The Cleveland Clinic Foundation Intensive Review of Internal Medicine

SIXTH EDITION
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Dedication

I dedicate this book to the memory of my father, Alfred Stoller (1919–2011), whose unending love, support, and relentless tenacity have forged his sons; to my wife, Terry, whose unceasing support and love have allowed all things; and to my son, Jake, whose huge spirit, energy, and drive light the way forward.

James K. Stoller, MD, MS

I would like to dedicate this edition to my lovely wife Simone for her continued support and encouragement and to my Father, Earl Nielsen, MD, for consistently role-modeling excellence.

Craig Nielsen, MD, FACP

To my daughters, my family, and my residents, who motivate and inspire me every day.

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Preface

The sixth edition of the Cleveland Clinic Foundation Intensive Review of Internal Medicine reflects our ongoing fascination with how physicians learn best and our continued passion for clinical medicine, medical education, and scholarship—values that define the culture of the Cleveland Clinic. This sixth edition also embraces new models of learning by blending a printed text with an on-line question bank, both meant to enhance the reader’s knowledge of internal medicine and preparedness for certifying examinations.

This book has its origins in the Clinic’s Intensive Review of Internal Medicine Symposium, a 6-day course offered annually since 1989, that is designed for physicians preparing for the certification and recertification examinations in internal medicine, and for those wishing for a comprehensive, state-of-the-art review of the field. The Symposium celebrated its 20th offering in the United States in June 2008 and has been presented four times internationally.

We continue to be humbled and gratified by the success of the Symposium and of the first five editions of this book. Experience has taught us that practicing physicians learn best when using a case-driven format, and that factual knowledge and new developments in the field are best integrated into clinical practice through a discussion of case management. Never meant to be a comprehensive textbook of internal medicine, this sixth edition of the book builds on this concept and continues to use bulleted points, clinical vignettes, and review exercises to convey important “clinical pearls.” This edition newly blends a printed text with an expanded and updated question bank which is available as an online adjunct learning tool.

Each chapter in the sixth edition has been extensively reviewed and carefully updated where necessary, and many chapters have been substantially revised or completely rewritten. Several chapters are new since the fifth edition, reflecting input from our readers and attendees of the Intensive Review of Internal Medicine Symposium. Updated references have been provided in the suggested readings at the end of each chapter. Enhanced chapter features include call-out boxes with bulleted “Points to Remember” and the uniform inclusion of review exercises (with discussions) to test the reader’s knowledge of key points.

This book continues to serve as the syllabus for both domestic and international offerings of the Cleveland Clinic Intensive Review of Internal Medicine Symposium. It also provides an independent study guide for those preparing for the certification and recertification examinations in internal medicine.

We remain extraordinarily grateful to our colleagues and contributors who have supported the Symposium and this book over the years. They represent the best and brightest among clinician-educators, adept at teaching the art and science of medicine, and facile in distilling their clinical wisdom into a concise and practical document. In addition, we are indebted to our many students, residents, fellows, and colleagues who have taught us so much over the years about clinical medicine and about how physicians learn best. Finally, there are several people without whom this book would not have come to fruition. We are indebted to David Longworth, M.D., our colleague and former editor, now Chair of the Medicine Institute at Cleveland Clinic. As one of the founding editors of this book, his wisdom and organizational skills are still very evident in this sixth edition. We also thank Dr. Brian Mandell and Dr. Frank Michota, both colleagues at Cleveland Clinic who ably served as co-editors of the fourth and fifth editions of the book and whose creativity and craftsmanship are reflected in these pages. We are grateful to Sonya Seigafuse of Lippincott Williams & Wilkins (LWW) for her ongoing support of the book, both editorial and intellectual, in building on past editions. Tom Conville provided superb developmental editorial help in preparing and organizing the manuscript. We also offer our deep thanks to our administrative assistants, Maria Hernandez and Carolyn Albert, who contributed energy, and craftsmanship in shepherding each chapter through editorial revision, completion, and submission to the publisher. Finally, we are grateful for our families, who graciously tolerated and supported the many hours we devoted to preparing this book.

As editors, we take extreme pride in this book’s content, and we accept sole responsibility for its shortcomings. We hope that this book deepens your own passion for clinical medicine and for medical education, just as it has continued to fuel our own.

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Please see the companion ebook for an interactive question bank and for expanded chapters containing full subspecialty review content.

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RAPID BOARD REVIEW—KEY POINTS TO REMEMBER:

**Primary prevention** aims to reduce the incidence of a disease.

**Secondary prevention** aims to reduce the prevalence of a disease.

**CARDIOVASCULAR DISEASE**

**Blood Pressure**
- Screen asymptomatic persons at least every 2 years, beginning at age 18 years.

**Diabetes Mellitus**
- Screen asymptomatic patients with sustained blood pressure (treated or untreated) $>135/80$ mmHg (U.S. Preventive Services Task Force—USPSTF). The American Diabetes Association has broader screening recommendations.
- Fasting plasma glucose levels $>126$ mg/dL on two separate occasions or a hemoglobin A1C $>6.5\%$ are diagnostic of type 2 diabetes mellitus.

**Cholesterol**
- Screen with a total and high-density lipoprotein serum cholesterol level in a nonfasting state “asymptomatic” adults, every 5 years beginning at age 35 years in men and 45 years in women, and those with additional cardiovascular risk factors (USPSTF) at younger ages (20 to 35 years in men and 20 to 45 years in women).
- Screen with a fasting lipid profile all adults, at least every 5 years, beginning at age 20 years. An age to stop screening is not established (National Cholesterol Education Program).

**Abdominal Aortic Aneurysms**
- Screen with an abdominal ultrasound all men between the ages of 65 and 75 years who have ever smoked at least the equivalent of 100 cigarettes.

**Electrocardiography, Exercise Treadmill Test, Calcium Scoring, Computed Tomography Angiography**
- Do not screen adults at low risk for coronary heart disease events (USPSTF).

**Aspirin**
- Use aspirin for men aged 45 to 79 years when the benefit to reduce myocardial infarctions outweighs the potential harm due to gastrointestinal hemorrhage (USPSTF).
- Use aspirin for women aged 55 to 79 years when the benefit to reduce ischemic strokes outweighs the potential harm due to gastrointestinal hemorrhage (USPSTF).

**CANCER SCREENING**

**Breast Cancer**
- Annual or biennial mammography screening after the age of 40 years.
- Magnetic resonance imaging only in patients at very high risk for breast cancer.

**Lung Cancer**
- Annual low-dose computed tomography screening for individuals aged 55 to 79 years with at least a 30 pack-year history of smoking (American Association for Thoracic Surgery).
Colons and Rectal Cancer
- In the low- or average-risk patients, start screening at the age of 50 years, with a fecal occult blood test yearly, sigmoidoscopy every 5 years, or colonoscopy every 10 years.
- In high-risk patients, start screening at an earlier age, usually around age 40 years, or 10 years earlier than the earliest diagnosed colon cancer in the family, whichever number is lower, with a colonoscopy every 5 years.
- In very high-risk patients (e.g., familial polyposis, inflammatory bowel disease), refer to a specialty center for more aggressive screening and monitoring.

Prostate Cancer
- Definitive evidence supporting prostate cancer screening is still lacking.
- Offer annual digital rectal examination and prostate-specific antigen testing to men older than 50 years (45 years in high-risk patients), whose life expectancy is at least 10 years (American Cancer Society).
- Discuss with the patients the potential benefits, risks, and uncertainties of the screening.

Cervical Cancer
- Start screening at age 21 years with Papanicolaou (Pap) smear testing every 3 years.
- Human papillomavirus testing along with Pap smear testing is recommended every 3 to 5 years in patients older than 30 years.
- Beyond age 65 to 70 years, screening should be continued based on the patient risk.

Vaccinations
- In general, live attenuated viral vaccines should be avoided in immunocompromised and pregnant patients.
- Be familiar with recommended vaccines in certain patient populations (e.g., the patient with splenectomy or with newly diagnosed HIV).
- Be familiar with recommended immunizations for healthy adults without chronic diseases or special circumstances (e.g., pregnancy, immunocompromised state).

Suggested Readings


RAPID BOARD REVIEW—KEY POINTS TO REMEMBER:

Amenorrhea

- Pregnancy should be considered as the number one cause of secondary amenorrhea.
- The differential diagnosis includes polycystic ovarian disease (most common ovarian cause), chronic anovulation, structural changes (cervical stenosis and Asherman’s syndrome), adrenal or thyroid dysfunction, endometrial atrophy (i.e., continuous progesterone use), pituitary prolactinoma, gestational trophoblastic disease, and nutritional disorders.

Premature Menopause or Premature Ovarian Insufficiency

- Occurs before the age of 40 years.
- Tests to order: pregnancy test (negative), follicle-stimulating hormone (FSH) (>40 IU/L), estradiol (<12 pg/mL), serum antimüllerian hormone (low), prolactin level (normal), transvaginal ovarian ultrasound (small to absent ovaries with minimal follicular activity).
- Tests to consider: karyotype (Turner’s syndrome—45,XO, trisomy X, Swyer’s syndrome—XY gonadal dysgenesis, or mosaicism), thyroid peroxidase antibodies (positive in autoimmune thyroiditis), fragile X mutation (FMR-1 gene mutation positive), celiac antibodies, adrenal antibodies, B12, adrenocorticotropic hormone stimulation test, and baseline dual X-ray absorptiometry (may be low in estrogen-deficient women).

Perimenopause or “Menopause Transition”

- The time before and after the last period, when hormone fluctuations occur.
- Diagnosis is made clinically; no serologic testing can predict the time of menopause.
- A persistent elevation in FSH [and luteinizing hormone (LH)] can signal that menopause is imminent.

Hormonal Contraceptives

- In the perimenopausal woman who is a nonsmoker and in general good health without venous thromboembolism risks, hormonal contraceptives (HCs) can be continued up to ages of 50 to 55 years.
- Factor V Leiden mutation testing is not recommended before starting HCs in a patient without a family or personal history of thromboembolic disease.
- HCs control the irregular cycles associated with the menopausal transition state, can control vasomotor symptoms, and provide contraceptive protection.
- Once the woman becomes menopausal, if symptomatic, HCs can be converted to progestin/estrogen therapy. Progestin/estrogen menopausal therapy does not provide contraceptive protection.

Menopause

- The diagnosis is made retrospectively after the cessation of menses for 1 year.
- In most cases, FSH and estradiol levels are not needed for the diagnosis.
- Any postmenopausal vaginal bleeding requires an endometrial biopsy.
- Bone mass declines starting in a woman’s 30s and is accelerated during the menopausal transition and early postmenopausal time. Screening for osteoporosis should be done in all women above the age of 65, or before 65 if one or more of the following are present: natural and surgically induced menopause, premature ovarian insufficiency, maternal or personal history of hip fracture, a weight of less than 128 lb, smoking, glucocorticoids use, eating disorders, anticonvulsant therapy, height loss, and history of prolonged amenorrhea (National Osteoporosis Foundation).

Hormone Therapy

- Hormone therapy (HT) should be considered in select patients. The benefits and risks should be discussed. The lowest effective dose should be used, individualized, and periodically reviewed.
- Both estrogen and progestin therapies should be given, unless the woman has had hysterectomy, in which case estrogen therapy alone is prescribed.
- Absolute contraindications to HT include pregnancy and undiagnosed vaginal bleeding.
Most ovarian cancers are not usually believed to be estrogen dependent and therefore do not constitute a contraindication to HT.

A remote history of a provoked deep venous thrombosis (DVT) is not an absolute contraindication to HT. Any patient with a history of recurrent DVT or a family history of thromboembolic events, however, should be evaluated for the presence of a hypercoagulable state and should use only transdermal HT, not oral HT.

Alternative treatments for hot flashes include selective serotonin reuptake inhibitors (citalopram), norepinephrine serotonin reuptake inhibitors (venlafaxine), anticonvulsants (gabapentin), vitamin E, megestrol acetate (Megace), soy products containing soy proteins and isoflavones, dong quai, black cohosh, and red clover.

**SUGGESTED READINGS**


RAPID BOARD REVIEW—KEY POINTS TO REMEMBER:

- Most medications used in pregnancy are category B or C.
- Examples of category D and X drugs and their potential effects include the following:

<table>
<thead>
<tr>
<th>CATEGORY D</th>
<th>EFFECTS</th>
<th>CATEGORY X</th>
<th>EFFECTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Angiotensin-converting enzyme inhibitors</td>
<td>Unsafe after the first trimester; renal failure and death in neonate</td>
<td>Measles, mumps, rubella, varicella live-attenuated vaccines</td>
<td>Congenital viral syndromes</td>
</tr>
<tr>
<td>Anticholinergic drugs</td>
<td>Neonatal meconium ileus</td>
<td>Danazol</td>
<td>Ambiguous genitalia</td>
</tr>
<tr>
<td>Antithyroid drugs</td>
<td>Neonatal goiter and hypothyroidism, aplasia cutis (methimazole)</td>
<td>Warfarin</td>
<td>Embryopathy: hypoplastic nose, epiphysial stippling, optic atrophy, microcephaly, and growth restriction</td>
</tr>
<tr>
<td>Carbamazepine</td>
<td>Neural tube defects (NTDs)</td>
<td>Diethylstilbestrol</td>
<td>Vaginal adenosis and clear cell carcinoma in offspring</td>
</tr>
<tr>
<td>Lithium</td>
<td>Ebstein's anomaly</td>
<td>Vitamin A</td>
<td>Spontaneous abortions and fetal malformations</td>
</tr>
<tr>
<td>Nonsteroidal anti-inflammatory drugs</td>
<td>Constriction of the ductus arteriosus in third trimester</td>
<td>Isotretinoin</td>
<td>Isotretinoin syndrome</td>
</tr>
<tr>
<td>Phenytoin</td>
<td>Fetal hydantoin syndrome</td>
<td>Triazolam</td>
<td>Cleft palate</td>
</tr>
<tr>
<td>Psychoactive drugs</td>
<td>Fetal withdrawal syndrome</td>
<td>Lovastatin</td>
<td>Bone malformation</td>
</tr>
<tr>
<td>Tetracycline</td>
<td>Tooth discoloration, bone malformation</td>
<td>Thalidomide</td>
<td>Limb-shortening defects</td>
</tr>
<tr>
<td>Valproic acid</td>
<td>NTDs</td>
<td>Ribavirin</td>
<td>Embryocidal</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Lead, methyl mercury, polychlorinated and polybrominated biphenyls, organic solvents, ionizing radiation</td>
<td>Assorted mental, physical, and metabolic effects</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Miscarriage</td>
</tr>
</tbody>
</table>

MEDICAL DISEASES DURING PREGNANCY

Anemia

- Defined as a hematocrit ≤30% or hemoglobin ≤10 g/dL.
- Causes: dilution, iron, folate deficiencies, thalassemias, sickle cell disease.
- Sickle trait carriers are at risk for urinary tract infections and should be screened.
- No mortality or cardiac failure in patients with hemoglobin >4.5 mg/dL.

Asthma

- Continue prepregnancy treatment (most medications safe) and minimize triggers.
- During a severe attack, fetal monitoring may be indicated:
  - $P_{O_2} \leq 60$ mmHg correlates with fetal compromise.
  - $P_{CO_2} > 38$ mmHg or $pH < 7.35$ may reflect retention and require intubation.

Cardiac Diseases

- Most cardioactive medications are Food and Drug Administration categories B or C.
CHAPTER 3  Medical Diseases in Pregnancy

- Endocarditis prophylaxis is of limited value. Treat the patient with a cesarean section after a long labor with prophylactic antibiotics.
- Peripartum cardiomyopathy can occur in the last month of pregnancy or the first 6 months after delivery. Treat similarly to other cardiomyopathies.
- Treat mechanical valve prostheses with (low-molecular-weight heparin (LMWH) in the first trimester to avoid fetal anomalies, and a combination of LMWH and unfractionated heparin in the third trimester for easy reversibility.

Deep Vein Thrombosis
- The risk of thrombosis increases during pregnancy and postpartum.
- Coumadin is relatively contraindicated because of teratogenesis in the first trimester and risk of bleeding later in pregnancy or at delivery.
- Vena cava ligation or placement of a filter are acceptable during pregnancy.

Diabetes Mellitus
- Tight glucose control is desired:
  - Fasting serum glucose level <100 mg/dL
  - 2 hour postprandial level <120 mg/dL
- Universal screening for gestational diabetes mellitus is done with a 50-g, 1-hour screening Glucola test in the second trimester. If abnormal, a 100-g, 3-hour Glucola diagnostic test is done. Follow-up 4 months after delivery and every 1 to 2 years thereafter.
- Continue metformin throughout the pregnancy (decreased chance of miscarriage and gestational diabetes). Do not use other oral hypoglycemics.

Human Immunodeficiency Virus
- Universal screening of all pregnant women for human immunodeficiency virus (HIV) is recommended.
- Antivirals given orally to the mother from 14 weeks' gestation to delivery, intravenously during labor, and orally to the infant for ≥6 weeks; a triple-drug regimen is usually recommended.

Chronic Hypertension
- Methyldopa, hydralazine, labetalol, nifedipine do not affect the fetal outcome.
- Chronic hypertension (HTN; ≥140/90 mmHg) exists before or appears during the first 20 weeks of pregnancy; poor maternal and fetal outcome with diastolic pressures >110 mmHg.

Preeclampsia or Pregnancy-Induced Hypertension
- Preeclampsia (renal)
  - Proteinuria, edema, HTN, decreased renal function

- Eclampsia (neurologic)
  - Convulsions

HELLP syndrome (hepatic microvascular)
- Hemolysis, Elevated Liver enzymes, Low Platelets, possible liver rupture
- Delivery is the only “cure.”
- Use intravenous magnesium during labor and 12 to 24 hours afterward to prevent seizures.

Hyperthyroidism
- The free thyroxine level is the best way to measure the thyroid function.
- Hyperthyroidism is treated with propylthiouracil.
- If thyroid storm is precipitated by terbutaline, treat with propranolol.

Hypothyroidism
- No adverse effects of medication use during pregnancy.

Urinary Tract Infections
- Treat asymptomatic bacteriuria or urinary tract infections with 3 day antibiotics.

SUGGESTED READINGS


The relationship between a dichotomous classification of a diagnostic test result and the presence or absence of the disease can be summarized using a 2 × 2 table.

<table>
<thead>
<tr>
<th>TRUE DISEASE STATUS</th>
</tr>
</thead>
<tbody>
<tr>
<td>TEST RESULT</td>
</tr>
<tr>
<td>Positive</td>
</tr>
<tr>
<td>Negative</td>
</tr>
<tr>
<td>Total</td>
</tr>
</tbody>
</table>

- The sensitivity of a diagnostic test is the proportion of patients with disease who have a positive test, that is, the true-positive rate.
  
  \[
  \text{Sensitivity} = \frac{A}{A+C}
  \]

- The specificity of a diagnostic test is the proportion of patients without disease who have a negative test, that is, the true-negative rate.
  
  \[
  \text{Specificity} = \frac{D}{B+D}
  \]

- The accuracy of a diagnostic test depends on the cut-point value of the test used to distinguish between a positive and a negative test.

- For diagnosis, what is important are the positive and negative predictive values of the test. The positive (negative) predictive value is the proportion of patients with positive (negative) results who are correctly diagnosed.
  
  Positive predictive value = \( \frac{A}{A+B} \)

  Negative predictive value = \( \frac{D}{C+D} \)

- Positive and negative predictive values of a diagnostic test depend on the prevalence of the disease, that is, on the probability of disease before the test is done.

  Positive predictive value = \( \frac{(\text{Prevalence}) \times (\text{Sensitivity})}{(\text{Prevalence}) \times (\text{Sensitivity}) + (1 - \text{Prevalence}) \times (1 - \text{Specificity})} \)

  Negative predictive value = \( \frac{(1 - \text{Prevalence}) \times (\text{Specificity})}{(1 - \text{Prevalence}) \times (\text{Specificity}) + (\text{Prevalence}) \times (1 - \text{Sensitivity})} \)
A person’s pretest probability of having the disease is modified to a posttest probability by incorporating information on the accuracy of the diagnostic test.

The ratio of the true-positive and false-positive rates of a diagnostic test is called the *likelihood ratio* of the test.

\[
\text{Likelihood ratio} = \frac{\text{Sensitivity}}{(1 - \text{Specificity})}
\]

**SUGGESTED READINGS**


Ocular Manifestations of Systemic Disease

Jack Shao and Careen Y. Lowder

RAPID BOARD REVIEW—KEY POINTS TO REMEMBER:

- The leading causes of blindness in the United States are macular degeneration, diabetic retinopathy, glaucoma, and cataract.
- Vital signs to ophthalmologists mean vision, pupillary response, and intraocular pressure.
- Cotton-wool spots, hard exudates, and intraretinal hemorrhages are the most common nonspecific manifestations of retinopathy.
- Papilledema usually does not cause reduction in visual acuity unless it is long standing.

Giant Cell Arteritis and Temporal Arteritis

- May present with sudden loss of vision in one or both eyes, diplopia, and systemic symptoms.
- If suspected, the initiation of corticosteroids should be instituted immediately, even before the temporal artery biopsy.

Hypertension—Phases

- Arterial narrowing and tortuosity.
- Change in the light reflex of the vessel wall, arteriovenous crossing.
- Flame-shaped hemorrhages, cotton-wool spots, or microinfarcts.
- Papilledema.

Malignant Hypertension

- A medical emergency, but do not decrease the systemic blood pressure too rapidly because it may lead to infarction of the optic nerve.

Diabetic Retinopathy

- In type 1 diabetes there is a 5-year delay. In type 2 diabetes the retinopathy may be present at the time of diagnosis.
- Retinal hemorrhages and hard exudates are not specific, but their distribution and relative proportions have a characteristic and essentially pathognomonic appearance.
- Diabetic patients should be evaluated by an ophthalmologist at least once a year.

Retinal Artery Occlusion

- Sudden loss of vision.
- The retina is opacified with a cherry-red spot in the macular area.

Granulomatosis with Polyangiitis

- Orbital disease, the most common ophthalmic manifestation, presents with pain, tenderness, limited extraocular movement, and proptosis.

Rheumatoid Arthritis

- Keratoconjunctivitis sicca is the most common ocular problem. It requires frequent instillation of tears or bland ointment to prevent corneal opacification and melting.
- Scleritis is the second most common ocular finding. It requires systemic treatment with nonsteroidal anti-inflammatory drugs, in addition to topical corticosteroids.
- Screen for antimalarial drug toxicity. Hydroxychloroquine may cause bull’s-eye pigmentary maculopathy.

HLA-B27–Associated Uveitis

- More than 50% of acute anterior uveitis is associated with the HLA-B27 antigen.
- Iritis is characterized by severe pain, redness, and photophobia. A marked conjunctival injection and ciliary flush are present. The cornea may be hazy. Fibrinous exudates or a hypopyon may be present. The anterior lens surface may be obscured by fibrin.

Thyroid Eye Disease

- Includes proptosis, eyelid retraction and lagophthalmos, and restriction of the extraocular muscles, resulting in diplopia.

Leukemia

- Leukemic infiltrates may be seen in the iris, retina, choroid, and optic nerve.

Acquired Immunodeficiency Syndrome

- The most common ocular manifestation in acquired immunodeficiency syndrome is the cotton-wool spot.
- The most common and sight-threatening ocular infection is cytomegalovirus retinitis.
Glaucoma
- A multifactorial disease process in which the end result is the characteristic optic neuropathy.
- All medical and surgical treatments are aimed at lowering intraocular pressure.
- Topical medications for glaucoma can have systemic side effects.

Macular Degeneration
- No cure, but smoking cessation and vitamins can halt the progression of the dry form.
- The most effective treatment is the intraocular injection of antivascular endothelial growth factor medication.

Retinal Detachment
- Loss of side and/or central vision, a dark shadow, a veil, or, with total detachment, loss of vision. Frequently, patients describe seeing new floaters or flashes of light within the eye.

SUGGESTED READINGS


Noninvasive stress testing can be performed in patients with unreliable histories or poor functional capacity, or in patients scheduled for high- or intermediate-risk surgery when additional clinical risk factors are present. It should not be done in patients undergoing low-risk surgery. It should be avoided in high-risk patients with unstable myocardial ischemia, where coronary angiography is recommended.

Cardiovascular Risk Reduction
Coronary revascularization with coronary artery bypass graft (CABG) or percutaneous coronary intervention (PCI) in

- Survivors of sudden cardiac death
- ST segment elevation myocardial infarction (STEMI). Urgent CABG indicated in patients that are not candidates for PCI and have:
  - Ongoing/recurrent ischemia
  - Severe heart failure
  - High-risk features
- Non-STEMI with refractory angina, hemodynamic or electrical instability
- Symptomatic stable ischemic heart disease (SIHD) with
  - Significant unprotected left main coronary artery stenosis
  - Three vessel disease with/without proximal left anterior descending (LAD) stenosis
  - Two vessel disease with proximal LAD stenosis or extensive ischemia, especially in patients with left ventricular dysfunction and ejection fraction <50%

Pulmonary Risk Assessment

- Evaluation not indicated in patients requiring emergency surgery.
- Diagnostic spirometry indicated in all patients requiring elective resectional thoracic surgery. Carbon monoxide diffusing capacity (DLCO) required in patients having excessive dyspnea on exertion or evidence of interstitial lung disease on radiographs.
  - If forced expiratory volume in one second (FEV1) ≥2 L or ≥80% predicted, pneumonectomy can be performed without further evaluation.
  - If FEV1 ≥1.5 L, lobectomy can be performed.
If FEV1 or DLCO is <80% predicted, additional testing should be done.
If FEV1 or DLCO is <40% predicted, exercise testing is recommended.

Other indications for spirometry include dyspnea of unknown etiology and uncontrolled asthma or chronic obstructive pulmonary disease.

- **Chest radiographs**: not recommended routinely.
- **Arterial blood gas**: no role in the routine preoperative assessment.

### Pulmonary Risk Reduction

- **Smoking cessation**: at least 6 to 8 weeks prior to surgery
- **Lung expansion techniques**: at least 2 weeks prior to surgery
- **Continuous positive airway pressure**: in patients with obesity or obstructive sleep apnea
- **Laparoscopic surgery**: in bariatric surgery patients
- **No role for routine nasogastric decompression after abdominal surgery**, total parenteral nutrition, or pulmonary artery catheterization

### Infective Endocarditis Prophylaxis

- Recommended for dental procedures that require manipulation of the gingival tissue or periapical region of teeth, perforation of the oral mucosa, in patients with
  - Prosthetic cardiac valves or prosthetic materials
  - Previous infective endocarditis
  - Congenital heart diseases
    - Cyanotic unrepaired, including palliative shunts and conduits
    - Repaired with residual defects
    - Completely repaired, during the first 6 postoperative months
  - Valvular heart diseases in cardiac transplant recipients
- No longer recommended in aortic stenosis, mitral stenosis, or mitral valve prolapse
- Not recommended for genitourinary or gastrointestinal tract procedures

### Hypertension

- A systolic blood pressure >180 mmHg and diastolic blood pressure >110 mmHg are indications for preoperative intervention.

