzymes are versatile and can catalyze different types of chemical reactions.

6. Glucose is converted to pyruvate in which stage of cellular respiration?
   a. glycolysis
   b. intermediate stage
   c. citric acid cycle
   d. electron transport system

7. NAD⁺ and FAD are examples of
   a. enzymes.
   b. high-energy organic molecules that are digested in cellular respiration.
   c. allosteric inhibitors, which participate in regulating enzymes.
   d. coenzymes that are required by some enzymes to function.

8. All stages of cellular respiration are decreased in conditions of insufficient oxygen except
   a. glycolysis.
   b. the intermediate stage.
   c. the citric acid cycle.
   d. the electron transport system.

9. In glycolysis, ______ ATP are formed, and if sufficient oxygen is present, ______ ATP are formed.
   a. 2, 2
   b. 36, 38
   c. 2, 30
   d. 10, 30

10. Oxidative phosphorylation involves
    a. electrons transported in the electron transport chain and accepted by O₂.
    b. ATP synthase harnessing the energy in a H⁺ gradient.
    c. coenzymes NADH and FADH₂ giving up their electrons.
    d. all of these processes.

11. List and define the different forms of energy, and give one example each of their application in the human body.

12. Describe the different ways of classifying chemical reactions, and explain the category to which oxidation-reduction belongs.

13. Explain ATP cycling.

14. Describe the structure and mechanism of enzymes.

15. Describe a metabolic pathway, and explain how it is controlled by negative feedback.

16. Summarize glycolysis, including where it occurs in a cell, if it requires oxygen, the substrate and final product, and the formation of energy-containing molecules (i.e., ATP, NADH, FADH₂).

17. In general terms, explain the fate of pyruvate if there is (a) sufficient oxygen and (b) insufficient oxygen.

18. Describe how oxygen becomes part of water during cellular respiration.

19. Identify the source of carbon in carbon dioxide.

20. Based on what you know about glycolysis and aerobic cellular respiration, explain the advantage in terms of ATP production of a healthy respiratory and cardiovascular system.

Can You Apply What You've Learned?

1. Albinism (achromia) is a genetic condition in which an individual cannot synthesize melanin from tyrosine (an amino acid), a brown pigment of the hair, skin, and eyes. These individuals lack
   a. specific fatty acids.
   b. a protein that contains tyrosine.
   c. an enzyme that converts tyrosine to melanin.
   d. cofactors that convert tyrosine to melanin.
2. If an individual has impaired respiratory function, as occurs with emphysema, you would expect all of the following except:
   a. production of additional lactate.
   b. an impaired ability to make ATP.
   c. low energy levels and complaints of being tired.
   d. increased aerobic cellular respiration.

3. Another challenge to a patient with impaired respiratory function is the buildup of CO$_2$ in the blood. What would you predict, given the following reversible enzymatic reaction that occurs in the blood?

   \[ 
   H_2O + CO_2 \rightleftharpoons H_2CO_3 \rightleftharpoons H^+ + HCO_3^- \n   \]
   a. increased production of H$_2$O
   b. increased production of H$^+$ (with an accompanying decrease in pH)
   c. decreased production of H$^+$ (with an accompanying increase in pH)
   d. all of the above

4. You would expect decreased production of ATP in all of the following individuals except
   a. an individual with impaired ability to transport oxygen in the blood, such as a person with anemia.
   b. an individual with severe asthma.
   c. an individual in congestive heart failure.
   d. an athlete.

5. Brown adipose tissue contains cells that allow H$^+$ to fall down the concentration gradient in the electron transport chain without producing ATP. Instead, all of the kinetic energy is converted to heat. If scientists could increase the amount of brown adipose tissue in our bodies, then
   a. our body temperature would be cooler than 98.6°F.
   b. brown adipose tissue cells would be more efficient at producing ATP.
   c. we could eat more and not gain weight.
   d. we would be able to run faster.

**Can You Synthesize What You’ve Learned?**

1. Tiffany had returned to her college dorm and was having difficulty breathing. She knew she was having an asthma attack. What changes in her energy level are predicted?

2. Provide a general explanation to a patient on the advantages of aerobic fitness in terms of ATP production.

3. What occurs to the amount of product formed in a metabolic pathway if inhibition does not occur?
Heart cells contract to pump blood out of the heart chambers; retinal cells of the eye detect light; phagocytic white blood cells engulf foreign substances (e.g., bacteria, viruses); and pancreatic cells synthesize and secrete the hormone insulin. All human body processes are ultimately dependent upon cells and their activities. For this reason, the cell is often referred to as the “functional unit of the body.” Knowledge of cellular structure and function is critical for understanding the concepts of all later chapters.

Throughout this chapter, we present a broad discussion of a cell by describing how cells are studied and the general structural components and functions of cells. Subsequent chapters examine specialized cells and provide details of their unique functions.
4.1 Introduction to Cells

Our examination of cells begins with a description of how we study them. We then describe how the cells that compose the human body vary in both size and shape, and that these differences reflect their specific function. This section concludes with a discussion of the common structural features all cells possess and the general functions that all cells must perform.

4.1a How Cells Are Studied

**LEARNING OBJECTIVE**

1. Distinguish among light microscopy, scanning electron microscopy, and transmission electron microscopy.

The study of cells is called **cytology** (sī-tō′l-ō-jē′; kyōtōs = a hollow [cell]). The small size of cells is the greatest obstacle to determining their nature. Cells were discovered after microscopes were invented because high-magnification microscopes are required to see the smallest human body cells.

**Microscopy** is the use of a microscope to view small-scale structures, and it is an invaluable asset in anatomic investigations. The most commonly used instruments are the light microscope, the scanning electron microscope, and the transmission electron microscope.

One of the challenges with viewing anatomic specimens with a microscope is that microscopy samples prepared from body tissues have no inherent contrast (difference between specimen and background). To provide contrast so microscopic structures can be seen more clearly, colored-dye stains are used with light microscopes, and heavy-metal stains are used with both scanning electron and transmission electron microscopes. **Figure 4.1** allows us to compare the images produced when each of these types of microscopes is used to examine the same specimen. Notice the remarkable difference between these images of the same body structure—in this case, hairlike cilia (see section 4.6c) on the inner lining of the respiratory tract.

The **light microscope** (LM) produces a two-dimensional image by passing visible light through the specimen stained with colored dyes. Glass lenses focus and magnify the image as it is projected toward the eye. A stained image of the magnified specimen is produced with an LM (figure 4.1a). A typical LM used in a college laboratory might magnify a specimen 40×, 100×, or 1000× (depending upon the objective lens that is used). The specimen in figure 4.1a is magnified 720× (as indicated on the side of the image).

The **electron microscope** (EM) uses a beam of electrons to “illuminate” the specimen stained with heavy metal. Electron microscopes easily exceed the magnification obtained by light microscopy—but more importantly, they improve the resolution (ability to see details) by more than a thousand-fold over the light microscope. A **scanning electron microscope** (SEM) directs electrons across the surface of a specimen to produce a three-dimensional image that is captured on a screen. An SEM allows us to visualize the specimen’s surface features (figure 4.1b). The specimen in figure 4.1b is magnified 3000×.

A **transmission electron microscope** (TEM) directs an electron beam through a thin-cut section of the specimen. A two-dimensional image of the specimen is focused either onto a screen or onto photographic film. A TEM allows us to visualize the details of the specimen’s internal structures (figure 4.1c). The specimen in figure 4.1c is magnified 50,000×!

**WHAT DID YOU LEARN?**

1. What is the advantage of using a TEM instead of an LM to study intracellular structure?

4.1b Cell Size and Shape

**LEARNING OBJECTIVES**

2. Describe the range in size of human cells.
3. Identify some of the shapes cells may exhibit.

Cells are typically depicted as being of one size and either spherical or cubelike in shape, when in reality the structure of the approximately 75 trillion cells of the adult human shows great variety. Most cells are microscopic in size, but some are large enough to be seen with the naked eye (figure 4.2). For example, red blood cells (erythrocytes) are relatively small with a diameter of about 7–8 μm, whereas a human oocyte has a diameter of about 120 μm. To help you to relate to how small some cells are, consider that about 5 million erythrocytes would fit on the head of a pin. Cells also vary greatly in shape (figure 4.3). Although some cells are spherical or

![Figure 4.1 Microscopic Techniques for Cellular Studies](image-url)
**Figure 4.2** The Range of Cell Sizes. Most cells in the human body are between 1 micrometer (μm) and 100 μm in diameter.

**Figure 4.3** The Variety of Cell Shapes. Cells throughout the body exhibit different shapes that support various functions.

cubelike, others are columnlike, cylindrical, disc-shaped, or irregular-shaped. Note that a relationship exists between the size and shape of a cell and its function in the body.

WHAT DID YOU LEARN?

2. Which cell is larger, an erythrocyte or a human oocyte? What are their respective sizes?

4.1c Common Features and General Functions

**LEARNING OBJECTIVES**

4. Describe the three main structural features of a cell.
5. Identify the membrane-bound and non-membrane-bound organelles.
6. Distinguish between organelles and cell inclusions.
7. Explain the general functions that cells must perform.

Most cells are composed of characteristic parts that work together to allow each cell type in the body to perform certain common functions.

Overview of Cellular Components

The generalized cell shown in figure 4.4 is not an actual body cell, but rather a representation of a cell that combines features of different types of body cells. The common features include the following:

- **Plasma membrane.** The plasma (plaz’mə; plasso = to form) membrane is the cell membrane that forms the outer, limiting barrier (of approximately 5–10 nm) that separates
the internal contents of the cell from the interstitial fluid (fluid that surrounds the cell). Modified extensions of the plasma membrane include cilia, a flagellum, and microvilli.

- **Nucleus.** The nucleus (nū′klē-əs; nux = the kernel) is the largest structure within the cell (approximately 5–10 μm in diameter) and is enclosed by a nuclear envelope. Much of the internal content of the nucleus is the genetic material, deoxyribonucleic acid (DNA). The fluid within the nucleus is called the nucleoplasm. Within the nucleus is a dark-staining body called the nucleolus.

- **Cytoplasm.** Cytoplasm (sī′tō-plazm; plasma = a thing formed) is a general term for all cellular contents located between the plasma membrane and the nucleus. The three primary components of the cytoplasm are the cytosol, organelles, and inclusions.

### Cytoplasmic Components

The cytosol (sī′tō-sōl; sol = soluble), also called the intracellular fluid (ICF) or cytoplasmic matrix, is the viscous, syruplike fluid of the cytoplasm. It has a high water content and contains many dissolved macromolecules that include carbohydrates, lipids, proteins, and small molecules such as glucose and amino acids. Cytosol also contains various types of ions, such as potassium ion (K⁺) and phosphate ion (PO₄³⁻).

**Organelles** (or′gă-nēl; organon = organ, elle = the diminutive suffix), meaning little organs, are complex, organized structures within cells that have unique characteristic shapes and functions. Two categories of organelles are recognized: membrane-bound organelles and non-membrane-bound organelles. **Membrane-bound organelles**, or membranous organelles, are enclosed by a membrane similar to the plasma membrane. The membrane separates the organelle’s contents from the cytosol so that the specific activities of the organelle can proceed without disruption from other cellular activities. Membrane-bound organelles include the endoplasmic

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**Figure 4.4 The Structure of a Cell.** This generalized cell illustrates most of the common features found in mature human cells, which include the plasma membrane, nucleus, and cytoplasm. Composing the cytoplasm is cytosol and organelles that are either membrane-bound or non-membrane-bound. Some cells also contain inclusions, which are temporary stores of specific molecules.
reticulum (rough and smooth), Golgi apparatus, lysosomes, peroxisomes, and mitochondria (figure 4.4). Vesicles are temporary membrane-bound structures formed from the endoplasmic reticulum, Golgi apparatus, and plasma membrane. The non-membrane-bound organelles, or nonmembranous organelles, are not enclosed within a membrane. These structures are generally composed of protein and include ribosomes (either attached [bound] to the external surface of the endoplasmic reticulum or free within the cytosol), the centrosome, proteasomes, and the cytoskeleton. Each of these organelles is discussed in detail in section 4.6.

The cytosol of some cells temporarily stores inclusions. Cell inclusions are not considered organelles, but rather are aggregates (clusters) of a single type of molecule. Molecules are continuously being added to and removed from inclusions. Pigments (e.g., melanin, a stored pigment in some skin, hair, and eye cells) and nutrient stores (e.g., glycogen in liver cells and triglycerides in adipose connective tissue) are examples of cell inclusions.

General Cell Functions

Cells must perform general functions, including:

- **Maintain integrity and shape of a cell.** The integrity and shape of a cell are dependent upon both the plasma membrane, which forms the external boundary of the cell, and the internal contents, which function to support the cell.
- **Obtain nutrients and form chemical building blocks.** Each cell must get nutrients and other needed substances from its surrounding fluid. Cells form new chemical structures and harvest the energy necessary for survival through diverse metabolic processes.
- **Dispose of wastes.** Cells must dispose of the waste products they produce so they do not accumulate and disrupt normal cellular activities.

In addition, some cells are capable of undergoing cell division to make more cells of the same type, as described in section 4.9. These new cells help to maintain the tissue or organ to which they belong by providing cells for new growth and replacing cells that die. However, during development, some cells do not retain this ability (e.g., most nerve cells typically do not; see section 12.2a).

WHAT DID YOU LEARN?

3. What are the three main structural features of a cell?

4. What cellular structure is responsible for forming the boundary of a cell and maintaining its integrity?

4.2 Chemical Structure of the Plasma Membrane

The plasma membrane is not a rigid boundary, but rather is a fluid matrix composed of approximately an equal mixture, by weight, of lipids and proteins. It regulates the movement of most substances both into and out of a cell.

4.2a Lipid Components

**LEARNING OBJECTIVE**

8. List the lipid components of the plasma membrane, and explain the actions of each component.

The plasma membrane contains several different types of lipids (see section 2.7b), including phospholipids, cholesterol, and glycolipids (figure 4.5).

Most of the plasma membrane lipids are phospholipids (see section 2.3c). Often these molecules are artistically portrayed in the membrane as an icon that looks similar to a balloon with two tails (see table 2.4). The balloon-like “head” is polar and hydrophilic. In contrast, the two “tails” are nonpolar and hydrophobic. Phospholipid molecules readily associate to form two parallel sheets of molecules lying tail-to-tail, with the hydrophobic tails forming the internal environment of the membrane and their hydrophilic polar heads positioned adjacent to either the cell’s cytoplasm or the interstitial fluid. This basic structure of the plasma membrane framework is called the phospholipid bilayer. The phospholipid bilayer ensures that cytosol remains inside the cell, and interstitial fluid remains outside.

**Cholesterol** is scattered within the inner hydrophobic regions of the phospholipid bilayer. It strengthens the membrane and stabilizes it at temperature extremes.

**Glycolipids** (glī′kō-lip′id; glykys = sweet) are lipids with attached carbohydrate groups. Each carbohydrate group of a glycolipid is attached to a phospholipid molecule located on the outer phospholipid layer of the plasma membrane. These carbohydrates extend like “sugar
antennae” from the cell’s external phospholipid surface, where they are exposed to the interstitial fluid. These molecules contribute to the glycocalyx, which is described at the end of this section.

The lipid portion of the plasma membrane is insoluble in water, which ensures that the plasma membrane will not simply dissolve when it comes into contact with water. Rather, this boundary is an effective nonpolar physical barrier to most substances. Only small and nonpolar substances can readily penetrate (move through) this barrier without assistance (see section 4.3a).

**WHAT DID YOU LEARN?**

How do lipids maintain the basic physical barrier of the plasma membrane?

### 4.2b Membrane Proteins

**LEARNING OBJECTIVES**

9. Differentiate between the two types of membrane proteins based upon their relative position in the plasma membrane.

10. Name the six major roles played by membrane proteins.

Although lipids form the main component of the plasma membrane, the proteins dispersed within the lipids make up about half of the plasma membrane by weight. Proteins can “float” and move about the phospholipid bilayer, much like a beach ball floating on the water surface in a swimming pool. Most of the membrane’s specific functions are determined by its resident proteins.
Membrane proteins are classified as one of two structural types: integral or peripheral. **Integral proteins** are embedded within, and extend completely across, the phospholipid bilayer (figure 4.5). Hydrophobic regions within the integral proteins interact with the hydrophobic interior of the membrane. In contrast, the hydrophilic regions of the integral proteins are exposed to the aqueous environments on either side of the membrane. Many integral membrane proteins are **glycoproteins** that have carbohydrates exposed to the interstitial fluid. These carbohydrates (like those of glycolipids) extend like “sugar antennae” from a cell’s external surface. In contrast, **peripheral proteins** are not embedded within the lipid bilayer. They are attached loosely to either the external or the internal surfaces of the membrane and are often “anchored” to the exposed parts of an integral protein.

Membrane proteins are also categorized functionally based upon the specific role they serve (figure 4.6).

- **Transport proteins** provide a means of regulating the movement of substances across the plasma membrane. Different types of transport proteins include **channels**, **carriers**, **pumps**, **symporters**, and **antiporters** (see section 4.3).
- **Cell surface receptors** bind specific molecules called ligands. **Ligands** are molecules that bind to macromolecules (e.g., binding to a receptor). An example of a ligand is a neurotransmitter released from a nerve cell that binds to the cell surface receptor of a muscle cell to initiate contraction (see section 10.3a).

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**Figure 4.6 Plasma Membrane Proteins.** The major functional categories of plasma membrane proteins include the several types of transport proteins (e.g., channels, carrier proteins, pumps), cell surface receptors, identity markers, enzymes, anchoring sites for the cytoskeleton, and cell-adhesion proteins.

**Figure 4.7 Membrane Transport.** Membrane transport is organized into passive processes and active processes depending upon the requirement for cellular energy. Passive processes do not require cellular energy, whereas active processes do.
• **Identity markers** communicate to other cells that they belong to the body. Cells of the immune system use identity markers to distinguish normal, healthy cells from foreign, damaged, or infected cells that are to be destroyed (see section 22.4c).

• **Enzymes** may be attached to either the internal or the external surface of a cell for catalyzing chemical reactions (see section 3.3b).

• **Anchoring sites** secure the cytoskeleton (the internal, protein support of a cell) to the plasma membrane (see section 4.6b).

• **Cell-adhesion proteins** are for cell-to-cell attachments. Proteins that form membrane junctions perform a number of functions, including binding cells to one another (see section 22.3d).

One additional cellular feature of a cell’s plasma membrane is a “coating of sugar” at the cell’s external surface called the **glycocalyx** (glkö-ká’liks; kalyx = husk). The carbohydrates of both glycolipids and glycoproteins that extend outward from the plasma membrane compose the glycocalyx (figure 4.5). The glycocalyx is unique to each cellular type and is important in cell-to-cell recognition (see sections 4.5a, 22.4c, and 29.2a).

### 4.3a Passive Processes: Diffusion

#### LEARNING OBJECTIVES

11. Summarize the general concept of diffusion.

12. Distinguish between the cellular processes of simple diffusion and facilitated diffusion.

Molecules and ions have kinetic energy (see section 3.1a) due to their random, constant motion. They continuously move about, and when they strike obstacles such as other molecules and ions they bounce off, moving in a different direction. If a concentration gradient exists for a given type of ion or molecule, it becomes more evenly distributed over time. This net movement of a substance from where it is more concentrated to where it is less concentrated is called **diffusion** (di-fú’zhun; diffundo = to pour in different directions). Diffusion, if unopposed, occurs until the substance reaches **equilibrium** (i.e., the molecules or ions become evenly distributed throughout a given area or areas (figure 4.8).

The rate at which substances diffuse is not constant, but is dependent upon environmental conditions, including:

- The **“steepness” of its concentration gradient**. Steepness of a concentration gradient is a measure of the difference in concentration of a substance between two areas. A steeper concentration gradient causes a faster rate of diffusion.

- **Temperature.** Temperature reflects the kinetic energy (or random movement) of a substance. When the temperature is higher, there is a greater random movement of the molecules and ions composing a substance, resulting in a faster rate of diffusion.

### Cellular Diffusion

Several concepts are important in understanding diffusion involving a cell. (1) The distribution of most molecules and ions associated with cellular energy. Instead, these processes simply depend upon the kinetic energy (or random movement) of ions and molecules as each moves down its concentration gradient (i.e., from where there is more of it to where there is less). Diffusion (which involves the movement of **solute**s down their concentration gradient) and **osmosis** (which involves the movement of **water** across a semipermeable membrane down its concentration gradient) are the two major types of passive processes.

**Active processes** differ from passive processes in that they require expenditure of cellular energy. The cellular energy could be used for active transport, where a solute (ion or molecule) is moved up its concentration gradient (i.e., from where there is less of it to where there is more). The cellular energy could also be used for vesicular transport, which involves either a vesicle releasing its contents from a cell or a vesicle being formed as material is moved into a cell.

#### Figure 4.8 Diffusion. When a drop of dye is placed into a beaker of water, the dye molecules diffuse within the water down their concentration gradient, spreading out until equilibrium has been reached.
cells is not equal between the inside and the outside of a cell. Some substances generally have a greater concentration inside the cell than outside the cell (e.g., CO$_3^-$, K$^+$), whereas others have a greater concentration outside the cell than inside (e.g., O$_2$, Na$^+$). (2) The concentration gradient between the inside and the outside of the cell determines whether the solute diffuses into the cell or out of the cell. As noted, solutes always diffuse from an area where they are more concentrated to an area where they are less concentrated. (3) The chemical characteristics of the diffusing solute dictate whether it moves across the plasma membrane unassisted by the process of simple diffusion or it is assisted with a protein by the process of facilitated diffusion.

**Simple Diffusion** Molecules that are small and nonpolar move into or out of a cell down their concentration gradient by simple diffusion. These molecules move unassisted across the plasma membrane (i.e., they do not require a transport protein). Their chemical characteristics (i.e., small and nonpolar) allow these molecules to simply pass between the phospholipid molecules of the plasma membrane (Figure 4.9). Molecules that move via simple diffusion include respiratory gases (O$_2$ and CO$_2$), small fatty acids, ethanol, and urea (a nitrogenous waste produced from amino acids).

The plasma membrane cannot regulate simple diffusion—rather, the movement of these molecules is dependent only upon the concentration gradient. Each type of molecule continues to diffuse across the plasma membrane as long as its concentration gradient exists. Impaired respiratory and cardiovascular function can alter the concentration gradients of oxygen and carbon dioxide, resulting in decreased diffusion of these gases (see sections 23.6b and c).

**Facilitated Diffusion** Small solutes that are charged ions or polar molecules are effectively blocked from passing through the plasma membrane by the nonpolar phospholipid bilayer. Their transport either into or out of the cell, down their concentration gradient, must be assisted by plasma membrane proteins in a process called facilitated (fa-sil′i-ta-ted) diffusion. Two types of facilitated diffusion—channel-mediated diffusion and carrier-mediated diffusion—are distinguished by the type of transport protein used to move the substance across the plasma membrane (see figure 4.7).

**Channel-mediated diffusion** is the movement of small ions across the plasma membrane through water-filled protein channels (Figure 4.10a). Each channel is typically specific for one type of ion. The channel is either a leak channel, which (as a general rule) is continuously open, or a gated channel. A gated channel is usually closed, opens only in response to a stimulus (e.g., chemical, light, voltage change), and then stays open for just a fraction of a second before it closes. For example, Na$^+$ leak channels allow Na$^+$ to pass through continuously. In contrast, chemically gated Na$^+$ channels open to allow Na$^+$ to move through the channel only when it temporarily opens in response to the presence of a particular chemical (e.g., neurotransmitter). Channel-mediated diffusion of ions is important in the normal function of both muscle cells and nerve cells.

**Carrier-mediated diffusion** is the movement of polar molecules (e.g., glucose or amino acids) across the plasma membrane. The relatively larger size of polar molecules (in comparison to ions) requires that their movement across the plasma membrane be assisted by a carrier protein. Three primary events take place in carrier-mediated diffusion: (1) The carrier protein within the plasma membrane binds the polar molecule, which (2) induces the carrier protein to change shape and move or carry the polar molecule to the other side of the plasma membrane, where (3) it is released. Like channels, a carrier moves a substance down its gradient; however, note that carrier-mediated diffusion involves a conformational change in the carrier protein for the transport of the
The number of channels and carriers in a plasma membrane determines the maximum rate at which a substance can be transported. Thus, a cell can alter the transport rate of a given substance down its concentration gradient by changing the number of channel or carrier proteins in the plasma membrane. A greater rate occurs with increased numbers of these transport proteins, and a lesser rate with decreased numbers (see section 24.6b).

Osmosis is unlike the other types of passive membrane transport, because it involves water movement and does not involve the movement of solutes (see figure 4.7). Osmosis (os-mōˈsis; osmos = a thrusting) is the passive movement of water through a semipermeable (or selectively permeable) membrane. This movement occurs in response to a difference in relative concentration of water on either side of a membrane. Please refer to figure 4.11 as you read through this section.

**Plasma Membrane: A Selectively Permeable Membrane**

The plasma membrane is a semipermeable membrane that allows the passage of water, but its phospholipid bilayer prevents the movement of most solutes. A plasma membrane is also more specifically a selectively permeable membrane because the movement of most solutes is regulated (selectively) by this barrier.

Water molecules cross the plasma membrane in one of two ways: Either they “slip between” the molecules of the phospholipid bilayer (limited amounts) or they move through integral protein water channels called aquaporins (ak-kwā′pər′in; aqua = water, porus = channel). Thus, cells can alter the amount of water that crosses the plasma membrane by changing the number of aquaporins.

The phospholipid bilayer of the plasma membrane is non-permeable to most solutes. In the context of osmosis, solutes are classified into two categories based upon whether their passage across the plasma membrane is prevented by the phospholipid bilayer. Permeable solutes (e.g., small and nonpolar solutes such as oxygen, carbon dioxide, and urea) pass through the bilayer, and non-permeable solutes (e.g., charged, polar, or large solutes such as ions, glucose, and proteins) are prevented from crossing the bilayer. (The term solutes in this discussion on osmosis will refer to non-permeable solutes.)

**Concentration Gradients Across the Plasma Membrane**

A difference in solute concentration can exist between the cytosol and the interstitial fluid because solutes are prevented from moving across the phospholipid bilayer of the plasma membrane. Note that when a solute concentration exists, a water concentration also exists. A solution with a greater concentration of solutes contains a lower concentration of water. For example, a solution containing 3% solutes has a lower water concentration (97% water) than a solution with 1% solutes (99% water). Note that solute percentage reflects the collective percentage of all of the solutes (e.g., glucose, proteins, Na+).

**Figure 4.11 Osmosis in Cells.** Osmosis occurs in cells across the plasma membrane, which is permeable to water but non-permeable to most solutes. Water always moves across the plasma membrane from an area of high water concentration to an area of low water concentration until equilibrium is reached. [AP R]

**Movement of Water into or Out of a Cell by Osmosis**

The net movement of water by osmosis is dependent upon the concentration gradient between the cytosol and the solution in which the cell is immersed. For example, water moves down its concentration gradient from the solution containing 1% solutes (and 99% water) into the solution containing 3% solutes (and 97% water). Water continues to move until equilibrium is reached (the concentration of water in the cell equals the concentration of the surrounding fluid). Note that water moves toward the solution with the lower water concentration (stated another way, water moves toward the solution with the greater solute concentration).

Figure 4.11 shows water moving across the plasma membrane by osmosis from an area of high water concentration to an area of low water concentration.
**Osmotic Pressure**

Osmotic pressure is the pressure exerted by the movement of water across a semipermeable membrane due to a difference in solution concentration. The steeper the gradient, the greater the amount of water moved by osmosis and the higher the osmotic pressure.

**Figure 4.12** helps us to visualize the movement of water by osmosis. Each U-shaped tube has two areas separated by a semipermeable membrane that allows the passage of water but restricts the passage of solutes. Initially, side A has more solutes and less water than side B. Water moves from side B into side A by osmosis (against the force of gravity) until the two fluids are equal in concentration.

Osmotic pressure can be measured indirectly. Imagine placing a stopper on side A in figure 4.12 and exerting force to return the fluid to its original level. The force exerted increases hydrostatic pressure within the U-shaped tube. (Hydrostatic pressure is the pressure exerted by a fluid on the inside wall of its container.) The osmotic pressure exerted in this setup is equal to the hydrostatic pressure produced to return the fluid to its original level.

**WHAT DO YOU THINK?**

Which setup would exhibit the greater osmotic pressure: a cell with a cytosol concentration of 0.9% immersed in (a) pure water or (b) a 0.2% NaCl solution? Explain.

**Osmosis and Tonicity**

When water crosses the plasma membrane of a cell by osmosis, the cell either gains or loses water with an accompanying change in the cell’s volume and osmotic pressure. The ability of a solution to change the volume or pressure (sometimes called the tone) of the cell by osmosis is called tonicity. Three specific terms are used to describe the relative concentration of solutions: isotonic, hypotonic, and hypertonic (figure 4.13). We describe them based on cells immersed in solutions with different concentrations.

An isotonic (iso-tōn’ik; iso = equal, tonus = stretching) solution has the same relative concentration of solutes as the cytosol. An example of a solution that is isotonic to erythrocytes is normal saline with a concentration of 0.9% NaCl. Under these conditions, the relative amounts of water inside and outside the cell are equal, and no net movement of water occurs (figure 4.13a). (Normal saline is used commonly in intravenous [IV] solutions to maintain a patient’s fluid balance.)

A hypotonic (hi-pō-ton’ik; hypo = under) solution has a lower concentration of solutes and a higher concentration of water than the cytosol. Pure water contains no solutes, so it is the most extreme example of solution that is hypotonic to erythrocytes. Under these conditions, water moves down its concentration gradient from where there is more water (outside the cell) to where there is less water (inside the cell). The entry of water increases both the volume and the osmotic pressure as the pressure that is exerted by the movement of water across a semipermeable membrane.

Hemolysis (hē-mol’i-sis; hem = blood, lysis = destruction) is the specific term for rupturing erythrocytes. Hemolysis is why nurses do not administer intravenous (IV) solutions of pure water—an error that results in cell lysis and depending on the amount administered can be fatal (see Clinical View 25.1: “Intravenous (IV) Solution”).

A hypertonic (hī-per-ton’ik; hyper = above) solution has a higher concentration of solutes, and thus a lower concentration of water than in the cytosol. For example, a solution that

**Figure 4.12** Osmotic Pressure. The semipermeable membrane allows the passage of water but restricts the passage of solutes. If a water gradient exists, water moves by osmosis from where it is more concentrated (side B) to where it is less concentrated (side A) until equilibrium is reached. Osmotic pressure is the pressure exerted by this movement of water.
Interstitial fluid is the same concentration as cytosol.

No net movement of water

Interstitial fluid is more concentrated than cytosol.

(a) Erythrocytes are immersed in an isotonic solution (e.g., 0.9% NaCl). As a result, there is no net movement of water between the erythrocytes and the solution, and the cell shape remains unchanged. (b) Erythrocytes are immersed in a hypotonic solution (e.g., pure water). As a result, water moves from the solution (where there is more water) into the erythrocytes (where there is less water), and the erythrocytes swell. (c) Erythrocytes are immersed in a hypertonic solution (e.g., 3% NaCl). As a result, water moves from the erythrocytes (where there is more water) into the solution (where there is less water), and the erythrocytes shrivel.

Osmosis is important in several significant physiologic processes that are discussed later in the text, including capillary exchange between the blood and body cells (see section 20.3), formation of urine (see section 24.6), and regulation of fluid balance (see section 25.2).

WHAT DID YOU LEARN?

9. Define osmosis.

10. What occurs to the tonicity of a cell when it is placed into an isotonic, a hypotonic, or a hypertonic solution?

11. What general conclusion can you make concerning the movement of water? There is always a net movement of water by osmosis toward (a) an isotonic solution, (b) a hypotonic solution, or (c) a hypertonic solution.

4.3c Active Processes

LEARNING OBJECTIVES

16. Compare and contrast primary and secondary active transport.

17. Explain the difference between exocytosis and endocytosis.

18. Describe the endocytotic processes of phagocytosis, pinocytosis, and receptor-mediated endocytosis.

Active processes of membrane transport are those that require the expenditure of cellular energy and occur only in living organisms. Active processes are organized into active transport and vesicular transport (see figure 4.7).
Active Transport

Active transport is the movement of a solute against its concentration gradient (i.e., movement from a low concentration to a high concentration) across a cellular membrane. Recall from section 4.3a that most molecules and ions associated with cells are not distributed equally between the inside and the outside of a cell. The energy-requiring processes of active transport are essential in maintaining these differences. The two types of active transport are primary active transport and secondary active transport, which are distinguished by their specific energy source (see figure 4.7).

Primary Active Transport  

Primary active transport uses energy derived directly from the breakdown of ATP (see figure 3.7). This breakdown also provides the phosphate group that is added to the membrane transport pump, resulting in a change in the protein’s shape and the subsequent movement of a solute across the membrane. The addition of the phosphate to a protein is called phosphorylation (see section 3.3g).

Cellular protein pumps that move ions across the membrane are more specifically called ion pumps. Ion pumps are a major factor in a cell’s ability to maintain its internal concentrations of ions. As an example, Ca$^{2+}$ pumps embedded in the plasma membranes of erythrocytes move calcium out of the erythrocyte to prevent it from becoming rigid due to the accumulation of calcium (figure 4.14). Therefore, the erythrocyte remains flexible enough to move through capillaries (the smallest blood vessels; see section 20.1c). H$^+$ pumps are another type of transport protein that function in maintaining cellular pH (see section 3.4e).

The sodium-potassium (Na$^+$/K$^+$) pump is a special type of ion pump. It is specifically called an exchange pump because it moves one type of ion into a cell against its concentration gradient, while moving another type of ion out of the cell against its concentration gradient. (You may find it helpful to think of the Na$^+$/K$^+$ pump as a “dual pump” because it moves two different ions against their respective concentration gradients.) The plasma membrane preserves steep concentration gradient differences for these ions by continuously exporting Na$^+$ out of the cell and moving K$^+$ into the cell.

Figure 4.15 shows the steps in the process in which 3 Na$^+$ ions are pumped out of a cell for every 2 K$^+$ ions that are pumped into a cell. The cell must expend ATP to maintain the levels of these ions on each side of the membrane. The Na$^+$/K$^+$ pump is also called a sodium-potassium ATPase because the protein pump is an enzyme that splits ATP to power the pump. There is a 1:2:3 ratio for this pump: 1 ATP is required to pump 2 K$^+$ ions into the cell and 3 Na$^+$ ions out of the cell.

Secondary Active Transport  

Secondary active transport is also called cotransport, or coupled transport. The movement of a substance (e.g., Na$^+$) down its concentration gradient provides the energy to move a different substance (e.g., glucose, H$^+$) up its concentration gradient. Put another way, the kinetic energy of one substance (usually Na$^+$) moving down its concentration gradient across the membrane provides the “power” to pump the other substance against its concentration gradient across the membrane (much as water moving over a dam and turning a water wheel can generate electricity; see section 3.1a). The Na$^+$ gradient is often the source of energy because its concentration gradient across the plasma membrane is extremely steep (about 99% of Na$^+$ is in the interstitial fluid, with only 1% in the cytosol). The Na$^+$ concentration gradient has potential energy that is harnessed as it is converted to kinetic energy when Na$^+$ moves into the cell down its concentration gradient in secondary active transport. The two types of secondary active transport include (see figure 4.7)

- **Symport.** If the two substances are moved in the same direction, these transport proteins are called symporters (or cotransporters), and the process is symport secondary active transport.
- **Antiport.** If the two substances are moved in opposite directions, the transport proteins are called antiporters (or countertransporters) and the process is antiport secondary active transport.

Figure 4.16 compares the processes of transporting a substance by a symporter or an antiporter using the movement of Na$^+$ as the energy source. In the symporter example, glucose binds to the symporter in the membrane (figure 4.16a). This binding helps alter the shape of the symporter and then both glucose and Na$^+$ are transported into the cell. The Na$^+$ moves down its
Transport protein resumes original shape

1. Three sodium ions (Na⁺) and ATP bind to sites on the cytoplasmic surface of the Na⁺/K⁺ pump.

2. ATP is split into ADP and Pᵢ, resulting in both the binding of the free phosphate (Pᵢ) to the pump and release of energy that causes the Na⁺/K⁺ pump to change conformation (shape) and release the Na⁺ ions into the interstitial fluid.

3. Two K⁺ ions from the interstitial fluid then bind to sites on the outer cellular surface of the Na⁺/K⁺ pump. At the same time, the Pᵢ produced earlier by ATP splitting is released into the cytosol.

4. This transport protein reverts back to its original shape, resulting in the release of the K⁺ ions into the cytosol. The Na⁺/K⁺ pump is now ready to begin the process again.

Figure 4.15 Na⁺/K⁺ Pump. The Na⁺/K⁺ pump is a plasma membrane transport protein that uses ATP to move both Na⁺ and K⁺ ions through the plasma membrane in opposite directions from their region of low concentration to their region of high concentration (1 ATP is split for moving 3 Na⁺ out of the cell and 2 K⁺ into the cell). [AP/R]

Secondary active transport mechanisms are ultimately dependent upon the primary active transport mechanisms of Na⁺/K⁺ pumps (described earlier). The activity of these pumps produce and sustain a distinct concentration gradient difference between Na⁺ on opposite sides of the plasma membrane, with substantially more Na⁺ in the interstitial fluid and less Na⁺ in the cytosol.
Vesicular Transport

Vesicular transport, also called bulk transport, involves a vesicle (ves′i-kl; vesica = bladder), which is a membrane-bound sac filled with materials. These energy-requiring processes allow for the transport of large substances (or large amounts of a substance) across the plasma membrane and are organized into exocytosis and endocytosis (see figure 4.7).

Exocytosis The means by which either large substances or large amounts of substances are secreted from the cell is called exocytosis (ek′so-st-i-tō′sis; exo = outside, osis = condition of) (figure 4.17). Macromolecules, such as large proteins and polysaccharides, are too big to be moved across the plasma membrane, even with the assistance of transport proteins. The material for secretion typically is packaged within intracellular transport vesicles. When the vesicle and plasma membrane come into contact, the phospholipid molecules of the vesicle and plasma membrane bilayers rearrange themselves so that the two membranes fuse. The fusion of these lipid bilayers requires the cell to expend energy by splitting ATP. Following fusion, the vesicle contents are released to the outside of the cell. An example of exocytosis is the release of neurotransmitter molecules from nerve cells (see section 12.8d).

Endocytosis The cellular uptake of either large substances or large amounts of substances from the external environment into the cell is called endocytosis (en′dō-st-i-tō′sis; endon = within). Endocytosis is used for the uptake of nutrients and extracellular debris for digestion, retrieval of membrane regions added to the plasma membrane during exocytosis, and regulation of composition of membrane proteins to alter cellular processes (e.g., cell communication by altering the number of receptors within the plasma membrane; see figure 17.9a).

The steps of endocytosis are similar to the exocytosis steps, only in reverse. Endocytosis occurs when substances within the interstitial fluid are packaged into a vesicle that forms at the cell surface for internalization into the cell (figure 4.18). A small area of plasma membrane folds inward into the cytosol to form a pocket, or invagination (in-vaj′i-nā-žun; vagina = a sheath). The pocket deepens as endocytosis proceeds and then it pinches off when the lipid bilayer fuses. Severing of the newly forming vesicle from the plasma membrane requires

Figure 4.16 Secondary Active Transport. Secondary active transport is powered by the movement of a substance (usually Na⁺) down its concentration gradient to move a different substance up its concentration gradient. (a) A symporter transports both substances in the same direction. (b) An antiporter transports the two substances in opposite directions. Remember, in both symport and antiport, the kinetic energy of Na⁺ moving down its concentration gradient is harnessed to move a different substance (e.g., glucose, H⁺) up its concentration gradient.
Specialized proteins and is the energy-expending step. The new intracellular vesicle now present contains material that was formerly outside the cell.

The three types of endocytosis include phagocytosis, pinocytosis, and receptor-mediated endocytosis. They are differentiated based upon the specific material being transported and the mechanism involved (see figure 4.7).

**Phagocytosis** (fag′-o-st′-o′sis; phago = to eat) means *cellular eating*. It is a nonspecific process that occurs when a cell engulfs or captures a large particle external to the cell by forming membrane extensions that are called *pseudopodia* (sū-dō-pō′-dē-ā; pseudes = false, pous = foot) or false feet, to surround the particle (figure 4.18a). Once the particle is engulfed by the pseudopodia, it is enclosed...

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**Figure 4.17 Exocytosis.** In exocytosis, the cell secretes bulk volumes of materials within cellular vesicles into the interstitial fluid as a vesicle fuses with the plasma membrane. Fusion of the vesicle to the plasma membrane is the energy-requiring step.

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**CLINICAL VIEW 4.1**

**Familial Hypercholesteremia**

*Familial hypercholesteremia* is an inherited genetic disorder that involves either defective or absent cellular receptor proteins that bind low-density lipoproteins (LDLs), defects in the proteins of the LDLs, or other possible mutations (see Clinical View 29.9: "Genetics of Familial Hypercholesteremia"). Defects in either the LDL receptor or the proteins of the LDLs interfere with the normal process of receptor-mediated endocytosis of cholesterol into cells. LDLs that contain cholesterol remain in the blood, resulting in greatly elevated levels of blood cholesterol. Consequently, cholesterol accumulates in the blood vessels, causing plaque buildup and narrowing of the blood vessels (i.e., atherosclerosis; see Clinical View 20.1: “Atherosclerosis”), especially those providing blood to the heart (coronary vessels). Individuals with this genetic defect are likely to experience blockage of the coronary arteries, resulting in a heart attack (see Clinical View 19.5: “Coronary Heart Disease, Angina Pectoris, and Myocardial Infarction”). The age of occurrence of a heart attack depends upon the severity of the protein defect. In severe cases, an individual may experience a heart attack during the teen years.
with what was previously part of the plasma membrane. This newly formed vesicle typically fuses with a lysosome (a cellular organelle containing digestive enzymes, described in section 4.6a). The molecules composing the ingested material are broken down or digested by the enzymes within the lysosome. Only a few types of cells are able to perform phagocytosis. For example, it occurs regularly when a white blood cell engulfs and digests a microbe (e.g., bacterium; see section 22.3b).

**Pinocytosis** (pin′ō-sī′tōs or pīn′ō-sē′; pineo = to drink) is known as cellular drinking. This process occurs when multiple, small regions of the plasma membrane invaginate and multiple, small vesicles are formed as the cell internalizes interstitial fluid that contains dissolved solutes (figure 4.18). This process is considered nonspecific because all solutes dissolved within the interstitial fluid are taken into the cell. Most cells perform this type of membrane transport.

**Receptor-mediated endocytosis** uses receptors on the plasma membrane to bind molecules within the interstitial fluid and bring the molecules into the cell. This enables the cell to obtain bulk quantities of certain substances, even though those substances may not be very concentrated in the interstitial fluid.

Receptor-mediated endocytosis begins when specific molecules in the interstitial fluid attach to their distinct integral membrane protein receptors in the plasma membrane to form a ligand-receptor complex (figure 4.18c). Following the binding of the ligand, the ligand-receptor complexes move laterally in the plane of the plasma membrane and accumulate at special membrane regions that contain clathrin protein on the internal surface of the membrane. The clathrin-coated regions of the plasma membrane housing the ligand-receptor complex folds inward to form an invagination called a clathrin-coated pit. This invagination deepens and pinches off, and the lipid bilayer of the plasma membrane fuses to form a clathrin-coated vesicle, which then moves into the cytosol. Following the formation of the clathrin-coated vesicles, the clathrin coat must be enzymatically removed before the vesicle may proceed to its intracellular destination. Again, it is the fusion of these lipid bilayers that requires the cell to expend energy. Following entry, receptors and ligands are uncoupled. Ligands may be stored, modified, or destroyed, and receptors (unless damaged) are returned to the plasma membrane.

The transport of cholesterol from the blood to a cell is an example of receptor-mediated endocytosis. When cholesterol is transported in the blood, it is bound to protein molecules in structures called low-density lipoproteins (or LDLs). LDLs move from the blood into the interstitial fluid and then bind to LDL receptors in the cell’s plasma membrane. LDLs are then internalized by the process of receptor-mediated endocytosis just described (see section 27.6b).

Figure 4.18 Three Forms of Endocytosis. Endocytosis is the process whereby a vesicle is formed as the cell acquires materials from the interstitial fluid. (a) Phagocytosis occurs when plasma membrane extensions called pseudopodia engulf a relatively large particle and internalize it into a vesicle. (b) Pinocytosis is the incorporation of numerous droplets of interstitial fluid into the cell in small vesicles as many regions of the plasma membrane invaginate. (c) Receptor-mediated endocytosis occurs when specific molecules bind to receptors in the plasma membrane. These receptors with bound molecules then aggregate within the membrane, and are internalized when the membrane invaginates, forming a vesicle. The formation of the vesicle is the energy-requiring step.
The various types of membrane transport mechanisms are integrated in figure 4.19. Passive processes are depicted on the left and active processes on the right in this two-page summary figure. Note as you observe this figure that the passive processes of diffusion and osmosis (which allow molecules and ions to move down their concentration gradient) facilitate the reaching of equilibrium (equal distribution of ions and molecules) across the plasma membrane. In comparison, active transport (which moves molecules and ions up their concentration gradient) opposes the reaching of equilibrium across the plasma membrane. It is the active transport processes that maintains cellular concentration gradients at the plasma membrane, which are necessary for normal cellular function.

### WHAT DID YOU LEARN?
- **12** What transport process involved in the movement of Na\(^+\) down its gradient is used to power another substance up its gradient?
- **13** Engulfing of a bacterium by a white blood cell occurs by what type of cellular transport?

## 4.4 Resting Membrane Potential

The plasma membrane also functions in establishing and maintaining an electrochemical gradient at the plasma membrane called the resting membrane potential (RMP), which is essential in the normal function of both muscle cells (see section 10.2d) and nerve cells (see section 12.7b). We first define an RMP and then discuss how resting membrane potentials are established and maintained. Refer to figure 4.20 as you read through this section.

### 4.4a Introduction

#### LEARNING OBJECTIVES
- **19.** Define a resting membrane potential (RMP).
- **20.** Describe the cellular conditions that are significant for establishing and maintaining a resting membrane potential.

Cells have an electrical charge difference at the plasma membrane. This electrical charge difference represents potential energy (see section 3.1a), and thus is appropriately called the membrane potential. The membrane potential when a cell is at rest is more specifically called the resting membrane potential (RMP). Two cellular conditions are significant in establishing and maintaining an RMP.

First, a cell has an unequal distribution of ions and charged molecules across the plasma membrane. The cytosol close to the plasma membrane contains relatively more K\(^+\) than does the surrounding interstitial fluid that is close to the plasma membrane. In comparison, the interstitial fluid close to the plasma membrane contains relatively more Na\(^+\) than the cytosol close to the plasma membrane. These relative distributions of K\(^+\) (more inside) and Na\(^+\) (more outside) are the result of the activity of Na\(^+\)/K\(^+\) pumps (described in section 4.3c). In addition, the cytosol has negatively charged protein molecules, which are formed by protein synthesis (see section 4.8). Note that these negatively charged proteins are too large to pass through the plasma membrane.

Second, the relative amounts of positive and negative charges are not equally distributed at the plasma membrane. There is relatively more positive charge on the outside of a cell than on the inside of a cell. Thus, the inside of the cell is relatively negative compared to the outside of the cell near the plasma membrane. This difference in charge can be measured by electrodes, which are positioned with one just inside the cell and the other outside the cell. Cell types vary in the specific value of their resting membrane potential, which typically ranges between −50 millivolts (mV) and −100 mV. Nerve cells (i.e., neurons), for example, have a resting membrane potential of −70 mV (see section 12.7b).

### 4.4b Establishing and Maintaining an RMP

#### LEARNING OBJECTIVES
- **21.** Explain the role of both K\(^+\) and Na\(^+\) in establishing an RMP.
- **22.** Discuss how Na\(^+\)/K\(^+\) pumps are necessary in maintaining an RMP.

A resting membrane potential (RMP) is primarily a consequence of the relative movement of ions across the plasma membrane. The two most significant ions are K\(^+\) and Na\(^+\). The net movement of each of these is dependent upon both the number of its leak channels and the electrochemical gradient, which is the combination of the electrical gradient at the plasma membrane and the chemical concentration gradient of the specific ion. Here we first discuss the role of K\(^+\) and the role of Na\(^+\) in establishing an RMP. We then describe the role of Na\(^+\)/K\(^+\) pumps.

### Establishing an RMP

**The Role of K\(^+\)** Potassium diffusion is the most important factor in establishing the specific value of the RMP. Movement of K\(^+\) is dependent upon its electrochemical gradient. Potassium ions exit the cell through K\(^+\) leak channels moving down their relatively steep chemical concentration gradient from the cytosol into the interstitial fluid. This loss of K\(^+\) leaves relatively more negatively charged structures (e.g., proteins) inside the cell. They remain within the cell because they are too large to cross the plasma membrane. The movement of K\(^+\) to the outside of a cell is, however, opposed by the electrical gradient. The positive charge on the outside of the cell repels the movement of K\(^+\), and the negative charge on the inside of the cell attracts K\(^+\). Thus, K\(^+\) movement out of the cell is facilitated by its chemical concentration gradient but opposed by the electrical gradient. As additional K\(^+\) diffuses out of the cell into the interstitial fluid, the inside becomes more negative. Consequently, the pull to keep K\(^+\) within the cell is greater. At some point, the electrical gradient that opposes the movement of K\(^+\) out of the cell becomes equal to the force of the chemical concentration gradient allowing K\(^+\) out of a cell. Thus, K\(^+\) movement has reached equilibrium. In a nerve cell, for example, if only K\(^+\) leak channels were present, the loss of the K\(^+\) from the nerve cell would result in an RMP with a specific value of −90 mV.

**The Role of Na\(^+\)** Sodium diffusion into cells occurs simultaneously to the loss of K\(^+\) from the cell, and it is dependent upon its electrochemical gradient. Sodium ions enter the cell through Na\(^+\) leak channels moving down their chemical concentration gradient from the interstitial fluid into the cytosol. Sodium ions are also “pulled” into the cell by the electrical gradient. Both of these forces (the chemical gradient and the electrical gradient) facilitate the
Transport processes are separated into two major categories. (a) Passive processes, which do not require expenditure of cellular energy, include simple diffusion, facilitated diffusion (channel-mediated and carrier-mediated), and osmosis. (b) Active processes, which require cellular energy, include active transport (primary and secondary) and vesicular transport (exocytosis and various forms of endocytosis).

(a) Passive Processes

Do not require expenditure of cellular energy; substance moves into or out of a cell down its concentration gradient.

DIFFUSION: Movement of a solute from an area of higher concentration to an area of lower concentration across a plasma membrane.

Simple Diffusion: Small and nonpolar solutes move unassisted between phospholipid molecules of the plasma membrane; no transport protein required.

Facilitated Diffusion: Ions and small polar molecules are assisted across the plasma membrane by a transport protein (channel or carrier).

Channel-Mediated: Ion (e.g., Na⁺) movement is facilitated by channels across the plasma membrane.

Carrier-Mediated: Polar molecule movement (e.g., glucose) is facilitated by protein carriers across the plasma membrane.

OSMOSIS: Movement of water across a semipermeable membrane from an area of higher water concentration to an area of lower water concentration (through either the phospholipid bilayer or aquaporins).
(b) Active Processes

Require expenditure of cellular energy; substance is moved up its concentration gradient or involves a vesicle.

**ACTIVE TRANSPORT:** Movement of a substance against its concentration gradient via a protein pump, symporter, or antiporter.

**Primary Active Transport:** Pumps are powered by splitting an ATP molecule.

- Pump changes shape (requires energy from ATP breakdown)
- ADP + P$_i$ → ATP
- Na$^+$
- K$^+$
- Note: The two types of ions are not simultaneously attached to the pump
- Interstitial fluid

**Secondary Active Transport:** Transport protein (symporter or antiporter) is powered by energy harnessed as a second substance (usually Na$^+$) moves down a concentration gradient.

- Symport: Two substances are moved in the same direction by a symporter protein.
- Antipor: Two substances are moved in opposite directions by an antiporter protein.

**VESICULAR TRANSPORT:** Movement of a substance out of or into a cell via a vesicle.

**Exocytosis:** Vesicular content is released from a cell.

- Vesicle fuses with plasma membrane and the vesicle contents are released

**Endocytosis:** Material is brought into a cell as vesicle is formed. The three types of endocytosis include phagocytosis, pinocytosis, and receptor-mediated endocytosis.

**Receptor-Mediated Endocytosis:** Following the binding of specific ligands to receptors, the ligand-receptor complexes are brought into a cell as a vesicle forms.

**Phagocytosis:** Particulate matter external to the cell is engulfed by pseudopodia and vesicle forms (e.g., white blood cells engulfing a bacterium).

**Pinocytosis:** Interstitial fluid is taken into a cell as vesicles form.
movement of Na\(^+\) into a cell. However, limited numbers of Na\(^+\) leak channels prevent as much Na\(^+\) movement into the nerve cell as K\(^+\) out. This movement of Na\(^+\) results in the inside becoming more positive. Thus, in a nerve cell, this movement of Na\(^+\) typically accounts for an approximately +20 mV addition of charge to the inside of the cell, which results in the resting membrane potential being −70 mV (instead of the −90 mV if only K\(^+\) leak channels were present).

**Maintaining an RMP**

The Na\(^+\)/K\(^+\) pumps are significant in maintaining the gradients of both K\(^+\) and Na\(^+\) following their diffusion. Each type of ion is pumped back up its concentration gradient by Na\(^+\)/K\(^+\) pumps (see section 4.3c). Na\(^+\) and K\(^+\) are moved in opposite directions; Na\(^+\) are pumped out of the cell and K\(^+\) are transported into the cell. We will see in later chapters that changes in the RMP caused by the regulated opening and closing of gated channels can alter the passage of specific ions, and these movements are essential to both contraction of muscle cells (see section 10.3) and relaying an impulse in nerve cells (see section 12.8).

**4.5 Cell Communication**

The plasma membrane plays a significant role in communication between cells in addition to serving as a physical barrier, functioning in membrane transport, and establishing and maintaining a resting membrane potential. Numerous structures in the membrane, including glycolipids and glycoproteins, facilitate both direct interaction with other cells and recognition and response to certain molecular signals external to the cell when these molecules bind with cellular receptors.

**4.5a Direct Contact Between Cells**

**LEARNING OBJECTIVE**

23. Explain how cells communicate through direct contact.

Physical or direct contact between two cells is important in the normal functioning of some cells, especially those of the immune system. One of the primary functions of the immune system is to make contact with and destroy both unhealthy cells (e.g., infected cells, cancer cells) and foreign cells (e.g., bacterial cells, transplanted cells). Body cells communicate to our immune cells that they both belong to the body and are healthy through direct contact that involves the glycocalyx. Recall that the glycocalyx is the coating of carbohydrates on the external surface of a cell (see section 4.2b). These carbohydrates extend from the lipids and proteins of the plasma membrane. The pattern of sugars is unique to each individual except identical twins. The immune system is able to distinguish normal, healthy cells from unwanted cells by making direct contact with a cell to determine if it exhibits the same pattern of sugars of the glycocalyx as the body’s cells. It is because unhealthy cells and foreign cells express a different pattern that they are subsequently destroyed.

Another example of direct contact between cells is the contact that occurs between sperm and an oocyte (egg) during the process of fertilization. The sperm recognizes and binds to the oocyte by its unique glycocalyx (see section 29.2a).
Direct contact is also critical in the process of development and in cellular regrowth following injury. If you cut the skin of your finger, the cells in the upper layer of the skin (the epidermis) begin to divide (see section 6.3). Cell division continues to fill in the gap created by the injury. When the damaged tissue has been replaced, overgrowth of skin tissue is prevented by inhibition caused by cellular contact.

**WHAT DID YOU LEARN?**

What are some examples of how cells communicate through direct contact?

### 4.5b Ligand-Receptor Signaling

**LEARNING OBJECTIVE**

24. Describe the three general mechanisms of response to the binding of a ligand with a receptor.

Most communication between cells occurs through ligands (see section 4.2b). Recall that ligands are molecules that bind with macromolecules (e.g., receptors). Ligands involved in communication include neurotransmitters from nerve cells and hormones from endocrine cells. The cell that receives the information has a receptor that can bind the ligand. Binding initiates mechanisms for controlling the growth, reproduction, and other cellular processes of individual cells.

There are three general types of receptors that bind ligands. They differ in their response to ligand binding as follows (figure 4.21):

- **Channel-linked receptors** (or chemically gated channels) permit ion passage either into or out of a cell in response to ligand (e.g., neurotransmitter) binding (figure 4.21a). Channel-linked receptors are required to initiate electrical changes to the resting membrane potential in skeletal muscle cells (see section 10.3), cardiac muscle cells (see section 19.7b), and nerve cells (see section 12.8).

- **Enzymatic receptors** function as protein kinase enzymes and are activated to directly phosphorylate (add a phosphate to) other enzymes within the cell (figure 4.21b). Recall that enzymes can be either turned on or turned off through phosphorylation (see section 3.3g). This provides a mechanism for altering enzymatic activity within a cell in response to external signals.

![Figure 4.21 Membrane Receptors](image)

**Figure 4.21 Membrane Receptors.** Receptors bind ligands that will initiate a cellular change. *(a)* Channel-linked receptors bind a ligand and open to allow a specific ion to move down its concentration gradient. *(b)* Enzymatic receptors (generally protein kinase enzymes) bind a ligand and are activated to phosphorylate other enzymes. *(c)* G protein–coupled receptors bind ligand and activate protein kinase enzymes indirectly through a G protein, as described in steps 1–5.
4.6 Cellular Structures

The cellular structures described in this section include membrane-bound organelles, non-membrane-bound organelles, vesicles for transport, and structures that extend from the cell’s surface.

4.6a Membrane-Bound Organelles

LEARNING OBJECTIVES

25. List the membrane-bound organelles of a typical human cell.
26. Describe the structure and main function(s) of each.

Membrane-bound organelles within the cytoplasm are surrounded by a membrane (similar in composition to the plasma membrane) that separates the organelle’s contents from the cytosol (the fluid part of the cytoplasm). This allows the activities of each organelle to proceed in a relatively isolated and controlled environment. Each organelle differs in its shape, membrane composition, and associated enzymes (see section 3.3a). These differences account for the unique functions of each. Membrane-bound intracellular organelles include the endoplasmic reticulum, Golgi apparatus, lysosomes, peroxisomes, and mitochondria (see figure 4.4). We first describe the structure and then the function of each.

Endoplasmic Reticulum

The endoplasmic reticulum (en’də-plas’mik re-tik’ů-lum; rete = net) (ER) is an extensive, interconnected membrane network that varies in shape (e.g., tubules, sacs, cisternae [flattened membrane sacs]), but with one continuous lumen (space within a tube) (figure 4.22). The ER typically extends from the nuclear envelope to the plasma membrane and composes about one-half of the membrane within a cell. The extensive ER membrane surface serves as a point of attachment for ribosomes (an organelle described in section 4.6b) and various types of enzymes. Endoplasmic reticulum with ribosomes attached is referred to as rough ER, whereas ER portions without ribosomes attached is referred to as smooth ER.

Rough ER The ribosomes of rough ER produce proteins that will be released from the cell (e.g., insulin from the pancreas), incorporated into the plasma membrane (see figure 4.6), and serve as digestive enzymes within lysosomes. These newly synthesized proteins are initially inserted either into the ER membrane or through the ER membrane into the lumen of the ER as they are formed. The protein may be changed by either the addition of other molecules (e.g., carbohydrates...
to form glycoproteins) or the removal of part of what was originally synthesized. A molecular tag (called a signal sequence) can be added to the protein that determines its destination. (This is much like adding an address to a letter before mailing it.) The modified proteins are packaged and then stored until their release. Transport from the ER occurs when small, enclosed membrane sacs pinch off from the ER. These sacs are termed transport vesicles (figure 4.22). They shuttle proteins from the rough ER lumen to the Golgi apparatus for further modification. The amount of rough ER is greater in cells producing large amounts of protein for secretion, such as a cell in the pancreas that releases insulin to control blood glucose (sugar). The ER also helps form peroxisomes.

**Smooth ER** The smooth ER carries out diverse metabolic processes that vary by cell type. Smooth ER functions include synthesis, transport, and storage of different types of lipids (e.g., phospholipids, steroids); carbohydrate metabolism (e.g., glycogen synthesis and breakdown in liver cells); and detoxification of drugs and poisons. Abundant amounts of smooth ER are present, for example, within the cells of the testes to produce the steroid hormone testosterone, and in the cells of the liver to detoxify alcohol.

**Golgi Apparatus**

The **Golgi apparatus**, also called the **Golgi complex** or **Golgi body**, is composed of several (e.g., about four or five) elongated, flattened, membranous sacs (cisternae) (figure 4.23). The Golgi apparatus exhibits a distinct polarity. The two poles are called the cis-face and trans-face. The cis-face is closer in proximity to the ER and the diameter of its flattened sac is larger compared to the trans-face.

One of the primary functions of the Golgi apparatus is to modify, package, and sort proteins (and glycoproteins) that are made by the rough ER (figure 4.22). Transport vesicles arrive from the ER and fuse the cis-face of the Golgi apparatus. Molecules move between cisterne

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**Functions of Golgi Apparatus**

1. **Synthesis**: Forms proteoglycans
2. **Processing molecules**: Modifies and stores protein (that was formed by rough ER)
3. **Organelle formation**: Synthesizes digestive enzymes for lysosomes
4. **Vesicle formation**: Forms secretory vesicles for delivering components of the plasma membrane and releasing contents from the cell by exocytosis

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**Figure 4.23** The **Golgi Apparatus and Endomembrane System**. Each Golgi apparatus is composed of several flattened membrane sacs (cisternae). The arrangement of these sacs exhibits both structural and functional polarity. (a) A TEM and a drawing provide different views of the Golgi apparatus. (b) The Golgi apparatus is part of the endomembrane system, which is a system of membranous structures of a cell that provide a means of transporting substances into, out of, and within a cell. [APR]
from the cis-face to the trans-face. Within the lumen of the Golgi apparatus, molecules are modified; this may involve removal of portions of a molecule, or additions to a molecule (e.g., addition of a carbohydrate or a phosphate group). As in the ER, a signal sequence may be added. The Golgi apparatus also synthesizes its own molecules, including long, unbranched polysaccharides (see section 2.7c), which are modified with the addition of small amounts of protein to form proteoglycans (e.g., glycosaminoglycans; see section 5.2a). At the trans-face, secretory vesicles form and carry both the modified and newly formed molecules away from the Golgi apparatus for different fates. Some molecules (which are located within the secretory vesicle’s membrane) become components of the plasma membrane as the two membranes fuse, whereas others (which are within the secretory vesicle’s lumen) are released from the cell into the interstitial fluid by exocytosis (see figure 4.17). Thus, the Golgi apparatus is especially extensive and active in cells specialized for protein, glycoprotein, and proteoglycan secretion.

 Vesicles released from the trans-face of the Golgi apparatus may also contain hydrolytic enzymes required for lysosomes. You may find it helpful to think of the Golgi apparatus as the “warehouse” center. Molecules arrive at the receiving region (cis-face), are modified and packaged within the lumen (and along with some new structures that are produced), and are then shipped out at the shipping region (trans-face).

Lysosomes

Lysosomes (Lī’sō-sōm; ly = a loosening, soma = body) are small, membrane-enclosed, spherical sacs, which contain digestive enzymes that are immersed in acidic fluid (pH 5) (figure 4.24). These enzymes are contributed to lysosomes as portions of the Golgi apparatus containing digestive enzymes pinch off to form vesicles, and these vesicles then fuse with the lysosome.

Lysosomes participate in digestion of unneeded or unwanted biological molecules (see section 2.7). Within a healthy cell, lysosomes digest the contents of endocytosed vesicles. For example, following phagocytosis of microorganisms by certain white blood cells, the vesicle containing the microorganism fuses with a lysosome. Its digestive enzymes break down the large biological molecules composing the microorganism (e.g., proteins, polysaccharides) into smaller molecules (see figure 22.3a).

Lysosomes also digest molecular structures of damaged organelles in a similar fashion; this process is specifically called autophagy (aw-tōf′ā-je; auto = self, phago = to eat). When a cell is damaged or dies, enzymes from its lysosomes are eventually released into the cytosol, resulting in the rapid digestion of the molecular components of the cell itself. This process is called autolysis (aw-tōl′i-sis; ly = dissolution). Two nicknames have been given to lysosomes: (1) “garbagemen” because of their “clean-up” activities of eliminating unwanted structures and (2) “suicide packets” because of their function in autolysis.

WHAT DO YOU THINK?

What would happen to a cell if it did not contain any lysosomes (or if its lysosomes were not functioning)? Would the cell be able to survive?

INTEGRATE

CLINICAL VIEW 4.2

Lysosomal Storage Diseases

Lysosomal storage diseases are an extensive group of heritable disorders that are characterized by accumulation of incompletely digested biological molecules within lysosomes. Lysosomal storage diseases occur because of mutations in the genes that code for one of the more than 40 different lysosomal enzymes. Tay-Sachs disease is one example of a lysosomal storage disease. Lysosomes in affected individuals lack an enzyme needed to break down complex membrane lipids (gangliosides). As a result, these complex lipids accumulate within nerve cells.

The cellular signs of Tay-Sachs disease are swollen lysosomes due to accumulation of the lipid. Affected infants appear normal at birth but begin to show signs of the disease by the age of 6 months. The nervous system bears the brunt of the damage. Paralysis, blindness, and deafness typically develop over a period of 1 or 2 years, followed by death, usually by the age of 4. Unfortunately, there is no treatment or cure for this fatal disease.

Peroxisomes

Peroxisomes (per-ok′si-sōm) are small, membrane-enclosed, spherical sacs that contain over 50 different enzymes that vary by cell type. They are usually smaller in diameter than lysosomes (figure 4.25). Peroxisomes are initially formed by vesicles first pinching off from the rough ER. Proteins (formed from ribosomes free in the cytosol; see section 4.6b) are then incorporated into the peroxisomes to serve as their enzymes. As additional membrane (formed by the ER) and proteins are added, a peroxisome increases in size. When a critical size is reached, it splits, forming two peroxisomes.

Although peroxisomes appear simple in structure, they engage in numerous metabolic functions. They were first named based on their role in chemical digestion, which involves removal of hydrogen from a molecule with the accompanying production of hydrogen peroxide. The hydrogen peroxide is subsequently broken down into water and oxygen (by catalase enzyme). Molecules broken down within peroxisomes by this process include fatty acids, amino acids, and uric acid (a waste product of nucleic acid breakdown). The breakdown of fatty acids is a process
that removes two hydrogen-carbon units at a time from the fatty acid chain (a process called \textit{beta oxidation}). These units are then converted to acetyl CoA and may be taken up by the mitochondria within the cell, where they are oxidized to transfer energy to form ATP (see section 3.4h).

Peroxisomes also engage in lipid synthesis (a role it shares with the smooth ER). Lipids formed by peroxisomes include specialized phospholipids (e.g., plasmalogens) within the cells of the heart and brain and bile salts within the cells of the liver. Notice that peroxisomes function in both digestion and synthesis of molecules.

**Endomembrane System**

The endomembrane system is an extensive array of membrane-bound structures that includes the endoplasmic reticulum, Golgi apparatus, vesicles, lysosomes, and peroxisomes. The plasma membrane and nuclear envelope are also considered part of this membrane system. All of these structures are either directly attached to one another or connected through vesicles that move between them. They are involved in various forms of metabolic processes that occur within a cell, and they provide a means of both transporting molecules within the cell and releasing molecules from the cell, as shown in figure 4.23b. Substances (e.g., bacteria, interstitial fluid, cholesterol) are also brought into the cell as new vesicles are formed by endocytosis (see figure 4.18). Note that mitochondria, described next, are the only membrane-bound organelles that are not components of the endomembrane system.

**Mitochondria**

Mitochondria (\textit{mi-tō-kon′drē-ə; sing., mitochondrion, \textit{mi-tō-kon′drē-on; mitos = thread, chondros = granule}) were first described in section 3.4c. They are oblong-shaped organelles that have a double membrane with the folds of the inner membrane called cristae (figure 4.26). The matrix, which is the inner region of a mitochondrion, contains a small, unique, circular fragment of (maternally inherited) DNA that has genes for producing mitochondrial proteins (not shown in figure 4.26). Mitochondria engage in aerobic cellular respiration to complete the digestion of glucose and other fuel molecules, such as fatty acids, for the transfer of energy to synthesize ATP molecules, the cell’s energy currency. For this reason, mitochondria are called the “powerhouses” of the cell. Mitochondria numbers within cells increase (by fission) with greater demands for ATP production. (See section 3.4 for a detailed discussion of cellular respiration.) Mitochondria also function in apoptosis (programmed cell death), as described in section 4.10.

**Figure 4.25 Peroxisomes.** A TEM and drawing show a peroxisome within a cell. Peroxisomes are small, spherical, membrane-bound organelles that contain enzymes that function in both digestion and synthesis of molecules. ©Don W. Fawcett/Science Source

**Figure 4.26 Mitochondria.** A drawing and TEM show the parts of a mitochondrion. Mitochondria are the double-membrane-bound organelles within the cell that engage in aerobic cellular respiration to produce ATP for energy-requiring cellular processes. ©Don W. Fawcett/Science Source

**LEARNING OBJECTIVES**

2. List the non-membrane-bound organelles of a typical human cell.

28. Describe the structure and main function(s) of each.

**4.6b Non-Membrane-Bound Organelles**

Ribosomes

Ribosomes are non-membrane-bound organelles containing protein and ribonucleic acid (RNA) that are arranged into both a large and a small subunit. The large subunit has three hollow areas designated as the A, P, and E sites (figure 4.28). You can think of the ribosomal...
subunits as puzzle pieces that are made within the nucleolus and then moved into the cytosol, where the pieces are put together into one complete puzzle (a ribosome).

Ribosomes are either bound or free. **Bound ribosomes** are attached to the external surface of the ER membrane to form rough ER. Recall that bound ribosomes of the rough ER are used to synthesize proteins destined for export out of the cell, to become an integral part of the plasma membrane, or to serve as enzymes within lysosomes. **Free ribosomes** are suspended within the cytosol. In general, all other proteins that function within the cell are synthesized by free ribosomes. The details of how ribosomes function in synthesizing protein are described in section 4.8b.

**Centrosome**

The **centrosome** is a structure typically in close proximity to the nucleus. It contains a pair of perpendicularly oriented, cylindrical **centrioles** (sen’trē-ōl; *kentron* = a point, center) surrounded by protein that is amorphous (without a distinctive shape) (figure 4.28). The paired centrioles are positioned perpendicular to each other with each composed of triplets of microtubules arranged in a circle. The primary function of a centrosome is organizing microtubules within the cytoskeleton (described shortly). The centrosome is best known for its function in cellular division, during which microtubules form spindle fibers to facilitate chromosome movement, as described in section 4.9b.

**Proteasomes**

Large, barrel-shaped protein complexes called **proteasomes** (pro’tē-ásōm) are major protein-digesting organelles located within both the cytosol and nucleus of cells (figure 4.29). Proteasomes degrade cell proteins through an ATP-dependent pathway; these proteins include damaged proteins, incorrectly folded proteins, and normal proteins that are no longer needed by the cell. The action of proteasomes also provides a means to control the quality of exported cell proteins. This latter function is especially critical during the regulation of cellular

Figure 4.27 Ribosomes. Ribosomes function in protein synthesis and are either bound to the endoplasmic reticulum or free within the cytosol. (a) Each ribosome consists of both a small and large subunit with each subunit composed of protein and RNA. (b) A TEM shows both bound and free ribosomes in the cell cytosol.

Figure 4.28 Centrosome. A TEM and a drawing show that a region of the cytoplasm called the centrosome contains a centriole pair immediately adjacent to the nucleus.
Protein to be degraded is first "tagged" with a ubiquitin molecule. Proteins of the infectious agent are cleaved by a proteasome. These degraded peptide fragments of the infectious agent are considered "nonself" and are presented to specialized white blood cells, alerting the immune system that the body has been "invaded" (see section 22.4c).

Recent research has shown that significant age-related alterations in proteasome structure and function may prevent or inhibit the normal removal of proteins from the cell.

The Cytoskeleton

The cytoskeleton is a framework of diverse proteins that extends both beneath the plasma membrane and through the interior of the cell. It both supports the cell (as the skeleton supports the body) and organizes the organelles. Three separate types of protein molecules form the cytoskeleton—microfilaments, microtubules, and intermediate filaments (figure 4.30).

Figure 4.29 Proteasomes. These organelles maintain order within the cell by digesting abnormal and unwanted cellular proteins. Both a sketch and a drawing are shown.

INTEGRATE
CONCEPT CONNECTION

A specific example of proteasome action occurs when a virus or other infectious agent enters a cell. Proteins of the infectious agent are cleaved by a proteasome. These degraded peptide fragments of the infectious agent are considered "nonself" and are presented to specialized white blood cells, alerting the immune system that the body has been "invaded" (see section 22.4c).
Microfilaments (mi-krō-fil′-a-ment; micro = small) are the smallest components of the cytoskeleton, with a diameter of about 7 nanometers. They are composed of globular actin protein monomers that are organized into two thin, intertwined protein filaments (actin filaments) similar to two twisted pearl strands. Individual globular actin proteins are added to one end of the microfilament for growth in a particular direction and removed from the other end for shortening. They form an interlacing web or network of protein on the cytoplasmic side of the plasma membrane. This network of protein provides internal structural support of the plasma membrane, including the plasma membrane extensions called microvilli (described in section 4.6c). A contractile ring of these proteins separates the two cells formed during cytokinesis (a process of cell division described in section 4.9b). Microfilaments are also located throughout the cell to facilitate movement of organelles, vesicles, and molecules within the cell (through cytoplasmic streaming) and participate in muscle contraction (see section 10.3c).

Microtubules (mi-krō-tū′-būl; tubus = tube) are the largest components of the cytoskeleton, with a diameter of about 25 nanometers. They are composed of globular tubulin protein monomers that are organized into hollow cylinders. Microtubules, like microfilaments, may be elongated or shortened as needed, by the addition or removal of tubulin monomers. Microtubules are arranged like railway tracks for directing the movement of organelles and vesicles within a cell (e.g., fast axonal transport in neurons; see section 12.2c). They also extend into the core of both cilia (see figure 4.1b) and flagella, where they slide past one another for the movement of these hairlike cellular projections (see section 4.6c). New microtubules are formed during cellular division (as spindle fibers) to separate chromosomes during mitosis (see section 4.9b).

Intermediate filaments are intermediate in size relative to the microfilaments and microtubules, with a diameter between 8 and 12 nanometers. These less flexible proteins extend across the inside of the cell and function as rigid rods to both support the cell and stabilize junctions between them (see desmosomes in section 4.6d). Their protein composition differs, depending upon the cells in which they occur. Keratin, a protein of the skin, hair, and nails, is an example of one type of intermediate filament (see section 6.1a); another type forms neurofilaments of nerve cells (see section 12.2b).

Microvilli

Microvilli are thin, microscopic membrane extensions of the plasma membrane. Microvilli are shorter and narrower than cilia (average about 1 µm high and 0.08 µm wide), are more densely packed together, and lack powered movement (figure 4.31). Each microvillus is supported by microfilaments (actin proteins are cross-linked into a dense bundle that serves as its structural core). Microvilli provide a more extensive plasma membrane surface area for more efficient membrane transport (see section 4.3). Just as not all cells have cilia, not all cells have microvilli. Cells with microvilli occur, for example, throughout the small intestine, where increased surface area is needed to absorb digested nutrients (see section 26.3b).

WHAT DID YOU LEARN?

21 Which cellular surface structure functions in (a) increasing the cell’s surface area and (b) moving material past the cell?
4.6d Membrane Junctions

LEARNING OBJECTIVE

31. Compare and contrast the structure and function of the three major types of membrane junctions.

Membrane junctions are composed of both integral and peripheral membrane proteins (see section 4.2b), which function to connect and support cells. Most of our cells are arranged into structural units called tissues that act together in a common function (see section 1.4b). To provide an orderly arrangement between some cells and coordinate their interactions, membrane junctions are located between adjacent cells. There are three major types of membrane junctions: tight junctions, desmosomes, and gap junctions (figure 4.32).

Tight Junctions

A tight junction (or zonula occludens) is composed of plasma membrane proteins that form strands or rows of proteins (e.g., claudins and occludins). These cell membrane junctions are positioned at the apical surfaces around the circumference of each of the adjacent cells. Tight junctions function as spot welds to seal off the intercellular space and prevent substances from passing between the cells; this requires all materials to move through, rather than between, the cells. For example, tight junctions associated with epithelial cells that form the lining of the small intestine prevent corrosive digestive enzymes that are within the lumen of the intestine from moving between cells and damaging other body structures (see section 26.3b). These junctions also prevent leakage of urine through the urinary bladder wall (see section 24.8b).

Desmosomes

A desmosome (dez’mōsōm; desmos = a band), also called macula adherens (“adhering spot”), is composed of several different proteins that bind neighboring cells. A thickened structure called a protein plaque is located on the internal surface of the plasma membrane of adjoining cells. Numerous protein filaments (e.g., desmogleins) extend from the plaque through the plasma membrane of both adjoining cells. These filamentous proteins extend across the small space between the two cells, where they are anchored to one another. Also anchored to each protein plaque are intermediate filaments of the cytoskeleton that extend from the protein plaque throughout the cell to provide support and strength. Observe in figure 4.32 the pattern of these proteins forming a desmosome between two adjoining cells: intermediate filaments, protein plaque, adjoining protein filaments, protein plaque, and intermediate filaments. This anatomic arrangement provides structural integrity to cells that are exposed to stress, such as the external layer of the skin (see section 6.1a) and cardiac muscle (see section 19.3f). Hemidesmosomes (i.e., half of a desmosome) anchor the basal layer (attached surface) of cells of the epidermis to the underlying basement membrane (see section 6.1a).

Gap Junctions

A gap junction is composed of six integral plasma membrane proteins, called connexons (kon-neks’onz), that form a tiny, fluid-filled tunnel or pore that extends across a small gap (about 2 nanometers) between adjacent cells. Gap junctions provide a direct passageway for substances to move between neighboring cells. Ions, glucose, amino acids, and other small solutes can pass directly from the cytosol of one cell into the neighboring cell through these pores. The flow of ions between cells allows spread of electrical activity in cardiac muscle of the heart (see section 19.3f).

Cellular structures and their associated functions are integrated in figure 4.33. This figure includes the three primary components of a cell: the cytoplasm, the nucleus, and the plasma membrane.

WHAT DID YOU LEARN?

22 Which cellular junction (a) provides resistance to mechanical stress, (b) allows the passage of ions between cells, and (c) prevents leakage between cells?

4.7 Structure of the Nucleus

The nucleus is the largest structure in the cell, typically averaging about 5 µm to 7 µm in diameter. It is often called the cell’s control center (figure 4.34). A cell typically has one nucleus. However, erythrocytes contain no nucleus, and skeletal muscle cells have many nuclei. The shape of the nucleus generally mirrors the shape of a cell. For example, a cuboidal cell has a spherical nucleus in the center of the cell, whereas a thin, flattened cell has a nucleus elongated in the same direction as

Chapter Four  Biology of the Cell  133
**Golgi apparatus:**
Modifies, packages, and sorts molecules from ER, synthesizes proteoglycans.

*INTEGRATE CONCEPT OVERVIEW*

**Figure 4.33 Cellular Structures and Their Functions.** Cells are responsible for all body functions. Most of the cellular functions occur within (1) the cytoplasm, which includes (1a) cytosol, (1b) membrane-bound organelles and non-membrane-bound organelles, and (1c) cell inclusions. (2) The nucleus is enclosed by the nuclear envelope and contains DNA and the nucleolus. (3) The plasma membrane is composed of a phospholipid bilayer, proteins, cholesterol, and glycolipids and glycoproteins.

**1) CYTOPLASM**

**(1a) Cytosol**
Viscous fluid medium of cell

**Endoplasmic reticulum**

**Smooth ER:**
Synthesizes and stores lipids, metabolizes carbohydrates, detoxifies drugs and poisons

**Rough ER:**
Synthesizes, modifies, transports, and stores protein formed by attached ribosomes

**Ribosome**
Forms
Contributes to formation

**Transport vesicle**
Forms

**Endoplasmic reticulum**

**Peroxisomes:**
Digest molecules, synthesize some lipids

**Contributes digestive enzymes**

**Forms**

**Golgi apparatus:**
Modifies, packages, and sorts molecules from ER, synthesizes proteoglycans

**Mitochondrion:**
Breaks down fuel molecules (e.g., pyruvate, fatty acids) in the presence of oxygen to release energy for the synthesis of ATP molecules

**Lysosomes:**
Digest molecules of cell or ingested material

**Secretory vesicles**
Exocytosis of contents

**(1b) Organelles: Membrane-Bound Organelles**

**Transport vesicle (transports)**

**Centrosome:**
Organizes microtubules for cell division

**Proteasome:**
Digests unwanted protein

**Cytoskeleton:**
Intracellular structural support and organization of organelles, participates in cell division; facilitates movement

**Aggregates of one type of molecule**

**(1c) Cell Inclusions**

**Nuclear envelope**

**Cytosol**

**Nuclear pore**

**Cholesterol**

**Phospholipid bilayer**

**Interstitial fluid**

**Glycolysis**

**Pyruvate**

**Glucose**

**DNA:**
Genetic blueprint for synthesizing new protein

**Nucleus:**
Houses nuclear DNA

**Nucleolus:**
Synthesizes ribosomes

**Carbohydrate**

**Protein**

**Transport proteins**

**DNA: mRNA**

**Ribosome:**
Synthesizes protein

**Mitochondrion:**
Breaks down fuel molecules in the presence of oxygen to release energy for the synthesis of ATP molecules

**Transport vesicles**

**Secretory vesicles**

**Exocytosis of contents**
**Golgi apparatus:**
Modifies, packages, and sorts molecules from ER, synthesizes proteoglycans.

**Organelles:**
- **Cytosol:** Viscous fluid medium of cell.
- **Centrosome:** Organizes microtubules for cell division.
- **Proteasome:** Digests unwanted protein.
- **Cytoskeleton:** Intracellular structural support and organization of organelles, participates in cell division; facilitates movement.
  - Microtubule
  - Microfilament
  - Intermediate filament
- **Ribosome:** Synthesizes protein.

**Nucleus:**
- Houses nuclear DNA.
- **Nucleolus:** Synthesizes ribosomes.
- **DNA:** Genetic blueprint for synthesizing new protein.

**Transport vesicle**
- Contributes to formation
- Establishes and maintains electrochemical gradients at the plasma membrane.

**Mitochondrion:**
Breaks down fuel molecules (e.g., pyruvate, fatty acids) in the presence of oxygen to release energy for the synthesis of ATP molecules.

---

Some cells may have extensions of the plasma membrane that include cilia (to sweep material past the cell’s surface), microvilli (to increase surface area), or both. Sperm have a flagellum to propel them through the female reproductive tract.
Some cells contain a uniquely shaped nucleus. For example, some white blood cells (e.g., neutrophils) have a multilobed nucleus that may have two or more segments (see table 18.7).

4.7a Nuclear Envelope and Nucleolus

LEARNING OBJECTIVES

32. Describe the nuclear envelope.
33. Explain the structure and function of a nucleolus.

The nucleus is enclosed within a double membrane that is called the nuclear envelope (or nuclear membrane). It separates the cytoplasm from the nucleoplasm (the fluid within the nucleus). This boundary controls the movement of materials between the nucleus and the surrounding cytoplasm. Each of the two layers of the nuclear envelope is a phospholipid bilayer, similar in structure to the plasma membrane. Externally it is continuous with the rough ER. Nuclear pores are open passageways formed by proteins that extend through fused regions of the nuclear envelope. They are larger than ion channels and allow for the passage of larger molecules both into the nucleus (e.g., proteins) and out of the nucleus (e.g., messenger RNA). Ions and water-soluble molecules also pass through nuclear pores.

The cell nucleus typically contains one dark-staining, usually spherical body called a nucleolus (nū-kle-ō-lūs) (figure 4.34a). (The plural term is nucleoli [nū-kle′-ō-lī].) A nucleolus is not membrane-bound. It is composed of protein and RNA, and it is responsible for producing the large and small subunits of ribosomes, which synthesize proteins.

Not all cells contain a nucleolus. Its presence and relative number indicate the protein synthesis activity of a cell. For example, nerve cells contain more than one nucleolus because numerous ribosomes are needed for the production of its many proteins. In contrast, sperm have no nucleoli because they produce no proteins.

WHAT DID YOU LEARN?

23. What is the function of nuclear pores within the nuclear envelope?
24. What is the function of the nucleolus?

4.7b DNA, Chromatin, and Chromosomes

LEARNING OBJECTIVE

34. Describe the relationship of DNA, chromatin, and genes.

The nucleus houses the nuclear DNA (a nucleic acid molecule) along with the nucleolus and nucleoplasm. Recall that a nucleic acid molecule is composed of nucleotides, including nitrogenous bases, sugars, and phosphate groups. The DNA is organized into chromosomes, which are tightly coiled structures. Histones, a type of protein, play a role in the condensation of DNA into chromosomes. When a cell needs to use a specific gene, the DNA is uncoiled to allow for transcription into RNA. The functional unit of DNA is the gene, which is a sequence of DNA that directs the synthesis of a specific protein.
acid molecule is formed by repeating monomers called **nucleotides** (see figure 2.21). DNA is specifically composed of **deoxyribonucleotides**, which include the five-carbon sugar deoxyribose, a phosphate, and one of four nitrogenous bases: adenine (A), cytosine (C), guanine (G), and thymine (T). Nucleotide monomers are linked through the phosphate groups by **phosphodiester bonds** to form a polymer strand. Each DNA molecule contains two complementary strands of nucleotides. They are bonded together by weak hydrogen bonds between the nucleotide bases to form a double helix structure. Note that the base adenine pairs only with the base thymine, whereas the base guanine pairs only with the base cytosine. This specific interaction between bases is called **complementary base pairing**: A to T, and C to G.

Think of the DNA as a spiral ladder, where the sugar and phosphate components of the nucleotide monomers form the vertical “struts” of the ladder. The horizontal “rungs” of the ladder are formed by pairs of nucleotide bases interconnected by weak hydrogen bonds to the complementary strand. The order of the bases in the nucleotides ultimately codes for specific proteins that the body needs.

DNA is an enormous macromolecule that comprises most of the genetic material of the cell (a small amount is found within mitochondria). The amount of DNA in a human cell contains over 3 billion pairs of nucleotides. A human somatic (body) cell nucleus has 46 separate double-stranded DNA molecules. To help package the DNA within the nucleus, each long DNA double helix winds around a cluster of special nuclear proteins, called **histones**, forming a complex called a **nucleosome** (figure 4.34b). Many nucleosomes are present along each DNA strand. When a cell is not dividing, the DNA and its associated proteins are in the form of a finely filamented mass called **chromatin** (kro′ma-tin; chroma = color), which resembles an unrolled spool of thread. Chromatin becomes tightly coiled masses called **chromosomes** only when a cell is dividing.

DNA is organized functionally into discrete units called **genes** (figure 4.34c). Genes are segments of nucleotides within DNA that provide the instructions for the synthesis of specific proteins. About 1–2% of the total amount of DNA composes genes. The average length of a gene is about 3000 nucleotide base pairs. Associated with each gene is a **promoter** region that is analogous to a “start” signal, and a **terminal** region that is analogous to a “stop” signal for the transcription, or copying, of a gene into an RNA molecule to direct the synthesis of a protein (see section 4.8b). Although you are probably more familiar with the term **chromosome** (than chromatin), our genetic DNA is typically present in our cells as chromatin. This looser arrangement of DNA allows cellular structures access to genes. As we will see, the tightly coiled mass of chromosomes is needed only to prevent the DNA from becoming tangled during cell division (see section 4.9).

### What Did You Learn?

**Describe the structural relationship of DNA and chromatin, and the functional relationship of DNA and genes.**

### 4.8 Function of the Nucleus and Ribosomes

We continue our discussion of cellular functions by describing protein synthesis, the central process upon which all other cellular activities ultimately depend. The DNA directs protein synthesis, which occurs at ribosomes in the cytosol. Consequently, two major events are involved: (1) **transcription**, which is the formation of a ribonucleic acid (RNA) copy of a gene from DNA in the nucleus, and (2) **translation**, which uses the information coded in RNA for the synthesis of the protein by ribosomes in the cytosol (figure 4.35).

For both processes, we first describe the required structures and then the mechanism involved.

### 4.8a Transcription: Synthesizing RNA

#### Learning Objectives

35. List the required structures for transcription.

36. Explain the three steps of transcription.

**Transcription** occurs within the nucleus of the cell. This process occurs when a segment of DNA is “read” and copied to produce a newly formed strand of RNA.

#### Required Structures

DNA is the major structure required in transcription. DNA serves as the template to form an RNA molecule that is complementary to the sequence of nucleotides in the gene. RNA (as described in section 2.7d) is a nucleic acid composed of repeating ribonucleotide monomers. Each **ribonucleotide** has a five-carbon sugar ribose, a phosphate, and one of four nitrogenous bases that include adenine (A), cytosine (C), guanine (G), and uracil (U). Unlike DNA, RNA is only a single strand of nucleotides (see figure 2.21).

Forming RNA during transcription requires both large numbers of ribonucleotides and the enzyme RNA polymerase. These structures
are located within the nucleoplasm in the nucleus. The enzyme RNA polymerase assembles the ribonucleotides by complementary base-pairing ribonucleotides with DNA as follows:

Although other enzymes and many regulatory factors are involved in the process, we limit our discussion to the basic process of transcription that involves DNA, ribonucleotides, and the enzyme RNA polymerase.

Process of Transcription

Three functional types of RNA are produced during transcription: messenger RNA (mRNA), transfer RNA (tRNA), and ribosomal RNA (rRNA). The general process of transcription includes three major events: initiation, elongation, and termination (figure 4.36).

**LEARNING STRATEGY**

The process of transcription may be compared to writing down a recipe. The DNA is the recipe book, and a gene is a specific recipe. The recipe book is opened (initiation), the specific recipe is written down (elongation), and the recipe book is closed (termination).

**Initiation** DNA is usually coiled into a double helix, so it first must be unwound in the region of the gene so its information is available for “reading” (copying). Specific enzymes help to partially unwind the DNA and make it accessible to RNA polymerase, the enzyme that catalyzes the synthesis of an mRNA (messenger RNA) molecule. After the partial unwinding of DNA, RNA polymerase attaches to the DNA strand and moves along its length until it comes in contact with the promoter region (the “start” region) associated with a gene.

The gene is marked for transcription by a number of regulatory factors that reflect a requirement for the specific protein coded for by that gene. The promoter serves as the start point for gene transcription. When identification of the gene and binding of the appropriate factors occurs, the hydrogen bonds between the two strands of DNA break, thus allowing expansion, or opening up, in that region. That permits the nitrogenous bases in the region to be available DNA.

**Elongation** Free ribonucleotides (which are within the nucleoplasm) are base-paired in a complementary way with the exposed bases in the DNA template strand during the elongation process. The enzyme RNA polymerase assists in this base pairing. Base pairing involves the formation of hydrogen bonds between a base of a ribonucleotide and its complementary base of the DNA strand. For example, if the base sequence of a DNA template strand is TTAGCTAGC, then the base sequence of the newly formed RNA strand will be AAUCAUAGC. (Recall that RNA contains the nitrogenous base uracil instead of thymine.) A phosphodiester bond is formed between each of the ribonucleotides to form the RNA polymer. RNA polymerase continues to move along the length of DNA until the entire gene has been transcribed. As a result, a new mRNA is formed from the “information” in the gene.

**Termination** When the terminal region at the end of the gene is reached, RNA polymerase is released from the DNA as hydrogen bonds are broken between the DNA strand and newly formed mRNA strand. The DNA rewinds into a double helix. The newly formed mRNA is a “recipe” copied from DNA for synthesizing a specific protein (e.g., insulin).

**Modifications to mRNA**

Several significant changes are made to the newly formed mRNA before it leaves the nucleus. The initially synthesized strand of mRNA is more specifically called the pre-mRNA (or primary transcript). The changes result in the formation of a mature mRNA, which is then used as the recipe to make the protein.

**Splicing** Pre-mRNA includes introns, which are noncoding regions. These introns are removed (most are degraded, but some have specialized functions in regulating gene expression). Exons are the coding region and are subsequently spliced together. This process is catalyzed by a ribonucleoprotein molecule complex (composed of RNA and protein) called a spliceosome. The pattern of splicing varies depending on several factors, including the organism’s stage of development and the cell type. Thus, splicing provides a means of producing a larger number of proteins from the available DNA.

**Other Changes** Further modifications to form the mature mRNA include capping and addition of a polyA tail. Capping involves the unique bonding of a ribonucleotide containing guanine to the lead end of the mRNA. This increases the stability of an mRNA strand, helping to prevent its digestion by nucleic acid digesting enzymes (nucleases) that are present within the cytosol. The polyA tail addition involves removing terminal segments of the mRNA and placing numerous adenine-containing ribonucleotides at the tail end of the mRNA. The addition of a polyA tail, like the splicing, provides a means of producing more than one mature mRNA transcript, because the segment that is removed and the addition of the polyA tail can be done at different sites. One function of the polyA tail is to serve as a measure of age of the mRNA. These nucleotides are subsequently removed over time, and the tail is shortened. When only a certain amount of the poly A tail remains, nuclease enzymes will destroy the mRNA.
Translation is the synthesis of a new protein, and it takes place at a ribosome within the cytosol. The mRNA is moved through a ribosome, and its information is “read.” The code in the nucleotide sequence of mRNA is translated, meaning that it is converted into a specific sequence of amino acids to produce newly formed strands of protein.

**WHAT DID YOU LEARN?**

What are the three major structures required for transcription? Explain where and how transcription occurs.

4.8b Translation: Synthesizing Protein

**LEARNING OBJECTIVES**

37. List the required structures for translation.
38. Name the three functional forms of RNA, explain what is meant by codon, and identify three types of codon sequences.
39. Describe the three steps of translation.

**LEARNING STRATEGY**

The required components of translation may be compared to a chef cooking up a masterpiece. The ribosome is the kitchen, the mRNA is the recipe, the tRNAs are the chef’s assistants, the amino acids are the ingredients, and the protein is the completed dish. The tRNA assistants bring the amino acid ingredients to the kitchen, as directed by the mRNA recipe, to produce a protein masterpiece.

**Figure 4.36 Process of Transcription.** Transcription occurs within the nucleus of the cell. RNA is formed from a template strand of DNA during transcription. It has three major events that include initiation, elongation, and termination.
Required Structures

Translation requires ribosomes, mRNA, tRNA, and large numbers of free amino acids. Protein is the product formed.

Ribosomes were introduced in section 4.6b (see figure 4.27). These globular organelles are composed of a large subunit and a small subunit synthesized by the nucleolus. Each subunit is considered to be a ribonucleoprotein because each is assembled from one to two RNA molecules and various proteins. The large subunit has three associated grooves or spaces: (1) the A (aminoacyl) site, which is where new amino acids are added; (2) the P (peptidyl) site, which holds the newly forming polypeptide (protein); and (3) the E (exit) site for the tRNA that is exiting the ribosome.

Three functional types of RNA are required for protein synthesis: ribosomal RNA, messenger RNA, and transfer RNA (figure 4.37).

Ribosomal RNA (rRNA) is so named because it is the specific type of RNA forming ribosomes. Research has shown that rRNAs within the ribosomal structure serve as the catalysts during assembly of amino acids into a protein molecule.

Messenger RNA is the molecule that is transcribed from a gene. It carries the instructions for synthesizing a protein. Messenger RNA is a linear sequence of nucleotides varying in length, depending upon the size of the protein to be made. The mRNA is read three nucleotide bases at a time. Each three-base unit is called a codon. A molecule of mRNA contains the following three categories of codons (figure 4.38):

- A **start codon** that always contains the three bases AUG, which codes for the amino acid methionine; this is the signal that indicates where protein synthesis begins.

**Figure 4.37 Required Structures for Translation.** The process of translation uses the information in the mRNA to direct protein synthesis. (a) Translation occurs at ribosomes (composed of protein and rRNA) and requires both messenger RNA and transfer RNA. (b) Amino acids are the building blocks used to produce the newly formed protein molecule.
The tRNA is now called a charged tRNA after the binding of the amino acid has occurred. The second function of the anticodon of each tRNA is to serve as the “adapter site” for binding a tRNA to its complementary codon of a mRNA.

As noted, there are 20 different amino acids normally found in the proteins of living organisms. We discussed in section 2.8 that the properties of the R groups form the basis for organizing and grouping amino acids. Thus, to synthesize a new protein, which may contain hundreds to thousands of individual amino acids, the necessary amounts of the different amino acids must be available in the cytosol in proximity to ribosomes.

Process of Translation

Translation of the mRNA sequence into a functional protein also involves three major events, as those identified for transcription: initiation, elongation, and termination (figure 4.39).

### CONCEPT CONNECTION

Chemical reactions are generally catalyzed by enzymes that are globular proteins (see section 3.3b). Ribosomes are composed of both protein and rRNA. It is the rRNA of the ribosome—and not the protein—that catalyzes the synthesis of protein. For this reason, the rRNA of the ribosome is called a ribozyme, a catalytic RNA molecule. The protein of the ribosome in this case primarily serves a structural role to hold the rRNA molecules in the correct orientation.

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### Figure 4.38 The Genetic Code.


- The consecutive codons following the start codon and before the stop codon direct the assembly of amino acids into a newly synthesized protein. Each codon determines the specific amino acid to be added to the newly forming protein strand. For example, ACG codes for the amino acid threonine, and UUC codes for the amino acid phenylalanine.
- The stop codon follows the codons used to assemble the new protein, and it is always one of the three sequences of bases: UAA, UAG, or UGA. These three codons do not code for an amino acid. Collectively, they serve as the point where the synthesis of protein is stopped.

<table>
<thead>
<tr>
<th>First Letter</th>
<th>Second Letter</th>
<th>A</th>
<th>G</th>
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<tbody>
<tr>
<td>U</td>
<td>UUU</td>
<td>Tyr</td>
<td>Cys</td>
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<tr>
<td></td>
<td>UUC</td>
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<td></td>
<td>UUA</td>
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<tr>
<td>C</td>
<td>CUU</td>
<td>Histidine</td>
<td>CGU</td>
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<td></td>
<td>CUC</td>
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<td></td>
<td>CUU</td>
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<tr>
<td></td>
<td>AUG</td>
<td>Methionine; “Start”</td>
<td>ACG</td>
</tr>
<tr>
<td>A</td>
<td>AUU</td>
<td>Asparagine</td>
<td>Arg</td>
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<tr>
<td></td>
<td>AAC</td>
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<td></td>
<td>GUG</td>
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</table>

A codon consists of three nucleotides read in the sequence shown. For example, ACU codes for threonine. The first letter, A, is in the First Letter column; the second letter, C, is in the Second Letter column; and the third letter, U, is in the Third Letter column. Each of the mRNA codons is recognized by a corresponding anticodon sequence on a tRNA molecule. Many amino acids are specified by more than one codon. For example, threonine is specified by four codons, which differ only in the third nucleotide (ACU, ACC, ACA, and ACG).
Initiation  Initiation (figure 4.39, step 1) requires the formation of a complex composed of a small subunit of a ribosome, a large subunit of a ribosome, the newly formed mRNA, and a tRNA. The small subunit of a ribosome moves along the mRNA until it reaches the start codon (AUG). A charged tRNA that possesses the anticodon UAC then base-pairs to the start codon AUG in the mRNA. The amino acid methionine is bound to this tRNA. Methionine is always the first amino acid to be used in the synthesis of a protein, but later it may be removed as protein synthesis continues and the protein matures. The large subunit then joins with the small subunit of the ribosome. The start codon now occupies the P site of the ribosome.

Elongation  Elongation (figure 4.39, step 2) involves the orderly delivery of all subsequent amino acids by specific tRNAs to form the protein. Three primary steps occur, as follows:

2a. A charged tRNA with a complementary anticodon base-pairs with the codon of the mRNA in the A site.
2b. A peptide bond is formed between the amino acid in the P site and the amino acid in the A site (as the bond of amino acid to tRNA in P site breaks).
2c. The ribosome then moves three nucleotide positions (the equivalent of a codon) “downstream” (beyond) the start codon on the mRNA. There is, of course, an accompanying change in position of the tRNAs. The tRNA that was in the A site is now in the P site, and the A site is again open. (The E site is the exit site from which the now uncharged tRNA is released.)

These processes (steps 2a–2c) repeat until the entire mRNA sequence has been translated. The product is a protein composed of a linear strand of amino acids.

Termination  Termination (figure 4.39, step 3) is when a stop codon (UAA, UAG, or UGA) enters the A site to end translation. A release factor enters the A site at this point instead of a charged tRNA. When the ribosome hits the factor bound to the mRNA stop codon, the two subunits of the ribosome are separated from the mRNA and the newly synthesized protein is released.

Note that a single mRNA can be read by more than one ribosome simultaneously, and thus many copies of that protein can be made quickly. An mRNA with many ribosomes attached along its length is called a polyribosome.

**What do you think?**

3. What might be the potential consequences to protein structure and ability to function if DNA is mutated in a specific gene?

**What did you learn?**

27. What is a codon and an anticodon?
28. How is mRNA attached to ribosomes and translated into the language of protein?

4.8c DNA as the Control Center of a Cell

**Learning Objective**

40. Explain why DNA is considered the cell’s control center.

Recall from section 2.7e that the human body is estimated to contain approximately 50,000 different proteins. These proteins serve a vast array of functions that include catalyzing reactions, defense, transport, support, movement, regulation, and storage. DNA is responsible for directing the synthesis of the proteins that carry out body functions.

Additionally, DNA is indirectly responsible for other metabolic changes that occur within a cell—including the synthesis of steroids and other lipids, and the enzymatic pathway of glucose oxidation—because...
DNA controls synthesis of the enzymes that are responsible for catalyzing both the decomposition and the synthesis of chemical structures (see section 3.3a). All of these roles explain why DNA is considered the control center of the cell and sometimes is referred to as the “boss” of the cell.

**WHAT DID YOU LEARN?**

29. The genetic code of DNA is the specific instructions to make what biological molecule?

4.9 Cell Division

Cells divide in two ways, depending upon the cell type. Mitosis (mī-tō’sis; mitos = thread) occurs in somatic cells, and meiosis occurs in sex cells. Somatic cells are all of the cells in the body other than the sex cells, and sex cells form either sperm or oocytes. Meiosis is discussed in detail in section 28.2. Here we define and describe somatic cell division that involves mitosis.

Somatic cell division occurs when one cell divides, resulting in two identical cells. Somatic cell division is essential to produce the trillions of new cells for development and growth, as well as to replace old or dying cells and those destroyed from trauma or disease.

4.9a Cellular Structures

**LEARNING OBJECTIVES**

41. Explain the structure and function of centrioles in cell division.

42. Describe the structural difference between chromatin and chromosomes, and note when each is present in a cell.

We saw earlier that a centrosome is a structure containing a pair of perpendicularly oriented, cylindrical centrioles located in close proximity to the nucleus (see figure 4.28). The centrosome organizes the microtubules that facilitate movement of chromosomes during cell division. In addition, the nucleus of human somatic cells typically has 46 separate DNA molecules that are organized as either loosely coiled chromatin or tightly coiled chromosomes (see figure 4.34).

**WHAT DID YOU LEARN?**

30. How is chromatin distinguished from a chromosome?

### 4.9b The Cell Cycle

**LEARNING OBJECTIVES**

43. Summarize the phases of the cell cycle and the activities that occur in each phase.

44. Name and explain the four main stages of mitosis.

45. Explain the function of cytokinesis.

The cell cycle depicts the steps in the replication of a somatic cell. It consists of all changes the cell undergoes as it divides into two identical cells called daughter cells. There are two major phases in the cell cycle: interphase and the mitotic (M) phase. The phases and events of the somatic cell cycle are described here and summarized in figure 4.40.

**Interphase**

Interphase is the time the cell prepares for division. This phase is distinctive in a light microscope because the DNA within the nucleus remains in the form of loosely coiled chromatin.

Interphase has three distinct phases: G1, S, and G2. During the G1 phase (also called the first gap stage) of the cell cycle, cells grow and produce new organelles and other structures needed for DNA replication. Replication of the centrioles to produce two centriole pairs is also initiated in this phase.
During the S phase (also called synthesis), the 46 double helix strands of DNA are replicated. Forming DNA requires large numbers of deoxyribonucleotides and the enzyme DNA polymerase. All of these components are located in the nucleoplasm within the nucleus.

The following steps in DNA replication (figure 4.41) involve unwinding, breaking, assembly, and restoration:

1. **Unwinding of DNA molecule.** The spiral, complementary DNA strands are unwound from each other by specific enzymes.

2. **Breaking the parent strands apart.** The hydrogen bonds holding the complementary bases together in the DNA strands are broken. Once the portions of strands are separated, binding proteins (not shown) ensure that the strands remain separated.

3. **Assembly of new DNA strands.** Both strands of DNA are read as templates by DNA polymerase enzymes that move along both parental strands (one called the leading strand and the other the lagging strand because of how transcription takes place on each). DNA polymerase assembles new strands of DNA as complementary deoxyribonucleotides are paired. For example, if the base sequence of a small portion of a DNA strand is TTAGCTAGC, then the base sequence of the newly formed complementary DNA strand assembled by DNA polymerase would be AATCGATCG. Complementary base pairs are held together by hydrogen bonds. The bond between nucleotides in the DNA polymer is a phosphodiester bond.

4. **Restoration of DNA double helix.** The DNA double strands are returned to their coiled, helix structure.

The process continues until the entire length of both strands of DNA are replicated. The replicated DNA strands, now called sister chromatids, remain attached at a region called a centromere (sen’trō-mē; kentron = center, meros = part). The joined sister chromatids form a chromosome. The sister chromatids are separated at the centromeres during mitosis; following their separation, each is called a chromosome.

**WHAT DO YOU THINK?**

4. Describe the difference in DNA replication and transcription in terms of (a) the type of nucleic acid formed and (b) the amount of DNA copied.

The last part of interphase, called the G2 phase (or the second gap phase), is brief (figure 4.40). During this phase, centriole replication is completed (having produced two centriole pairs present within the cell) and enzymes and other structures needed for cell division are synthesized.

**LEARNING STRATEGY**

To prevent confusion between the process of DNA replication and transcription (formation of RNA from DNA), remember that transcription of mRNA is analogous to copying one recipe from a cookbook. The recipe is written as DNA. In contrast, DNA replication is analogous to printing a replica of an entire cookbook. The cookbook is printed as DNA.
M Phase (Mitotic Phase)

Following interphase, cells enter the M (mitotic) phase. Two distinct events occur in this phase to produce two new cells: mitosis, which is division of the nucleus, and cytokinesis, which is the division of the cytoplasm. Mitosis begins first with cytokinesis starting and overlapping with later stages of mitosis.

Four consecutive phases take place during mitosis: prophase, metaphase, anaphase, and telophase, which can be remembered with the acronym P-MAT. Each phase merges smoothly into the next in a nonstop process. The events of each stage are summarized in figure 4.42.

Prophase is the first stage of mitosis (step b). Chromatin becomes supercoiled into the chromosomes that are more maneuverable and are less likely to become tangled during cell division. The DNA and protein within the chromatin coil, wrap, and twist, forming the chromosomes. Chromosomes are composed of the two sister chromatids, which resemble relatively short, thick rods, and chromosomes become noticeable with a light microscope during the prophase stage as dark-staining structures within the nucleus.

In addition, the nucleolus breaks down and disappears. Elongated microtubules (see figure 4.30) called spindle fibers begin to grow from the centrioles. The two centriole pairs are pushed apart by the elongating microtubules composing the spindle fibers; eventually, the centriole pairs come to lie at opposite poles (ends) of the cell. The end of prophase is marked by the dissolution (disassembly) of the nuclear envelope. This permits the chromosomes to be moved by spindle fibers through the cytoplasm during the next stages of mitosis.

Metaphase is the second stage of mitosis (step c), during which the chromosomes are aligned along an imaginary line in the middle of the cell (region called the equatorial plate). This alignment occurs through the growth of spindle fibers from each centriole toward the chromosomes. Some fibers attach to the centromere of each chromosome, directing their movement to the equatorial plate.

Anaphase, which is the third stage of mitosis, initiates as the spindle fibers cause the sister chromatids to be moved apart toward the cell’s poles; the centromere leads the way, and its “arms” trail behind (step d). Each chromatid is now a chromosome composed of one DNA double helix with its own centromere.

Telophase begins with the arrival of a group of chromosomes at each cell pole. Essentially, the processes of prophase are reversed in telophase. The chromosomes begin to uncoil and return to the form of dispersed threads of chromatin, each new nucleus forms a nucleolus, the mitotic spindle breaks up and disappears, and a new nuclear envelope forms around each set of chromosomes. Telophase signals the end of nuclear division.

Cytokinesis Cytokinesis (sītō-kī-nē′sīs; kinesis = movement) is the other major event in the mitotic phase, and it is the division of the cytoplasm between the two newly forming cells. This phase usually overlaps with anaphase and telophase of mitosis. A ring of microfilament proteins (see figure 4.30) on the inner surface of the cell’s...
INTEGRATE

LEARNING STRATEGY
These tips should help you remember the major events of each phase of mitosis:

- The **p** in **prophase** stands for the **puffy** ball of chromosomes that forms within the nucleus.
- The **m** in **metaphase** stands for **middle**: During this phase, the chromosomes align along the **middle** of the cell.
- The **a** in **anaphase** stands for **apart**: During this phase, the sister chromatids are pulled **apart**.
- The **t** in **telophase** stands for **two**: During this phase, two new cells become noticeable as a cleavage furrow deepens to divide the cytoplasm.

plasma membrane contracts at the cell’s equator. It pinches the mother cell into two separate cells in a manner analogous to the tightening of a belt. The resulting **cleavage furrow** that appears indicates where the cytoplasm is dividing (figure 4.42e). Two new daughter cells are formed and cell division is complete.

WHAT DID YOU LEARN?

31. Describe the process of DNA replication that occurs during the **S** phase of interphase.

32. What are the events that occur during the mitotic phase (mitosis and cytokinesis)? Explain each.

4.10 Cell Aging and Death

LEARNING OBJECTIVES

46. Define apoptosis.
47. List the actions that occur in a cell during apoptosis.

Aging is a normal, continuous process that often exhibits obvious body signs. In contrast, changes within cells at the molecular level due to aging are neither obvious nor well understood. The reduced metabolic functions of normal cells often have wide-ranging effects throughout the body, including a reduced ability of cells to maintain homeostasis. These signs of aging reflect a lower number of normally functioning body cells, and may even suggest abnormal functions of some remaining cells.
Cells affected by aging may exhibit alteration in either the structure or number of specific organelles. For example, if mitochondrial function begins to fail, the cell’s ability to synthesize ATP diminishes. Additionally, changes in the distribution and structure of the chromatin and chromosomes within the nucleus may occur. Often, both chromatin and chromosomes clump, shrink, or fragment as a result of repeated divisions.

Essentially, cells die by one of two mechanisms: (1) they are killed by harmful agents or mechanical damage or (2) they are induced to commit suicide, a process of programmed cell death called **apoptosis** (ap’op-tō’sis; apo = off, ptosis = a falling).

**CLINICAL VIEW 4.3**

**Tumors**

Normally, many regulatory mechanisms signal a cell when it should divide and when to stop dividing. **Tumors** arise when cells either proceed through the cell cycle without a start signal or fail to respond to signals that normally stop cell division. The tumor may, due to its size, interfere with the function of the normal surrounding cells. A cancerous tumor is invasive, and cells may enter the blood or lymph and metastasize to other areas of the body and establish secondary tumors.

Apoptosis occurs in orderly, well-defined, continuous, degradative steps to destroy and remove cellular components and eventually cell remnants. This biochemical mechanism is initiated by ligand-receptor signaling. Upon binding of ligand to a receptor, inactive, self-destructive enzymes within the cytosol are turned on and initiate the following actions:

- Destruction of DNA polymerase to prevent the synthesis of new DNA
- Digestion of the DNA into small fragments
- Digestion of the cytoskeleton, thus destroying structural support for organelles and the nucleus—the cell appears to shrink and become rounded and the nuclear shape changes
- Formation of small, irregular blebs (bubbles) on the plasma membrane surface
- Condensation of the cytosol and destruction of organelles—specifically, the mitochondria to deprive the cell of ATP needed for energy-requiring processes
- Release of proteins within mitochondria, activating specific digestive enzymes (caspase proteaseses) in cytosol; these enzymes digest cellular structures and signal for engulfment of the cell by phagocytosis

Programmed cell death occurs both to promote proper development and to remove harmful cells. For example, the proper development of fingers and toes begins with the formation of a paddlelike structure at the distal end of the developing limb. Programmed cell death removes the cells and tissues between the fingers and toes developing within this paddle structure.

Programmed cell death sometimes destroys harmful cells, reducing potential health threats. Cells of our immune system promote programmed cell death in some virus-infected cells to reduce the further spread of infection (see section 22.3c). Cells that have damage to their DNA often appear to promote events leading to apoptosis, presumably to prevent these cells from causing developmental defects or becoming cancerous. Some cancer therapy treatments lead to apoptosis in certain types of cancer cells.

**WHAT DID YOU LEARN?**

What are the specific changes that occur to DNA during apoptosis?
### CHAPTER SUMMARY

<table>
<thead>
<tr>
<th><strong>4.1 Introduction to Cells</strong></th>
<th><strong>4.2 Chemical Structure of the Plasma Membrane</strong></th>
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<tbody>
<tr>
<td>- Cells are the structural and functional units of the body.</td>
<td>- The plasma membrane is a fluid matrix that has approximately an equal mixture of lipids and proteins by weight.</td>
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<tr>
<td>- Cells vary in size and shape, but they have certain common features and functions.</td>
<td><strong>4.2a Lipid Components</strong></td>
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<tr>
<td>- Cells are microscopic and can be studied using a light microscope (LM), scanning electron microscope (SEM), and transmission electron microscope (TEM).</td>
<td>- The plasma membrane is composed of a bilayer of phospholipids with embedded cholesterol molecules. Glycolipids are lipids with carbohydrates extending from the outer surface of the cell.</td>
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<tr>
<td><strong>4.1b Cell Size and Shape</strong></td>
<td><strong>4.2b Membrane Proteins</strong></td>
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<tr>
<td>- Although some cells are round or cubelike, other cells are flat, cylindrical, oval, or quite irregular in shape.</td>
<td>- Plasma membrane proteins are integral proteins that extend through the plasma membrane, whereas peripheral proteins reside on either the internal or external surface of the plasma membrane.</td>
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<tr>
<td><strong>4.1c Common Features and General Functions</strong></td>
<td>- Functionally, the plasma membrane proteins include several types of transport proteins, receptors, identity markers, enzymes, attachment sites for the cytoskeleton, and cell-adhesion proteins.</td>
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<td>- The three major structural components of a cell include the nucleus, plasma membrane, and cytoplasm (composed of cytosol, organelles, and perhaps cell inclusions).</td>
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<td>- All cells must maintain their integrity and shape, obtain nutrients and form chemical building blocks, dispose of wastes, and if possible, replace cells.</td>
<td><strong>4.3 Membrane Transport</strong></td>
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<tr>
<td><strong>4.3a Passive Processes: Diffusion</strong></td>
<td><strong>4.3b Passive Processes: Osmosis</strong></td>
</tr>
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<td>- Diffusion is the movement of a solute from an area where it is more concentrated to an area where it is less concentrated.</td>
<td>- Osmosis is the passive movement of water across a semipermeable membrane down a water concentration gradient.</td>
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<tr>
<td>- Simple diffusion is the unassisted movement of small, nonpolar molecules through the phospholipid bilayer.</td>
<td>- Osmotic pressure is the pressure exerted by the movement of water across a semipermeable membrane due to a difference in solution concentration; the greater the difference, the greater the osmotic pressure.</td>
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<td>- Channel-mediated facilitated diffusion is the transport of ions through channels that either are always open (leak channels) or open and close as a result of a stimulus (gated channels).</td>
<td>- The terms isotonic, hypotonic, and hypertonic describe the relative concentration of solutions.</td>
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<tr>
<td>- Carrier-mediated facilitated diffusion is the transport of polar molecules through a carrier that is induced to change shape to move the molecules across the plasma membrane.</td>
<td><strong>4.3c Active Processes</strong></td>
</tr>
<tr>
<td><strong>4.4 Resting Membrane Potential</strong></td>
<td>- Active processes require the expenditure of cellular energy and include both active transport and vesicular transport.</td>
</tr>
<tr>
<td>- The plasma membrane functions in establishing and maintaining the resting membrane potential (RMP).</td>
<td>- The two types of active transport are primary active transport, which obtains its energy directly from ATP, and secondary active transport, which is “powered” by the movement of a second substance (usually sodium ion) down its concentration gradient.</td>
</tr>
<tr>
<td><strong>4.4a Introduction</strong></td>
<td>- Vesicular transport occurs through energy-requiring processes that involve a vesicle for transporting large materials or relatively large amounts of a substance either out of a cell or into a cell.</td>
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<tr>
<td>- The RMP is the electrical charge difference at the plasma membrane when a cell is at rest; it typically ranges between −50 millivolts (mV) and −100 mV.</td>
<td>- Exocytosis moves material out of a cell, and endocytosis moves substances into a cell.</td>
</tr>
<tr>
<td><strong>4.4b Establishing and Maintaining an RMP</strong></td>
<td>- The three types of endocytosis are phagocytosis, pinocytosis, and receptor-mediated endocytosis.</td>
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<tr>
<td>- K⁺ leaks out of a cell through K⁺ leak channels, and Na⁺ leaks into a cell through Na⁺ leak channels. This movement of ions is primarily responsible for establishing an RMP. The Na⁺/K⁺ pumps maintain ion gradients following movement of these ions.</td>
<td><strong>(continued on next page)</strong></td>
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</table>
### 4.5 Cell Communication
- Cell communication occurs either through direct contact or through binding of ligands released from other cells.

#### 4.5a Direct Contact Between Cells
- Direct contact is used as a means of cell communication by the cells of the immune system in protecting the body from potentially harmful substances. It is also used during fertilization, development, and cellular repair.

#### 4.5b Ligand-Receptor Signaling
- Three general types of receptors are distinguished by their different response to the binding of a ligand: They include channel-linked receptors, enzymatic receptors, and G protein–coupled receptors.

### 4.6 Cellular Structures
- Cellular structures include membrane-bound and non-membrane-bound organelles, vesicles, and structures extending from the cell surface.

#### 4.6a Membrane-Bound Organelles
- Membrane-bound organelles are surrounded by a membrane that separates the organelle’s contents from the cytosol so that the specific activities of the organelle can proceed without being disrupted by other cellular activities.
- The membrane-bound organelles include the endoplasmic reticulum, the Golgi apparatus, lysosomes, peroxisomes, and mitochondria. They are involved in various forms of metabolic processes, including synthesis and degradation processes that occur within a cell.

#### 4.6b Non-Membrane-Bound Organelles
- Non-membrane-bound organelles are composed of either protein alone or protein and RNA; they include ribosomes, centrosomes with centrioles, proteasomes, and the cytoskeleton.

#### 4.6c Structures of the Cell’s External Surface
- Cilia and flagella are extensions of the plasma membrane supported by microtubules; cilia sweep materials along the cell’s outer surface; a flagellum, located only on sperm, moves the sperm through the female reproductive tract.
- Microvilli are extensions of the plasma membrane supported by microfilaments, which increase cell surface area for more efficient membrane transport.

#### 4.6d Membrane Junctions
- Membrane junctions include tight junctions, desmosomes, and gap junctions.

### 4.7 Structure of the Nucleus
- The nucleus is the largest structure within a cell; it has a shape that typically mirrors the cell’s shape.

#### 4.7a Nuclear Envelope and Nucleolus
- The nuclear envelope is a double phospholipid bilayer that serves as the boundary between nucleoplasm and the cytoplasm.
- A cell typically contains one nucleolus within its nucleus. It is a structure responsible for synthesizing the large and small subunits of ribosomes.

#### 4.7b DNA, Chromatin, and Chromosomes
- DNA is wrapped around histone proteins and packaged as chromatin.
- Chromatin is supercoiled into chromosomes only when a cell is proceeding through cell division.
- DNA contains functional units called genes; a gene is a segment of DNA that carries instructions for making a specific protein.

### 4.8 Function of the Nucleus and Ribosomes
- The nucleus and ribosomes are required to synthesize proteins, a process that involves transcription and translation.

#### 4.8a Transcription: Synthesizing RNA
- RNA is formed from DNA through transcription, a process that occurs in the nucleus and requires DNA, free ribonucleotides, and the enzyme RNA polymerase.

#### 4.8b Translation: Synthesizing Protein
- Translation occurs in the cytosol. It requires ribosomes (composed of protein and rRNA), messenger RNA (mRNA), transfer RNA (tRNA), and large numbers of free amino acids and results in the synthesis of a new protein.

#### 4.8c DNA as the Control Center of a Cell
- DNA is responsible for directing the synthesis of proteins.

### 4.9 Cell Division
- Mitosis is one of two types of dividing a nucleus during cell division that occurs in cells.
- Cell division involving mitosis produces two identical cells when one divides. It is a necessary process for development, tissue growth, replacement of old or dying cells, and tissue repair.