### Diabetes Mellitus

- Blood glucose should be kept under moderate control (140 to 200 mg/dL) in surgical patients treated with insulin in the intensive care unit.

### Suggested Readings


RAPID BOARD REVIEW—KEY POINTS TO REMEMBER:

Hypertension

- Secondary analysis of major hypertensive studies in older adults finds a nadir for adverse cardiovascular outcomes of 130 to 140 mmHg for systolic blood pressure (sBP) and 80 to 90 mmHg for diastolic blood pressure (dBP).
- New guidelines for hypertension in older adults state that blood pressures below 130 mmHg for sBP and below 65 mmHg for dBP should be avoided, and that a target for sBP of 140 to 145 mmHg can be acceptable for those 80 years and over.

Falls

- Accidental falls are common in older patients, but high-risk patients can be identified in the office by asking them if they have fallen in the previous year or have a balance or gait problem.
- Interventions to reduce the risk of falls should always include the exercise triad: balance, endurance, and resistance training. T’ai chi is explicitly recognized as reducing the risk of future falls.
- Falls may be reduced if the number of medications can be reduced.
- Extraction of the first cataract may lower hip fracture risk in very old adults, particularly those with osteoporosis and severe cataracts.
- Vitamin D 800 to 1,000 units daily may reduce falls and fractures in elders.
- A health-care professional should assess the home to reduce fall risk; a handout that lists potential home hazards is insufficient.

Urinary Incontinence

- Nonpharmacologic therapies for urinary incontinence including behavioral therapies (e.g., patient continence logs, biofeedback, habit training) reduce the number of incontinence episodes in cognitively intact women with mixed (stress/urge) types of incontinence, often obviating the need for medications.
- Neurostimulation of the sacral nerve or the posterior tibial nerve may reduce the incontinence in those with urge or mixed incontinence intolerant to or not responding to medications and nonpharmacologic interventions.
- Consider bladder outlet obstruction causing overflow incontinence early in males with incontinence; a bedside postvoid residual can be helpful in diagnosing this condition.

Delirium

- An acute change in mental status with disturbed consciousness, impaired cognition, and fluctuating course is characteristic of delirium.
- Delirium in a hospitalized patient is a sign of a serious underlying illness and should be evaluated and managed promptly with attention to contributing factors.
- The risk of delirium in hospitalized older adults increases with age, cognitive impairment, vision impairment, poor nutrition or hydration, and severity of illness.
- Hospital delirium may be precipitated or maintained by the use of physical restraints, malnutrition in the hospital, prescription of more than three new medications or any psychoactive medication, use of a bladder catheter, or occurrence of any iatrogenic event.
- Hypoactive delirium may be mistaken for depression.
- The risk of delirium can be reduced 25% to 40% in acute care medical and surgical patients by nonpharmacologic interventions such as maintaining hydration, optimizing cognitive function, encouraging mobility, facilitating satisfactory sleep with nursing interventions, and providing hearing and vision aids as required.
- Treating contributing conditions (shared risk factors, such as generalized weakness, impaired mobility, and use of psychotropic medications) can reduce the incidence of falls, delirium, and urinary incontinence.

Ethics

- The Durable Power of Attorney for Healthcare is a very useful device when a patient lacks capacity, even temporarily.
- The Living Will as the sole advance directive has a very limited utility in most of the decision-making processes.
SUGGESTED READINGS


Sanders KM, Stuart AL, Williamson EJ, et al. Annual high-dose oral vitamin d and falls and fractures in older women: a randomized controlled trial. *JAMA.* 2010;303(18):1815-1822.


RAPID BOARD REVIEW—KEY POINTS TO REMEMBER:

- An awareness and appreciation of the cutaneous manifestations of systemic diseases help guide the internist in determining the diagnosis, therapy, or need for referral to a dermatologist.

Common Benign Cutaneous Disorders
- Acne vulgaris: comedones, papules, pustules, and nodules, occasionally with scars, on the face, neck, chest, and back. Concomitant hyperandrogenism may occur in women with acne, hirsutism, and irregular menses.
- Rosacea: erythema, telangiectasia, papules, and pustules.
- Seborrheic dermatitis: erythematous plaques with greasy, yellow scale. Common and extensive in adults with neurologic disorders such as Parkinson's disease and human immunodeficiency virus infection.
- Seborrheic keratoses: warty, age-related plaques. May indicate an underlying adenocarcinoma of the gastrointestinal tract.
- Urticaria: pruritic, edematous, evanescent wheals that usually resolve within 24 hours.
- Pruritus: aquagenic pruritus is unique to polycythemia vera.
- Drug eruptions: occur in approximately 2% of all hospitalized patients.
- Erythema multiforme: the most common cause is recurrent herpes simplex virus infection; less common: Mycoplasma pneumonia and medications.
- Psoriasis: silvery-white scaly papules and plaques commonly on the scalp, elbows, and knees, and/or nail dystrophy. Patients are at an increased risk for the metabolic syndrome.
- Vitiligo: depigmented macules. Some patients have an associated autoimmune disease.

Autoimmune Bullous Diseases
- Pemphigus vulgaris: painful mucosal erosions and flaccid eroded blisters. Immunoglobulin (Ig)G deposits within the epidermis. Even with treatment, associated with a high morbidity and mortality.
- Bullous pemphigoid: large, tense blisters and urticarial plaques; mucosal disease is rare; almost invariably affects the elderly. IgG deposits at the dermal–epidermal junction. With treatment has a good prognosis.
- Dermatitis herpetiformis: symmetric groups of vesicles, papules, and wheals that appear on the elbows, knees, scalp, and buttocks; neutrophils are present in the dermal papillae and IgA deposits at the dermal–epidermal junction.
- Epidermolysis bullosa acquisita: skin fragility, milia, scarring alopecia, and nail dystrophy; typically follows trauma. IgG deposits at the dermal–epidermal junction.

Primary Skin Cancer
- Basal cell carcinoma (BCC) and squamous cell carcinoma (SCC) are the most common types of skin cancer.
  - BCC is usually a “pearly” papule, plaque, or nodule with a telangiectatic surface and a rolled border.
  - SCC is typically an ill-defined indurated papule, plaque, or nodule with central ulceration and a hyperkeratotic edge.
- Melanoma affects approximately 60,000 people each year in the United States. The lifetime risk in fair-skinned individuals is 1 in 75 (approximately 1%).
  - Most have asymmetry, an irregular border, uneven color, and a large diameter (greater than 6 mm), all of which constitute the “ABCD” signs of melanoma.
  - Thin melanomas (<0.75 mm) have an excellent prognosis (>95% 5-year survival), but thick melanomas (>3.5 mm) carry a much graver prognosis (35% to 40% 5-year survival).

Sarcoidosis
- Chronic, often multisystem, granulomatous disease. Approximately one-third of patients have skin disease,
which has a variety of presentations, including nasal edema, midfacial papules, annular or scaly plaques, or nodules.

**Skin Disease with Diabetes**

- Approximately half of all patients with diabetes have skin disease, most commonly diabetic dermopathy (shin spots), thickened skin, acanthosis nigricans, yellowed nails and skin, or cutaneous infections (fungal or yeast, or bacterial most commonly).

**Porphyrias**

- Group of disorders related to abnormalities in heme biosynthesis; may be erythropoietic, hepatic, or mixed; each type, whether inherited or acquired, has a specific enzyme defect.

*Porphyria cutanea tarda:* photosensitivity, skin fragility, vesicles, bullae, and erosions on the hands, forearms, and face; hyperpigmentation and hypertrichosis on the face.

**SUGGESTED READINGS**


RAPID BOARD REVIEW—KEY POINTS TO REMEMBER:

Asphyxiants—Carbon Monoxide
- Nonexposed persons have $\leq 1\%$ blood carboxyhemoglobin. Smokers as high as 18%.
- At levels of 10% to 30%, patients may complain of headache, nausea, weakness, and dizziness. Mentation begins to be impaired at 30% to 35%, and levels of 35% to 40% may result in coma. “Cherry red color” of the skin and mucous membranes is only seen in lethal levels of carbon monoxide poisoning. Death can occur with levels exceeding 50%.
- A key diagnostic clue is the discordance between the oxygen saturation as measured by pulse oximetry (falsely normal) and that measured by an arterial blood gas (decreased).
- Measurement of the carboxyhemoglobin level confirms the diagnosis.
- 100% oxygen reduces the half-life for carbon monoxide elimination from 5.5 hours to 1.5 hours. Oxygen at 3 atm reduces the half-life to 23 minutes.

Cholinesterase Inhibitors—Organophosphate Insecticides
- Clinical effects, nicotinic (ganglionic and neuromuscular) and muscarinic (parasympathetic), through phosphorylation of the acetylcholinesterase enzyme at nerve endings:
  - STUMBLED = Salivation, Tremors, Urination, Miosis, Bradycardia, Lacrimation, Emesis, and Diarrhea.
- Measure:
  - Plasma cholinesterase (pseudocholinesterase), synthesized by the liver, declines sooner and regenerates faster (days to a few weeks).
  - Red cell cholinesterase (true acetylcholinesterase), depressed more slowly and for longer periods of time (regeneration time is 1 to 3 months).

Heavy Metals—Lead Intoxication
- Organic lead can be absorbed via skin; distributed to the erythrocytes, liver, and kidneys.
- Insidious gastrointestinal symptoms, including vague abdominal discomfort, anorexia, and constipation. A bluish gray line along the gingiva called “Lead line.”
- Involvement of the peripheral nervous system and lead encephalopathy are rare.
- Anemia, microcytic, hypochromic or normocytic, normochromic; reticulocytosis and basophilic stippling of red blood cells.
- Heavy persistent exposure $\geq 10$ years may result in lead nephropathy, tubular dysfunction, Fanconi-like syndrome with aminoaciduria, glucosuria, and hyperphosphaturia.
- Hyperuricemia with saturnine gout.
- Blood lead is the single most useful diagnostic test. Free erythrocyte protoporphyrin and zinc protoporphyrin levels begin to increase when the blood lead level is $>40 \mu g/dL$. They stay elevated longer than blood lead and are therefore better indicators of chronic intoxication.

Asbestos

Pleural Disease
- Pleural Plaques: smooth, white, raised, irregular lesions on the parietal pleura; typically asymptomatic, recognized only on chest imaging.
- Benign Asbestos Pleural Effusions: silent or pain, fever, and shortness of breath; early manifestation of asbestos exposure (within 15 years); diagnosis of exclusion.
- Pleural Fibrosis: progressive shortness of breath; focal or diffuse fibrosis; remote exposure, but short-lived and heavy in intensity (more than 20 years before).
- Malignant Mesothelioma: insidious onset of nonpleuritic chest wall pain, 20 to 40 years after the initial exposure, often associated with dyspnea and systemic symptoms.

Asbestosis
- Pulmonary fibrosis secondary to asbestos exposure; may appear and progress long after exposure has ceased.

Carcinogen
- Asbestos is classified as a class I carcinogen: lung cancer and mesothelioma.
Silica

Silicosis

- **Chronic silicosis**: fibronodular parenchymal lung disease, with more than 20 years of silica exposure; radiographically multiple small nodules with an upper lobe predominance and hilar adenopathy with “eggshell” calcification.

- **Progressive massive fibrosis**: “conglomerate silicosis and progressive massive fibrosis”; shortness of breath and cough can become debilitating.

- **Acute silicosis**: within months of exposure progressive shortness of breath and coughing; proteinosis with proteinaceous material in the alveoli, but interstitial involvement and early nodule formation can be seen; rapid progression to acute respiratory failure is common.

- **Accelerated silicosis**: after 5 to 15 years of exposure; patients usually symptomatic and often progress to respiratory failure and death; recognized by the development of upper zone nodules and fibrosis on radiographs.

Mycobacterial Disease

- Patients with silicosis should be screened for latent tuberculosis.

Coal Dust

Coal Worker’s Pneumoconiosis

- **Simple Coal Worker’s Pneumoconiosis (CWP)**: most are asymptomatic; chest imaging reveals small nodules with upper and posterior zone predominance; hilar lymph node enlargement is not uncommon.

- **Progressive massive fibrosis**: can occur, more frequently, when there has also been exposure to silica; the small nodules seen in simple CWP coalesce, forming opacities larger than 1 cm.

- **Caplan’s syndrome**: nodular form of CWP seen in individuals with rheumatoid arthritis.

SUGGESTED READINGS


Work-Related Lung Disease Surveillance Report, 1999. USDHHS, CDC, Division of Respiratory Disease Studies; DHHS (NIOSH) publication no. 2003-111.
RAPID BOARD REVIEW—KEY POINTS TO REMEMBER:

DEPRESSION

- Patient should have been depressed or dysphoric most of the day, for ≥2 weeks, with difficulties in social interactions or at work, and ≥4 of the following problems:

  - S Sleep—poor or excessive
  - I Interest in normal activities—diminished
  - G Guilt—excessive or inappropriate
  - E Energy—lower than normal
  - C Concentration—poor
  - A Appetite—reduced or increased, with weight change
  - P Psychomotor retardation, slowed speech, physical involvement or agitation
  - S Suicidal thoughts or thoughts of death

- Patients with a diagnosis of major depression can often present with physical symptoms.
- Depressed patients have a two- to fourfold greater risk for a recurrent cardiovascular event.
- The first-line treatment is a selective serotonin reuptake inhibitor (SSRI) such as escitalopram. If patients do not achieve remission, switch to another SSRI or another class of antidepressant. Augmenting the response with either buspirone or bupropion is also effective.
- All antidepressant medications can increase the suicidal behavior and ideation in children, adolescents, and young adults ages 18 to 24 years.

SOMATIC SYMPTOM DISORDERS

- The DSM criteria include finding a history of many physical complaints beginning before age 30 years that occur over a period of several years and result in treatment being sought or significant impairment in social, occupational, or other area of functioning. Symptoms cannot fully be explained by a known medical condition or effects of a substance.

- Somatic symptom disorders respond better when the intervention is early, without reinforcement by the excessive ordering of tests and evaluations.

PANIC DISORDER

- To establish a diagnosis of panic disorder, both 1 and 2 must be present:
  1. Recurrent unexpected panic attacks.
  2. At least one of the attacks has been followed by ≥1 month of ≥1 of the following:
     a) Persistent concern about having additional attacks
     b) Worry about the implications of the attack or its consequences
     c) Significant change in behavior related to attacks
     d) The episodes are not caused by a physical, other emotional, or substance disorder
- Low-dose antidepressants for long-term treatment, benzodiazepines for the short-term anxiolysis.

MANIA

- The symptoms of a classic hypomanic/manic phase include pressured speech, racing thoughts, little to no sleep, boundless energy, euphoric mood, grandiose plans, and inappropriate judgment.

DELIRIUM

- Acute impairment in attention and concentration with a fluctuating course.

DEMENTIA

- Cholinesterase inhibitors and N-methyl-D-aspartate (NMDA) antagonists can slow the course of the illness and antipsychotics can control the agitation.
SUGGESTED READINGS


RAPID BOARD REVIEW—KEY POINTS TO REMEMBER:

- Most diseases encountered in the practice of medicine have genetic components in both the cause and the pathogenesis.
- The process of considering, ordering, and interpreting a genetic test is not straightforward.

Inheritance Patterns

**Autosomal Dominant**
- Multigenerational presence of symptoms and equal involvement of sexes
- One copy of a gene pair needs to be altered for clinical symptoms to appear (heterozygous)
- Conditions often caused by aberrant structural or developmental processes, and only a minority result from enzymatic defects

**Autosomal Recessive**
- Two gene copies altered (homozygous); heterozygotes are unaffected
- Equal involvement of both sexes; affected individuals in the same single generation; absence of the disease appearing in multiple generations

**X-Linked Recessive**
- Virtually all males are affected clinically, with rare symptomatic females
- All daughters of an affected male are carriers of the mutated allele; the risk for any of the daughters’ sons to inherit the gene responsible for the condition is 50%

**X-Linked Dominant**
- Both heterozygote males and females affected; females affected less severely, unless they are homozygous
- Multigenerational involvement; presence of symptoms in all daughters and none of the sons of an affected male; equal involvement of both sexes when transmitted by females

**Uniparental Disomy**
- A meiosis error with two intact chromosomes from one parent

**Mosaicism**
- At least two cell lines within an individual or a specific tissue, that differ genetically, but are derived from a single fertilized egg
- May be the underlying etiology in families with unusual clinical pictures and/or pedigrees

**Mitochondrial Disorders**
- Clinically heterogenous and associated with mutations of either nuclear or mitochondrial DNA; nuclear gene defects are primarily inherited in an autosomal recessive manner
- Parent point mutations in mitochondrial DNA are variably transmitted to children, with pronounced intrafamilial phenotypic variability

**Triple Repeats Disorders**
- A segment of DNA containing a repeat of three nucleotides increases in number when passed from generation to generation, undergoing expansion; once a critical degree of expansion occurs, a change in gene expression and function ensues leading to a disease phenotype

SUGGESTED READINGS


RAPID BOARD REVIEW—KEY POINTS TO REMEMBER:

DISORDERS OF CONSCIOUSNESS

- Disorders of consciousness are divided into two categories:
  - Disorders of arousal—confusion, drowsiness, stupor, and coma.
  - Disorders of awareness—an abnormal interaction with the environment when the patient is apparently awake.
- Vegetative state—complete unawareness of the self and environment despite preservation of some brain functions (often cardiovascular and autonomic control).
- Persistent vegetative state >1 month after initial injury.
- Permanent vegetative state >6 months of unresponsiveness.

HEADACHE

- Tension-type or muscle contraction headache is the most common type of primary headache.
- Migraine headache, the second most common type of primary headache, has four phases:
  - The prodrome—premonitory phenomena occurring hours to days prior to headache onset.
  - The aura—focal neurologic symptoms, usually <60 minutes.
  - The headache—unilateral, throbbing pain, moderate to severe intensity, and aggravated by exertion. Other symptoms: nausea, vomiting, sensory excitability, systemic symptoms.
  - The postdrome—feeling tired, washed out, or depressed.
- Chronic daily headache—any type of headache that occurs ≥15 days per month.
- Medication overuse headaches, when related to overuse of medications (e.g., nonsteroidal anti-inflammatory drugs).
- Cluster headache—≥5 attacks of severe, unilateral, orbital, supraorbital, and/or temporal pain lasting 15 to 180 minutes and associated with ipsilateral lacrimation, conjunctival injection, rhinorrhea, nasal congestion, forehead and facial sweating, miosis, ptosis, or eyelid edema.
- Thunderclap headache—maximal at onset.
- Hemicrania continua—continuous, daily unilateral headache, associated with autonomic features (miosis, ptosis, lacrimation, rhinorrhea).

DEMENTIA

- Group of symptoms that include memory impairment affecting social interactions.
- Recommended neuroimaging study—a noncontrast head CT or a brain MRI.
- Check vitamin B12 level and a thyroid test.
- The most common cause of dementia is Alzheimer’s disease (AD).
- Centrally acting anticholinesterase drugs are indicated in mild to moderate AD to slow the disease progression.
- Vascular dementia—secondary to multiple cerebral infarcts or chronic cerebral ischemia causing white matter injury (Binswanger’s disease).
- Normal-pressure hydrocephalus—dementia, gait abnormalities, and urinary incontinence.

DIZZINESS

- Vertigo—an illusion of movement caused by a disorder of the vestibular system.
- Near syncope (lightheadedness)—a sensation of almost fainting caused by an inadequate cerebral perfusion pressure.
- Disequilibrium—a sensation of dizziness caused by a gait disorder.

SEIZURES AND EPILEPSY

- Seizure—any stereotypical experience or activity arising from hypersynchronous discharges in the cerebral cortex and perhaps some subcortical structures.
- Epilepsy—a disorder characterized by two, three, or more seizures that are unprovoked by any known proximate insult.
Status epilepticus—continuous seizures lasting for longer than 30 minutes or repeated seizures lasting a total of 30 minutes from which the patient does not recover awareness between episodes.

STROKE

- A stroke is the sudden or rapid onset of a neurologic deficit, lasting for more than 24 hours, in a vascular territory, and caused by an underlying cerebrovascular disease. A transient ischemic attack (TIA) lasts less than 24 hours.
- Based on the results of the diagnostic studies and the time window, the stroke patient may be a candidate for intravenous or intra-aortic thrombolytic therapy.
- Antiplatelet therapy is an important treatment for stroke unless a high-risk condition such as atrial fibrillation is present.
- Carotid endarterectomy or stenting is recommended for patients with a recent TIA or ischemic stroke (<6 months), with ipsilateral severe (70% to 99%) carotid artery stenosis.

PERIPHERAL NEUROPATHY

- Mononeuropathy involves the loss of motor or sensory function in the distribution of one nerve.
- Polyneuropathies involve multiple peripheral nerves, usually symmetrically, and tend to be a length-dependent process (starts distally and progresses proximally).
- Mononeuritis multiplex is a process that affects multiple nerves and can be associated with pain and loss of reflexes.
- Autonomic neuropathies selectively affect the nerves involved with the autonomic nervous system.

MOVEMENT DISORDERS

- Hypokinetic disorders include paralysis, rigidity, and akinesia.
- Tremor is the most common hyperkinetic movement disorder. Resting tremors are obvious when resting, intention tremors are present with action.
  - A resting tremor that is relieved by action is most likely due to Parkinson’s disease.
  - A resting tremor that is exaggerated with action is known as a rubral or cerebellar outflow tremor.
- Action tremors present only with goal-directed action, such as pointing at a particular object, are due to a cerebellar disease either in the cerebellum itself or in fibers going to or coming from the cerebellum.
- Action tremors that are activated simply by a particular position (e.g., antigravity posture) are known as postural action tremors.

- Parkinson’s disease classic features include (a) resting tremor (usually a pill-rolling tremor), (b) bradykinesia (slow movements, difficulty initiating movements), (c) cogwheel rigidity, and (d) shuffling gait with a stooped posture.

DISEASES OF MYELIN

- Multiple sclerosis is a disease of the central nervous system myelin that is manifested by attacks separated in both time and space: lesions must occur in more than one location, and they must have occurred at more than one time.

SUGGESTED READINGS


Question 1

A 55-year-old woman with a past medical history of hypertension, diabetes mellitus, and proteinuric chronic kidney disease from uncontrolled diabetes is admitted to the hospital with a methicillin-sensitive *Staphylococcus aureus* bloodstream infection from a tunneled dialysis catheter. Your patient reports a history of penicillin allergy and requests desensitization. All the following statements are true, except:

a) It is important to verify the history because the patient may incorrectly assume that a nonallergic side effect, such as a gastrointestinal side effect, is allergic in origin.
b) Fatal reactions to penicillin skin tests have been reported.
c) Skin testing should not be performed in patients with a high risk of an anaphylactic reaction, unless no alternative drug to a β-lactam is available.
d) Patients with a positive skin test to penicillin are at a fourfold increased risk of an allergic reaction to cephalosporins.
e) Desensitization helps reduce the incidence of Stevens-Johnson syndrome, hemolytic anemia, and serum sickness associated with penicillin.

Answer and Discussion

The answer is e.

Objective: Identify the benefits of penicillin desensitization.

Desensitization has no effect on the incidence of Stevens-Johnson syndrome, hemolytic anemia, or serum sickness associated with penicillin because these are all non–immunoglobulin E (IgE)-mediated reactions. Fatal reactions to penicillin skin tests have been reported, but they occur in <1% of those tested.

Question 2

The optimal timing for the administration of the pneumococcal vaccination includes which of the following?

a) In the immediate postoperative period after splenectomy

b) Every 10 years in a patient with chronic renal failure who received the vaccination previously

c) In a healthy 55-year-old patient

d) When a person is found to be human immunodeficiency virus (HIV) positive

e) After immunosuppressive therapy, in a patient undergoing organ transplantation

Answer and Discussion

The answer is d.

Objective: Identify indications for the pneumococcal vaccination.

The pneumococcal vaccination is recommended in all patients aged 65 years or older. Generally, it should also be given to immunosuppressed patients before their immunosuppression occurs or becomes advanced. Therefore, the vaccination should be given before a planned splenectomy, before the administration of chemotherapy or immunosuppressant therapy, and when HIV infection is first detected. Because of waning immunity, the vaccination should be given every 5 years in a patient with chronic renal failure who received the vaccination previously. Therefore, the correct answer is d.

Question 3

Which of the following statements regarding influenza vaccination is true?

a) It cannot be given at the same time as the pneumococcal vaccination.
b) It is 90% effective.
c) It often causes an influenza-like illness.
d) It is contraindicated in the presence of allergy to eggs.
e) It should not be postponed in the setting of a febrile illness.

Answer and Discussion

The answer is d.

Objective: Identify contraindications to influenza vaccination.

A common misconception among patients is that the influenza vaccination causes an influenza infection. The vaccine may cause a local skin reaction, fever, myalgia, and malaise, side effects that the patient may mistake for influenza symptoms. The vaccine does not cause influenza because the vaccine is made from an inactivated virus. The vaccine is contraindicated in those allergic to eggs because the vaccine is made from the inactivated virus grown in eggs. It should be postponed in those with a febrile illness. It is 60% to 80% effective and can be given safely at the same time as the pneumococcal vaccination. Therefore, the correct answer is d.
Question 4

A 50-year-old woman complains of headaches. She has never had headaches before and has no history of neurologic or psychiatric diseases. The headaches began about 6 weeks before and are not severe, but they seem to be getting worse and are beginning to worry her. They wax and wane throughout the day without any particular pattern. They respond well to aspirin but seem to return when the aspirin wears off. They do not wake her from sleep, nor do they cause nausea or vomiting. No neurologic prodrome is present, and she cannot think of anything that exacerbates the pain. It is difficult to localize the headache, and it is not pulsating in character. The pain sometimes improves when her husband massages her neck. No significant past medical, family, or social history is present. She takes no drugs and does not drink alcohol, or smoke. The general physical examination is normal, as is the mental status and cranial nerve examination. The motor examination shows a slight but definite pronation of the left arm on the extension of upper limbs. A careful sensory examination shows some extinction to double simultaneous stimulation on the left.

Coordination is normal. Reflexes are symmetric and of average amplitude. Both plantars are flexor. Which of the following is the most appropriate next step?

a) Reassurance
b) Prescribe paroxetine
c) Lumbar puncture
d) Computed tomography (CT) of the head without contrast
e) Magnetic resonance imaging (MRI) of the head with gadolinium

Answer and Discussion

The answer is d.