#### 4.9a Cellular Structures
- The major structures required in cell replication are chromatin (chromosomes), centrioles, free deoxyribonucleotides, and the enzyme DNA polymerase.

#### 4.9b The Cell Cycle
- The cell cycle consists of a series of changes the cell undergoes between its formation and the time it divides into two identical cells, called daughter cells. It is divided into two major phases: interphase and the mitotic phase.

### 4.10 Cell Aging and Death
- Cellular changes associated with aging are neither obvious nor well understood.
- Cell death occurs by harmful agents or mechanical damage, or through induction that leads to suicide, a process called apoptosis.
1. All of the following general functions are carried out by all cells except:
   a. obtaining nutrients and chemical building blocks.
   b. maintaining integrity of the plasma membrane.
   c. replacing cells through cell division.
   d. disposing of wastes.

2. The molecule that is responsible for most functions of the plasma membrane is:
   a. the phospholipid bilayer.
   b. cholesterol.
   c. glycolipid.
   d. protein.

3. Which process does not require cellular energy (and thus, it is a passive process)?
   a. primary active transport.
   b. carrier-mediated facilitated diffusion.
   c. endocytosis.
   d. exocytosis.

4. One substance flows down its concentration gradient, and the energy is harnessed to move another substance up its gradient in the same direction. This best describes:
   a. primary active transport.
   b. endocytosis.
   c. symport secondary active transport.
   d. antiport secondary active transport.

5. Which of the following is a non-membrane-bound organelle?
   a. ribosomes.
   b. lysosomes.
   c. the Golgi apparatus.
   d. the endoplasmic reticulum.

6. This organelle is composed of extensive amounts of membrane. It synthesizes lipids and detoxifies harmful substances such as alcohol. This organelle is:
   a. the smooth endoplasmic reticulum.
   b. a mitochondrion.
   c. a proteasome.
   d. a lysosome.

7. Which of the following organelles destroys malformed proteins, proteins that do not fold normally, and proteins that are no longer needed by a cell?
   a. centriole
   b. peroxisome
   c. proteasome
   d. nucleolus

8. The process of forming RNA from DNA is called:
   a. mitosis.
   b. DNA replication.
   c. translation.
   d. transcription.

9. During this stage of mitosis, the chromatin coils to form chromosomes, the nuclear envelope disappears, the nucleolus dissolves, spindle fibers are formed, and the centrioles migrate to the poles.
   a. prophase
   b. metaphase
   c. anaphase
   d. telophase

10. Erythrocytes do not have a nucleus. In what two cellular processes can they not engage?
    a. apoptosis and synthesis of lipid
    b. protein synthesis and cell division
    c. digestion of unwanted protein and cell division
    d. formation of vesicles and protein synthesis

11. Describe the general structure and function of the three major structures of a cell.

12. List and describe the functions of plasma membrane proteins.

13. Describe the passive processes of membrane transport, including simple diffusion, facilitated diffusion, and osmosis.

14. Describe the active processes of membrane transport, including primary active transport, secondary active transport, and the various forms of vesicular transport.

15. List the membrane-bound structures, and describe the structure and function of each.

16. Describe the three types of proteins that form the cytoskeleton, and explain the general function of each.

17. Compare and contrast the structure and function of cilia and microvilli.

18. Describe the processes of transcription and translation.

19. Explain how DNA either directly or indirectly controls the processes of a cell.

20. Explain the processes that occur in the different stages of the cell cycle, including DNA replication, mitosis, and cytokinesis.

Can You Apply What You've Learned?

1. Michael was born with Tay-Sachs disease. Which of the following organelles in Michael’s cells lacks a specific enzyme that digests organic molecules?
   a. mitochondria
   b. lysosomes
   c. Golgi apparatus
   d. centrioles
2. A young man in his 20s has a heart attack and is rushed to the hospital. Blood is drawn, and his cholesterol level is tested and found to be very high. The doctor tells him that he has a genetic condition in which he is unable to effectively remove LDL particles containing cholesterol from his blood and into his cells. Which cellular process is not functioning normally?
   a. channel-mediated facilitated diffusion
   b. receptor-mediated endocytosis
   c. exocytosis
   d. simple diffusion

3. Tumors involve a malfunction in this cellular process.
   a. transcription
   b. translation
   c. phagocytosis
   d. mitosis

4. A rare genetic disease involves the inability of the cells to respond to testosterone. The cells are lacking
   a. enzymes for testosterone.
   b. protein carriers for testosterone.
   c. receptors for testosterone.
   d. all plasma membrane proteins.

5. The hormone insulin is a protein composed of repeating units of amino acids. It is produced through the process(es) of
   a. transcription and translation.
   b. DNA replication.
   c. mitosis.
   d. differentiation.

**Can You Synthesize What You’ve Learned?**

1. The liver produces a protein called albumin. The major function of albumin is to exert osmotic pressure to pull fluid back into the blood. Predict what happens to blood osmotic pressure in a patient who has cirrhosis of the liver and is not producing adequate levels of albumin.

2. In a patient with pneumonia (a respiratory condition that results in lower levels of oxygen in the blood), will diffusion of oxygen increase, decrease, or stay the same in comparison to normal? Explain.

3. Explain to a young man, with reduced numbers of receptors for LDL, why his cholesterol level is elevated.
The trillions of cells in the human body are organized into more complex units called tissues. Tissues typically are groups of similar cells and extracellular material that perform a common function, such as providing protection or facilitating body movement. The study of tissues is called histology (his-tol’ō-jē; histos = web). Histological images are viewed using various types of microscopes, which provide different levels of detail (see section 4.1a).

Tissues in the body are classified into four major types: epithelial tissue, connective tissue, muscle tissue, and nervous tissue (table 5.1). You can remember the four major tissue types with the acronym Con-MEN. These four tissue types vary in the structure of their cells, the functions of these cells, and the composition of an extracellular matrix (mā’trik’s; matrix = womb). The extracellular matrix is composed of varying amounts of protein fibers, water, and dissolved molecules (e.g., glucose, oxygen). Its consistency ranges from fluid to semifluid to solid.
An epithelium (ep-i-thē′lē-um; epi = upon, thele = nipple; pl., epithelia), also referred to as epithelial tissue, is composed of one or more layers of closely packed cells, and it contains little to no extracellular matrix between these cells. Epithelial tissue covers the body surfaces, lines the body cavities and organ cavities, and forms glands.

5.1a Characteristics of Epithelial Tissue

All epithelia exhibit the following common characteristics, some of which are shown in figure 5.1:

- **Cellularity.** Epithelial tissue is composed almost entirely of tightly packed cells. There is a minimal amount of extracellular matrix between the cells.
- **Polarity.** An epithelium has an apical (āp′i-kāl) surface (free, or superficial), which is exposed either to the external environment or to some internal body space. The apical surface may have either microvilli or cilia. Recall from section 4.6c that cilia are numerous, slightly longer, membranous projections that move fluid, mucus, and materials past the cell surface, whereas microvilli are small, membranous projections on the apical surface of the cell that increase its surface area for secretion and absorption. The lateral surfaces may contain membrane (intercellular) junctions (see section 4.6d). Additionally, each epithelium has a basal (bā′sāl) surface (a fixed or deep surface), where the epithelium is attached to a basement membrane with underlying connective tissue.
- **Attachment to a basement membrane.** The epithelial layer is bound at its basal surface to a thin basement membrane. It may be seen as a single noncellular (or molecular) layer using junctions (see section 4.6d). Additionally, each epithelium has a basal (bā′sāl) surface (a fixed or deep surface), where the epithelium is attached to a basement membrane with underlying connective tissue.

### Table 5.1 Overview of Tissues

<table>
<thead>
<tr>
<th>Tissue Type</th>
<th>Epithelial Tissue</th>
<th>Connective Tissue</th>
<th>Muscle Tissue</th>
<th>Nervous Tissue</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Composition</strong></td>
<td>Tightly packed cells with minimal extracellular matrix</td>
<td>Contains cells, protein fibers, and ground substance</td>
<td>Cells that may be cylindrical, branching, or spindle-shaped; contain contractile proteins (myofilaments)</td>
<td>Contains neurons and glial cells</td>
</tr>
<tr>
<td><strong>Functions</strong></td>
<td>Covers body and organ surfaces, lines body cavities and organ cavities, forms glands</td>
<td>Binds, supports, and protects other tissues and organs</td>
<td>Moves the skeleton, organ walls, or body structures</td>
<td>Transmits nerve impulses and processes information</td>
</tr>
<tr>
<td><strong>Subtypes</strong></td>
<td>Simple Epithelium</td>
<td>Connective Tissue Proper</td>
<td>Skeletal</td>
<td>(None)</td>
</tr>
<tr>
<td></td>
<td>Simple squamous</td>
<td>Loose (areolar, adipose, reticular)</td>
<td>Cardiac</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Simple cuboidal</td>
<td>Dense (regular, irregular, elastic)</td>
<td>Smooth</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Simple columnar</td>
<td>Supporting Connective Tissue</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Pseudostratified columnar</td>
<td>Cartilage (hyaline, elastic, fibrocartilage)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Stratified Epithelium</td>
<td>Bone</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Stratified squamous</td>
<td>Fluid Connective Tissue</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Stratified cuboidal</td>
<td>Blood</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Stratified columnar</td>
<td>Lymph</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Transitional</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

5.1 Epithelial Tissue: Surfaces, Linings, and Secretory Functions

An epithelium (ep-i-thē′lē-um; epi = upon, thele = nipple; pl., epithelia), also referred to as epithelial tissue, is composed of one or more layers of closely packed cells, and it contains little to no extracellular matrix between these cells. Epithelial tissue covers the body surfaces, lines the body cavities and organ cavities, and forms glands.

### Figure 5.1 Characteristics of Epithelia

An epithelium is composed mostly of cells, it exhibits its polarity, and the lateral surfaces of cells are connected by membrane junctions (see figure 4.32). An epithelium attaches to underlying tissue via a basement membrane.
Epithelia have several functions, although no one epithelium performs all of them:

- **Physical protection.** Epithelial tissues protect both external and internal surfaces from dehydration, abrasion, and destruction by physical, chemical, or biological agents.
- **Selective permeability.** An epithelium typically exhibits a range of permeability; it may be relatively non-permeable to some substances, while promoting and assisting the passage of other ions and molecules. All substances that enter or leave the body must pass through an epithelium, and thus epithelial cells act as “gatekeepers.”
- **Secretions.** Some epithelial cells are specialized to produce and release secretions. These cells form glands. Glands may be individual cells scattered among other cell types in an epithelium (e.g., goblet cells) or arranged in small, organized clusters within a multicellular gland (see section 5.1d).
- **Sensations.** Epithelial tissues are innervated by sensory nerve endings to detect or respond to a stimulus (see section 16.1a). These nerve endings—and those in the underlying connective tissue—continuously relay sensory input to the central nervous system (i.e., brain and spinal cord) concerning touch, pressure, temperature, and pain. Additionally, several organs contain a specialized epithelium, called a neuroepithelium, that houses specific cells responsible for the senses of sight, taste, smell, hearing, and equilibrium (as described in chapter 16).

**WHAT DO YOU THINK?**

1. Why do you think epithelial tissue does not contain any blood vessels? Can you think of any epithelial function that could be compromised if blood vessels were running through the tissue?

2. Why is an epithelium considered selectively permeable?

**WHAT DID YOU LEARN?**

1. Why does an epithelium need to be highly regenerative?

**5.1b Functions of Epithelial Tissue**

**LEARNING OBJECTIVE**

2. Explain the four functions of epithelial tissues.

**LEARNING OBJECTIVES**

3. Name the classes of epithelia based on cell layers and cell shapes.
4. Give examples of each type of epithelium.

The body contains many different types of epithelia, and the classification of each type is indicated by a two-part name. The first part of the name refers to the number of epithelial cell layers, and the second part describes the shape of cells at the apical (superficial) surface of the epithelium.

**Classification by Number of Cell Layers**

Epithelia are classified as either simple or stratified (figure 5.2a). A simple epithelium is one layer of epithelial cells, and all of the epithelial cells are in direct contact with the basement membrane. A simple epithelium is found in areas where stress is minimal and filtration, absorption, or secretion is the primary function.

A stratified epithelium contains two or more layers of epithelial cells. Only the cells in the deepest (basal) layer are in direct contact with the basement membrane. A stratified epithelium resembles a brick wall, where the bricks in contact with the ground represent the basal layer and the bricks at the top of the wall represent the apical (superficial) layer. This tissue provides either more structural support or better protection for underlying tissue. A stratified epithelium is found in areas likely to be subjected to abrasive activities or mechanical stresses, as multiple layers of cells are better able to resist the wear and tear. Cells in the basal layer continuously regenerate as the cells in the apical layer are lost due to abrasion or stress.

**Classification by Cell Shape**

Epithelia are also classified by the shape of the cell at the apical surface. In a simple epithelium, all of the cells display the same shape, whereas in a stratified epithelium, a difference in shape can be seen between cells within the basal layer and those within the apical layer. Figure 5.2b shows the three common cell shapes seen in epithelia: squamous, cuboidal, and columnar. (Note that the cells in this figure all appear hexagonal when viewed from their apical surface. Thus, these terms describe the cells’ shapes when viewed laterally, or from the side.)
Squamous (skwā’mūs; squamosus = scaly) cells are flat, wide, and somewhat irregular in shape. The cells are arranged like floor tiles, and the nucleus is somewhat flattened. Cuboidal (kū-boy’dāl) cells are about as tall as they are wide. The cells do not resemble perfect cubes because their edges are somewhat rounded. The cell nucleus is spherical and located within the center of the cell. Columnar (kol-ūm’nār) cells are slender and taller than they are wide. The cell nucleus is oval and usually oriented lengthwise and in the basal region of the cell. Another shape classification that occurs in epithelial cells is called transitional. These cells can readily change their shape from polyhedral to more flattened, depending upon the degree to which the epithelium is stretched. The shape change occurs when the epithelium cycles between distended and relaxed states, such as in the lining of the bladder, which fills with urine and is later emptied.

Using the classification system just described, epithelium can be broken down into the primary types shown in figure 5.3.

**Simple Squamous Epithelium**

A simple squamous epithelium consists of a single layer of flattened cells (table 5.2a). When viewed en face (looking onto the surface), the irregularly shaped cells display a spherical to oval nucleus, and the cells are tightly bound together. Each squamous cell resembles a fried egg, with the slightly bulging nucleus of the cell representing the yolk. This epithelium is extremely delicate and represents the thinnest possible barrier to allow rapid movement of molecules and ions across the epithelium by membrane transport processes (see section 4.3). Simple squamous epithelium forms the lining of the air sacs (alveoli) of the lung (see section 23.3d), where this thin epithelium is well suited for the exchange of oxygen and carbon dioxide between the blood and the inhaled air. Simple squamous epithelium also is found lining the lumen (inside space) of blood vessel walls (see section 20.1a), where it allows for rapid exchange of nutrients and waste between the blood and the interstitial fluid surrounding the blood vessels. Serous membranes, which cover body organs and secrete serous fluid, are also formed by a simple squamous epithelium.
### Simple Epithelia

#### (a) SIMPLE SQUAMOUS EPITHELIUM

**Structure**

Single layer of thin, flat cells resembling irregular floor tiles; the single nucleus of each cell bulges at its center.

**Function**

Thinnest possible barrier to allow for rapid diffusion and filtration; secretion in serous membranes.

**Location**

Air sacs in lungs (alveoli); lining of lumen of blood vessels and lymph vessels (endothelium); serous membranes of body cavities (mesothelium).

#### (b) SIMPLE CUBOIDAL EPITHELIUM

**Structure**

Single layer of cells about as tall as they are wide; spherical and centrally located nucleus.

**Function**

Absorption and secretion; forms secretory tissue of most glands and small ducts.

**Location**

Kidney tubules, thyroid gland follicles; surface of ovary; secretory regions and ducts of most glands.

#### (c) NONCILIATED SIMPLE COLUMNAR EPITHELIUM

**Structure**

Single layer of cells taller than they are wide; oval-shaped nucleus oriented lengthwise in basal region of cell; apical regions of cell may have microvilli; may contain goblet cells that secrete mucin.

**Function**

Absorption and secretion; secretion of mucin.

**Location**

Inner lining of most of digestive tract (stomach, small intestine, and large intestine).

#### (d) CILIATED SIMPLE COLUMNAR EPITHELIUM

**Structure**

Single layer of ciliated cells taller than they are wide; oval-shaped nucleus oriented lengthwise in basal region of cell; may contain goblet cells.

**Function**

Secretion of mucin and movement of mucus along apical surface of epithelium by cilia; oocyte movement through uterine tube.

**Location**

Lining of the larger bronchioles (air passageways) of the lung and the uterine tubes.

#### (e) CILIATED PSEUDOSTRATIFIED COLUMNAR EPITHELIUM

**Structure**

Single layer of cells with varying heights; all cells connect to the basement membrane, but not all cells reach the apical surface; has goblet cells and cilia.

**Function**

Protection; secretion of mucin and movement of mucus along apical surface of epithelium by cilia.

**Location**

Lining of the larger airways of respiratory tract, including nasal cavity, part of pharynx, parts of larynx, trachea, and bronchi.

#### (f) NONCILIATED PSEUDOSTRATIFIED COLUMNAR EPITHELIUM

**Structure**

Single layer of cells with varying heights; all cells connect to the basement membrane, but not all cells reach the apical surface; lacks goblet cells and cilia.

**Function**

Protection.

**Location**

Rare—lining of part of the male urethra and epididymis.
Specific names are used to refer to the simple squamous epithelia in certain locations within the body. **Endothelium** (en-dô-thel′ē-ūn; *endon* = within) is the name of the simple squamous epithelium that lines both blood vessels and lymph vessels (see sections 20.1a and 21.1a), and **mesothelium** (me-zô-thel′ē-ūn; *mesos* = middle) is the name given to the simple squamous epithelium that forms the serous membranes of body cavities (see section 1.4e). Mesothelium gets its name from the embryonic primary germ layer called mesoderm, from which it is derived (see section 5.6a).

### Simple Cuboidal Epithelium

A **simple cuboidal epithelium** contains one layer of uniformly shaped cells that are about as tall as they are wide with a centrally located, spherical nucleus (table 5.2a). This epithelium allows for both absorption and secretion. Its cells’ uniformity in shape makes them ideal to form the structural components of glands. For example, a simple cuboidal epithelium forms the follicles (spherical structures) of the thyroid gland and covers each ovary. Simple cuboidal epithelium also composes the walls of small ducts (or tubules), including those of kidney tubules.

### Simple Columnar Epithelium

A **simple columnar epithelium** is composed of a single layer of cells that are taller than they are wide. The nucleus is oval, oriented lengthwise, and located in the basal region of the cell. This type of epithelium is ideal for both absorptive and secretory functions. Simple columnar epithelium has two forms: One type has no cilia, whereas the apical surface of the other type is covered with cilia.

- **Nonciliated simple columnar epithelium** often contains microvilli (see section 4.6c) and a scattering of unicellular glands called **goblet cells** (table 5.2c). Individual microvilli cannot be distinguished under the microscope; rather, the microvilli collectively appear as a bright, fuzzy structure known as a **brush border**. Goblet cells secrete mucin (mu′sin), which is a glycoprotein that when hydrated (mixed with water) forms mucus. Nonciliated simple columnar epithelium lines most of the digestive tract from the stomach to the anal canal.

- **Ciliated simple columnar epithelium** has cilia that project from the apical surfaces of the cells (table 5.2d). Mucus covers the apical surface and is moved along by the beating of the cilia. Goblet cells typically are interspersed throughout this epithelium. Ciliated columnar epithelium lines the larger bronchioles (air passageways) in the lung. It also lines the luminal (internal) surface of the ureter (a tube that conveys urine from the urinary bladder to the outside of the body) and epididymis (the structure that stores sperm within the testes).

### Pseudostratified Columnar Epithelium

A **pseudostratified columnar epithelium** (**sôd′stras′i-f′d; *pseudes* = false, *stratum* = layer) is so named because upon first glance, it appears to consist of multiple layers of cells. However, this epithelium is not really stratified because all of its cells are in direct contact with the basement membrane. Although it may look stratified because the nuclei are scattered at different distances from the basal surface, not all of the cells reach the apical surface in this epithelium. Its columnar cells always reach the apical surface, and the shorter cells are stem cells (see Clinical View 5.4: “Stem Cells”) that give rise to the columnar cells.

Pseudostratified columnar epithelium consists of two forms: **pseudostratified ciliated columnar epithelium**, which contains cilia on its apical surface (table 5.2e), and **pseudostratified nonciliated columnar epithelium**, which lacks cilia (table 5.2f). Both types perform protective functions. Pseudostratified ciliated columnar epithelium houses goblet cells that secrete mucin, which hydrates to become the mucus that traps foreign particles and is moved by the beating cilia. This type is found in the larger air passageways of the respiratory system (e.g., the nasal cavity, part of the pharynx [throat], part of the larynx [voice box], trachea, and bronchi [see section 23.1b]). Pseudostratified nonciliated columnar epithelium is rare, lacks goblet cells and cilia, and occurs primarily in part of the male urethra (the tube that conveys urine from the urinary bladder to the outside) and epididymis (the structure that stores sperm within the testes).

### Stratified Squamous Epithelium

- **A stratified squamous epithelium** has multiple cell layers, and only the deepest layer of cells is in direct contact with the basement membrane. The cells in the basal layers have a cuboidal or polyhedral shape, whereas the apical cells display a flattened, squamous shape. A stratified squamous epithelium is so named because of its multiple cell layers and the shape of its apical cells. This epithelium is adapted to protect underlying tissues from damage caused by abrasion and friction. Stem cells in the basal layer continuously divide, to produce a new stem cell and a committed cell that is gradually displaced toward the surface to replace those cells that have been lost. This type of epithelium exists in two forms: keratinized and nonkeratinized.

  - In **keratinized stratified squamous epithelium**, the superficial layers are composed of cells that are dead. These cells lack nuclei and all organelles, and instead are filled with the protein keratin (ker′ā-tin; keras = horn), which is a tough, protective protein that strengthens the tissue (table 5.3a). The epidermis (outer layer) of the skin consists of keratinized stratified squamous epithelium (see section 6.1a).

  - The cells in **nonkeratinized stratified squamous epithelium**, including those at the tissue’s apical surface, lack keratin and remain alive. Because all of the cells are alive, the nuclei characteristic of squamous cells are visible throughout the tissue (table 5.3b). This tissue is kept moist with secretions such as saliva or mucus. Nonkeratinized stratified squamous epithelium forms the surface tissue of mucous membranes that line the oral cavity (mouth), part of the pharynx (throat), part of the larynx (voicebox), the esophagus, the vagina, and the anus (see figure 5.12).

### Stratified Cuboidal Epithelium

- **A stratified cuboidal epithelium** contains two or more layers of cells, and the superficial cells tend to be cuboidal in shape (table 5.3c). Stratified cuboidal epithelium, like simple cuboidal epithelium, forms tubes and ducts, and it functions in protection and secretion. However, stratified cuboidal epithelium is thicker than simple cuboidal epithelium. This tissue forms the walls of the ducts of most exocrine glands (see section 5.1d), such as the ducts of the sweat glands in the skin and the periphery of ovarian follicles.

### Stratified Columnar Epithelium

- **A stratified columnar epithelium** is relatively rare in the body. It consists of two or more layers of cells, but only the cells at the apical surface are columnar in shape (table 5.3d). This type of epithelium protects and secretes. It is found in the large ducts of salivary glands, the conjunctiva covering the eye, and a segment of the male urethra (i.e., membranous urethra).

### Transitional Epithelium

- **A transitional epithelium** is limited to the urinary tract (urinary bladder, ureters, and part of the urethra). It varies in appearance, depending upon whether it is in a relaxed state or a distended...
### Table 5.3 Stratified Epithelia

<table>
<thead>
<tr>
<th>Type</th>
<th>Structure</th>
<th>Function</th>
<th>Location</th>
</tr>
</thead>
<tbody>
<tr>
<td>(a) Keratinized Stratified Squamous Epithelium</td>
<td>Multiple cell layers; basal cells are cuboidal or polyhedral, whereas apical cells are squamous; apical cells are dead and filled with the protein keratin.</td>
<td>Protection of underlying tissue from abrasion</td>
<td>Epidermis of skin</td>
</tr>
<tr>
<td>(b) Nonkeratinized Stratified Squamous Epithelium</td>
<td>Multiple cell layers; basal cells are cuboidal or polyhedral, whereas apical (superficial) cells are squamous; cells lack keratin; superficial cells are alive and kept moist.</td>
<td>Protection of underlying tissue from abrasion</td>
<td>Lining of oral cavity, part of pharynx, part of larynx, esophagus, lining of vagina, and anus</td>
</tr>
<tr>
<td>(c) Stratified Cuboidal Epithelium</td>
<td>Two or more layers of cells; cells at the apical surface are about as tall as they are wide.</td>
<td>Protection and secretion</td>
<td>Ducts of most exocrine glands and ovarian follicles</td>
</tr>
<tr>
<td>(d) Stratified Columnar Epithelium</td>
<td>Two or more layers of cells; cells at the apical surface are taller than they are wide.</td>
<td>Protection and secretion</td>
<td>Large ducts of salivary glands, conjunctiva covering the eye, and membranous part of male urethra</td>
</tr>
<tr>
<td>(e) Transitional Epithelium</td>
<td>Epithelial appearance varies, depending upon whether tissue is relaxed or distended (stretched); relaxed epithelium (top) has cuboidal or polyhedral cells and the apical cells are large and rounded, whereas distended epithelium (bottom) has flattened cells at the apical surface; some cells are binucleated.</td>
<td>Accommodates urine volume changes (by distending or relaxing) in the urinary bladder, ureters, and part of urethra</td>
<td>Lining of urinary bladder, ureters, and part of urethra</td>
</tr>
</tbody>
</table>

(photos): (a, b, c, d) ©McGraw-Hill Education/Al Telser; (e) ©McGraw-Hill Education/Al Telser; ©Victor P. Eroschenko

(stretched) state (table 5.3e). In a relaxed state, the basal cells appear cuboidal or polyhedral, and the apical cells are large and rounded. When transitional epithelium stretches, it thins and the apical cells flatten and become almost squamous in shape. One distinguishing feature of transitional epithelium is the presence of some binucleated (containing two nuclei) cells. By being able to stretch as the bladder...
**INTEGRATE CONCEPT OVERVIEW**

**Figure 5.4 The Relationship Between Epithelial Tissue Type and Function.** (a) Simple epithelium functions in absorption, secretion, and diffusion. In contrast, (b) a stratified epithelium’s many layers make it best suited for protection.

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**SIMPLE SQUAMOUS EPITHELIUM**

**Location:** Walls of each alveolus in lung and walls of capillary blood vessels

**Function:** A single thin layer of cells allows for rapid diffusion of gases between an alveolus of the lung and a capillary

---

**SIMPLE CUBOIDAL EPITHELIUM**

**Location:** Convoluted tubules of the kidney

**Function:** A single layer of cuboidal cells functions in absorption and secretion of materials between filtrate and the blood

---

**SIMPLE COLUMNAR EPITHELIUM**

**Location:** Small intestine

**Function:** The microvilli and single layer of cells facilitate absorption of nutrients and the goblet cells secrete mucus

---

**PSEUDOSTRATIFIED CILIATED COLUMNAR EPITHELIUM**

**Location:** Ciliated form in most of upper respiratory tract, including the trachea

**Function:** Protection, secretion of mucus; cilia propel mucus along epithelial surface

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(b) Stratified Epithelia | Best suited for physical protection

(Nonkeratinized stratified and keratinized epithelium are shown.)

**Nonkeratinized Stratified Squamous Epithelium**
- **Location:** Lining of the oral cavity and esophagus
- **Function:** The multiple layers of cells withstand abrasion from ingested materials

**Keratinized Stratified Squamous Epithelium**
- **Location:** Epidermis of the skin
- **Function:** The strong multiple layers of keratinized cells protect underlying tissue from abrasion; offers greater protection than nonkeratinized epithelium

**Transitional Epithelium**
- **Location:** Lining of the urinary bladder, ureters, and part of the urethra
- **Function:** The distensible, multilayer tissue protects deeper tissue from urine, distends and relaxes to accommodate urine volume changes
fills, this tissue ensures that urine does not seep into the underlying tissues of these organs.

**WHAT DO YOU THINK?**

2. Which types of epithelia are well suited for protection and why?

**LEARNING STRATEGY**

Integrate lab and lecture material: Ask yourself the following questions to help distinguish the type of epithelium under the microscope:

1. Is the epithelium one layer or many layers thick? If it is one layer thick, then you are looking at some type of simple epithelium. If it appears many layers thick, you are looking at either some type of stratified epithelium or pseudostratified epithelium.
2. What is the shape of the cells at the apical surface of the epithelium? If the cells are flattened, it is a squamous epithelium; if they are about as tall as they are wide, the cells are cuboidal; and if the cells are tall and narrow, they are columnar.

Your answer for question 1 gives you the first part of the epithelium name (e.g., simple). Your answer for question 2 gives you the second part of the epithelium name (e.g., squamous). Put these answers together, and you get the name of the tissue (e.g., simple squamous).

Now that you have examined all the different types of epithelia, refer to **Figure 5.4** to reexamine the relationship between epithelial type and function. Note in this figure that the simple epithelia function in diffusion, absorption, and secretion functions, because these epithelia are thinner than stratified epithelium. Stratified epithelia are best suited for protective functions. Thus, when you examine organs with different epithelia, you will have a clue about the organ’s function based on its epithelium.

**WHAT DID YOU LEARN?**

2. How does simple epithelium differ from stratified epithelium?
4. What type of epithelial tissue lines the air sacs of the lungs?
6. What epithelial tissue contains multiple layers of cells, and the most superficial cells are squamous, dead, and filled with the protein keratin?

### 5.1d Glands

**LEARNING OBJECTIVES**

5. Define glands.
6. Distinguish between endocrine and exocrine glands.
7. List exocrine gland types based on both anatomic form and physiologic method of secretion.

**Glands** are either individual cells or multicellular organs composed predominantly of epithelial tissue. They secrete substances either for use elsewhere in the body or for elimination from the body. Glandular secretions may include mucin, ions, hormones, enzymes, or urea (a nitrogenous waste produced by the body).

**Endocrine and Exocrine Glands**

Endocrine (en′dō-krin; krino = to separate) glands lack ducts and secrete their products, called hormones, into the blood to be transported throughout the body. Hormones act as chemical messengers (or ligands) to influence cell communication (see section 4.5b). Endocrine glands, such as the thyroid and adrenal glands, are discussed in depth in chapter 17.

Exocrine (ek′sō-krin) glands typically originate from an invagination of epithelium that burrows into the underlying connective tissue. These glands usually maintain their connection with the epithelial surface by means of a duct, an epithelium-lined tube through which the gland secretions are discharged onto the epithelial surface. Examples of exocrine glands include sweat glands, mammary glands, and salivary glands.

Exocrine glands may be unicellular (one-celled) or multicellular. **Unicellular exocrine glands** typically do not contain a duct, and they are located close to the surface of the epithelium in which they reside. The most common type of unicellular exocrine gland is the goblet cell, which is usually found in both simple columnar epithelium and pseudostratified ciliated columnar epithelium (refer to table 5.2c and e for examples). In contrast, **multicellular exocrine glands** contain numerous cells that work together to produce a secretion (**Figure 5.5**). The gland often consists of acini (as′i-nē; acinus = grape), which are the clusters of cells that produce the secretion, and one or more smaller ducts, which merge to form a larger duct that transports the secretion to the epithelial surface. Multicellular exocrine glands typically are surrounded by a fibrous capsule, and extensions of the capsule called septa partition the gland into lobes.

**Classification of Exocrine Glands**

Multicellular exocrine glands may be classified either by anatomic form or by method of secretion, which may be thought of as a physiologic classification.

**Classification by Anatomic Form** Exocrine glands may be classified anatomically based on the structure and complexity of their ducts. **Simple glands** have a single, unbranched duct; **compound glands** have branched ducts. In addition, glands may be classified according to the shape of their secretory portions. The gland is called

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**Figure 5.5 General Structure of Multicellular Exocrine Glands.**

Exocrine glands may contain secretory portions called acini, and conducting portions composed of many ducts that merge to form a larger duct that transports the secretion to the epithelial surface.
tubular if the secretory portion and the duct have the same diameter. If the secretory portion forms an expanded sac, the gland is called acinar. Finally, a gland with both tubules and acini is called a tubuloacinar gland. Figure 5.6 shows several types of exocrine glands based on their anatomic form.

**Classification by Method of Secretion** Exocrine glands may be classified physiologically by their method of secretion. The three basic types of exocrine glands in this classification are merocrine glands, apocrine glands, and holocrine glands (figure 5.7).

**Merocrine** (mer′ō-krin; meros = share) glands package their secretions into secretory vesicles and release the secretions by exocytosis (see section 4.3c). The glandular cells remain intact and are not damaged in any way by producing the secretion. Examples of merocrine glands include lacrimal (tear) glands; salivary glands; some sweat glands, also known as eccrine glands; the exocrine glands of the pancreas (see section 26.3c); and the gastric glands of the stomach (see section 26.2d).

**Apocrine** (ap′ō-krin; apo = away from, off) glands produce their secretory material in the following way: Secretion occurs when the cell’s apical portion pinches off, releasing cytoplasmic content. Thereafter, the cell repairs itself in order to repeat its secretory activity. Examples include the mammary glands (see section 28.3f) and ceruminous glands of the ear (see section 16.5a).

**Holocrine** (hol′ō-krin; holos = whole) glands are formed from cells that accumulate a product; the entire cell then disintegrates. Thus, a holocrine secretion is a viscous mixture of both cell fragments and the product the cell produced prior to its disintegration. The ruptured, dead cells are continuously replaced by other epithelial cells undergoing cellular division. The oil-producing glands (sebaceous glands) in the skin are examples of holocrine glands (see section 6.2c).

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**WHAT DID YOU LEARN?**

6. What are the two basic parts of a multicellular exocrine gland?
7. What are the differences between holocrine and merocrine glands?
5.2 Connective Tissue: Cells in a Supportive Matrix

Connective tissue is the most diverse, abundant, and widely distributed of the tissues. Connective tissue functions to support, protect, and bind organs. Examples of connective tissue include tendons (structures that attach muscle to bone) and ligaments (structures that attach bone to bone), adipose connective tissue (fat), cartilage, bone, and blood. (See table 5.1.)

All connective tissues share a common origin; they are all derived from an embryonic connective tissue called mesenchyme (discussed in section 5.2c). In addition, while almost all connective tissue is vascular, the different types of connective tissue exhibit a range of vascularity, from very vascular (in areolar connective tissue) to poorly vascular (in dense regular connective tissue) to avascular (in mature cartilage).

### 5.2a Characteristics of Connective Tissue

**LEARNING OBJECTIVES**

- **8.** Describe the three components of connective tissue.
- **9.** Give examples of resident cells and wandering cells in connective tissue proper.
- **10.** Name three types of protein fibers found in connective tissue.
- **11.** Identify three types of molecules that may be found in ground substance.

All connective tissues share three basic components: cells, protein fibers, and ground substance (figure 5.8). Together, the ground substance and the protein fibers it houses form an extracellular matrix. Its specific cell types may differ between the various classes of connective tissue. However, the diversity in connective tissue is due primarily to the different types and amounts of protein fibers, as well as the varying proportions of the ground substance.

**Cells**

Each kind of connective tissue contains specific types of cells. For example, dense regular connective tissue, which forms ligaments and tendons, contains fibroblasts, adipose connective tissue (fat) contains adipocytes, and cartilage is composed of chondrocytes. Unlike cells of epithelial tissue, most connective tissue cells are not in direct contact with each other and usually are randomly scattered throughout the tissue.
Connective tissue proper contains two classes of cells: resident cells and wandering cells. **Resident cells** are stationary cells that are permanently housed within the connective tissue. They help support, maintain, and repair the extracellular matrix. Examples of resident cells include the following:

- **Fibroblasts** (ˈfɪbrə-bʌllst; *fibra* = fiber, *blastos* = germ) are relatively flat cells with tapered ends and are the most abundant resident cells in connective tissue proper. They produce the fibers and ground substance components of the extracellular matrix.

- **Adipocytes** (adˈɪ-pə-sīt; *adip* = fat), also called fat cells, appear in small clusters within some types of connective tissue proper. If large clusters of these cells dominate an area, the connective tissue is called adipose connective tissue.

- **Mesenchymal** (me-sengˈki-məl) cells are a type of embryonic stem cell within connective tissue. If the tissue becomes damaged, these cells will divide. One cell that is produced replaces the mesenchymal stem cell, while the other cell becomes a committed cell that moves into the damaged area and differentiates into the type of connective tissue cell that is needed. (More discussion about stem cells is in Clinical View 5.4: “Stem Cells.”)

- **Fixed macrophages** are relatively large, irregular-shaped cells that are derived from a type of white blood cell called a monocyte (see section 18.3c). They are dispersed throughout the matrix, where they phagocytize (engulf) damaged cells or pathogens. When they encounter foreign materials, the cells also release chemicals that stimulate the immune system and attract numerous wandering cells to the tissue.

**Wandering cells** continuously move throughout the connective tissue proper and are components of the immune system (see section 22.2). They also may help repair damaged extracellular matrix. These cells are primarily types of **leukocytes** (ˌlûˈkJə-tīz; *leukos* = white), also known as white blood cells, and protect the body against harmful agents. Examples of wandering cells and their specific functions include the following:

- **Mast cells** are small, mobile cells that usually are found close to blood vessels; they secrete heparin to inhibit blood clotting and histamine to dilate blood vessels and increase blood flow, which is significant in the inflammatory response (see section 22.3b).
• **Plasma cells** are formed when B-lymphocytes are activated by exposure to foreign materials (see section 22.6b). Plasma cells produce **antibodies**, which are proteins that immobilize a foreign material and prevent it from causing further damage.

• **Free macrophages** are mobile, phagocytic cells that wander through the connective tissue (see section 22.3b). They function as fixed macrophages, yet they are able to move throughout the tissue.

• **Other leukocytes** also migrate through the blood vessel walls into the connective tissue. These include neutrophils, a type of leukocyte that phagocytizes bacteria, and T-lymphocytes, a type of leukocyte that attacks that materials.

**Protein Fibers**

The protein fibers in connective tissue usually strengthen and support the tissue. Three basic types of protein fibers may be found in connective tissue: collagen fibers, reticular fibers, and elastic fibers.

**Collagen fibers** are unbranched, “cablelike,” long protein fibers that are strong, flexible, and resistant to stretching. These fibers are stronger than steel of the same diameter. Collagen comprises about 25% of the body’s protein, and the fibers appear white in fresh tissue, so they often are called white fibers. In tissue sections stained with hematoxylin and eosin, they appear pink. Collagen fibers are numerous in structures such as tendons and ligaments.

**Reticular fibers** are similar to collagen fibers but much thinner. They contain the same protein subunits found in collagen, but their subunits are combined in a different way. These fibers form a branching, interwoven framework that is tough but flexible. Reticular fibers are especially abundant in the **stroma** (connective tissue framework) of organs such as the lymph nodes, spleen, and liver.

Finally, **elastic fibers** contain the protein elastin. The fibers branch and rejoin, and appear wavy. Elastic fibers stretch and recoil easily. Fresh elastic fibers have a yellowish color and often are called yellow fibers. These fibers are visible only in tissue sections that have been stained with special stains, which make the elastic fibers appear black. Elastic fibers are abundant in the skin, arteries, and lungs, to allow them to return to their normal shape after being stretched.

**Ground Substance**

**Ground substance** is a noncellular material produced by the connective tissue cells, and it is within this substance that the connective tissue cells and protein fibers reside. The ground substance may be viscous (as in blood), semisolid (as in cartilage), or solid (as in bone). Together, the ground substance and the protein fibers it houses form the **extracellular matrix**. The viscous nature of the extracellular matrix restricts the movement and spread of disease-causing organisms.

Ground substance contains different large molecules as well as varying amounts of water. **Glycosaminoglycans** (glī-kōs-am-i-nō-glyk’ān; glyks = sweet, glycan = saccharide), or GAGs, are one type of large molecule in the ground substance. A GAG is a polysaccharide (see section 2.7c) that is composed completely of carbohydrate building blocks, some of which have an attached amine group. GAGs are negatively charged and hydrophilic. The negative charges attract cations, such as sodium (Na⁺), and as a result water follows the movement of the positive ion. Thus, GAGs are able to attract and absorb water. Different GAGs attract varying amounts of water, depending on their number of negative charges, so the fluidity of the ground substance varies as a result. Different types of GAGs include chondroitin sulfate, heparan sulfate, and hyaluronic acid.

When a GAG is linked to a protein, it forms an even larger molecule within the ground substance called a **proteoglycan**. Proteoglycans have over 90% of their structure composed of carbohydrates, in the form of GAGs. The large structure of a proteoglycan is due primarily to the large number of negative charges in its GAGs, which then repel each other and cause the molecule to spread out and occupy more space. As we will see in this and future chapters, GAGs and proteoglycans perform numerous important functions in the body.

The ground substance includes other molecules, like adherent **glycoproteins** (proteins with carbohydrates attached; see section 4.2b), which act as glue to bond connective tissue cells and fibers to the ground substance.

**CLINICAL VIEW 5.1**

**Scurvy**

Collagen is an important protein that strengthens and supports almost all body tissues, especially connective tissue. Vitamin C (ascorbic acid) is essential for the production and maintenance of healthy collagen fibers. **Scurvy**, a disease caused by vitamin C deficiency, is marked by weakness, ulceration of gums resulting in tooth loss, hemorrhages, abnormal bone growth, and easily ruptured capillaries (microscopic blood vessels). Scurvy was prevalent among nineteenth-century sailors who, on long sea voyages, lacked vitamin C in their food. Sailors eventually learned that eating citrus fruits, such as limes and lemons, on their voyages prevented scurvy (this also explains why sailors received the nickname *limeys*). Today, collagen production disorders that are caused by nutritional deficiencies are treated by consuming foods high in vitamin C, such as citrus fruits, broccoli, cauliflower, peppers, spinach, and tomatoes, or by taking vitamin C supplements.

**WHAT DID YOU LEARN?**

9. What is the function of GAGs in ground substance?

**5.2b Functions of Connective Tissue**

**LEARNING OBJECTIVE**

12. Describe the functions of connective tissue.

The many types of connective tissue collectively perform a wide variety of functions. These functions include physical protection, support and structural framework, binding of structures, storage, transport, and immune protection. Note that each connective tissue type may perform only some of these functions. The specific functions of each connective tissue type will be discussed in the following sections.
WHAT DID YOU LEARN?
10. What are some of the general functions of connective tissue?

5.2c Embryonic Connective Tissue

**LEARNING OBJECTIVE**

13. Compare and contrast mesenchyme and mucous connective tissue.

Two types of embryonic connective tissue have been identified: mesenchyme and mucous connective tissue. They have different names because they occupy different locations, but both are embryonic connective tissues. **Mesenchyme** (mes’en-kīm; enkyma = infusion) is the first type of connective tissue to emerge in the developing embryo. It has star-shaped (stellate) or spindle-shaped mesenchymal cells dispersed within a gel-like ground substance that contains fine, immature protein fibers (table 5.4a). In fact, ground substance makes up a larger proportion than mesenchymal cells in this type of tissue. Mesenchyme is the tissue from which all other connective tissues are formed. Adult connective tissues often house numerous mesenchymal cells that act as stem cells to provide support in the repair of the tissue following damage or injury.

A second type of embryonic connective tissue is **mucous connective tissue**, also known as Wharton’s jelly (table 5.4b). The immature protein fibers in this tissue are more numerous than those within mesenchyme. Mucous connective tissue is located within the umbilical cord only.

**WHAT DID YOU LEARN?**

11. What is the composition of mesenchyme, and what is its function?

### Table 5.4 Embryonic Connective Tissue

<table>
<thead>
<tr>
<th>(a) MESENCHYME</th>
<th>Structure</th>
<th>Function</th>
<th>Location</th>
</tr>
</thead>
<tbody>
<tr>
<td>Immature protein fiber</td>
<td>Mesenchymal cells are stellate or spindle-shaped; ground substance is a viscous fluid with some immature protein fibers</td>
<td>Common origin for all other connective tissue types</td>
<td>Throughout the body of the embryo and fetus</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>(b) MUCOUS CONNECTIVE TISSUE</th>
<th>Structure</th>
<th>Function</th>
<th>Location</th>
</tr>
</thead>
<tbody>
<tr>
<td>Immature protein fiber</td>
<td>Mesenchymal cells scattered within a viscous ground substance; immature protein fibers are more abundant here than in mesenchyme</td>
<td>Support of structures in umbilical cord</td>
<td>Umbilical cord of fetus</td>
</tr>
</tbody>
</table>

**CLINICAL VIEW 5.2**

What Are You Planning to Do with Your Baby’s Umbilical Cord?

A fetus’s blood contains stem cells that are the same as those found in a child’s red bone marrow, and these cells can be used to treat a variety of life-threatening diseases. Cord blood can be harvested immediately following the birth of a baby, and the blood specimen can be shipped to a cord blood bank for testing, processing, and storage. Some conditions successfully treated to date with cord blood stem cells include lymphoma (cancer of the lymph nodes); leukemia (cancer of the blood); anemia resulting from bone marrow damage, which may happen as a complication of cancer chemotherapy; and even sickle-cell disease.

Although this technology offers hope, it is expensive and is not covered by most insurance plans. Further, each cord blood sample contains relatively few stem cells. Although these stem cells can be used in unrelated recipients, it takes longer for the cells to complete the engraftment process, which leaves the patient vulnerable to infections for a longer amount of time than when using bone marrow–derived stem cells.
All connective tissue is ultimately derived from mesenchyme. Mesenchyme begins to differentiate in the developing fetus as it forms the connective tissues that ultimately are found in the adult body. The connective tissue types present after birth are classified into three broad categories: connective tissue proper, supporting connective tissue, and fluid connective tissue (figure 5.9).

**Connective Tissue Proper**

Connective tissue proper is divided into two broad groups: loose connective tissue and dense connective tissue. This classification is based upon the relative proportions of cells, fibers, and ground substance.

**Loose Connective Tissue**

Loose connective tissue contains relatively fewer cells and protein fibers than dense connective tissue. The protein fibers are sparse and irregularly arranged (hence, the name loose connective tissue), and there is abundant, viscous ground substance. Loose connective tissues act as the body’s “packing material” by supporting and surrounding structures and organs. Loose connective tissue subtypes are all well vascularized. There are three types of loose connective tissue: areolar connective tissue, adipose connective tissue, and reticular connective tissue.

*Areolar* (ä-rē’ō-lār) connective tissue has an unconfined organization of collagen and some elastic fibers and is highly vascularized (table 5.5a). This connective tissue type contains all of the fixed and wandering cells of connective tissue proper, although the predominant cell is the fibroblast. The ground substance is abundant and viscous. Areolar connective tissue is present nearly everywhere in the body. It is found in the skin (papillary layer of the dermis) and is a major component of the subcutaneous layer that is deep to the skin. It binds skin and some epithelia to deeper tissues. It also protects and surrounds organs, some individual nerve and muscle cells, and blood vessels.

*Adipose connective tissue* (commonly known as fat) is a highly vascularized loose connective tissue composed primarily of adipocytes (table 5.5b). Adipocytes are filled with lipid droplets, causing the nucleus to be pushed to the inside edge of the plasma membrane. On a histology slide, the lipid is extracted during tissue processing so all that is left is the plasma membrane and nucleus of the adipocyte. There are two types of adipose connective tissue: white and brown. *Brown adipose connective tissue* is found in newborns and is designed to generate heat. As we age, we lose most of our brown adipose connective tissue and instead predominantly have white adipose connective tissue. *White adipose connective tissue* functions in long-term energy storage (stores triglyceride molecules), acts as an insulator, and serves both as packing around structures and as a cushion against shocks. It is located throughout the body in places such as the subcutaneous layer deep to the skin and surrounding various organs. Typically, the number of adipocytes remains relatively stable in an individual,
### Table 5.5 Connective Tissue Proper: Loose Connective Tissue

| (a) AREOLAR CONNECTIVE TISSUE | Structure | Abundant, viscous ground substance; few collagen and elastic fibers; scattered fibroblasts; many blood vessels |
|                              | Function   | Protects tissues and organs; binds skin and some epithelia to deeper tissue |
|                              | Location   | Papillary layer of the dermis (skin); subcutaneous layer (deep to skin); surrounds organs, nerve cells, some muscle cells, and blood vessels |
| Collagen fiber               |            |                                |
| Elastic fiber                |            |                                |
| Fibroblast                   |            |                                |
| Ground substance             |            |                                |

| (b) ADIPOSE CONNECTIVE TISSUE | Structure | Closely packed adipocytes; nucleus pushed to edge of cell by large fat droplet; contains many blood vessels |
|                              | Function   | Stores energy; insulates, cushions, and protects |
|                              | Location   | Subcutaneous layer; surrounds and covers some organs |
| Adipocyte nucleus            |            |                                |
| Adipocyte                    |            |                                |

| (c) RETICULAR CONNECTIVE TISSUE | Structure | Viscous ground substance; meshwork of reticular fibers, leukocytes, and some fibroblasts |
|                               | Function   | Provides stroma (supportive framework) to lymphatic organs |
|                               | Location   | Spleen, lymph nodes, and red bone marrow |
| Ground substance              |            |                                |
| Reticular fibers              |            |                                |
| Leukocyte                     |            |                                |

**CLINICAL VIEW 5.3**

**Marfan Syndrome**

Marfan syndrome is a rare genetic disease of connective tissue that causes skeletal, cardiovascular, and visual system abnormalities. It results from an abnormal gene on chromosome 15. Patients with Marfan syndrome tend to have (1) abnormally long fingers, toes, and upper and lower limbs; (2) malformation of the thoracic cage, vertebral column, or both, as a result of excessive growth of ribs; and (3) easily dislocated joints, resulting from weak ligaments, tendons, and joint capsules. Cardiovascular system problems involve a weakness in the aorta and abnormal heart valves. Visual system abnormalities develop because the thin fibers (called suspensory ligaments) that hold the lens of the eye in place are weak, allowing the lens to slip out of place.

Patients usually exhibit symptoms of Marfan syndrome by age 10. Marfan syndrome symptoms may range from mild to severe. In severe cases, individuals may die of cardiovascular-related problems before age 50. However, those with milder symptoms and who receive early diagnosis and medical management may have long life spans.

Individuals with Marfan syndrome may have abnormally long fingers and highly flexible joints.
and weight gain or loss is due to the adipocytes enlarging or shrinking in size, respectively.

Reticular connective tissue houses abundant leukocytes and some fibroblasts within a meshwork of reticular fibers (table 5.5c). This tissue forms the stroma (structural framework) of many lymphatic organs, such as the spleen, lymph nodes, and red bone marrow.

**Dense Connective Tissue** Dense connective tissue is composed primarily of protein fibers and has proportionately less ground substance than loose connective tissue. It also is known as collagenous tissue because collagen fibers usually are the dominant fiber type. There are three categories of dense connective tissue: dense regular connective tissue, dense irregular connective tissue, and elastic connective tissue.

**Dense regular connective tissue** contains few fibroblasts and limited ground substance yet abundant collagen fibers that are packed tightly and aligned parallel to one another. The fibers resemble lasagna noodles stacked one on top of another (table 5.6a). This tissue type is found in tendons (which attach muscle to bone) and ligaments (which attach bone to bone), where stress typically is applied in a single direction. Dense regular connective tissue has few blood vessels, and thus it takes a long time to heal following injury, because a rich blood supply is necessary for quick healing.

**Dense irregular connective tissue** contains bundles and clumps of collagen fibers that extend in all directions, with an extensive blood supply between the collagen fibers (table 5.6b). This tissue provides support and resistance to stress in multiple directions. Dense irregular connective tissue is found in most of the dermis of the skin, the epimysium (sheath surrounding a skeletal muscle), the epineurium (sheath surrounding a nerve), the periostium (sheath surrounding bone), and the perichondrium (sheath surrounding cartilage). It also forms capsules around some internal organs, such as the liver, kidneys, and spleen.

**Elastic connective tissue** is composed of numerous fibroblasts among branching, densely packed elastic fibers (table 5.6c). The elastic fibers provide the ability for the tissue to stretch and recoil. This tissue is found in the walls of large arteries, the trachea, and the vocal cords.

### WHAT DO YOU THINK?

What type of connective tissue have you damaged when you sprain your ankle?

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**Table 5.6** Connective Tissue Proper: Dense Connective Tissue

#### (a) DENSE REGULAR CONNECTIVE TISSUE

| Structure | Densely packed, parallel arrays of collagen fibers; fibroblasts squeezed between layers of fibers; scarce ground substance; limited blood supply |
| Function | Attaches bone to bone (most ligaments) as well as muscle to bone (tendon); resists stress applied in one direction |
| Location | Tendons (attach muscle to bone); ligaments (typically attach bone to bone) |

#### (b) DENSE IRREGULAR CONNECTIVE TISSUE

| Structure | Collagen fibers randomly arranged and clumped together; fibroblasts in spaces among fibers; more ground substance than in dense regular connective tissue; extensive blood supply |
| Function | Withstands stresses applied in all directions; durable |
| Location | Most of dermis of skin; periostium covering bone; perichondrium covering cartilage, epineurium covering nerves, epimysium covering skeletal muscle, some organ capsules |

#### (c) ELASTIC CONNECTIVE TISSUE

| Structure | Predominantly composed of elastic fibers; fibroblasts occupy some spaces between fibers |
| Function | Allows for stretching and recoil |
| Location | Walls of elastic arteries (such as the aorta), trachea, vocal cords |
Supporting Connective Tissue

There are two types of supporting connective tissue: cartilage and bone. Both form a strong, durable framework that protects and supports the soft body tissue. The extracellular matrix contains many protein fibers and a ground substance that ranges from semisolid (cartilage) to solid (bone).

**Cartilage**

Cartilage has a firm, semisolid extracellular matrix that contains variable amounts of collagen and elastic protein fibers. Mature cartilage cells are called chondrocytes (kon’drō-sīt; chondros = gristle, cartilage). These cells occupy small spaces called lacunae (lä-kū’nē; lacus = a hollow, a lake) within the extracellular matrix. Cartilage is stronger and more resilient than previously discussed connective tissue types, and it provides more flexibility than bone. It is present in areas of the body that need support and must withstand deformation, such as the tip of the nose or the auricle (external part) of the ear.

Chondrocytes produce and secrete a chemical that prevents blood vessel growth and formation within the extracellular matrix. Thus, mature cartilage is avascular, and as a result the chondrocytes must exchange nutrients and waste products by diffusion with blood vessels outside the cartilage.

Three major types of cartilage are found in the body: hyaline cartilage, fibrocartilage, and elastic cartilage. They exhibit both differences in density and dispersal of chondrocytes within the extracellular matrix.

**Hyaline** (hī′lā-lin; hyalos = glass) cartilage provides flexible support to structures and is the most common type of cartilage. It is named for its clear, glassy appearance when viewed under the microscope (table 5.7a). Its chondrocytes are irregularly scattered, and collagen within the extracellular matrix is not readily observed by light microscopy. If this tissue type is stained with hematoxylin and eosin and examined under the microscope, the tissue resembles carbonated grape soda, where the lacunae represent the bubbles in the soda. Hyaline cartilage functions in support and is found in many areas of the body, including structures of the respiratory tract (nose, trachea, bronchi, and most of the larynx; see sections 23.2 and 23.3), costal cartilage (cartilage attached to ribs; see section 8.6b), and both the epiphyseal (growth) plates and the articular ends of long bones (see section 7.1). It also forms most of the fetal skeleton (see section 7.4b).

**Fibrocartilage** (fi’brō-kār’ti-lāj; fibro = fiber) is a weight-bearing cartilage. It has numerous coarse, readily visible protein fibers that are arranged as irregular bundles between large

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**Table 5.7 Supporting Connective Tissue: Cartilage**

<table>
<thead>
<tr>
<th>Type</th>
<th>Structure</th>
<th>Function</th>
<th>Location</th>
</tr>
</thead>
<tbody>
<tr>
<td>(a) Hyaline Cartilage</td>
<td>Glassy-appearing matrix; irregularly arranged chondrocytes in lacunae</td>
<td>Provides support; forms most of fetal skeleton</td>
<td>Tip of nose; trachea; most of larynx, costal cartilage; both the epiphyseal (growth) plates and articular ends of long bones; most of fetal skeleton</td>
</tr>
<tr>
<td>(b) Fibrocartilage</td>
<td>Readily visible, numerous, parallel collagen fibers with limited ground substance; large chondrocytes in lacunae</td>
<td>Resists compression; acts as shock absorber in some joints</td>
<td>Intervertebral discs; pubic symphysis; menisci of knee joints</td>
</tr>
<tr>
<td>(c) Elastic Cartilage</td>
<td>Abundant elastic fibers that form weblike mesh; closely packed chondrocytes in lacunae</td>
<td>Maintains shape while permitting extensive flexibility</td>
<td>External ear; epiglottis of larynx</td>
</tr>
</tbody>
</table>

(photos): (a, b) ©Ed Reschke; (c) ©McGraw-Hill Education/Al Telser
chondrocytes (table 5.7b). There is only a sparse amount of ground substance. The densely interwoven collagen fibers contribute to the durability of this cartilage. Fibrocartilage resists compression and acts as a good shock absorber. It is located in the intervertebral discs (circular supportive structures between adjacent vertebrae; see section 8.5c), pubic symphysis (between the anterior parts of the hip bones; see section 8.10), and the menisci of the knee joint (see section 9.7e).

**Elastic cartilage** is the flexible, springy cartilage. It is so named because it contains numerous elastic fibers within its extracellular matrix (table 5.7c). The chondrocytes are closely packed and surrounded by a small amount of extracellular matrix. The elastic fibers are densely packed together and ensure that this tissue is both resilient and very flexible. Note that both elastic cartilage and elastic connective tissue contain abundant amounts of elastic fibers. However, elastic cartilage has a semisolid ground substance and contains chondrocytes, whereas elastic connective tissue has a fluid ground substance formed by fibroblasts.

Elastic cartilage is found in the external ear and the epiglottis (a structure of the larynx that prevents swallowed materials from entering the trachea). You can see for yourself how flexible elastic cartilage is by performing this experiment: Fold your external ear over your finger, hold for 10 seconds, and release. Your ear springs back to its original shape because the elastic cartilage resists the deformational pressure you applied. (This also explains why our ears aren’t permanently misshapen if we sleep on them in an unusual way!)

**Bone**  
Bone connective tissue is also known as osseous connective tissue and makes up the mass of most of the structures referred to as bones. Bone connective tissue is more solid than cartilage and provides greater support, although it is not as flexible. Bone tissue is extensively vascularized. Section 7.2e provides a detailed description of the histology of bone connective tissue.

The extracellular matrix of bone connective tissue consists of organic components (collagen fibers and glycoproteins) and inorganic components composed of a mixture of calcium salts, primarily calcium phosphate. The bone cells are called **osteocytes** (os′tē-ō-sīt) and are housed within spaces in the extracellular matrix called **lacunae**.

The two forms of bone tissue are compact bone and spongy (cancellous, trabecular) bone. **Compact bone** appears completely solid but is, in fact, perforated by a number of neurovascular canals (table 5.8). It has a uniform histologic pattern. Compact bone is formed from cylindrical structures called osteons (os′tē-on), which display concentric rings of bone connective tissue called lamellae. The lamellae encircle a central canal that houses blood vessels and nerves. **Spongy bone** is located within the interior of a bone, and it contains a latticework structure of bone connective tissue that is very strong yet lightweight (see figure 7.8).

Bone serves a variety of functions. As an organ, bones provide support and serve as levers for skeletal muscle movement, and they support soft tissues as well as protect vital body organs. The hard extracellular matrix of bone connective tissue stores important minerals, such as calcium and phosphorus. Finally, some spongy bone houses **hemopoietic** (hē′mō-poy-et′ik; hemat = blood) cells, which form a type of reticular connective tissue that makes blood cells (a process called hemopoiesis, see section 18.3a).
Fluid Connective Tissue

There are two types of fluid connective tissue: blood and lymph. **Blood** is a fluid connective tissue composed of **formed elements**. Formed elements include cells, both erythrocytes (red blood cells) and leukocytes (white blood cells), and cellular fragments called platelets (table 5.9). The liquid ground substance is called **plasma**, and within it are proteins and solutes.

Blood has numerous functions. The erythrocytes transport respiratory gases (oxygen and carbon dioxide), and the leukocytes protect the body from infectious agents. Platelets and the protein fibers help clot the blood. Plasma transports nutrients, wastes, and hormones throughout the body. Blood is discussed in greater detail in chapter 18. **Lymph** is derived from blood plasma, but it contains no cellular components or fragments (which is why we don’t examine it histologically here). Ultimately, lymph is returned to the bloodstream. We discuss it in greater detail in section 21.1.

Figure 5.10 summarizes the relationships between connective tissue types and their functions.

**WHAT DID YOU LEARN?**

12. Compare loose connective tissue to dense connective tissue with respect to fiber density, fiber distribution, and the amount of ground substance.

13. Describe the composition and location of fibrocartilage.

14. Why is blood considered a connective tissue?
(a) Connective Tissue Proper | Binds structures together

**DENSE CONNECTIVE TISSUE**

- **Dense Regular Connective Tissue**
  - **Location:** Interosseous membrane (ligament between radius and ulna bones in forearm)
  - **Main function:** Forms tendons that bind muscle to bone and ligaments that bind bone to bone

- **Dense Irregular Connective Tissue**
  - **Location:** Dermis of the skin
  - **Main function:** Binds tissues (e.g., connects epidermis to underlying subcutaneous layer)

- **Elastic Connective Tissue**
  - **Location:** Aorta
  - **Main function:** Allows for stretching and recoil in some structures

**LOOSE CONNECTIVE TISSUE**

- **Adipose Connective Tissue**
  - **Location:** Subcutaneous layer inferior to skin
  - **Main function:** Supports and surrounds structures and organs; forms the subcutaneous layer, which binds the skin and muscle
  - **Other functions:** Long-term energy storage (triglycerides), insulates and cushions

- **Areolar Connective Tissue**
  - **Location:** Subcutaneous layer inferior to skin
  - **Main function:** Protects tissues and organs; binds skin and some epithelia to deeper tissue

- **Reticular Connective Tissue**
  - **Location:** Spleen
  - **Main function:** Supports and surrounds various structures and organs
  - **Other functions:** Houses leukocytes, which offer protection

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**INTEGRATE CONCEPT OVERVIEW**

Figure 5.10 The Relationship Between Connective Tissue Type and Function. (a) Connective tissue proper binds structures together, whereas (b) supporting connective tissue either provides a framework for or protects underlying soft tissues. (c) Fluid connective tissue is responsible for fluid, nutrient, gas, and waste transport.
(b) Supporting Connective Tissue

Provides physical protection to underlying tissues or a structural framework for soft body tissues.

**CARTILAGE**

- **Elastic Cartilage**
  - **Location:** External ear
  - **Main function:** Maintains shape while permitting extensive flexibility

- **Hyaline Cartilage**
  - **Location:** Costal cartilage of ribs
  - **Main function:** Protection and structural support, with more flexibility than bone

- **Fibrocartilage**
  - **Location:** Intervertebral discs
  - **Main function:** Withstands compression, acts as a shock absorber in some joints

**BONE**

- **Location:** Bones of the skeletal system
- **Main functions:** Protection and structural support, more rigid and solid than cartilage; serves as a reservoir for calcium and phosphorus

(c) Fluid Connective Tissue

Transports nutrients, gases, and wastes

**BLOOD**

- **Location:** Within blood vessels and the heart
- **Main function:** Transport of nutrients, gases, and wastes through the body
Muscle tissue is a well-vascularized tissue; it is composed of specialized cells that contain contractile proteins. When muscle tissue is stimulated to contract, it produces movement, such as the voluntary motion of body parts, contraction of the heart, and propulsion of materials through the digestive and urinary tracts. The three types of muscle tissue are skeletal muscle, cardiac muscle, and smooth muscle. These tissues are described briefly here and discussed in greater detail in sections 10.2, 19.3e, and 10.10, respectively.

**Skeletal muscle tissue**, also known as striated or voluntary muscle tissue, is primarily responsible for movement of the skeleton (although this tissue also moves some nonskeletal structures, such as the skin of the face and the external urethral and external anal sphincters). This tissue also functions in thermoregulation, as when our skeletal muscle contracts it generates heat, which increases body temperature (see section 10.1a). It is composed of long, cylindrical cells called skeletal muscle fibers. These fibers are arranged in parallel bundles that typically run the length of the entire muscle. Such long fibers need more than one nucleus to control and carry out all cellular functions; thus, each skeletal muscle fiber is multinucleated (see figure 10.2), with nuclei located at the periphery of the fiber (table 5.10a). Under the light microscope, skeletal muscle fibers exhibit alternating light and dark bands, called striations, that reflect the overlapping pattern of parallel thick and thin contractile protein filaments. Additionally, skeletal muscle is considered voluntary because it usually does not contract unless stimulated by the somatic (voluntary) nervous system (see section 12.1b). Skeletal muscle generally has reduced ability to repair itself through cell division.

**Cardiac muscle tissue** is confined to the thick middle layer of the heart wall, called the myocardium (see section 19.3b); it is responsible for the pumping action of the heart to move blood through the cardiovascular system (heart and blood vessels). Cardiac muscle tissue is composed of cells that are medium-sized and often bifurcating (branching) (table 5.10b). Cardiac muscle cells contain one or two centrally located nuclei. When viewed with the light microscope, cardiac muscle cells also have visible striations because of the same type of overlapping pattern of parallel protein filaments. In addition, the cells are connected by intercalated (in-ter′kə-lə-ted; intercalates = inserted between) discs, which are intercellular junctions between the cells composed of

<table>
<thead>
<tr>
<th>Table 5.10 Muscle Tissue</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>(a) SKELETAL MUSCLE TISSUE</strong></td>
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<td><strong>Structure and characteristics</strong></td>
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<tr>
<td>Long, cylindrical fibers (cells) arranged parallel and unbranched; fibers are multinucleated with visible striations; fiber is under voluntary control</td>
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<tr>
<td><strong>Function</strong></td>
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<td>Primarily responsible for moving skeleton and for thermoregulation (increases body temperature when muscles contract)</td>
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<td><strong>Location</strong></td>
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<td>Attaches to bones or sometimes to skin (e.g., facial muscles); forms external urethral and anal sphincters</td>
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| **(b) CARDIAC MUSCLE TISSUE** |
| **Structure and characteristics** |
| Medium-sized, typically branching cells; contain one or two centrally located nuclei with visible striations; intercalated discs between cells; under involuntary control |
| **Function** |
| Pumps blood through heart and blood vessels |
| **Location** |
| Heart wall (myocardium) |

| **(c) SMOOTH MUSCLE TISSUE** |
| **Structure and characteristics** |
| Cells are short and fusiform in shape; contain one centrally located nucleus; cells do not have visible striations; under involuntary control |
| **Function** |
| Moves and propels materials through internal organs; controls the size of the lumen |
| **Location** |
| Walls of hollow internal organs, such as intestines, stomach, airways, urinary bladder, uterus, and blood vessels; iris of the eye |
desmosomes and gap junctions (see section 4.6d). Intercalated discs appear as dark, thick lines when viewed with the microscope. Intercalated discs strengthen the connection between cells and promote the rapid conduction of electrical activity through many cells at once, allowing the cells of a heart chamber to contract as a unit. Cardiac muscle cells are considered involuntary because they cannot be controlled by the somatic (voluntary) nervous system activity to initiate a contraction; instead, specialized cardiac muscle cells (pacemaker cells) in the heart wall initiate the contraction (see section 19.6a).

Smooth muscle tissue, also called visceral or involuntary muscle tissue, is so named because it lacks the striations seen in other muscle tissue, so this tissue appears smooth (table 5.10). Smooth muscle cells are fusiform (spindle-shaped), which means they are thick in the middle and tapered at their ends. These cells are relatively short and contain one centrally located, oval nucleus. Smooth muscle tissue is also called visceral muscle tissue because it is found in the walls of most viscera (internal organs), such as the intestines, stomach, airways, urinary bladder, uterus, and blood vessels. It is also located in specialized structures where involuntary muscle contraction is required, such as the iris of the eye (which adjusts the size of the pupil; see section 16.4b). The contraction of smooth muscle helps propel material movement through these organs or controls the size of the lumen. This tissue is considered involuntary because we do not have voluntary control over the muscle. Smooth muscle can engage in cell division to provide growth and healing of the tissue.

WHAT DID YOU THINK?
4 Why do you think smooth muscle lacks striations?

INTEGRATE

LEARNING STRATEGY
Integrate your learning of lecture and lab material: Ask the following questions to help distinguish the types of muscle tissue viewed microscopically:

1. What is the shape of the cell? Skeletal muscle cells are long and cylindrical, cardiac muscle cells are short and bifurcated, and smooth muscle cells are spindle-shaped.

2. How many nuclei are present, and are the nuclei centrally located or at the periphery of the cell? Skeletal muscle has multiple nuclei that are located at the periphery of the cell. Cardiac muscle has one or two centrally located nuclei. Smooth muscle has a single centrally located nucleus.

3. Do the cells have striations? Skeletal and cardiac muscle have striations, but smooth muscle does not. Further, only cardiac muscle has intercalated discs between the cells.

WHAT DID YOU LEARN?
16 Compare and contrast the structure of skeletal and cardiac muscle tissue.

5.4 Nervous Tissue: Information Transfer and Integration

LEARNING OBJECTIVES
17. Describe the structure of nervous tissue.
18. List the functions of nervous tissue.

Nervous tissue is located within the brain, the spinal cord, and the nerves that traverse through the body. It consists of cells called neurons (núr’onz) that receive, process, and transmit nerve impulses. It also contains a larger number of cells called glial cells (or supporting cells), which do not transmit nerve impulses but instead are responsible for the protection, nourishment, and support of the neurons (see section 12.4) (table 5.11). Nervous tissue is well vascularized.

Each neuron has a prominent cell body that houses both the nucleus and other organelles. Extending from the cell body are branches called nerve cell processes. The shorter and more numerous processes are dendrites (den’drites; dendrites = relating to a tree), which receive incoming signals and transmit the information to the cell body. The single long process extending from the cell body is the axon (ak’son; axon = axis), which carries outgoing signals to other cells. Because of the extensive lengths of some axons, neurons are usually the longest cells in the body; some are longer than 1 meter. We discuss nervous tissue in detail in chapter 12.

Table 5.11 Nervous Tissue

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<th>NERVOUS TISSUE</th>
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Structure
Contains neurons, which have a cell body, dendrites, and an axon that extend from the cell body; also contains glial cells, which lack the processes seen in neurons

Function
Neurons receive, process, and transmit nerve impulses, whereas glial cells help protect, nourish, and support neurons

Location
Brain, spinal cord, and nerves

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5.5 Integration of Tissues in Organs and Body Membranes

We have learned that a tissue is a group of similar cells that perform a common function. Organs and body membranes also perform certain specialized functions, and they consist of two or more tissues that support their function (see section 1.3b).

5.5a Organs

**LEARNING OBJECTIVES**

19. Define an organ.
20. Explain the roles of different tissues in an organ.

An organ is a structure that is composed of two or more tissue types that work together to perform specific, complex functions. The key to organ structure is that the different tissue types must work in concert.

For example, the stomach contains all four types of tissue (figure 5.11). It is lined by an epithelium, has both areolar and dense connective tissue in its walls, contains three layers of smooth muscle in those walls, and possesses abundant nervous tissue. All these tissues work together to perform the functions of the stomach. Glands associated with epithelial tissue secrete substances for chemical digestion of ingested nutrients. Connective tissue houses the blood vessels and nerves that supply the stomach as well as provides shape and support. Smooth muscle contracts and relaxes so that contents within the stomach may be mechanically mixed and broken down. Nervous tissue is responsible for both regulating the contraction of muscle and stimulating secretion by glands.

5.5b Body Membranes

**LEARNING OBJECTIVES**

21. Explain the structure and functions of mucous, serous, cutaneous, and synovial membranes.
22. Identify the locations of these membranes.

Epithelial and connective tissue together form structures called body membranes, which should not be confused with the plasma membranes of cells. Body membranes are formed from an epithelial layer that is bound to an underlying connective tissue. These membranes line body cavities, cover the viscera, or cover the body’s external surface. There are four types of body membranes: mucous, serous, cutaneous, and synovial, shown in figure 5.12.

A mucous membrane, also called a mucosa (mû-kō’sä), lines passageways and compartments that eventually open to the external environment; these include the digestive, respiratory, urinary, and reproductive tracts. Mucous membranes perform absorptive, protective, or secretory functions or a combination of these functions. A mucous membrane is formed by an epithelium and an underlying connective tissue called the lamina propria. Often, this membrane is covered with a layer of mucus derived from goblet cells, multicellular glands, or both.

A serous membrane lines body cavities that typically do not open to the external environment and covers the external surface of many organs. Their locations were first introduced in section 1.4e. The membrane is composed of a simple squamous epithelium called mesothelium. Serous membranes produce a

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**Figure 5.11 Roles of Tissues in an Organ.** Different tissue types (epithelial, connective, muscle, and nervous) work together to perform the functions of the stomach.
Thin, watery serous fluid, or transudate (trans = across, sudo = to sweat), which is derived from blood plasma. Serous membranes form two associated layers: a parietal layer that lines the inside of the body cavity and a visceral layer that covers the surface of the internal organs. Between these two layers is a serous cavity, which is a potential space into which the serous fluid is secreted. The serous fluid reduces the friction between their opposing surfaces. Examples of serous membranes include part of the pericardium (which is associated with the heart), the pleura (associated with the lungs), and the peritoneum (associated with abdominal organs).

The largest body membrane is the cutaneous (kū-tā-nē-ŭs; cutis = skin) membrane, also known as the skin, which covers the external surface of the body. The cutaneous membrane is composed of a keratinized stratified squamous epithelium (called the epidermis) and an underlying layer of connective tissue (called the dermis). Its many functions include protecting internal organs and preventing water loss. This membrane is discussed in greater detail in chapter 6.

Some joints in the body are lined by a synovial (si-nō’ve-ăl) membrane that is composed of a specialized type of connective tissue. The cells within this membrane secrete a synovial fluid that reduces friction among the moving bone parts and distributes nutrients to the cartilage on the articular surfaces of bone (see section 9.4a).

**WHAT DID YOU LEARN?**

18. What are the differences between the parietal and visceral layers of the serous membrane?

**5.6 Tissue Development and Aging**

The process by which the many different tissues of the body are generated from a single cell, the fertilized egg, could take up an entire book. Here we describe the milestones of this complex process; you will learn more in chapter 29. In addition, we consider how tissues change over time and with different conditions. We conclude with a brief summary of how the aging process affects the body’s tissues.

**5.6a Tissue Development**

**LEARNING OBJECTIVES**

23. Explain the stages of tissue development in the embryo.

24. Describe the three primary germ layers and the tissues to which they give rise.

To understand how all tissues form, some basic information about the human embryo is required. When a secondary oocyte (egg) is fertilized by a sperm, it forms a diploid cell called a zygote. The zygote undergoes multiple cell divisions; eventually, a multicellular structure called a blastocyst is formed. The cells that form the embryo are collectively known as the embryoblast.

Embryoblast cells differentiate in the second and third weeks of development. By the third week of development, three primary germ layers are formed. All body tissues develop from these layers (figure 5.13). The three primary germ layers are called ectoderm, mesoderm, and endoderm. When these three primary germ layers have formed, the growing structure may now be referred to as an embryo.
**Ectoderm** is initially located on the dorsal and external surfaces of the embryo. It is responsible for forming many externally placed structures, such as the epidermis of the skin, hair, nails, and exocrine glands of the skin. Thus, some but not all epithelial tissues are derived from ectoderm. Tooth enamel, the lens of the eye, and the adrenal medulla are derived from ectoderm, as is all nervous tissue such as the brain, spinal cord, and nerves.

**Mesoderm** is the middle primary germ layer. It forms all muscle tissue and both the epithelial lining of vessels and the serous membranes that line the body cavities. Mesoderm becomes mesenchyme, which then goes on to form all connective tissues in the body. The dermis of the skin, adrenal cortex, heart, spleen, kidneys and ureters, and internal reproductive organs are mesoderm-derived.

**Endoderm** becomes the innermost germ layer when the embryo undergoes shape changes. It forms the epithelial linings of the tympanic cavity (middle ear) and auditory tube, as well as the digestive, respiratory, reproductive, and urinary tracts. Endoderm also forms organs such as the thyroid gland, the parathyroid glands, the thymus, and portions of the palatine tonsils, as well as most of the liver, gall bladder, and pancreas.

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**WHAT DID YOU LEARN?**

19. What are the three primary germ layers, and when do they form?

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**5.6b Tissue Modification**

**LEARNING OBJECTIVE**

25. Describe how tissues may change in form, size, or number of cells.

Tissues may change in size, form, or number of cells in response to a stimulus. **Hypertrophy** refers to an increase in the size of the existing cells in a tissue, although the number of cells remains constant. For example, skeletal muscle cells may hypertrophy when a person undergoes a long-term rigorous exercise regimen. **Hyperplasia** (plasso = to form) is an increase in the number of cells in a tissue. Developing a “callus” on the palm of your hand is an example of these skin cells undergoing hyperplasia.

Shrinkage of tissue by a decrease in either cell size or cell number is called **atrophy** (at′ro-f). Atrophy may result from normal aging (senile atrophy) or from failure to use an organ or a tissue (disuse atrophy). If an individual becomes bedridden or must wear a cast for a broken bone, the affected muscles exhibit disuse atrophy as the skeletal muscle fibers become smaller. If the atrophy is not due to long-term problems, then typically physical therapy and a reuse of the tissues can minimize or reverse the atrophic changes.

As we place different stresses on our bodies, our tissues may actually transform into another type of tissue. Sometimes a mature
INTEGRATE

CLINICAL VIEW 5.4
Stem Cells

Why all the interest in stem cells?

Stem cells are immature, undifferentiated cells. These cells are able to divide into two cells, the first of which is another stem cell, and the other is a cell that could differentiate into a specialized, mature cell with a unique function. Stem cells have generated interest in the scientific and medical communities because of their potential for repair or replacement of damaged or dying tissue.

What are the two basic characteristics of stem cells?

All stem cells exhibit two characteristics: self-renewal and potency. Self-renewal refers to their ability to divide repeatedly to produce both new cells for maturation and new stem cells. Potency is the potential for differentiation: Different stem cells have varying ability to differentiate into almost any type of cell. Stem cells exhibit the following four levels of potency: totipotency, pluripotency, multipotency, and unipotency:

- **Totipotent** stem cells have a “total potential,” meaning that they exhibit the ability to differentiate into any cell type within an organism. A totipotent cell is produced when a secondary oocyte is fertilized by a sperm, giving rise to a zygote. The first few cell divisions of the zygote result in equally totipotent cells. Thus, only embryonic (not adult) stem cells have the potential to be totipotent.

- **Pluripotent** stem cells are derived from totipotent stem cells. These stem cells are formed from the embryoblast portion (inner cell mass) of the blastocyst. The blastocyst is a ball of cells that develops during the first week of development from the zygote. The embryoblast is the portion of the blastocyst that will eventually become an embryo and then a fetus. Pluripotent stem cells can form cells in any of the tissue layers of the embryo, but they cannot form structures such as the placenta. Again, only embryonic stem cells have the potential to be pluripotent.

- **Multipotent** stem cells are derived from pluripotent stem cells. They have the capability to differentiate into a restricted number of some cell types but not others. For example, stem cells in the red bone marrow may be stimulated to mature and differentiate into different types of blood cells, but not into some other types of cells. Some adult stem cells have the potential to be multipotent.

- **Unipotent** stem cells can differentiate into a single type of cell, yet these cells still retain the ability to renew themselves. Epithelial stem cells are examples of unipotent stem cells. Many adult stem cells are unipotent.

What are the differences between embryonic and adult stem cells?

Stem cells have long been used for bone marrow replacement and skin grafts. Research into the use of stem cells for treatment of Parkinson disease, Alzheimer disease, spinal cord injuries, and type 1 diabetes mellitus is ongoing.

Stem cells may be categorized as either embryonic stem cells or adult stem cells. Embryonic stem cells include those that have begun to divide in the zygote and the cells in the blastocyst. Embryonic stem cells exhibit the greatest degree of potency—and thus the greatest potential to differentiate into multiple cell types. In contrast, adult stem cells are the immature cells found in postnatal (already born) organisms. Adult stem cells typically are multipotent or unipotent, and thus they exhibit less potency than embryonic stem cells.

How are stem cells harvested?

Most embryonic stem cells must be harvested from a structure no more differentiated than a blastocyst. Most of these blastocysts are donated by families undergoing in vitro fertilization who stored more blastocysts than needed for a successful pregnancy. If these blastocysts are not used by the family and not donated for research, they typically are destroyed. Note that opponents of embryonic stem cell research counter that these blastocysts could be implanted and lead to viable infants who could be adopted, and any medical benefit from embryonic stem cell research does not justify using them in research. Opponents also maintain that adult stem cell research should be explored instead.

Adult stem cells may be extracted from the red bone marrow or tissue of an individual. These adult stem cells have been used to successfully treat certain blood and bone cancers. The main problem with adult stem cells is their limited potency, which suggests that their use in treatment for diseases is limited. Embryonic stem cells exhibit greater promise for treatment because of their greater potency.
epithelium changes to a different form of mature epithelium, a phenomenon called **metaplasia** (met-ā-plā’zē-ā; *metaplasia* = transformation). Metaplasia may occur as an epithelium adapts to environmental conditions. For example, smokers typically experience metaplastic changes in the epithelium of the trachea (windpipe). The smoke and its by-products are the environmental stressors that change the normal pseudostratified ciliated columnar epithelium lining the trachea to a nonkeratinized stratified squamous epithelium. (If a person quits smoking, his or her metaplastic epithelium will fairly quickly revert back to its pseudostratified ciliated columnar epithelium.) Another example occurs in some individuals with chronic acid reflux, also known as heartburn. Here, the nonkeratinized stratified squamous epithelium of the inferior esophagus may transform to a simple columnar epithelium, like that seen in the stomach.

**Dysplasia** (dis-plā’zē-ā; dys = bad, plasis = molding) refers to abnormal tissue development. For example, cervical dysplasia may develop when a woman is exposed to the human papillomavirus. Dysplasias have the potential to turn into cancer (and thus are sometimes described as precancerous), but they also have the potential to revert to normal tissue. Thus, cervical dysplasia has the potential to either turn into cancer or revert to normal tissue, which is why dysplastic cells are closely monitored by health-care professionals.

When tissue growth proceeds out of control, a tumor composed of abnormal tissue develops, and the condition is called **neoplasia** (nē-ō-plā’zē-ā; neo = new). Neoplasms (tumors) may be benign or malignant. A **benign** (bē-nīn’; benig-nus = kind) neoplasm typically is localized in its growth and does not spread, whereas a **malignant** neoplasm is characterized by invading local tissues and potentially **metastasizing**, or spreading, to other
tissues of the body. A malignant neoplasm is commonly known as cancer. It is thought that most cancers are a result of DNA damage, through environmental factors, genetics, or a combination of both. The growth and proliferation of malignant cells can interfere with the normal functioning of other tissues and organs, leading to the morbidity and mortality of the individual.

Necrosis (nē-krōˈsis; nekros = corpse) is the term for tissue death. Necrosis typically occurs due to tissue damage that is not reversible, and an inflammatory response (see section 22.3d) usually occurs in the tissue in response to the damage. Gangrene is an example of tissue necrosis (see Clinical View 5.5: “Gangrene”).

WHAT DID YOU LEARN?

What is the difference between metaplasia, dysplasia, and a malignant neoplasia?

5.6c Aging of Tissues

LEARNING OBJECTIVE

26. List some changes that occur in tissues with age.

All tissues change as a result of aging. Proper nutrition, good health, normal circulation, and relatively infrequent wounds promote continued normal tissue functioning past middle age. Thereafter, the support, maintenance, and replacement of cells and extracellular matrix become less efficient. Physical damage and physiologic changes can alter the structure and chemical composition of many tissues. For example, as individuals age, epithelia become thinner and connective tissues lose their pliability and resiliency. The amount of collagen in the body declines with age, so tissue repair takes longer. Bones become brittle, and muscle and nervous tissue begin to atrophy. Poor diet, circulation problems, and smoking accelerate these tissue declines. Eventually, cumulative losses from relatively minor damage or injury may contribute to major health problems.

WHAT DID YOU LEARN?

How do epithelia and connective tissue change when we age?

INTEGRATE

CLINICAL VIEW 5.6

Tissue Transplant

Grafting is the process of surgically transplanting healthy tissue to replace diseased, damaged, or defective tissue. Tissue transplant may be characterized in four ways: an autograft, a syngenetic graft, an allograft, or a heterograft.

An autograft (awlō-graft; autos = self) is a tissue transplant from one site to a different site on the same individual. Autografts are often performed with skin, as healthy skin from one part of the body is grafted to another part of the body where the skin has been damaged by burns or chemicals. Because an autograft is a person’s own body tissue, the body will not reject the tissue as foreign. However, autografts may not be feasible in certain situations, such as when the amount of skin damaged is so great that it would not be possible to transplant such a large portion of tissue.

A syngenetic (sin-jē-netˈik; syn = together) graft, also called an isograft, is a tissue transplant from one person to a genetically identical person (i.e., identical twins). Very few of us, however, have an identical twin, so this type of graft is not possible for most people.

An allograft (alˈō-graft; allos = other) is a tissue transplant from one person to another person who is genetically different. Many tissue types have been used as allografts, including skin, muscle, bone, and cartilage. The term allograft also is used for the transplantation of organs or parts of organs, such as heart valves, kidneys, and the liver. The patient and the organ donor must be as genetically similar as possible, because the closer the match, the less likely the allograft will be rejected. The recipient of the transplanted organ(s) must take powerful immunosuppressant drugs, which help prevent the body from rejecting the organ. Unfortunately, these same drugs work by suppressing the entire immune system, making the transplant patient more susceptible to illness (see Clinical View 22.5: “Organ Transplants and MHC Molecules”).

A xenograft (zēˈnō-graft; xen = foreign), also called a heterograft (hēˈter-ō-graft; heteros = other), is a tissue transplant from an animal into a human being. For example, porcine (pig) and bovine (cattle) tissues have been used as replacements for heart valves, blood vessels, and bone. As with an allograft, xenografts may be prone to rejection and thus may not last as long as a syngenetic graft would.
<table>
<thead>
<tr>
<th>CHAPTER SUMMARY</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
</tr>
<tr>
<td>5.1 Epithelial Tissue: Surfaces, Linings, and Secretory Functions</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>5.1a Characteristics of Epithelial Tissue</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>5.1b Functions of Epithelial Tissue</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>5.1c Classification of Epithelial Tissue</td>
</tr>
<tr>
<td></td>
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<td>5.1d Glands</td>
</tr>
<tr>
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<tr>
<td></td>
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<tr>
<td>5.2 Connective Tissue: Cells in a Supportive Matrix</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>5.2a Characteristics of Connective Tissue</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>5.2b Functions of Connective Tissue</td>
</tr>
<tr>
<td></td>
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<tr>
<td>5.2c Embryonic Connective Tissue</td>
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<tr>
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<tr>
<td>5.2d Classification of Connective Tissue</td>
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<td>5.3 Muscle Tissue: Movement</td>
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</tr>
<tr>
<td>5.4 Nervous Tissue: Information Transfer and Integration</td>
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<td></td>
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<tr>
<td>5.5 Integration of Tissues in Organs and Body Membranes</td>
</tr>
<tr>
<td>5.5a Organs</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>5.5b Body Membranes</td>
</tr>
<tr>
<td></td>
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<td></td>
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<tr>
<td>5.6 Tissue Development and Aging</td>
</tr>
<tr>
<td>5.6a Tissue Development</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>5.6b Tissue Modification</td>
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<tr>
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<td>5.6c Aging of Tissues</td>
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Do You Know the Basics?

1. Which tissue contains a calcified ground substance and is specialized for structural support?
   a. muscle tissue
   b. dense regular connective tissue
   c. areolar connective tissue
   d. bone connective tissue

2. Which of the following is not a characteristic of areolar connective tissue?
   a. predominant cell type is the fibroblast
   b. abundant ground substance
   c. densely packed protein fibers
   d. occurs in the subcutaneous layer of the skin

3. ________ membranes line body cavities that typically open to the exterior, such as the nasal cavity.
   a. Mucous
   b. Serous
   c. Cutaneous
   d. Synovial

4. Which of the following is a correct statement about a simple epithelium?
   a. All of the cells are in direct contact with the basement membrane.
   b. It protects against mechanical abrasion.
   c. It is formed from multiple layers of cells.
   d. It may contain the protein keratin.

5. All of the following are characteristics of an epithelium except
   a. it is selectively permeable.
   b. it may form exocrine glands.
   c. its cells are highly regenerative.
   d. it contains abundant blood vessels.

6. Which connective tissue type is composed of cells called chondrocytes?
   a. bone
   b. dense irregular
   c. cartilage
   d. areolar

7. Which tissue type is formed from mesoderm?
   a. epidermis (outer layer) of skin
   b. nervous tissue
   c. smooth muscle tissue
   d. epithelial lining of the urinary bladder

8. Which muscle type consists of long, cylindrical, striated fibers with multiple nuclei located at the periphery of the fiber?
   a. smooth muscle
   b. skeletal muscle
   c. cardiac muscle
   d. All of these are correct.

9. Which epithelial tissue type lines the trachea (air tube)?
   a. simple columnar epithelium
   b. pseudostratified ciliated columnar epithelium
   c. simple squamous epithelium
   d. transitional epithelium

10. A gland that releases its secretion by exocytosis out of secretory vesicles is called a(n) ________ gland.
    a. merocrine
    b. apocrine
    c. holocrine
    d. All of these are correct.

11. What are some characteristics of all types of epithelium?

12. Describe the two main criteria by which epithelia are classified.

13. List the epithelium types that line (a) the lumen of the stomach, (b) the oral cavity, (c) the urinary bladder, and (d) the air sacs (alveoli) of the lungs.

14. What are the types of exocrine glands, classified by method of secretion, and how does each method of secretion work?

15. Name the four types of body membranes, and cite a location of each type.

16. What characteristics are common to all connective tissues?

17. What are the main structural differences between dense regular and dense irregular connective tissue?

18. In what regions of the body would you expect to find hyaline cartilage, fibrocartilage, and elastic cartilage, and why would these types be located in these regions?

19. What are the similarities and differences between skeletal muscle, cardiac muscle, and smooth muscle?

20. What is the difference between neurons and glial cells in nervous tissue?

Can You Apply What You’ve Learned?

1. John is a 53-year-old construction worker who has come into your office complaining of a sore knee joint. You see a buildup of fluid close to the patella (kneecap) but deep to the skin and suspect the soreness is due to bursitis, an inflammation of membranes that surround some joints. Which type of body membrane is inflamed?
   a. cutaneous membrane
   b. serous membrane
   c. synovial membrane
   d. mucous membrane

2. Your optometrist shines a light in your eye and notices your pupil constricts (becomes smaller) in response to the light. She tells you the iris (the colored part of the eye) is a muscle that adjusts the size of the pupil automatically in response to the amount of light entering the eye. Based on this information, which type of muscle do you think forms the iris?
   a. skeletal
   b. cardiac
   c. smooth
   d. visual

Use the following paragraph to answer questions 3–5.

During a biology lab, Erin used a cotton swab to remove some tissue from the inner side of her cheek. She then placed the tissue on a slide to examine it under the microscope.
3. Why was the tissue able to be removed so easily without causing injury to the rest of Erin’s cheek?
   a. The tissue contained abundant amounts of ground substance to keep the tissue puffy and relatively intact.
   b. The tissue contained multiple layers of cells, so removing a few cells wouldn’t harm the rest of the tissue.
   c. The tissue contained lots of blood vessels, so blood filled any gaps left when the original cells were removed.
   d. The remaining cells were interconnected by intercalated discs, which formed a strong bond between the cells.

4. When Erin examined the cells under the microscope, what shape were the cells?
   a. squamous
   b. cuboidal
   c. columnar
   d. circular

5. If Erin removed a large chunk of this tissue from the same site, the shape and characteristics of the deepest cells would be
   a. the same as the original cells under the microscope.
   b. cuboidal.
   c. binucleated and circular.
   d. squamous.

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**Can You Synthesize What You’ve Learned?**

1. During a microscopy exercise in the anatomy laboratory, a student makes the following observations about a tissue section: (a) The section contains some different types of scattered protein fibers—that is, they exhibit different widths, some are branched, and some are long and unbranched. (b) The observed section has some “open spaces”—that is, places between both cells and the fibers that appear clear with no recognizable features. (c) Several connective tissue cell types are scattered throughout the section, but these cells are not grouped tightly together. What type of tissue is the student observing? Where might this tissue be found in the body?

2. Your father is suffering from a painful knee joint. He has been told that he has either the early stages of arthritis or some inherent joint problems. His friend recommends that he take a chemical supplement, called chondroitin sulfate, which has been shown to help some people with joint aches and pains. Specifically, this supplement may alleviate symptoms caused by degenerated cartilage on the surfaces of bones in joints. Based on your knowledge of connective tissues, do you think the chondroitin sulfate supplements could help your father’s knee problems?
The integument (in-teg′u-ment; integumentum = a covering) is the skin that covers your body. Skin is also known as the cutaneous (kə-ta′nē-ūs; cutis = skin) membrane. The integumentary (in-teg′u-men′tā-rē) system consists of the skin and its derivatives: nails, hair, sweat glands, and sebaceous (oil) glands. On average, each square inch of skin contains up to 20 feet of blood vessels, 650 sweat glands, 100 sebaceous glands, and over 1000 nerve endings. Our skin is a barrier to the outside world and is subjected to trauma, harmful chemicals, pollutants, microbes, and damaging sunlight. Changes in the color of the skin may reflect body disorders or anomalies; skin changes or lesions sometimes reflect systemic infections or disease. The scientific study and treatment of the integumentary system is called dermatology (der-mā-to-lē-jē; derma = skin, logos = study). In this chapter, we examine the specific layers of the integument and the tissues that compose each layer. We also will see how the composition of the integumentary system is related to its functions. We conclude by discussing integument repair and how the integumentary system ages.
6.1 Composition and Functions of the Integument

The integument is the body’s largest organ and is composed of all the tissue types that function in concert to protect internal body structures. Its surface is an epithelium that protects underlying body layers. The connective tissue that is deep to the epithelium provides strength and resilience to the skin. This connective tissue also contains smooth muscle associated with hair follicles (arrector pili) that alters hair position. Finally, nervous tissue detects and monitors sensory stimuli in the skin, thus providing information about touch, pressure, temperature, and pain.

The integument accounts for 7% to 8% of the body weight and covers the entire body surface with an area that varies between about 1.5 and 2.0 square meters (m²). Its thickness ranges between 1.5 millimeters (mm) and 4 mm or more, depending on body location. (For comparison, a sheet of copier paper is about 0.1 mm thick, so the thickness of the skin would range between 15 and 40 sheets of paper.) The integument consists of two distinct layers: a layer of stratified squamous epithelium called the epidermis, and a deeper layer of both areolar and dense irregular connective tissue called the dermis (figure 6.1). Deep to the integument is a layer of areolar and adipose connective tissue called the subcutaneous layer, or hypodermis. The subcutaneous layer is not part of the integumentary system; however, it is described in this chapter because it is closely involved with both the structure and function of the skin.

6.1a Epidermis

LEARNING OBJECTIVES

1. Describe the five layers (strata) of the epidermis.
2. Differentiate between thick skin and thin skin.
3. Explain what causes differences in skin color.

The epithelium of the integument is called the epidermis (ep-i-derm′is; epi = on, derma = skin). It is a keratinized, stratified squamous epithelium (see section 5.1c).

Careful examination of the epidermis, from the basement membrane to its surface, reveals several specific layers, or strata. From deep to superficial, these layers are the stratum basale, stratum spinosum, stratum granulosum, stratum lucidum (found in thick skin only), and stratum corneum (figure 6.2). The first three strata listed are composed of living keratinocytes, whereas the most superficial two strata contain dead keratinocytes.

Figure 6.1 Layers of the Integument. A diagrammatic sectional view through the integument shows its relationship to the underlying subcutaneous layer.
Stratum Basale

The deepest epidermal layer is the stratum basale (strät’um bah-sä’lē), also known as the stratum germinativum, or basal layer. This single layer of cuboidal to low columnar cells is tightly attached by hemidesmosomes (see section 4.6d) to an underlying basement membrane that separates the epidermis from the connective tissue of the dermis. Three types of cells occupy the stratum basale (figure 6.2b):

1. **Keratinocytes** (ke-ra’ti-nō-sēt; keras = horn) are the most abundant cell type in the epidermis and are found throughout all epidermal strata. The stratum basale is dominated by large keratinocyte stem cells, which divide to generate new keratinocytes that replace dead keratinocytes shed from the surface. Their name is derived from their synthesis of **keratin**, a protein that strengthens the epidermis considerably. Keratin is one of a family of fibrous structural proteins that are both tough and insoluble. Fibrous keratin molecules can twist and intertwine around each other to form helical intermediate filaments of the cytoskeleton (see section 4.6b). The keratin proteins found in keratinocytes are called **cytokeratins**. Their structure in these keratinocytes gives skin its strength and makes the epidermis water resistant.

2. **Melanocytes** (mel’ā-nō-sēt; melano = black) have long, branching processes and are scattered among the keratinocytes of the stratum basale. They produce and store the pigment **melanin** (mel’ā-nīn) in response to ultraviolet light exposure. Their cytoplasmic processes transfer melanin pigment within granules called **melanosomes** (mel’ā-nō-sōmz) to the keratinocytes within the basal layer and sometimes in more superficial layers. This pigment (which includes the colors black, brown, tan, and yellow-brown) accumulates around the nucleus of the keratinocyte and shields the nuclear DNA from ultraviolet radiation. The darker tones of the skin result from melanin produced by the melanocytes. Thus, “tanning” is the result of the melanocytes producing melanin to block UV light from causing mutations in the DNA of your keratinocytes (in the epidermis) and fibroblasts (in the dermis).

3. **Tactile cells**, also called Merkel cells, are few in number and found scattered among the cells within the stratum basale (see section 16.2a). Tactile cells are sensitive to touch and, when compressed, they release chemicals that stimulate sensory nerve endings, providing information about objects touching the skin.

Stratum Spinosum

Several layers of polygonal keratinocytes form the stratum spinosum (spīn’ō-sūm), or spiny layer. Each time a keratinocyte stem cell in the stratum basale divides, a daughter cell is pushed toward the external surface from the stratum basale, while the other cell remains as a stem cell in the stratum basale. Once this new cell enters the stratum spinosum, it begins to differentiate into a nongrowing, highly specialized keratinocyte. The keratinocytes in the stratum spinosum attach to their neighbors by many membrane junctions called desmosomes (described in section 4.6d).

The process of preparing epidermal tissue for observation on a microscope slide shrinks the cytoplasm of the cells in the stratum spinosum. Because the cytoskeletal elements and desmosomes remain intact, the shrunken keratinocytes in the stratum spinosum resemble miniature porcupines that are attached to their neighbors. This spiny appearance accounts for the name of this layer.

In addition to the keratinocytes, the stratum spinosum also contains the fourth epidermal cell type, called **epidermal dendritic (Langerhans) cells** (figure 6.2b). Epidermal dendritic cells are immune cells that help fight infection in the epidermis. These immune cells are often present in the stratum spinosum and stratum granulosum, but they are not identifiable in standard histologic preparations. Their phagocytic activity initiates an immune response to protect the body against pathogens that have penetrated the superficial epidermal layers as well as epidermal cancer cells (see section 22.3b).
Stratum Granulosum

The stratum granulosum (gran-ú-ló’sum), or granular layer, consists of three to five layers of keratinocytes superficial to the stratum spinosum. Within this stratum begins a process called keratinization (ker’á-tin-i-za’shún), where the keratinocytes fill up with the protein keratin, and in so doing, cause both the cell’s nucleus and organelles to disintegrate and the keratinocyte dies. Keratinization is not complete until the keratinocytes reach the more superficial epidermal layers. A fully keratinized cell is dead (because it has neither a nucleus nor organelles), but it is structurally strong because of the keratin it contains.

Stratum Lucidum

The stratum lucidum (lú’sid-um), or clear layer, is a thin, translucent region of about two to three keratinocyte layers that is superficial to the stratum granulosum. This stratum is found only in the thick skin. Keratinocytes occupying this layer are flattened, pale cells with indistinct boundaries. They are filled with the translucent protein called eleidin (é-li’din), which is an intermediate product in the process of keratin maturation. This layer helps protect the skin from ultraviolet light.

Stratum Corneum

The stratum corneum (kór’né-úm; corneus = horny), or hornlike layer, is the most superficial layer of the epidermis. It is the stratum you see when you look at your skin. The stratum corneum consists of about 20 to 30 layers of dead, scala, interlocking, keratinized cells. The dead keratinocytes are anucleate (lacking a nucleus) and are tightly packed together.

A keratinized, or cornified, epithelium contains large amounts of keratin. After keratinocytes are formed from stem cells within the stratum basale, they change in structure and in their relationship to their neighbors as they progress through the different strata until they eventually reach the stratum corneum and are sloughed off its external surface. Major changes during keratinocyte migration include synthesis of keratin and loss of the nucleus and organelles as described. What remains of these keratinocytes in the stratum corneum is essentially keratin protein enclosed in a thickened plasma membrane. Migration of the keratinocyte to the stratum corneum occurs during the first 2 weeks of the keratinocyte’s life. The dead, keratinized cells usually remain for an additional 2 weeks in the exposed stratum corneum layer, providing a barrier before they are shed. Overall, individual keratinocytes are present in the integument for about 1 month following their formation.

The stratum corneum presents a thickened surface unsuitable for the growth of many microorganisms. Additionally, some exocrine gland secretions (e.g., sweat, which contains doricidin, an antimicrobial peptide) help prevent the growth of microorganisms on the epidermis, thus supporting its barrier function (see section 22.3a).

Variations in the Epidermis

The epidermis exhibits variations between different body regions within one individual as well as differences between individuals. The epidermis varies in its thickness, coloration, and skin markings.

Thick Skin Versus Thin Skin Over most of the body, the skin ranges in thickness between 1 mm and 2 mm. Skin is classified as either thick or thin based on the number of epidermal strata and the relative thickness of the epidermis, rather than the thickness of the entire integument (Figure 6.3).

Thick skin is found on the palms of the hands and the soles of the feet. All five epidermal strata occur in the thick skin. The epidermis of thick skin ranges between 0.4 mm and 0.6 mm thick. It houses sweat glands but has no hair follicles or sebaceous (oil) glands.

Thin skin covers most of the body. It lacks a stratum lucidum, so it has only four specific layers in the epidermis. Thin skin contains the following structures: hair follicles, sebaceous glands, and sweat glands. The epidermis of thin skin ranges from 0.075 mm to 0.150 mm thick.

WHAT DO YOU THINK?

1. Why do you think thick skin lacks hair follicles and sebaceous glands? Think about where thick skin is found and how that may interfere with the function of skin in that area.

Skin Color Normal skin color results from a combination of the colors of hemoglobin, melanin, and carotene. Hemoglobin (hē-mö-glo’bin; haima = blood) is an oxygen-binding protein present in red blood cells (see section 18.3b). It exhibits a bright red color upon

LEARNING STRATEGY

Integrate lab and lecture material: Follow these steps to help you identify the epidermal strata under the microscope:

1. Determine if the layer is closer to the free surface or is deeper. Remember the stratum corneum forms the free surface, whereas the stratum basale forms the deepest epidermal layer.
2. Examine the shape of the keratinocytes. The stratum basale contains cuboidal to low columnar keratinocytes, the stratum spinosum contains polygonal keratinocytes, and the stratum lucidum and corneum contain squamous keratinocytes.
3. See if the keratinocytes have a nucleus or are anucleate. When they are still alive (as in the strata basale, spinosum, and granulosum), you are able to see nuclei. The stratum lucidum and corneum layers contain dead, anucleate keratinocytes.
4. Count the layers of keratinocytes in the stratum. The stratum basale has only one layer of keratinocytes, and the stratum corneum contains 20 to 30 layers of keratinocytes. The other layers contain about two to five layers of keratinocytes.
5. Determine if the cytoplasm of each keratinocyte contains visible granules. If the keratinocytes contain visible granules, you likely are looking at the stratum granulosum.
binding oxygen, thus giving blood vessels in the dermis a reddish tint that is seen most easily in lightly pigmented individuals. If the blood vessels in the superficial layers vasodilate (i.e., the blood vessel diameter increases), such as during physical exertion, then the red tones are much more visible.

Melanin is a pigment produced and stored in melanocytes (described earlier in this section), and it occurs in a variety of black, brown, tan, and yellow-brown shades. Recall that melanin is transferred in melanosomes from melanocytes to keratinocytes in the stratum basale. Because keratinocytes are displaced toward the stratum corneum, melanocyte activity affects the color of the entire epidermis (figure 6.4).

The amount of melanin in the skin is determined by both heredity and light exposure. All people have about the same number of melanocytes. However, melanocyte activity and the color of the melanin produced by these cells vary among individuals and races, resulting in different skin color tones. Darker-skinned individuals have melanocytes that produce relatively more and darker melanin than lighter-skinned individuals. Further, these more active melanocytes tend to package melanin into cells in the more superficial epidermal layers, such as the stratum granulosum. Recall that exposure to ultraviolet light stimulates melanocytes to make more melanin.

Carotene (kar′ō-tēn) is a yellow-orange pigment that is acquired from various yellow-orange vegetables, such as carrots, corn, and squashes. Normally, it accumulates inside keratinocytes of the stratum corneum and in the subcutaneous fat. Within the body, carotene is converted into vitamin A, which plays an important role in normal vision (see section 16.4d). Vitamin A has also been thought to reduce potentially dangerous molecules called free radicals that form during normal metabolic activity in the body. Additionally, carotene may improve immune cell number and activity.

Albinism (al′bi-nizm) is an inherited recessive condition where the enzyme needed to produce melanin is nonfunctional. As a result, melanocytes are unable to produce melanin. Individuals who have albinism typically have white hair, pale skin, and pink irises.

Skin Markings A nevus (nē-vūs; pl., nevi), commonly called a mole, is a harmless, localized overgrowth of melanocytes. On rare
Friction ridges are another type of skin marking. These ridge patterns follow the contours of the skin, varying from small, conical pegs (in thin skin) to the complex arches and whorls. Friction ridges are found on the fingers (fingerprint), palms, soles, and toes (figure 6.5). These ridges are formed from large folds and valleys of both dermis and epidermis. They help increase friction on contact, so that our hands can firmly grasp items and our feet do not slip when we walk barefoot. Some researchers have suggested friction ridges also provide flexibility to the skin and allow it to deform without being damaged. When sweat glands and oil glands release their secretions, noticeable fingerprints may be left on touched surfaces. Each individual has a unique pattern of friction ridges, allowing matching of prints and identification of individuals.

WHAT DID YOU LEARN?

1. As you trim your roses, a thorn penetrates your palm through all epidermal strata. What are the layers of the epidermis penetrated, starting from the surface of the skin?

2. Briefly describe the process of keratinization. Where does it occur? Why is it important?

3. How does hemoglobin contribute to skin color?

4. What is the function of friction ridges?

Figure 6.5 Friction Ridges of Thick Skin. Friction ridges form fingerprints, palm prints, and toe prints. Shown here are four basic fingerprint patterns.
6.1b Dermis

LEARNING OBJECTIVES

4. Characterize the two layers of the dermis.
5. Explain the significance of cleavage lines.
6. Describe how dermal blood vessels function in temperature regulation.

The dermis (der′mis) is deep to the epidermis and ranges in thickness from 0.5 mm to 3.0 mm. This layer of the integument is composed of connective tissue proper (see section 5.2d) and contains primarily collagen fibers, although both elastic and reticular fibers also are found within the dermis. Additionally, researchers recently have discovered motile cells in the dermis called dendritic cells. These cells are similar to the epidermal dendritic cells in that they serve an immune function, except they are located in the dermis (see section 22.3b). Other structures within the dermis are blood vessels, sweat glands, sebaceous glands, hair follicles, nail roots, sensory nerve endings, and smooth muscle tissue associated with hair follicles (arrector pili). Two major regions of the dermis can be distinguished: a superficial papillary layer and a deeper reticular layer (figure 6.6).

Papillary Layer of the Dermis

The papillary (pap′i-lār-ē) layer is the superficial region of the dermis that is deep to the epidermis. It is composed of areolar connective tissue, and it derives its name from the projections of the dermis called dermal papillae (der′mă pă-pil′ē; papilla = a nipple). The dermal papillae interdigitate with deep projections of the epidermis called epidermal ridges, much like two sets of egg crate foam stacked on top of one another. Together, the epidermal ridges and dermal papillae increase the area of contact between the two layers and interlock them. Each dermal papilla contains the capillaries that supply nutrients to the cells of the epidermis. Additionally, dermal papillae contain sensory nerve endings that serve as tactile receptors (see figure 6.1); these receptors continuously monitor touch on the surface of the epidermis. Tactile receptors are discussed in detail in section 16.2a.

Reticular Layer of the Dermis

The reticular layer forms the deeper, major portion of the dermis that extends from the papillary layer to the underlying subcutaneous layer. The reticular layer consists primarily of dense irregular connective tissue through which large bundles of collagen fibers extend in all directions. These fibers are interwoven into a meshwork that surrounds structures in the dermis, such as the hair follicles, sebaceous glands and sweat glands, nerves, and blood vessels. The word reticular means “network” and refers to this meshwork of collagen fibers. Note that the reticular layer is different from reticular connective tissue, described in section 5.2d.

Lines of Cleavage and Stretch Marks

The majority of the collagen and elastic fibers in the skin are oriented in parallel bundles at specific body locations. The alignment of fiber bundles within the dermis is a result of the direction of applied stress during routine movement; therefore, the function of the bundles is to resist stress. Lines of cleavage (tension lines) in the skin identify the predominant orientation of collagen fiber bundles (figure 6.7). These are clinically and surgically significant because any procedure resulting in a cut perpendicular to a cleavage line usually is pulled
open as a result of the recoil resulting from cut elastic fibers. This often results in slow healing and increased scarring. In contrast, an incision made parallel to a cleavage line usually will remain closed. Therefore, surgical procedures should be planned to consider lines of cleavage, thus ensuring rapid healing and prevention of scarring.

Collagen fibers and elastic fibers together contribute to the visible physical characteristics of the skin. Whereas the collagen fibers impart tensile strength, elastic fibers allow some stretch and recoil in the dermis during normal movement activities. Stretching of the skin that may occur as a result of excessive weight gain or pregnancy often exceeds the elastic capabilities of the skin. When the skin is stretched beyond its capacity, some collagen fibers are torn and result in stretch marks, called striae (strī; stria = furrow). Both the flexibility and thickness of the dermis are diminished by effects of exposure to ultraviolet light and aging, causing either sagging or wrinkled skin.

WHAT DID YOU LEARN?

5. Compare and contrast the papillary versus reticular layer of the dermis, with respect to their tissue type and the structures they contain.

6. What is indicated by the lines of cleavage in the skin, and why is this medically important?

**INTEGRATE**

**CLINICAL VIEW 6.2**

**Tattoos**

Tattoos are permanent images produced on the integument through the process of injecting a dye into the dermis. The dermis doesn’t have a rapid cell turnover, so the injected dye remains in this area for a long time. Scar tissue surrounds the dye granules, which are too large for dendritic cells to ingest, and they become a permanent part of the dermis layer.

It is usually impossible to completely remove a tattoo, and some scarring may occur. Older methods include excision (cutting out the tattoo), dermabrasion (sanding down the tattooed skin), and cryosurgery (freezing the area of tattooed skin prior to its removal). Lasers are now used in some cases to break down the tattoo pigments. Newer tattoo inks have been introduced that allow for easier tattoo removal.

**Figure 6.7 Lines of Cleavage.** Lines of cleavage partition the skin and indicate the predominant direction of underlying collagen fibers in the reticular layer of the dermis.
6.1c Subcutaneous Layer

LEARNING OBJECTIVE

7. List the functions of the subcutaneous layer.

Deep to the integument is the subcutaneous (sub-kə-ta’né-ūs; sub = beneath, cutis = skin) layer, also called the hypodermis, or superficial fascia. It is not considered a part of the integument. This layer consists of both areolar connective tissue and adipose connective tissue (see figure 6.1). In some locations of the body, adipose connective tissue predominates; thus, the subcutaneous layer is called subcutaneous fat. The connective tissue fibers of the reticular layer of the dermis are extensively interwoven with those of the subcutaneous layer to stabilize the position of the skin and bind it to the underlying structures. The subcutaneous layer pads and protects the body, acts as an energy reservoir, and provides thermal insulation. Drugs often are injected into the subcutaneous layer because its extensive vascular network promotes rapid absorption of the drugs.

Normally, the subcutaneous layer is thicker in women than in men, and its regional distribution differs between the sexes. Adult males tend to accumulate subcutaneous fat primarily at the neck, upper arms, abdomen, lower back, and buttocks, whereas adult females accumulate adipose connective tissue primarily in the breasts, buttocks, hips, and thighs.

Table 6.1 reviews the layers of the integument and the subcutaneous layer.

Table 6.1 Integument Layers and the Subcutaneous Layer

<table>
<thead>
<tr>
<th>Layer</th>
<th>Specific Layer</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>INTEGUMENT: EPIDERMIS</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stratum corneum</td>
<td>Most superficial layer of epidermis; 20–30 layers of dead, flattened, anucleate, keratin-filled keratinocytes</td>
<td></td>
</tr>
<tr>
<td>Stratum lucidum</td>
<td>2–3 layers of anucleate, dead keratinocytes; seen only in thick skin (i.e., palms of hands, soles of feet)</td>
<td></td>
</tr>
<tr>
<td>Stratum granulosum</td>
<td>3–5 layers of keratinocytes with distinct granules in cytoplasm; keratinization begins in this layer</td>
<td></td>
</tr>
<tr>
<td>Stratum spinosum</td>
<td>Several layers of keratinocytes attached to neighbors by desmosomes; epidermal dendritic cells present</td>
<td></td>
</tr>
<tr>
<td>Stratum basale</td>
<td>Deepest, single layer of cuboidal to low columnar keratinocytes in contact with basement membrane; cell division occurs here; also contains melanocytes and tactile cells</td>
<td></td>
</tr>
<tr>
<td><strong>INTEGUMENT: DERMIS</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Papillary layer</td>
<td>Superficial layer of dermis; composed of areolar connective tissue; forms dermal papillae; houses capillaries and tactile receptors</td>
<td></td>
</tr>
<tr>
<td>Reticular layer</td>
<td>Deeper layer of dermis; composed of dense irregular connective tissue surrounding and supporting hair follicles, sebaceous glands and sweat glands, nerves, and blood vessels</td>
<td></td>
</tr>
<tr>
<td><strong>SUBCUTANEOUS LAYER</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No specific layers</td>
<td>Not considered part of the integument; deep to dermis; composed of areolar and adipose connective tissue</td>
<td></td>
</tr>
</tbody>
</table>
The integument system protects almost all body systems:

- The integument provides the first line of defense against pathogens and toxins trying to enter the body (see section 22.3a).
- The integument helps in preventing fluid loss, and thus assists the cardiovascular system in maintaining blood volume (see section 25.2a).
- When muscular exertion generates heat (see section 10.1a), the integumentary system helps release excess heat via sweating and vasodilation.
- The integument provides abundant sensory information to the nervous system (see section 16.2a).
- The integument can synthesize vitamin D, which is required for calcium homeostasis (see section 7.6a).
- Dendritic cells are components of the immune system that initiate an immune response (see section 22.2a).
- Hairs in the nasal cavity help the respiratory system filter inspired air (see section 23.2a).
- The integumentary system and the urinary system both excrete nitrogenous waste products (see section 24.1).

6.1d Functions of the Integument

**LEARNING OBJECTIVES**

- Name ways in which the integument protects the body and prevents water loss.
- Describe the integument’s involvement in calcium and phosphorus utilization.
- Describe the integument’s role in secretion and absorption.
- Identify the immune cells that reside in the integument, and describe their actions.
- Explain how the skin helps cool the body or retain warmth.
- List the sensations detected by the skin’s sensory receptors.

The epidermis serves a protective function, helps prevent water loss, and is involved with metabolic regulation. The epidermis and the dermis together secrete and absorb materials, and both play a role in immunity. We explore these functions in detail.

**Protection**

The epidermis acts as a physical barrier that protects the entire body from injury and trauma. It offers protection against harmful chemicals, toxins, microbes, and excessive heat or cold. The skin also protects deeper tissues from solar radiation, especially UV rays. When exposed to the sun, the melanocytes become more active and produce more melanin, thus giving the skin a tanned look. Even when you get a sunburn, the deeper tissues (muscles and internal organs) remain unaffected.

**Prevention of Water Loss and Water Gain**

The epidermis is water resistant, but not entirely waterproof. Some water is always lost through the skin when you sweat. More water is typically lost through respiration, a process in which fluids slowly penetrate through the epidermis and then evaporate into the surrounding air (see section 25.2a). We realize how important the skin is in preventing water loss when treating individuals with severe burns. One of the main dangers is dehydration, because without the protective skin barrier, much larger amounts of water can escape from body tissues.

The skin also helps prevent water gain. If the skin were not water resistant, then each time you took a bath you would swell up like a sponge as the skin absorbed water!

**Metabolic Regulation**

Vitamin D₃, also called cholecalciferol (kō’lē-kal-sif’er-ol), is synthesized from a steroid precursor by the keratinocytes when they are exposed to ultraviolet radiation. Vitamin D₃ is then released into the blood and transported to the liver, where it is converted to another intermediate molecule (calcidiol), and then transported to the kidney, where it is converted to calcitriol (kal-si-tr’lōl). Calcitriol is the active form of vitamin D and is considered a hormone (see section 7.6a). It increases absorption of calcium and phosphate from the small intestine into the blood, which results in a greater amount of the calcium being absorbed from the foods we eat. Thus, the synthesis of vitamin D₃ is important in regulating the levels of calcium and phosphate in the blood. As little as 10 to 15 minutes of direct sunlight a day provides your body with its daily vitamin D through this process.

The skin also is involved in other forms of metabolic regulation. It is able to convert some compounds to slightly different forms that may be used by the skin. For example, when topical corticosteroids (e.g., hydrocortisone) are applied to the skin, the corticosteroid medication enters the keratinocytes, where the cells convert and use the medication to stop inflammation and itching. (For further information about corticosteroids, see section 17.9a.)

**WHAT DO YOU THINK?**

During the Industrial Revolution, many children in cities spent little time outdoors and most of their time working in factories, leading to an increase in a disorder called rickets. Rickets is a bone disorder caused by inadequate vitamin D. Based on your knowledge of skin function, why do you think these children developed rickets?

**Secretion and Absorption**

Skin exhibits a secretory function when it discharges substances from the body during sweating. Sweating occurs to release excess heat from the body. Notice that sweat sometimes feels...
“gritty” because of the waste products being secreted onto the skin surface. The substances secreted in sweat include water, salts, and urea, a nitrogenous waste product of amino acid breakdown (see section 24.6e). The amount of water, salts, and urea secreted can be adjusted by the skin, and in so doing, the skin alters electrolyte levels in the body (see section 25.3). Thus, the skin also plays a role in electrolyte homeostasis. Sebum, excreted by sebaceous glands, lubricates the epidermis and hair, and helps make the integument water resistant.

The skin can absorb certain chemicals and drugs, such as estrogen from a birth control patch or nicotine from a nicotine patch. We refer to the skin as being selectively permeable because some materials are able to pass through it, whereas others are effectively blocked.

In a process called transdermal administration, drugs that are soluble either in oils or in lipid-soluble carriers may be administered transdermally by an adhesive patch that keeps the drug in contact with the skin surface. Drugs administered in this way slowly penetrate the epidermis and can be absorbed into the blood vessels of the dermis. Transdermal patches are especially useful because they release a continual, slow absorption of the drug into the blood over a relatively long period of time. The barrier to drug diffusion through the epidermis requires that the concentration of the drug in the patch be relatively high.

Immune Function

In section 6.1a, we described a small population of immune cells within the stratum spinosum called epidermal dendritic cells. These cells play an important role in initiating an immune response against pathogens that have penetrated the skin (see section 22.2a). These cells, along with dendritic cells of the dermis, also mount an attack against epidermal cancer cells.

Temperature Regulation

We previously discussed temperature regulation in section 1.6b. Body temperature can be influenced by the vast capillary networks and sweat glands in the dermis. Dermal blood vessels have an important role in body temperature and blood pressure regulation. Vasoconstriction (vā’sōktrı̄k’shən; vās = a vessel) means that the diameters of the vessels narrow, so relatively less blood is transported through them. Because less blood can flow through these dermal blood vessels, relatively more blood is transported through blood vessels deeper under the skin. The net effect is a shunting of blood away from the periphery of the body and toward deeper structures. Vasoconstriction of dermal blood vessels occurs to conserve heat. This is why we appear paler when we are exposed to cold temperatures. In addition, arrector pili (small bands of smooth muscle associated with hair follicles) are stimulated to contract to produce heat.

Conversely, vasodilation of the dermal blood vessels means that the diameter of the vessels increases, so relatively more blood is transported through them. The dermal blood vessels vasodilate so that more blood is transported close to the body surface. Here the net effect is a shunting of blood to the periphery of the body and away from deeper structures. Vasodilation of dermal blood vessels occurs to release excess heat. This additional blood flow through the dermis results in a more reddish/pinkish hue to the skin. This additional blood flow accounts for your face becoming flushed when you exercise. Consider how on a cold day your face may be paler than normal. When you come in from the cold, your face may become flushed as your body adjusts to the warmer temperature.