Objective: Identify the indications for imaging in patients with a headache.

This case raises many important issues encountered in the management of a patient complaining of headache. In this particular case, the history itself is worrisome and is enough to warrant further testing. Although the headaches are mild, for this patient, they are different than the usual pattern. This is probably the most important part of the history in a headache patient. Headaches that have changed in quality are more worrisome than severe headaches that are the same as always. The fact that the headaches respond to mild analgesic medication or to massage should not be reassuring to the physician. All sorts of pains respond to analgesic medication, and this in and of itself does not mean that the cause of the headache is benign. Of the greatest importance is the abnormality in the neurologic examination. A slight but definite pronation of the left arm on extension of the upper limbs indicates a mild left hemiparesis. A positive neurologic examination in the presence of headache should always lead to further evaluation. In some centers, it may be possible to do an MRI, but CT scanning is a more widespread and available technology. For this patient, there is really no reason to obtain skull radiographs or any other noninvasive evaluation other than a CT scan. The CT scan may be done without contrast, at which time a lesion may be found. If nothing is found, a decision about injecting contrast can be made later.

Question 5

A 35-year-old man presents to his physician’s office for the first time requesting a “routine physical examination.” He is on no medications, has no significant past medical or family history, and his review of systems is negative. In addition to checking blood pressure (BP), which of the following screening tests would be considered to be most appropriate?

a) Lipid panel, urinalysis, complete blood count
b) Lipid panel, glucose
c) Glucose
d) Lipid panel
e) Lipid panel, electrocardiogram (ECG)

Answer and Discussion

The answer is d.

Objective: Identify screening guidelines in a young, healthy patient.

In asymptomatic patients, routine ECGs and screening lab tests, such as urinalysis, complete blood counts, chemistry panels, and liver function tests, are generally not recommended. All major advisory groups recommend BP screening and lipid panel testing by the age of 35 years for all male patients and 45 years for all female patients. High-risk patients are recommended to have screening sooner if they are at increased risk for coronary artery disease. This patient is not at increased risk, and therefore, should have only screening lipids at this time. The U.S. Preventive Services Task Force recommends screening for diabetes in patients with sustained BP greater than 135/85, or at increased risk for impaired glucose tolerance. Assessment for left ventricular hypertrophy, typically with an ECG, is recommended in hypertensive patients only.

Question 6

During a preplacement examination for a bridge reconstruction job, a 32-year-old woman was found to have a blood lead level of 4.0 μg/dL (normal, 0.0 to 11.0 μg/dL) and a zinc protoporphyrin of 104 μg/dL (normal, 0.0 to 70.0 μg/dL). She is asymptomatic and her physical examination is normal. Her medical history is unremarkable, except for four pregnancies. The most likely explanation for these laboratory results is:

a) Unrecognized environmental lead exposure
b) Iron deficiency anemia
c) Erythropoietic protoporphyria
d) Laboratory error
e) Thalassemia minor
**Answer and Discussion**
The answer is b.

**Objective:** Understand the differential diagnosis of lead exposure.

An elevated zinc protoporphyrin with a normal blood lead level is most often due to iron deficiency anemia, particularly in a woman of reproductive age. Because these studies were obtained during the preplacement evaluation, the patient has not yet encountered lead exposure in the workplace. The physician always should inquire about possible environmental or household exposures, such as the use of glazed ceramic ware, folk remedies, and lead-soldered water pipes. A completely normal lead level excludes recent or ongoing lead exposure from any source.

Erythropoietic protoporphyrin is a rare disorder that results in significant symptoms, including photosensitivity. Thalassemia minor and laboratory error are theoretically possible, but highly unlikely explanations for these results.

**Question 7**

A 42-year-old woman presents with a pruritic erythematous rash around her neck after wearing a new necklace. In the past, she experienced a similar reaction to a cheap pair of earrings. All the following statements are true, except:

a) Perfumes and cosmetics can produce the same type of response.

b) Diagnosis can be confirmed with a patch test read in 48 hours.

c) This type of reaction can be caused by topical medications, including antibiotics.

d) Poison ivy produces the same type of response.

e) This is a type II cell-mediated response.

**Answer and Discussion**
The answer is e.

**Objective:** Understand the mechanisms of hypersensitivity reactions.

Gell and Coombs classification is a classification of the immune mechanisms of tissue injury, comprising four types: type I, immediate hypersensitivity reactions, mediated by the interaction of IgE antibodies and antigens and the release of histamine and other mediators; type II, antibody-mediated hypersensitivity reactions, due to antibody–antigen interactions on cell surfaces; type III, immune complex, local or general inflammatory responses, due to formation of circulating immune complexes and their deposition in tissues; and type IV, cell-mediated hypersensitivity reactions, initiated by sensitized T lymphocytes either by release of lymphokines or by T-cell–mediated cytotoxicity. Contact dermatitis is a type IV cell-mediated response.

**Question 8**

A 68-year-old woman and her husband are coming in for their annual evaluations. It is mid-November. They have many questions for you regarding prevention. As you begin to counsel them, you remember that which of the following statements is correct?

a) Herpes zoster vaccination is indicated in patients older than 55 years.

b) Prostate-specific antigen and digital rectal examinations are proven screening methods to reduce prostate cancer mortality.

c) Measles vaccine is recommended in individuals born before 1957.

d) Breast self-examination is a proven screening method to reduce breast cancer mortality.

e) The live attenuated influenza vaccine would not be recommended for this couple.

**Answer and Discussion**
The answer is e.

**Objective:** Identify appropriate screening and immunization guidelines in elderly patients.

Herpes zoster vaccine is recommended for patients aged 60 years and older. Definitive evidence supporting prostate cancer screening is still lacking. Patients born before 1957 are likely to have had the measles virus and need not be vaccinated. Adults born after 1957 who are not previously vaccinated and without demonstrated immunity should receive the vaccine. Advisory groups now list breast self-examination as an optional test because of lack of evidence regarding its effectiveness. Answer e is a true statement—the live attenuated influenza vaccine is only approved for use in patients younger than 50 years.

**Question 9**

A 45-year-old woman presents to you for a new patient evaluation and wants her “annual physical examination.” Her current medications include an oral contraceptive and ibuprofen as needed. Her mother has a history of hypertension. She is married and works as a legal secretary. Her review of systems is negative. Her previous records report that she had a normal liquid-based Pap smear and a human papilloma virus (HPV) screen 2 years ago. She does not remember any recent lab work and believes that her last immunizations were done when she was a teenager. Which of the following screening tests are most appropriate for this patient?

a) Pap smear, lipid panel

b) Td vaccination, lipid panel

c) Pap smear, Td

d) Td

e) Pap smear, HPV testing, lipid panel, Td

**Answer and Discussion**
The answer is b.

**Objective:** Identify appropriate screening and immunization guidelines in a healthy patient.

With both a normal Pap smear and negative HPV screen done 2 years ago, this patient does not need another Pap smear for another 3 years. If she just had a normal Pap smear,
but did not have HPV testing, the U.S. Preventative Services Task Force recommends to repeat cytology screening at 3 years. A Pap smear could be done sooner if this patient were considered to be at high risk for cervical cancer. There is no evidence of that in this patient. A tetanus booster immunization should be administered every 10 years after the primary series is completed. Most major advisory groups recommend cholesterol screening in asymptomatic patients with normal risk of coronary artery disease by 35 years of age for men and 45 years of age for women. Therefore, b is the correct answer.

**Question 10**

A 68-year-old man is complaining that his handwriting is deteriorating and that his hands shake when he tries to drink from a glass or coffee cup. He has no significant past medical history and no family history of neurologic or psychiatric diseases. He does not drink alcohol, or smoke. His only medication is Sinemet 10/100 four times a day given to him by a physician whom he saw once on vacation in Florida 2 years before. A physician friend of the patient has been rewriting the prescription since then. His general examination is normal. On motor examination, he is noted to have a rather expressionless face and sits rigidly in his chair with arms flexed, bent slightly forward. Tone is diffusely increased with "cogwheeling." Power is normal. There is a 2- to 3-second alternating tremor noted in both hands while he is seated. When asked to extend his hands, this tremor becomes finer but more rapid. On finger–nose–finger testing, the tremor intensifies, but no dysmetria is noted. When he attempts to write, the tremor becomes severe, leading to illegible script. The sensory examination is intact. Reflexes are average and symmetric. Both plantars are extensor. His gait is shuffling but with a narrow base. He has difficulty getting started, but, once he is going, he walks quite well although slightly bent forward. Which of the following is the most appropriate treatment plan for this patient’s tremors?

- a) Begin metoprolol
- b) Begin primidone
- c) Increase the Sinemet dose
- d) Decrease the Sinemet dose
- e) Recommend moderate alcohol consumption

**Answer and Discussion**

The answer is d.

**Objective:** Identify a physiologic tremor in a patient with underlying Parkinsonism.

This 68-year-old man has two separate problems. The first is a tendency not to move, known as akinesia or bradykinesia. This gives him the expressionless face and accounts for his sitting rigidly in a chair with his arms flexed and bent slightly forward. This akinesia is sometimes referred to as Parkinsonism. In addition to the akinesia, he shows the classic tremor of Parkinsonism, which is characterized as a slow alternating tremor with a frequency of about three cycles per second. This tremor is most prominent in the position of repose and improves when the limb moves into action. When a tremor is superimposed on rigidity, the phenomenon of cogwheeling develops. The tremor of his Parkinson disease is probably not bothering him because it is present only in repose and improves on action. His major complaint concerned the deterioration of handwriting. In fact, he is complaining about a second tremor, some form of postural tremor, which could be either an essential tremor or an exaggerated physiologic tremor. Tremor is defined as an alternating movement around some fulcrum. Tremors may be proximal or distal, rapid or slow, and synchronous or alternating. They may be greatest in the position of repose or on action. Action tremors are subdivided into goal-directed action tremors, which are present only when the patient attempts to make projected precise movements, and postural action tremors, which occur when the affected limb attains an antigravity posture, such as raising the hand. The physiologic tremor is a rapid postural action tremor and is most prominent in the distal extremities and interferes with carrying out fine motor activities, such as writing. It is caused by the peripheral action of catecholamines or their agonists on receptors in the muscle. It is usually not symptomatic, but it may become symptomatic, in which case it is called exaggerated physiologic tremor. Physiologic tremor is exaggerated by situations that increase the sensitivity of peripheral catecholamine receptors or increase the amount of circulating catecholamines. Such circumstances include anxiety, hyperthyroidism, or the use of drugs that functionally raise the circulating catecholamine levels, such as anti-asthmatic medications, lithium carbonate, theophylline, and caffeine. This tremor is treated best by reducing the exacerbating factors or, if necessary, with a small dose of β-blocker. Alcohol is also effective against this tremor, but it is not recommended as a therapy. The second form of postural tremor is known as essential tremor. It is slightly slower than the physiologic tremor, is also present in the extremities most commonly, may occur in families, and may develop only in older people (senile essential tremor). Treatment consists of either β-blocker or use of the antiepileptic drug primidone (Mysoline). Evidence suggests that the incidence of essential tremor is higher in patients with Parkinsonism than in age-matched controls; that is, it may be true that the action tremor is part of Parkinson disease. It is also possible that this man has an exaggerated physiologic tremor, possibly caused by the peripheral metabolism of Sinemet to norepinephrine, which then acts on receptors in the muscle. A tremor study done in an experienced neurophysiology laboratory might be helpful in distinguishing these two types of tremor, but a therapeutic trial of reduction in Sinemet may work just as well. In this case, the first choice would be to decrease or discontinue his Sinemet. If there was no effect on the tremor, then treatment with primidone or β-blocker would be appropriate.

**Question 11**

A 54-year-old woman presents to your office with the chief complaint of vaginal dryness. She became postmenopausal
spontaneously at 52 years of age and has had occasional non-descriptive hot flashes since then. She reports having at least two urinary tract infections in the past year, has noted that sexual intercourse has become more painful over the past year, and has experienced some stress urinary incontinence. Otherwise, she is healthy, has no history of breast or endometrial cancer, and has a normal Pap smear and screening mammogram. She is not interested in systemic hormone therapy (HT) at this time. Your best recommendations are which of the following?

a) Vaginal over-the-counter moisturizers and lubricants during intercourse
b) Estradiol vaginal ring
c) Oral contraceptive pills therapy
d) Assessment of bone status
e) Choices a, b, and d

Answer and Discussion

The answer is e.

Objective: Identify and manage postmenopausal symptoms.

The use of the estradiol vaginal ring would be an option for local estrogen treatment in a patient with vaginal atrophy and genitourinary symptoms. The estrogen ring provides local estrogen to the vaginal mucosa to help alleviate symptoms of vaginal dryness. The use of nonhormonal over-the-counter vaginal moisturizers and lubricants, including Silk-E and K-Y Jelly, may provide some relief during sexual intercourse.

In a woman not on systemic HT, it is important to establish her bone mineral density status because this might affect her decision to initiate HT, or select an alternative therapy with a bisphosphonate (Actonel or Fosamax) or selective estrogen receptor modulator (SERM) such as raloxifene (Evista).

Question 12

A 55-year-old Hispanic woman who became menopausal 3 years ago presents to your office for a routine physical examination. She is currently on conjugated equine estrogens (Premarin), 0.625 mg, since her hysterectomy. She has been on conjugated equine estrogens (Premarin), 0.625 mg, since her hysterectomy. She is also taking phenytoin and folic acid. She has an isolated elevation of her triglyceride levels to 250 mg/dL. You would recommend which of the following?

a) Adding progestin, 5 mg daily
b) Increasing her oral Premarin dose to 1.25 mg daily
c) Adding isoflavones to her diet and then stopping Premarin
d) Changing her estrogen therapy (ET) to a transdermal patch therapy such as weekly Climara

Answer and Discussion

The answer is d.

Objective: Identify drug–drug interactions between estrogen and other medications affecting the hepatic metabolism.

Because of her history of using phenytoin for seizure disorder, this patient probably metabolizes estrogen at a faster rate than normal. By changing her ET to a transdermal patch, consistent estrogen levels can be maintained, which should alleviate her symptoms. Simply increasing her oral CEE dosage does not account for the fluctuations in metabolism and is less favorable than changing to a transdermal patch. Addition of progestin would not help with the hot flashes. Adding isoflavones and other plant-based estrogens in addition to her ET may or may not also help her symptoms. Other causes for her hot flashes should also be excluded, including checking for the thyroid-stimulating hormone and fasting blood sugar level. The patient will also benefit from a transdermal patch therapy instead of the oral ET due to her elevated triglyceride level. Fasting lipid levels should be periodically monitored.

Question 14

A 43-year-old mother of four children presents to the office with complaints of headache, neck pain, some dizziness, and nausea. She has a history of chronic tension headaches and low back pain. She works as a pharmaceutical representative and reports spending a lot of time in her car. She has been seeing a chiropractor on and off for 20 years to treat her chronic symptoms, but despite a visit to the chiropractor...
yesterday, her headache remained. She reported nausea right after the visit. While cooking dinner that night she reported dizziness. “I turned my head to the left, and the room started spinning and I felt nauseated. It lasted only a second.” Today she reports similar episodes of spinning that have lasted longer and that were associated with nausea. Physical examination reveals a normal vascular examination without bruits. There is no hearing deficit. Neurologic examination is significant for horizontal nystagmus and left eyelid ptosis. Which of the following is the most likely cause of her vertigo?

a) Benign positional vertigo
b) Vestibular neuritis
c) Cerebrovascular stroke
d) Migraine
e) Cholesteatoma

**Answer and Discussion**

The answer is c.

**Objective:** Identify an ischemic etiology for vertigo.

Vertigo is defined as an illusion of movement and always reflects a disorder of the vestibular system. Vertigo originating from the central nervous system tends to spare hearing, produces less torsional vertigo, and is associated with other brainstem symptoms and signs, such as double vision, dysarthria, and ataxia. The horizontal nystagmus and the eyelid ptosis are concerning for a cerebrovascular stroke and consistent with her recent neck manipulation by her chiropractor. Although uncommon, extreme or abrupt twisting of the neck can damage the inner layer of vertebral arteries.

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**Question 15**

A 48-year-old African American woman with a history of total abdominal hysterectomy and bilateral salpingo-oophorectomy 4 years ago for benign reasons comes to your office complaining of low sexual interest and an inability to reach sexual climax. She is currently on esterified estrogen (Menest), 0.625 mg every day, and denies other symptoms. You check her total serum E₂ level, which is 50 pg/mL. She has a normal vaginal and pelvic examination. You recommend which of the following?

a) Sertraline (Zoloft), 25 mg by mouth every day and sex therapy
b) Vaginal lubrication
c) Changing to esterified estrogens, 0.625 mg, plus methyltestosterone, 1.25 mg (Estratest HS) by mouth every day
d) Increasing her dose of Premarin to 1.25 mg by mouth every day

**Answer and Discussion**

The answer is c.

**Objective:** Identify and treat female androgen deficiency (FAD).

This patient’s symptoms seem to correlate with a FAD, syndrome requiring therapy. Because she is already on adequate estrogen replacement, the only method currently available for androgen therapy is oral Estratet HS (1.25 methyltestosterone and 0.625 mg of esterified estrogen). At present, no agent is the Food and Drug Administration approved for FAD. She should have periodic monitoring of her triglycerides, cholesterol profile, and free and total testosterone level before and after therapy is initiated as there is an increased risk of cardiovascular disease, presumed to at least be partially related to higher levels of total cholesterol and low-density lipoprotein. Also, ~20% of women can have side effects of hair loss, deepening of voice, hirsutism, and so on, even with testosterone levels within the normal range, although the risk of this increases substantially with supratherapeutic levels.

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**Question 16**

A 56-year-old white woman who has been postmenopausal for 6 years comes to you for a routine examination. She has intermittent symptoms of gastroesophageal reflux disease and has a past medical history of esophagitis. She also had a recent dual-energy X-ray absorptiometry (DXA) scan of her spine and hip that showed a T score of −2.5 standard deviations below young normal. She states her mother was diagnosed with breast cancer, and she is not interested in hormone therapy. She has no personal or family history of deep venous thrombosis (DVT). You recommend which of the following?

a) Medroxyprogesterone acetate (Depo-Provera) injections every 3 months
b) Raloxifene, 60 mg by mouth every day
c) Alendronate, 70 mg by mouth every week
d) Calcium supplementation to a total of 1,500 mg daily with vitamin D, 400 to 800 IU daily
e) Both b and d

**Answer and Discussion**

The answer is e.

**Objective:** Manage osteoporosis (OP) in a patient with esophagitis.

This patient has OP on DXA, which is of concern and must be treated. Although calcium supplementation at 1.5 g plus vitamin D, 800 IU/day, is necessary but not sufficient to treat OP, she needs additional treatment to prevent further bone loss. The best option for treatment in this patient is a SERM such as raloxifene. Raloxifene will not only prevent further bone loss but also offer her a breast cancer risk reduction, as well as a decrease in the total cholesterol without an increase in the ultrasensitive C-reactive protein. Because of this patient’s past medical history of esophagitis and gastroesophageal reflux disease, Fosamax or Actonel can still be an option for treatment, but the gastrointestinal symptoms would have to be followed closely. Injectable Forteo, a bone-building agent, could be considered.

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**Question 17**

A 23-year-old man presents to your office after recently being discharged from the hospital with the diagnosis of new-onset seizures and epilepsy. He is currently taking valproic acid as
prescribed and denies any seizures for the past 2 weeks. He works as an electrician and drives a company van to and from his jobs. He is often climbing ladders and working with “live” wires. Which of the following is the most accurate statement in regard to returning to normal daily activities?

a) He should not be driving until he has been seizure free for 6 to 12 months.
b) As long as his valproic acid level is therapeutic, he may return to normal activities, including driving.
c) Epileptics, regardless of seizure control, should not climb ladders or work with heavy machinery.
d) He will need approval from the Bureau of Motor Vehicles and a special driver’s license to return to his job.

**Answer and Discussion**

**The answer is c.**

**Objective:** Identify appropriate lifestyle recommendations for patients with seizure disorders.

Seizures can be associated with a sudden alteration of consciousness that may interfere with the activities of daily living or put the patient in a dangerous situation. In general, patients should not drive unless the seizures are under control. Each state within the United States has specific rules about what is meant by the phrase “seizure free for a long enough period.” Generally, this period ranges between 6 and 12 months without a seizure while on an appropriate antiepileptic drug regimen. Some states require that the physician report such cases to the Registry of Motor Vehicles; in other states, this is not necessary. Familiarity with local laws on this subject is recommended. Other activities such as swimming, bathing, operating heavy machinery, and climbing great heights are usually not regulated specifically, but should be avoided when unsupervised.

**Question 18**

A 32-year-old woman with no past medical problems is seen at her primary care physician’s office. She is currently in her 12th week of gestation and was found to have HIV on routine screening. She is seeking further care for this. Which of the following is true?

a) The confirmatory Western blot test may be falsely positive in pregnancy.
b) Untreated, perinatal transmission approaches 60%.
c) Perinatal antiviral treatment will decrease the transmission rate to <7%.
d) *Pneumocystis jiroveci* pneumonia (PCP) prophylaxis should be started regardless of the CD4 count.
e) Termination of the pregnancy will offer some protection against the progression of her disease.

**Answer and Discussion**

**The answer is c.**

**Objective:** Manage HIV during pregnancy.

Two things are important about HIV during pregnancy: first, the management of HIV and HIV-related complications in the mother; and second, minimizing the risk of vertical transmission. The management of HIV and HIV-related complications is similar to the one recommended in the patients who are not pregnant, including the prophylaxis against opportunistic infections. As such, PCP prophylaxis should be initiated with a CD4 count of <200. Either trimethoprim/sulfamethoxazole or aerosolized pentamidine is used for PCP prophylaxis if indicated. Pregnancy does not affect the progression of the disease. In addition, HIV has no effect on the pregnancy course once social factors are controlled for.

The risk of transmission from the mother to the infant is believed to be related to the viral load. The risk of vertical transmission is as high as 33% of infants born to untreated mothers versus less than 7% in those infants born to mothers receiving perinatal antiviral medication.

The optimal timing and route of antivirals is debated, but most experts believe in treating with oral triple therapy (if possible) from 14 weeks of gestation to delivery followed by intravenous (IV) therapy during labor and oral therapy to the infant for 6 weeks. If triple therapy is not possible, intrapartum zidovudine conveys the most benefit if given alone. If a mother is on antiretrovirals at the time of conception, they should be continued during the first trimester.

**Question 19**

All the following statements concerning rhinitis are true, except

a) An increased risk of allergic rhinitis exists if there is a family history of allergic rhinitis.
b) Eosinophils can be seen on Wright-stained nasal secretions.
c) Over-the-counter oral sympathomimetic agents may provide some relief of congestive symptoms, but they can cause elevation of BP and can be dangerous in patients with hypertension or in those at risk for cardiac events.
d) Nasal sympathomimetic agents are an excellent choice for the long-term symptom relief.
e) Hot and spicy foods may produce an episodic rhinitis termed *gustatory rhinitis*, which is a vagally mediated reflex.

**Answer and Discussion**

**The answer is d.**

**Objective:** Understand key concepts about rhinitis.

Nasal sympathomimetic agents are not to be used for long-term symptom relief. Their use is limited to 2 to 3 days, to avoid the development of rhinitis medicamentosa. In rhinitis medicamentosa, rebound nasal congestion occurs after the discontinuation of a strong nasal decongestant, creating a vicious cycle, with the patient restarting the nasal spray to treat the congestion, which is directly caused by the nasal spray itself.

**Question 20**

A 28-year-old woman in her 20th week of gestation comes to the emergency department (ED) with shortness of breath.
She has had asthma since childhood that was previously well controlled. She stopped all medications because of concerns for the fetus. On examination, she appears to be in severe respiratory distress, with a respiratory rate (RR) of 28/minute. Her other vitals include a BP of 102/56 mmHg, pulse (P) of 100/minute, and 97% saturation on room air. Her lung examination is significant for wheezing in all lung fields. The rest of the examination is unremarkable. You diagnose her as having an exacerbation of asthma. Appropriate therapy might include all but

- a) Subcutaneous epinephrine
- b) Inhaled metaproterenol
- c) Oxygen by mask
- d) Inhaled albuterol
- e) IV steroids

**Answer and Discussion**

The answer is a.

**Objective: Identify the management of asthma during pregnancy.**

Minimizing the known risks of maternal hypoxia to the fetus is preferred to minimizing the theoretical risks of medications. Therefore, encouraging compliance with medications is important. Almost all asthma medications are used safely during pregnancy. The exception is epinephrine, which can decrease the uterine perfusion. A better choice is terbutaline, 0.25 mg subcutaneously, which is often used to treat preterm labor.

**Question 21**

A 34-year-old diabetic woman is in her 10th week of gestation. Her diabetes was previously well controlled, but she has had problems maintaining her blood sugar control with recent changes in diet. She is also concerned about her risk of hypoglycemia. Her examination is unremarkable. You advise her that all of the following have been associated with poor glycemic control in diabetic women who become pregnant, except

- a) Increased first-trimester miscarriages
- b) Increased neural tube defects
- c) Increased birth weight
- d) Increased neonatal glucose levels
- e) Increased neonatal respiratory distress syndrome

**Answer and Discussion**

The answer is e.

**Objective: Identify the risk of maternal diabetes to the fetus.**

Insulin does not cross the placenta, but glucose does. The fetus will make its own insulin to respond to the high glucose levels. This leads to hypoglycemia after the umbilical cord is cut, as the glucose supply is interrupted. Both large-for-gestational-age and growth-restricted babies are born to diabetics, depending on the effect on the placenta, which is also an end organ like the kidneys and the eyes. Larger babies tend to have less mature lungs; the mechanism for this is unknown.

Miscarriages and birth defects are more common in preexisting diabetics, as opposed to gestational diabetics.

**Question 22**

A 36-year-old woman with diabetes and hypertension has just found out that she is pregnant. Her BP has been well controlled with enalapril 10 mg daily. She has come for her annual primary care visit and has not yet seen an obstetrician. Her BP in your office is 136/78 mmHg. Which of the following medications is contraindicated for the treatment of hypertension in pregnancy?

- a) Propranolol
- b) Methyldopa
- c) Hydralazine
- d) Enalapril
- e) Labetalol

**Answer and Discussion**

The answer is d.