Sensory Reception

The dermis of the skin has an extensive innervation, which refers to its distribution of nerve fibers. Sensory nerve fibers in the skin (called sensory receptors) monitor stimuli in both the dermis and epidermis. For example, tactile cells (or Merkel cells) are large, specialized epithelial cells that stimulate specific sensory nerve endings when they are distorted by fine touch or pressure. In fact, seven major types of sensory receptors are housed within the skin to detect, distinguish, and interpret the many stimuli of our external environment that interact with our skin (see section 16.2a). In addition, motor nerve fibers extend through the skin to control glandular secretions and blood flow in blood vessels.

Figure 6.8 illustrates how the anatomy of the integument supports these various functions.

WHAT DID YOU LEARN?

8 How does the skin produce vitamin D?
9 Is the skin entirely waterproof? Explain.
10 What are some ways the skin can dissipate excess heat?
**Epidermis**

**PROTECTION**

Epidermal strata provide layers of protection against harmful chemicals, toxins, microbes, and excessive heat or cold. Skin also protects deeper tissues from UV radiation as melanocytes are stimulated to produce more melanin.

**PREVENTION OF WATER LOSS AND WATER GAIN**

The epidermis is water resistant and keeps water from either exiting or entering the skin easily.

**METABOLIC REGULATION**

Sunlight

Upon exposure to UV rays, keratinocytes produce vitamin D₃ and melanocytes are stimulated to produce more melanin, giving the skin a more tanned look.

**SECRETION AND ABSORPTION**

Materials (e.g., sebum, sodium, water, urea) secreted by dermal structures are released onto the epidermal surface. The skin is selectively permeable because some materials (e.g., certain drugs, like nicotine and estrogen within transdermal patches) may be absorbed while others are blocked.

**IMMUNE FUNCTION**

Epidermal dendritic cells engulf and destroy pathogens, alert the immune system to the presence of pathogens, and initiate an immune response. (Note: The dermis also contains its own dendritic cells.)
Epidermis

**PROTECTION**

Epidermal dendritic cells engulf and destroy pathogens, alert the immune system to the presence of pathogens, and initiate an immune response.

(Note: The dermis also contains its own dendritic cells.)

**IMMUNE FUNCTION**

Dermis

**METABOLIC REGULATION**

St. ratum

**SENSORY RECEPTION**

(a) Epidermis Functions

**PREVENTION OF WATER LOSS AND WATER GAIN**

The epidermis is water resistant and keeps water from either exiting or entering the skin easily.

Epidermal strata provide layers of protection against harmful chemicals, toxins, microbes, and excessive heat or cold. Skin also protects deeper tissues from UV radiation as melanocytes are stimulated to produce more melanin.

St. ratum

St. ratum spinosum

St. ratum lucidum

St. ratum granulosum

Stratum basale

Sunlight

Pathogen

Sensory receptor structures detect and relay pain, heat, cold, touch, pressure, and vibration. (Note: There also are some sensory receptors in the epidermis.)

Sensory receptors

Sensory nerve fiber

(b) Dermis Functions

**TEMPERATURE REGULATION**

Dilating blood vessels in the dermis release heat; constricting vessels conserve heat.

Sweat glands release fluid onto the skin surface, and the body cools off by evaporation of the sweat.

**SECRETION AND ABSORPTION**

Sweat glands secrete sodium, water, and urea onto the epidermal surface, and in so doing help maintain electrolyte homeostasis.

Sebaceous glands secrete sebum, which lubricates the skin and hair, and helps make the integument water resistant.

INTEGRATE CONCEPT OVERVIEW

Figure 6.8 How Integument Form Influences Its Functions.

(a) The epidermis is composed of multiple layers of keratinized epithelial cells that make it well suited for protection and prevention of water loss. It also participates in secretion and absorption, metabolic regulation, and immunity. (b) The dermis is composed of well-vascularized connective tissue that participates in secretion and absorption, temperature regulation, and sensory reception.
6.2 Integumentary Structures Derived from Epidermis

The nails, hair, and exocrine glands of the skin all are derived from the epidermal epithelium. These structures also are known as epidermal derivatives, or epidermal appendages, of the integument. They formed during embryologic development as portions of the epidermis invaginated into the dermis. Both nails and hairs are composed primarily of dead keratinocytes, whereas the exocrine glands are composed of living keratinocytes.

6.2a Nails

**LEARNING OBJECTIVES**

14. Describe the function of nails.
15. List the main components of the nail.

Nails are scalelike modifications of the stratum corneum layer of the epidermis that form on the dorsal edges of the fingers and toes. They protect the distal tips of the digits during jumping, kicking, or catching. Fingernails also assist us in grasping objects.

Each nail has a distal whitish free edge, a pinkish nail body, and a nail root, which is the proximal part embedded in the skin (figure 6.9). Together, these parts form the nail plate. The nail body covers a layer of epidermis called the nail bed, which contains only the deeper, living cell layers of the epidermis.

**INTEGRATE**

**CLINICAL VIEW 6.3**

Nail Disorders

Changes in the shape, structure, or appearance of the nails are clinically significant. A change may indicate the existence of a disease process affecting metabolism throughout the body. In fact, the state of a person’s fingernails and toenails can be indicative of his or her overall health. Nails are subject to various disorders.

**Brittle nails** are prone to vertical splitting and separation of the nail plate layers at the free edge. Overexposure to water or to certain household chemicals can cause brittle nails. Keeping the nails moisturized and limiting exposure to water and chemicals can alleviate brittle nails.

**An ingrown nail** occurs when the edge of a nail digs into the skin around it. This painful condition is first characterized by pain and inflammation at the site. If left untreated, some ingrown toenails can cause infection. Ingrown nails may result from overly tight shoes and improper trimming of the nails.

**Onychomycosis** (on′i-kō-mĭ-ko′sĭs; onych = nail, mykes = fungus, osis = condition) is a fungal infection that occurs in nails constantly exposed to warmth and moisture. The fungus starts to grow under the nail and eventually causes a yellowish discoloration, a thickened nail, and brittle, cracked edges. Fungal infections can result in permanent damage to the nail and a potential for spread of infection. Treatment involves taking oral fungal medications for long periods of time (a minimum of 6 to 12 weeks, and in some cases up to a year) to eradicate the fungal infection.

**Yellow nail syndrome** occurs when growth and thickening of the nail slows or stops completely. As the nail growth slows, the nails become yellowish or sometimes greenish. Yellow nail syndrome often, but not always, may be an outward sign of respiratory disease, such as chronic bronchitis.

**Spoon nails**, or **koilonychia** (koy-lō-nik′ē-ă; koilos = hollow), are a nail malformation where the outer surface of the nails are concave instead of convex. Spoon nails frequently are a sign of an iron deficiency. Treating the iron deficiency should alleviate the spoon nail condition.

**Beau’s lines** run horizontally across the nail and indicate a temporary interference with nail growth at the time this portion of the nail was formed. Injury to the nail or severe illness can cause Beau’s lines. They also may be seen in individuals suffering from chronic malnutrition.

**Vertical ridging** of the nails is common and usually does not indicate any serious medical problem. The condition occurs more frequently as we get older.
Most of the nail body appears pink because of the blood flowing in the underlying capillaries; the free edge of the nail appears white because there are no underlying capillaries. At the nail root and the proximal end of the nail body, the nail bed thickens to form the nail matrix, which is the actively growing part of the nail. The lunula (lūˈnə-lə; luna = moon) is the whitish, semilunar (semicircular) area of the proximal end of the nail body. It has a whitish appearance because a thickened stratum basale obscures the underlying blood vessels.

Along the lateral and proximal borders of the nail, folds of skin called nail folds overlap the nail. The eponychium (ep-ˈō-nikˈē-əm; onyx = nail), also known as the cuticle (kūˈti-kl), is a narrow band of epidermis extending from the margin of the nail wall onto the nail body. The hyponychium (hi-pō-nikˈē-əm) is the area of thickened epithelium underlying the free edge of the nail.

WHAT DID YOU LEARN?

11. What is the difference between the eponychium and the hyponychium of a fingernail?

6.2b Hair

LEARNING OBJECTIVES

16. Describe the structure of a hair and a follicle.
17. List the functions of hair.

Hair is found almost everywhere on the body except the palms of the hands and palmar surface of the fingers, the sides and soles of the feet and toes, the lips, and portions of the external genitalia. The general structure of hair and its relationship to the integument are shown in figure 6.10.

Hair Type and Distribution

A single hair, or pilus, has the shape of a slender filament; it is composed of keratinized cells growing from hair follicles that extend into the dermis, and often deeper into the underlying subcutaneous layer. Differences in hair density are due primarily to differences in the texture and pigmentation of the hair.
We produce three kinds of hair during our lives: lanugo, vellus, and terminal hair. Lanugo (làn-i-gō) is a fine, unpigmented, downy hair that first appears on the fetus in the last trimester of development. At birth, most of the lanugo has been replaced by similarly fine, unpigmented or lightly pigmented hair called vellus (vel’ús; vellus = fleece). Vellus is the primary human hair and is found on the upper and lower limbs.

Terminal hair is usually coarser, pigmented, and longer than vellus. It grows on the scalp, and it is the hair of eyebrows and eyelashes. At puberty, terminal hair replaces vellus hair in the axillary and pubic regions, and it forms the beard on the faces of males.

Hair Structure and Follicles

Three zones can be recognized along the length of a hair: the hair bulb, root, and shaft. The hair bulb consists of epithelial cells and is a swelling at the base where the hair originates in the dermis. The epithelium at the base of the bulb surrounds a small hair papilla, which is composed of a small amount of connective tissue containing tiny blood vessels and nerves. The root is the zone of the hair extending from the bulb to the skin surface. The shaft is the third portion of the hair that extends beyond the skin surface. The hair bulb contains living epithelial cells, whereas the root and shaft consist of dead epithelial cells.

Hair production involves a specialized type of keratinization that occurs within the hair matrix, a structure immediately adjacent to the hair papilla in the hair bulb. Epithelial cells near the center of the hair matrix divide, producing new cells that are gradually pushed toward the surface. The medulla, not found in all hair types, is a remnant of the soft core of the matrix. It is composed of loosely arranged cells and air spaces, and it contains soft keratin. Several layers of flattened cells closer to the outer surface of the developing hair form the relatively hard cortex. A single cell layer around the cortex forms the cuticle, which coats the hair.

The hair follicle (fol’i-kl) is an oblique tube that surrounds the hair root. It always extends into the dermis and sometimes into the subcutaneous layer. The cells of the follicle walls are organized into two principal concentric layers: an outer connective tissue root sheath, which originates from the dermis, and an inner epithelial tissue root sheath, which originates from the epidermis (figure 6.10b). Extending from the hair follicle to the dermal papillae are thin ribbons of smooth muscle that collectively are called the arrector pili (ár-ek’tör pī’lī). Stimulation of the arrector pili is usually a result of an emotional state, such as fear or rage, or as a response to exposure to cold temperatures. Upon stimulation, the arrector pili contracts, pulling on the hair follicle and elevating the hair, producing goose bumps.

Functions of Hair

The millions of hairs distributed on the surface of the human body have important functions:

- **Protection.** The hair on the head protects the scalp from sunburn and injury. Hair within the nostrils entraps particles and prevents their entry deeper into the respiratory system, whereas hairs within the external ear canal protect the ear from insects and foreign particles. Eyelashes protect the eyes.

- **Heat retention.** Hair on the head prevents the loss of conducted heat from the scalp to the surrounding air. Individuals who have lost their scalp hair release much more heat through the scalp than those who have a full head of hair.

- **Sensory reception.** Hair follicles have associated tactile receptors (root hair plexuses) that detect light touch (see section 16.2a).

- **Visual identification.** Hair characteristics are important in determining age and sex, and in identifying individuals.

Hair Color

Hair color is determined by the melamin synthesized in the matrix adjacent to the hair papillae. Variations in hair color reflect genetically determined differences in the structure of the melanin. Additionally, environmental and hormonal factors may influence the color of the hair. As people age, the production of pigment decreases, and thus hair becomes lighter in color. Gray hair results from the gradual reduction of melanin production within the hair follicle; white hair occurs due to a complete stoppage of melanin production.

Hair Growth and Replacement

There are three stages of the hair growth cycle: anagen, catagen, and telogen:

1. The anagen phase is the active phase of growth where living cells of the hair bulb are rapidly growing, dividing, and transforming into hair. It is the longest part of the growth cycle and lasts from about 18 months to as much as 7 years, depending on both the specific body location of the hair (e.g., scalp, eyebrows) and the genetics of the person. During the anagen phase, each hair strand grows about one-third of a millimeter per day, which equals 0.5 to 1.0 cm per month. On a normal scalp, 80–95% of follicles are in anagen phase.

2. The catagen phase is a brief regression period where cell division ceases and the follicle undergoes involution. This very short phase lasts for about 3 to 4 weeks.

3. The telogen phase is the resting phase and is usually the phase when the hair is shed (these hairs are the ones we find in our comb or brush). After 3 to 4 months in the telogen phase, the cells of the hair bulb start regrowing, and the follicle reenters the anagen phase.

The hair growth rate and the duration of the hair growth cycle vary; however, the scalp normally loses between 10 and 100 hairs per day. Continuous losses that exceed 100 hairs per day often indicate a health problem. Sometimes hair loss may be temporary as a result of one or more of the following factors: exposure to drugs, dietary factors, radiation, high fever, or stress. Alopecia (al-ō-pē’shē-ā; alopéckia = a disease like fox mange) areata, also known as spot baldness for the circular bald patches that develop on the scalp or the body, can occur in both sexes. Alopecia areata is an autoimmune disorder where the body mistakes selected hair follicles as foreign and attacks them. In diffuse hair loss, a condition that is both dramatic and distressing, hair is shed from all parts of the scalp. Women primarily suffer from this condition, which may be due to hormones, drugs, or iron deficiency.

In males, the condition called male pattern baldness causes loss of hair first from only the crown region of the scalp rather than uniformly. It is caused by a combination of genetic and hormonal influences. The relevant gene for male pattern baldness has two alleles, one for uniform hair growth and one for baldness. The baldness allele is dominant in males and is expressed only in the presence of a high level of testosterone, which causes the terminal hair of the scalp to be replaced by thinner vellus, beginning on the top of the head and later at the sides. In females, the baldness allele is recessive.
Excessive male pattern hairiness in areas of the body that normally do not have terminal hair is called hirsutism (herˈsə-tizm; hirsutus = shaggy). This hair growth typically occurs on the face, chest, and back and may affect both sexes. Hirsutism most commonly is caused by an excess of male sex hormones called androgens, either through a medical condition (such as polycystic ovarian syndrome) or by certain medications that cause a rise in androgens, such as illegal anabolic steroid use (see Clinical View 10.8: “Anabolic Steroids as Performance-Enhancing Compounds”).

**WHAT DID YOU LEARN?**
12. What are the three zones of a hair?
13. How does hair function in protection and heat retention?

### 6.2c Exocrine Glands of the Skin

#### LEARNING OBJECTIVES
18. Differentiate between the two types of sweat glands.
19. Describe the function of sebaceous glands.
20. Name two other modified integumentary glands.

The skin houses many types of exocrine glands. The two most common types of exocrine glands are sweat (sudoriferous) glands and sebaceous glands; these are shown in figure 6.11.

**Sweat Glands**

The two different groups of sweat glands in the skin are merocrine (eccrine) sweat glands and apocrine sweat glands (see section 5.1d). Both have a coiled, tubular secretory portion that is located in the reticular layer of the dermis and a sweat gland duct that transports the secretion to the surface of the epidermis (in a merocrine sweat gland) or into a hair follicle (in an apocrine sweat gland). The opening of the sweat gland duct on the epidermal surface is an indented region called a sweat pore.

Both types of sweat glands contain myoepithelial cells (specialized epithelial cells with contractile proteins like muscle). These specialized epithelial cells are sandwiched between the secretory gland cells and the underlying basement membrane. In response to nervous system stimulation, myoepithelial cells contract to squeeze the gland, causing it to discharge its accumulated secretions.

**WHAT DO YOU THINK?**

3. The autonomic nervous system is a part of the nervous system that can be activated when we are frightened or nervous. What would you expect to happen to sweat gland production and secretion when we are frightened or nervous?

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**Figure 6.11 Exocrine Glands of the Skin.** (a) The integument contains sweat glands and sebaceous glands. (b) Merocrine sweat glands have a duct with a narrow lumen that opens onto the skin surface through a pore. (c) Apocrine sweat glands exhibit a duct with a larger lumen to convey secretion products into a hair follicle. (d) The cells of sebaceous glands are destroyed during the release of their oily secretion into the hair follicle.
Merocrine Sweat Glands  Merocrine (eccrine) sweat glands (figure 6.11b) are the most numerous and widely distributed sweat glands. The adult integument contains between 3 and 4 million merocrine sweat glands. They are simple, coiled, tubular glands that discharge their secretions directly onto the surface of the skin. The clear secretion they release by exocytosis (see section 5.1d) is called sweat; it consists of approximately 99% water and 1% other chemicals that include electrolytes (primarily sodium and chloride), metabolites (e.g., lactate), and waste products (urea and ammonia).

The major function of merocrine sweat glands is thermoregulation, which is the regulation of body temperature by evaporation of fluid from the skin (see sections 1.5b, 25.2a). Merocrine sweat gland secretions provide a means for the loss of both water and electrolytes. The secretions also may help eliminate a number of ingested drugs. Finally, merocrine sweat gland secretions provide some protection from environmental hazards both by diluting harmful chemicals and by preventing the growth of microorganisms (antibacterial and antifungal activity; see section 22.3a).

Apocrine Sweat Glands  Apocrine sweat glands (figure 6.11c) are coiled, tubular glands that release their secretion into hair follicles in the axillae, around the nipples, in the pubic region, and in the anal region. Originally, these glands were called apocrine because their cells were thought to secrete their product by an apocrine mechanism (meaning that the apical portion of the cell’s cytoplasm pinches off and, along with cellular components of the apical region, becomes the secretory product—see section 5.1d). Now, researchers have shown that both apocrine and merocrine sweat glands produce their secretion by exocytosis. However, the secretory portion of an apocrine gland has a much larger lumen than that of a merocrine gland, and the secretions they produce are different, so these glands continue to be called apocrine glands. The secretion they produce is viscous and cloudy, and it contains both proteins and lipids that are acted upon by bacteria to produce a distinct, noticeable odor. (Underarm deodorant is designed to mask the odor, whereas a deodorant with antiperspirant also helps prevent the formation of sweat.) These sweat glands become active and produce secretions beginning around puberty.

Sebaceous Glands

Sebaceous glands are holocrine glands (see section 5.1d) that produce an oily, waxy secretion called sebum (se´bəm; sebum = tallow) that is usually discharged into a hair follicle and onto the hair itself. Sebum acts as a lubricant to keep the skin and hair from becoming dry, brittle, and cracked. Sebum also has some bactericidal (bacteria-killing) properties. Several sebaceous glands may open onto a single follicle.

The secretion of sebum in both sexes is stimulated by hormones, especially androgens (male sex hormones). Sebaceous glands are relatively inactive during childhood; however, they are activated during puberty in both sexes, when the production of sex hormones increases (see section 28.1b).

Other Integumentary Glands

Some specialized glands of the integument are restricted to specific locations. Two important examples are the ceruminous glands and the mammary glands.

INTEGRATE

CLINICAL VIEW 6.4

Acne and Acne Treatments

Acne (ak’né) is the term used to describe plugged sebaceous ducts. Acne typically becomes pronounced beginning at puberty, because increases in hormone levels stimulate sebaceous gland secretion, making the pores more prone to blockage. Acne is prevalent during the teenage years, although any age group may experience acne.

The types of acne lesions include

- **Comedo** (kom’è-dō). A sebaceous gland plugged with sebum. An open comedo is called a blackhead, because the plugged material has a dark, blackish appearance. A closed comedo is called a whitehead, because the top surface is whitish in color.
- **Papule** (pap’úl) and pustule (pús’túl). Both are dome-shaped lesions. Papules typically are fluid-filled, form red elevations on the skin, and do not contain pus. Pustules may become pustules, which are filled with a mixture of white blood cells, dead skin cells, and bacteria (called pus).

- **Nodule** (nod’úl). Similar to a pustule, but extending into the deeper skin layers and usually rupturing the hair follicle wall. Nodules can be prone to scarring.
- **Cyst**. A large, fluid-filled nodule that can become severely inflamed and painful and can lead to scarring of the skin.

Many medicinal treatments are available for acne, depending upon the type and severity. The effectiveness of the following medications varies from individual to individual. These treatments include benzoyl peroxide, salicylic (sal-i-sil’ik) acid, topical and oral antibiotics, topical vitamin A–like compounds (e.g., retinoids such as tretinoin [Retin-A]), and systemic retinoids such as isotretinoin (e.g., Accutane).

Other treatments include light chemical skin peels and comedo extraction by a dermatologist. Untreated acne, if severe, can lead to scarring, as can picking at the acne lesions.
Ceruminous (sĕ-rŭ′mi-nūs) glands are modified apocrine sweat glands located only in the external acoustic meatus (ear canal), where their secretion forms a waterproof earwax called cerumen (sĕ-rŭ′men). Both cerumen and the tiny hairs in the meatus help trap foreign particles or small insects and keeps them from reaching the eardrum. Cerumen also helps lubricate the external acoustic meatus and eardrum (see section 16.5a).

The mammary glands of the breasts are modified apocrine sweat glands. Both males and females have mammary glands, but these glands become functional only in pregnant and lactating females, when they produce milk, a secretion that nourishes offspring. The development of the glands and its secretions are controlled by a complex interaction between gonadal and pituitary hormones, discussed in section 28.3f.

**WHAT DID YOU LEARN?**

14. How do apocrine sweat glands differ from merocrine sweat glands in terms of their location, secretions, and function?

15. What do sebaceous glands secrete, and where is this material secreted?

### 6.3 Repair and Regeneration of the Integumentary System

**LEARNING OBJECTIVES**

- 21. Distinguish between regeneration and fibrosis.
- 22. Describe the process of wound healing.

The components of the integumentary system exhibit a tremendous ability to respond to stressors, trauma, and damage. Repetitive mechanical stresses applied to the integument stimulate cell division in the stem cells of the stratum basale, resulting in a thickening of the epidermis and an improved ability to withstand stress. For example, walking about without shoes causes the soles of the feet to thicken, thus providing more protection for the underlying tissues.

Damaged tissues are normally repaired in one of two ways. The replacement of damaged or dead cells with the same cell type is called regeneration. This restores organ function. When regeneration is not possible because part of the organ is too severely damaged or its cells lack the capacity to divide, the body fills in the gap with scar (fibrous) tissue. This process of scar tissue deposition in connective tissue during healing is referred to as fibrosis, and it binds the damaged parts together. The replacement scar tissue is produced by fibroblasts and is composed primarily of collagen fibers. Some structural restoration occurs; however, functional activities are not restored.

Both regeneration and fibrosis may occur in the healing of damage to the skin. Figure 6.12 illustrates stages in wound healing of the skin:

1. Cut blood vessels initiate bleeding into the wound. The blood brings clotting proteins, numerous leukocytes (white blood cells; see section 18.3c), and antibodies (see section 22.8).

2. A blood clot forms, temporarily patching the edges of the wound together and acting as a barrier to prevent the entry of pathogens into the body. Internal to the clot, macrophages and neutrophils (two types of leukocytes; see section 18.3c) clean the wound of cellular debris. (For more information about blood clotting, see section 18.4.)

3. The cut blood vessels regenerate and grow in the wound. A soft mass deep in the wound becomes granulation (gran′ū-lā-shən) tissue, which is a vascular connective tissue that initially forms in a healing wound. Macrophages within the wound begin to remove the clotted blood. Fibroblasts produce new collagen fibers in the region.

4. Epithelial regeneration of the epidermis occurs due to division of epithelial cells at the edge of the wound. These new epithelial cells migrate over the wound, moving internally to the now superficial remains of the clot (the scab). The connective tissue is replaced by fibrosis.

The skin repair and regeneration process is dependent on the extent of the injury. The wider and deeper the surface affected, the longer it takes for skin to be repaired. Additionally, the area under repair usually is more susceptible to complications due to fluid loss and infection. As the severity of the damage increases, the repair and regeneration ability of the integument is strained and its return to its original condition becomes much less likely. Some integumentary
system components that are not repaired following severe damage to the integument include hair follicles, exocrine glands, nerves, and the arrector pili muscle cells.

**WHAT DID YOU LEARN?**

16 What is granulation tissue, and when does it appear during wound healing of the skin?

### 6.4 Development and Aging of the Integumentary System

The integumentary system structures are derived from both ectoderm and mesoderm germ layers (see section 5.6a). The ectoderm is the origin of the epidermis, whereas the mesoderm is the origin of the dermis.
**CLINICAL VIEW 6.6**

Burns

Burns are a major cause of accidental death and are usually caused by heat, radiation, harmful chemicals, sunlight, or electrical shock. The immediate threat to life results primarily from fluid loss, infection, and the effects of burned, dead tissue.

Burns are classified by depth of tissue involvement. First- and second-degree burns are called partial-thickness burns; third-degree burns are called full-thickness burns.

**How are first-, second-, and third-degree burns distinguished?**

**First-degree burns**, often referred to as superficial burns, involve only the epidermis and are characterized by redness, pain, and slight edema. An example is a mild sunburn. Treatment involves immersing the burned area in cool water or applying cool, wet compresses, possibly followed by covering the burn with sterile, nonadhesive bandages. The healing time averages about 3 to 5 days, and typically there is no scarring.

**Second-degree burns** involve the epidermis and part of the dermis. The skin also is blistered and painful. Examples include very severe sunburns (where the skin also blisters) or scalding from hot liquids or chemicals. The treatment is similar to that for first-degree burns, and care must be taken not to break the blisters, which would increase risk of infection. Applying ointments to the blisters is not recommended, because the ointments can retain heat in the burned area. In addition, burned limbs should be elevated to prevent swelling. Healing times are approximately 2 to 4 weeks, and slight scarring may occur.

**Third-degree burns** involve the epidermis, dermis, and subcutaneous layer, which often are destroyed. Third-degree burns typically are caused by contact with corrosive chemicals or fire, or prolonged contact with extremely hot water. Dehydration is a major concern with a third-degree burn, because the entire portion of skin has been lost, and water cannot be retained in the area. Most third-degree burns require hospitalization. Skin grafting typically is needed for patients with third-degree burns, because the entire dermis and its vasculature are destroyed and regeneration is limited (see Clinical View 5.6: “Tissue Transplant” for more information about skin grafts).

**How is the overall severity of a burn injury determined?**

The severity of a burn injury is measured not only by the degree of the burn but also by the age of the patient, the general size of the burn, and the location of the burn. For example, a burn on the face may require more extensive treatment than a similar burn on an extremity. The rule of nines is used to estimate surface area of a burn. Simply put, most (but not all) major body areas approximately account for some factor of 9% of the total body surface area. In adults, the anterior and posterior parts of the head and neck count 9% of the total body surface area, each upper limb counts 9%, each lower limb and gluteal region counts 18%, the anterior trunk counts 18%, the posterior trunk counts 18%, and the perineum is 1%. Estimating surface area of a burn is critical for determining appropriate fluid replacement. The greater the surface area of the burn, the greater the volume of fluids that are lost, and these fluids must be replaced, either orally or intravenously.

Burns are considered very severe or critical if one of the following criteria is met:

1. Over 25% of the body has second-degree burns.
2. Over 10% of the body has third-degree burns.
3. Third-degree burns are present on the hands, feet, face, or perineum.

**What treatments are used for burn injuries?**

In general, acute treatment involves managing fluid loss, relieving swelling, managing pain, removing dead tissue and foreign material from the wound (debridement), controlling infection, and increasing caloric intake.

Swelling also may occur as the blood capillaries become more permeable (“leaky”), and fluid may collect in localized tissues, which exacerbates the overall fluid loss in the circulation. In severe cases, a procedure called an escharotomy (es-kā-rotˈō-mē) is performed, where an incision is made in the dermis to lessen the constriction caused by the swelling.

Pain medications may be given to alleviate any discomfort from the burn and resulting swelling. Antibiotics and other medications may be given to help limit and prevent infection.

Finally, individuals with severe burns become hypermetabolic as the body attempts to heal, so their demand for nutrition greatly increases. The burn patient must be given additional caloric intake, sometimes as much as two to three times their normal caloric intake, to meet the demands. Typically, this supplementary nutrition is given through feeding tubes, IVs, or both.
Chapter Six

Integumentary System

6.4a Development of the Integument and Its Derivatives

LEARNING OBJECTIVES

23. Describe how integument develops from two germ layers.

24. Explain the developmental origins of nails, hair, and glands.

By the end of week 7 of development, the ectoderm forms a layer of squamous epithelium that flattens and then becomes both a covering layer, called the periderm, and an underlying basal layer. The basal layer will form the stratum basale and all other epidermal layers. By week 21, the stratum corneum and friction ridges form. During the fetal period (weeks 9-38), the periderm is eventually sloughed off. The sloughed-off cells mix with sebum secreted by the sebaceous glands, producing a waterproof protective coating called the vernix caseosa that coats the skin of the fetus.

The dermis is derived from mesoderm. During weeks 3-8, this mesoderm becomes mesenchyme. The mesenchymal cells begin to form the components of the dermis at about 11 weeks.

Fingernails and toenails start to form in the tenth week of development. The fingernails reach the tips of the fingers by 32 weeks, whereas the toenails become fully formed by about 36 weeks.

Hair follicles begin to appear between 9 and 12 weeks of development as pockets of cells, called hair buds, invade the dermis from the overlying stratum basale of the epidermis. These hairs do not become easily recognizable in the fetus until about 20 weeks. Finally, sweat and sebaceous glands develop from the stratum basale of the epidermis and first appear at about 20 weeks on the palms and soles and later in other regions.

WHAT DID YOU LEARN?

17. What two primary germ layers form the integument?

6.4b Aging of the Integument

LEARNING OBJECTIVES

25. Explain changes to the skin with age.

26. List factors that contribute to skin aging.

Although some adolescents develop acne when they enter puberty, most skin changes do not become obvious until an individual reaches middle age. Then, the skin repair processes take longer to complete because of a reduced number and activity of stem cells. Skin repair and regeneration activities that took 3 weeks in a healthy young person often take twice that time for a person in the seventh decade of life. Additionally, the reduced stem cell activity in the epidermis results in a thinner skin that is less likely to protect against abrasive, mechanical trauma.

CLINICAL VIEW 6.7

Botox and Wrinkles

Many individuals have explored ways to diminish the appearance of age-related wrinkles. One popular treatment for wrinkles caused by repeated facial muscle expression is botulinum toxin type A (Botox). This medicine is derived from the toxin produced by the bacterium Clostridium botulinum. Although large doses of this toxin may be deadly, small therapeutic doses temporarily block nerve impulses to the facial expression muscles, thereby decreasing or eliminating the wrinkles they produce.

The procedure is done in a doctor’s office, where the doctor injects Botox in the specific facial muscles responsible for the wrinkles, such as frown lines and crow’s feet. The effect is temporary, and an individual must repeat the procedure after about 4 months, as the muscles regain their function.

Botox is relatively safe, but some individuals may experience adverse effects, and overuse of Botox can produce a face that appears frozen and devoid of facial expression.

INTEGRATE

Botox is relatively safe, but some individuals may experience adverse effects, and overuse of Botox can produce a face that appears frozen and devoid of facial expression.

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Collagen fibers in the dermis decrease in number and organization, and elastic fibers lose elasticity. Years of particular facial expressions (squinting, smiling) produce crease lines in the integument. As a result, the skin forms wrinkles and becomes less resilient. In addition, the skin’s immune responsiveness is diminished by a decrease in the number and efficiency of epidermal dendritic cells. Also, hair follicles either produce thinner hairs or stop production entirely.

Chronic overexposure to UV rays can damage the DNA in epidermal cells and accelerate aging, and it is the predominant factor in the development of nearly all skin cancers. Skin cancer is the most common type of cancer. It occurs most frequently on the head and neck regions, followed by other regions commonly exposed to the sun. Fair-skinned individuals, especially those who had severe sunburns as children, are most at risk for skin cancer.

Skin cancer can arise in anyone at any age. Individuals should use sunscreen regularly and avoid prolonged exposure to the sun. An individual should regularly and thoroughly inspect his or her skin for any changes, such as an increase in the number or size of moles or the appearance of new skin lesions. In addition, a person should be examined routinely by a dermatologist. Table 6.2 compares and describes the three main types of skin cancer.

**Table 6.2 Skin Cancer**

<table>
<thead>
<tr>
<th>Skin Cancer</th>
<th>Characteristics</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>BASAL CELL CARCINOMA</strong></td>
<td>- Most common type of skin cancer</td>
</tr>
<tr>
<td></td>
<td>- Least dangerous type, as it seldom metastasizes (i.e., spreads to other locations within the body)</td>
</tr>
<tr>
<td></td>
<td>- Originates in stratum basale</td>
</tr>
<tr>
<td></td>
<td>- First appears as small, shiny elevation that enlarges and develops central depression with pearly edge</td>
</tr>
<tr>
<td></td>
<td>- Usually occurs on face</td>
</tr>
<tr>
<td></td>
<td>- Treated by surgical removal of lesion</td>
</tr>
<tr>
<td><strong>SQUAMOUS CELL CARCINOMA</strong></td>
<td>- Arises from keratinocytes of stratum spinosum</td>
</tr>
<tr>
<td></td>
<td>- Lesions usually appear on scalp, ears, lower lip, or dorsum of hand.</td>
</tr>
<tr>
<td></td>
<td>- Early lesions are raised, reddened, scaly; later lesions form concave ulcers with elevated edges.</td>
</tr>
<tr>
<td></td>
<td>- Treated by early detection and surgical removal of lesion</td>
</tr>
<tr>
<td></td>
<td>- May metastasize to other parts of the body</td>
</tr>
<tr>
<td><strong>MALIGNANT MELANOMA</strong></td>
<td>- Most deadly type of skin cancer due to aggressive growth and metastasis</td>
</tr>
<tr>
<td></td>
<td>- Arises from melanocytes, usually in a preexisting mole</td>
</tr>
<tr>
<td></td>
<td>- Individuals at increased risk include those who have had severe sunburns, especially as children.</td>
</tr>
<tr>
<td></td>
<td>- Characterized by change in mole diameter, color, shape of border, and symmetry</td>
</tr>
<tr>
<td></td>
<td>- Survival rate improved by early detection and surgical removal of lesion</td>
</tr>
<tr>
<td></td>
<td>- Advanced cases (metastasis of disease) are difficult to cure and are treated with chemotherapy, interferon therapy, and radiation therapy.</td>
</tr>
</tbody>
</table>

The usual signs of melanoma may be easily remembered using the **ABCDE rule**. Report any of the following changes in a birthmark or mole to your physician:

- **A** = Asymmetry: One-half of a mole or birthmark does not match the other.
- **B** = Border: Edges are notched, irregular, blurred, or ragged.
- **C** = Color: Color is not uniform; differing shades (usually brown or black and sometimes patches of white, blue, or red) may be seen.
- **D** = Diameter: Affected area is larger than 6 mm (about 1/4 inch) or is growing larger.
- **E** = Evolving: Change in the size, shape, or color of a mole or a change in symptoms, such as how a mole feels (how itchy or tender it feels) or what happens on the surface of a mole (especially bleeding).
**CHAPTER SUMMARY**

- The integumentary system includes both the skin (integument) and its derivatives (nails, hair, sweat glands, and sebaceous glands).

### 6.1 Composition and Functions of the Integument

- The integument has a superficial epidermis (composed of keratinized stratified squamous epithelium) and a deeper dermis (that is composed of both areolar and dense irregular connective tissue).
- Deep to the integument is the subcutaneous layer, which helps adhere the integument to underlying structures.

#### 6.1a Epidermis

- Cell types in the epidermis include keratinocytes (the most abundant cell type), melanocytes (produce melanin), epidermal dendritic cells (initiate an immune response), and tactile cells (sensitive to touch).
- The epidermis is organized into specific layers called strata. From deepest to most superficial, they are the stratum basale (deepest layer, with actively dividing keratinocytes), stratum spinosum, stratum granulosum, stratum lucidum, and stratum corneum (many layers of dead keratinocytes).
- Keratinization is the process by which keratinocytes fill up with the protein keratin, and as a result the cell dies. Keratinization begins in the stratum granulosum.
- Thick skin (palms of hands, soles of feet) has five epidermal strata, whereas thin skin (on the rest of the body) has four.
- Skin color is a result of hemoglobin in the blood vessels of the dermis, melanin pigment, and carotene pigment.

#### 6.1b Dermis

- The dermis has a superficial papillary layer and a deep reticular layer.
- The papillary layer is primarily composed of areolar connective tissue. Its dermal papillae interlock with the epidermal ridges of the epidermis.
- The reticular layer is composed of dense irregular connective tissue, and it contains hair follicles, the secretory portions of glands, and blood vessels and nerves.

#### 6.1c Subcutaneous Layer

- The subcutaneous layer protects body parts, acts as an energy reservoir, and provides thermal insulation.

#### 6.1d Functions of the Integument

- The integument has numerous functions, including protection, prevention of water loss and water gain, metabolic regulation, secretion and absorption, immune function, temperature regulation, and sensory reception.

### 6.2 Integumentary Structures Derived from Epidermis

- Nails, hair, and the exocrine glands of the skin are all derived from the epidermis and are known as epidermal derivatives.

#### 6.2a Nails

- Nails are formed from the stratum corneum layer of the epidermis; they protect the digits and aid in grasping objects.

#### 6.2b Hair

- Hair consists of a bulb (a swelling where the hair originates in the dermis), a root (the portion of the hair deep to the skin surface), and the shaft (the portion of the hair that extends beyond the skin surface).
- Arrector pili muscles can contract to elevate the hair.
- Among the functions of hair are protection, heat retention, sensory reception, and visual identification.

#### 6.2c Exocrine Glands of the Skin

- Merocrine sweat glands produce a watery secretion called sweat.
- Apocrine sweat glands produce a viscous secretion that, when acted upon by bacteria, produces a noticeable odor.
- Sebaceous glands discharge sebum onto hair follicles by holocrine secretion.
- Ceruminous glands are modified apocrine sweat glands which produce cerumen (earwax) to lubricate the external acoustic meatus and eardrum.
- Mammary glands are modified apocrine sweat glands that produce breast milk.

### 6.3 Repair and Regeneration of the Integumentary System

- Regeneration is the replacement of damaged or dead cells. Fibrosis is the replacement of damaged tissues with scar tissue.
- The wider and deeper the surface affected, the longer it takes for the skin to be repaired, and generally the more extensive the scarring that results.

### 6.4 Development and Aging of the Integumentary System

- The epidermis and epidermal derivatives are derived from ectoderm, and the dermis is derived from mesoderm.

#### 6.4a Development of the Integument and Its Derivatives

- The integument begins to form during weeks 3-9.
- Nails start to form in the tenth week of development, hair follicles first appear between 9 and 12 weeks of development, and exocrine glands first appear during week 20.

#### 6.4b Aging of the Integument

- As an individual ages, the skin repair processes take longer, wrinkles appear, the epidermis becomes thinner (due to reduced stem cell activity), and skin cancers become more likely.
1. Which statement about sebaceous glands is false?
   a. They release their secretion onto a hair follicle.
   b. They release their product by apocrine secretion.
   c. They are located in the dermis.
   d. The product they secrete acts as a lubricant and waterproofer.

2. The layer of the epidermis in which cells begin the process of keratinization is the
   a. stratum corneum.
   b. stratum basale.
   c. stratum lucidum.
   d. stratum granulosum.

3. The sweat glands that communicate with skin surfaces throughout the body, producing a secretion that is primarily water, are
   a. apocrine glands.
   b. merocrine glands.
   c. sebaceous glands.
   d. ceruminous glands.

4. Which of the following is not a function of the integument?
   a. acts as a physical barrier
   b. stores calcium in the dermis
   c. regulates temperature through vasoconstriction and vasodilation of dermal blood vessels
   d. participates in immune defense

5. What layer is correctly matched with the tissue that forms it?
   a. papillary layer of dermis; areolar connective tissue
   b. subcutaneous layer; dense irregular connective tissue
   c. reticular layer of dermis; stratified squamous epithelium
   d. epidermis; dense irregular connective tissue.

6. Which statement is accurate about melanin or melanocytes?
   a. Melanin is produced by cells that are located in the stratum spinosum.
   b. Melanin is a pigment that accumulates inside keratinocytes.
   c. Darker-skinned individuals have more melanocytes than lighter-skinned individuals.
   d. Albinism is caused by a lack of melanocytes in the body.

7. A _____ degree burn typically involves the epidermis and part of the dermis. The subcutaneous layer is not affected.
   a. first-
   b. second-
   c. third-
   d. fourth-

8. The cells in a hair follicle that are responsible for forming hair are the
   a. hair papilla cells.
   b. matrix cells.
   c. medullary cells.
   d. cortex cells.

9. Which epidermal cell type is responsible for detecting touch sensations?
   a. keratinocyte
   b. melanocyte
   c. tactile cell
   d. epidermal dendritic cell

10. At what stage of wound healing does granulation tissue first form?
    a. after scar tissue forms along the wound
    b. before the blood completely clots
    c. before leukocytes enter the site and clean the wound
    d. after a blood clot forms and prior to scar tissue forming

11. Describe the composition of the layers of the epidermis.

12. List the four main cell types in the epidermis, their function, and the layer(s) of the integument in which they reside.

13. Describe the tissue type and structure of the two specific layers of the dermis.

14. Describe how the skin is involved in vitamin D production.

15. Compare the structure and composition of the following nail parts: nail body, nail bed, eponychium, and lunula.

16. What are the three types of hair?

17. Where are ceruminous glands located, and what do they secrete?

18. Discuss the steps involved in wound repair of the integument.

19. What embryonic tissues form the integument?

20. What are some effects of aging on the integument?

Can You Apply What You’ve Learned?

1. Alexander is a 15-year-old boy with extensive acne on his nose, forehead, and cheeks. He reached puberty at age 14, at which point his acne became more abundant in these areas. What is the anatomic basis for his acne?
   a. His merocrine sweat glands have begun producing abundant amounts of sweat.
   b. His sebaceous gland ducts have become blocked.
   c. His sebaceous glands are not producing enough sebum to lubricate his skin.
   d. His apocrine sweat glands are producing a secretion that has a marked odor.
2. During anatomy lab, Susan scratched her arm and noticed that some skin cells had sloughed off. She prepared a slide of these cells and examined them under a microscope. What characteristics do you expect the cells to have?
   a. polygonal cells with prominent nuclei
   b. cuboidal cells, some undergoing mitosis
   c. flattened anucleate cells
   d. oval cells surrounded by abundant collagen

3. While running to class, Jennifer slipped and skinned her knee. The wound appeared superficial, yet there was extensive bleeding. Based on this information, and her knowledge of integument composition, she determined that the wound penetrated
   a. the stratum corneum layer of the epidermis only.
   b. all layers of the epidermis but not the dermis.
   c. all layers of the epidermis and part of the dermis.
   d. all layers of the epidermis and dermis, as well as the subcutaneous layer.

Can You Synthesize What You’ve Learned?

1. When you are outside on a cold day, your skin is much paler than normal. Later, when you enter a warm room, your face becomes flushed. What are the reasons for the change in color of your face?

2. Teri was involved in a chemical accident where she suffered third-degree burns on 30% of her body. What potential complications could Teri develop as a result of these burns? As Teri’s physician, how would you help minimize these complications?

3. At the age of 50, John noticed that one of the moles on his face looked different than normal. The mole appeared larger than normal, darkened, and asymmetrical. John’s dermatologists suspected skin cancer. Based on this description, what type of skin cancer is most likely, and should John be concerned?
Skeletal System: Bone Structure and Function

Mention of the skeletal system conjures up images of dry, supposedly lifeless bones in various sizes and shapes. But the skeleton (skelˈē-ton; skeletos = dried) is much more than a supporting framework for the soft tissues of the body. The skeletal system is composed of dynamic, living tissues; it interacts with all of the other organ systems and continually rebuilds and remolds itself.

We begin this chapter with a brief description of the skeletal system and a detailed discussion of bone anatomy, the primary organ of this system. Then we examine several important concepts of bone physiology, including cartilage growth, bone formation, bone growth and bone remodeling, the regulation of blood calcium, and the effects of aging on the skeletal system. Our chapter concludes with a discussion of bone fracture and repair.
7.1 Introduction to the Skeletal System

**LEARNING OBJECTIVES**

1. List the structures of the skeletal system.
2. Compare and contrast compact and spongy bone.
3. Identify the types and locations of cartilage within the skeletal system.

Our skeletal system includes the bones of the skeleton as well as cartilage, ligaments, and other connective tissues that stabilize or connect the bones.

**Bones** of the skeleton are the primary organs of the skeletal system. They form the rigid framework of the body and perform other functions, described shortly. Two types of bone connective tissue are present in most of the bones of the body: compact bone and spongy bone (see section 5.2d). **Compact bone** (also called dense or cortical bone) is a relatively rigid connective bone tissue that appears white, smooth, and solid. It makes up approximately 80% of the total bone mass. **Spongy bone** (also called cancellous or trabecular bone) is located internal to compact bone, appears porous, and makes up approximately 20% of the total bone mass.

**Cartilage** is a semirigid connective tissue that is more flexible than bone. Mature cartilage is avascular (lacks a blood supply). Recall from section 5.2d that there are three subtypes of cartilage; the two subtypes associated with the skeletal system are described next (figure 7.1).

- **Hyaline cartilage** attaches ribs to the sternum (costal cartilage), covers the ends of some bones (articular cartilage), and is the cartilage within growth plates (epiphyseal plates). Hyaline cartilage also provides a model during development for the formation of the fetal skeleton.
- **Fibrocartilage** is a weight-bearing cartilage that withstands compression. It forms the intervertebral discs, the pubic symphysis (cartilage between bones of the pelvis), and the cartilage pads of the knee joints (menisci).

The roles of **ligaments** (dense regular connective tissue that anchors bone to bone), **tendons** (dense regular connective tissue that connects muscle to bone), and other connective tissue structures associated with the skeletal system are described in section 9.4a.

**WHAT DID YOU LEARN?**

1. Compare the appearance of compact bone and spongy bone.
2. In what three locations of the body do you find fibrocartilage?

7.2 Bone: The Major Organ of the Skeletal System

Our bones—such as the bone of the thigh (femur) or bone of the upper arm (humerus)—are organs. Note that living bone is not white (like the bones you may be seeing in your lab). Rather, living bone may be yellowish in color. (In contrast, the dead bones you see in lab likely were bleached to acquire that whitish appearance. Here we describe the general functions, classification based upon shape, gross anatomy, and histology of bone.

7.2a General Functions

**LEARNING OBJECTIVE**

4. Describe the general functions of bone.

Bones perform several basic functions: support and protection, levers for movement, hemopoiesis, and storage of mineral and energy reserves.

**Support and Protection**

Bones provide structural support and serve as a framework for the entire body. Bones also protect many delicate tissues and organs from injury and trauma. The rib cage shields the heart and lungs; the cranial bones enclose and protect the brain; the vertebrae enclose the spinal cord; and the pelvis cradles urinary and reproductive organs, as well as the terminal end of the gastrointestinal tract.

**INTEGRATE**

**CONCEPT CONNECTION**

Both the muscular system and the nervous system need calcium to function properly. Fortunately, the skeletal system typically houses a sufficient supply of calcium, which may be “tapped” when blood calcium levels are low.
### Levers for Movement

Bones serve as attachment sites for skeletal muscles, other soft tissues, and some organs. Muscles attached to the bones of the skeleton contract and exert a pull on the skeleton, which then functions as a system of levers. The bones of the skeleton can alter the direction and magnitude of the forces generated by the skeletal muscles. Potential movements range from powerful contractions needed for running and jumping to delicate and precise movements required to remove a splinter from the finger.

### Hemopoiesis

**Hemopoiesis** (he’mō-poy-ě’sis; haima = blood, poiesi = making) is the process of blood cell production. It occurs in red bone marrow connective tissue, which contains stem cells that form blood cells and platelets. (The process of hemopoiesis is described in greater detail in section 18.3a.)

### Storage of Mineral and Energy Reserves

Most of the body’s reserves of the minerals calcium and phosphate are stored within and then released from bone. Calcium is an essential mineral for such body functions as muscle contraction (see section 10.3), blood clotting (see section 18.4), and release of neurotransmitter from nerve cells (see section 12.8d). Phosphate is a structural component of ATP, other nucleotides, and phospholipids (see sections 2.7b and 2.7d) and is an important component of the plasma membrane (see section 4.2a).

When calcium or phosphate is needed by the body, some bone connective tissue is broken down, and the minerals are released into the blood. In addition, potential energy in the form of lipids is stored in yellow bone marrow in the shafts of some adult bones.

### WHAT DID YOU LEARN?

3. What two minerals are stored in bone, and what are their functions in the body?

### 7.2b Classification of Bones

#### Learning Objective

5. Describe the four major classes of bones as determined by shape.

Bones appear in various shapes and sizes, depending upon their function. The four classes of bone as determined by shape are long bones, short bones, flat bones, and irregular bones (figure 7.2).

**Long bones** are greater in length than width. These bones have an elongated, cylindrical shaft (diaphysis). This is the most common bone shape. Long bones are found in the upper limbs (namely, the arm, forearm, palm, and fingers) and lower limbs (thigh, leg, sole of the foot, and toes). Long bones vary in size. The small bones in the fingers and toes are long bones, as are the larger tibia and fibula of the lower limb.

**Short bones** have a length nearly equal to their width. Examples of short bones include the carpals (wrist bones) and tarsals (bones in the foot). Sesamoid bones, which are small, sesame seed–shaped bones along the tendons of some muscles, are also classified as short bones. The patella (kneecap) is the largest sesamoid bone.

**Flat bones** are so named because they have flat, thin surfaces that may be slightly curved. They provide extensive surface areas for muscle attachment and protect underlying soft tissues. Flat bones form the roof of the skull, the scapulae (shoulder blades), the sternum (breastbone), and the ribs.

**Irregular bones** have elaborate, sometimes complex shapes and do not fit into any of the preceding categories. The vertebrae; the osa coxae (hip bones); and several bones in the skull, such as the ethmoid, sphenoid, and sutural bones, are examples of irregular bones.

### WHAT DID YOU LEARN?

4. What are several examples of flat bones in the body?

### 7.2c Gross Anatomy of Bones

#### Learning Objectives

6. Describe the structural components of a long bone.
7. Compare the gross anatomy of other bones to that of a long bone.
8. Explain the general function of blood vessels and nerves that serve a bone.

Our discussion continues with details of the gross anatomy of a long bone. First we compare it to other classes of bones, then we discuss the vascularization and innervation of bone.
Gross Anatomy of a Long Bone

Long bones are the most common bone shape in the body and thus serve as a useful model of bone structure \((\text{figure 7.3a})\).

**Regions of a Long Bone**  One of the principal gross features of a long bone is its shaft, which is called the **diaphysis** \((\text{di}-\text{af}^{	ext{i}-}	ext{s}^{	ext{i}-}\text{s}^{	ext{i}}; \text{pl.}, \text{d}^{	ext{i}-}\text{af}^{	ext{i}-}	ext{s}^{	ext{i}-}	ext{es}; \text{growing between})\). The elongated, usually cylindrical diaphysis provides for the leverage and major weight support of a long bone. Extending internally from the compact bone along the length of the diaphysis are spicules (thin, needlelike structures) of spongy bone. The hollow, cylindrical space within the diaphysis is called the **medullary** (marrow) **cavity**. In children, this cavity contains red bone marrow, which later is replaced by yellow bone marrow in adults.

An expanded, knobby region called the **epiphysis** \((\text{e}-\text{pif}^{	ext{i}-}	ext{s}^{	ext{i}}; \text{pl.}, \text{e}^{	ext{i}-}\text{pif}^{	ext{i}-}	ext{s}^{	ext{i}-}	ext{es}; \text{epi} = \text{upon}, \text{physis} = \text{growth})\) is at each end of a long bone. A **proximal epiphysis** is the end of the bone closest to the body trunk, and a **distal epiphysis** is the end farthest from the trunk. An epiphysis is composed of an outer, thin layer of compact bone and an inner, more

![Figure 7.3 Gross Anatomy of a Long Bone](image-url)

*Figure 7.3 Gross Anatomy of a Long Bone.* Long bones support soft tissues in the limbs. \((a)\) A typical long bone, such as the humerus, contains both compact and spongy bone. \((b)\) The endosteum lines the medullary cavity. \((c)\) The periosteum lines the external surface of the bone shaft.
extensive region of spongy bone. Spongy bone within the epiphysis resists stress that is applied from many directions. Covering the joint surface of an epiphysis is a thin layer of hyaline cartilage called the **articular cartilage.** This cartilage helps reduce friction and absorb shock in movable joints.

The **metaphysis** (mě-ta-fi′sis) is the region in a mature bone sandwiched between the diaphysis and the epiphysis. This region contains the **epiphysial plate** (or **growth plate**) in a growing bone. It is a thin layer of hyaline cartilage that provides for the continued lengthwise growth of the bone. The remnant of the epiphysial plate in adults is a thin, defined area of compact bone called the **epiphyseal line.**

**Coverings and Linings of Bone** A tough sheath called **periosteum** (per-ē-os′tē-ūm; peri = around, osteon = bone) covers the outer surface of the bone except for the areas covered by articular cartilage (figure 7.3a, c). The periosteum consists of two layers. The outer, fibrous layer of dense irregular connective tissue protects the bone from surrounding structures, anchors blood vessels and nerves to the surface of the bone, and serves as an attachment site for ligaments and tendons. The inner, cellular layer includes osteoprogenitor cells, osteoblasts, and osteoclasts. The function of these cells is described in section 7.2e. The periosteum is anchored to the bone by numerous collagen fibers called **perforating fibers,** or Sharpey's fibers, which run perpendicular to the diaphysis.

The **endosteum** (en-dos′tē-ūm; endo = within) is an incomplete layer of cells that covers all internal surfaces of the bone within the medullary cavity (figure 7.3a, b). The endosteum, like the periosteum, contains osteoprogenitor cells, osteoblasts, and osteoclasts.

**Gross Anatomy of Other Bone Classes**

Short, flat, and irregular bones differ in their gross anatomic structure from long bones. The external surface generally is composed of compact bone, the interior is composed entirely of spongy bone, and there is no medullary cavity. **Figure 7.4** shows the compact and spongy bone arrangement in a skull bone. Observe the layer of spongy bone in between the roughly parallel segments of compact bone. In a flat bone of the skull, the spongy bone is also called **diploë** (dip′lō-ē; diplous = double).
Blood Supply and Innervation of Bone

Bone is highly vascularized (supplied by many blood vessels), especially in regions containing spongy bone (figure 7.3a). Blood vessels enter bones from the periosteum. Typically, only one nutrient artery enters and one nutrient vein exits the bone via a small opening or hole in the bone called a nutrient foramen. Blood vessels supply nutrients and oxygen required by cells and remove waste products from bone cells.

Nerves that supply bones accompany blood vessels through the nutrient foramen and innervate the bone as well as its periosteum, endosteuem, and marrow cavity. These are mainly sensory nerves (see section 12.1b) that signal injuries to the skeleton.

**WHAT DID YOU LEARN?**

1. How do the diaphysis and epiphysis of a bone differ in structure?
2. What is the function of a nutrient foramen in bone?

7.2d Bone Marrow

**LEARNING OBJECTIVE**

9. Compare and contrast the structure and location of the two types of bone marrow.

Bone marrow is the soft connective tissue of bone that includes both red bone marrow and yellow bone marrow (figure 7.5). Red bone marrow (also called myeloid tissue) is hematopoietic (i.e., blood cell–forming) and contains reticular connective tissue, developing blood cells (see figure 18.3), and adipocytes.

The locations of red bone marrow differ between children and adults. In children, red bone marrow is located in the spongy bone of most of the bones of the body as well as the medullary cavity of long bones. Much of the red bone marrow changes as children mature into adults. Primarily within the medullary cavities of long bones and inner core of most epiphyses there is a progressive decrease in developing blood cells and an increase in adipocytes. This fatty-appearing substance is called yellow bone marrow (figure 7.5b). As a result, adults have red bone marrow only in selected portions of the axial skeleton, such as the flat bones of the skull, the vertebrae, the ribs, the sternum, and the ossa coxae (hip bones). Adults also have red bone marrow in the proximal epiphyses of each humerus and femur.

Note that severe anemia—a condition in which erythrocyte (red blood cell) numbers are lower than normal, resulting in insufficient oxygen reaching the cells of the body—may trigger conversion of yellow bone marrow back to red bone marrow, a change that facilitates the production of additional erythrocytes. (See Clinical View 18.2: “Anemia.”)

**WHAT DID YOU LEARN?**

6. Where is red bone marrow found in the adult skeleton?

---

**INTEGRATE**

**CLINICAL VIEW 7.1 Bone Marrow Transplant**

Red bone marrow may be transplanted in an individual whose red bone marrow was destroyed by radiation or chemotherapy, or who has abnormally functioning red bone marrow (as is the case in an individual with leukemia, where the marrow produces abnormal blood cells)—see Clinical View 18.5: “Leukemia.” Donor red bone marrow is most commonly harvested from the hip bone or, less commonly, from the sternum. The harvested cells are injected into the blood of the recipient, where they will be transported to the normal locations for red bone marrow. Bone marrow must be “matched” between donor and recipient, just as blood types must be matched so the immune system will not attack the tissue as something foreign (see Clinical View 22.5: “Organ Transplants and MHC Molecules”). Thus, an individual can receive red bone marrow only from a donor that is a close match.
7.2e Microscopic Anatomy: Bone Connective Tissue

LEARNING OBJECTIVES

10. Name the four types of bone cells and their functions.
11. Describe the composition of bone's matrix.
12. Explain bone matrix formation and resorption.
13. Compare the structure of compact bone and spongy bone.

The primary component of bone is bone connective tissue, also called osseous (os′ˈe-ūs; os = bone) connective tissue. Bone is composed of both cells and extracellular matrix, like all connective tissue. We now describe the cells and matrix that compose bone connective tissue, how the matrix is formed and resorbed, and the two microscopic arrangements (compact bone and spongy bone).

Cells of Bone

Four types of cells are found in bone connective tissue: osteoprogenitor cells, osteoblasts, osteocytes, and osteoclasts (figure 7.6).

Osteoprogenitor (os′te-o-prō-jen′i-ter) cells are stem cells derived from mesenchyme (see section 5.2c). When they divide through the process of cellular division, another stem cell is produced along with a “committed cell” that matures to become an osteoblast. As mentioned in section 7.2c, these stem cells are located in both the periosteum and the endosteum.

Osteoblasts (blast = germ) are formed from osteoprogenitor stem cells. Often, osteoblasts are positioned side by side on bone surfaces. Active osteoblasts exhibit a somewhat cuboidal shape and have abundant rough endoplasmic reticulum and Golgi apparatus.

Figure 7.6 Types of Cells in Bone Connective Tissue. Four different types of cells are found in bone connective tissue.
(a) Osteoprogenitor cells develop into osteoblasts, many of which differentiate to become osteocytes. (b) Some bone marrow cells fuse to form osteoclasts. (c) A photomicrograph shows osteoblasts, osteocytes, and osteoclasts. ©Alvin Telser, Ph.D.
Reflecting the activity of these cells, osteoblasts perform the important function of synthesizing and secreting the initial semisolid organic form of bone matrix called osteoid (os′tē-oíd; eidos = resemblance). Osteoid later calcifies as a result of salt crystal deposition. As a consequence of this mineral deposition on osteoid, osteoblasts become entrapped within the matrix they produce and secrete, and thereafter they differentiate into osteocytes.

Osteocytes (kytos = a hollow [cell]) are mature bone cells derived from osteoblasts that have lost their bone-forming ability when enveloped by calcified osteoid. Connections between some of the original neighboring osteoblasts are maintained as they become osteocytes. Osteocytes maintain the bone matrix and detect mechanical stress on a bone. If stress is detected, osteoblasts are signaled, and it may result in the deposition of new bone matrix at the surface.

Osteoclasts (os′tē-ō-klast; klastos = broken) are large, multinuclear, phagocytic cells. They are derived from fused bone marrow cells similar to those that produce monocytes (described in section 18.3c). These cells exhibit a ruffled border where they contact the bone, which increases their surface area exposure to the bone. An osteoclast is often located within or adjacent to a depression or pit on the bone surface called a resorption lacuna (Howship’s lacuna). Osteoclasts are involved in breaking down bone in an important process called bone resorption (described shortly).