**Objective: Identify antihypertensives safe during pregnancy.**

Angiotensin-converting enzyme inhibitors (ACEIs) are associated with fetal compromise and death when exposure occurs during the second and third trimesters. ACEIs are considered class D medications during pregnancy, meaning that they have known teratogenic properties. Methyldopa is a class B medication during pregnancy, indicating that while there are no well-designed human trials, there are no teratogenic effects noted in animal models, and there is no anecdotal evidence of teratogenic effects in humans or there are teratogenic effects in animal models but not in human models. The rest of the medications above are considered class C medications, suggesting that either animal studies have shown risks and there are no human studies, or no animal or human studies have been conducted. Clinically, all the medications listed other than enalapril are used during pregnancy.

**Question 23**

A 26-year-old woman in her seventh month of pregnancy presents to the ED with increasing shortness of breath. She also complains of left leg swelling. She has no other medical problems and is not currently taking any prescription medications. On examination, she is in moderate respiratory distress. Her vital signs are as follows: RR = 28/minute, BP = 108/64 mmHg, P = 120/minute, and pulse oximetry = 89% on room air. Cardiac examination is significant for a regular, tachycardic rhythm; chest examination reveals no abnormalities; abdominal examination shows an enlarged uterus with palpable fetus; and extremities reveal left leg redness and swelling at the level of the calf. In addition to oxygen, what would be the most appropriate next step?

- a) Doppler study of leg, then IV heparin if positive
- b) Spiral CT, then weight-adjusted low molecular weight heparin (LMWH) subcutaneously if indicated
- c) Ventilation–perfusion scan, then IV heparin if positive
d) IV heparin while awaiting radiographic studies  
e) Doppler leg study and vena cava filter to prevent pulmonary embolism (PE) if positive

Answer and Discussion  
The answer is d.

Objective: Identify and manage Deep Vein Thrombosis/Pulmonary Embolism in pregnancy.

In patients with DVT/PE, early anticoagulation with heparin or LMWH decreases mortality. Also, the risk of DVT and PE is increased during pregnancy. Heparin does not cross the placenta and is easily reversed, so immediate anticoagulation carries little risk. Once that is done, do not hesitate to make the definitive diagnosis. Fetal risk from radiation is minimal compared with the risk of untreated DVT or PE, or ongoing anticoagulation without a documented diagnosis. Ventilation-perfusion scanning, spiral CT, angiography, and venography are all worth the risk. Long-term full anticoagulation with heparin or LMWH is preferred to warfarin. A filter is indicated only if anticoagulation cannot be safely accomplished.

Question 24  
Assume that 20% of patients truly have disease X. Using a new test (X-ometry) to test 100 patients in your office for disease X, a total of 40 of these 100 patients are found to have positive X-ometry. The specificity of X-ometry is known to be 60%. What is the positive predictive value of positive X-ometry under these conditions?

a) 10%  
b) 20%  
c) 40%  
d) 60%

Answer and Discussion  
The answer is b.

Objective: Calculate the positive predictive value given the sensitivity, specificity, and prevalence.

Complete the following table using the partial information provided:

<table>
<thead>
<tr>
<th>TEST RESULT</th>
<th>TRUE DISEASE STATUS</th>
<th>TOTAL</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>X DISEASE PRESENT</td>
<td></td>
</tr>
<tr>
<td></td>
<td>X DISEASE ABSENT</td>
<td></td>
</tr>
</tbody>
</table>

The steps to calculate the positive predictive value are as follows:

Step 1. The example specifies a population prevalence of disease X of 20%. Thus, of 100 patients who are tested, 20 are expected to have the condition disease X— that is, the frequencies A and C add to 20.

Step 2. The problem specifies that 40 of the 100 patients tested have a positive test, so A + B is 40, and the other marginal values of the table can be determined by subtracting the known values from 100, which is the total number of patients examined in this example.

Step 3. The specificity of the test is designated to be 60%, so that 60% of the 80 patients without disease X in this example have a negative X-ometry test result. Frequency D is thus 60% of 80, or 48. The frequency in each of the other cells in this $2 \times 2$ table can then be specified.

Step 4. Once the cells are all filled in, it is possible to calculate the value of the positive predictive value of X-ometry in this example by calculating cell $A (= 8)$ divided by the sum of cells $A + B (= 8 + 32, or 40)$. The correct answer for the positive predictive value is therefore 8/40, or 20%, in this example.

Question 25  
Suppose that a screening mammography test for breast cancer has both high sensitivity and specificity, say 95% and 90%, respectively. What are the positive and negative predictive values of the test when applied to women with a 1% prevalence of breast cancer?

Positive predictive value is:

a) 0.514  
b) 0.333  
c) 0.154  
d) 0.088

Negative predictive value is:

a) 0.999  
b) 0.994  
c) 0.989  
d) 0.950

Answer and Discussion  
The answers are d and a.

Objective: Calculate the positive and negative predictive values given the sensitivity, specificity, and prevalence.

Bayes’ theorem can be applied to calculate the positive and negative predictive values given the specified values of sensitivity, specificity, and prevalence. The Bayes’ theorem for positive predictive value is generally calculated with the following equation:

\[
\text{Positive predictive value} = \frac{(\text{Prevalence})(\text{Sensitivity})}{(\text{Prevalence})(\text{Sensitivity})+((1-\text{Prevalence})(1-\text{Specificity}))}
\]

The prevalence is 0.01, so the positive predictive value is 

\[
\frac{(0.01)(0.95)}{(0.01)(0.95) + ((1 – 0.01) (1 – 0.90))},
\]

which equals 0.0095/(0.0095 + 0.099), or 0.088.
Likewise, the Bayes’ theorem for negative predictive value is generally calculated with the following equation:

\[
\text{Negative predictive value} = \frac{(1-\text{Prevalence})(\text{Specificity})}{(1-\text{Prevalence})(\text{Specificity}) + (\text{Prevalence})(1-\text{Sensitivity})}
\]

Therefore, the negative predictive value is \((1−0.01)(0.90)/[(1−0.01)(0.90) + (0.01)(1−0.95)]\), which equals \(0.891/(0.891 + 0.0005)\), or 0.999.

**Question 26**

Using the same sensitivity and specificity as in question 25, what are the positive and negative predictive values of the test when applied to women with a 10% prevalence of breast cancer (e.g., those with a self-diagnosed lump in a breast)?

Positive predictive value is:

a) 0.667  
b) 0.514  
c) 0.333  
d) 0.167

Negative predictive value is:

a) 0.994  
b) 0.989  
c) 0.950  
d) 0.900

**Answer and Discussion**

The answers are b and a.

**Objective: Correlate statistical power to the sensitivity of a test.**

In a statistical test, rejecting the null hypothesis given that it is truly false is called the power of the test. This is equivalent to having a diagnostic test reject the presence of “no disease” to conclude that there is disease. Hence, this is analogous to sensitivity, the probability that the diagnostic test indicates there is disease when in fact there is disease present. Likewise, in hypothesis testing, the type I error rate (i.e., significance level) of rejecting the null hypothesis when it is really true is analogous to 1 – specificity of a diagnostic test, the false-positive rate.

**Question 28**

The most common cause of visual decline in a patient with diabetes mellitus is

a) Macular edema  
b) Proliferative diabetic retinopathy  
c) Diabetic papillopathy  
d) Tractional retinal detachment

**Answer and Discussion**

The answer is a.

**Objective: Identify macular edema as the most common cause of visual decline in diabetic patients.**

In the Western Hemisphere, diabetic retinopathy is the leading cause of blindness in patients younger than 65 years. While all of these conditions are associated with diabetic retinopathy, the leading cause of irreversible vision loss in patients with diabetes is macular edema given the significantly higher prevalence of macular edema compared with these other conditions. Proliferative diabetic retinopathy is rare in the initial stages of the disease, but can be as high as 11% to 15% in the end stages of the disease. Even at this time, nonproliferative diabetic retinopathy is more common. The pathophysiology of visual loss in nonproliferative diabetic retinopathy is most commonly associated with macular edema.

**Question 29**

The most appropriate initial intervention for a patient with a corneal ulcer is

a) No treatment  
b) Corneal cultures and sensitivities  
c) Eye patch  
d) Broad-spectrum topical antibiotics four times a day

**Answer and Discussion**

The answer is b.

**Objective: Identify and manage a corneal ulceration.**

Most corneal ulcers are caused by infections. People who wear contact lenses are at an increased risk for corneal ulcers.
The risk of corneal ulcerations increases 10-fold when using extended-wear soft contact lenses. Patching is not indicated because it creates a warm, dark environment that allows bacterial growth. Once a pathogen has been identified, targeted antibiotic eye drops and oral pain medications are the mainstay of therapy.

**Question 30**

The most common ocular manifestation in patients with rheumatoid arthritis is

a) Uveitis  

b) Keratoconjunctivitis sicca  

c) Conjunctivitis  

d) Keratitis

**Answer and Discussion**

The answer is b.  

**Objective: Identify ocular problems in rheumatoid arthritis.**

The most common ocular problem in patients with rheumatoid arthritis is keratoconjunctivitis sicca or secondary Sjögren syndrome associated with connective tissue disease. Dry eyes occur in 11% to 13% of patients and this condition is characterized by lymphocytic infiltration of lacrimal and salivary glands with subsequent glandular destruction.

Scleritis is the second most common ocular finding, occurring in 1% to 6% of patients with rheumatoid arthritis. Posterior segment lesions due to rheumatoid arthritis are rare.

**Question 31**

In the Western Hemisphere, the leading cause of irreversible blindness in patients older than 65 years is

a) Cataract  

b) Diabetic retinopathy  

c) Glaucoma  

d) Age-related macular degeneration (AMD)

**Answer and Discussion**

The answer is d.  

**Objective: Identify the etiology of visual loss in elderly patients.**

In the Western Hemisphere, diabetic retinopathy is the leading cause of blindness in patients younger than 65 years; AMD is the most common cause of irreversible blindness in patients older than 65 years. Macular degeneration affects up to 10% of patients between the ages of 65 and 75 years and up to 30% of patients between 75 and 85 years. There are two types of macular degeneration, dry type and wet type. Dry AMD accounts for up to 90% of cases of AMD. Patients will generally get a central visual field loss that is progressive over time.

**Question 32**

Which of the following is a known cause of retinal detachment?

a) Diabetes  

b) Cataract surgery

c) Ocular trauma  

d) Severe nearsightedness (long eyeballs)  

e) All of the above

**Answer and Discussion**

The answer is e.  

**Objective: Identify etiologies of retinal detachment.**

Retinal detachment occurs when the lining of the eye comes off, thus causing loss of vision. Causes of retinal detachment include ocular trauma, posterior vitreous detachment, traction from an inflamed vitreous, long eyeballs (as in very nearsighted people), family predisposition, degenerative changes in the retina, complications from diabetes, and complications of intraocular surgery, including cataract surgery.

**Question 33**

You are asked to see a 54-year-old man for a preoperative evaluation prior to total hip arthroplasty. He has a 15-year history of non-insulin-dependent diabetes mellitus, chronic renal insufficiency, and hypertension. His medications include glyburide, metformin, and lisinopril. He has mild retinopathy and 300 mg/day of proteinuria. His last laboratory studies 2 weeks ago showed a creatinine of 2.1 mg/dL, total cholesterol of 256 mg/dL, high-density lipoprotein cholesterol 39 mg/dL, low-density lipoprotein cholesterol of 152 mg/dL, triglycerides of 210 mg/dL, and glycosylated hemoglobin of 7.2%. He has no past history of cardiovascular disease and denies current chest pain, palpitations, or dyspnea on exertion. For the past year, he has had limited physical activity due to progressive osteoarthritis of the hip. On examination, his weight is 220 lb with a body mass index of 32, BP 132/84 mmHg, and P 84/minute. His funduscopic examination shows mild background retinopathy. His cardiac and pulmonary examinations are normal, whereas the remainder of his examination is otherwise unremarkable except for mildly diminished dorsalis pedis pulses and a decreased position sense in his toes. His ECG shows nonspecific ST-T wave changes. Which of the following is the most appropriate preoperative recommendation at this time?

a) Ultrasound vascular evaluation of the lower extremities  

b) Dobutamine stress echocardiography or dipyridamole thallium imaging  

c) No further cardiac testing and proceed with surgery  

d) Cardiac catheterization

**Answer and Discussion**

The answer is b.  

**Objective: Identify indications for preoperative cardiac testing.**

Using the American College of Cardiology and the American Heart Association (ACC/AHA) guidelines, this patient has several clinical risk predictors (h/o type 2 diabetes mellitus and chronic renal insufficiency) and is scheduled for an intermediate-risk surgery. Because his functional class is poor with...
activity <4 metabolic equivalent of tasks (METs), he should undergo further risk stratification with noninvasive testing.

Once high risk features have been ruled out (active ischemia, decompensated congestive heart failure, and ventricular arrhythmia), patients going for intermediate-risk surgery should have their functional status assessed. If the patient is able to consistently undergo at least 4 METs of activity, then no further preoperative testing for cardiovascular disease is needed. However, this patient is not able to do 4 METs due to his osteoarthritis and has multiple (at least three) risk factors for coronary artery disease. With an abnormal baseline ECG, stress testing with an imaging modality may be indicated.

**Question 34**

You are asked to evaluate a 73-year-old man with stable class II angina treated with nitrates and atenolol, and no previous myocardial infarction or coronary heart failure. He has mild hypertension controlled with lisinopril and no history of diabetes. He had excellent exercise capacity (7 METs) until he injured his ankle 2 weeks ago. At that time, he was found to have a 5.2-cm abdominal aortic aneurysm. His examination is unremarkable, his BP is 144/86 mmHg, and his heart rate is 65/minute. His ECG is normal. He is scheduled to undergo abdominal aortic aneurysm repair. Which of the following is the most appropriate recommendation at this time?

a) Exercise stress test  
b) Dobutamine stress echocardiography or dipyridamole thallium imaging  
c) No further cardiac testing and proceed with surgery  
d) Cardiac catheterization

**Answer and Discussion**

**Objective: Identify indications for preoperative testing to assess for the cardiovascular risk.**

Applying the ACC/AHA guidelines to this patient with chronic stable class II angina with excellent functional class would suggest that he did not undergo any further risk stratification with a stress test unless there would be a change in management.

This patient is able to consistently do >4 METs of activity and is safe to proceed to surgery. No further testing is indicated given his good functional capacity.

**Question 35**

A 48-year-old woman is referred for preoperative evaluation before a planned elective laparoscopic cholecystectomy. She has no prior cardiac history but has had asthma since age 16 years. Her current medications are oral theophylline and inhaled albuterol. She does not smoke and notes no dyspnea on moderate exertion. On examination, her weight is 97 kg (213.4 lb), height 163 cm (5’ 4”), BP 144/78 mmHg, and P 76/minute and regular. Her lungs reveal moderate wheezing that does not clear with cough. Her heart is normal, and, other than obesity, the remainder of her examination is normal. Which of the following is the most appropriate next step?

a) Add inhaled salbutamol before surgery  
b) Add inhaled betamethasone before surgery  
c) Reassure her that her risk is low because of the planned laparoscopic approach  
d) Cancel the surgery and optimize antiasthma treatment regimen before rescheduling

**Answer and Discussion**

**Objective: Manage perioperative pulmonary complaints.**

The presence of active wheezing places this patient at greater risk for postoperative pulmonary complications and increased bronchospasm risk during anesthesia induction. The patient’s surgery should be delayed until her asthma treatment is optimized. The laparoscopic approach may reduce the risk of pulmonary complications compared with the open cholecystectomy, but a level of risk remains because of gaseous peritoneal distention and postoperative pain.

**Question 36**

A 27-year-old man is evaluated in the emergency room for the abrupt onset of neck pain associated with dizziness, slurred speech, and difficulty walking. He was in his usual state of health until 3 hours ago, when he developed the acute onset of posterior-lateral neck pain, shortly after he left an appointment with his chiropractor. Soon after, he noticed a sense of spinning and began slurring his words. He is unsteady when he walks, and within the last 30 minutes, he has had difficulty swallowing. His past medical history is negative except for occasional musculoskeletal complaints. He does not take any regular medications. He drinks alcohol socially and does not use tobacco. He is not married, and he works as a bank manager. His vital signs are as follows: T = 37.1°C, P = 81 beats/minute, RR = 22/minute, and BP = 126/81 mmHg. Head, eyes, ears, nose, and throat (HEENT) examination reveals left ptosis with anisocoria (left pupil smaller than the right). Nystagmus is present. The neck is supple but tender to palpation. There is no jugular venous distention (JVD), adenopathy, or bruits. Cardiopulmonary and abdominal examinations are normal. Neurologic examination demonstrates left-sided dysmetria and decreased pain and temperature sensation on the left side of the face and right side of the body. A chemistry profile, complete blood cell count, and coagulation studies are normal. CT scan of the head without contrast is normal. Which of the following is the most appropriate next step in the evaluation of this patient?

a) Carotid ultrasound  
b) Lumbar puncture  
c) Transcranial Dopplers  
d) MRI/magnetic resonance angiography (MRA) of the brain and neck  
e) Repeat CT scan of the head without contrast in 24 hours
**Question 37**

A 55-year-old man was brought to the ED via squad. His wife called 911 after the patient awoke this morning with a posterior headache, dizziness, and unsteady gait. His past medical history is significant for hypertension and known coronary artery disease. His medications include a baby aspirin, metoprolol, atorvastatin, and clonidine. He was not able to take his medications before arrival. In the emergency room upon presentation, he was awake, alert, and afebrile. He described severe vertigo. Vital signs were as follows: P = 65 beats/minute, RR = 24/minute, and BP = 175/97 mmHg. His HEENT examination revealed bidirectional nystagmus. His lungs were clear. Cardiac examination displayed normal heart tones with a +S4 gallop. Abdominal examination was normal. Neurologic testing revealed gait ataxia but normal muscle strength. Laboratory tests were unremarkable, and the CT scan of the head without contrast was normal. He was admitted for further observation, and examination several hours later revealed lethargy alternating with agitation, intractable hiccups, bidirectional nystagmus, and dysmetria of the right upper and lower extremities. Which of the following is the most likely diagnosis?

- a) Vestibular neuronitis
- b) Cerebellar infarction
- c) Benign positional vertigo
- d) Vestibular migraine
- e) Ménière disease

**Answer and Discussion**

The answer is b.

**Objective: Recognize symptoms concerning for cerebellar stroke.**

This patient presents with headache, vertigo, and ataxia, which are the classic presenting symptoms of ischemic or hemorrhagic cerebellar stroke. Although CT scan can exclude hemorrhage, infarcts may not be well visualized early, especially in the brainstem and cerebellum. The patient’s deterioration following the day, with signs of brainstem compression (altered level of consciousness and intractable hiccups), indicates a dire situation, and urgent neurosurgical decompensation is required. Peripheral vertigo may be a result of many disorders of the ear, including vestibular neuronitis, benign positional vertigo, vestibular migraine, acoustic neuroma, and Ménière disease, but none of these causes limb ataxia, dysarthria, or hiccups. Headache may accompany vestibular migraine but is not a feature of the other peripheral disorders.

**Question 38**

A 35-year-old man is referred to you for preoperative evaluation prior to an inguinal hernia repair. He has no prior cardiac history and does not smoke or drink. On examination, he weighs 80 kg (176 lb), BP 140/80 mmHg, and P 80/minute. His heart and lungs, as well as the remainder of his examination, are normal. You recommend which of the following?

- a) Complete metabolic profile
- b) Complete blood count
- c) Urine analysis
- d) All of the above
- e) None of the above

**Answer and Discussion**

The answer is e.

**Objective: Identify the preoperative testing in a healthy individual.**

This patient is completely healthy, and the evidence would suggest that ordering routine preoperative blood work would be both unnecessary and costly, and not indicated in this patient’s case. A screening urine analysis is never indicated unless symptoms suggest that the patient may have an underlying infection.

**Question 39**

A 50-year-old woman with a 20-year history of rheumatoid arthritis is scheduled for a spine surgery. Her medications include prednisone 10 mg/day orally for the past year, vitamin E, gingko biloba, garlic, and aspirin. Her functional class is limited, but she can still climb a flight of stairs with her groceries (>4 METs). She denies any history of chest pain, shortness of breath, and prior cardiac problems. Her examination reveals a weight of 60 kg and height of 5’ 5”, BP of 120/70 mmHg, and heart rate of 80/minute. Heart and lung examinations are normal. Her neck examination reveals a decreased range of motion, and her extremities reveal deformities consistent with rheumatoid arthritis. Which of the following is the most appropriate recommendation?

- a) Discontinue vitamin E, gingko biloba, and garlic
- b) Discontinue aspirin 10 days before surgery
c) Obtain cervical spine films  
d) Stress-dose steroids  
e) All of the above

**Answer and Discussion**

**Objective: Manage medications perioperatively.**

The current evidence and consensus would support discontinuing vitamin E, ginkgo, and garlic about 2 weeks prior to surgery because they may all increase the risk of bleeding. Aspirin irreversibly inhibits the platelet cyclooxygenase and should be stopped 7 to 10 days before surgery. Cervical spine films are indicated in patients with rheumatoid arthritis before they undergo general anesthesia because the presence of severe atlantoaxial disease can cause a compromise of the cervical cord during manipulation of the neck during intubation; however, there is no role for further spine imaging. Although the risk of perioperative adrenal insufficiency is low, it is potentially catastrophic. Stress-dose steroids would be recommended to prevent this.

**Question 40**

A previously well 78-year-old man is admitted to the hospital for the treatment of a community-acquired pneumonia. The nurses report that he is sometimes hard to arouse, quiet, and withdrawn, while at other times he is agitated, disoriented, and accusatory, and behaves inappropriately. Physical examination is unremarkable except for the findings of pneumonia. Which of the following is the most accurate statement about his mental status?

a) He has dementia with “sundowning.”

b) The symptoms are potentially preventable.

c) A head CT scan is needed.

d) He has the “pseudodementia” of depression.

**Answer and Discussion**

**Objective: Identify and manage delirium in an elderly hospitalized patient.**

The acute onset of the change in mental status, the fluctuating course, and the altered level of consciousness are diagnostic of delirium. Although the cognitive dysfunction at night in a new environment (sundowning) can occur in patients with either dementia or delirium, the patient does not have a history of dementia, in which symptoms usually progress over a duration of months to years, and attention and level of consciousness are normal. A head CT scan is rarely useful in the diagnostic evaluation of a patient with delirium and is reserved for patients with new or focal neurologic signs or suspected head trauma. Patients with major depressive disorder often have cognitive dysfunction (“pseudodementia”), but are alert and attentive and do not have a fluctuating course. A clinical trial with hospitalized elderly patients demonstrated a 40% decrease in the incidence of delirium with an intervention that targeted the risk factors for delirium (cognitive impairment, sleep deprivation, immobility, visual and hearing impairment, and dehydration); the total number of days with delirium was also reduced by the intervention.

**Answer and Discussion**

**Objective: Manage the urinary incontinence in the elderly.**

The patient has a urinary tract infection and is likely to respond to an antibiotic that will reduce his lower urinary tract symp-
toms as well. Acute causes of urinary incontinence can be recalled by the pneumonic DRIP: Delirium, Restricted mobility, Impaction oriatrogenic (physical restraints and excessive IV fluids) or Infection, Polypufia (glucosuria, loop diuretics, and anticholinergics), or Pharmaceuticals. The transurethral resection of prostate is indicated for men with severe lower urinary tract symptoms and/or bladder outlet obstruction unrelieved by medications, but this patient’s symptoms are acute and not associated with a large postvoid residual urine. An α-adrenergic blocker is often effective in reducing the irritative and obstructive symptoms of benign prostatic hyperplasia, but the patient did not have a history of chronic symptoms and an improvement with these medications might not be seen for several days or weeks. A bladder relaxant might reduce the intensity of the urinary urgency but would not eliminate the infection. A cholinergic agent would not eradicate the infection and might exacerbate the urge symptoms because it increases the detrusor muscle contractions.

**Question 43**

An 84-year-old man is recovering from an abdominal surgery in the hospital. Four days after surgery, he attempts to get out of bed for the first time. He feels light-headed and unsteady and falls without an injury. He is now afraid to walk. Before the operation, he walked normally. He is taking a cardioselective β-blocker, a statin, and acetaminophen. Physical examination reveals normal cognition and vital signs and generalized weakness. He appears worried. Laboratory studies are unremarkable. Which of the following is most likely to improve his symptoms?

a) A β-blocker with intrinsic sympathomimetic activity rather than the cardioselective agent  
b) Low-intensity resistive exercises for his lower extremities  
c) A low dose of a psychostimulant (e.g., methylphenidate)  
d) A four-prong cane  
e) A benzodiazepine (e.g., lorazepam) to treat anxiety

**Answer and Discussion**

The answer is b.

**Objective:** Identify and manage deconditioning in an elderly patient.

The patient probably has deconditioning associated with major surgery and prolonged immobility. With prolonged bed rest, a generalized weakness of the extensor and flexor muscles of the knees and hip muscles is common. Low-intensity exercises, active resistance against flexion or extension, and therapeutic bands or tubes increase muscle strength and lessen the chance of a fall. A β-blocker with intrinsic sympathomimetic activity could cause orthostatic hypotension and more light-headedness. A psychostimulant might be considered for a patient with depression and delayed recovery from surgery but would not increase the muscle strength. A four-prong cane is helpful when patients have weakness in one extremity, but is not indicated for patients with generalized weakness due to deconditioning. An anxiolytic could cause gait impairment and increase the risk of a fall.

**Question 44**

A 71-year-old woman presents with an 8-month history of urinary urgency, frequency, and nocturia, and daily urinary incontinence. Her past medical history is significant for occasional “stress incontinence” (with sneezing, coughing, and straining) for 12 years. She takes no daily medications. Physical examination reveals slight anterior vaginal prolapse and no visible leakage or pelvic mass. A screening urinalysis and basic metabolic panel are normal. Which of the following is most likely to relieve her urinary incontinence?

a) Bladder relaxant (oxybutynin)  
b) Topical (vaginal) estrogen  
c) α-Agonist (pseudoephedrine)  
d) Behavioral therapies  
e) Periurethral injections (collagen)

**Answer and Discussion**

The answer is d.

**Objective:** Identify and manage mixed urinary incontinence.

The patient has mixed stress and urge incontinence. The stress incontinence is most likely a result of urethral hypermobility, whereas the urge incontinence likely represents an overactive bladder. Although bladder relaxants alone reduce the frequency of incontinent episodes due to urge incontinence, they have little or no effect on stress incontinence. Behavioral therapies (training), including pelvic floor exercise, pelvic floor stimulation, and biofeedback, are more effective than placebo or bladder muscle relaxants for mixed forms of incontinence. In one study, biofeedback to teach pelvic floor muscle control, verbal feedback based on vaginal palpation, and a self-help booklet in a first-line behavioral training program all achieved comparable improvements in urine incontinence in community-dwelling older women. Periurethral injections with bulking agents (collagen) are indicated for intrinsic sphincter deficiency (ISD) and have no effect on urge incontinence. The α-agonists and vaginal estrogen are of questionable value in the treatment of stress incontinence and have no proven effect in women with ISD.

**Question 45**

A 20-year-old man presents to the ED with altered mental status, diaphoresis, urinary incontinence, and shortness of breath. He is agitated, has pinpoint pupils, as well as diffuse wheezing. Family reports that he is a college student, and does odd jobs on the side to help make some additional money. Most recently, he had been working for a landscaping company and tutoring fellow students. The appropriate management of this patient includes all of the following, except

a) Atropine  
b) Sodium nitrite  
c) Pralidoxime chloride (Protopam)  
d) Maintenance of airway  
e) Decontamination

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Answer and Discussion
The answer is b.

Objective: Identify and manage organophosphate poisoning.

This patient has organophosphate poisoning as evidenced by his muscarinic and nicotinic overactivation, which may include altered mental status, diaphoresis, lacrimation, miosis, urination, defecation, bradycardia, and diffuse wheezing. Atropine blocks the muscarinic effects of organophosphates and should be administered promptly. Pralidoxime chloride (Protopam) reactivates the enzyme cholinesterase by breaking the acetylcholinesterase–phosphate complex. Its advantages over atropine include its ability to reverse muscle paralysis and possibly central nervous system depression.

Decontamination procedures may include removal of contaminated clothing, washing of skin and hair, and, if indicated by route of exposure, emptying the stomach. In severe cases, a patent airway needs to be established for the removal of excess secretions and institution of ventilatory support.

Sodium nitrite is used in cyanide poisoning. It has no role in the management of organophosphate toxicity.

Question 46

Which of the following side effects is most commonly seen with selective serotonin reuptake inhibitors (SSRIs)?

a) Weight gain
b) Sexual dysfunction
c) Sedation
d) QTc prolongation
e) None of the above

Answer and Discussion
The answer is b.

Objective: Identify the side effects from SSRIs.

SSRIs are the most often prescribed medication class in depression. While a relatively safe and effective medication class, they are associated with some side effects. Sexual dysfunction is a very common side effect. Patients taking SSRIs (fluoxetine, sertraline, paroxetine, citalopram, and escitalopram) are more likely to report sexual dysfunction than those taking other agents such as bupropion and mirtazapine. The other side effects, notably weight gain and sedation, have been associated with many SSRIs, but not nearly as frequently as sexual dysfunction. QTc prolongation, while reported, is very rare and should often prompt investigation of other medications.

c) These disorders respond better when the intervention is early, without reinforcement by the excessive ordering of tests and evaluations.
d) Patients should be told that the symptoms are “real” but not life-threatening.
e) All of the above

Answer and Discussion
The answer is e.

Objective: Identify and manage somatic symptom disorders.

The Diagnostic and Statistical Manual of Mental Disorders criteria include finding a history of many physical complaints beginning before age 30 years that occur over a period of several years and result in a current diagnosis being sought or a significant impairment in the social, occupational, or other area of functioning.

Treating the patient with short but regularly scheduled visits; reassurance; referral to a psychoeducational group, if available, to enhance optimal health; ordering only “necessary” testing; and treating comorbid psychiatric disorders, such as depression, are the cornerstones of managing these cases.

Question 47

Which of the following statements about somatic symptom disorders is correct?

a) There is a history of many physical complaints beginning before age 30 years.
b) When a related general medical condition exists, physical complaints are in excess of what would be expected.
c) These disorders respond better when the intervention is early, without reinforcement by the excessive ordering of tests and evaluations.
d) Patients should be told that the symptoms are “real” but not life-threatening.
e) All of the above

Answer and Discussion
The answer is c.

Objective: Identify symptoms that associate with panic attacks.

Panic attacks are characterized by intense fear triggering many somatic symptoms when no apparent threat is present. Panic attacks are very debilitating and while most individuals tend to only have one or two, the fear of having recurrent panic attacks can be crippling. Symptoms of panic attacks are generally quick in onset and can mimic a hyperadrenergic state, including chest pain, palpitations, light-headedness, dizziness, shortness of breath, nausea, difficulty swallowing, and paresthesias. Diarrhea is not a characteristic feature of panic attacks and should prompt an investigation of an alternative or concurrent diagnosis. Nausea and abdominal distress may be seen.

Question 49

Which of the following medications increases the risk of lithium toxicity?

a) Enalapril
b) Hydrochlorothiazide
c) Ibuprofen
d) Losartan
e) All the above
**Answer and Discussion**

The answer is e.

**Objective: Identify drug–drug interactions that affect renal clearance.**

Lithium has renal clearance and is not hepatically metabolized. Therefore, any medications that alter sodium excretion and subsequently lithium excretion should be used with caution (e.g., diuretics, ACEIs, and nonsteroidal anti-inflammatory drugs) because lithium levels may increase to the point of toxicity in only several days.

**Question 50**

A 56-year-old man is transferred from the intensive care unit (ICU) to the general medicine ward for a severe urinary tract infection. He is being treated with ciprofloxacin for this urinary tract infection and seems to be improving. He is not requiring ventilatory or vasopressor support. Overnight, he has an acute change in mental status and becomes agitated. He is not on any narcotics, benzodiazepines, antihistamines, anticholinergics, or sleep aids. His repeat lab work, including electrolytes, is within normal range. The nurse asks for some haloperidol, as this is what he would get in the ICU when he was agitated. Which of the following should be obtained before initiating haloperidol?

a) Thyroid-stimulating hormone  
b) Hematocrit  
c) ECG  
d) Liver function tests  
e) All of the above

**Answer and Discussion**

The answer is c.

**Objective: Identify the risk of QTc prolongation with haloperidol.**

Haloperidol may alter the cardiac conduction and prolong QT Interval; life-threatening arrhythmias have occurred with therapeutic doses of antipsychotics, but the risk may be increased with doses exceeding recommendations and/or with IV administration (unlabeled route). Haloperidol should be used with caution or avoided in patients with electrolyte abnormalities (e.g., hypokalemia and hypomagnesemia), hypothyroidism, familial long QT syndrome, concomitant medications that may augment QT prolongation, or any underlying cardiac abnormality that may also potentiate the risk.

**Question 51**

A thin, 21-year-old white woman presents to the ED with an acute onset of shortness of breath. The examination is consistent with a pneumothorax. Chest radiography confirms this finding, along with evidence of mild hyperinflation and ring shadows in the upper lobes. She states that she was adopted and grew up in foster homes, noting that she was a “sickly” child with many episodes of sinusitis and bronchitis, and that lately she cannot get rid of a productive cough.

**Answer and Discussion**

The answer is e.

**Objective: Identify and manage cystic fibrosis (CF).**

This patient has CF. In white populations, CF, which occurs in approximately 1 in 2,500 live births, is the most common lethal autosomal recessive genetic disorder, with a carrier frequency of 1 in 25 persons. During the past three decades, however, the number of adults with CF has increased dramatically, attributable in large part to a significant improvement in survival. For patients born in the 1990s, the median survival is now predicted to be longer than 40 years. More than one-third of the patients in the Cystic Fibrosis Foundation Registry are now older than 30 years. CF is a mono- genetic disorder caused by mutation in the CFTR gene on chromosome 7. The clinical manifestations are due primarily to the dysfunction of exocrine glands, producing viscid dehydrated secretions. Clinically, CF is characterized by chronic airway infections leading to bronchiectasis and bronchiolectasis, exocrine pancreatic deficiency, abnormal sweat glands, and urogenital dysfunction. Patients with CF exhibit characteristic sputum microbiology, with *Haemophilus influenzae* and *S. aureus* often being the first organisms recovered from lung samples in patients newly diagnosed with CF. After multiple clinical exacerbations and antibiotic exposures, *P. aeruginosa* becomes the predominant organism recovered. Almost 50% of patients have *Aspergillus fumigatus* in their sputum, with up to 10% exhibiting the syndrome of allergic bronchopulmonary aspergillosis. The infection with *Burkholderia cepacia* species is pathogenic and causes a rapid clinical deterioration, often with fulminating pneumonia, bacteremia, and death (cepacia syndrome). Female sex and pneumothorax are poor prognostic indicators in CF.

**Question 52**

A 43-year-old man undergoes a preoperative evaluation for an inguinal hernia repair. He is a tall, thin man without previous medical problems. Examination reveals normal vital signs, pectus excavatum, mild kyphoscoliosis, and a mitral regurgitation murmur. A subsequent echocardiography demonstrates normal left ventricular function, 2+ mitral
regurgitation, and a mild ascending aortic aneurism. Further workup reveals a negative urine cyanide–nitroprusside test result and a slit-lamp examination consistent with ectopia lentis. Which of the following is the most likely diagnosis?

a) Ehlers-Danlos syndrome type IV  
b) Homocystinuria  
c) Marfan syndrome  
d) Familial aortic aneurysm  
e) Ehlers-Danlos syndrome type VI

Answer and Discussion
The answer is c.

Objective: Identify a patient with Marfan syndrome.
This case illustrates the clinical presentation of Marfan syndrome. Marfan syndrome is inherited as an autosomal dominant disorder with a wide phenotypic range both within affected families and between families. Severe Marfan syndrome is characterized by a triad of features: (a) long, thin extremities frequently associated with other skeletal changes; (b) reduced vision as the result of dislocations of the lenses (ectopia lentis); and (c) aortic aneurysm that typically begins at the base of the aorta. Other skeletal abnormalities include severe chest deformities, scoliosis, kyphosis, and pes planus. Joint hypermobility may be seen, although not commonly. Other clinical manifestations include spontaneous pneumothorax and inguinal and incisional hernias. Marfan syndrome shares clinical characteristics with other syndromes, and in the absence of classic features, diagnosis may be difficult. Patients with homocystinuria may have tall stature, pectus deformities, scoliosis, pes planus, and progressive lens dislocation. Homocystinuria may be detected by a positive urinary nitroprusside test result or elevated urinary homocystine by amino acid chromatography. Ehlers-Danlos syndrome type IV (vascular type) presents with aortic aneurysms and rupture, joint hypermobility, mitral valve prolapse, and spontaneous pneumothorax. Ehlers-Danlos syndrome type VI (ocular type) may exhibit characteristics similar to those of type IV, with the addition of retinal detachment and ocular symptoms. Ectopia lentis is not a feature of Ehlers-Danlos syndrome.

Question 53
Which of the following patients would not be appropriate for hospice care?

a) A 45-year-old woman with metastatic breast cancer who is not going to receive any further chemotherapy  
b) A 85-year-old man with widespread metastatic prostate cancer who wants to be do not resuscitate (DNR) and has received his first dose of HT  
c) A 74-year-old bed-confined and nonverbal dementia patient with a feeding tube whose family does not want to make him a DNR  
d) A 38-year-old man with type 1 diabetes complicated by kidney disease requiring dialysis, and advanced, progressive HIV  
e) A 58-year-old man with ischemic cardiomyopathy and an implantable cardiac defibrillator (ICD) who wants to continue his cardiac medications

Answer and Discussion
The answer is b.

Objective: Identify indications for Hospice care.
Metastatic malignancy with no plans for therapy is almost always an appropriate hospice diagnosis. The only exceptions could be diseases with very slow progression such as carcinoid tumors and, occasionally, head and neck primaries. Medicare guidelines specifically state that hospices may not require a DNR order for admission. Dementia patients who have reached a functional state with one or less understandable words in 24 hours and an inability to independently get out of a chair have an average life expectancy of less than 6 months; therefore, the patient with dementia could be admitted to hospice. The dialysis patient will be admitted for a diagnosis other than his renal disease, so the hospice would not be responsible for it, and it may continue. Cardiac medications in heart failure are used to improve symptoms so they would be appropriate. The ICD can be turned off at a later date or not at all. The 85-year-old with prostate cancer has just started therapy with a high probability of response with life prolongation and so would be inappropriate for hospice.

Question 54
Dr. X has personal religious beliefs that one should always provide and never discontinue artificial nutrition and hydration, regardless of the specific circumstances. He has been caring for an advanced dementia patient who did not complete a living will but did specify a legal medical proxy—his daughter. The nursing home has approached the daughter about placing a percutaneous endoscopic gastrostomy tube because the patient has begun to lose weight. She has been reading on the Internet and questions whether there is any evidence that feeding tubes do not provide comfort and may actually cause distress. Discuss her goals of care for her father and, if focused regardless of the specific circumstances. He has been caring for an advanced dementia patient who did not complete a living will but did specify a legal medical proxy—his daughter. The nursing home has approached the daughter about placing a percutaneous endoscopic gastrostomy tube because the patient has begun to lose weight. She has been reading on the Internet and questions whether there is any evidence that feeding tubes do not provide comfort and may actually cause distress.

a) Transfer the care to a physician with different religious beliefs  
b) Explain that although he has particular religious beliefs, the evidence is that feeding tubes do not provide comfort and may actually cause distress  
c) Discuss his concern that her father will starve to death and be very uncomfortable without nutritional support  
d) Discuss her goals of care for her father and, if focused predominantly on comfort, suggest a hospice referral and further discussion of the role of nutritional support by the hospice team  
e) Support her reading of the literature and the lack of evidence of benefit without mentioning his religious beliefs

Answer and Discussion
The answer is c.

Objective: Identify options for care given conflict between the caregiver and the patient beliefs.
Physicians with personal beliefs may not force their particular beliefs on other individuals, but they are also not required to provide care that they feel is ethically inappropriate. Therefore,
because the evidence for feeding tubes in dementia does not support an improvement in quality of life, Dr. X should not use emotionally charged words such as “starve” to persuade a family member to his point of view. He may transfer the care to another physician, allow the hospice team to have a conversation he personally feels uncomfortable with but maintain care of the patient, or present the evidence in an unbiased way. One can argue whether he should acknowledge his personal beliefs because the power imbalance between the physician and the family could be considered coercive, but this is preferred to allowing the bias to remain unspoken.

**Question 55**

Mr. M is a 79-year-old man who has suffered a major intracerebral bleed. He was maintained on ventilator support for a week but has been successfully weaned. The team approaches the wife to discuss placing a feeding tube. She believes that her husband would not want to be sustained in this condition and requests that he just be kept comfortable. He is unresponsive and does not appear to have any active symptoms. Which of the following choices is most appropriate?

- a) Start a morphine infusion
- b) Discontinue any labs and any imaging
- c) Discontinue chronic medications, except PRN medications for symptomatic relief
- d) All of the above
- e) All of the above except choice a

**Answer and Discussion**

The answer is e.

**Objective: Manage symptoms in an unresponsive patient.**

One could support any of the other answers, depending on how one clarifies the goals with the patient’s wife. Given the transition of goals of care to comfort measures only, any intervention that does not focus and enhance the patient’s comfort should be discontinued. This includes any laboratory and imaging modalities, and chronic medications other than those for comfort. Because he is unresponsive, he may well not have any symptoms so one could wait until/if something developed and provide medication then. It will save the nurse and the patient time and distress if the needs are anticipated and medications already available, rather than having to page if something develops. Starting an infusion in an unresponsive patient, even with family consent, is not proportional to the need and therefore crosses the ethical boundaries of palliative sedation, is not supported by the concept of double effect, and approaches active euthanasia, which is illegal in all states. There is no intractable symptom to address.

**Question 56**

Mrs. L is a 60-year-old woman with a history of severe osteoarthritis and chronic pain secondary to her osteoarthritis. She was maintained with reasonable comfort on naproxen until recently, when she was diagnosed with congestive heart failure. Her cardiologist stopped the naproxen and advised her that she could not take it again. She is coming to see you for uncontrolled pain. She has been taking eight extra-strength acetaminophen daily and has been using her husband’s tramadol 50 mg without any benefit. She rates her pain as 8/10 in her knees and hands and constant, although it gets worse with walking or cooking. Functionally, she is not able to perform most of the activities that she could while taking the naproxen. Which of the following would be the most appropriate order for her?

- a) Propoxyphene/acetaminophen one to two tablets every 4 to 6 hours as needed
- b) Celecoxib 200 mg/day
- c) Fentanyl patch 25 μg every 3 days
- d) Oxycodone 5 mg every 4 hours as needed, with a plan to convert to sustained-release oxycodone once need is determined
- e) Morphine 5 mg liquid every 4 hours, with a plan to convert to sustained-release morphine once need is determined

**Answer and Discussion**

The answer is e.

**Objective: Identify the pain regimen in patients with other chronic conditions.**

Propoxyphene has not been shown to be better than placebo and therefore should not be given in this setting. Celecoxib has less gastrointestinal toxicity but is no different in fluid retention than other nonsteroidal anti-inflammatory drugs; therefore, it is contraindicated in congestive heart failure. Fentanyl patches should never be started in opioid-naïve individuals because deaths have been reported. This dose is equivalent to 60 mg of oral morphine in 24 hours. Of the choice of oxycodone or morphine, morphine has a generic; therefore, this should be the first opioid tried. Oxycodone would be a reasonable alternative, although the sustained-release version is the most expensive way to orally manage pain.

**Question 57**

Mr. R is a 79-year-old man with end-stage lung cancer admitted to home hospice. He is DNR. He has been quite functional at home on 2 liters/minute of nasal O2. He had recently returned from a cross-country trip to visit his first great grandchild. He calls the hospice nurse with sudden onset of severe dyspnea and acute anxiety. The nurse calls you for recommendations and also wants to give him morphine for his dyspnea. Which of the following is the most appropriate action?

- a) Let her give him as much morphine as needed and keep him comfortable at home
- b) Let her give him 5 mg of oral morphine that may be repeated every 15 minutes three times and then arrange an admission to look for a PE
- c) Morphine may decrease his respirations; thus, he may have lorazepam for his anxiety as needed. The nurse should recheck him tomorrow.
- d) Send him to the emergency room
- e) Start him on a fentanyl patch 12 μg/24 hours
Answer and Discussion

The answer is b.

Objective: Identify and manage the shortness of breath in a hospice patient.

Given the history, the likelihood of a PE is quite high. An admission to hospice does not rule out the evaluation of acute new problems. Patient goals should be considered in light of his functional status at the time the new symptom developed. If he was bed bound or did not want to be admitted, then answer a is appropriate. There is evidence to support the role of morphine in cancer dyspnea management (Cochrane Review) and also in nonhospice chronic obstructive pulmonary disease (COPD). In one Australian study, patients with COPD were started on 20 mg of sustained-release morphine once daily for dyspnea. The worse the COPD, the more benefit they obtained from the medication. No one developed a clinical worsening of their respiratory status even though CO₂ was not tested. Because hospice provides inpatient benefits, the care should be given in that setting rather than in an emergency room. Although the fentanyl dose might ultimately be appropriate, at the present time, it will take 12 to 16 hours for the patch to have an effect; therefore, it will not relieve patient’s current distress. Even at the lower dose, starting this in a naïve patient is not recommended.

Question 58

In the proper medical management of lead toxicity, all the following are true, except

a) Patient removal from exposure is mandatory.
b) Symptomatic patients with high lead levels should undergo chelation therapy.
c) All patients with elevated blood lead levels should be chelated even if asymptomatic.
d) Ca-EDTA is the preferred parenteral agent.
e) 2,3-Dimercaptosuccinic acid (Succimer) is the oral agent of choice.

Answer and Discussion

The answer is c.

Objective: Understand the management of lead toxicity.

The first step in the management of lead toxicity is patient removal from exposure and, in some cases, this may be all that is necessary. Chelation therapy in adults should be reserved for patients with significant signs or symptoms (e.g., encephalopathy or renal injury). Commonly used chelators have potential side effects (e.g., Ca-EDTA can cause acute tubular necrosis) and should not be used routinely in asymptomatic patients. The indications for chelation therapy in children are more liberal. The Centers for Disease Control and Prevention recommend that children with blood levels of 45 μg/dL be referred for therapy, and some practitioners routinely treat children with levels between 25 and 44 μg/dL.

Although several chelators have been used in the treatment of lead poisoning, Ca-EDTA is the drug of choice when a parenteral agent is needed. When an oral agent is preferred (e.g., in children), Succimer is used.

Question 59

According to the National Quality Forum, all patients should receive which of the following on admission to the hospital?

a) Screening compression ultrasound of the lower extremities
b) Risk assessment for venous thromboembolism (VTE)
c) Graded compression stockings
d) D-Dimer assay
e) Hypercoagulability testing

Answer and Discussion

The answer is b.

Objective: Identify appropriate guidelines for hospitalized patient regarding DVT prophylaxis.

In its Best Health Care Practice Report in 2003, the National Quality Forum recommended that all patients admitted to the hospital undergo a formal risk assessment for VTE, and those found to be at risk should receive appropriate methods of prevention. Ultrasonography and D-dimers should be reserved for patients with signs and symptoms of DVT for which a diagnostic evaluation is indicated. A hypercoagulability testing is only indicated in patients with a previous history of idiopathic DVT and in whom a diagnosis would alter long-term management. Graded compression stockings may be used to prevent VTE in low-risk populations. They offer little incremental benefit in patients already receiving pharmacologic prophylaxis.

Question 60

You are consulted on a 65-year-old woman with no significant past medical history who just underwent an elective left hip arthroplasty. She is noted to have increased swelling of her contralateral leg. The surgical team is concerned about a DVT and wants to know what diagnostic modality they should choose. Which of the following statements regarding the diagnosis of DVT is true?

a) CT venography is the initial diagnostic test of choice.
b) Compression ultrasonography of the lower extremities has the greatest sensitivity in asymptomatic patients.
c) Elevated D-dimers help confirm the diagnosis.
d) MRI is an effective strategy for DVT diagnosis, but it is costly.
e) All the statements are true.

Answer and Discussion

The answer is d.

Objective: Diagnose DVT.

Compression ultrasonography is the initial imaging test of choice, not CT venography, given the relative cost, risk of
adverse events to the patient, and diagnostic yield. However, compression ultrasonography has the greatest sensitivity in symptomatic patients, not in asymptomatic patients. D-Dimers have a very high sensitivity, but lack specificity. Therefore, d-dimers are best used to help rule out, not rule in, DVT. MRI is an effective diagnostic strategy, but due to cost concerns it is not feasible as an initial choice.

**Question 61**

A 70-year-old man presents to the office for a health assessment. Which BP reading would indicate the highest risk for a cardiovascular event?

a) 110/90 mmHg  
b) 120/90 mmHg  
c) 130/70 mmHg  
d) 140/80 mmHg  
e) 150/70 mmHg

**Answer and Discussion**

The answer is e.

**Objective:** Understand the Joint National Committee 7 categories for BP.

Prehypertension signifies an increased cardiovascular risk as well as a risk of developing true hypertension.

**Question 62**

You are performing a routine physical examination on a 30-year-old man. His office BP is 124/70 mmHg. He has been checking his own BP and has been getting similar values. You should tell him that his current BP falls within the range of

a) Normal  
b) Optimal  
c) Prehypertension  
d) Borderline hypertension  
e) Stage 1 hypertension

**Answer and Discussion**

The answer is c.

**Objective:** Recognize that the systolic BP is more important in determining the cardiovascular risk than the diastolic BP, particularly after 55 years of age.

The elevated pulse pressure (80 mmHg) in choice e gives an additional reason that this reading signifies a higher risk than any of the other choices.

**Question 63**

A 38-year-old woman was admitted to the hospital 2 hours ago because of a 2-hour history of aching pain in her neck accompanied by severe headache. She recently had an upper respiratory tract infection (URI) that resolved after treatment with pseudoephedrine. She takes no other medications and has no history of chronic illness. She has a history of cocaine use during her late 20s. On admission, vital signs were as follows: T = 37.2°C, P = 120 beats/minute, RR = 24/minute, and BP = 167/112 mmHg. The patient is now unresponsive to verbal stimuli. Noxious stimuli elicit decortication on the left and no response on the right. CT scan of the head shows a subarachnoid bleed. Which of the following is the most likely complication of this patient’s current condition?

a) Carotid artery dissection  
b) Subdural empyema  
c) Thalamic bleed  
d) Cerebral vasospasm  
e) Acute basilar artery thrombosis

**Answer and Discussion**

The answer is d.

**Objective:** Identify the red flags associated with headache.

This patient has concerning symptoms associated with her headache. The International Headache Society has identified “red flags” to help clue the clinician there is an underlying organic cause of the headache. These include new headache beginning after 50 years of age, sudden onset, increasing frequency and severity, signs of a systemic illness, immunocompromised host, or focal neurologic signs. Severe, sudden onset headaches may be caused by a subarachnoid hemorrhage—bleeding in the area between the arachnoid membrane and the pia mater surrounding the brain. This may occur spontaneously, usually from a ruptured cerebral aneurysm, or may result from head injury. Blood in the subarachnoid space causes chemical meningitis that commonly increases intracranial pressure for days or a few weeks. Secondary vasospasm may cause focal brain ischemia; about 25% of patients develop signs of a transient ischemic attack (TIA) or ischemic stroke. Brain edema is maximal, and risk of vasospasm and subsequent infarction (called angry brain) is highest between 72 hours and 10 days. Secondary acute hydrocephalus is also common. A second rupture (rebleeding) sometimes occurs, most often within about 7 days.

**Question 64**

A 73-year-old woman is evaluated in the ED for worsening of left hemiparesis that began this morning. She has a past medical history of a right middle cerebral artery territory stroke 2 years ago that was attributed to her atrial fibrillation. At that time, she had very severe left hemiparesis but gradually improved with 3 months of rehabilitation. At her most recent office visit, she had a very mild left central facial palsy, no response on the right. CT scan of the head shows a subarachnoid bleed. What is the most likely complication of this patient’s current condition?

a) Cerebral vasospasm  
b) Acute basilar artery thrombosis  
c) Acute ischemic stroke  
d) Carotid artery dissection  
e) Subdural empyema

**Answer and Discussion**

The answer is c.