Composition of the Bone Matrix

The matrix of bone connective tissue has both organic and inorganic components. The organic component is osteoid, which is produced by osteoblasts. Osteoid is composed of both collagen and a semisolid ground substance of proteoglycans (including chondroitin sulfate) and glycoproteins that suspend and support the collagen fibers. These organic components give bone tensile strength by resisting stretching and twisting, and contribute to its overall flexibility.

The inorganic portion of the bone matrix is made up of salt crystals that are primarily calcium phosphate, \( \text{Ca}_3(\text{PO}_4)_2 \). Calcium phosphate and calcium hydroxide, \( \text{Ca}(_2\text{OH})_2 \), interact to form crystals of hydroxypatite (hi′-drok′sē-ap-a-tīt), which is \( \text{Ca}_10(\text{PO}_4)_6(\text{OH})_2 \). The crystals also incorporate other salts (e.g., calcium carbonate) and ions (e.g., sodium, magnesium, sulfate, and fluoride) during the process of calcification. These crystals deposit around the long axis of collagen fibers in the extracellular matrix. The crystals harden the matrix and account for the rigidity or relative inflexibility of bone that provides its compressional strength.

The correct proportion of organic and inorganic substances in the matrix of bone allows it to function optimally. A loss of protein, or the presence of abnormal protein, results in brittle bones; insufficient calcium results in soft bones.

Bone Matrix: Its Formation and Resorption

Bone formation begins when osteoblasts secrete osteoid. Calcification (kal′si-fi-kā’shūn), or mineralization, subsequently occurs to the osteoid when hydroxypatite crystals deposit in the bone matrix. Calcification is initiated when the concentration of calcium ions and phosphate ions reaches critical levels and precipitate out of solution, thus forming the hydroxypatite crystals that deposit in and around the collagen fibers. The entire process of bone formation requires a number of substances, including vitamin D (Table 27.2) (which enhances calcium absorption from the gastrointestinal tract; see section 7.6b) and vitamin C (which is required for collagen formation), as well as calcium and phosphate for calcification.
Bone resorption is a process whereby bone matrix is destroyed by substances released from osteoclasts into the extracellular space adjacent to the bone. Proteolytic enzymes released from lysosomes within the osteoclasts chemically digest the organic components (collagen fibers and proteoglycans) of the matrix, while hydrochloric acid (HCl) dissolves the mineral parts (calcium and phosphate) of the bone matrix. The liberated calcium and phosphate ions enter the blood. Bone resorption may occur when blood calcium levels are low (described in detail in section 7.6b).

Comparison of Compact and Spongy Bone Microscopic Anatomy

Compact bone and spongy bone have unique microscopic architecture (figure 7.7).

Figure 7.7 Components of Bone. (a) An expanded section of the humerus shows the arrangement of osteons within (b) the compact bone and (c) the arrangement of trabeculae within spongy bone.
LEARNING STRATEGY

The analogy of an archery target can help you remember the following components of an osteon:

- The entire target represents the osteon.
- The bull’s-eye of the target is the central canal.
- The rings of the target are the concentric lamellae.

Compact Bone Microscopic Anatomy  Compact bone is composed of small, cylindrical structures called osteons, or Haversian systems. An osteon is the basic functional and structural unit of mature compact bone (figure 7.7a, b). Osteons are oriented parallel to the diaphysis of the long bone. When an osteon is viewed in cross section, it has the appearance of a bull’s-eye target. An osteon has several components:

- **The central** (Haversian) **canal** is a cylindrical channel that lies in the center of the osteon and runs parallel to it. Extending through the central canal are the blood vessels and nerves that supply the bone.
- **Concentric lamellae** (lə-ˈmel-ə|-sing., lamella, lə-melˈə; lamina = plate, leaf) are rings of bone connective tissue that surround the central canal and form the bulk of the osteon. The numbers of concentric lamellae vary among osteons. Each lamella contains collagen fibers oriented at an angle in one direction; adjacent lamellae contain collagen fibers oriented at an angle that is 90 degrees different from both the previous and the next lamella. This alternating pattern of collagen fiber direction gives bone part of its strength and resilience.
- **Osteocytes** are mature bone cells found in small spaces (see next) between adjacent concentric lamellae. These cells maintain the bone matrix.
- **Lacunae** are the small spaces that each house an osteocyte.
- **Canaliculi** (kan-ˈəlikə-lī; sing., canaliculus, kan-ˈəlikə-lūs; canalis = canal) are tiny, interconnecting channels within the bone connective tissue that extend from each lacuna, travel through the lamellae, and connect to other lacunae and the central canal. Canaliculi house osteocyte cytoplasmic projections that permit intercellular contact and communication. Nutrients, minerals, gases, and wastes are transported through the cytoplasmic extensions within these passageways, allowing their exchange between the blood vessels of the central canal and the osteocytes.

Figure 7.8a, b shows cross sections of osteons as viewed through a light microscope and a scanning electron microscope. Several other structures occur in compact bone but are not part of the osteon proper, including the following (see figure 7.7a):

- **Perforating** (Volkmann) **canals** resemble central canals in that they also contain blood vessels and nerves. However, perforating canals run perpendicular to the central canals and help connect multiple central canals within different osteons, thus forming a channel for a vascular and innervation connection among the multiple osteons.
- **Circumferential lamellae** are rings of bone immediately internal to the periosteum of the bone (external circumferential lamellae) or immediately external to the endosteum (internal circumferential lamellae). Both external and internal circumferential lamellae extend the entire circumference of the bone itself (hence their name).
- **Interstitial lamellae** (interstitial systems) are either the components of compact bone that are between osteons or the leftover parts of osteons that have been partially resorbed—thus, they often look like a “bite” has been taken out of them. The interstitial lamellae are incomplete and typically have no central canal.

**Figure 7.8 Microscopic Anatomy of Bone.** (a) Light micrograph and (b) SEM of osteons in a cross section of compact bone. (c) Light micrograph of spongy bone. ©C Squared Studios/Getty Images RF; (a) ©Biophoto Associates/Science Source; (b) ©Carolina Biological Supply Company/Medical Images; (c) ©Andrew Syred/Science Source; (a, b) ©Carolina Biological Supply Company/Medical Images; (b) ©Andrew Syred/Science Source; (c) ©Biophoto Associates/Science Source
throughout the structure. This is accomplished because stresses and forces are distributed throughout the entire framework. As an analogy, visualize the bars and plates of small bone pieces. This structure provides great support for the canaliculi that open onto the surfaces of the trabeculae.

Note that the trabeculae often form a meshwork of crisscrossing bars and plates of small bone pieces. This structure provides great resistance to stresses applied in many directions by distributing the stress throughout the entire framework. As an analogy, visualize the jungle gym climbing apparatus on a children’s playground. It is capable of supporting the weight of numerous children, whether they are distributed throughout its structure or all localized in one area. This is accomplished because stresses and forces are distributed throughout the structure.

---

**WHAT DID YOU LEARN?**

1. What are the functions of the osteoprogenitor cell, osteoblast, osteocyte, and osteoclast?
2. What organic and inorganic substances compose bone matrix?
3. What are the major components of an osteon?

---

### 7.2f Microscopic Anatomy: Hyaline Cartilage Connective Tissue

**LEARNING OBJECTIVE**

14. Analyze the structure of hyaline cartilage and the cells in its matrix.

Hyaline cartilage contains a population of cells scattered throughout a glassy-appearing matrix of protein fibers (primarily collagen) embedded within a gel-like ground substance (see section 5.2d). This ground substance is similar to that of bone in that it includes proteoglycans, such as chondroitin sulfate, but it differs from bone because its inorganic salts do not include calcium. This makes hyaline cartilage both resilient and flexible. Additionally, cartilage also contains a high percentage of water (60% to 70% by weight). The high water content makes it highly compressible, allowing hyaline cartilage to function as a good shock absorber.

**Chondroblasts** (kon′drō-blast; *chondros* = grit or gristle) are derived from mesenchymal cells and they produce the cartilage matrix. Once chondroblasts become encased within the matrix they have produced and secreted, the cells are called **chondrocytes** (kon′drō-sīt) and occupy small spaces called **lacunae**. These mature cartilage cells maintain the matrix. Hyaline cartilage—except the articular cartilage—is covered by a dense irregular connective tissue sheet called the **perichondrium**, which helps maintain its shape. Mature cartilage is avascular (not penetrated by blood vessels) and contains no nerves. Nutrients and oxygen are supplied to the cartilage by diffusion from blood vessels in the perichondrium. Several important differences between bone connective tissue and hyaline cartilage connective tissue are summarized in **table 7.1**. (How the articular cartilage is supplied with oxygen and nutrients is described in section 9.4a.)

---

### 7.3 Cartilage Growth

**LEARNING OBJECTIVE**

15. Compare interstitial and appositional growth of cartilage.

We focus on the process of cartilage growth before discussing bone growth because certain types of bone formation and bone growth are dependent upon the growth of hyaline cartilage.

Cartilage development and growth begin during embryologic development. Cartilage can grow both in length through the process of interstitial growth and in width by appositional growth (figure 7.9).

**Interstitial** (in-ter-stish′ăl) growth is an increase in length that occurs within the internal regions of cartilage through the following series of four steps (figure 7.9a):

1. Chondrocytes housed within lacunae are stimulated to undergo mitotic cell division.
2. Following cell division, two cells occupy a single lacuna; they are now called chondroblasts.
3. As chondroblasts begin to synthesize and secrete new cartilage matrix, they are pushed apart. Each cell now resides in its own lacuna and is called a chondrocyte.
4. The cartilage continues to grow in the internal regions as chondrocytes continue to produce more matrix.

**Appositional** (ap-ô-zish′ün-ăl) growth is an increase in width along the cartilage’s outside edge, or periphery. The following three steps occur in this process (figure 7.9b):

1. Undifferentiated stem cells (see Clinical View 5.4: “Stem Cells”) at the internal edge of the perichondrium begin to divide. (Note the perichondrium contains mesenchymal cells as well as these stem cells.)
2. New undifferentiated stem cells and committed cells that differentiate into chondroblasts are formed. These chondroblasts are located at the periphery of the old cartilage, where they begin to produce and secrete new cartilage matrix.
3. The chondroblasts, as a result of matrix formation, push apart and become chondrocytes, with each occupying its own lacuna. The cartilage continues to grow at the periphery as chondrocytes continue to produce more matrix.

---

Table 7.1 Comparison of Bone Connective Tissue and Hyaline Cartilage Connective Tissue

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Bone Connective Tissue</th>
<th>Hyaline Cartilage Connective Tissue</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cells that form matrix</td>
<td>Osteoblasts</td>
<td>Chondroblasts</td>
</tr>
<tr>
<td>Mature cell type</td>
<td>Osteocytes</td>
<td>Chondrocytes</td>
</tr>
<tr>
<td>Mature cells in lacunae?</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Calcium present in matrix?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Blood supply in mature tissue</td>
<td>Extensive</td>
<td>Avascular</td>
</tr>
</tbody>
</table>

---

**WHAT DID YOU LEARN?**

11. What are the primary ways that hyaline cartilage tissue differs from bone tissue?
A chondrocyte within a lacuna begins to exhibit mitotic activity. Two cells (now called chondroblasts) are produced by mitosis from one chondrocyte and occupy one lacuna. Each cell produces new matrix and begins to separate from its neighbor. Each cell is now called a chondrocyte. Cartilage continues to grow internally. Mitotic activity occurs in stem cells within the perichondrium. New undifferentiated stem cells and committed cells that differentiate into chondroblasts are formed. Chondroblasts produce new matrix at the periphery. As a result of matrix formation, the chondroblasts push apart and become chondrocytes. Chondrocytes continue to produce more matrix at the periphery.

Figure 7.9 Formation and Growth of Cartilage. Cartilage grows either (a) from within by interstitial growth or (b) at its periphery (edge) by appositional growth.
During early embryonic development, both interstitial and appositional cartilage growth occur simultaneously. Note that interstitial growth declines rapidly as the cartilage matures because the cartilage becomes semirigid, and it is no longer able to expand. Further growth can occur only at the periphery of the tissue, so later growth is primarily appositional. Once the cartilage is fully mature, new cartilage growth typically stops. Thereafter, cartilage growth usually occurs only after injury to the cartilage, yet this growth is limited due to the lack of blood vessels in the tissue.

**WHAT DID YOU LEARN?**

**12.** Where do interstitial and appositional growth of cartilage occur?

### 7.4 Bone Formation

**Ossification** (os′î-ťa-kā′shŭn: facio = to make), or **osteogenesis** (os′tē-ŏ-jen′ĕ-sis; genesis = beginning), refers to the formation and development of bone connective tissue. Ossification begins in the embryo and continues as the skeleton grows during childhood and adolescence. By the eighth through twelfth weeks of embryonic development, the skeleton begins forming from either thickened condensations of mesenchyme (intramembranous ossification) or a hyaline cartilage model of bone (endochondral ossification).

#### 7.4a Intramembranous Ossification

**LEARNING OBJECTIVES**

**16.** Identify bones that are produced by intramembranous ossification.

**17.** Explain the four main steps in intramembranous ossification.

**Figure 7.10 Intramembranous Ossification.** A flat bone in the skull forms from mesenchymal cells in a series of continuous steps.

**1.** Ossification centers form within thickened regions of mesenchyme.

**2.** Osteoid undergoes calcification.

**3.** Woven bone and surrounding periosteum form.

**4.** Lamellar bone replaces woven bone, as compact and spongy bone form.
INTEGRATE CONCEPT OVERVIEW

Figure 7.11 The Process of Endochondral Ossification.
Endochondral ossification of a long bone occurs in progressive stages. Bone growth is complete when each epiphyseal plate has ossified and the epiphyseal line has formed. Depending upon the bone, epiphyseal plate ossification typically occurs between the ages of 10 and 25 years.

bone, or primary bone. Eventually, woven bone is replaced by lamellar bone, or secondary bone (see step 4). The mesenchyme that still surrounds the woven bone begins to thicken and eventually organizes to form the periosteum. Mesenchymal cells grow and develop to produce additional osteoblasts. Newly formed blood vessels also branch throughout this region. The calcified trabeculae and inter trabecular spaces are composed of spongy bone.

Lamellar bone replaces woven bone, as compact bone and spongy bone form. Lamellar bone replaces the trabeculae of woven bone. On the internal and external surfaces, spaces between the trabeculae are filled and the bone becomes compact bone. Internally, the trabeculae are modified slightly and produce spongy bone. The typical structure of a flat cranial bone is composed of two external layers of compact bone with a layer of spongy bone in between (see figure 7.4).

WHAT DID YOU LEARN?

13 When does intramembranous ossification begin? What bones are formed from this method?
**7.4b Endochondral Ossification**

**LEARNING OBJECTIVES**

18. Explain the steps in endochondral ossification of a long bone.

19. Differentiate between intramembranous ossification and endochondral ossification.

Endochondral (en-dō-kon’drål; endo = within, chondral = cartilage) ossification begins with a hyaline cartilage model and produces most bones of the skeleton, including those of the upper and lower limbs, the pelvis, the vertebrae, and the ends of the clavicle.

Long bone development is a good example of this process, which takes place in the following six steps (figure 7.11):

1. **The fetal hyaline cartilage model develops.** During the eighth to twelfth week of development, chondroblasts secrete cartilage matrix, and a hyaline cartilage model
Endochondral bone growth is a complex process. Before trying to remember every detail, first learn the following basics:

1. A hyaline cartilage model of bone forms.
2. Bone first replaces hyaline cartilage in the diaphysis.
3. Next, bone replaces hyaline cartilage in the epiphyses.
4. Eventually, bone replaces hyaline cartilage everywhere, except the epiphyseal plates and articular cartilage.
5. By a person’s late 20s, all epiphyseal plates typically have ossified, and lengthwise bone growth is complete.

Chondrocytes are trapped within lacunae, and a perichondrium surrounds the cartilage.

2. *Cartilage calcifies, and a periosteal bone collar forms.* Within the center of the cartilage model (future diaphysis), chondrocytes start to hypertrophy (enlarge) and resorb (eat away) some of the surrounding cartilage matrix, producing larger holes in the matrix. As these chondrocytes enlarge, the cartilage matrix begins to calcify. Chondrocytes in this region die and disintegrate because nutrients cannot diffuse to them through this calcified matrix. The result is a calcified cartilage shaft with large holes where living chondrocytes had been.

As the cartilage in the shaft is calcifying, blood vessels grow toward the cartilage and start to penetrate the perichondrium around the shaft. Stem cells within the perichondrium divide to form osteoblasts. The osteoblasts develop as this supporting connective tissue becomes highly vascularized, and the perichondrium becomes a periosteum. The osteoblasts within the internal layer of the periosteum start secreting a layer of osteoid around the calcified cartilage shaft. The osteoid hardens and forms a periosteal bone collar around this shaft.

3. **The primary ossification center forms in the diaphysis.** A growth of capillaries and osteoblasts, called a *periosteal bud*, extends from the periosteum into the core of the cartilage shaft, invading the spaces where the living chondrocytes had been. The remains of the calcified cartilage serve as a template on which osteoblasts begin to produce osteoid. This region is called the *primary ossification center* because it is the first major center of bone formation. Bone development extends in both directions toward the epiphyses from the primary ossification center. Healthy bone connective tissue quickly displaces the calcified, degenerating cartilage in the shaft. Most, but not all, primary ossification centers have formed by the twelfth week of development.

4. **Secondary ossification centers form in the epiphyses.** The same basic process that formed the primary ossification center occurs later in the epiphyses. Beginning around the time of birth, the hyaline cartilage in the center of each epiphysis calcifies and begins to degenerate. Epiphyseal blood vessels and osteoprogenitor cells enter each epiphysis. *Secondary ossification centers* form as bone displaces calcified cartilage. Note that not all secondary ossification centers form at birth; some form later in childhood. As the secondary ossification centers form, osteoclasts resorb some bone matrix within the diaphysis, creating a hollow medullary cavity.

5. **Bone replaces almost all cartilage, except the articular cartilage and epiphyseal cartilage.** By late bone development, almost all of the hyaline cartilage has been
displaced by bone. Hyaline cartilage remains as articular cartilage only on the articular surface of each epiphysis and at the epiphyseal plates.

**Lengthwise growth continues until the epiphyseal plates ossify and form epiphyseal lines.** Lengthwise bone growth continues into puberty until the epiphyseal plate is converted to the epiphyseal line, indicating that the bone has reached its adult length. Depending upon the bone, most epiphyseal plates ossify to become epiphyseal lines between the ages of 10 and 25. (The last epiphyseal plates to ossify are those of the clavicle in the late 20s.)

**WHAT DO YOU THINK?**

1. Why does endochondral bone formation involve so many complex steps? Instead of having the hyaline cartilage model followed by the separate formation of the diaphysis and epiphyses, why can’t bone simply be completely formed in the fetus?

**WHAT DID YOU LEARN?**

14. Briefly describe the process by which a long bone forms by endochondral ossification.
**7.5 Bone Growth and Bone Remodeling**

Bone growth and bone remodeling both begin during embryologic development. We examine both processes here and the major hormones that regulate them.

### 7.5a Bone Growth

#### LEARNING OBJECTIVES

20. Compare and contrast the five zones of the epiphyseal plate, and describe how growth in length occurs there.

21. Describe the steps of appositional growth.

As with cartilage growth, a long bone’s growth in length is called interstitial growth, and its growth in diameter or thickness is termed appositional growth.

**Interstitial Growth**

Interstitial growth is dependent upon growth of cartilage within the epiphyseal plate. The epiphyseal plate exhibits five distinct microscopic zones that are continuous from the first zone nearest the epiphysis to the last zone nearest the diaphysis (figure 7.12):

1. **Zone of resting cartilage.** This zone is farthest from the medullary cavity of the diaphysis and nearest the epiphysis. It is composed of small chondrocytes distributed throughout the cartilage matrix. It resembles mature and healthy hyaline cartilage. This region secures the epiphysis to the epiphyseal plate.

2. **Zone of proliferating cartilage.** Chondrocytes in this zone undergo rapid mitotic cell division, enlarge slightly, and become aligned like a stack of coins into longitudinal columns of flattened lacunae. These columns are parallel to the diaphysis.

3. **Zone of hypertrophic cartilage.** Chondrocytes cease dividing and begin to hypertrophy (enlarge in size) in this zone. The walls of the lacunae become thin because the chondrocytes resorb matrix as they hypertrophy.

4. **Zone of calcified cartilage.** This zone usually is composed of two or three layers of chondrocytes. Minerals are deposited in the matrix between the columns of lacunae; this calcification destroys the chondrocytes and makes the matrix appear opaque.

5. **Zone of ossification.** The walls break down between lacunae in the columns, forming longitudinal channels. These spaces are invaded by capillaries and osteoprogenitor cells from the medullary cavity. New matrix of bone is deposited on the remaining calcified cartilage matrix.

Growth in bone length occurs specifically within both zone 2 as chondrocytes undergo mitotic cell division and zone 3 as chondrocytes hypertrophy. These activities combine to push the zone of resting cartilage toward the epiphysis. Note that it is the flexible matrix of hyaline cartilage, and not the hard, calcified matrix of bone, that permits this growth. Once growth in length has occurred, new bone connective tissue is then produced at the same rate in zone 5. Thus, growth in length is due to growth in hyaline cartilage connective tissue, which is later replaced with bone. This process is similar to the endochondral ossification process that occurs during bone development.

The epiphyseal plate maintains its thickness during childhood as it is pushed away from the center of the shaft. At maturity, the rate of epiphyseal cartilage production slows, and the rate of osteoblast activity accelerates. As a result, the epiphyseal plate continues to narrow until it ultimately disappears, and interstitial growth completely stops. Eventually, the only remnant of each epiphyseal plate is an internal thin line of compact bone called an epiphyseal line. The loss of the hyaline cartilage and the appearance of the remnant epiphyseal line signal the end of interstitial growth.

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**Figure 7.12 Epiphyseal Plate.** (a) In a growing long bone, the epiphyseal plate, located at the boundary between the diaphysis and the epiphysis, exhibits five distinct but continuous zones. Zones 1–4 are cartilage, and zone 5 is bone. (b) A colorized x-ray of a child’s hand shows the cartilaginous epiphyseal plate as a dark line between the epiphysis and the diaphysis of a long bone. 

(a) McGraw-Hill Education/Al Telser; (b) Yoav Levy/Medical Images
INTEGRATE

CLINICAL VIEW 7.4

Achondroplastic Dwarfism

Achondroplasia (ā-kon-drō-plā’zē-ă) is characterized by abnormal conversion of hyaline cartilage to bone. The most common form is achondroplastic dwarfism, in which the long bones of the limbs stop growing in childhood, whereas the other bones usually continue to grow normally. Thus, an individual with achondroplastic dwarfism is short in stature but generally has a large head. Those affected may have bowed lower limbs and lordosis (exaggerated curvature of the lumbar spine). Achondroplastic dwarfism results from a failure of chondrocytes in the second and third zones of the epiphyseal plate (figure 7.12a) to multiply and enlarge. As a result, there is inadequate endochondral ossification. Most cases result from a spontaneous mutation during DNA replication (see section 4.9b), whereas other cases are due to inheriting the disorder from an affected parent (see section 29.9b).

7.5b Bone Remodeling

LEARNING OBJECTIVES

22. Define bone remodeling, and give examples of how it varies in different bones and different portions of the same bone.

23. Explain the effect of mechanical stress on bone remodeling.

Even when adult bone size has been reached, the bone continues to renew and reshape itself throughout a person’s lifetime. This constant, dynamic process of continual addition of new bone tissue (bone deposition) and removal of old bone tissue (bone resorption) is a process called bone remodeling. This ongoing process occurs at both the peristeal and endosteal surfaces of a bone.

It is estimated that about 20% of the adult human skeleton is replaced yearly. However, bone remodeling does not occur at the same rate everywhere in the skeleton. For example, the compact bone in our skeleton is replaced at a slower rate than the spongy bone. The distal part of the femur (thigh bone) is replaced every 4 to 6 months, whereas the diaphysis of this bone may not be completely replaced during an individual’s lifetime.

Clearly, bone remodeling is dependent upon the coordinated activities of osteoblasts, osteocytes, and osteoclasts. The relative activities of these cells are influenced by two primary factors: hormones (described in section 7.5c) and mechanical stress to the bone.

Mechanical stress occurs in the form of weight-bearing movement and exercise, and it is required for normal bone remodeling. Stress is detected by osteocytes and communicated to osteoblasts. Osteoblasts increase the synthesis of osteoid, and this is followed by deposition of mineral salts. Bone strength increases over a period of time in response to mechanical stress.

Mechanical stresses that significantly affect bone result from skeletal muscle contraction and gravitational forces. Typically, the bones of athletes become noticeably thicker as a result of repetitive and stressful exercise. Weight-bearing activities, such as weight lifting, walking, or running, help build and retain bone mass. Research has shown that regular weight-bearing exercise can increase total bone mass in adolescents and young adults prior to its inevitable reduction later in life. In fact, research suggests that even 70- and 80-year-olds who perform moderate weight training can increase their bone mass.
Effect on Bone
Inhibits osteoprogenitor cells from differentiating
Effects of Hormones on Bone
Promotes calcium deposition in bone and inhibits growth
Stimulates liver to produce the hormone IGF, resulting in the rates of chondrocyte, osteoblast, and osteoclast activity (table 7.2).

In contrast, removal or significant decrease of mechanical stress weakens bone through both reduction of collagen formation and demineralization. When a person has a fractured bone and wears a cast or is bedridden, the strength of the unstressed bone decreases in the immobilized limb. Thus, while in space, astronauts must exercise to reduce the effects of loss of bone mass due to lack of gravity.

**WHAT DID YOU LEARN?**
What is bone remodeling, where does it occur, and when does it occur?

7.5c Hormones That Influence Bone Growth and Bone Remodeling

LEARNING OBJECTIVE
24. Identify the hormones that influence bone growth and bone remodeling, and describe their effects.

Hormones are molecules that are released from one cell into the blood and are transported throughout the body to affect other cells (see section 17.1a). Certain hormones influence bone composition and growth patterns by altering the rates of chondrocyte, osteoblast, and osteoclast activity (table 7.2).

<table>
<thead>
<tr>
<th>Table 7.2 Effects of Hormones on Bone Maintenance and Growth</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Hormone</strong></td>
</tr>
<tr>
<td>Growth hormone</td>
</tr>
<tr>
<td>Thyroid hormone</td>
</tr>
<tr>
<td>Calcitonin</td>
</tr>
<tr>
<td>Calcitriol</td>
</tr>
<tr>
<td>Parathyroid hormone</td>
</tr>
<tr>
<td>Sex hormones (estrogen and testosterone)</td>
</tr>
<tr>
<td>Glucocorticoids</td>
</tr>
<tr>
<td>Serotonin</td>
</tr>
</tbody>
</table>

Growth hormone, also called somatotropin (sŏ-mā-tō-trō-pin), is produced by the anterior pituitary gland (see section 17.7d). It affects bone growth by stimulating the liver to form another hormone called insulin-like growth factor (IGF) (also called somatomedin; sŏ-mā-tō-mē’din). Both growth hormone and IGF directly stimulate growth of cartilage at the epiphyseal plate.

Thyroid hormone is secreted by the thyroid gland and stimulates bone growth by influencing the basal metabolic rate of bone cells (see section 17.8b). If maintained in proper balance, growth hormone and thyroid hormone regulate and maintain normal activity at the epiphyseal plates until puberty.

Sex hormones (estrogen and testosterone; see tables R.9 and R.10), which begin to be secreted in relatively large amounts at puberty (see section 28.1b), dramatically accelerate bone growth. Sex hormones increase the rate of both cartilage growth and bone formation within the epiphyseal plate. Ironically, the appearance of high levels of sex hormones at puberty also signals the beginning of the end for growth at the epiphyseal plate. This happens because bone formation occurs at a faster rate than cartilage growth. Bone growth eventually overcomes the region of cartilage, replacing all cartilage with bone at the epiphyseal plates.

**WHAT DID YOU THINK?**
Given what you know about the effects of testosterone, explain why there is a risk of stunted growth to a young boy (pre-puberty) taking anabolic steroids (substances that have effects similar to those of testosterone).

Glucocorticoids are a group of steroid hormones that are released from the adrenal cortex and regulate blood glucose levels (see section 17.9b). High amounts increase bone loss and, in children, impair growth at the epiphyseal plate. It is because of this relationship that a child’s growth is monitored if receiving high doses of glucocorticoids as an anti-inflammatory, such as a treatment for severe asthma.

Serotonin (ser-0-tō’nin) was previously discussed in section 1.7. Researchers have discovered that most bone cells have serotonin receptors and specifically that, when levels of circulating serotonin are too high, osteoprogenitor cells are prevented from differentiating into osteoblasts. Thus, serotonin appears to play a role in the rate and regulation of normal bone remodeling because it affects osteoblast differentiation. Further research is ongoing to see if abnormally high levels of serotonin are linked to low bone density disorders.

Three additional hormones—parathyroid hormone, calcitriol, and calcitonin—participate in both regulating bone remodeling and regulating blood calcium levels. These hormones are discussed in detail in section 7.6.

**WHAT DID YOU LEARN?**
What are the effects of growth hormone and thyroid hormone on bone growth and bone mass?
7.6 Regulating Blood Calcium Levels

Regulating calcium concentration in blood (between 8.9 and 10.1 milligrams per deciliter [mg/dL]) is essential because calcium is required for numerous physiologic processes such as initiation of muscle contraction (see section 10.3a); exocytosis of molecules from cells (see section 4.3c), including nerve cells (neurons) (see section 12.8d); stimulation of the heart by pacemaker cells (see section 19.6a); and blood clotting (see section 18.4c). The two primary hormones that regulate blood calcium are calcitriol (an active form of vitamin D) and parathyroid hormone. We describe blood calcium regulation here because of the role of the skeleton in storage of calcium. (Also see table R.2 for information about the hormones involved in regulating blood calcium levels.)

7.6a Activation of Vitamin D to Calcitriol

LEARNING OBJECTIVE

25. Explain the activation of vitamin D to calcitriol.

To effectively describe the actions of calcitriol and parathyroid hormone we first describe the enzymatic pathway of activating vitamin D to calcitriol. The three steps are as follows (figure 7.14):

1. Ultraviolet light converts the precursor molecule in keratinocytes of the skin (7-dehydrocholesterol, a modified cholesterol molecule) to vitamin D₃ (cholecalciferol), which is released into the blood. (Vitamin D₃ also is absorbed from the small intestine into the blood from the diet.)

2. Vitamin D₃ circulates throughout the blood. As it passes through the blood vessels of the liver, it is converted by liver enzymes to calcidiol by the addition of a hydroxyl group (—OH). Both steps 1 and 2 occur continuously with limited regulation.

3. Calcidiol circulates in the blood: As it passes through blood vessels of the kidney, it is converted to calcitriol by kidney enzymes (when another —OH group is added). Calcitriol is the active form of vitamin D₃. The presence of parathyroid hormone increases the rate of this final enzymatic step in the kidney. Thus, greater amounts of calcitriol are formed when parathyroid hormone is present.

Figure 7.14 Calcitriol Production. Calcitriol is produced as follows: When keratinocytes are exposed to UV rays, a precursor molecule (7-dehydrocholesterol) in keratinocytes is transformed to vitamin D₃ (cholecalciferol). Humans also may obtain vitamin D₃ from dietary sources, such as milk. The liver then synthesizes calcidiol from the vitamin D₃. Finally, the kidneys will convert calcidiol to calcitriol.
Vitamin D in its active form of calcitriol hormone has the unique function of stimulating absorption of calcium ions (Ca\(^{2+}\)) from the small intestine into the blood.

**WHAT DID YOU LEARN?**

What organs are involved in activating vitamin D\(_3\) to calcitriol?

### 7.6b Parathyroid Hormone and Calcitriol

**LEARNING OBJECTIVES**

26. Discuss the release of parathyroid hormone.

27. Explain how parathyroid hormone and calcitriol function together to regulate blood calcium levels.

**Parathyroid hormone (PTH)** is secreted and released by the parathyroid glands (see section 17.11b) in response to reduced blood calcium levels (figure 7.15). The final enzymatic step converting calcidiol to calcitriol in the kidney occurs more readily in the presence of PTH.

PTH and calcitriol interact with selected major organs as follows:

- **Bone.** PTH and calcitriol act synergistically (their combined effect is greater than the sum of their individual effects) to increase the release of calcium from the bone into the blood, by increasing osteoclast activity.

- **Kidneys.** PTH and calcitriol act synergistically to stimulate the kidneys to excrete less calcium in the urine (and thus retain more calcium in the blood). This occurs by increasing calcium reabsorption in the tubules in the kidneys (see section 24.6).

**Figure 7.15 Effects of Parathyroid Hormone and Calcitriol on Blood Calcium Levels.** Blood calcium levels are closely regulated by a negative feedback mechanism that involves the parathyroid gland, calcitriol, and various effectors (bone, kidneys, and small intestine). A low blood calcium level is the initial stimulus for the parathyroid glands to release parathyroid hormone. Together, PTH and calcitriol target various effectors to ultimately instigate a rise in blood calcium levels and return to homeostasis.
**Small intestine.** A function unique to calcitriol is to increase absorption of calcium from the small intestine into the blood.

The removal of calcium from bone, the decrease in loss of calcium from the kidney, and the increase in calcium absorption from the gastrointestinal tract result in elevating blood calcium and returning it to within the normal homeostatic range. Subsequently, the release of additional PTH is inhibited by negative feedback.

**WHAT DID YOU LEARN?**

When are parathyroid hormone and calcitriol produced and/or secreted, and what organs respond to them?

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### 7.6c Calcitonin

**LEARNING OBJECTIVE**

28. Discuss the homeostatic system involving the hormone calcitonin and its effect on blood calcium levels.

Calcitonin (kal-si-tō′nin; calx = lime, tonos = stretching) is another hormone that aids in regulating blood calcium levels—however, it has a less significant role than either PTH or calcitriol. Calcitonin is released from the thyroid gland—specifically, from its parafollicular cells (see section 17.8c) in response to high blood calcium levels; it is also secreted in response to stress from exercise. Although the entire function of calcitonin is unclear, it is known that calcitonin primarily inhibits osteoclast activity. In addition, calcitonin stimulates the kidneys to increase the loss of calcium in the urine. The result is a reduction in blood calcium levels.

The following limitations are observed with calcitonin:

- Calcitonin seems to have the greatest effect under conditions where there is the greatest turnover of bone, such as in growing children.

**WHAT DID YOU LEARN?**

If high doses of calcitonin are administered, blood calcium levels decrease only temporarily. Thus, therapeutic injections of calcitonin cannot provide long-term decrease in blood calcium.

### 7.7 Effects of Aging

**LEARNING OBJECTIVE**

29. Describe how age influences bone structure.

Aging affects bone connective tissue in two ways. First, the tensile strength of bone decreases due to a reduced rate of protein synthesis by osteoblasts. Consequently, the relative amount of inorganic minerals in the bone matrix increases (due to decreased matrix protein), and the bones of the skeleton become brittle and susceptible to fracture.

- If high doses of calcitonin are administered, blood calcium levels decrease only temporarily. Thus, therapeutic injections of calcitonin cannot provide long-term decrease in blood calcium.

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**INTEGRATE**

**CLINICAL VIEW 7.7**

**Osteoporosis**

Osteoporosis, meaning porous bones, is a disease that results in decreased bone mass and leads to weakened bones that are prone to fracture. The occurrence of osteoporosis is greatest among the elderly, especially Caucasian women, and the severity is closely linked to both age and onset of menopause. Smoking is also a risk factor for osteoporosis. Postmenopausal women are at risk because (1) women have less bone mass than men, (2) women begin losing bone mass earlier and faster in life (sometimes around 35 years of age), and (3) postmenopausal women no longer produce significant amounts of estrogen, which appears to help protect against osteoporosis by stimulating bone growth. As a result of osteoporosis, the incidence of fractures increases, most frequently in the wrist, hip, and vertebral column.

One’s bone density may be determined through the use of a dual-energy x-ray absorptiometry scan, also known as a DEXA scan. The procedure is similar to a traditional x-ray and is noninvasive. The DEXA scan provides both images and calculations to determine if the bone examined is at normal-for-age bone mass or reduced bone mass.

The best treatment for osteoporosis seems to be prevention. Young adults should maintain good nutrition and physical activity to ensure adequate bone density, thus allowing for the normal, age-related loss later in life. Calcium supplements with vitamin D help maintain bone health but by themselves will not stimulate new bone growth.

Medical treatments involve two strategies: (1) slowing the rate of bone loss and (2) attempting to stimulate new bone growth. A class of medications called bisphosphonates (e.g., alendronate [Fosamax], risedronate [Actonel], ibandronate [Boniva]) are prescribed to slow the progression of osteoporosis. These drugs work by interfering with osteoclast function and thus retarding the removal of bone during remodeling. Unfortunately, these drugs have also been implicated in increased risk of osteonecrosis (bone death) of the jaw and some other bone growth abnormalities, so it is recommended that patients not take the drugs for longer than 5 years at a time.
Second, bone loses calcium and other minerals (demineralization). The bones of the skeleton become thinner and weaker, resulting in insufficient ossification, a condition called osteopenia (os’tē-ō-pē′né-ā; pē′-nē-ā = poverty). Aging causes all people to become slightly osteopenic. This reduction in bone mass may begin as early as 35–40 years of age, when osteoblast activity declines, while osteoclast activity continues at previous levels. Different parts of the skeleton are affected unequally. Vertebrae, jaw bones, and epiphyses lose large amounts of mass, resulting in reduced height, loss of teeth, and fragile limbs.

Every decade, women lose roughly more of their skeletal mass than do men. A significant percentage of older women and a smaller proportion of older men suffer from osteoporosis (os’tē-ō-pōr-o’sīs; poros = pore, osis = condition), a condition characterized by reduction in bone mass sufficient to compromise normal function (see Clinical View 7.7: “Osteoporosis”).

In addition, vitamin D and numerous hormones, including growth hormone, estrogen, and testosterone, decrease with age. This decrease in hormone levels contributes to reduction in bone mass.

**WHAT DID YOU LEARN?**

**Explain why women are more likely than men to develop osteoporosis.**

---

**7.8 Bone Fracture and Repair**

**LEARNING OBJECTIVE**

30. Explain the four steps by which fractures heal.

Bone has great mineral strength, but it may break as a result of unusual stress or a sudden impact. Breaks in bones are called fractures and are classified in several ways. A stress fracture is a thin break caused by increased physical activity in which the bone experiences repetitive loads (e.g., as seen in some runners). A pathologic fracture usually occurs in bone that has been weakened by disease. In a simple fracture, the broken bone does not penetrate the skin, whereas in a compound fracture, one or both ends of the broken bone pierce the overlying skin. Figure 7.16 shows the classifications of fractures.

The healing of a simple fracture takes about 2 to 3 months, whereas a compound fracture takes longer to heal. Fractures heal much more quickly in young children (average healing time, 3 weeks) and become slower to heal as we age. In the elderly, the normal thinning and weakening of bone increase the incidence of fractures, and

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**Classification of Bone Fractures**

<table>
<thead>
<tr>
<th>Fracture</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Avulsion</td>
<td>Complete severing of a body part (typically a toe or finger)</td>
</tr>
<tr>
<td>Colles</td>
<td>Fracture of the distal end of the lateral forearm bone (radius); produces a “dinner fork” deformity</td>
</tr>
<tr>
<td>Comminuted</td>
<td>Bone is splintered into several small pieces between the main parts</td>
</tr>
<tr>
<td>Complete</td>
<td>Bone is broken into two or more pieces</td>
</tr>
<tr>
<td>Compound (open)</td>
<td>Broken ends of the bone protrude through the skin</td>
</tr>
<tr>
<td>Compression</td>
<td>Bone is squashed (may occur in a vertebra during a fall)</td>
</tr>
<tr>
<td>Depressed</td>
<td>Broken part of the bone forms a concavity (as in skull fracture)</td>
</tr>
<tr>
<td>Displaced</td>
<td>Fractured bone parts are out of anatomic alignment</td>
</tr>
<tr>
<td>Epiphyseal</td>
<td>Epiphysis is separated from the diaphysis at the epiphyseal plate</td>
</tr>
<tr>
<td>Greenstick</td>
<td>Partial fracture; one side of bone breaks—the other side is bent</td>
</tr>
<tr>
<td>Hairline</td>
<td>Fine crack in which sections of bone remain aligned (common in skull)</td>
</tr>
<tr>
<td>Impacted</td>
<td>One fragment of bone is firmly driven into the other</td>
</tr>
<tr>
<td>Incomplete</td>
<td>Partial fracture extends only partway across the bone</td>
</tr>
<tr>
<td>Linear</td>
<td>Fracture is parallel to the long axis of the bone</td>
</tr>
<tr>
<td>Oblique</td>
<td>Diagonal fracture is at an angle</td>
</tr>
<tr>
<td>Pathologic</td>
<td>Weakening of a bone caused by disease process (e.g., cancer)</td>
</tr>
<tr>
<td>Pott</td>
<td>Fracture is at the distal ends of the tibia and fibula</td>
</tr>
<tr>
<td>Simple (closed)</td>
<td>Bone does not break through the skin</td>
</tr>
<tr>
<td>Spiral</td>
<td>Fracture spirals around axis of long bone; results from twisting stress</td>
</tr>
<tr>
<td>Stress</td>
<td>Thin fractures due to repeated, stressful impact such as running (these fractures often are difficult to see on x-rays, and a bone scan may be necessary to accurately identify their presence)</td>
</tr>
<tr>
<td>Transverse</td>
<td>Fracture is at right angles to the long axis of the bone</td>
</tr>
</tbody>
</table>
Fracture Repair. The repair of a bone fracture occurs in a series of steps:

1. **A fracture hematoma forms.** A bone fracture tears blood vessels inside the bone and within the periosteum, causing bleeding. This bleeding results in a fracture hematoma that forms from the clotted blood.

2. **A fibrocartilaginous (soft) callus forms.** Regenerated blood capillaries infiltrate the fracture hematoma. First, the fracture hematoma is reorganized into an actively growing connective tissue called a procallus. Fibroblasts within the procallus produce collagen fibers that help connect the broken ends of the bones. Chondroblasts in the newly growing connective tissue form a dense regular connective tissue associated with the cartilage. Eventually, the procallus becomes a fibrocartilaginous (soft) callus (kal′ús; hard skin). The fibrocartilaginous callus stage lasts at least 3 weeks.

3. **A hard (bony) callus forms.** Within a week after the injury, osteoprogenitor cells in areas adjacent to the fibrocartilaginous callus become osteoblasts and produce trabeculae of primary bone. The fibrocartilaginous callus is then replaced by this bone, which forms a hard (bony) callus. The trabeculae of the hard callus continue to grow and thicken for several months.

4. **The bone is remodeled.** Remodeling is the final phase of fracture repair. The hard callus persists for at least 3 to 4 months as osteoclasts remove excess bony material from both exterior and interior surfaces. Compact bone replaces primary bone. The fracture usually leaves a slight thickening of the bone (as detected by x-ray); however, in some instances, healing occurs with no persistent obvious thickening.

**WHAT DID YOU LEARN?**

- **22** What are the four basic steps in fracture repair?
- **23** Explain the risk of bearing weight on a bone when the fibrocartilage callus is forming.
# Chapter Summary

## 7.1 Introduction to the Skeletal System
- The skeletal system is composed of dynamic, living tissue.

## 7.2 Bone: The Major Organ of the Skeletal System
- Bones, cartilage, ligaments, and other connective tissue that stabilize or connect bones compose the skeletal system.

### 7.2a General Functions
- The functions of bone include support and protection, levers for movement, hemopoiesis, and storage of minerals and energy reserves.

### 7.2b Classification of Bones
- Bones are classified by shape as long, short, flat, or irregular.

### 7.2c Gross Anatomy of Bones
- A long bone contains the following regions: diaphysis, epiphysis, metaphysis, articular cartilage, medullary cavity.
- A long bone is covered externally by the periosteum and lined internally by the endosteum.
- All bones contain a rich blood supply and innervation.

### 7.2d Bone Marrow
- Bone marrow fills the internal spaces of bone and includes red bone marrow (hemopoietic tissue) and yellow bone marrow.

### 7.2e Microscopic Anatomy: Bone Connective Tissue
- Osteoprogenitor cells are bone stem cells; osteoblasts produce osteoid; osteocytes maintain the bone matrix; and osteoclasts resorb bone.
- The bone matrix is made up of collagen fibers and ground substance (composed of glycoproteins, proteoglycans, and hydroxyapatite crystals).
- Compact bone forms the dense outer, solid region of bone, whereas spongy bone is located internally.

### 7.2f Microscopic Anatomy: Hyaline Cartilage Connective Tissue
- Hyaline cartilage is composed of chondrocytes in lacunae within a semirigid matrix.

## 7.3 Cartilage Growth
- Cartilage growth includes both interstitial growth (growth from within preexisting cartilage) and appositional growth (growth around the periphery of cartilage).

## 7.4 Bone Formation
- Ossification, or osteogenesis, is the process of bone connective tissue formation.

### 7.4a Intramembranous Ossification
- In intramembranous ossification, bone forms from a thin layer of mesenchyme (sometimes called a membrane).

### 7.4b Endochondral Ossification
- Endochondral ossification uses a hyaline cartilage model that is gradually replaced by newly formed bone tissue.

## 7.5 Bone Growth and Bone Remodeling
- Bone growth and bone remodeling begin during development.

### 7.5a Bone Growth
- Bone growth occurs in length through interstitial growth within the epiphyseal plate and in width through appositional growth at the periosteum.
- The epiphyseal plate contains five zones where cartilage grows and eventually is replaced by bone.

### 7.5b Bone Remodeling
- The continual deposition of new bone tissue by osteoblasts and resorption of bone by osteoclasts are called bone remodeling.

### 7.5c Hormones That Influence Bone Growth and Bone Remodeling
- Growth hormone, thyroid hormone, and sex hormones stimulate bone growth by increasing osteoblast activity.
- High doses of glucocorticoids interfere with normal bone growth, and high doses of serotonin interfere with normal bone remodeling.
- Calcitonin inhibits osteoclast activity and stimulates osteoblast activity, whereas parathyroid hormone and calcitriol stimulate osteoclast activity.

## 7.6 Regulating Blood Calcium Levels
- Calcium homeostasis requires precise controls over calcium uptake, calcium loss, and calcium storage.

### 7.6a Activation of Vitamin D to Calcitriol
- Vitamin D is a pre-hormone that is activated to calcitriol through several enzymatic steps.

### 7.6b Parathyroid Hormone and Calcitriol
- Parathyroid hormone is released from the parathyroid gland in response to decreased blood calcium levels, and its release increases the final step in the synthesis of calcitriol.
- The combined actions of parathyroid hormone and calcitriol increase blood calcium levels to within the normal range.

### 7.6c Calcitonin
- Calcitonin is a hormone released from the thyroid gland in response to increased blood calcium levels. It appears to be less significant in regulating blood calcium levels than parathyroid hormone and calcitriol, at least in adults.

## 7.7 Effects of Aging
- Due to aging, the tensile strength of bone decreases, and bone loses calcium and other minerals (demineralization).

## 7.8 Bone Fracture and Repair
- A fracture is a break in a bone that can usually be healed if portions of the blood supply, endosteum, and periosteum remain intact.
CHALLENGE YOURSELF

Do You Know the Basics?

1. Which bone is formed from intramembranous bone growth?
   a. femur
   b. rib
   c. os coxae (hip bone)
   d. frontal bone

2. All of the following are functions of cartilage except
   a. cartilage serves as a site for hemopoiesis.
   b. cartilage provides support for soft tissue.
   c. cartilage forms the initial model in endochondral ossification.
   d. cartilage provides a smooth gliding surface at the end of bones in freely movable joints.

3. Which is not a function of bone?
   a. It protects some internal organs, such as the brain, heart, and lungs.
   b. It serves as levers for movement by skeletal muscle.
   c. It stores phosphorus within the bone connective tissue.
   d. Its yellow bone marrow forms blood cells.

4. The femur is an example of a(n)
   a. short bone.
   b. flat bone.
   c. long bone.
   d. irregular bone.

5. Which cell type is most likely to have created the medullary cavity in a long bone?
   a. osteocytes
   b. osteoblasts
   c. osteoclasts
   d. osteoprogenitor cells

6. Which long bone structure is correctly matched with its description or function?
   a. epiphysis; the end of a bone that is composed of compact bone only
   b. articular cartilage; fibrocartilage located at the ends of a bone
   c. periosteum; responsible for growth in bone width
   d. perforating fibers; blood vessels that penetrate the bone

7. Which statement is correct about an osteon?
   a. The circumferential lamellae surround the blood vessels and nerves within an osteon.
   b. Canaliculi allow for nutrient and waste exchange among the osteocytes.
   c. The middle region of an osteon is called the perforating canal.
   d. An osteon is oriented perpendicular to the diaphysis of a long bone.

8. All of the following accurately describe hyaline cartilage except
   a. the matrix of hyaline cartilage contains calcium.
   b. hyaline cartilage is avascular.
   c. hyaline cartilage lacks nerves.
   d. hyaline cartilage is a flexible, semirigid connective tissue.

9. To elevate blood calcium levels, all of these must occur except
   a. calcitonin is secreted by the thyroid gland.
   b. less calcium is excreted in the urine.
   c. parathyroid hormone is secreted by the parathyroid glands.
   d. increased calcium is absorbed from the small intestine into the blood.

10. An epiphyseal line appears when
    a. epiphyseal plate growth has ended.
    b. epiphyseal plate growth is just beginning.
    c. growth in bone diameter is just beginning.
    d. the bone is fractured at that location.

11. Describe the structure of a typical long bone.

12. Describe the general function of both osteoblast and osteoclast activity.

13. Describe the microscopic anatomy of compact bone.


15. List the steps involved in endochondral ossification.

16. Which of the five zones in the epiphyseal plate cartilage are specifically responsible for bone growth in length? Explain.

17. Discuss the effect of exercise on bone mass.

18. Compare and contrast the effects of growth hormone and glucocorticoids on bone growth.

19. Describe how parathyroid hormone regulates blood calcium concentration.

20. What are the steps in fracture repair?

Can You Apply What You’ve Learned?

1. Jorge is donating bone marrow to a friend who has leukemia (a type of blood cell cancer). Jorge is 30 years old, so the doctor knows she must insert the needle into
   a. the diaphysis of the femur.
   b. the hip bone.
   c. the distal epiphysis of the tibia.
   d. the diaphysis of the humerus.

2. You are given the following assignment. Obtain two small chicken or turkey bones. Bake one bone in the oven at a high temperature for approximately 30 minutes. Place the other in vinegar (acidic pH) for several days. Which of the following would most accurately reflect what occurred?
   a. Proteins in the bone matrix have denatured in the bone that is baked, and the vinegar has denatured the proteins in the soaked bone, so both bones are flexible.
   b. Proteins in the bone matrix are lost from the baked bone, and the bone becomes flexible. The soaked bone loses calcium and results in a brittle bone.
   c. Proteins in matrix have denatured from high temperature, and the bone is brittle; calcium has been removed from the bone soaked in vinegar and it has become flexible.
   d. Proteins are lost in the baked bone matrix, and this bone becomes flexible. Calcium loss from the bone soaked in vinegar results in a flexible bone.
3. Your dog is chewing on an adult cow long bone and breaks it open. He pulls out some fleshy material within the diaphysis of the bone. You know that this fleshy material
   a. produced red blood cells for the adult cow.
   b. contains fat.
   c. was formed from osteoblasts.
   d. is abnormal and is not normally found in bone.

4. To identify the approximate age of skeletal remains of a body found in the forest, the forensic anthropologists are most interested in which of the following?
   a. whether the epiphyses have fused to the diaphyses
   b. number of bones in the skeleton
   c. length of the long bones in the legs
   d. presence or absence of articular cartilage

5. In your anatomy and physiology laboratory, you look at prepared slides of developing bone. In the epiphyseal plate region, you note the chondrocytes are slightly enlarged and stacked in a longitudinal array. What epiphyseal plate zone is in your field of view?
   a. zone of rest
   b. zone of proliferation
   c. zone of hypertrophy
   d. zone of calcification

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Can You Synthesize What You’ve Learned?

1. The traditional surgical procedure to treat advanced thyroid gland tumors is to remove the affected organ. Some concerns with the results of this surgery were raised regarding the parathyroid glands, which are small attachments on the posterior side of the thyroid gland. Why should the surgeon be concerned about the removal of these glands? A new procedure has been developed to sequester some parathyroid gland tissue into a plastic mesh holder and implant this small holder back into the body. Why is this implant an advantage to the patient?

2. A fireman fell from a ladder while fighting a fire and severely fractured the thigh and leg bones in his right leg. He was hospitalized for several weeks; then he was wheelchair-bound for several months while his leg bones healed. Upon removal of the cast, it was apparent that his right thigh and leg bones were thin and weak. What factors contributed to this thinning and weakening of the bones, and what should the fireman do to improve the strength of these bones?

3. Elise is 14 and lives in an apartment in the city. She does not like outdoor activities, so she spends most of her spare time watching TV, playing video games, drinking soft drinks, and talking to friends on the phone. One afternoon, Elise tries to run down the stairs while talking on the phone and falls, breaking her leg. Although she appears healthy, her leg takes longer to heal than expected. What might cause the longer healing time?
The bones of the skeleton form an internal framework to support soft tissues, protect vital organs, bear the body’s weight, and function as levers to help us move. An adult skeleton typically has 206 named bones, although this number varies slightly in some individuals. Bones differ in size, shape, and weight, and this diversity is related directly to the skeleton’s many functions. Bones can tell an intricate anatomic story for criminologists, pathologists, and anthropologists. The skeleton can provide information about an individual, such as his or her sex, age at death, and possible pathologies. In this chapter, not only will you learn the names of and features on the individual bones but we also provide an overview of how you can determine age at death from the skeletal remains, as well as how you can tell the difference in sex between certain bones of the skeleton. You can practice determining age at death and determining sex using the bones in your anatomy and physiology lab. This will permit you to learn some of the variations seen in bone morphology so you can start to unlock the mysteries of the bones in front of you in the lab.
8.1 Components of the Skeleton

We first examine the two subdivisions of the skeleton: the axial skeleton and the appendicular skeleton. Then we discuss the names for characteristic markings on bones.

8.1a Axial and Appendicular Skeleton

LEARNING OBJECTIVE
1. Compare and contrast the composition and functions of the axial and appendicular skeletons.

The skeletal system is organized into two divisions: the axial skeleton and the appendicular skeleton (figure 8.1).

The axial skeleton is so named because it is composed of the bones along the central axis of the body, which include the bones of the skull, vertebral column, sternum, and ribs. The main function of the axial skeleton is to form a framework that supports and protects the organs. Additionally, the spongy bone of most of the axial skeleton contains hemopoietic tissue that is responsible for blood cell formation (see section 18.3a).

The appendicular skeleton includes the bones of the upper and lower limbs, and the girdles of bones that attach the upper and lower limbs to the axial skeleton. The pectoral girdle consists of bones that

---

**Figure 8.1 Axial and Appendicular Skeleton.** (a) Anterior and (b) posterior views compare the axial and appendicular components of the skeleton. The axial skeleton is colored blue and the appendicular skeleton is colored tan.
hold the upper limbs in place, whereas the pelvic girdle consists of bones that hold the lower limbs in place.

**WHAT DID YOU LEARN?**

1. What is the general function of the axial skeleton, and which bones are considered part of the axial skeleton?

### 8.1b Bone Markings

**LEARNING OBJECTIVE**

2. Become familiar with terminology for common bone markings.

Distinctive bone markings are the surface features that characterize each bone in the body. Projections from the bone surface mark the points where muscles, tendons, and ligaments attach. Sites of articulation between adjacent bones tend to be smooth areas. Depressions, grooves, and openings through bones indicate sites where blood vessels and nerves travel. Anatomists use specific terms to describe these characteristics (figure 8.2).

Knowing the names of bone markings will help you learn about specific bones described in this chapter. For example, when trying to locate the foramen magnum of the skull, you have an advantage if you know that foramen means hole or passageway.

**WHAT DID YOU LEARN?**

2. What is the difference between a foramen and a fissure?

### Figure 8.2 Bone Markings

Specific anatomic terms describe the characteristic features on bones.

<table>
<thead>
<tr>
<th>General Structure</th>
<th>Anatomic Term</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Articulating surfaces</td>
<td>Condyle</td>
<td>Large, smooth, rounded, oval structure</td>
</tr>
<tr>
<td></td>
<td>Facet</td>
<td>Small, flat, shallow surface</td>
</tr>
<tr>
<td></td>
<td>Head</td>
<td>Prominent, rounded epiphysis</td>
</tr>
<tr>
<td></td>
<td>Trochlea</td>
<td>Smooth, grooved, pulleylike process</td>
</tr>
<tr>
<td>Depressions</td>
<td>Alveolus (pl., alveoli)</td>
<td>Deep pit or socket in the maxillae or mandible</td>
</tr>
<tr>
<td></td>
<td>Fossa (pl., fossae)</td>
<td>Flattened or shallow depression</td>
</tr>
<tr>
<td></td>
<td>Sulcus</td>
<td>Narrow groove</td>
</tr>
<tr>
<td>Projections for tendon and ligament attachment</td>
<td>Crest</td>
<td>Narrow, prominent, ridgelike projection</td>
</tr>
<tr>
<td></td>
<td>Epicondyle</td>
<td>Projection adjacent to a condyle</td>
</tr>
<tr>
<td></td>
<td>Line</td>
<td>Low ridge</td>
</tr>
<tr>
<td></td>
<td>Process</td>
<td>Any marked bony prominence</td>
</tr>
<tr>
<td></td>
<td>Ramus (pl., ramus)</td>
<td>Angular extension of a bone relative to the rest of the structure</td>
</tr>
<tr>
<td></td>
<td>Spine</td>
<td>Pointed, slender process</td>
</tr>
<tr>
<td></td>
<td>Trochanter</td>
<td>Massive, rough projection found only on the femur</td>
</tr>
<tr>
<td></td>
<td>Tubercle</td>
<td>Small, round projection</td>
</tr>
<tr>
<td></td>
<td>Tuberosity</td>
<td>Large, rough projection</td>
</tr>
<tr>
<td>Openings and spaces</td>
<td>Canal</td>
<td>Passageway through a bone</td>
</tr>
<tr>
<td></td>
<td>Fissure</td>
<td>Narrow, slitlike opening through a bone</td>
</tr>
<tr>
<td></td>
<td>Foramen (pl., foramina)</td>
<td>Rounded passageway through a bone</td>
</tr>
<tr>
<td></td>
<td>Meatus</td>
<td>Passageway through a bone</td>
</tr>
<tr>
<td></td>
<td>Sinus</td>
<td>Cavity or hollow space in a bone</td>
</tr>
</tbody>
</table>

### General Structure Diagrams

- **Skull, anterior view**
  - **Trochanter**
  - **Sinus**
  - **Meatus**
  - **Canal**
  - **Foramen**
  - **Ramus**
  - **Alveolus**

- **Skull, sagittal view**
  - **Tubercle**
  - **Sulcus**
  - **Tuberosity**
  - **Humerus**
  - **Fossa**
  - **Epicondyle**
  - **Ramus**
  - **Foramen**
  - **Alveolus**

- **Pelvis**
  - **Facet**
  - **Crest**
  - **Fossa**
  - **Spine**
  - **Line**
  - **Foramen**
  - **Ramus**

- **Femur**
  - **Head**
  - **Trochanter**
  - **Epicondyle**
  - **Condyle**

- **Skull**
  - **Sinus**
  - **Meatus**
  - **Canal**
  - **Foramen**
  - **Ramus**
  - **Alveolus**

- **Humerus**
  - **Tubercle**
  - **Sulcus**
  - **Tuberosity**
  - **Fossa**
  - **Epicondyle**
  - **Ramus**
  - **Foramen**
  - **Alveolus**

**Figure 8.2 Bone Markings.** Specific anatomic terms describe the characteristic features on bones.
8.2 Bones and Features of the Skull

We begin our examination of the skeleton by discussing its most complex structure, the skull. The skull is made up of 22 bones. Here we describe the anatomy and landmarks of the skull, the sutures (a type of fibrous joint; see section 9.2) that connect the bones of the cranium, and the specialized features of the orbital and nasal complexes and paranasal sinuses.

8.2a General Anatomy of the Skull

LEARNING OBJECTIVE
3. Distinguish between the cranial and the facial bones.

The skull is composed of both cranial and facial bones. Cranial bones form the rounded cranium (krā’nē-um; kranion = skull), which completely surrounds and encloses the brain. The cranium consists of eight bones that form a roof and a base. The roof of the cranium, called the calvaria (kal-vā’rē-ā), is composed of part of the frontal bone, the parietal bones, and part of the occipital bone. The base of the cranium is composed of portions of the ethmoid, sphenoid, occipital, and temporal bones. Some skulls in the anatomy lab have had their calvariae cut away, making the distinction between the calvaria and base easier to distinguish.