**Objective:** Identify the red flags associated with headache.

This patient has concerning symptoms associated with her headache. The International Headache Society has identified “red flags” to help clue the clinician there is an underlying organic cause of the headache. These include new headache beginning after 50 years of age, sudden onset, increasing frequency and severity, signs of a systemic illness, immunocompromised host, or focal neurologic signs. Severe, sudden onset headaches may be caused by a subarachnoid hemorrhage—bleeding in the area between the arachnoid membrane and the pia mater surrounding the brain. This may occur spontaneously, usually from a ruptured cerebral aneurysm, or may result from head injury. Blood in the subarachnoid space causes chemical meningitis that commonly increases intracranial pressure for days or a few weeks. Secondary vasospasm may cause focal brain ischemia; about 25% of patients develop signs of a transient ischemic attack (TIA) or ischemic stroke. Brain edema is maximal, and risk of vasospasm and subsequent infarction (called angry brain) is highest between 72 hours and 10 days. Secondary acute hydrocephalus is also common. A second rupture (rebleeding) sometimes occurs, most often within about 7 days.
chills, nausea, vomiting, or diarrhea. Her arthritis is not active at the moment. She reports taking her medications on schedule, and there have been no recent changes to her medications. On examination, she appears anxious. Vital signs are as follows: T = 38.1°C, P = 80 beats/minute and irregular, RR = 21/minute, and BP = 118/70 mmHg. HEENT examination is normal. Lungs are clear. Cardiac examination reveals an irregularly irregular rhythm. Abdomen is soft, and there is mild suprapubic tenderness noted, positive bowel sounds, and no organomegaly. Extremities show hand changes consistent with destructive arthritis, but no synovitis is detected. There is no peripheral edema. Neurologic examination demonstrates a normal mental status and visual fields. Moderate left hemiparesis is present, along with a moderate left central facial palsy. Laboratory studies are as follows:

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Na = 139 mmol/L</td>
<td>WBC = 13,100 /μL</td>
</tr>
<tr>
<td>K = 4.0 mmol/L</td>
<td>Hgb = 9.8 g/dL</td>
</tr>
<tr>
<td>Cl = 105 mmol/L</td>
<td>Platelets = 439,000 /μL</td>
</tr>
<tr>
<td>HCO₃ = 27 mmol/L</td>
<td>INR = 2.5 s</td>
</tr>
<tr>
<td>Cr = 0.9 mg/dL</td>
<td>ESR = 23 mm/h</td>
</tr>
<tr>
<td>BUN = 22 mg/dL</td>
<td>6–10 WBC/hpf</td>
</tr>
<tr>
<td>Glucose = 134 mg/dL</td>
<td>0–5 RBC/hpf</td>
</tr>
</tbody>
</table>

CT scan of the head without contrast shows a chronic hypodensity in the right middle cerebral artery territory. Which of the following is the most likely diagnosis?

a) Acute cerebral infarction  
b) Postictal paresis  
c) Hemorrhage into previous infarction  
d) Unmasking of a chronic deficit due to infection  
e) Rheumatoid vasculitis

**Answer and Discussion**

The answer is d.

**Objective:** Understand the treatment of hypertension during pregnancy.

Eighty-five percent of women with preexisting mild hypertension do well through pregnancy. Of those taking medication, some may be able to reduce the dose or stop the antihypertensive agent during the second trimester because of the usual drop in BP. Studies have shown that treatment of mild hypertension before and during pregnancy does not reduce the risk of preeclampsia or eclampsia and does not improve maternal or fetal health. Indications for drug treatment usually include a diastolic BP of >100 mmHg or evidence of end-organ damage from the hypertension. Methyldopa and hydralazine have been shown to be safe for the fetus, as opposed to ACEIs, which have been associated with poor fetal outcome, perhaps related to dysregulation of uteroplacental blood flow.

**Question 65**

A 32-year-old woman is referred to you from her obstetrician. She has had mild hypertension for several years but has been hesitant to start any medications. She is now attempting to have a baby and is concerned that her elevated BP may pose a risk to her baby. She is also concerned that any medications that she takes could be harmful to the fetus. At a preconception visit, her obstetrician recommended a consultation with you. She denies any complaints. Her BP during this visit is 160/90 mmHg and heart rate is 85 beats/minute. She has a normal physical examination. Urinalysis is negative. You tell her all the following, except:

a) Methyldopa and hydralazine have been shown to be safe to the developing fetus.  
b) Reducing her BP will reduce the chances of preeclampsia or eclampsia developing.  
c) Eighty-five percent of hypertensive women have uncomplicated pregnancies.  
d) Some women with mild hypertension can stop antihypertensive medications in the second trimester.  
e) Drug treatment would be indicated if hypertensive end-organ damage were found on evaluation.

**Answer and Discussion**

The answer is b.

**Objective:** Recognize neurologic deficits in the setting of a systemic illness caused by unmasking a previous infarction.

This woman presents with right hemispheric dysfunction, but these symptoms are similar to and less severe than the previous stroke in that area. The head CT does not demonstrate hemorrhage, so this cause is excluded. Recurrent stroke in the same territory as the previous stroke with identical symptoms is not likely to occur with atrial fibrillation, which can send emboli to any part of the brain. Seizure cannot be refuted or confirmed with the existing information, but the lack of any other signs of seizure and the duration of several hours makes postictal paresis less likely. There is no evidence of active vasculitis on skin examination or laboratory testing. Unmasking of a chronic deficit due to infection is most likely because of the temperature and urinalysis findings.

**Question 66**

A 28-year-old woman reports palpitations for the past 6 months. They are accompanied by light-headedness, chest pressure, and nausea. Initially, they tended to occur only two or three times a day; however, they have now become more frequent, and she has missed work on several occasions and has stopped socializing with friends except at her own home. She has no psychiatric history and does not drink alcohol or abuse drugs. Her caffeine intake is limited. Her family history is notable for maternal hypertension; her father suffered a stroke 7 months ago. The workup reveals no evidence of thyroid disease. Ambulatory ECG monitoring shows that
her symptoms are accompanied by sinus tachycardia. All the following statements about her condition are true, except
a) She may benefit from a short-acting benzodiazepine, such as alprazolam.
b) She may benefit from a serotonin reuptake inhibitor, such as paroxetine, in a dose similar to that used for depression.
c) First-degree relatives have an increased incidence of the same condition.
d) Behavioral exposure techniques may be helpful.
e) Patients using alcohol to relax in social situations have a lower incidence of this condition.

Answer and Discussion
The answer is e.
Objective: Recognize the features and appropriate treatment of panic disorder.
Symptoms of panic disorder are characterized by discrete attacks of anxiety associated with a sensation of chest pain, palpitations, or nausea. Patients may have multiple ED visits before they are diagnosed. The embarrassment or fear of having panic attacks in public without an easy escape often disrupts social interactions. Alcohol can actually intensify the symptoms.

Question 67
A new ultrasound technique is available to screen for ovarian cancer. The sensitivity is said to be 80% and the specificity 95%. The prevalence of ovarian cancer is believed to be 2% in a sample population of adult women. If the entire sample population undergoes imaging with the new technique, what will be the predictive value of a positive test?

a) 10%
b) 49%
c) 24%
d) 80%
e) 95%

Answer and Discussion
The answer is c.
Objective: Understand the calculation for the positive predictive value.
Suppose a sample population of 1,000: The reader should construct a 2 × 2 table. A prevalence of 2% would mean 20 patients have the disease (a + c = 20). The sensitivity is 80%, and of the 20 patients with the disease, 16 would test positive (a = 20 × 0.8). Of the 980 patients without disease, 931 would test negative (d = 980 × 0.95 [specificity]). This now means 49 patients (b = 931) would test positive despite the absence of disease. The positive predictive value is calculated as a/(a + b).

Question 68
All the following statements about the cough associated with ACEIs are true, except
a) Dry and hacking
b) More frequent in asthmatics
c) Women affected more often than men
d) Generally occurring on rechallenge
e) Usually begin within 1 to 2 weeks of institution of therapy

Answer and Discussion
The answer is b.
Objective: Recognize ACEI-associated cough.
The cough associated with ACEIs does not occur more frequently in asthmatics than in nonasthmatics, although it may be accompanied by bronchospasm.

Question 69
A 67-year-old man reports “lethargy.” The history and physical examination suggest no physical disease, but he is not sleeping well, has lost his appetite, is not enjoying his retirement, and is staying in bed for much of the day. He states that his wife has been trying to get him to play golf and bridge with his friends, which he used to enjoy doing, but he feels too lethargic and is not interested in socializing. You are concerned that he may be depressed, and you consider his suicidal risk. All the following statements about suicide are true, except
a) His age puts him in a high-risk group.
b) Women are more likely to attempt suicide and successfully complete it than men.
c) Family history of suicide is a risk factor for suicide.
d) History of recent loss, such as retirement, is a risk factor for suicide.
e) Being single puts one at greater risk of suicide than being divorced.

Answer and Discussion
The answer is b.
Objective: Recognize those at risk for suicide.
Suicide among men peaks at age 75 years and among women at 55 years. The predominant age groups for suicide are the elderly (older than 65 years) and adolescents (15 to 24 years). Women are more likely to attempt suicide (3:1), but men are more likely to complete it (3:1). History of recent loss, such as retirement or bereavement, is a risk factor for suicide. Marital status is important in assessing suicide risk. Single individuals have a higher suicide risk than those who are divorced. Widowed individuals are at higher risk than those who are married.

Question 70
An 87-year-old woman presents for a checkup. She has no complaints and considers herself healthy. On direct questioning, she confesses to falling in her home a few weeks ago but states that she was in no way injured. She is taking no medications. She remains in the family home where she raised her seven children and had lived with her husband for 65 years until he died there 5 years ago. Her children live nearby and visit her frequently. You perform a full history
and physical examination and assess her risk for falls. All the following are risk factors for falls, except:

a) Increasing age  
b) Female sex  
c) A history of falls  
d) Arthritis  
e) Hypertension

**Answer and Discussion**

**Objective:** Recognize those at risk for falls.

Postural hypotension, rather than hypertension, has been associated with falls. In the elderly, it is important to assess the risk factors for falls and to address them in order to prevent the falls, because falls are some of the most common problems that threaten the independence of the elderly and are associated with a significant morbidity and mortality.

**Questions 71 to 73**

Match the host defense defect with the clinical presentation

<table>
<thead>
<tr>
<th>a)</th>
<th>b)</th>
<th>c)</th>
<th>d)</th>
<th>e)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Common variable immunodeficiency</td>
<td>Selective IgA deficiency</td>
<td>Reduced activity of the late components of serum complement pathway: C6, C7, or C8</td>
<td>Complement deficiency factors H and I (alternate pathways)</td>
<td>Job syndrome</td>
</tr>
</tbody>
</table>

**Question 71**

A 19-year-old white woman with a history of recurrent sinus and lung infections presents with weight loss, anemia, night sweats, and mediastinal lymph nodes enlargement by chest radiograph.

**Question 72**

Recurrent *Neisseria meningitidis* and *Neisseria gonorrhoeae* infections.

**Question 73**

Recurrent “cold” staphylococcal abscesses, failure to shed primary teeth, eczema, hyperimmunoglobulinemia E, and impaired neutrophil chemotactic responses.

**Answers and Discussion**

**Objective:** Understand the key features of immunodeficiency syndromes.

**Question 71:** The answer is a.

**Question 72:** The answer is c.

**Question 73:** The answer is e.

Common variable immunodeficiency is a primary immunodeficiency characterized by a defective antibody formation. Among populations of European origin, common variable immunodeficiency is the most frequent of the primary specific immunodeficiency diseases. It affects men and women equally. The usual age at presentation is the second or third decade of life. The clinical presentation of common variable immunodeficiency disease is generally that of recurrent pyogenic sinopulmonary infections. Recurrent attacks of herpes simplex are common, and herpes zoster develops in approximately one-fifth of patients. An unusually high incidence of malignant lymphoreticular and gastrointestinal conditions is present in common variable immunodeficiency. A 50-fold increase in gastric carcinoma has been observed. Lymphoma, which seems to be the presenting illness in this patient, is approximately 300 times more frequent in women with common variable immunodeficiency than in affected men.

Deficiencies in both the late and early components of the complement system can lead to an increased susceptibility to meningococcal infections. The risk of meningococcal disease for a person with a complement deficiency is estimated to be 0.5% per year. This represents a relative risk of 5,000, as compared with the incidence of meningococcal disease among persons without a complement deficiency.

Job syndrome is an autosomal recessive disorder characterized by a defective neutrophil chemotactic response, with the development of recurrent cold staphylococcal abscesses and eczema. Patients also have elevated levels of IgE in the serum.

**Question 74**

A 65-year-old man presented to the ED after awakening with right-side weakness. His family says that for about a year he has complained of brief episodes of blurred vision in his left eye. On the evening before admission, he had a short period of difficulty finding words, which cleared after about 5 minutes, and he seemed to be normal when he retired for the night. On examination, his BP is 160/100 mmHg. The neurologic examination shows a mild degree of difficulty naming and mild pronation of the right arm on extension of the limb. Circumduction of the right leg occurs when walking, and mild deficits to all sensory modalities can be discerned on the right side. Reflexes are 2+ on the left and 1+ on the right, and a right-side Babinski sign is present. Carotid pulses are faint but palpable bilaterally without bruits. Flow in the external carotid branches on the face cannot be estimated clinically. During the examination, he has a 5-minute episode of dense right hemiplegia and mutism, from which he recovers and returns to his baseline, except for a short period of difficulty finding words, which cleared as described. Which of the following is the most accurate statement?

a) This patient has a right middle cerebral artery disorder.

b) Given the resolution between attacks, any impending stroke is likely to be mild.

c) The physical examination yields little information about the severity of the carotid disease.

d) Dynamic palpations of facial pulses can distinguish a tight stenosis from an occlusion of the internal carotid artery.

e) Neurodiagnostic studies must be performed in all patients with TIAs.
**Answer and Discussion**

The answer is c.

**Objective: Identify the appropriate diagnostic and prognostic information about TIAs.**

This patient is complaining of episodes of TIAs. A TIA is defined as the sudden onset of a neurologic deficit that fits a vascular territory and lasts less than 24 hours. This patient’s spell fits a disorder in the distribution of a left middle cerebral artery. Although the spells seem mild and completely disappear between attacks, one should not feel comfortable that this does not foreshadow a serious subsequent stroke. There is no way to predict, based on the severity or quality of the attack, whether a patient will go on to develop a stroke and whether this stroke will be severe or mild. The physical examination yields little information about the severity of the carotid disease. The presence or absence of a cervical bruit is nearly useless, although bruits often represent vascular disease; however, the bruit may be on the wrong side (as in this patient) or not present at all if flow through a tight stenosis is slowed sufficiently. Dynamic palpations of facial pulses are a way of evaluating the direction of flow in the external carotid branches in the face. With a tight stenosis or occlusion of the internal carotid distal to the takeoff of the external carotid, it is often possible to demonstrate reversed flow in the branches of the external carotid artery of the face. This test, however, does not distinguish between a tight stenosis and an occlusion, an important distinction because surgical intervention is possible only in a case of tight stenosis, not in a case of total occlusion. Once it is recognized that this patient is undergoing TIAs in the distribution of the left carotid artery, the most difficult decision will involve which maneuver should be carried out next. Some experienced physicians would not investigate such a patient any further but would simply give the patient aspirin. Most neurologists and neurosurgeons probably would carry out some form of neurodiagnostic study to evaluate the carotid. The simplest test, which gives the most information, is a magnetic resonance angiogram. This obtains a reasonably good angiogram at the lowest risk. If a tight carotid stenosis is found, most neurologists would recommend a carotid endarterectomy done by an experienced neurosurgeon or vascular surgeon. If the carotid is occluded, most physicians would recommend the use of aspirin in an attempt to prevent further TIAs, which may be due to platelet emboli from the distal stump of the occlusion. If no carotid disease is found, a careful evaluation of the heart would follow, including a transthoracic echocardiography, a set of blood cultures, and a careful cardiac examination, probably including a Holter monitor study.

**Question 75**

A 76-year-old man admitted to the hospital 2 weeks ago for pneumonia and transferred to the ICU 1 week ago has been deteriorating for the past 3 days, requiring mechanical ventilation with full support and 100% oxygen. He has a history of coronary artery disease and COPD. Given the poor prognosis, the ICU team meets with his wife. Which of the following statements is most valid?

a) Instruct the wife that the patient’s prognosis is poor and that she will need to make a decision regarding her husband’s thoughts on end-of-life issues.

b) Instruct the wife that there is no “DNR” order on the chart, even if her husband’s physicians believe that cardiopulmonary resuscitation is futile, it will have to be performed in the event of cardiopulmonary arrest.

c) If a durable power of attorney for health care is appointed, that person should be making decisions, but only in the absence of the patient’s wife.

d) Because the prognosis is poor, the ICU team should be instructed to only run “slow” codes on this patient.

e) Use of pain medications can be construed as a form of physician-assisted suicide because these medications can hasten the patient’s death.

**Answer and Discussion**

The answer is a.

**Objective: Understand the ethics of treatment in those with severe medical illness.**

Because this man cannot make decisions about end-of-life issues, the responsibility falls on his wife to make the decision on his behalf. Essentially, she is being asked to decide what he would want to be done, not what she would want to be done. In addition, if a durable power of attorney for health care has been appointed, this individual would be the surrogate decision maker, even if the wife were involved in the patient’s hospitalization or illness. The individual with the power of attorney must also act on behalf of the patient and not merely project his or her own view. Finally, “slow” codes have no role in the care of a terminally ill patient because there is also no requirement that cardiopulmonary resuscitation be performed in the event that it has been deemed futile. Competent physicians who use standard pain medications in terminally ill patients who suffer from chronic pain are not engaging in physician-assisted suicide.

**Question 76**

The appropriate management of a patient poisoned by organophosphate cholinesterase-inhibiting agents includes all of the following, except

a) Atropine
b) Sodium nitrite
c) Pralidoxime chloride (Protopam)
d) Maintenance of airway
e) Decontamination

**Answer and Discussion**

The answer is b.

**Objective: Understand the management of organophosphates toxicity.**

Atropine blocks the muscarinic effects of organophosphates and should be administered promptly. Pralidoxime chloride...
(Protopam) reactivates the enzyme cholinesterase by breaking the acetylcholinesterase–phosphate complex. Its advantages over atropine include its ability to reverse the muscle paralysis and possibly the central nervous system depression.

Decontamination procedures may include removal of contaminated clothing, washing of skin and hair, and, if indicated by the route of exposure, emptying the stomach. In severe cases, a patent airway needs to be established for removal of excess secretions and institution of ventilatory support.

Sodium nitrite is used in cyanide poisoning. It has no role in the management of organophosphate toxicity.

**Question 77**

A 74-year-old man is brought to the emergency room by paramedics after the acute onset of aphasia and weakness while eating at a restaurant with his family. According to the family, he was fine until he spilled his glass of water and was unable to speak or follow commands. They called for an ambulance immediately and arrived to the ED within 1 hour of symptom onset. His past medical history is significant for COPD and a prior history of excessive alcohol use. His medications include an ipratropium and albuterol inhaler. He quit smoking 7 years ago but has a 100 pack-year history of tobacco use. He has not had alcohol in over 20 years. He is single and lives alone independently. His review of systems is otherwise unremarkable, and he has had no recent surgery, trauma, or bleeding. His vital signs are as follows: T = 36.8°C, P = 82 beats/minute, RR = 20/minute, and BP = 175/102 mmHg. HEENT demonstrates a right central facial palsy. The neck is supple without JVD, adenopathy, or bruits. Lungs have diminished breath sounds throughout with scattered rhonchi. Cardiac and abdominal examinations are normal. Examination of the skin shows eczema of the hands, but no stigmata of chronic liver disease. Neurologic examination reveals severe global aphasia without an understandable speech or ability to follow commands. He has a mild right pronator drift. Strength and sensation are normal. Laboratory studies are as follows:

- Na = 139 mmol/L
- K = 4.0 mmol/L
- Cl = 99 mmol/L
- HCO₃ = 29 mmol/L
- Cr = 1.3 mg/dL
- BUN = 22 mg/dL
- Glucose = 87 mg/dL
- ALT = 28 U/L
- AST = 23 U/L
- WBC = 8,200/μL
- Hgb = 14.7 g/dL
- Platelets = 231,000/μL
- ALT = 28 U/L
- AST = 23 U/L
- WBC = 8,200/μL

Head CT of the brain without contrast is normal.

Which of the following is the most appropriate therapy for this patient?

a) Aspirin
b) Clopidogrel
c) Alteplase
d) Abciximab
e) Unfractionated heparin

**Answer and Discussion**

The answer is c.

Objective: Identify the treatment for an acute stroke.

This patient has an acute infarction in the left middle cerebral artery territory. He can be treated within 3 hours after the onset of his stroke and meets all the eligibility criteria for IV thrombolytic therapy. Contraindications to tissue plasminogen activator include any history of intracerebral hemorrhage, gastrointestinal or any serious hemorrhage within 3 weeks, major surgery or trauma within 2 weeks, arterial puncture at a noncompressible site within 7 days, stroke or head trauma within 3 months, uncontrolled hypertension (systolic BP > 185 mmHg or diastolic BP > 110 mmHg), coagulopathy (protime > 15 seconds), heparin given within 48 hours, PTT elevated, and platelet count < 100,000. Aspirin is useful in the early treatment of stroke because it prevents early recurrences but does not have a major impact on clinical outcome. The addition of clopidogrel or use of abciximab as a treatment for acute ischemic stroke is currently under investigation. Unfractionated heparin is not helpful in acute ischemic strokes, except in fixed doses to help prevent VTE.

**Question 78**

You have encouraged a 42-year-old male patient to exercise more. He has recently started to play soccer and now comes to you, complaining of back pain. The pain is worse on standing and bending and eased by sitting or lying down. The pain does not radiate. Pain is not reproducible on straight leg raising, and neurologic examination is intact. All the following statements concerning this patient’s condition are true, except

a) Spinal manipulation can be helpful, if used in the first month of symptoms.
b) Biofeedback has proved to be helpful in reducing recovery time.
c) Controlled physical activity, nonsteroidal anti-inflammatory drugs, and muscle relaxants have a role in the initial management.
d) Bed rest for more than 4 days may lead to debilitation.
e) Lumbosacral strain is the most likely diagnosis.

**Answer and Discussion**

The answer is b.

Objective: Understand the natural history and treatment of routine low back pain.

The most likely diagnosis is lumbosacral strain. Biofeedback has not been proven to reduce the recovery time. The other choices are reasonable approaches to the patient with low back pain and no “red flag” symptoms. Red flag symptoms that may require a more aggressive approach include recent trauma, age ≥ 70 years, unexplained weight loss or fever, immunosuppressed state, history of cancer, prior IV drug abuse, history of OP or prolonged treatment with glucocorticoids, focal neurologic deficit, or persistence past 6 weeks.
Question 79

A 21-year-old woman reports a thin, malodorous vaginal discharge and vulvar itching. She is sexually active with more than one partner and does not use condoms. She thinks her last menstrual period was 3 weeks ago. Examination of the discharge reveals a pH of 5.0 and a fishy odor on addition of 20% potassium hydroxide solution. The saline wet preparation is significant for squamous cells covered by adherent bacteria. Which of the following statements relating to this patient is the most accurate?

a) Treatment of choice is oral metronidazole, 2 g.
b) Treatment of choice is oral metronidazole, 500 mg twice daily for 7 days.
c) There is no need for pregnancy testing at this time.
d) There are no findings indicating an increased risk of cervical carcinoma.
e) Treatment with ketoconazole is effective.

Answer and Discussion

The answer is b.

Objective: Recognize the etiologies of vaginal discharge.

Bacterial vaginosis is characterized by the appearance of clue cells on a saline wet preparation, as described. The vaginal pH is usually >4.5 and a fishy odor may be present on addition of 20% potassium hydroxide solution. The treatment of choice is metronidazole, 500 mg twice daily for 7 days. Intravaginal clindamycin cream may also be used in the first trimester of pregnancy, when metronidazole is contraindicated. Human papillomavirus has been implicated in the etiology of cervical cancer. Multiple sex partners, smoking, and HIV infection are considered to be risk factors for cervical cancer. Ketoconazole is an antifungal agent and is not effective for bacterial vaginosis.

Question 80

A 46-year-old overweight male postal worker has had multiple ED visits for chest pain. Cardiac catheterization done 1 month ago was significant for mild atherosclerotic disease. His past medical history is notable for hypercholesterolemia. Exercise stress testing was negative for ischemia. He is worried that he should not continue working and seeks further evaluation. Which of the following tests would be the most appropriate for this patient?

a) Bernstein test
b) Ambulatory ECG monitoring
c) 24-Hour pH monitoring
d) Endoscopy
e) Esophageal manometry

Answer and Discussion

The answer is a.

Objective: Understand the diagnostic evaluation of non-cardiac chest pain.

This man has chest pain that is unlikely to be of cardiac origin. Reflux disease may mimic cardiac chest pain. A positive Bernstein test would imply that the symptoms are due to reflux and should be treated as such. With convincing evidence that the cause is noncardiac, further evaluation for atherosclerotic disease is redundant. The use of pH monitoring helps establish whether reflux is present, but it may not explain symptoms. Similarly, endoscopy and manometry evaluate for esophagitis and the mechanism of reflux, respectively.

Question 81

A 56-year-old woman reports urinary incontinence. She explains that she has leakage of urine associated with laughing or making sudden movements. Her past medical history is notable for migraines and two uncomplicated pregnancies. A postvoid residual volume is recorded as 30 mL. Urinalysis is unremarkable. What would be the most appropriate management at this time?

a) Prompted voiding
b) Intermittent catheter drainage
c) Environmental manipulation
d) Fluid intake modification
e) Pelvic muscle exercises

Answer and Discussion

The answer is e.

Objective: Recognize the etiologies of female incontinence and their appropriate treatment.

This postmenopausal woman has stress incontinence. The history shows leakage associated with increased intra-abdominal pressure. Instruction in pelvic muscle exercises can be effective, as can bladder training. Prompted voiding, fluid-intake modification, and environmental manipulation are strategies used in functional incontinence. Intermittent catheter drainage can be used in overflow incontinence.

Question 82

All the following are common presenting symptoms of major depression

a) Fatigue or loss of energy
b) Beliefs of worthlessness or guilt
c) Recurring thoughts of death or suicide
d) Auditory hallucinations
e) Significant weight loss or weight gain

Answer and Discussion

The answer is d.

Objective: Recognize the diagnostic criteria for major depressive disorder.

Auditory hallucinations are not common symptoms of depression and are not included among the nine Diagnostic and Statistical Manual of Mental Disorders, criteria, of which at least five are required for the diagnosis of major depression. The nine criteria for major depressive episode include
depressed mood, anhedonia, weight loss or gain, insomnia or hypersomnia, psychomotor agitation or retardation, fatigue, feelings of worthlessness, difficulty concentrating, and suicidal ideation.

Question 83

A 40-year-old woman presents to you after reading an article in the newspaper about screening for ovarian cancer. She is concerned because although she comes for annual physical examinations and has her regular pelvic examinations, Pap tests, and all the tests that are recommended to her, nobody has told her that she needs to have screening tests for ovarian cancer. She feels very well and wants to remain so. She has no family history of ovarian cancer, but a friend was recently diagnosed with it. Her history and physical examination reveal nothing that suggests any increased risk of ovarian cancer. What would be the most appropriate next step for this patient?

a) Call your lawyer in case she has ovarian cancer and you missed it
b) Test for the tumor marker CA125
c) Perform transvaginal ultrasonography
d) Test for the tumor marker CA125 and perform transabdominal ultrasound
e) Explain to her why no screening is indicated

Answer and Discussion

The answer is e.

Objective: Understand the indications for ovarian cancer screening.

No expert group in the United States recommends screening for ovarian cancer in asymptomatic women. A National Institutes of Health consensus conference on ovarian cancer recommends a family history and annual pelvic examination for all women. Ovarian cancer has the highest mortality rate of all types of gynecologic cancer and is the fifth leading cause of cancer death among women. Although the mortality rate associated with ovarian cancer is high, the disease occurs infrequently in the general U.S. population, with an age-adjusted incidence of 13 cases per 100,000 women. As a result, the positive predictive value of screening for ovarian cancer—which directly depends on the prevalence of the disease—is low, and most women with a positive screening test result will have a false-positive result. Screening for CA125 and vaginal ultrasound are recommended only for those with a presumed hereditary cancer syndrome (e.g., BRCA mutations).

Question 84

A 34-year-old woman reports a shooting pain between the third and fourth toes of her left foot that has progressively worsened over the past 5 months. The pain occurs with walking and is relieved by stopping and massaging the affected area. On examination, compression of the forefoot causes the patient to wince in pain. Which of the following is the most accurate statement relating to this patient’s condition?

a) Elevating the heel of her shoe will help alleviate her pain.
b) Nonsteroidal anti-inflammatory drugs are effective.
c) Men and women are affected in equal numbers.
d) The condition is caused by the compression of interdigital nerves.
e) Surgical treatment is never indicated.

Answer and Discussion

The answer is d.

Objective: Recognize common features of Morton neuroma.

This is a description of Morton neuroma, a common cause of metatarsalgia. The condition is not caused by a true neuroma, but is due to an interdigital nerve fibrosis caused by irritation. Women are affected approximately five times more often than men, and wearing high-heeled or restrictive shoes aggravates symptoms. Patients should be instructed to wear low-heeled shoes with a wide toe box. Local injection with lidocaine can be helpful in avoiding surgery, which may be necessary.

Question 85

A 38-year-old woman comes in with a history of nightly insomnia for the past 5 years. She has “weird” sensations in her legs at night when she tries to sleep. This feeling is relieved when she moves her legs or gets up and walks. Her husband complains that she kicks during her sleep. All the following are true regarding her condition, except

a) The prevalence is twice as high for women compared with men.
b) A trial of oral iron therapy is indicated in premenopausal women.
c) Pregnancy causes temporary relief of the symptoms.
d) It is associated with diabetes.
e) Dopaminergic agents are considered the first line of treatment.

Answer and Discussion

The answer is c.

Objective: Identify key features of restless leg syndrome (RLS).

RLS refers to an upsetting and overwhelming urge to move the legs, or sometimes even the arms or trunk, when the patient lies down to sleep. A dramatic relief is provided by movement. The prevalence of RLS increases with age up to 80 years and is twice as high in women as in men. Primary (or idiopathic) RLS may show a dominant inheritance pattern in 40% of the cases. Secondary causes include iron deficiency, dialysis, diabetes mellitus, venous insufficiency, vitamin deficiencies, lumbosacral radiculopathy, spinal
stenosis, hypoglycemia, Parkinson disease, and hypothyroidism. Pregnancy can cause or worsen RLS. Dopaminergic agents (levodopa, bromocriptine, pergolide, and pramipexole) are considered the first line of treatment in idiopathic RLS. Opiates (propoxyphene, oxycodone, and methadone), benzodiazepines (clonazepam), and anticonvulsant agents (carbamazepine and gabapentin) have been shown to improve the symptoms of RLS. Among patients with RLS, a high prevalence of iron deficiency is seen, and treatment of the iron deficiency has been reported to improve symptoms. A trial of oral iron therapy is indicated for all patients with RLS.

**Question 86**
A 32-year-old previously healthy female secretary complains of the recent (3 months) onset of progressive pain in her right arm involving the second and third fingers, forearm, and upper arm. It awakens her from sleep and worsens while she is driving. It is at times associated with painful tingling. Physical examination reveals normal neck motion, negative Spurling and Adson tests, and a normal shoulder examination. Examination of pulses, deep tendon reflexes, pinprick, strength, and elbow are normal. What diagnostic test should be performed next?

a) Nerve conduction of the distal median nerve  
b) MRI of the cervical spine  
c) Upper extremity angiography  
d) Chemical sympathetic block

**Answer and Discussion**

The answer is a.

Objective: Identify the appropriate diagnostic testing for carpal tunnel syndrome.

The patient has carpal tunnel syndrome. Nerve conduction testing of the median nerve would likely provide the diagnosis. Local provocative testing with Tinel sign, Phalen maneuver, or direct compression might also provide suggestive information. Prolonged keyboard typing may be a risk factor. Other tests are not warranted based on the history and examination, which do not suggest radiculopathy, thoracic outlet, reflex sympathetic dystrophy, or Raynaud syndrome. Causes include wrist synovitis, hypothyroidism, diabetes mellitus, pregnancy, trauma, primary amyloidosis, acromegaly, and possibly polymyalgia rheumatica.

**Question 87**
A 75-year-old man presents with fatigue and decreased energy. He has lived alone since his wife died 2 years ago. His last physical examination was in 1978, when he changed jobs. He is edentulous and cooks for himself. On examination, temperature is 36.5°C, RR is 18 breaths/minute, heart rate is 83 beats/minute, and BP is 142/87 mmHg. His lung, heart, and abdominal examinations are unremarkable. Perifollicular hyperkeratotic papules containing hemorrhages and a purpuric rash are noted on the back of his thighs. Laboratory tests reveal the following:

<table>
<thead>
<tr>
<th>Test</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>WBCs</td>
<td>4,239/mm³ (normal differential)</td>
</tr>
<tr>
<td>Hemoglobin</td>
<td>9.8 g/dL</td>
</tr>
<tr>
<td>Platelets</td>
<td>145,000/μL</td>
</tr>
<tr>
<td>Mean corpuscular volume</td>
<td>101</td>
</tr>
<tr>
<td>Blood smear cells</td>
<td>Hypersegmented neutrophils and macrocytic RBCs</td>
</tr>
<tr>
<td>BUN</td>
<td>32 mg/dL</td>
</tr>
<tr>
<td>Serum creatinine</td>
<td>1.3 mg/dL</td>
</tr>
<tr>
<td>Antinuclear antibody</td>
<td>Positive</td>
</tr>
</tbody>
</table>

The most likely diagnosis is:

a) Vitamin A deficiency  
b) Vitamin B₁₂ deficiency  
c) Folic acid deficiency  
d) Vitamin C deficiency  
e) Lead poisoning

**Answer and Discussion**

The answer is d.

Objective: Identify key features of vitamin C deficiency.

Although rare in the United States, ascorbic acid deficiency (vitamin C deficiency, scurvy) occurs mostly in severely malnourished individuals, drug and alcohol abusers, or those living in poverty. One group at particularly increased risk comprises adults living alone, most commonly men (“bachelor” or “widower” scurvy) but sometimes women, who have deficient dietary intake because of factors such as poverty, poor access to groceries, dementia, or nutritional ignorance. They mostly prepare their own meals.

The clinical syndrome seen in vitamin C deficiency is due to impaired collagen synthesis. The most distinctive cutaneous finding in scurvy is hemorrhagic skin lesions that usually occur in a perifollicular distribution, especially on the legs, where the hydrostatic pressure is highest. Besides fatigue and decreased exercise tolerance, symptoms of scurvy include ecchymoses, bleeding gums, petechiae, hyperkeratosis, Sjögren syndrome, arthralgias, and impaired wound healing.

Vitamin A deficiency classically presents with night blindness. Vitamin B₁₂ deficiency causes gradual deterioration of the spinal cord and very gradual brain deterioration, resulting in sensory or motor deficiencies. Mental disorders from the gradual brain damage begin as fatigue, irritability, depression, or bad memory. As the disease progresses over several years, psychosis and mania can appear. Folic acid deficiency can present with anorexia and weight loss, weakness, headaches, and megaloblastic anemia. Lead poisoning presents with headache, nausea, vomiting, weakness, and paresthesias.

**Question 88**
A 64-year-old former male construction worker presents with increasing exertional bilateral calf pain and leg tingling. Leg symptoms have been present for 1 year but have
worsened during the cardiac rehabilitation for his recent myocardial infarction. He could only walk 0.4 mile on the treadmill because of the leg pain. He switched to an exercise cycle, on which he could ride for 3 miles. Physical examination demonstrated decreased left distal pulses and a left iliac bruit, with normal foot temperature, color, deep tendon reflexes, pinprick, and strength. The study with high yield for diagnosis is

a) Angiography  
b) Abdominal ultrasonography  
c) Spinal MRI  
d) Electromyography

**Answer and Discussion**

The answer is c.

**Objective: Identify the appropriate diagnostic testing for spinal stenosis.**

Although the MRI of the spine has limited specificity for diagnosing disc disease and back pain, it is excellent for diagnosing spinal stenosis. This patient has peripheral vascular disease, but the positional aspects of claudication symptoms argue for the presence of a neurogenic, not vascular, claudication. Spinal stenosis frequently coexists with peripheral vascular disease, and neurologic examination is often normal for age. Osteoarthritis of the spine is common. Physical therapy is often effective, and surgery may be curative.

**Questions 89 to 95**

Correctly match the vitamin or mineral deficiency with their symptoms.

<table>
<thead>
<tr>
<th>Question</th>
<th>Symptom</th>
</tr>
</thead>
<tbody>
<tr>
<td>Question 89</td>
<td>Bleeding gums, easy bruising, impaired wound healing, joint pains, loose teeth, malaise, and tiredness.</td>
</tr>
<tr>
<td>Question 90</td>
<td>Acne, dry hair, fatigue, growth impairment, insomnia, hyperkeratosis, immune impairment, and night blindness.</td>
</tr>
<tr>
<td>Question 91</td>
<td>Loss of vibration sensation, low stomach acid, mental disturbances, numbness, and spinal cord degeneration.</td>
</tr>
<tr>
<td>Question 92</td>
<td>Myocardial infarction, hyperactivity, insomnia, muscular irritability, restlessness, and weakness.</td>
</tr>
<tr>
<td>Question 93</td>
<td>Anxiety, fatigue, glucose intolerance, and adult-onset diabetes.</td>
</tr>
<tr>
<td>Question 94</td>
<td>Delayed sexual maturation, impotence, alopecia, dysgeusia, delayed wound healing, and decubitus ulcers.</td>
</tr>
<tr>
<td>Question 95</td>
<td>Cardiomyopathy and skeletal muscle dysfunction.</td>
</tr>
</tbody>
</table>

**Answers and Discussion**

**Objective: Identify key features of vitamin deficiencies.**

Question 89: The answer is g.

Question 90: The answer is e.

Question 91: The answer is f.

Question 92: The answer is d.

Question 93: The answer is a.

Question 94: The answer is b.

Question 95: The answer is c.

**Question 89**

Vitamin C deficiency causes bleeding gums, easy bruising, dental cavities, low infection resistance, nosebleeds, poor digestion, stress, weakened cartilages, blood clots, and impaired healing.

**Question 90**

Vitamin A deficiency causes acne, allergies, colds, dry hair and skin, eye sties, hyperkeratosis, fatigue, insomnia, impaired growth, loss of smell, and night blindness.

**Question 91**

Vitamin B_{12} deficiency causes appetite loss, diminished reflexes, fatigue, irritability, memory impairment, mental depression and confusion, pernicious anemia, and spinal cord degeneration.

**Question 92**

Magnesium deficiency causes hypotension, hypothermia, tachycardia, confusion, disorientation, hair loss, hyperactivity, muscle tremors, nervousness, noise sensitivity, depression, muscle weakness, twitching, heart disease, and disruption in proper pH balance.

**Question 93**

Chromium deficiency causes disturbed amino acid metabolism, increased serum cholesterol, impaired glucose tolerance, lack of energy, myopia, and protein/calorie malnutrition.

**Question 94**

Zinc deficiency causes acne, brittle nails, decreased learning ability, delayed sexual maturity, eczema, fatigue, loss of taste...
and smell, poor appetite, poor circulation, poor memory, prolonged wound healing, and decubitus ulcers.

**Question 95**

Selenium deficiency causes cardiomyopathy and skeletal muscle dysfunction.

**Question 96**

A 33-year-old woman at 34-week gestation presents with a petechial rash and epistaxis. Laboratory tests reveal the following:

<table>
<thead>
<tr>
<th>Test</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>WBC</td>
<td>6,000/mm³ (normal differential)</td>
</tr>
<tr>
<td>Hemoglobin</td>
<td>14.8 g/dL</td>
</tr>
<tr>
<td>Platelets</td>
<td>18,000/µL</td>
</tr>
<tr>
<td>Chemistry profile</td>
<td>Normal</td>
</tr>
<tr>
<td>Bone marrow aspirate</td>
<td>Normal with abundant megakaryocytes</td>
</tr>
</tbody>
</table>

She is started on prednisone (60 mg/day). Four days later, she begins to have contractions, and delivery is expected within the next 12 hours. Repeat complete blood count reveals a platelet count of 31,000/µL. Your next step in management is which of the following?

a) Pulse glucocorticoid (methylprednisolone, 1 g/day IV for 3 days)
b) Danazol, orally
c) Continuous platelet transfusion until 6 hours after delivery
d) Emergent plasma exchange
e) IV gamma globulin

**Answer and Discussion**

The answer is e.

Objective: Identify the appropriate treatment plan for idiopathic thrombocytopenic purpura.

The management of idiopathic thrombocytopenic purpura in the early stages of pregnancy is similar to the management of the disease in nonpregnant patients. Prednisone is the drug of choice for patients whose platelet counts are between 30,000 and 50,000/µL. Although splenectomy remains the most effective treatment for severe idiopathic thrombocytopenic purpura, splenectomy should be reserved for refractory cases that fail medical therapy. IV immunoglobulin is a temporary therapy, especially useful for patients with severe thrombocytopenia who have to undergo urgent surgical procedures or those who go into labor.

**Question 97**

A 36-year-old, G2P2, African American woman presents to your office for a routine Papanicolaou test. She reports feeling well, although admits she is overweight. During the visit, she inquires about contraception. She states that she has been happily married for 11 years and denies extramarital partners. She has two healthy children. She denies any history of sexually transmitted diseases. She takes a calcium supplement and prescription medications. She takes a calcium supplement and daily. She is 5′ tall and weighs 138 kg. On examination, her heart has regular rate and rhythm with no murmurs or gallops. Abdomen is obese. Her vagina is normal. Cervix is large and multiparous without discharge. Her uterus is anteverted.

**Question 98**

A 19-year-old man presents with dysuria and penile discharge for 5 days. He reports having unprotected sexual encounters with multiple prostitutes over the past 3 weeks. On examination, an indurated 2- to 4-cm warm, tender, inguinal mass is palpated. An ultrasound examination of the groin suggests that the mass represents enlarged inguinal lymph nodes. A Gram stain of the discharge shows numerous neutrophils and Gram-negative intracellular diplococci. Rapid plasma reagin is nonreactive, and HIV serology is negative. The next most appropriate step in management is

a) Give a single dose of ceftriaxone intravenously, 250 mg
b) Give a single dose of ceftriaxone intravenously, 250 mg, and doxycycline for 7 days
c) Give a single dose of ceftriaxone orally, 2 g, and doxycycline for 14 days
d) Give a single dose of ceftriaxone (250 mg intramuscularly) and doxycycline (100 mg two times a day for 7 days), until *Chlamydia trachomatis* serology is back
e) Await the results of culture and sensitivity testing, and counsel him regarding safe sex practices

**Answer and Discussion**

The answer is d.

Objective: Identify the correct treatment plan for sexually transmitted diseases.

Penile discharge should be treated aggressively, and the physician should look carefully for clinical and laboratory clues for coinfections with sexually transmitted diseases. The Centers for Disease Control and Prevention recommend concomitant chlamydia treatment for cases of presumed or confirmed gonorrheal infection at any site. Choice d represents the preferred recommended therapy.

Conversely, the history of exposure to several prostitutes and presence of inguinal lymph node enlargement in this patient is suspicious for concomitant lymphogranuloma venereum (LGV) infection. The diagnosis of LGV is difficult because there is no characteristic clinical presentation. Sexual partners of patients diagnosed with *N. gonorrhoeae* who have had sexual contact with the infected patient within the past 60 days should be evaluated and treated, even if they were asymptomatic.

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and normal in size, shape, and consistency. You counsel her on weight reduction and smoking cessation. Regarding her contraception, which of the following is the most appropriate choice for this patient at this time?

- a) Intrauterine contraceptive device (IUD or IUS-Mirena)
- b) Ethinyl estradiol 50/norethindrone 1000 (Ovcon 50)
- c) Medroxyprogesterone acetate injection (Depo-Provera)
- d) 1.25 mg of esterified estrogens/2.5 mg of methyltestosterone (EstraTest)
- e) Ethinyl estradiol 20/drospirenone 3000 (Yasmin)

**Answer and Discussion**

**The answer is a.**

**Objective: Understanding the indications and contraindications for contraceptive therapy.**

The patient is older than age 35 and currently smoking. This patient is at increased risk for venous thromboembolic disease if placed on birth control pills such as Yasmin or Ovcon 50. Regardless, Ovcon 50 is a first-generation birth control pill with a high dose of ethinyl estradiol. This dose is only indicated in women with recurrent ovarian cysts needing ovarian suppression or in women with a seizure disorder on anticonvulsant therapy who may metabolize contraceptives at a faster rate. EstraTest is an estrogen replacement therapy, not a contraceptive. Depo-Provera may cause a weight gain in this already obese patient and make weight loss that much more difficult. The best choice in this married, monogamous woman with no risk factors for pelvic inflammatory disease would be an intrauterine contraceptive device.

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**Question 99**

Acute poisoning from organophosphate insecticides can result in which of the following delayed neurologic effects?

- a) Cerebellar degeneration
- b) Dementia
- c) Bell palsy
- d) Motor polyneuropathy
- e) Seizure disorder

**Answer and Discussion**

**The answer is d.**

**Objective: Identify the neurologic complications of acute poisoning with organophosphates.**

Acute poisoning with organophosphate insecticides can result in a variety of central nervous system manifestations. A small percentage of patients may exhibit neuropsychiatric or cognitive complaints, such as irritability, depression, anxiety, and short-term memory impairment, weeks to months after the initial intoxication. It is often difficult, however, to distinguish organically based neurobehavioral symptoms from the psychological or emotional responses likely to occur after acute chemical exposures.

A delayed peripheral neuropathy has been reported after poisoning by some organophosphates. This condition, organophosphate-induced delayed neuropathy, is a predominantly motor polyneuropathy that occurs 2 to 3 weeks after acute poisoning.

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**Question 100**

A 28-year-old woman presents 2 months postpartum, complaining of 4 months of burning pain in her left thigh. She was told of carpal tunnel syndrome during her pregnancy and has been wearing wrist splints, but is now concerned regarding the possibility of multiple sclerosis (MS). Physical examination reveals bilateral wrist Tinel sign with a positive Phalen maneuver. The results of the hip examination are normal, with a negative straight-leg-raising test. Deep tendon reflexes are preserved. No motor weakness is detected. There is an area approximately the size of a hand with marked dysesthesias to light touch on the anterior lateral left thigh. In addition to the clinical diagnosis, a positive test result would include

- a) Electromyography of the sacral plexus
- b) Tinel sign over the lateral inguinal ligament
- c) Pelvic CT scan
- d) Cerebrospinal fluid oligoclonal bands

**Answer and Discussion**

**The answer is b.**

**Objective: Identify the diagnostic maneuvers for meralgia paresthetica.**

The patient has meralgia paresthetica caused by entrapment of the lateral femoral cutaneous nerve, which often occurs as it exits through the lateral inguinal ligament. It can be diagnosed clinically and usually requires no workup or treatment. It may accompany a weight gain, the wearing of constricting garments, or overtight seat belts. Often self-limiting, it may respond to local steroid injection. A differential diagnosis might include prezoster neuralgia.
Breast examination is normal. Her lungs are clear to auscultation. Heart has regular rate and rhythm with no murmurs or gallops. Abdomen is obese. Her pelvic examination reveals atrophic vaginal mucosa but is otherwise normal. There are bilateral varicosities on the lower extremities. Neurologic examination is normal.

You discuss the risks, benefits, and alternatives of HT with her but advise her against HT due to which of the following absolute contraindications?

a) Early family history of cardiovascular disease and stroke
b) Personal history of VTE
c) Strong family history of breast cancer
d) Undiagnosed uterine bleeding
e) Alcohol use

**Answer and Discussion**

The answer is d.

**Objective: Understand the contraindications for HT.**

Absolute contraindications to HT include pregnancy and undiagnosed vaginal bleeding. Any postmenopausal vaginal bleeding must be investigated with an endometrial biopsy due to a 5% to 10% incidence of simple or complex hyperplasia (with or without atypia), adenomatous endometrial hyperplasia, or frank endometrial cancers. A remote history of DVT is not an absolute contraindication to HT. Although a strong family history of breast cancer or cardiovascular disease is an important consideration when advising women on HT, these factors do not make the decision for or against starting HT. There is no relationship between alcohol use and adverse events in association with HT.

**Question 102**

A 36-year-old white woman presents to your office for contraceptive counseling. Her past medical history is significant for hypertension, and her only medication is daily enalapril. She is married, has two children, and has no history of sexually transmitted diseases, pelvic inflammatory disease, or VTE. She has normal periods with no heavy bleeding or clots. She reports feeling well, and her complete review of systems is negative. She drinks socially and reports smoking one-half pack of cigarettes daily. She is 5’ 4” tall and weighs 94 kg. On examination, her vital signs are as follows: T = 36.4°C, P = 77 beats/minute, RR = 16 breaths/minute, and BP = 125/77 mmHg. HEENT examination is normal. Breast examination is normal. Her lungs are clear to auscultation. Heart has regular rate and rhythm with no murmurs or gallops. Abdomen is obese. Neurologic, skin, and musculoskeletal exams are without abnormalities. Which of the following is the most appropriate contraceptive recommendation?

a) Ethinyl estradiol/drospirenone (Yasmin)
b) Medroxyprogesterone/ethinyl estradiol (Lunelle) injection
c) Ethinyl estradiol (second-generation birth control pill)
d) Medroxyprogesterone acetate (Depo-Provera) injection
e) Intrauterine device

**Answer and Discussion**

The answer is e.

**Objective: Understanding the indications and contraindications for contraceptive therapy.**

Because she is a smoker and older than age 35, this patient is at risk for thromboembolic disease if placed on birth control pills. The best choice in this married, monogamous woman with no risk factors for pelvic inflammatory disease would be the intrauterine device. Depo-Provera may cause a weight gain in this already obese patient. Yasmin should be used with caution in women taking medications that predispose to hyperkalemia, such as potassium-sparing diuretics, ACEIs, and nonsteroidal anti-inflammatory medications.

**Question 103**

A researcher wished to see whether women who have taken the oral contraceptive pill have an earlier or later menopause than other women. He decided to study a group of women born in 1930 because these women would be young enough for some to have taken the pill but old enough for some to have reached menopause. He obtained the names of all 132 women in one general practice who were born in 1930, using the practice’s age-sex register. Women claiming to have had menopause were checked by measuring their follicle-stimulating hormone (FSH) levels. Of the 132 women, 101 were available (21 not contactable, 1 refused); 60 = premenopausal; 14 = hysterectomy; 1 = radium-induced menopause; 2 = unmarried; and 2 = FSH < 30 IU/L.

Of the 31 women studied, 12 had taken an oral contraceptive pill (mean age of menopause, 47.2 years), and 19 had not (mean age of menopause, 47.5 years). Which of the following best describes this study design?

a) Observational cohort
b) Cross-sectional
c) Prospective, experimental
d) Case-control

**Answer and Discussion**

The answer is b.

**Objective: Describe features of different study designs.**

Research designs can be classified in several ways. In an observational study, the researcher collects information on the attributes or measurements of interest but does not influence the events. In contrast, experiments deliberately influence events and investigate the effects of the intervention. Prospective or cohort studies collect data forward in time from the start of the study. Cross-sectional studies are those in which individuals are observed only once. The study in this case was an observational, cross-sectional design.

**Question 104**

You are reviewing a research paper that describes a multicenter, randomized, double-blind, placebo-controlled trial
with 3,023 intermediate- to high-risk patients undergoing coronary artery bypass grafting surgery with cardiopulmonary bypass. Patients received an investigation drug X or placebo immediately before and for 30 days after surgery to assess the efficacy and safety in reducing cardiovascular death or nonfatal myocardial infarction. The primary efficacy outcome occurred in 100 of 1,510 patients (6.6%) receiving study drug X and 140 of 1,486 patients (9.4%) in the placebo group (risk ratio = 0.69; 95% confidence interval, 0.52 to 0.86; \( p = 0.012 \)). Which of the following statements regarding this study result is the most accurate?

a) There is a 1.2% chance that drug X is no better than placebo.
b) There is a 95% chance that drug X is better than placebo.
c) There is a 1.2% probability that the study result is arising by chance.
d) The confidence interval is too wide to make any conclusions from this study.

**Answer and Discussion**

**The answer is a.**

**Objective: Understand the meaning of a \( p \) value.**

There is a 1.2% chance of getting the observed effect if the null hypothesis is true. The \( p \) value is the probability of having the observed data when the null hypothesis is true. Therefore, the \( p \) value reflects the likely variation in a sample due to chance when the null hypothesis is true in the population. The \( p \) value is not the probability of the data having arisen by chance, or equivalently, \( p \) is not the probability that the observed effect is not a real one. The observed effect in the study sample is real (genuine), but we do not know what is true in the population at large. Thus, in this study, drug X is better than placebo; and there is only a 1.2% chance (\( p = 0.012 \)) that this result would be seen if drug X was equal to placebo in the population at large. The confidence interval is a range of values that we can be confident includes the true value. Thus, 95% of the study population will have a risk ratio between 0.52 and 0.86, and 5% will not.

**Question 105**

You are designing a research study to investigate variables that might increase the risk of DVT recurrence following 6 months of standard anticoagulation therapy. Your data collection sheet is shown below:

Patient study number______
Age______
Sex: M, F
\( \text{d-dimer level: } \leq 500, \ 500-1,000, \ >1,000 \)
US Day 0
  - Marder score______
US Day 30
  - Marder score______
US Day 180
  - Marder score______

Which of the following best describes the \( \text{d-dimer} \) variable?

a) Nominal (categorical)
b) Ordinal (categorical)
c) Continuous
d) Discrete
e) Dichotomous (categorical)

**Answer and Discussion**

**The answer is b.**

**Objective: Define variable types in research.**

Variables are continuous (quantified on an infinite arithmetic scale), discrete (quantified on a finite numeric scale), or categorical (classified in categories). Categorical variables are further classified as nominal (unordered) and ordinal (ordered) and according to whether or not they are dichotomous (only two categories). The patient study number, age, and Marder scores would be continuous variables. Sex is a dichotomous categorical variable. The \( \text{d-dimer} \) level is an ordinal categorical variable.