Facial bones form the face. They also protect the entrances to the digestive and respiratory systems. Touch your cheeks, your jaws, and the bridge of your nose; these bones are facial bones. The facial bones give shape and individuality to the face, form part of the orbit and nasal cavities, support the teeth, and provide for the attachment of muscles involved in facial expression and mastication (chewing). There are 14 facial bones, including the paired zygomatic bones, lacrimal bones, nasal bones, inferior nasal conchae, palatine bones, maxillae, and unpaired vomer and mandible.

The skull contains several prominent cavities (figure 8.3). The largest is the cranial cavity (or endocranium) that encloses, protects, and supports the brain. (The volume of an

1Osteologists (scientists who study bones) define the cranium as the entire skull minus the mandible. In this text, we use the term cranium to denote the bones that directly surround the brain only.

---

Figure 8.3 Major Cavities of the Skull. A coronal section diagram highlights the cranial cavity, orbits, three of the four sets of paranasal sinuses, nasal cavity, and oral cavity.
adult cranial cavity ranges from approximately 1300 to 1500 cubic centimeters, which is about 50 fluid ounces.) The skull also forms and has several smaller cavities, including the orbits (eye sockets), the oral cavity, the nasal cavity, and the paranasal sinuses.

**WHAT DID YOU LEARN?**

1. What bones form the skull? Which of these bones are cranial bones? Which of these bones are facial bones?

**8.2b Views of the Skull and Landmark Features**

**LEARNING OBJECTIVES**

1. Identify the locations of cranial and facial bones in various views of the skull.
2. Learn key bone markings and features of each of the bones of the cranium.
3. Compare and contrast the locations and contents of three cranial fossae.

To best understand the complex nature of the skull, we first examine the skull as a whole and learn which bones are best seen from a particular view. Note that only some major features will be mentioned in this section. In table 8.2, we examine the individual skull bones in detail.

**WHAT DO YOU THINK?**

1. What is the benefit of the skull’s being made of multiple smaller bones, rather than one big bone?

A cursory glance at the skull reveals numerous bone markings, such as canals, fissures, and foramina that serve as passageways for blood vessels and nerves. The major foramina of the cranial and facial bones are summarized in table 8.1. Refer to this table as we examine the skull from various directions. (This table also will be important when we study cranial nerves in section 13.9 and blood vessels in section 20.10.)

<table>
<thead>
<tr>
<th>Table 8.1</th>
<th>Passageways Within the Skull</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Passageway</strong></td>
<td><strong>Location</strong></td>
</tr>
<tr>
<td>Carotid canal</td>
<td>Petrous part of temporal bone</td>
</tr>
<tr>
<td>Cribriform foramina</td>
<td>Cribriform plate of ethmoid bone</td>
</tr>
<tr>
<td>Foramen lacerum</td>
<td>Between petrous part of temporal bone, sphenoid bone, and occipital bone</td>
</tr>
<tr>
<td>Foramen magnum</td>
<td>Occipital bone</td>
</tr>
<tr>
<td>Foramen ovale</td>
<td>Greater wing of sphenoid bone</td>
</tr>
<tr>
<td>Foramen rotundum</td>
<td>Greater wing of sphenoid bone</td>
</tr>
<tr>
<td>Foramen spinosum</td>
<td>Greater wing of sphenoid bone</td>
</tr>
<tr>
<td>Hypoglossal canal</td>
<td>Anteromedial to occipital condyle of occipital bone</td>
</tr>
<tr>
<td>Inferior orbital fissure</td>
<td>Junction of maxilla, sphenoid, and zygomatic bones</td>
</tr>
<tr>
<td>Jugular foramen</td>
<td>Between temporal bone and occipital bone (posterior to carotid canal)</td>
</tr>
<tr>
<td>Mastoid foramen</td>
<td>Posterior to mastoid process of temporal bone</td>
</tr>
<tr>
<td>Optic canal</td>
<td>Posteromedial part of orbit in lesser wing of sphenoid bone</td>
</tr>
<tr>
<td>Parietal foramen</td>
<td>Parietal bone near sagittal suture</td>
</tr>
<tr>
<td>Stylostomastoid foramen</td>
<td>Between mastoid and styloid processes of temporal bone</td>
</tr>
<tr>
<td>Superior orbital fissure</td>
<td>Posterior part of orbit between greater and lesser wings of sphenoid bone</td>
</tr>
<tr>
<td>Supraorbital foramen or notch</td>
<td>Supraorbital margin of orbit in frontal bone</td>
</tr>
</tbody>
</table>

**CRANIAL BONES**

**FACIAL BONES**

| Greater and lesser palatine foramina | Palatine bone | Palatine vessels; greater and lesser palatine nerves (branches of CN V2) |
| Incisive foramen | Posterior to incisor teeth in hard palate of the maxilla | Nasopalatine nerve (branch of CN V2) |
| Infraorbital foramen | Inferior to orbit in maxilla | Infraorbital artery; infraorbital nerve (branch of CN V2) |
| Lacrimal groove | Lacrimal bone | Nasolacrimal duct |
| Mandibular foramen | Medial surface of ramus of mandible | Inferior alveolar blood vessels; inferior alveolar nerve (branch of CN V3) |
| Mental foramen | Inferior to second premolar on anterolateral surface of mandible | Mental blood vessels; mental nerve (branch of CN V3) |
Figure 8.4 Anterior View of the Skull. The frontal bone, nasal bones, maxillae, and mandible are prominent in this view.

Frontal bone
Parietal bone
Glabella
Supraorbital notch
Temporal bone
Sphenoid bone
Ethmoid bone
Lacrimal bone
Nasal bone
Infraorbital foramen
Zygomatic bone
Maxilla
Glabella
Supraorbital notch
Supraorbital margin
Mandible
Supraorbital foramen
Perpendicular plate of ethmoid bone
Vomer
Superior orbital fissure
Inferior orbital fissure
Supraorbital notch
Supraorbital margin
Nasal septum
Inferior nasal concha
Anterior nasal spine
Alveolar processes
Mental foramen
Mental protuberance
Anterior nasal spine
Alveolar processes
Mental foramen
Mental protuberance

Anterior view
Anterior View

An anterior view (figure 8.4) shows several major bones of the skull. The frontal bone forms the forehead. The left and right orbits (figure 8.3) are formed from a complex articulation of multiple skull bones. There are two large openings within each orbit called the superior orbital fissure and the inferior orbital fissure (figure 8.4). Superior to the orbits on the anterior surface of the frontal bone are the superciliary (sū-per-sil′-ē-ar-ē; super = above, cilium = eyelid) arches, otherwise known as the brow ridges. Male skulls tend to have larger and more pronounced superciliary arches than do female skulls. The left and right nasal bones form the bony bridge of the nose. Superior to the nasal bones and between the orbits is a landmark area called the glabella (glā-bel′ā; glabellus = smooth).

The left and right maxillae (mak-sil′ė; sing., maxilla, mak-sil′-ā; jawbone), also called maxillary bones, fuse in the midline to form most of the upper jaw and the lateral boundaries of the nasal cavity. The maxillae also help form a portion of both the floor of each orbit and the roof of the oral cavity. Inferior to each orbit in the maxilla is an infraorbital foramen, which is a passageway for blood vessels and nerves to the face.

The lower jaw is formed by the mandible. The prominent chin of the mandible is called the mental protuberance. The oral margins of the maxillae and mandible each have alveolar (al-vē′-ō-lār) processes that contain the teeth.

The nasal cavity is also seen in an anterior view. Its inferior border is marked by a prominent anterior nasal spine. The thin ridge of bone that divides the nasal cavity into left and right halves is called the nasal septum. Along the inferolateral walls of the nasal cavity are two scroll-shaped bones called the inferior nasal conchae (kon′kē; sing., concha, kon′kä; shell).

Superior View

The superior view of the skull in figure 8.5a primarily shows four of the cranial bones: the frontal bone, both parietal (pā-rī-tāl; paries = wall) bones, and the occipital (ok-sip′-i-tāl; occiput = back of head) bone. The articulation between the frontal and parietal bones is the coronal suture, so named because it runs along a coronal plane. The sagittal suture connects the left and right parietal bones along the midline of the skull.

Along the posterior one-third of the sagittal suture is either a single parietal foramen or paired parietal foramina, which serve as the passageway of small veins between the brain and the scalp. The lateral surface of each parietal bone exhibits a rounded, smooth area called the parietal eminence. The superior part of the lambdoid suture represents the articulation of the occipital bone with both parietal bones.

Posterior View

The posterior view of the skull in figure 8.5b shows a portion of the occipital, parietal, and temporal bones, as well as the lambdoid suture between the occipital and parietal bones. Within the lambdoid suture, there may be one or more sutural bones. The external occipital protuberance (prō-tū′ber-ans) is a prominence on the posterior aspect of the skull. Palpate the back of your head; males tend to have a prominent, pointed external occipital protuberance, whereas females have a more subtle, rounded protuberance. Intersecting the external occipital protuberance are two horizontal ridges, the superior and inferior nuchal (nu-kāl) lines (see figure 8.7).
A lateral view of the skull (figure 8.6) shows one parietal bone, temporal bone, and zygomatic (zi'gō-mat'ık; zygoma = a joining, a yoke) bone. This view also shows part of the maxilla, mandible, frontal bone, and occipital bone. The superior and inferior temporal

**Figure 8.6 Lateral View of the Skull.** The parietal, temporal, zygomatic, frontal, and occipital bones, as well as the maxilla and mandible, are prominent in this view. ©McGraw-Hill Education/Christine Eckel
lines are across the surface of the parietal and frontal bones and mark the attachment site of the temporalis muscle (see section 11.3c). The small lacrimal (lakˈriː-məl; lacrima = a tear) bone articulates with the maxilla anteriorly and with the ethmoid bone posteriorly. A portion of the sphenoid (sfeⁿˈɔid; wedge-shaped) bone articulates with the frontal, parietal, and temporal bones. This region is called the ptéridon (tēˈrē-on; ptéron = wing) and is circled on figure 8.6. Pterion includes the H-shaped set of sutures of these four articulating bones.

The temporal process of the zygomatic bone and the zygomatic process of the temporal bone fuse to form the zygomatic arch. Put your fingers along the bony prominences (“apples”) of your cheeks and move your fingers posteriorly toward your ears; you are feeling the zygomatic arch. The zygomatic arch terminates superior to the point where the mandible articulates with the mandibular (man-diˈbə-lər) fossa of the temporal bone. This articulation is called the temporomandibular joint (TMJ) and is described further in section 9.7a. By putting your finger anterior to your external ear opening and then opening and closing your jaw, you can feel that joint moving.

The squamous part of the temporal bone lies directly inferior to the squamous suture. Immediately posterolateral to the mandibular fossa is the tympanic (tim-panˈık; tympanon = drum) part of the temporal bone. This is a small, bony ring surrounding the external ear opening called the external acoustic meatus (mē-ˈtātəs; a passage), or external auditory canal (see section 16.5a). Inferior and posterior to this meatus is the mastoid (masˈtoyd; masto = breast, eidos = resemblance) process, the bump you feel behind your external ear opening. The styloid (stīˈloyd; stylos = pillar, post) process is a thin, pointed projection of bone located anteromedial to the mastoid process. It serves as an attachment site for several hyoid and tongue muscles (see section 11.3c).

Sagittal Sectional View

Cutting the skull along a sagittal sectional plane reveals bones that form the endocranium and the nasal cavity (figure 8.7a). The cranial cavity is formed from a complex articulation of the frontal, parietal, temporal, occipital, ethmoid (ethˈmōid; ethmos = sieve), and sphenoid bones. Vessel impressions may be visible on the internal surface of the skull. The frontal sinus (a space within the frontal bone) and the sphenoidal sinus (open space within the sphenoid bone) are visible in a sagittal view.

A sagittal sectional view also shows the bones that form the nasal septum more clearly. The perpendicular plate of the ethmoid forms the posterosuperior portion of the nasal septum, whereas the vomer (vōˈmer; plowshare) forms the posteroinferior portion. (The anterior part of the nasal septum is cartilaginous.) The ethmoid bone serves as the division between the anterior floor of the cranial cavity and the roof of the nasal cavity. The palatine process of the maxillae and the palatine (palˈa-tı-n) bones form the hard palate (figure 8.7b), which acts as both the floor of the nasal cavity and a portion of the roof of the mouth. Move your tongue along the roof of your mouth; you are palpating the maxillae anteriorly and palatine bones posteriorly.

Inferior (Basal) View

In an inferior (basal) view, the most anterior structure is the hard palate (figure 8.7b). On the posterior aspect of either side of the palate are the medial and lateral pterygoid (terˈi-goyd; pteryx = winglike) plates of the sphenoid bone. Together, both plates form a pterygoid process. Medially adjacent to these structures are the internal openings of the nasal cavity, called the choanae (kōˈan-ē; sing., choana, kōˈan-ə; funnel).

Between the mandibular fossa and the pterygoid processes are several paired foramina and canals. Typically, these openings provide passage for specific blood vessels and nerves. For example, the jugular (jūgˈə-lər; jugulum = throat) foramen is an opening between the temporal and occipital bones that provides a passageway for the internal jugular vein and several nerves. The foramen lacerum (anteromedial to the carotid canal) extends between the occipital and temporal bones. This opening is covered by cartilage in a living individual. The entrance to the carotid (ka-rotˈid; karoo = to put to sleep) canal is anteromedial to the jugular foramen; the internal carotid artery passes through this canal.

The stylomastoid foramen lies between the mastoid process and the styloid process. The facial nerve (CN VII) extends through the stylomastoid foramen to innervate the facial muscles (see sections 11.3a and 13.9).

The largest foramen of all is the foramen magnum, literally meaning big hole. Through this opening, the spinal cord enters the cranial cavity and is continuous superiorly with the brainstem. On either side of the foramen magnum are the rounded occipital condyles, which articulate with the first cervical vertebra of the vertebral column. At the anteromedial edge of each condyle is a hypoglossal canal through which the hypoglossal nerve (CN XII) extends to innervate tongue muscles (see sections 11.3c and 13.9).
Figure 8.7 Sagittal Section and Inferior View of the Skull. (a) Features such as the perpendicular plate of the ethmoid bone, the vomer, and the frontal and sphenoidal sinuses, as well as the internal relationships of the skull bones, are best seen in sagittal section. (b) The hard palate, the sphenoid bone, parts of the temporal bone, and the occipital bone with its foramen magnum may be seen in the inferior view.
Internal View of Cranial Base
When the top of the skull is cut and removed, the internal view of the cranial base (figure 8.8) is revealed. Here we see the frontal bone surrounding the delicate cribriform (krib’ri-form; cribrum = sieve, forma = form) plate of the ethmoid bone. The plate has numerous perforations called the cribriform foramina, which provide passageways for the olfactory nerves (CN I; see sections 13.9 and 16.3a) into the superior portion of the nasal cavity. The anteromedial part of the cribriform plate exhibits a midsagittal elevation called the crista galli (kris’tâ = crest; gal’lë = of a rooster), to which the cranial dural septa of the brain attach (see section 13.2a).

The relatively large sphenoid is located posterior to the frontal bone. It is often referred to as a “bridging bone” because it unites the cranial and facial bones. The lateral expansions of the sphenoid bone are called the greater wings and the lesser wings of the sphenoid. The pituitary gland (see section 17.7a) is suspended inferiorly from the brain into a prominent midline depression between the greater and lesser wings. This depression is termed the hypophyseal fossa, and the bony enclosure around the hypophyseal fossa is called the sella turcica (sel’â = saddle; tur’si-ka = Turkish). Anterior to the sella turcica are the optic canals through which the optic nerves (CN II) extend from the eyes in the orbits to the brain (figure 8.8).

The lateral regions of the cranial base are formed by the petrous (pet’rûs; petra = a rock) part of each temporal bone, whereas the posterior region is formed by the occipital bone. The internal acoustic meatus (also called the internal auditory canal) opens in the more medial portion of the temporal bone and contains the facial nerve (CN VII) and the vestibulocochlear nerve (CN VIII; see section 13.9).

An internal landmark of the occipital bone is the internal occipital protuberance. The internal occipital crest extends from the protuberance to the posterior border of the foramen magnum. Large grooves along the internal aspect of the cranium are formed from impressions from the dural venous sinuses of the brain that lie within them (see section 13.2a).

Each bone of the cranium has specific surface features, and each specific bone is shown and summarized in table 8.2. The facial bones are summarized in table 8.3.
## Table 8.2 Cranial Bones and Selected Features

<table>
<thead>
<tr>
<th>(a) Frontal Bone</th>
<th>(b) Parietal Bone</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Associated Passageways</strong></td>
<td><strong>Associated Passageways</strong></td>
</tr>
<tr>
<td>Supraorbital foramen or notch</td>
<td>Parietal foramen</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Description and Boundaries of Bone</strong></th>
<th><strong>Description and Boundaries of Bone</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Forms the superior and anterior parts of the skull; part of anterior cranial fossa and orbit</td>
<td>Each forms most of lateral and superior walls of the skull</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Selected Features and Their Functions</strong></th>
<th><strong>Selected Features and Their Functions</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Frontal crest</strong>: Attachment site for meninges to help stabilize brain within the skull</td>
<td>Superior and inferior temporal lines: Attachment sites for temporalis muscle</td>
</tr>
<tr>
<td><strong>Frontal sinuses</strong>: Lighten bone, moisten inhaled air, and give resonance to voice</td>
<td><strong>Parietal eminence</strong>: Forms rounded prominence on each side of the skull</td>
</tr>
<tr>
<td><strong>Orbital part</strong>: Forms roof of orbit</td>
<td><strong>Squamous part</strong>: Attachment of scalp muscles</td>
</tr>
<tr>
<td><strong>Squamous part</strong>: Forms protective superior border of orbit</td>
<td><strong>Supraorbital margin</strong>: Forms protective superior border of orbit</td>
</tr>
<tr>
<td><strong>Zygomatic process</strong>: Articulates with zygomatic bone</td>
<td><strong>Zygomatic process</strong>: Articulates with zygomatic bone</td>
</tr>
</tbody>
</table>

---

1. Not all features listed in the table may be shown in the accompanying art; please also refer to figures 8.3–8.8 in this chapter.
### (c) Temporal Bone [AP R]

<table>
<thead>
<tr>
<th>Associated Passageways</th>
<th>Description and Boundaries of Bone</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stylomastoid foramen</td>
<td>Each forms inferolateral wall of the skull; forms part of middle cranial fossa. Three parts are included below.</td>
</tr>
<tr>
<td>Carotid canal</td>
<td></td>
</tr>
<tr>
<td>External acoustic meatus</td>
<td></td>
</tr>
<tr>
<td>Internal acoustic meatus</td>
<td></td>
</tr>
<tr>
<td>Mastoid foramen</td>
<td></td>
</tr>
<tr>
<td>Jugular foramen (with occipital bone)</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Selected Features and Their Functions¹</th>
<th>External occipital condyles: Articulate with first cervical vertebra</th>
</tr>
</thead>
<tbody>
<tr>
<td>Petrous part: Protects sensory structures in inner ear</td>
<td></td>
</tr>
<tr>
<td>Squamous part: Attachment site of some jaw muscles</td>
<td></td>
</tr>
<tr>
<td>Tympanic part: Houses external acoustic meatus</td>
<td></td>
</tr>
<tr>
<td>Mastoid process: Attachment site of some neck muscles to extend or rotate head</td>
<td></td>
</tr>
<tr>
<td>Styloid process: Attachment site for hyoid bone ligaments and muscles</td>
<td></td>
</tr>
<tr>
<td>Zygomatic process: Articulates with zygomatic bone to form zygomatic arch</td>
<td></td>
</tr>
<tr>
<td>Mandibular fossa: Articulates with mandible</td>
<td></td>
</tr>
<tr>
<td>Articular tubercle: Limits displacement of head of mandible within mandibular fossa</td>
<td></td>
</tr>
</tbody>
</table>

¹ Not all features listed in the table may be shown in the accompanying art; please also refer to figures 8.3–8.8 in this chapter.

### (d) Occipital Bone [AP R]

<table>
<thead>
<tr>
<th>Associated Passageways</th>
<th>Description and Boundaries of Bone</th>
</tr>
</thead>
<tbody>
<tr>
<td>Foramen magnum</td>
<td>Forms posteroinferior part of the skull, including most of posterior cranial fossa; forms part of base of the skull</td>
</tr>
<tr>
<td>Hypoglossal canal</td>
<td></td>
</tr>
<tr>
<td>Jugular foramen (with temporal bone)</td>
<td></td>
</tr>
<tr>
<td>Condylar canal</td>
<td></td>
</tr>
</tbody>
</table>

| Selected Features and Their Functions¹ |                                                                      |
| External occipital crest: Attachment site for ligaments                  |                                                                      |
| External occipital protuberance: Attachment site for neck ligaments and muscles |                                                                      |
| Inferior and superior nuchal lines: Attachment sites for neck ligaments and muscles |                                                                      |
| Occipital condyles: Articulate with first cervical vertebra              |                                                                      |
### Table 8.2 Cranial Bones and Selected Features1 (continued)

<table>
<thead>
<tr>
<th>Sphenoid Bone</th>
<th>Ethmoid Bone</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Associated Passageways</strong></td>
<td><strong>Associated Passageways</strong></td>
</tr>
<tr>
<td>Foramen lacerum (with temporal and occipital bones)</td>
<td>Cribriform foramina</td>
</tr>
<tr>
<td>Foramen ovale</td>
<td></td>
</tr>
<tr>
<td>Foramen rotundum</td>
<td></td>
</tr>
<tr>
<td>Foramen spinosum</td>
<td></td>
</tr>
<tr>
<td>Optic canal</td>
<td></td>
</tr>
<tr>
<td>Pterygoid canal</td>
<td></td>
</tr>
<tr>
<td>Superior orbital fissure</td>
<td></td>
</tr>
<tr>
<td><strong>Description and Boundaries of Bone</strong></td>
<td><strong>Description and Boundaries of Bone</strong></td>
</tr>
<tr>
<td>Forms part of the base of the skull; posterior part of orbit; part of anterior and middle cranial fossae</td>
<td>Forms part of anterior cranial fossa; part of nasal septum, roof and lateral walls of nasal cavity; part of medial wall of orbit</td>
</tr>
<tr>
<td><strong>Selected Features and Their Functions</strong>¹</td>
<td><strong>Selected Features and Their Functions</strong>¹</td>
</tr>
<tr>
<td>Hypophyseal fossa: Depression that houses pituitary gland</td>
<td>Cribriform plate: Contains cribriform foramina for passageway of olfactory nerves (CN I)</td>
</tr>
<tr>
<td>Body: Houses sphenoidal sinuses</td>
<td>Crista galli: Attachment site for cranial dural septa to help stabilize brain within the skull</td>
</tr>
<tr>
<td>Sella turcica: Bony enclosure around hypophyseal fossa</td>
<td>Ethmoidal labyrinth: Contain ethmoidal sinuses and nasal conchae</td>
</tr>
<tr>
<td>Optic groove: Depression on body between the optic canals</td>
<td>Ethmoidal sinuses (cells): Lighten bone, moisten inhaled air, and give resonance to voice²</td>
</tr>
<tr>
<td>Medial and lateral pterygoid plates: Attachment sites for chewing muscles</td>
<td>Nasal conchae (superior and middle): Increase airflow turbulence through nasal cavity so air can be adequately moistened and cleaned by nasal mucosa</td>
</tr>
<tr>
<td>Lesser wings: Form part of anterior cranial fossa; contain optic canals</td>
<td>Orbital plate: Forms part of medial wall of orbit</td>
</tr>
<tr>
<td>Greater wings: Form part of middle cranial fossa, lateral surface of skull, and orbits</td>
<td>Perpendicular plate: Forms superior part of nasal septum</td>
</tr>
<tr>
<td>Sphenoidal sinuses: Lighten bone, moisten inhaled air, and give resonance to voice²</td>
<td></td>
</tr>
</tbody>
</table>

1. Not all features listed in the table may be shown in the accompanying art; please also refer to figures 8.3–8.8 in this chapter.
2. See figure 8.13.
<table>
<thead>
<tr>
<th>Table 8.3</th>
<th>Facial Bones and Selected Features¹</th>
</tr>
</thead>
<tbody>
<tr>
<td>(a) Zygomatic Bone</td>
<td>(b) Lacrimal Bone</td>
</tr>
<tr>
<td>Associated Passageways</td>
<td>None</td>
</tr>
<tr>
<td>Description and Boundaries of Bone</td>
<td>Each forms a cheek and lateral part of the orbit</td>
</tr>
<tr>
<td>Selected Features and Their Functions</td>
<td>Frontal process: Articulates with frontal bone</td>
</tr>
<tr>
<td></td>
<td>Temporal process: Articulates with temporal bone to form zygomatic arch</td>
</tr>
<tr>
<td></td>
<td>Maxillary process: Articulates with maxilla</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>(c) Vomer</th>
<th>(d) Inferior Nasal Concha</th>
</tr>
</thead>
<tbody>
<tr>
<td>Associated Passageways</td>
<td>None</td>
</tr>
<tr>
<td>Description and Boundaries of Bone</td>
<td>Forms inferior and posterior part of nasal septum</td>
</tr>
<tr>
<td>Selected Features and Their Functions</td>
<td>Ala: Articulates with sphenoid bone</td>
</tr>
<tr>
<td></td>
<td>Vertical plate: Articulates with perpendicular plate of ethmoid bone</td>
</tr>
</tbody>
</table>

¹ Nasal bones are not in the table and are shown on figures 8.4 and 8.6.
Table 8.3  Facial Bones and Selected Features\(^1\) (continued)

<table>
<thead>
<tr>
<th>(e) Palatine Bone</th>
<th>(f) Maxilla</th>
<th>Associated Passageways</th>
<th>Description and Boundaries of Bone</th>
<th>Description and Boundaries of Bone</th>
<th>Associated Passageways</th>
<th>Description and Boundaries of Bone</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Greater and lesser palatine foramina</td>
<td>Each forms posterior part of hard palate; also forms small part of nasal cavity and orbit wall</td>
<td>Each forms anterior portion of face; upper jaw and parts of hard palate, inferior parts of orbits, and part of the walls of nasal cavity</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Horizontal plate: Forms posterior part of hard palate</td>
<td></td>
<td>Anterior nasal spine: Anterior projection formed by union of left and right maxillae</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Perpendicular plate: Forms part of nasal cavity and orbit</td>
<td></td>
<td>Alveolar process: Houses the teeth</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Frontal process: Forms part of lateral aspect of the nasal bridge</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Infraorbital margin: Forms inferolateral border of orbit</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Maxillary sinus: Lightens bone</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Orbital surface: Forms part of orbit</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Palatine process: Forms most of bony palate</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Zygomatic process: Articulates with zygomatic bone</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

\(^1\) Not all features listed in the table may be shown in the accompanying art; please refer to figures 8.3–8.8 in this chapter.
**Table 8.3**

<table>
<thead>
<tr>
<th>Passageways Associated with Boundaries and Description</th>
<th>Functions</th>
<th>Their Features and Selected Features of Bone</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Palatine Bone</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Greater and lesser palatine foramina, part of nasal cavity and orbit wall</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Forms part of nasal cavity and orbit</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

1. **Right maxilla, lateral view**

<table>
<thead>
<tr>
<th>Structures</th>
<th>Functions and Position</th>
</tr>
</thead>
<tbody>
<tr>
<td>Palatine process</td>
<td>Forms most of bony palate</td>
</tr>
<tr>
<td>Orbital surface</td>
<td>Forms part of orbit</td>
</tr>
<tr>
<td>Maxillary sinus</td>
<td>Lightens bone</td>
</tr>
<tr>
<td>Infraorbital margin</td>
<td>Forms inferolateral border of orbit</td>
</tr>
<tr>
<td>Frontal process</td>
<td>Forms part of lateral aspect of the nasal bridge</td>
</tr>
<tr>
<td>Alveolar process</td>
<td>Houses the teeth</td>
</tr>
<tr>
<td>Anterior nasal spine</td>
<td>Articulates with zygomatic bone</td>
</tr>
</tbody>
</table>

1. **Medial view**

<table>
<thead>
<tr>
<th>Structures</th>
<th>Functions and Position</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alveolar process</td>
<td>Houses the teeth</td>
</tr>
<tr>
<td>Zygomatic process</td>
<td>Forms part of lateral aspect of the nasal bridge</td>
</tr>
<tr>
<td>Anterior nasal spine</td>
<td>Articulates with zygomatic bone</td>
</tr>
<tr>
<td>Orbital surface</td>
<td>Forms part of orbit</td>
</tr>
<tr>
<td>Infraorbital margin</td>
<td>Forms inferolateral border of orbit</td>
</tr>
<tr>
<td>Frontal process</td>
<td>Forms part of lateral aspect of the nasal bridge</td>
</tr>
</tbody>
</table>

1. **Maxilla**

<table>
<thead>
<tr>
<th>Structures</th>
<th>Functions and Position</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mandibular foramen</td>
<td>Forms the lower jaw</td>
</tr>
</tbody>
</table>

1. **Mandible**

<table>
<thead>
<tr>
<th>Structures</th>
<th>Functions and Position</th>
</tr>
</thead>
<tbody>
<tr>
<td>Head of mandible</td>
<td>Forms the chin</td>
</tr>
<tr>
<td>Angle of the mandible</td>
<td>Junction between the body and ramus</td>
</tr>
<tr>
<td>Ramus (rą’məs)</td>
<td>Vertical portion of mandible</td>
</tr>
<tr>
<td>Mental protuberance</td>
<td>U-shaped depression between coronoid and condylar processes</td>
</tr>
<tr>
<td>Condylar process</td>
<td>Articulates with temporal bone</td>
</tr>
<tr>
<td>Coronoid process</td>
<td>Anterior projection off ramus</td>
</tr>
<tr>
<td>Mandibular foramen</td>
<td>Houses the teeth</td>
</tr>
<tr>
<td>Alveolar process</td>
<td>Houses the teeth</td>
</tr>
</tbody>
</table>

**CLINICAL VIEW 8.1 Cleft Lip and Palate**

A **cleft lip** is the incomplete fusion of upper jaw components of the developing embryo, resulting in a split upper lip extending from the mouth to the side of one nostril. Cleft lip appears in 1 per 1000 births and tends to be more common in males. The etiology of cleft lip is multifactorial, in that both genetic and environmental factors (such as cigarette smoking or alcohol ingestion during pregnancy) appear to contribute to the condition.

Another anomaly that can develop is **cleft palate**, a congenital fissure in the midline of the palate. A cleft palate results when the left and right maxillary and palatine bones fuse incompletely or do not fuse at all. In the more severe cases, children have swallowing and feeding problems because food can easily pass from the oral cavity into the nasal cavity. Cleft palate occurs in about 1 per 2500 births and tends to be more common in females. Like cleft lip, the etiology of cleft palate is multifactorial. Cleft palate sometimes occurs in conjunction with cleft lip.

**Figure 8.9 Internal Bones of the Skull**

Several bones of the skull, such as the ethmoid and sphenoid, are primarily located deep to other bones. This figure illustrates the positioning of these internal bones, relative to the externally placed skull bones.

Articulations of selected cranial and facial bones that are obscured by more superficial bones are shown in **figure 8.9**.
Cranial Fossae

The contoured floor of the cranial cavity exhibits three curved depressions called the cranial fossae (figure 8.10).

The anterior cranial fossa is the shallowest of the three depressions. It is formed by the frontal bone, the ethmoid bone, and the lesser wings of the sphenoid bone. The anterior cranial fossa houses the frontal lobes of the brain (see section 13.3b).

The middle cranial fossa is inferior and posterior to the anterior cranial fossa. It ranges from the posterior edge of the lesser wings of the sphenoid bone (anteriorly) to the anterior region of the petrous part of the temporal bone (posteriorly). It houses the temporal lobes of the brain and the pituitary gland.

The posterior cranial fossa is the most inferior and posterior cranial fossa and extends from the posterior region of the petrous part of the temporal bones to the occipital bone. This fossa supports part of the brainstem and the cerebellum (see sections 13.5 and 13.6).

WHAT DID YOU LEARN?

4. What bones may be prominently seen in an anterior view of the skull?

5. What bones form the middle cranial fossa, and which part of the brain resides in this fossa?

8.2c Sutures

LEARNING OBJECTIVE

7. Describe the locations of the sutures between the cranial bones.

Sutures (sūˈchər; sutura = a seam) are immovable fibrous joints (see section 9.2b) that form the boundaries between the cranial bones (see figures 8.5–8.7). Dense regular connective tissue connects cranial bones firmly together at a suture. The sutures often have intricate, interlocking forms resembling puzzle pieces.

Numerous sutures are present in the skull, each with a specific name. Many of the smaller sutures are named for the bones or features they interconnect. For example, the occipitomastoid suture connects the occipital bone with the portion of the temporal bone that houses the mastoid process. Here we discuss only the largest sutures—the coronal, lambdoid, sagittal, and squamous sutures:
• The **coronal** (kō-rō’nal; coron = crown) **suture** extends laterally across the superior surface of the skull along a coronal plane. It represents the articulation between the anterior frontal bone and the more posterior parietal bones.

• The **lambdoid** (lam’doyd) **suture** extends like an arc across the posterior surface of the skull. This suture is the site where the parietal bones and the occipital bone articulate. It is named for the Greek letter lambda, which its shape resembles.

• The **sagittal** (sa’j-i-tāl; sagitta = arrow) **suture** extends between the coronal and lambdoid sutures along the midsagittal plane. It is the site where the right and left parietal bones articulate.

• A **squamous** (skwā’mus) **suture** (or squamosal suture) on each side of the skull is the site where the temporal bone and the parietal bone of that side articulate. The squamous part of the temporal bone typically overlaps the parietal bone.

One common variation in sutures is the presence of **sutural bones** (Wormian bones) (see figure 8.5b). Sutural bones may range in size from a tiny pebble to a quarter, but they can be much larger. Sutural bones represent independent bone ossification centers and are most common and numerous in the lambdoid suture.

In adulthood, the sutures typically are obliterated (closed) as the adjoining bones fuse. This fusion starts internally and is followed by fusion on the skull’s external surface. Although the timing of suture closure can be highly variable, the coronal suture typically is the first to fuse, usually in the late 20s to early 30s, followed by the sagittal suture (usually in the 30s or later) and then the lambdoid suture (usually in the 40s). The squamous suture usually does not fuse until late adulthood (60-plus years), or it may not fuse at all. Osteologists can estimate the approximate age at death of an individual by examining the extent of suture closure in the skull.

**WHAT DID YOU LEARN?**

What bones articulate at the lambdoid suture? When does this suture typically fuse?

---

**CLINICAL VIEW 8.2**

**Craniosynostosis and Plagiocephaly**

**Sagittal synostosis**

Dr. John A. Jane, Sr., David D. Weaver
Professor of Neurosurgery, Department of Neurological Surgery, University of Virginia Health System, Charlottesville, Virginia

**Coronal synostosis**

Dr. John A. Jane, Sr., David D. Weaver
Professor of Neurosurgery, Department of Neurological Surgery, University of Virginia Health System, Charlottesville, Virginia

Sutures in the skull allow the cranium to grow and expand during childhood. In adulthood, when cranial growth has stopped, the sutures fuse and are obliterated. **Craniosynostosis** (krä’né-o-sin’os-tō’sis) refers to the premature fusion or closing of one or more of these cranial sutures. If this premature fusion occurs early in life or in utero, skull shape is dramatically affected. If not surgically treated, a craniosynostotic individual often grows up with an unusual craniofacial shape. For example, if the sagittal suture fuses prematurely (a condition called **sagittal synostosis**), the skull cannot grow and expand laterally as the brain grows, and compensatory skull growth occurs in an anterior-posterior fashion. A child with sagittal synostosis develops a very elongated, narrow skull shape, a condition called **scaphocephaly**, or **dolichocephaly**. **Coronal synostosis** refers to premature fusion of the coronal suture, which causes the skull to be abnormally short and wide.

**Plagiocephaly** is the term used to describe an asymmetric head shape, where one part of the skull (usually the frontal or occipital region) has an oblique flattening. Plagiocephaly may be caused by unilateral coronal craniosynostosis or asymmetric lambdoid synostosis. It also is commonly caused by normal deformational factors, such as consistently sleeping on the same side of the head. Incidence of plagiocephaly has risen in the United States since the 1990s, primarily due to the National Institute of Child Health and Human Development Safe to Sleep Campaign (formerly called the Back to Sleep Campaign), which encourages parents to place children on their backs to sleep (instead of on their stomachs) so as to reduce the incidence of SIDS. Mild forms of plagiocephaly may be corrected by wearing a corrective helmet; more severe forms may necessitate surgery.

---

**Plagiocephaly**

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8.2d Orbital and Nasal Complexes, Paranasal Sinuses

LEARNING OBJECTIVES

8. List the bones that form the orbital and nasal complexes.
9. Describe the location and function of the paranasal sinuses.

The bony cavities called orbits enclose and protect the eyes and the muscles that move them. The orbital complex consists of seven bones that form each orbit. The borders of the orbital complex are shown and listed in Figure 8.11.

The nasal complex is composed of bones and cartilage that enclose the nasal cavity and the paranasal sinuses (see section 23.2a). Most of these bones are best seen in sagittal section, as shown in Figure 8.12.

Figure 8.11 Left Orbit. Several bones compose the orbit of the eye and collectively form the orbital complex.
Chapter Eight  Skeletal System: Axial and Appendicular Skeleton  261

We have already described the ethmoidal, frontal, maxillary, and sphenoidal sinuses in connection with the bones where they are located. As a group, these air-filled chambers that open into the nasal cavities are called the paranasal sinuses (figure 8.13). The term paranasal refers to their being located adjacent to the nasal cavity. The sinuses have a mucous membrane lining that helps to humidify and warm inhaled air. Additionally, the sinus spaces reduce the weight of the skull bones in which they are located, and they provide resonance to the voice.

**WHAT DID YOU LEARN?**

7. What bones form the floor of the orbit?

8. In which four bones are the paranasal sinuses located?

---

### INTEGRATE

**CONCEPT CONNECTION**

The respiratory system could not function as effectively were it not for the paranasal sinuses (see section 23.2b) housed within selected skull bones. We would not be able to efficiently warm and humidify inhaled air, and our voices would sound dramatically different without these sinuses. When you speak while holding your nose, you can tell that your voice sounds different—that is because the sounds aren’t resonating in your paranasal sinuses.

---

**WHAT DID YOU LEARN?**

9. What are the names of the auditory ossicles, and in which specific bone are they found?

---

#### 8.3 Bones Associated with the Skull

**LEARNING OBJECTIVES**

10. Locate and identify the auditory ossicles.

11. Describe the structure and function of the hyoid bone.

The auditory ossicles and the hyoid bone are bones of the axial skeleton associated with the skull. **Auditory ossicles** (os′i-kl) are three tiny ear bones housed within the petrous part of each temporal bone. These bones—the **malleus** (mal′e-us), the **incus** (ing′kūs), and the **stapes** (stā′pēz)—are discussed in detail in section 16.5a.

The **hyoid bone** is a slender, curved bone located inferior to the skull between the mandible and the larynx (voice box) (figure 8.14). It does not articulate with any other bone in the skeleton. The hyoid has a medial **body** and two paired, hornlike processes, the **greater cornua** (kor′nū-ä = horn; sing. **cornu**, kōr′nū) and the **lesser cornua**. The cornua and body serve as attachment sites for tongue and anterior neck muscles and ligaments (see section 11.3d).

---

**Figure 8.13 Paranasal Sinuses.** The paranasal sinuses are air-filled chambers within the frontal, ethmoid, and sphenoid bones and the maxillae. They are shown in (a) anterior and (b) lateral views. They are lined with a mucous membrane and are connected by ducts to the nasal cavity.

**Figure 8.14 Hyoid Bone.** The hyoid bone is inferior to the mandible and is not in direct contact with any other bone.
8.4 Sex and Age Determination from Analysis of the Skull

The skull can provide insight into the sex and age of an individual. We first describe some diagnostic features of the skull used to determine the sex of an individual. Then we compare how the skull changes through the fetal period, childhood, early adulthood, and old age.

8.4a Sex Differences in the Skull

**LEARNING OBJECTIVE**

12. Identify the similarities and differences between male and female skulls.

Human female and male skulls display some obvious differences in general shape and size, a phenomenon known as sexual dimorphism. Typical “female” features tend to be gracile (delicate, small), whereas “male” features tend to be more robust (larger, sturdier, bulkier). Table 8.4 summarizes the general sex differences seen in the skull.

However, caution is required when a skull and other skeletal remains are used to determine an individual’s sex. Both skeletons and skeletal features vary in their general size and robusticity among populations. For example, some male Asian skeletal remains may be less robust than those of a female Native American. Further, it often is difficult or impossible to determine the sex of infant and juvenile remains, because skull characteristics appear female-like until well after puberty.

The most accurate method of determining sex is to look at multiple skeletal features and make a judgment based on the majority of features present. For example, if a skull displays two female-like characteristics and four male-like characteristics, the skull will likely be classified as male. If your anatomy lab uses real skulls, use Table 8.4 to try to determine the sex of the skull you are studying.

**WHAT DO YOU THINK?**

It is difficult to determine the sex of a young child’s skull because both male and female skulls at this stage of development appear female-like. What factors do you think cause those features to change in males by adulthood?

**WHAT DID YOU LEARN?**

What are some features that differ between female and male skulls?

8.4b Aging of the Skull

**LEARNING OBJECTIVES**

13. Compare the structure of fetal, child, and adult skulls.
14. List the fontanelles and the ages at which they close.

The shape and structure of cranial elements differ between infants and adults, causing variations in their proportions and size. The most significant growth in the skull occurs before age 5, when the brain is still growing and exerting pressure against the developing skull bones’ internal surface. Brain growth is 90–95% complete by age 5, at which time cranial bone growth is close to completion, and the cranial sutures are almost fully developed. Note that early in life the skull grows at a much faster rate than does the rest of the body. Thus, a young child’s cranium is relatively larger compared to the rest of its body than that of an adult.
## Table 8.4
### Sex Differences in the Skull

<table>
<thead>
<tr>
<th>View</th>
<th>Female Skull Characteristic</th>
<th>Male Skull Characteristic</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Anterior View</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>General size and appearance</td>
<td>More gracile (delicate and small); less prominent muscle markings</td>
<td>More robust (big and bulky); more prominent muscle markings</td>
</tr>
<tr>
<td>Nuchal lines and external occipital protuberance</td>
<td>External surface of occipital bone is relatively smooth, with no major bony projections; external occipital protuberance is rounded</td>
<td>Well-demarcated nuchal lines and a prominent bump or “hook” for external occipital protuberance</td>
</tr>
<tr>
<td>Mastoid process</td>
<td>Relatively small</td>
<td>Large, may project inferior to external acoustic meatus</td>
</tr>
<tr>
<td>Squamous part of frontal bone</td>
<td>Usually more vertically oriented and rounded than males</td>
<td>Exhibits a sloping angle</td>
</tr>
<tr>
<td>Supraorbital margin</td>
<td>Thin, sharp border</td>
<td>Thick, rounded, blunt border</td>
</tr>
<tr>
<td>Superciliary arches</td>
<td>Little or no prominence</td>
<td>More prominent and bulky</td>
</tr>
<tr>
<td>Mandible (general features)</td>
<td>Smaller and lighter</td>
<td>Larger, heavier, more robust</td>
</tr>
<tr>
<td>Mental protuberance</td>
<td>More pointed and triangular-shaped, less forward projection</td>
<td>Squarish, more forward projection</td>
</tr>
<tr>
<td>Mandibular angle</td>
<td>Typically greater than 125 degrees</td>
<td>Typically less obtuse and less than 125 degrees (closer to 90 degrees); angle edges may flare outward</td>
</tr>
</tbody>
</table>

*(photos): (top left, top right, bottom left, bottom right) ©McGraw-Hill Education/Christine Eckel*
A neonatal (infant) cranium is shown in lateral and superior views in figure 8.15. The infant’s cranial bones are not yet large enough to surround the brain completely, so some cranial bones are interconnected by flexible areas of dense regular connective tissue in regions called fontanelles (fon′t˘ a-nel = little spring; sometimes spelled fontanels). Fontanelles are sometimes referred to as the “soft spots” on a baby’s head. The fontanelles enable some flexion in the bony plates within the skull during birth, thus allowing the child’s head to pass through the birth canal to ease the baby’s passage (see section 29.6d). Newborns frequently have a “cone-shaped” head due to this temporary deformation, but the cranial bones usually return to their normal position by a few days after birth. Some fontanelles, such as the small mastoid and sphenoidal fontanelles, close relatively quickly after birth. However others are present until many months after birth, when skull bone growth finally starts to keep pace with brain growth. The posterior fontanelle normally closes around 9 months of age; the larger anterior fontanelle doesn’t close until about 15 months of age.

The skull undergoes many more changes as we age. The maxillary sinus becomes more prominent after age 5, and by age 10 the frontal sinus is becoming well formed. Later, the cranial sutures start to fuse and ossify. As a person ages, the teeth start to wear down from dental attrition. Finally, if an individual loses some or all of his or her teeth, the alveolar processes of the maxillae and mandible regress and eventually disappear.

WHAT DID YOU LEARN?

What are the two largest fontanelles, and when do they disappear?

8.5 Bones of the Vertebral Column

The adult vertebral column is composed of 26 bones, including 24 individual vertebrae (ver′t˘ e-br˘ e; sing., vertebra, ver′t˘ e-br˘ a) and the fused vertebrae that form both the sacrum and the coccyx. Each vertebra (except the first and the last) articulates with one superior vertebra and one inferior vertebra. Here we consider the vertebral column’s general function and regions, the curves of the spine, anatomy of a generalized vertebra, and anatomic details of the components of the five regions of the vertebral column.

8.5a Types of Vertebrae

LEARNING OBJECTIVES

15. Describe the functions of the vertebral column.
16. List the five types of vertebrae.

The vertebral column provides vertical support for the body and supports the weight of the head. It helps maintain an upright body position. Most important, it houses and protects the delicate spinal cord.

The vertebral column is partitioned into five divisions, or regions (figure 8.16). Vertebrae are identified by using a capital letter to denote their region, followed by a numerical subscript that indicates their sequence, going from a superior to an inferior location:

- Seven cervical (ser′vi-kal; cervix = neck) vertebrae (designated C₁–C₇) form the bones of the neck (cervical region). The first cervical vertebra (C₁) articulates superiorly with the occipital condyles of the skull. The seventh cervical vertebra articulates inferiorly with the first thoracic vertebra.
- Twelve thoracic vertebrae (designated T₁–T₁₂) form the superior region of the back (thoracic region). Each thoracic vertebra articulates laterally with one or two pairs of ribs. The twelfth thoracic vertebra articulates inferiorly with the first lumbar vertebra.
- Five lumbar vertebrae (designated L₁–L₅) form the inferior concave region (“small”) of the back (lumbar region). The fifth lumbar vertebra articulates inferiorly with the first sacral vertebra.
- The sacrum (sä′kr˘ ūm) is formed from five sacral vertebrae (designated S₁–S₅) that fuse into a single bony structure by the mid to late 20s. The sacrum articulates with L₅ superiorly, the first coccygeal vertebra inferiorly, and laterally with the two osa coxae (hip bones).
- The coccyx (kok′siks) is commonly called the tailbone and is formed from four coccygeal vertebrae (designated C₀–C₄) that start to unite during puberty and is complete by the
mid 20s. The first coccygeal vertebra (Co₁) articulates with the inferior end of the sacrum. In much later years, the coccyx also may fuse to the sacrum.

**WHAT DID YOU LEARN?**

12. Which vertebrae are located in the "small" of the back, and how many of these vertebrae are there?

### 8.5b Spinal Curvatures

**LEARNING OBJECTIVES**

17. Name the four spinal curvatures of an adult vertebral column.

18. Explain the sequence of curvature development.

The vertebral column has some flexibility because it is not straight and rigid. When viewed from a lateral perspective, the adult vertebral column has four **spinal curvatures**: the **cervical**, **thoracic**, **lumbar**, and **sacral curvatures**. This arrangement better supports the weight of the body when standing than could a straight spine.

**INTEGRATE**

**CLINICAL VIEW 8.3**

**Spinal Curvature Abnormalities**

There are three main spinal curvature deformities: kyphosis, lordosis, and scoliosis.

**Kyphosis** (ki-fō’sis) is an exaggerated thoracic curvature that is directed posteriorly, producing a *hunchback* look. Kyphosis often results from osteoporosis but also may occur due to a vertebral compression fracture, osteomalacia (a disease in which adult bones become demineralized), abnormal vertebral growth, or chronic contractions in muscles that insert on the vertebrae.

**Lordosis** (lōr-dō’sis) is an exaggerated lumbar curvature, often called *swayback*, that is seen as a protrusion of the abdomen and buttocks. Lordosis may have the same causes as kyphosis, or it may result from the added abdominal weight associated with pregnancy or obesity.

**Scoliosis** (skō-lē-ō’sis) is the most common spinal curvature deformity. It is an abnormal lateral curvature that sometimes results during development when both the vertebral arch and body fail to form, or form incompletely, on one side of a vertebra. It can also be caused by unilateral muscular paralysis, or spasm, in the back. Mild cases of scoliosis may be treated in adolescence by wearing a back brace, whereas more severe cases may require surgical intervention.

The spinal curvatures appear sequentially during fetal, newborn, and child developmental stages. The **primary curves** are the thoracic and sacral curvatures, and they are present at birth. These curvatures arch posteriorly and result in the vertebral column being C-shaped.

The **secondary curves** are called the cervical and lumbar curvatures, and they appear after birth. These curvatures arch anteriorly and are also known as *compensation curves* because they help shift the trunk weight over the legs. The cervical curvature appears when the child is first able to hold up its head without support (usually around 3–4 months of age). The lumbar curvature appears when the child is learning to stand and walk (typically by the first year of life). These curvatures become accentuated as the child becomes more adept at walking. The sacral curvature is less pronounced in females than in males, to allow for a greater pelvic outlet to accommodate the passage of an infant through the birth canal.
Most vertebrae share some common structural features (Figure 8.17). The anterior region of each vertebra is a thick, cylindrical body, or centrum, which is the weight-bearing structure of each vertebra. Posterior to the vertebral body is the vertebral arch, also called the neural arch. The body together with the vertebral arch enclose an opening called the vertebral foramen. All the stacked vertebral foramina collectively form a superior-to-inferior directed vertebral canal that contains the spinal cord. Lateral openings between adjacent vertebrae are the intervertebral foramina. The intervertebral foramina provide a horizontally directed passageway through which spinal nerves extend to various parts of the body (see section 14.5).

The vertebral arch is composed of two pedicles and two laminae. The pedicles (ped′i-kĕl; pes = foot) originate from the posterolateral margins of the body, whereas the laminae (lam′i-nĕ; sing., lamina, lam′i-n˘a = layer) extend posteromedially from the posterior edge of each pedicle. A spinous process projects posteriorly from the junction of the left and right laminae. Most of these spinous processes can be palpated along the skin of the back. Lateral projections on both sides of the vertebral arch are called transverse processes.

### Table 8.5 Characteristic Features of Cervical, Thoracic, and Lumbar Vertebrae

<table>
<thead>
<tr>
<th>View</th>
<th>(a) Cervical Vertebra</th>
<th>(b) Thoracic Vertebra</th>
<th>(c) Lumbar Vertebra</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Superior View</strong></td>
<td>Transverse process</td>
<td>Superior articular facet</td>
<td>Transverse process</td>
</tr>
<tr>
<td></td>
<td>Body</td>
<td>Vertebral arch</td>
<td>Pedicle</td>
</tr>
<tr>
<td><strong>Lateral View</strong></td>
<td>Superior articular facet</td>
<td>Transverse foramen</td>
<td>Superior articular facet</td>
</tr>
<tr>
<td></td>
<td>Body</td>
<td>Transverse foramen</td>
<td>Inferior articular facet</td>
</tr>
<tr>
<td></td>
<td>Transverse process</td>
<td>Transverse process</td>
<td>Inferior articular facet</td>
</tr>
<tr>
<td></td>
<td>Spinal process</td>
<td>Spinal process</td>
<td>Spinal process</td>
</tr>
<tr>
<td></td>
<td>Intervertebral disc</td>
<td>Intervertebral disc</td>
<td>Intervertebral disc</td>
</tr>
<tr>
<td></td>
<td>Body</td>
<td>Body</td>
<td>Body</td>
</tr>
</tbody>
</table>

**Table 8.5 Characteristic Features of Cervical, Thoracic, and Lumbar Vertebrae**

- **Relative size**: Small
- **Body shape**: Kidney-bean-shaped
- **Costal facets for ribs**: Not present
- **Transverse processes**: Small (contain transverse foramina)
- **Transverse foramina**: Present (except sometimes for C7)
- **Spinous process**: Slender; C2–C4 are often bifid (note: C1 has no spinous process)
Each vertebra has superior and inferior articular processes that originate at the junction between the pedicles and laminae. Each articular process has a smooth surface called an articular facet (fas’t, fă-set’). The facets on the inferior articular processes of each vertebra articulate with the facets on the superior articular processes of the vertebra immediately inferior to it.

The stack of vertebral bodies is stabilized and interconnected by ligaments. Adjacent vertebral bodies are separated by pads of fibrocartilage, called the intervertebral (in-ter-ver’te-brəl) discs. Intervertebral discs are composed of an outer ring of fibrocartilage, called the anulus fibrosus (an’ū-lūs ft-brō’sus), and an inner gelatinous, circular region, called the nucleus pulposus (shown in Clinical View 8.4: “Herniated Discs”). Intervertebral discs make up approximately one-quarter of the entire vertebral column length. They act as shock absorbers between the vertebral bodies and permit the vertebral column to bend. For example, when you bend your torso anteriorly, the intervertebral discs are compressed at the bending (anterior) surface and pushed out at the opposite (posterior) surface.

Over the course of a day, as body weight and gravity act on the vertebral column, the intervertebral discs become compressed and flattened. But while a person is lying horizontally during sleep, the intervertebral discs are able to expand and spring back to their original shape.

In general, the vertebrae are smallest near the skull. They become gradually larger moving inferiorly through the body trunk as weight-bearing increases. Although vertebrae are divided into regions, there typically are no anatomically discrete “cutoffs” between the regions. For example, the most inferior cervical vertebra has some structural similarities to the most superior thoracic vertebra, as the two vertebrae are adjacent to one another. Likewise, the most inferior thoracic vertebra may look similar to the first lumbar vertebra. Table 8.5 compares the characteristics of the cervical, thoracic, and lumbar vertebrae and lists unique features of each regional group of vertebrae.

<table>
<thead>
<tr>
<th>(b) Thoracic Vertebra</th>
<th>(c) Lumbar Vertebra</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Superior articular facet</strong></td>
<td><strong>Superior articular facet</strong></td>
</tr>
<tr>
<td><strong>Costal facet</strong></td>
<td><strong>Costal facet</strong></td>
</tr>
<tr>
<td><strong>Transverse process</strong></td>
<td><strong>Transverse process</strong></td>
</tr>
<tr>
<td><strong>Body</strong></td>
<td><strong>Body</strong></td>
</tr>
<tr>
<td><strong>Costal demifacet</strong></td>
<td><strong>Spinous process</strong></td>
</tr>
<tr>
<td><strong>Inferior articular facet</strong></td>
<td><strong>Inferior articular facet</strong></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Thoracic Vertebra</strong></th>
<th><strong>Lumbar Vertebra</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Medium-sized (larger than cervical)</td>
<td>Largest</td>
</tr>
<tr>
<td>Heart-shaped</td>
<td>Large, oval or round</td>
</tr>
<tr>
<td>Present on body and transverse processes</td>
<td>Not present</td>
</tr>
<tr>
<td>Medium-sized</td>
<td>Large, thick, and blunt</td>
</tr>
<tr>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>Long; most project inferiorly</td>
<td>Short (thick and blunt); project posteriorly</td>
</tr>
</tbody>
</table>

*(photos): (a, b,c) ©McGraw-Hill Education/Christine Eckel*
Cervical Vertebrae

The cervical vertebrae are the most superiorly located vertebrae. They typically have kidney-bean-shaped bodies and extend inferiorly from the occipital bone of the skull through the neck to the thorax. Because cervical vertebrae support only the weight of the head, their vertebral bodies are relatively small and light. Most cervical vertebrae are distinguished from other vertebrae by the presence of transverse foramina in their transverse processes that house the vertebral artery and vein (sometimes C7 does not have these foramina). Table 8.5 summarizes the key features of the typical cervical vertebra (C3–C6); the other cervical vertebrae are described here.

**Atlas (C1)** The first cervical vertebra, called the atlas (at′las), supports the head through its articulation with the occipital condyles of the occipital bone (figure 8.18a). This vertebra is named for the Greek mythological figure Atlas, who carried the world on his shoulders. The articulation between the occipital condyles and the atlas, called the atlanto-occipital joint, permits us to nod our heads “yes.” The atlas is readily distinguished from the other vertebrae because it lacks both a body and a spinous process. Instead, the atlas has lateral masses that are connected by semicircular anterior and posterior arches, each containing slight protuberances, the anterior and posterior tubercles (tū′bər-kēl). The atlas has depressed, oval superior and inferior articular facets (table 8.5a) that articulate with the occipital condyles and the axis (C2), respectively. Finally, the atlas has an articular facet for dens on its anterior arch.

**Axis (C2)** The body of the atlas separates from the atlas and fuses during development to the body of the second cervical vertebra, called the axis (ak′sis) (figure 8.18b). This fusion produces the most distinctive feature of the axis, the prominent dens, or odontoid (ō-don′toyd; odont = tooth). The dens acts as a pivot for the lateral rotation of both the atlas and the skull. This articulation between the atlas and axis, called the atlantoaxial joint, permits us to shake our heads “no” (figure 8.18c). This joint is stabilized by a transverse ligament.

**Vertebra Prominens (C7)** The seventh cervical vertebra represents a transition from cervical to the thoracic vertebral region (see figure 8.16). The spinous processes of both C7 and all the thoracic vertebrae are nonbifid (not forked)—however, this process in C7 is much longer than it is within the other cervical vertebrae. It is easily palpated through the skin between the shoulder blades and inferior to the neck. Thus, C7 also is called the vertebra prominens (prom′i-nens; prominent). This vertebra may or may not have transverse foramina.

Thoracic Vertebrae

There are 12 thoracic vertebrae, and each articulates with the ribs (table 8.5). Thoracic vertebrae typically have heart-shaped bodies and are distinguished from all other types of vertebrae by the presence of costal facets or costal demifacets (semicircular facets) on the lateral
side of the body and on the sides of the transverse processes. The head of the rib (see section 8.6b) articulates with the costal facet or demifacet on the body of the thoracic vertebra. The tubercle of the rib (see section 8.6b) articulates with the costal facets on the transverse processes of the vertebra.

The thoracic vertebrae vary slightly with respect to their transverse costal facets. Vertebrae T1–T10 have transverse costal facets on their transverse processes; T11 and T12 lack these transverse costal facets because the eleventh and twelfth ribs do not have tubercles (and thus do not articulate with the transverse processes). The costal facets on the bodies of the thoracic vertebrae also display variations. Some vertebrae may have a single whole facet; others may have two demifacets.

**Lumbar Vertebrae**

The largest vertebrae are the lumbar vertebrae, as they bear most of the weight of the body. A typical lumbar vertebra body is thicker than that of all the other vertebrae, and its body is oval or round (table 8.5).

The lumbar vertebrae are distinguished by the features they lack—that is, lumbar vertebrae have neither transverse foramina (like the cervical vertebrae) nor costal facets (like the thoracic vertebrae). The thick spinous processes provide extensive surface area for the attachment of inferior back muscles that reinforce or adjust the lumbar curvature.

**Sacrum**

The sacrum is an anteriorly curved, somewhat triangular bone that forms the posterior wall of the pelvic cavity (figure 8.19). The apex of the sacrum is a narrow, pointed portion of the bone that projects inferiorly, whereas the bone’s broad superior surface forms the base.
The sacrum is composed of five fused sacral vertebrae. These vertebrae start to fuse shortly after puberty and are usually completely fused between ages 20 and 30. The horizontal lines of fusion that remain are called **transverse ridges**. Superiorly, the sacrum articulates with L₅ via a pair of **superior articular processes**. The vertebral canal becomes much narrower and continues through the sacrum on its posterior side as the **sacral canal**. The sacral canal terminates in an inferior opening called the **sacral hiatus** (hī-ˈātəs; hio = to yawn). On either side of the sacral hiatus are bony projections called the **sacral cornua**.

The anterosuperior edge of the first sacral vertebra bulges anteriorly into the pelvic cavity and is called the **promontory**. The paired **anterior and posterior sacral foramina** permit the passage of nerves to the pelvic organs and the gluteal region, respectively. A
dorsal ridge, termed the **median sacral crest**, is formed by the fusion of the spinous processes of individual sacral vertebrae. On each lateral surface of the sacrum is the **ala** (meaning *wing*). On the lateral surface of the ala is the **auricular surface**, which marks the site of articulation with the os coxae of the pelvic girdle, forming the **sacroiliac** (sā-krō-ī′-lē-ak) joint (see table 9.5).

**Coccyx**

Four small coccygeal vertebrae fuse to form the coccyx. These individual vertebrae begin to fuse by about age 25. The coccyx is an attachment site for several ligaments and some muscles. The first and second coccygeal vertebrae have unfused vertebral arches and transverse processes. The prominent laminae of the first coccygeal vertebrae are known as the **coccygeal cornua**, which curve to meet the sacral cornua. In males, the coccyx tends to project anteriorly, but in females it tends to project more inferiorly. In very elderly individuals, the coccyx may fuse with the sacrum.

**WHAT DID YOU LEARN?**

14. Compare the locations and functions of the transverse foramina, intervertebral foramina, and vertebral foramen.
15. How do the atlas and axis differ from other cervical vertebrae?

**8.6 Bones of the Thoracic Cage**

The bony framework of the chest is called the **thoracic cage** and consists of the thoracic vertebrae posteriorly, the ribs laterally, and the sternum anteriorly (figure 8.20). The thoracic cage acts as a protective enclosure around the thoracic organs and provides attachment points for many muscles.

![Figure 8.20 Thoracic Cage](image)

The thoracic cage is composed of the thoracic vertebrae, ribs, and sternum. It protects and encloses the organs in the thoracic cavity.
INTEGRATE

CLINICAL VIEW 8.6

Sternal Foramen

In up to 4–10% of all adults, a midline sternal foramen is present in the body of the sternum. The sternal foramen represents failure of the left and right ossification centers of the sternal body to fuse completely. Sometimes, this opening may be misidentified as a bullet wound. Thus, a crime scene investigator must be aware of this congenital anomaly when examining skeletal remains. In rare instances, individuals with previously undetected sternal foramina have died after an acupuncture session, when the acupuncture needle was unknowingly inserted through the sternal foramen and into the heart.

8.6a Sternum

LEARNING OBJECTIVE

21. Identify the three main components of the sternum and their features.

The sternum (sterˈnəm; sternon = the chest), also referred to as the breastbone, is a flat bone that forms in the anterior midline of the thoracic wall. Its shape has been likened to that of a sword. The sternum is composed of three parts: the manubrium, the body, and the xiphoid process.

The manubrium (mänˈəbrē-əm) is the widest and most superior portion of the sternum (the handle of the bony sword). The two clavicular notches of the sternum articulate with the left and right clavicles. The shallow superior indentation between the clavicular notches is called the suprasternal (or jugular) notch. A single pair of costal notches represent articulations for the first ribs’ costal cartilages.

The body is the longest part of the sternum and forms its bulk (the blade of the bony sword). Individual costal cartilages from ribs 2–7 are attached to the body at indented articular costal notches. The body and the manubrium articulate at the sternal angle, a horizontal ridge that may be palpated under the skin. The sternal angle is an important landmark in that the costal cartilages of the second ribs attach there; thus, it may be used to count the ribs.

The xiphoid (ziˈfəd; xiphos = sword) process represents the very tip of the sword. This small, inferiorly pointed, cartilaginous projection often doesn’t ossify until after age 40.

WHAT DID YOU LEARN?

What sternal structures form the sternal angle, and what is its clinical significance?

8.6b Ribs

LEARNING OBJECTIVES

22. Describe the features found on all ribs.

23. Differentiate between true ribs and false ribs.

The ribs are elongated, curved, flattened bones that originate on or between the thoracic vertebrae and end in the anterior wall of the thorax (figure 8.21a). Both males and females have 12 pairs of ribs. Ribs 1–7 are called true ribs. True ribs articulate directly and individually to the sternum by separate cartilaginous extensions called costal (kosˈtal; costa = rib) cartilages (figure 8.20). The smallest true rib is the first.

Ribs 8–12 are called false ribs because their costal cartilages do not articulate directly to the sternum. The costal cartilages of ribs 8–10 fuse to the costal cartilage of rib 7 and thus indirectly articulate with the sternum. The last two pairs of false ribs (ribs 11 and 12) are called floating ribs because they have no articulation with the sternum.

The vertebral bodies articulate with the head of a rib (figure 8.21). The articular surface of the head is divided into superior and inferior articular facets by an articular crest. The surfaces of these facets articulate with the costal facets or demifacets on the bodies of the thoracic vertebrae. The neck of the rib lies between the head and the tubercle. The tubercle of the rib has an articular facet for the costal facet on the transverse process of the thoracic vertebra. Figure 8.21b, c illustrates how most of the ribs articulate with the thoracic vertebrae.

INTEGRATE

CLINICAL VIEW 8.7

Variations in Rib Development

In 1 out of every 200 people, the costal element of the seventh cervical vertebra elongates and forms a rudimentary cervical rib. Cervical ribs may compress the artery and nerves extending toward the upper limb, producing tingling or pain. Less commonly, an extra pair of ribs may form from the costal elements of the first lumbar vertebra. Some individuals lack a pair of twelfth ribs, because their costal elements from the twelfth thoracic vertebra failed to elongate. Another rib development anomaly is fused (bicipital) ribs. Finally, bifid ribs occur in 1.2% of the world’s population (and up to 8.4% of Samoans). A bifid rib splits into two separate anterior portions when it reaches the sternum.
The angle (border) of the rib indicates the site where the tubular shaft begins to curve anteriorly toward the sternum. A prominent costal groove along its inferior internal border marks the path of spinal nerves (see section 14.5c) and blood vessels to the thoracic wall.

**WHAT DID YOU LEARN?**

17. Where specifically do the head and tubercle of a rib each articulate?

### 8.7 The Upper and Lower Limbs: A Comparison

**LEARNING OBJECTIVES**

24. Identify skeletal features common to the upper and lower limbs.

25. Describe the functional reasons for differences between the upper and lower limb skeletons.

Humans evolved from quadrupeds, which are animals that move on four feet. Quadruped limbs are very similar because all of the limbs are structured to support the body weight and move the animal. However, as our ancestors evolved into modern human beings, we became bipedal. Only our lower limbs normally support our body weight and are responsible for moving our bodies when we walk or run. In contrast, our upper limbs have been freed from these functions and are able to do other things, such as grasping objects and utilizing tools with our hands.

Our upper and lower limb skeletons share some common features based on this evolutionary history, and they exhibit some differences based on the primary functions of each limb. Figure 8.22 summarizes the similarities. The proximal part of both upper and lower limbs is supported by a girdle of bones; the pectoral girdle (clavicles and scapulae) holds the upper limbs in place, whereas...
The proximal part of the limb contains a single bone with a rounded head.

The rounded heads of the humerus and femur fit within their respective girdles, and allow for a wide range of movement at the shoulder and hip joints.

A girdle supports each limb.

Each girdle has a rounded, cuplike depression (socket) in which the head of the proximal part of each limb bone fits.

Pectoral girdle = left and right clavicles and scapulae

Pelvic girdle = left and right ossa coxae

Upper Limb

Lower Limb

The styloid processes of the radius and ulna are structurally similar to the malleoli of the tibia and fibula.

The interosseous membrane keeps the bones a fixed distance apart and allows these bones to pivot about one another.

(Note: Pivoting is much more limited in the lower limb.)
The distal part of each limb contains two bones connected by an interosseous membrane.

The interosseous membrane keeps the bones a fixed distance apart and allows these bones to pivot about one another. (Note: Pivoting is much more limited in the lower limb.)

The styloid processes of the radius and ulna are structurally similar to the malleoli of the tibia and fibula.

(b) Distal part of the limb

The hands and the feet have similar arrangements of bones.

Both the hand and the foot have 5 metacarpals or metatarsals, respectively, and 14 phalanges. Note the thumb and the big toe are the most robust of the digits, yet they each have only 2 phalanges.

The multiple carpal and tarsal bones allow for a wide range of movement at either the wrist or the ankle joints.
the pelvic girdle (i.e., both ossa coxae) articulates with the lower limb. The proximal part of each limb has one large bone: the humerus in the upper limb and the femur in the lower limb. The distal part of each limb contains two bones; these bones are able to pivot slightly about one another. Both the wrist and the proximal foot contain multiple bones (carpal and tarsal bones, respectively) that allow for a range of movement. Finally, the feet and hands are very similar in that both contain either 5 metacarpals (palm of hand) or 5 metatarsals (arch of foot), and each contains a total of 14 phalanges (bones of the fingers and toes, respectively).

The structural differences between the upper and lower limb skeletons arise from the functional differences. Understanding these general differences between upper and lower limbs will make the study of their individual bones easier. Because the lower limb is weight bearing and is used for locomotion, some mobility at specific joints has been lost for greater stability. The upper limb is not weight bearing, so both arm and forearm bones are relatively smaller and lighter than the similar respective lower limb bones. Additionally, the upper limb joints are relatively more mobile than the respective lower limb joints, so we may utilize the upper limbs for a wide range of activities. Unfortunately, more mobile joints are less stable, and that is why some of the upper limb joints (such as the shoulder joints) are the most frequently injured.

### 8.8 The Pectoral Girdle and Its Functions

The pectoral (pek′to-răl; pectus = breastbone) girdle articulates with the trunk and supports the upper limbs. A pectoral girdle consists of the clavicles and the scapulae.

#### 8.8a Clavicle

**LEARNING OBJECTIVE**

26. Identify and locate the clavicle and its landmarks.

The clavicle (klav′i-kĕl; clavis = key), commonly known as the collarbone, is an elongated, S-shaped bone that extends between the manubrium of the sternum and the acromion of the scapula (figure 8.23). Its sternal end (medial end) is roughly pyramidal in shape and articulates with the manubrium of the sternum, forming the sternoclavicular joint (see section 9.7b). The acromial end (lateral end) of the clavicle is broad and flattened. The acromial end articulates with the acromion of the scapula, forming the acromioclavicular joint. You can palpate your own clavicle by first locating the superior aspect of your sternum and then moving your hand laterally. The curved bone you feel under your skin, and close to the neck opening of your shirt, is your clavicle.

The superior surface of the clavicle is relatively smooth and the inferior surface is roughened (figure 8.23). On the inferior surface, near the acromial end, is a rough tuberosity called the conoid (kō′nōyd; konoëides = cone-shaped) tubercle for the conoid ligament (part of the coracoclavicular ligament of the shoulder joint; see section 9.7b). The inferiorly located prominence at the sternal end of the clavicle is the costal tuberosity, for the attachment of the shoulder's costoclavicular ligament.

### 8.8b Scapula

**LEARNING OBJECTIVE**

27. Describe the landmarks and features of the scapula.

The scapula (skap′yŏ-lă) is a broad, flat, triangular bone that forms the shoulder blade (figure 8.24). You can palpate your scapula by putting your hand on your superolateral back region and moving
your upper limb; the bone you feel moving is the scapula. The spine of the scapula is a ridge of bone on the posterior aspect of the scapula. It is easily palpated under the skin. The spine is continuous with a larger, posterior process called the acromion (a-krō'-mē-on; akron = tip, omos = shoulder), which forms the bony tip of the shoulder. Palpate your upper shoulder; the prominent bump you feel is the acromion. The coracoid (kōr′-ā-koyd) process is the smaller, more anterior, hook-shaped projection that is a site for muscle attachment.

The triangular shape of the scapula forms three sides, or borders. The superior border is the horizontal edge of the scapula superior to the spine of the scapula; the medial border (also called the vertebral border) is the edge of the scapula closest to the vertebrae; and the lateral border (also called the axillary border) is closest to the axilla. A suprascapular notch (which in some individuals is a suprascapular foramen) in the superior border provides passage for the suprascapular nerve and blood vessels.

Between these borders are the superior, inferior, and lateral angles. The superior angle is located between the superior and medial, while the inferior angle is positioned between the medial and lateral borders. The lateral angle is primarily made up of the cup-shaped, shallow glenoid (glē'noyd; glen′oyd; resembling a socket) cavity, or glenoid fossa, which articulates with the humerus, the bone of the arm.

The broad, relatively smooth anterior surface of the scapula is called the subscapular (sūb-skap′yū-lār; sub = under) fossa. A large muscle called the subscapularis overlies this fossa. The spine subdivides the posterior surface of the scapula into two shallow fossae. The depression superior to the spine is the supraspinous (sū-prā-spi′nūs; supra = above) fossa; inferior to the spine is a broad, extensive surface called the infraspinous fossa. The supraspinatus and infraspinatus muscles, respectively, occupy these fossae (see section 11.8b).

**WHAT DID YOU LEARN?**

20. What fossae are located on the scapula, and what is located in each fossa?

### 8.9 Bones of the Upper Limb

The upper limb consists of the brachium (arm), antebrachium (forearm), and hand. The complex structure of the hand in particular gives humans capabilities beyond those of most other vertebrates. Each upper limb contains a total of 30 bones:

- 1 humerus, located in the brachium region
- 1 radius and 1 ulna, located in the antebrachium region
- 8 carpal bones, which form the wrist
- 5 metacarpal bones, which form the palm of the hand
- 14 phalanges, which form the fingers

#### 8.9a Humerus

**LEARNING OBJECTIVES**

28. Describe the articulations of the humerus.

29. List landmarks and features of the humerus.

The humerus (hū′měr-ūs) is the longest and largest upper limb bone (figure 8.25). Its proximal end has a hemispherical head that...
articulates with the glenoid cavity of the scapula. The prominent greater tubercle is positioned lateral to the head and helps form the rounded contour of the shoulder. The lesser tubercle is smaller and located more medial to the head. Between the two tubercles is the intertubercular sulcus (also called bicipital sulcus or bicipital groove), a depression that contains the tendon of the long head of the biceps brachii muscle (see section 11.8c).

Between the tubercles and the head of the humerus is the anatomical neck, an almost indistinct groove that marks the location of the former epiphyseal plate. The surgical neck is a narrowing of the bone immediately distal to the tubercles, at the transition from the head to the shaft. This feature is called the “surgical” neck because it is a common fracture site.

The shaft of the humerus has a roughened area, termed the deltoid (del’toyd; deltoides = like the Greek letter Δ) tuberosity (tū’bér-os’-ı-te), which extends along its lateral surface for about half the length of the humerus. The deltoid muscle of the shoulder attaches to this roughened surface (see section 11.8b). The radial groove (or spiral groove) is located adjacent to the deltoid tuberosity and is the location of the radial nerve (see section 14.5e) and some blood vessels.

Together, the bones of the humerus, radius, and ulna form the elbow joint (figure 8.25c). The medial and lateral epicondyles (ep-i-kon’dil; epi = upon, kondylos = a knuckle) are bony side projections on the distal humerus that provide surfaces for muscle attachment. Palpate the sides of your elbow; the bumps you feel are the medial and lateral epicondyles. Placed posterior to the medial epicondyle is the ulnar nerve (see table 14.4 and section 14.5e). (You actually are hitting this nerve when you hit your funny bone.)

The distal end of the humerus has two smooth, curved surfaces for articulation with the bones of the forearm. The rounded capitulum (kä-pit’yü-lüm; caput = head) is located laterally and articulates with the head of the radius. The pulley-shaped trochlea (trok’le-a; trochileia = a pulley) is located medially and articulates with the trochlear notch of the ulna. Additionally, the distal end of the humerus exhibits three depressions, two on its anterior surface and one on its posterior surface. The anterolaterally placed radial fossa accommodates the head of the radius; the anteromedially placed coronoid (kōr’ō-noid; korone = a crow, eidos = resembling) fossa accommodates the coronoid process of the ulna. The posterior depression,
8.9b Radius and Ulna

LEARNING OBJECTIVES

30. Compare and contrast the features of the radius and the ulna.
31. Explain how the radius, ulna, and humerus articulate.
32. Differentiate between supination and pronation of the forearm.

The radius and ulna form the forearm (Figure 8.26). In anatomic position, these bones are parallel, and the radius (rā’dē-ās; spoke of...
The shaft of the radius curves slightly and leads to a wider distal end, where there is a laterally placed styloid (stĭl’oid) process. This bony projection can be palpated on the lateral side of the wrist, just proximal to the thumb. On the distal medial surface of the radius is an ulnar notch, which articulates with the medial surface of the distal end of the ulna at the distal radioulnar joint.

The ulna (ʻūl’nà) is the longer, medially placed bone of the forearm. At the proximal end of the ulna, a C-shaped trochlear notch interlocks with the trochlea of the humerus. The posterosuperior aspect of the trochlear notch has a prominent projection called the olecranon. The olecranon articulates with the olecranon fossa of the humerus and forms the posterior “bump” of the elbow. The inferior lip of the trochlear notch, called the coronoid process, articulates with the humerus at the coronoid fossa. Lateral to the coronoid process, a smooth, curved radial notch accommodates the head of the radius and helps form the proximal radioulnar joint. Also at the proximal end of this bone is the tuberosity of ulna. At the distal end of the ulna, the shaft narrows and terminates in a knoblike head that has a posteromedial styloid process. The styloid process of the ulna may be palpated on the medial (little finger) side of the wrist.

Both the radius and the ulna exhibit interosseous borders, which face each other; the ulna’s interosseous border faces laterally, whereas the interosseous border on the radius faces medially. These interosseous borders are connected by an interosseous membrane (interosseous ligament) composed of dense regular connective tissue. This membrane helps keep the radius and ulna a fixed distance apart from one another and provides a pivot of rotation for the forearm. The bony joints that move during this rotation are the proximal and distal radioulnar joints.

In anatomic position, the palm of the hand is facing anteriorly, and the bones of the forearm are said to be in supination (sŭ-pĭn′a-shun) (figure 8.26c). Note that the radius and the ulna are parallel with one another. If you view your own supinated forearm, the radius is on the lateral (thumb) side of the forearm, and the ulna is on the medial (little finger) side.

Pronation (prŏ-nă-shun) of the forearm requires that the radius cross over the ulna and that both bones pivot along the interosseous membrane (figure 8.26d). When the forearm is pronated, the palm of the hand is facing posteriorly and the head of the radius is still along the lateral side of the elbow, but the distal end of the radius has crossed over and become a more medial structure.

When an individual is in anatomic position (i.e., has the upper limbs extended and forearms supinated), note that the bones of the forearm may angle laterally from the elbow joint. This positioning is referred to as the carrying angle of the elbow, and this angle positions the bones of the forearms such that the forearms will clear the hips during walking as the forearms swing. Females have wider carrying angles than males, presumably because they have wider hips than males.

**LEARNING STRATEGY**

No matter what the position of the forearm (pronated or supinated), the distal end of the radius is always near the thumb, and the distal end of the ulna is near the little finger.

**WHAT DID YOU LEARN?**

23. What are some bony features that the radius and ulna share?

24. Describe how the radius and ulna are positioned when the forearm is pronated.

**8.9c Carpals, Metacarpals, and Phalanges**

**LEARNING OBJECTIVES**

33. Locate and identify the carpals and metacarpals.

34. Describe the phalanges and their relative locations.

The bones that form the wrist and hand are the carpals, metacarpals, and phalanges (figure 8.27). The carpals (kar’păls; karpus = wrist) are small, short bones that form the wrist. They are arranged in two rows (a proximal row and a distal row) of four bones each and allow for the multiple movements possible at the wrist.

The proximal row of carpals, listed from lateral to medial, are the scaphoid (skaf’oid; skaphe = boat), lunate (lùn’āt; luna = moon), triquetrum (trî-kwē’strūm; triquetrum = three-cornered), and pisiform (pis’i-fŏrm; pisum = pea, forma = appearance).

The distal row of the carpals, listed from lateral to medial, are the trapezium (tra-pĕz’ē-ūm; trapeza = table), trapezoid (trap’e-zoyd), capitate (kap’ĭ-tăt), and hamate (ha’mät; hamus = hook).

Bones in the palm of the hand are called metacarpals (met’ă-kar’păls; meta = beyond). Five metacarpal bones articulate with the distal carpal bones and support the palm. Roman numerals I–V denote the metacarpal bones, with metacarpal I located at the base of the thumb, and metacarpal V at the base of the little finger.

A total of 14 bones are present in the digits; these are called phalanges (fă-lan’jē; sing., phalanx, fă’langks; line of soldiers). Three
The scaphoid bone is one of the more commonly fractured carpal bones. A fall on the outstretched hand may cause the scaphoid to fracture into two separate pieces. Usually, blood vessels are torn on the proximal part of the scaphoid, resulting in avascular necrosis, which is death of the bone tissue due to inadequate blood supply. Scaphoid fractures take a very long time to heal properly due to this complication.

8.10 The Pelvic Girdle and Its Functions

The adult pelvis (pel’vis; pl., pelves, pel’vēz; basin) is composed of four bones: the sacrum, the coccyx, and the right and left osa coxae (os′ă kok’sā; sing., os coxae; hip bone) (figure 8.28). The pelvis protects and supports the viscera in the inferior part of the ventral body cavity (see section 1.5e).
The term **pelvic girdle** refers to both the left and right ossa coxae only. The pelvic girdle articulates with the trunk and provides an attachment point for each lower limb. When a person is standing upright, the pelvis is angled slightly anteriorly.

### 8.10a Os Coxae

**LEARNING OBJECTIVES**

35. Name the three bones that make up each os coxae.
36. Describe how the osa coxae articulate with each femur and sacrum.
37. Describe landmarks and features of an os coxae.

The os coxae is commonly referred to as the *hip bone* (and sometimes as the *coxal bone* or the *innominate bone*). Each os coxae is formed from three separate bones: the ilium, ischium, and pubis (figure 8.29). These three bones fuse between the ages of 13 and 15 years to form the single os coxae.

Each os coxae articulates posteriorly with the sacrum at the sacroiliac joint (figure 8.28). The femur articulates with a deep, curved depression on the lateral surface of the os coxae called the acetabulum (as-ē-tab′y-ō-lum; shallow cup). The acetabulum contains a smooth, curved surface, called the lunate surface, which is C-shaped and articulates with the femoral head. The ilium, ischium, and pubis all contribute a portion to the acetabulum—thus, it represents a region where these bones have fused.

**WHAT DO YOU THINK?**

Compare and contrast the glenoid cavity of the scapula with the acetabulum of the os coxae. Which girdle maintains stronger, more tightly fitting bony connections with its respective limb—the pectoral girdle or the pelvic girdle? Explain.

The largest of the three coxal bones is the ilium (il′ē-ŭm; groin, flank), which forms the superior region of the os coxae and part of the acetabular surface. The wide, fan-shaped portion of the ilium is called the ala (ā′lā). The ala terminates inferiorly at a ridge called the arcuate (ar′ky-ū-ät; arcuat us = bowed) line on the medial surface of the ilium. On the medial side of the ala is a depression termed the iliac fossa. On the lateral surface of the ilium, the anterior, posterior, and inferior gluteal (glū′tē-ăl; gloutos = buttock) lines are attachment sites for the gluteal muscles of the buttock (see section 11.9a). The postero medial side of the ilium exhibits a large, roughened area called the auricular (aw-rik′y-ŭ-lār; auris = ear) surface, where the ilium articulates with the sacrum.

The superiormost ridge of the ilium is the iliac crest. Palpate the posterosuperior edges of your hips; the ridge of bone you feel on each side is the iliac crest. The iliac crest arises anteriorly from a projection called the anterior superior iliac spine and extends posteriorly to the posterior superior iliac spine. Located inferiorly to the ala of the ilium are the anterior inferior iliac spine and the posterior inferior iliac spine. The posterior inferior iliac spine is adjacent to a prominent greater sciatic notch (st-at′ik; sciatic us = hip joint), through which the sciatic nerve extends to the lower limb (see section 14.5g).

The ilium fuses with the ischium (is′kē-ŭm; ischion = hip) near the superior and posterior margins of the acetabulum. Posterior to the acetabulum, the prominent triangularischial (is′kē-āl) spine projects medially. The bulky bone superior to the ischial spine is called the body of the ischium. The lesser sciatic notch is a semicircular depression inferior to the ischial spine. The posterolateral border of the ischium is a roughened projection called the ischial tuberosity. The ischial tuberosities also are called the sitz bones by some health professionals and fitness instructors because they support the weight of the body when seated. If you palpate your buttocks while in a sitting position, you can feel the large ischial tuberosities. An elongated ramus (rā′mūs; pl., rami, rā′mē) of the ischium extends from the ischial tuberosity toward its anterior fusion with the pubis.

The pubis (pyū′bis) fuses with the ilium and ischium at the acetabulum. The ramus of ischium fuses anteriorly with the inferior pubic ramus to form the ischiopubic ramus (figure 8.28). The superior pubic ramus originates at the anterior margin of the acetabulum. Between the superior and inferior pubic rami is an anteriorly placed mass of bone called the body of the pubis. The obturator (ob′tō-rā-tōr; obturo = to occlude) foramen is a space in the os coxae that is circled by both pubic and ischial rami. In a living individual, this foramen is covered with a connective tissue membrane. A roughened ridge, called the public crest, is located on the anterosuperior surface of the superior pubic ramus, and it ends at the pubic tubercle. A roughened area on the body of the pubis, called the symphysial (sim-fiz′ē-āl; growing together) surface or pubic symphysis, denotes the site of articulation between the pubic bones. On the medial surface of the
pubis, the **pectineal** (pek-tin′-é-al) **line** originates and extends diagonally across the pubis to merge with the arcuate line.

**WHAT DID YOU LEARN?**

26. What three bones fuse to form the os coxae?
27. Where are the ischial tuberosities located, what is an alternative name for them, and what is their function?

---

**Figure 8.29 Os Coxae.** Each os coxae is formed by the fusion of three bones: an ilium, an ischium, and a pubis. Diagrams show the features of these bones in (a) lateral and (b) medial views.
8.10b True and False Pelves

**LEARNING OBJECTIVES**

38. Differentiate between the true and false pelves.

39. Compare and contrast the pelvic inlet and pelvic outlet.

The **pelvic brim** is a continuous, oval ridge that extends from the pubic crest, pectineal line, and arcuate line to the rounded inferior edges of the sacral ala and promontory. This pelvic brim helps subdivide the entire pelvis into a true pelvis and a false pelvis (figure 8.30). The true pelvis, also known as the lesser pelvis, lies inferior to the pelvic brim. It encloses the pelvic cavity and forms a deep bowl that contains the pelvic organs. The false pelvis, also known as the greater pelvis, lies superior to the pelvic brim. It is enclosed by the alae of the ilia. It forms the inferior region of the abdominal cavity and houses the inferior abdominal organs.

The pelvis also has a superior and an inferior opening, and each has clinical significance. The **pelvic inlet**, also known as the superior pelvic aperture, is the superiorly positioned space enclosed by the pelvic brim. In other words, the pelvic brim is the bony, oval ridge of bone, whereas the pelvic inlet is the space surrounded by the pelvic brim. The pelvic inlet is the opening at the boundary between the true pelvis and the false pelvis.

The **pelvic outlet**, also known as the inferior pelvic aperture, is the inferiorly placed opening bounded by the coccyx, the ischial tuberosities, and the inferior border of the symphysial surface. In males, the ischial spines commonly project into the pelvic outlet, thereby narrowing the diameter of this outlet. In contrast, female ischial spines less frequently project into the pelvic outlet (so the birth canal will not be obstructed by these bony prominences). The pelvic outlet is covered with muscles and skin, and it forms the body region called the perineum (per′i-nē′īm) (see figure 11.17). The width and size of the pelvic outlet are especially important in females, because the opening must be wide enough to accommodate the fetal head during childbirth (see section 29.6).

**WHAT DID YOU LEARN?**

28. How is the pelvic inlet distinguished from the pelvic outlet?

8.10c Sex Differences in the Pelvis

**LEARNING OBJECTIVE**

40. Compare and contrast the anatomy of male and female pelves.

Although it is possible to determine the sex of a skeleton by examining the skull, the most reliable indicator of sex is the pelvis, primarily the ossa...
The ossa coxae are the most sexually dimorphic bones of the body due to the demands of pregnancy and childbirth in females. For example, the female pelvis is shallower and wider than the pelvis of a male to accommodate the infant’s head as it passes through the birth canal.

Some of these differences are obvious, such as that males have narrower hips than females. But we can find many other differences by examining the shapes and orientations of the pelvic bones. For example, the female ilium flares more laterally, whereas the male ilium projects more superiorly, which is why males typically have narrower hips. Because the female pelvis is wider, the acetabulum projects more laterally, and the greater sciatic notch is much wider. In contrast, the male acetabulum projects more anteriorly, and the male greater sciatic notch is much narrower, deeper, and U-shaped. Females tend to have a preauricular sulcus, which is a depression or groove between the greater sciatic notch and the sacroiliac articulation. Males tend not to have this sulcus. The sacrum tends to be shorter and wider in females.

The body of the pubis in females is much longer and almost rectangular in shape, compared to the shorter, triangular-shaped male pubic body. The subpubic angle (or pubic arch) is the angle formed when the left and right pubic bones are aligned at their symphysial surfaces. Because females have much longer pubic bones, the corresponding subpubic angle is much wider and more convex, usually much greater than 100 degrees. The male subpubic angle is much narrower and typically does not extend past 90 degrees.

Several significant differences between the female and male pelvises are shown and listed in Table 8.6.

### Concept Connection

The skeletal system and female reproductive system (see section 28.3) are linked by the fact that the shape of the bony pelvis has a direct relation on whether a female will have a difficult labor and delivery.

### Table 8.6 Sex Differences Between the Female and Male Pelvis

<table>
<thead>
<tr>
<th>View</th>
<th>Female Characteristic</th>
<th>Male Characteristic</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Medial View</strong></td>
<td>Wider and more flared ilium</td>
<td>Narrower and more vertical ilium</td>
</tr>
<tr>
<td></td>
<td>Preauricular sulcus</td>
<td>Narrow greater sciatic notch</td>
</tr>
<tr>
<td></td>
<td>Wide greater sciatic notch</td>
<td></td>
</tr>
<tr>
<td><strong>Anterior View</strong></td>
<td>Wider pelvis and more flared ilia</td>
<td>Narrow pelvis and more vertical ilia</td>
</tr>
<tr>
<td></td>
<td>Rectangular body of pubis</td>
<td>Triangular body of pubis</td>
</tr>
<tr>
<td></td>
<td>Triangular obturator foramen</td>
<td>Large, oval obturator foramen</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Wide subpubic angle</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Narrow subpubic angle</td>
</tr>
</tbody>
</table>

**Feature**  
- **General appearance**: Less massive; gracile processes, less prominent muscle markings  
- **General width**: Pelvis wider; ilia more flared  
- **Pelvic inlet**: Spacious, wide and oval  
- **Greater sciatic notch**: Wide and shallow  
- **Obturator foramen**: Smaller and triangular  
- **Subpubic angle**: Broader, more convex; usually greater than 100 degrees  
- **Body of pubis**: Longer; more rectangular  
- **Preauricular sulcus**: Usually present  
- **Sacrum**: Shorter and wider; flatter sacral curvature  
- **Ischial spine**: Rarely projects into pelvic outlet

**Male Characteristic**: More massive; more robust processes, more muscle markings  
- **General width**: Pelvis narrower; ilia more vertically oriented and less flared  
- **Pelvic inlet**: Heart-shaped  
- **Greater sciatic notch**: Narrow and U-shaped, deep  
- **Obturator foramen**: Larger and oval  
- **Subpubic angle**: Narrow, V-shaped; usually less than 90 degrees  
- **Body of pubis**: Short; triangular  
- **Preauricular sulcus**: Usually absent  
- **Sacrum**: Narrower and longer; more curved (greater sacral curvature)  
- **Ischial spine**: Frequently rotated inward; projects into pelvic outlet

(photos): (medial view female, male) ©David Hunt/Smithsonian Institution; (anterior view female, male) ©VideoSurgery/Science Source
**WHAT DID YOU LEARN?**

How do male and female pelves differ with respect to the shape of the pubis, subpubic angle, greater sciatic notch, and overall shape of the pelvis?

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### 8.10d Age Differences in the Ossa Coxae

#### LEARNING OBJECTIVE

41. Describe changes to the ossa coxae as a person ages.

The ossa coxae are an excellent indicator of both sex and age, and they can provide a reliable estimate of age at death. These estimates are given in age ranges (as opposed to precise numbers) because some variation may occur in how an os coxae exhibits the age-related changes.

Osteologists have noted age-related changes to the auricular surface of the ilium. The auricular surface of a young adult typically has some billowing texture to it (e.g., appears to have “hills” and “valleys”), and the surface is fine-grained. As the auricular surface ages, the billowing flattens out and the surface becomes more coarse and granular. In much older individuals, the surface may develop some bony lipping (evidence of osteoarthritic changes) and the surface becomes even more rough and irregular.

Osteologists also have documented that the symphysial surface of the pubis undergoes uniform, age-related changes as well. In fact, the symphysial surface has become one of the most reliable indicators for estimating age at death. In a young adult (age range 15–24), the symphysial surface is billowed, and no well-formed rim is found around the surface. As the person ages, this billowing becomes more flattened, and a bony rim begins to form around the circumference of the symphysial surface. This rim is completed about ages 35–50 for most individuals. Once the rim is complete, the symphysial surface becomes depressed and concave and may become pitted in much older individuals. The rim or border may start to break down, and bony lipping (arthritis) develops along the edges of the symphysial surface. These last stages typically occur after age 50.

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### 8.11 Bones of the Lower Limb

The lower limb is made up of the thigh, leg, and foot. The structure of the foot enables it to support the body during bipedal walking and running.

The arrangement and numbers of bones in the lower limb are similar to those of the upper limb. Each lower limb contains a total of 30 bones:

- 1 femur, located in the femoral region
- 1 patella (kneecap), located in the patellar region
- 1 tibia and 1 fibula, located in the crural region
- 7 tarsal bones, which form the bones of the ankle and proximal foot
- 5 metatarsal bones, which form the arched part of the foot
- 14 phalanges, which form the toes

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### 8.11a Femur and Patella

#### LEARNING OBJECTIVES

42. Describe the articulations of the femur.
43. Identify key landmarks and features of the femur.
44. Describe the location and function of the patella.

The **femur** (fē′mūr; thigh) is the longest bone in the body as well as the strongest and heaviest (figure 8.31). The nearly spherical **head** of the femur articulates with the os coxae at the
acetabulum. There is a small depression within the head of the femur, called the fovea (fō’ve-ā; a pit), or fovea capitis. Here a small ligament connects the head of the femur to the acetabulum. Distal to the head, an elongated, constricted neck joins the shaft of the femur at an angle. This results in a medial angling of the femur, which brings the knees closer to the midline.

The greater trochanter (trō-kan’ter; a runner) projects laterally from the junction of the neck and shaft. A lesser trochanter is located on the femur’s posteromedial surface. These are rough processes that serve as attachment sites for powerful gluteal and thigh muscles (see section 11.9a). The greater and lesser trochanters are connected on the posterior surface of the femur by a thick oblique ridge of bone called the intertrochanteric (in’ter-trō-kan-tăr’ik) crest. Anteriorly, a raised intertrochanteric line extends between the two trochanters and marks the distal edge of the hip joint capsule. Inferior to the intertrochanteric crest, the pectineal line marks the attachment of the pectineus muscle; the gluteal (glō’tē-āl; gloutos = buttock) tuberosity marks the attachment of the gluteus maximus muscle (see section 11.9a).

The gluteal tuberosity and pectineal line merge inferiorly into an elevated, midline ridge called the linea aspera (lin’e-ā as’për-ā), where many thigh muscles attach. Distally, the linea aspera branches into medial and lateral supracondylar lines. A flattened, triangular area,
The patella is a sesamoid bone located within the tendon of the quadriceps femoris muscle. These views show the right patella.

**WHAT DID YOU LEARN?**

31. What are the locations and functions of the greater and lesser trochanter?
32. Where does the patella articulate with the femur?

### 8.11b Tibia and Fibula

**LEARNING OBJECTIVES**

45. Describe the features of the tibia and fibula.
46. Explain how the function of the tibia differs from that of the fibula.
47. Describe how the tibia and fibula articulate.

The skeleton of the leg (crural region) has two parallel bones: the thick, strong tibia and the slender fibula (figure 8.33). Like the radius and ulna, these two bones are connected by an interosseous membrane that extends between their interosseous borders. The interosseous membrane stabilizes the relative positions of the tibia and fibula, and provides a pivot of minimal rotation for the two bones.

The **tibia** (tib′ë-ä; large shinbone) is the medially placed bone and the only weight-bearing bone of the leg (crural region). Its broad, superior head has two relatively flat surfaces, the medial and lateral condyles, which articulate with the medial and lateral condyles of the femur, respectively. Separating the condyles of the tibia is a prominent ridge called the intercondylar eminence (em′i-nens). On the proximal posterolateral side of the tibia is a fibular articular facet, where the head of the fibula articulates to form the superior (or proximal) tibiofibular joint.

The rough anterior surface of the tibia near the proximal condyles is the **tibial tuberosity**, which can be palpated just inferior to the patella and marks the attachment site for the patellar ligament. The **anterior border** (or margin), often referred to as the shin, is a prominent ridge that extends distally along the anterior tibial surface from the tibial tuberosity.

The tibia narrows distally, but at its medial border it forms a large, prominent process called the **medial malleolus** (ma-łē′ō-lūs; malleus = hammer). Palpate the medial side of your ankle; the bump you feel is your medial malleolus. There is a **fibular notch** on the distal posterolateral side of the tibia where the fibula articulates and forms the **inferior (or distal) tibiofibular joint**. On the inferior distal surface of the tibia is the smooth **inferior articular surface** for the talus, one of the tarsal bones.

The **fibula** (fib′yū-lā; buckle, clasp) is the long, thin, lateral bone of the leg. The fibula does not bear any weight, but several muscles attach to it. The rounded, knoblike **head** of the fibula is slightly inferior and posterior to the lateral condyle of the tibia. Distal to the fibular head is the **neck** of the fibula, followed by its **shaft**. The fibula’s distal tip, called the **lateral malleolus**, extends laterally to the ankle joint, where it provides lateral stability. Palpate the lateral side of your ankle; the bump you feel is your lateral malleolus.
WHAT DO YOU THINK?

5. The medial and lateral malleoli of the leg are similar to what bony features of the forearm?

WHAT DID YOU LEARN?

33. What are some bony features that are similar or the same between the tibia and fibula?

24. What is the primary function of the tibia?
The bones that form the ankle and foot are the tarsals, metatarsals, and phalanges (figure 8.34). The seven tarsals (tar’sål; tarsus = flat surface) of the ankle and proximal foot are similar to the eight carpal bones of the wrist in some respects, although their shapes and arrangement are different from those of their carpal bone counterparts.

The talus, calcaneus, and navicular bone are considered the proximal row of tarsal bones. The superiormost and second largest tarsal bone is the talus (tä’lūs; ankle bone), which articulates with the tibia. The calcaneus (kal-kā’nē-ūs) is the largest tarsal bone and forms the heel. Its posterior end is a rough, knob-shaped projection that is the point of attachment for the calcaneal (Achilles) tendon extending from the strong posterior leg muscles (see section 11.9c). The navicular (nā-vik’yū-lār; navis = ship) bone is on the medial side of the ankle.
The distal row of four tarsal bones includes the cuneiforms and the cuboid bone. The medial cuneiform (kū′nē-i-fōrm; cuneus = wedge), intermediate cuneiform, and lateral cuneiform bones are wedge-shaped bones that articulate with and are positioned anterior to the navicular bone. The laterally placed cuboid (kyū′boyd; kybos = cube) bone articulates at its medial surface with the lateral cuneiform and at its posterior surface with the calcaneus.

The metatarsals (met′a-tar′sāl) of the foot are five long bones similar in arrangement and name to the metacarpal bones of the hand. They form the arched sole of the foot and are identified with Roman numerals I–V, proceeding medially to laterally. The metatarsals articulate proximally with either the cuneiform bones or the cuboid bone. Distally, each metatarsal bone articulates with a proximal phalanx. At the head of the first metatarsal are two tiny sesamoid bones, which insert on the tendons of the flexor hallucis brevis muscle and help these tendons move more freely (see section 11.9d).

The bones of the toes (like the bones of the fingers and pollex) are called phalanges. The toes contain a total of 14 phalanges. The great toe is the hallux (hal′ûks; hallex = great toe), and it has only 2 phalanges (proximal and distal); each of the other four toes has 3 phalanges (proximal, middle, and distal).

**WHAT DID YOU LEARN?**

35. What are the seven tarsal bones?

### 8.11d Arches of the Foot

**LEARNING OBJECTIVE**

50. Describe the three arches of the foot and their functions.

Normally, the sole of the foot is arched, which helps it support the weight of the body and ensures that the blood vessels and nerves on the sole of the foot are not pinched when we are
standing. The three arches of the foot are the medial longitudinal, lateral longitudinal, and transverse arches (Figure 8.35).

The **medial longitudinal arch** is the highest of the three arches and extends from the heel to the great toe. It is formed from the calcaneus, talus, navicular, and cuneiform bones and metatarsals I–III. The medial longitudinal arch prevents the medial side of the foot from touching the ground and gives our footprint its characteristic shape (Figure 8.35d).

The **lateral longitudinal arch** is not as high as the medial arch, so the lateral part of the foot does contribute to a footprint. This arch extends between the little toe and the heel, and it is formed from the calcaneus and cuboid bones and metatarsals IV and V.

The **transverse arch** runs perpendicular to the longitudinal arches. It is formed from the distal row of tarsals and the bases of all five metatarsals.

The shape of the foot arches is maintained primarily by the foot bones themselves. These bones are shaped so that they can interlock and support their weight in an arch, much as the wedge-shaped blocks of an arched bridge can support the bridge without other mechanical supports. Secondarily, strong ligaments that attach to the bones and contracting muscles pull on the tendons, thereby helping to maintain the arches’ shapes.

**WHAT DID YOU LEARN?**

Why is it preferable to have an arched (versus a flat) foot?

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**Figure 8.35 Arches of the Foot.** The foot’s two longitudinal arches and one transverse arch allow for better weight support. (a) Medial longitudinal arch. (b) Lateral longitudinal arch. (c) Transverse arch as seen in cross-sectional view. (d) A footprint illustrates the placement of the longitudinal arches.
The appendicular skeleton begins to develop during the fourth week of development, when limb buds appear as small ridges along the lateral sides of the embryo. The upper limb buds appear early in the fourth week (approximately day 26), and the lower limb buds appear a few days later (day 28) (figure 8.36). Lower limb development lags behind upper limb development by about 2 to 4 days. The upper and lower limbs form proximodistally, meaning that the more proximal parts of the limbs form first (in weeks 4–5), whereas the more distal parts differentiate later.

Early limb buds are composed of lateral plate mesoderm and covered by a layer of ectoderm (see section 5.6a). The musculature of the limbs forms from somitic mesoderm that migrates to the developing limbs during the fifth week of development.

At the apex of each limb bud, part of the ectoderm forms an elevated thickening called the apical ectodermal ridge. By mechanisms not completely understood, this ridge “signals” the underlying tissue to form the various components of the limb.

Initially, the limb buds are cylindrical. The distal portion of the upper limb bud forms a rounded, paddle-shaped hand plate by the early fifth week. It later becomes both the palm and fingers. In the lower limb bud, a corresponding foot plate forms during the sixth week. These plates develop longitudinal thickenings called digital rays, which eventually form the digits. The digital rays in the hand plate appear in the late sixth week, and the foot digital rays appear during the early seventh week. The digital rays initially are connected by intermediately placed tissue, which later undergoes programmed cell death (apoptosis; see section 4.10). Thus, as this intermediate tissue dies, notching occurs between the digital rays, and separate digits are formed. This process occurs in the seventh week and is complete by the eighth week for both the fingers and the toes.

As mentioned in section 7.4, bone forms by either intramembranous ossification or endochondral ossification. The flat bones of the skull; several facial bones, including the zygomatic, maxilla, and mandible; and the central part of the clavicle are formed from intramembranous ossification, whereas almost all of the remaining bones of the skeleton form through endochondral ossification.

**Figure 8.36 Development of the Appendicular Skeleton.** The upper and lower limbs develop between weeks 4 and 8. Upper limb development precedes corresponding lower limb development by 2 to 4 days.
The adult skeleton is typically composed of 206 bones; skeletal features can be used to determine height, age at death, sex, and general health.

8.1 Components of the Skeleton

- The adult skeleton is typically composed of 206 bones; skeletal features can be used to determine height, age at death, sex, and general health.

8.1a Axial and Appendicular Skeleton

- The axial skeleton includes the skull, vertebral column, and thoracic cage.
- The appendicular skeleton includes the pectoral and pelvic girdles, the bones of the upper limb, and the bones of the lower limb.

8.1b Bone Markings

- Specific anatomic terms are used to describe various features on bones.

8.2b Views of the Skull and Landmark Features

- Specific bones, foramina, processes, and bone landmarks of the skull are seen in multiple views of the skull.
- The cranial bones include the frontal bone, paired parietal bones, occipital bone, paired temporal bones, nasal bone, inferior nasal conchae, nasal bone, inferior nasal conchae, and maxillary bone.
- The cranial bones include the paired zygomatic bones, lacrimal bones, nasal bones, inferior nasal conchae, palatines bones, maxillae, single vomer bone, and single mandible.
- The anterior, middle, and posterior cranial fossae are located within the cranial cavity and house specific regions of the brain.
8.2c Sutures
- Sutures are immobile joints between skull bones. They allow for growth of the skull bones during childhood.

8.2d Orbital and Nasal Complexes, Paranasal Sinuses
- Seven bones form the orbital complex: the maxilla, frontal, lacrimal, ethmoid, sphenoid, palatine, and zygomatic bones.
- The nasal complex is composed of bones and cartilage that enclose the nasal cavity and paranasal sinuses.
- Paranasal sinuses function to lighten the skull and give resonance to the voice.

8.3 Bones Associated with the Skull
- Auditory ossicles (malleus, incus, stapes) are tiny ear bones housed in each temporal bone.
- The hyoid bone does not articulate with any other bone but serves as an attachment site for several muscles and ligaments.

8.4 Sex and Age Determination from Analysis of the Skull
- Diagnostic features of the skull may be used to determine the sex and age at death.

8.4a Sex Differences in the Skull
- Female skulls tend to be more gracile, have more pointed (versus squared-off) chins, and have sharper supraorbital margins.
- Male skulls tend to be more robust, have more prominent bone markings (e.g., nuchal lines and external occipital protuberance), and have squared-off chins and angles of the mandible.

8.4b Aging of the Skull
- Fontanelles permit the skulls of infants to distort during birth as well as expand as the brain grows.
- In adulthood, the sutures begin to fuse and ossify at regular rates, permitting determination of age at death.

8.5 Bones of the Vertebral Column
- The vertebral column is composed of 26 vertebrae.

8.5a Types of Vertebrae
- An adult typically has 7 cervical vertebrae, 12 thoracic vertebrae, 5 lumbar vertebrae, the sacrum, and the coccyx.

8.5b Spinal Curvatures
- Spinal curvatures help support the weight of the body better than a straight spine.

8.5c Vertebral Anatomy
- A typical vertebra has a body and a vertebral arch. Together they enclose a vertebral foramen, which, when stacked, form the vertebral canal that houses the spinal cord.
- Cervical vertebrae typically have both transverse foramina and bifid spinous processes.
- Thoracic vertebrae have costal facets on their bodies and on most of their transverse processes.
- Lumbar vertebrae are more massive than cervical and thoracic vertebrae. They lack costal facets and transverse foramina.
- The sacrum is a triangular-shaped bone with five fused vertebrae by the late 20s.
- Four small coccygeal vertebrae fuse to form the coccyx by the mid 20s.

8.6 Bones of the Thoracic Cage
- The thoracic cage is composed of the thoracic vertebrae, the ribs, and the sternum.

8.6a Sternum
- The sternum is composed of the manubrium, body, and xiphoid process.

8.6b Ribs
- There are 12 pairs of ribs. Ribs 1–7 are called true ribs, and ribs 8–12 are called false ribs. The last two false ribs (11–12) are floating ribs.

8.7 The Upper and Lower Limbs: A Comparison
- Each limb is held in place by a girdle (pectoral girdle for the upper limbs, pelvic girdle for the lower limbs).
- The arm and thigh each contain one bone, the forearm and leg contain two bones that pivot against one another, there are multiple short bones in the wrist and proximal foot, and both the hand and foot contain 14 phalanges each.

8.8 The Pectoral Girdle and Its Functions
- The pectoral girdle is composed of the clavicle and scapula; it articulates with the axial skeleton and supports the upper limb.

8.8a Clavicle
- The clavicle is the S-shaped bone that articulates with the sternum on its medial end and the scapula on its lateral end.

8.8b Scapula
- The scapula forms the “shoulder blade.” Its glenoid cavity articulates with the head of the humerus.

8.9 Bones of the Upper Limb
- Each upper limb contains a humerus, a radius, an ulna, 8 carpals, 5 metacarpals, and 14 phalanges.

8.9a Humerus
- The humerus is the bone of the arm. It articulates proximally with the scapula and distally with the radius and ulna at the elbow.

8.9b Radius and Ulna
- The radius and ulna are the bones of the forearm.

8.9c Carpals, Metacarpals, and Phalanges
- The 8 carpal bones form the wrist, the 5 metacarpals form the bones of the palm, and the 14 phalanges form the bones of the fingers.
**Chapter Eight**

**Skeletal System: Axial and Appendicular Skeleton**

### 8.10 The Pelvic Girdle and Its Functions
- The pelvic girdle consists of two osa coxae, whereas the pelvis is composed of the osa coxae, sacrum, and coccyx.

#### 8.10a Os Coxae
- Each os coxae forms through the fusion of an ilium, an ischium, and a pubis. The acetabulum of the os coxae articulates with the head of the femur.

#### 8.10b True and False Pelves
- The pelvic brim is an oval ridge of bone that divides the pelvis into a true pelvis and a false pelvis.

#### 8.10c Sex Differences in the Pelvis
- The osa coxae are the most sexually dimorphic bones of the body.
- The female pelvis is wider and has a broader greater sciatic notch and a more rectangular-shaped pubis than the male pelvis.

#### 8.10d Age Differences in the Ossa Coxae
- As a person ages, the symphysial surface transforms from a billowed surface to more flattened.

### 8.11 Bones of the Lower Limb
- Each lower limb is composed of the femur, the patella, the tibia, the fibula, 7 tarsals, 5 metatarsals, and 14 phalanges.

#### 8.11a Femur and Patella
- The femur has a rounded head and an elongated neck.
- The medial and lateral condyles of the femur articulate with the condyles on the tibia.
- The patella is the kneecap and is located within the quadriceps femoris tendon.

#### 8.11b Tibia and Fibula
- The tibia is the medially located, thick, and strong bone of the leg, and its medial malleolus forms the medial bump of the ankle.
- The fibula is the laterally located, slender bone, and its lateral malleolus forms the lateral bump of the ankle.

#### 8.11c Tarsals, Metatarsals, and Phalanges
- The 7 tarsal bones form the proximal foot, the 5 metatarsals form the bones of the arch of the foot, and the 14 phalanges form the bones of the toes.

#### 8.11d Arches of the Foot
- The three arches of the foot support the body’s weight and ensure plantar structures do not get compressed when we are standing.

### 8.12 Development of the Skeleton
- The appendicular skeleton forms from limb buds beginning in the fourth week. Development of the limbs is mostly complete by week 8.

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**Challenge Yourself**

**Do You Know the Basics?**

1. The bony portion of the nasal septum is formed by the
   a. perpendicular plate of the ethmoid bone and vomer.
   b. perpendicular plate of the ethmoid bone only.
   c. nasal bones and perpendicular plate of the ethmoid bone.
   d. vomer and sphenoid bones.

2. Which bone marking is matched with its correct description?
   a. foramen; bony prominence
   b. facet; opening in the bone
   c. tubercle; small, bony projection
   d. alveolus; narrow groove

3. The frontal and parietal bones articulate at the _____ suture.
   a. coronal
   b. sagittal
   c. lambdoid
   d. squamosal

4. The compression of an infant’s skull bones at birth is facilitated by spaces between unfused cranial bones called
   a. ossification centers.
   b. fontanelles.
   c. foramina.
   d. fossae.

5. Most _____ vertebrae have a heart-shaped body and a long spinous process that is angled inferiorly.
   a. cervical
   b. thoracic
   c. lumbar
   d. sacral

6. The female pelvis typically has which of the following characteristics?
   a. narrow, U-shaped greater sciatic notch
   b. wide subpubic angle, greater than 100 degrees
   c. short, triangular pubic body
   d. smaller, heart-shaped pelvic inlet
7. When the forearm is supinated,
   a. the pollex is laterally placed.
   b. the radius and ulna are crossed.
   c. the little finger is laterally placed.
   d. the pisiform is facing posteriorly.
8. The spine of the scapula separates which two fossae?
   a. supraspinous, subscapular
   b. subscapular, infraspinous
   c. infraspinous, supraspinous
   d. supraspinous, glenoid
9. The femur articulates with the tibia at the
   a. linea aspera.
   b. medial and lateral condyles.
   c. head of the femur.
   d. greater trochanter of the femur.
10. When sitting upright, you are resting on your
    a. pubic bones.
    b. ischial tuberosities.
    c. sacroiliac joints.
    d. iliac crest.
11. What are sutures, and how do they affect skull shape and
growth?
12. What cranial and facial bones may be seen easily on the
    inferior surface of the skull?
13. What are the functions of the paranasal sinuses?
14. What are the spinal curvatures, when do they form, and what
    are their functions?
15. Describe similarities and differences among true, false, and
    floating ribs.
16. Compare and contrast the anatomic and functional features
    of the pectoral and pelvic girdles.
17. What are the primary similarities and differences between the
    upper and lower limbs?
18. Distinguish between the true and false pelvis. What bony
    landmark separates the two?
19. What are the functions of the arches of the foot?
20. Discuss the development of the limbs. What primary germ
    layers form the limb bud? List the major events during each
    week of limb development.

**Can You Apply What You’ve Learned?**

*Use the following paragraph to answer questions 1–5.*

You are called to a crime scene reported in the woods. A hiker
found a skeleton underneath some leaves—and as the osteologist
of the team, it is up to you to identify the bones, as well as
determine the age and sex of the skeleton. You begin examining
the skeleton.

1. The first bone you identify is long and rather large. It has a
    rounded head, an elongated neck, and smooth condyles on its
    distal surface. There also are large, bony projections near the
    neck of this bone. Based on these features, you determine that
    the bone in question is a
    a. humerus.
    b. radius.
    c. femur.
    d. tibia.
2. As you examine the rest of the skeleton, you notice an
    S-shaped bone that appears to have been fractured prior to
defeat. This bone likely was fractured due to a fall on the
    outstretched hand. What bone is it?
    a. clavicle
    b. metacarpal
    c. rib
    d. phalanx
3. You pick up the skull and begin examining it. The mastoid
    process is rather small, and the external occipital protuberance
    is not well defined. The supraorbital margins are rather sharp,
    and the mental protuberance is pointed (instead of squared-off).
    All of these features lead you to the following
    conclusion:
    a. The skeleton has been buried for a long time.
    b. The skull is from a female.
    c. The skull is from a male.
    d. The skull is from a young child.
4. Based on the answer you gave to question 3, what feature(s)
    would you expect to see in the pelvis?
    a. narrow pelvic inlet
    b. elongated, rectangular pubic bones
    c. narrow, U-shaped sciatic notch
    d. 90-degree subpubic arch
5. The police officers also want to know if you can determine
    the age at death of the skeleton. You determine that all long
    bone epiphyses have fused to their diaphyses, and all
    permanent teeth are erupted. The cranial sutures are still open,
    and the symphysial surface is flattened, but there is no
    complete rim around the symphysis. Based on these features,
    a likely age range for the skeleton would be
    a. younger than 10 years.
    b. 10–20 years.
    c. 20–35 years.
    d. 35–50 years.

**Can You Synthesize What You’ve Learned?**

1. Paul viewed his newborn daughter through the nursery
    window at the hospital and was distressed because the infant’s
    skull was badly misshapen. A nurse told him not to worry—
    the shape of the infant’s head would return to normal in a few
days. What caused the misshapen skull, and what anatomic
    feature of the neonatal skull allows it to return to a more
    rounded shape?
2. A female in her first trimester of pregnancy sees her physician. She suffers from lupus and has read that the drug thalidomide has shown remarkable promise in treating the symptoms. Should the physician prescribe this drug for her at this time? Why or why not?

3. Forensic anthropologists are investigating portions of a human pelvis found in a cave. How can they tell the sex, the relative age, and some physical characteristics of the individual based on the pelvis only?
Our skeleton protects vital organs and supports soft tissues. Its marrow cavity is the source of new blood cells. When it interacts with the muscular system, the skeleton helps the body move. Bones are too rigid to bend—but they meet at joints that anatomists call articulations. In this chapter, we examine how bones articulate (connect) and permit varying degrees of freedom of movement, depending upon both the shapes and the supporting structures of the different joints.
Classification of Joints

**LEARNING OBJECTIVES**

1. Define a joint.
2. Compare the structural and the functional classification of joints.
3. Explain the inverse relationship between mobility and stability within a joint.

A joint, or an articulation (ar-tik’yə-lə-shən), is the place of contact between bones, between bone and cartilage, or between bones and teeth. Bones are said to articulate with each other at a joint. The scientific study of joints is called arthrology (ar-thrə-lə-je; arthr = joint, logos = study).

Joints are classified by both their structural characteristics and their functional characteristics, which are the movements they allow (table 9.1). Joints are categorized structurally on the basis of whether a space occurs between the articulating surfaces of the bones and the type of connective tissue that binds the articulating surfaces of the bones:

- A fibrous (fib’brús) joint has no joint cavity and occurs where bones are held together by dense regular (fibrous) connective tissue.
- A cartilaginous (kar-ti-laj’i-nəs) joint has no joint cavity and occurs where bones are joined by cartilage.
- A synovial (si-nəv’səl) joint has a fluid-filled joint cavity that separates the articulating surfaces of the bones. The articulating surfaces are enclosed within a connective tissue capsule, and the bones are attached to each other by various ligaments.

Joints are classified functionally based on the extent of movement they permit:

- A synarthrosis (si’nər-thrə-sis; pl., synarthroses, -sēz; syn = joined, together; osis = condition) is an immobile joint. Two types of fibrous joints and one type of cartilaginous joint are synarthroses.
- An amphiarthrosis (am’fē-ar-thrə-sis; pl., amphiarthroses, -sēz; amphi = around) is a slightly mobile joint. One type of fibrous joint and one type of cartilaginous joint are amphiarthroses.
- A diarthrosis (di-ar-thrə-sis; pl., diarthroses, -sēz; di = two) is a freely mobile joint. All synovial joints are diarthroses.

The motion permitted at a joint ranges from no movement, such as where some skull bones interlock at a suture, to extensive movement, such as that seen at the shoulder, where the humerus articulates with the scapula. The structure of each joint determines both its mobility and its stability. There is an inverse relationship between mobility and stability in articulations. When the mobility of a joint increases, its stability decreases. In contrast, if a joint is immobile, it has maximum stability. Figure 9.1 illustrates the tradeoff between mobility and stability for various joints. It allows you to view and compare the structural versus functional classification of some common joints.

### Table 9.1 Joint Classifications

<table>
<thead>
<tr>
<th>Structural Classification</th>
<th>Structural Characteristics</th>
<th>Structural Categories</th>
<th>Functional Classification</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fibrous (see figure 9.2)</td>
<td>Dense regular connective tissue holds together the ends of bones and bone parts; no joint cavity</td>
<td>Gomphosis</td>
<td>Synarthrosis (immobile) or amphiarthrosis (slightly mobile)</td>
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<td></td>
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<td>Suture</td>
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<td>Syndesmosis</td>
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<tr>
<td>Cartilaginous (see figure 9.3)</td>
<td>Pad of cartilage is wedged between the ends of bones; no joint cavity</td>
<td>Synchrondrosis</td>
<td>Synarthrosis (immobile) or amphiarthrosis (slightly mobile)</td>
</tr>
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<td></td>
<td>Symphyssis</td>
<td></td>
</tr>
<tr>
<td>Synovial (see figure 9.6)</td>
<td>Ends of bones covered with articular cartilage; joint cavity separates the articulating bones; joint enclosed by an articular capsule, lined by a synovial membrane; contains synovial fluid</td>
<td>Plane</td>
<td>Diarthrosis (freely mobile)</td>
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<td></td>
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<td>Hinge</td>
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<td>Pivot</td>
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<td>Condylar</td>
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<td>Saddle</td>
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<td>Ball-and-socket</td>
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</tr>
</tbody>
</table>

**INTEGRATE**

**LEARNING STRATEGY**

You can logically figure out the names of most joints by putting together the names of the bones that form them. For example, the glenohumeral joint is where the glenoid cavity of the scapula meets the head of the humerus, and the sternoclavicular joint is where the manubrium of the sternum articulates with the sternal end of the clavicle.

The following detailed discussion of articulations is based upon their structural classification, with functional categories included as appropriate.

**WHAT DID YOU LEARN?**

1. What is the relationship between mobility and stability in a joint?
2. Are all fibrous joints also synarthroses? Explain why or why not.