**Question 106**

Acute lower respiratory tract infection (LRI) is one of the most common causes of death among adults with sickle cell disease in developing countries. A simple test is needed to distinguish between those patients with acute respiratory infection who have LRI and should receive antibiotics from those with URI. The following data come from a study of the usefulness of the RR for this purpose in adults.

<table>
<thead>
<tr>
<th>Respiratory Rate (Breathe/min)</th>
<th>LRI (Number of patients (%))</th>
<th>URI (Number of patients (%))</th>
</tr>
</thead>
<tbody>
<tr>
<td>0–20</td>
<td>1 (1%)</td>
<td>16 (11%)</td>
</tr>
<tr>
<td>21–30</td>
<td>4 (3%)</td>
<td>77 (51%)</td>
</tr>
<tr>
<td>31–40</td>
<td>10 (7%)</td>
<td>46 (30%)</td>
</tr>
<tr>
<td>41–50</td>
<td>41 (29%)</td>
<td>9 (6%)</td>
</tr>
<tr>
<td>51+</td>
<td>86 (61%)</td>
<td>3 (2%)</td>
</tr>
<tr>
<td>Total</td>
<td>142 (100%)</td>
<td>151 (100%)</td>
</tr>
</tbody>
</table>

Which RR cutoff gives the best balance of sensitivity and specificity for LRI?

a) \( \leq 20 \)
b) \( \leq 30 \)
c) \( \leq 40 \)
d) \( \leq 50 \)
e) Not enough data have been given to answer this question

**Answer and Discussion**

**The answer is c.**

**Objective: Calculate sensitivity and specificity.**

A 2 \( \times \) 2 table of each cutoff reveals the sensitivity and specificity.
A new blood test that has been recently developed reports to identify patients who have pancreatic cancer before there is evidence of cancer on clinical imaging. The table below summarizes the sensitivity and specificity of the new blood test.

<table>
<thead>
<tr>
<th>CUTOFF</th>
<th>SENSITIVITY</th>
<th>SPECIFICITY</th>
</tr>
</thead>
<tbody>
<tr>
<td>20</td>
<td>141/142 = 99%</td>
<td>16/151 = 11%</td>
</tr>
<tr>
<td>30</td>
<td>137/142 = 96%</td>
<td>93/151 = 62%</td>
</tr>
<tr>
<td>40</td>
<td>127/142 = 89%</td>
<td>139/151 = 92%</td>
</tr>
<tr>
<td>50</td>
<td>86/142 = 61%</td>
<td>148/151 = 98%</td>
</tr>
</tbody>
</table>

The best cutoff is 40 breaths/minute, with an overall correct assessment for 266/293 = 91% of adults.

**Question 107**

A new blood test that has been recently developed reports to identify patients who have pancreatic cancer before there is evidence of cancer on clinical imaging. The table below summarizes the sensitivity and specificity of the new blood test.

<table>
<thead>
<tr>
<th>DISEASE STATUS</th>
<th>POSITIVE</th>
<th>NEGATIVE</th>
<th>TOTAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Test</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Positive</td>
<td>77</td>
<td>96</td>
<td>173</td>
</tr>
<tr>
<td>Negative</td>
<td>9</td>
<td>162</td>
<td>171</td>
</tr>
<tr>
<td>Total</td>
<td>86</td>
<td>258</td>
<td>344</td>
</tr>
</tbody>
</table>

What is the prevalence of pancreatic cancer in the study population?

a) 25%
b) 44%
c) 50%
d) 89%
e) There are not enough data available to answer this question.

**Answer and Discussion**

The answer is a.

**Objective: Use a 2 × 2 table to calculate prevalence.**

In a 2 × 2 table that is represented by a binary diagnostic test, prevalence can be determined by dividing the true positives by the total population. In this case, the true positives (n = 86) divided by the total population (n = 344) is 25%.

**Question 108**

An 88-year-old woman is admitted to the hospital after a fall that resulted in a fractured hip. She previously lived alone and cared for most of her daily needs. She had recently employed a helper to do the weekly shopping and the heavier housework because the arthritis in her knees was limiting her efficiency in performing this heavier work. She had hip surgery yesterday, and today you are asked by the orthopedic surgeon to see her as a medical consultant because she is combative and trying to get out of bed. The history and examination are difficult to perform because she fluctuates between falling asleep and shouting that she needs to go to the shops because the cupboards are empty and she has no food. She will listen to you and follow simple commands, but she is easily distracted by the noises of the hospital, is unable to concentrate, and wants to leave the bed to go shopping. All the following are true about the most likely cause of her confusion, except

a) It is a common condition in the hospitalized elderly.
b) Common causes include medications.
c) The best plan for her safety is to restrain her with soft restraints until the confusion resolves.
d) A reduced level of consciousness and inability to focus or sustain concentration are key characteristics.
e) Perceptual disturbances such as illusions, hallucinations, and delusions help establish the diagnosis.

**Answer and Discussion**

Delirium is a common condition in elderly hospitalized patients. Physical restraints are not the best plan in this case. The physical restraints have an associated morbidity and mortality and should be used only when other management possibilities, such as environmental changes or nursing and family support, cannot be established. As well as an immediate safety measure, the evaluation and determination of the underlying cause of delirium is important to enable the treatment of the underlying cause, and, consequently, the confusion.

**Question 109**

A 73-year-old morbidly obese woman is hospitalized for right lower extremity cellulitis. She presented to the ED last night in a taxicab and complained of severe pain in her right leg and difficulty ambulating. At that time, her vital signs were as follows: T = 38.2°C, P = 84 beats/minute, RR = 20 breaths/minute, and BP = 163/84 mmHg. The examination revealed a well-demarcated erythema and warmth of her right lower extremity involving her foot up to her mid-calf. There was no edema, but the extremity was painful to palpation. Duplex ultrasound in the ED was negative for DVT. Laboratory studies revealed a leukocyte count of 19,400 μL and a glucose of 325 mg/dL. She was subsequently placed on IV antibiotics along with subcutaneous insulin. Her past medical history is unremarkable, and she denies taking any medications. She is a retired history professor, and she does not smoke or drink alcohol. She is widowed and lives alone. She denies local family members, and she has full activities of daily living. She does not have a primary care physician and told the ED physician that, “I don’t like seeing doctors!” As you enter her room this morning on rounds, microbiology pages to alert you that her blood culture is positive for Gram-positive cocci. Before you even introduce yourself, she tells you that she is feeling much better and wants to go home immediately. Which of the following principles of medical ethics is most likely to guide your decision making at this time?

a) Nonmaleficence
b) Beneficence
c) Veracity
d) Autonomy
e) Justice
Answer and Discussion
The answer is d.

Objective: Understand the patient’s right of autonomy.
This patient has the right to determine what happens to her and her body. Western culture generally favors patient autonomy over beneficent protection offered by others. To override this, there has to be evidence for unintended irrepairable harm. So, even though continued hospital care is in this patient’s best interest (beneficence), patient autonomy dictates that she may choose to accept treatment or not. The clinician now must be sure that she is informed about her condition and has the mental capacity to make health-care decisions at this time. A formal capacity evaluation would include questions to assess her understanding of her condition, her current treatments, her treatment options, the consequences of refusing treatment, and questions to ensure that she is not depressed, delusional, or psychotic.

Question 110
A 32-year-old woman presents with double vision. The significant findings on examination include ptosis, diplopia, and facial weakness, causing her to appear to snarl when she attempts to smile. During counting aloud, her speech becomes progressively less distinct and more nasal. Proximal muscle weakness is present, which increases with repetitive movements and improves with rest. All the following statements are true about this disease, except:

a) It is more common in women.
b) The most common ages at presentation are the 20s and 30s for women and the 60s for men.
c) Pupils are small and irregular and react to accommodation but not to light.
d) The diagnostic test involves IV injection of an anticholinesterase inhibitor.
e) A pathophysiologically similar syndrome that affects proximal muscles but improves with brief exercise is associated with malignancy, most commonly, small cell carcinoma of the lung.

Answer and Discussion
The answer is c.

Objective: Recognize the features of myasthenia gravis.
Myasthenia gravis is the diagnosis suggested by the findings in this woman. The disease is more common in women than men (3:1). Pupillary reactions are always spared in myasthenia gravis. Small, irregular pupils that react to accommodation but not to light are described as Argyll Robertson pupils and are found in patients with neurosyphilis and, occasionally, in those with diabetes mellitus. The diagnostic test for myasthenia gravis involves IV injection of the anticholinesterase inhibitor edrophonium chloride.

Question 111
A 92-year-old woman is hospitalized for hypotension and suspected sepsis from an infected sacral decubitus ulcer. She is stabilized with fluids and broad-spectrum antibiotics, yet her BP remains low, and she is currently on a 100% nonrebreather mask to maintain oxygen saturations above 90%. The patient has been nonverbal and bedfast for the past 3 years, following a stroke. She is fed via a percutaneous gastrostomy tube and cared for by her family at home. Her past medical history is significant for known heart failure with an ejection fraction of 30% and chronic kidney injury with a baseline creatinine of 3.8 mg/dL. Today, she is anuric, and her creatinine is noted to be 5.5 mg/dL. The patient’s daughter has durable power of health for medical decision making. You raise resuscitation status with the daughter, and she is adamant that she is a “full code” and that the family expects all available life-saving treatments. The patient begins to desaturate, and you contact the ICU to arrange for a transfer. The intensivist does not recommend transfer or intubation unless nephrologist is willing to perform dialysis. Nephrologist declines dialysis on the grounds of medical futility. The family is getting increasingly upset and wants all life-saving measures; they are questioning why she is not in the ICU. They threaten to contact an attorney if you do not transfer the patient immediately. Which of the following is the most appropriate next step?

a) Intubate and transfer the patient to the ICU without dialysis
b) Contact your attorney for counsel
c) Order a bioethics consult
d) Call security to have the family removed
e) Begin palliative measures with morphine, benzodiazepines, and atropine

Answer and Discussion
The answer is a.

Objective: Identify Durable Power of Health’s legal rights in ethical dilemmas.
The daughter has Durable Power of Health and wishes all available treatments. To begin palliative measures or to have the family removed from the hospital would be against the expressed wishes of the patient surrogate decision maker and would violate the ethical principle of patient autonomy. Medical futility may override patient autonomy depending on the circumstances, such as the following: subversion of medical goals to heal and relieve suffering, when treatments deviate from professional standards, if there is no reasonable benefit of the treatment, and when treatment conflicts with reasonable stewardship of financial resources. In this case, the physician needs to determine the surrogate’s goals of care and apply futility against these goals. A bioethics consult will aid in this process and should be obtained, but it will take some time to accomplish this, and the patient needs to be stabilized first.
Question 112
A 75-year-old woman comes to your office as an urgent afternoon appointment. She complains of sudden, painless vision loss in her right eye. She reports that she was in her kitchen early this morning making breakfast when her right eye “went blank.” She states that she had similar symptoms last month but her vision improved in a couple of hours, but “It is not getting any better this time.” She denies headache, fevers, or myalgias. Her complete review of systems is positive for constipation. She has a past medical history of hypertension, coronary artery disease, and hypothyroidism. She lives alone and has full activities of daily living. She does not drink or smoke. Her past surgeries include coronary artery bypass grafting 7 years ago, bilateral cataract extraction, and a carpal tunnel release on her right hand. Her medications include a baby aspirin, simvastatin, enalapril, thyroid supplements, and hydrochlorothiazide. On examination, her vital signs are as follows: T = 36.5°C, P = 72 beats/minute, RR = 18 breaths/minute, and BP = 195/92 mmHg. Visual acuity testing is normal on the left. She can see shadows on the right but is unable to count fingers. Funduscopic examination on the right shows retinal edema with a cherry-red spot in the macula. Neck examination reveals no JVD, adenopathy, or carotid bruits. Lungs are clear to auscultation. Cardiac examination reveals a regular rhythm and paradoxical split S2 but no murmurs or gallops. Extremities show mild bipedal edema. Abdominal, muscular, and neurologic examinations are without abnormalities. You perform an ECG in the office, and it shows left bundle branch block. Which of the following most likely explains this patient’s problem?

a) Malignant hypertension
b) Giant cell arteritis
c) Cardiogenic embolism
d) Carotid artery atherosclerosis
e) Thyroid disease

Answer and Discussion
The answer is d.

Objective: Identify key features of central retinal artery occlusion (CRAO).

This patient has CRAO. These patients have sudden and painless loss of vision along with an opacified retina, markedly narrow arteries with boxcar segmentation, and a cherry-red spot in the macular area. Atherosclerotic disease of the ipsilateral carotid artery is the most common cause of retinal artery occlusion. The reported prevalence of significant carotid artery disease among patients with CRAO or branch retinal artery occlusion is 10% to 25% in most case series, but rates as high as 70% have been reported. A cardiogenic embolic source is second to carotid disease in causing retinal artery occlusion and is more frequent in younger patients (age < 40 years). Other etiologies include small vessel disease, hematoaglogenic disorders, and inflammatory states. Giant cell arteritis should be considered in all elderly patients (age > 50 years) because steroids may reverse the vision loss if given within 1 to 2 hours of symptom onset. In addition, without steroid treatment, vision loss may rapidly progress to involve the other eye.

Question 113
A 48-year-old man reports drooping of the face and difficulty speaking for 48 hours. On examination, a paralysis of the upper and lower face is present on the right side. He cannot raise his eyebrows or close his eye tightly. Drooping of the right side of the mouth is present, and the nasolabial fold is smoothed out. Which of the following is true about the most likely cause of this man’s symptoms?

a) This is an upper motor lesion.
b) The most common cause is herpes zoster of the external auditory meatus and geniculate ganglion, called Ramsay Hunt syndrome.
c) This is a rare condition occurring in approximately 1 in 10,000 persons in a lifetime.
d) This is permanent in 60% of patients.
e) There may be associated loss of taste sensation from the ipsilateral anterior two-thirds of the tongue.

Answer and Discussion
The answer is e.

Objective: Recognize the features of Bell palsy.

These clinical findings are consistent with Bell palsy, in which there may be an associated loss of taste sensation from the ipsilateral anterior two-thirds of the tongue. Clinically, this is a lower motor lesion. In an upper motor lesion of the facial nerve, there the frontalis muscle would be spared and the ability to raise the eyebrows would be preserved. Ramsay Hunt syndrome is a lower seventh cranial nerve lesion associated with herpes zoster of the external auditory meatus and geniculate ganglion, but it is not the most common cause of this facial nerve lesion; the most common cause is idiopathic. This is a common condition occurring in approximately 1 in 60 or 70 persons in a lifetime. Bell palsy is usually a self-limiting disease; most patients recover in a few weeks.

Question 114
A 64-year-old man presents to the emergency room with severe headache. The headache began 5 hours ago and is described as a unilateral dull ache over his left eye and temporal region. He took acetaminophen followed by ibuprofen for the symptoms, without relief. He states that this is the worst headache of his life and that pain intensifies with bright light. He also reports some nausea but no emesis. A complete review of symptoms is otherwise negative. He is a long-distance truck driver and lives out of state. He drinks 2 to 3 beers per week and smokes a half pack of cigarettes daily. His past medical history is significant for obesity, diabetes mellitus, and elevated cholesterol. His medications include metformin, simvastatin, and an
albuterol inhaler to use as needed. His surgeries include bilateral knee arthroscopies, cholecystectomy, and a vasectomy. On examination, he appears uncomfortable, and he is holding his hand over his left eye and forehead. Vital signs are as follows: T = 37.3°C, P = 92 beats/minute, RR = 23 breaths/minute, and BP = 138/86 mmHg. The head is atraumatic and normocephalic. Sclera is erythematous on the left with a fixed, mid-dilated pupil. Neck is supple, without JVD, adenopathy, or bruits. The lungs have scattered rhonchi but are otherwise clear. Cardiac examination reveals regular rate and rhythm and no gallops or bruits. Pulses are symmetric throughout. Abdominal and neurologic examinations are without abnormalities. CT scan of the head without contrast is normal. Laboratory studies are as follows:

- Sodium: 140 mEq/dL
- Potassium: 4.2 mEq/dL
- Chloride: 105 mEq/dL
- CO₂: 26 mEq/dL
- BUN: 18 mg/dL
- Serum creatinine: 1.2 mg/dL
- Leukocyte count: 9,600 μL
- Hematocrit: 32%
- Activated PTT: 33 seconds
- INR: 1.0

Which of the following is the most appropriate next step?

a) MRI of the head with gadolinium
b) Lumbar puncture
c) 100% oxygen via nonrebreather face mask
d) Sumatriptan
e) Iridotomy on the left eye

**Answer and Discussion**

The answer is e.

**Objective: Correctly treat acute angle glaucoma.**

This patient is having an acute angle glaucoma attack. Glaucoma is a condition in which the pressure caused by the fluid in the eye is abnormally high. The risk of developing glaucoma increases with age, the presence of diabetes, and a positive family history. About 90% of glaucoma cases are open angle glaucoma, a chronic and slowly progressive disorder that is amenable to medical therapy. Acute angle closure glaucoma leads to a sudden and dramatic increase in intraocular pressure. Patients typically complain of unilateral headache that is often described as the worst headache of their lives. Examination of the eye shows a ciliary flush or an injection most marked at the limbus (where the cornea undergoes transition to the sclera) with associated photophobia and nausea. The eye findings in this case are not consistent with subarachnoid hemorrhage or cluster headache or migraine. If the increased pressure is not relieved within hours, the patient may develop permanent vision loss. Immediate referral to an ophthalmologist is necessary for a laser iridotomy.

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**Question 115**

Which of the following features suggests a lower motor neuron lesion rather than an upper motor lesion?

a) Extensor plantar response
b) Hyperreflexia of the tendon reflexes
c) Increased tone (spasticity)
d) Fasciculation
e) Weakness

**Answer and Discussion**

The answer is d.

**Objective: Understand the localizing findings off the neurologic examination.**

Fasciculation suggests a lower motor neuron lesion rather than an upper motor lesion. Extensor plantar response, hyperreflexia of the tendon reflexes, and increased tone (spasticity) are all suggestive of an upper motor lesion. Weakness is a feature of both upper and lower motor lesions.

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**Question 116**

A 75-year-old African American woman presents to your office for routine follow-up for her hypertension and diabetes mellitus. She states that she has been doing well, although she is concerned that she may need a new prescription for her glasses, as things are looking “fuzzy” to her. She is widowed and lives with her daughter. She has full activities of daily living, and she has been driving until recently. She works part time at a local pet store. She states, “I love the puppies and kittens, but I don't like cleaning out the turtle tanks!” She does not smoke. She does report drinking one to two gin and tonics nightly. Her past medical history is significant for hypertension, diabetes mellitus, osteoarthritis, cervical cancer status post curative surgery and radiation, and remote Hashimoto thyroiditis. Her medications include diltiazem, amlodipine, hydrochlorothiazide, metformin, insulin, ibuprofen, and thyroid replacement. On examination, her vital signs are as follows: T = 37.5°C, P = 75 beats/minute, RR = 18 breaths/minute, and BP = 155/75 mmHg. Her HEENT examination is normal except for decreased visual acuity in her left eye. Her left eye with penlight examination is shown here.
Her neck is supple without JVD, adenopathy, or bruits. Her lungs show diminished breath sounds throughout, but they are clear without wheezing. Breast examination is normal without masses. Cardiac examination is normal. Abdomen shows a protuberant but nontender abdomen. Her liver margin is palpable and measures 7 cm at the midclavicular line. She has Heberden nodes on her fingers bilaterally. Neuromuscular examination is without abnormalities. Which of the following factors in this patient is associated with the etiology of her vision problem?

a) Occupation  
b) Race  
c) Diabetes  
d) Thyroid disease  
e) Liver size

**Answer and Discussion**

The answer is c.

**Objective:** Identify key features of cataracts.

This patient has a mature, senile cataract with loss of the red reflex. The risk factors associated with cataracts include advancing age, smoking, alcohol consumption, sunlight exposure, low education, systemic corticosteroid use, and diabetes mellitus. Cataract should be suspected in any patient who complains of a painless, progressive decline in vision. A lens opacity can be confirmed by a nondilated fundus examination with the direct ophthalmoscope; there may be darkening of the red reflex, opacities within the red reflex, or obscuration of ocular fundus detail. In the absence of other visual symptoms, a red eye, or other abnormality noted on fundus examination, these patients should be referred on a nonurgent basis for a comprehensive ophthalmic examination.

**Question 117**

A 32-year-old woman presents with slurred speech and ataxia. You have seen her previously, with two episodes of blurred vision, 10 and 6 months ago. On examination of her lower extremities, she has increased tone and bilateral spasticity and weakness. Bilateral ankle clonus is present, and the plantar reflexes are extensor. You consider the possibility of multiple sclerosis. Which of the following statements about MS is true?

a) It is more common in men.  
b) The predominant age at presentation is 50 to 65 years.  
c) Northern European descent or living in a temperate climate are risk factors for MS.  
d) CT and MRI are equally sensitive in the diagnosis of MS.  
e) Cerebrospinal fluid examination that suggests the diagnosis of MS includes a normal or slightly high protein level (50 to 100 mg/dL), high level of γ-globulin IgG, and negative serology for syphilis.

**Answer and Discussion**

The answer is c.

**Objective:** Recognize the features of MS.

Northern European descent or living in a temperate climate are risk factors for MS. MS is more common in women. The predominant age at presentation is 16 to 40 years. MRI is more sensitive than CT in the diagnosis of MS. Cerebrospinal fluid examination that suggests the diagnosis of MS includes a normal or slightly high protein level (50 to 100 mg/dL), high level of γ-globulin IgG, and negative serology for syphilis.

**Question 118**

A 52-year-old male employee of a local warehouse operation is seen at an urgent care center complaining of gradual onset of headache, nausea, and dizziness. He relates experiencing similar symptoms over the past few days, which tend to occur near the end of his workshift and resolve overnight. During this time, all windows in his warehouse have remained closed to reduce heating costs. None of his family members is ill, but he claims other employees in his work area are experiencing similar complaints. He has been in good health, in spite of having smoked one-half pack of cigarettes daily for the past 30 years. Physical examination is unremarkable. A blood carboxyhemoglobin level is 20%. An ECG and cardiac enzymes are normal. Proper medical management of this patient would entail the following:

a) Nothing, except removal from exposure  
b) Administration of 100% oxygen by face mask  
c) Assisted ventilation  
d) Hospitalization overnight for observation  
e) Hyperbaric oxygen at 2 to 3 atm

**Answer and Discussion**

The answer is b.

**Objective:** Understand the treatment of carbon monoxide (CO) poisoning.

Removal from further exposure is usually the first step in the management of any toxic event. This has already been accomplished in this case, at least for the time being. However, the treating physician does have an obligation to promptly report the diagnosis of work-related CO poisoning to the employer to ensure appropriate corrective measures are undertaken to lower further employee exposure below permissible limits.

While this patient would ultimately recover without a specific therapy, administration of 100% oxygen by face mask would reduce the half-life from 5.5 to 1.5 hours and hasten the patient’s symptomatic improvement.

Assisted ventilation, hospitalization, or hyperbaric oxygen are indicated only for those more severely affected than this patient.

**Question 119**

An 83-year-old man, who lives alone, is brought to the ED by ambulance after being found by his daughter lying down in his kitchen. He did not recognize her but told her he was cold. He denied shortness of breath or chest pain. Medical history is significant for hypertension and coronary artery disease. His medications include aspirin, metoprolol, hydro-
chlorothiazide, and atorvastatin. He is a former smoker, and according to the daughter, he does not drink alcohol. He has been independent in all of his activities of daily living until now. The daughter states that he was complaining of a “stomach flu” last weekend. Upon arrival to the ED, he is awake and mildly agitated. He is not oriented to time or place, and he responds inappropriately to questioning. His vitals are as follows: T = 38.5°C, P = 105 beats/minute, RR = 20/minute, and BP = 80/50 mmHg. Pulse oximetry is 95% on room air. Skin is clear, dry, and warm. HEENT examination is normal. The patient is edentulous. The neck is supple. Cardiac examination reveals a grade 2/6 systolic ejection murmur at the apex. Lungs have scattered rhonchi but otherwise are clear. Abdomen is soft and nontender without organomegaly or peritoneal signs. Gait is unobserved due to weakness. Prostate is enlarged and nontender to palpation. Lab studies reveal the following:

- BUN: 35 mg/dL
- Cr: 2.0 mg/dL
- Na: 149 mEq/L
- K: 4.6 mEq/L
- Cl: 105 mEq/L
- HCO₃⁻: 25 mEq/L
- WBC: 5,000 mm³
- Platelets: 110,000 mm³
- Urine specific gravity: 1.030
- WBC: 0 to 5/hpf
- RBC: 6 to 10/hpf
- Hycaline casts

ECG shows nonspecific ST segment-T wave changes that are unchanged from a baseline study on file. Head CT without contrast shows cortical atrophy and changes consistent with small vessel disease. Which of the following best explains his mental state?

a) Alzheimer dementia
b) Metabolic encephalopathy
c) Viral meningitis
d) Ischemic stroke
e) Postictal confusion

**Answer and Discussion**

The answer is b.

**Objective:** Identify key features of delirium.

This patient has delirium, a condition found in up to 40% of elderly patients who present to the ED. Delirium is a disturbance of consciousness with reduced ability to focus, sustain, or shift attention. The disturbance develops over a short period of time (hours to days) and fluctuates during the course of the day. Elderly patients with subclinical dementia or unrecognized cognitive deficits are susceptible to delirium with minimal noxious stimuli. In this case, the patient had a stomach “flu” with decreased oral intake, in the setting of continued diuretic use. His electrolytes confirm the dehydration and acute kidney injury. Dementia itself does not cause inattention, change in levels of consciousness, or inappropriate speech or thoughts. Strokes may cause delirium, but they need to involve both cerebral hemispheres or be large enough to cause edema with mass shift. The clinical picture and examination are not consistent with meningitis or postictal state.

**Question 120**

A 79-year-old woman is brought to your office by her daughter for a routine follow-up visit. The patient is currently living alone, but the daughter is concerned about her safety because she has suffered two falls in the past month. The patient reports that she feels fine and that she just innocently tripped on a rug. Her past medical history is significant for remote breast cancer, hypothyroidism, and hypertension. Her medications include synthroid 100 μg daily, diltiazem extended release 180 mg daily, vitamin D 800 IU daily, and calcium 1,200 mg daily. Her surgical history is significant for a left total hip arthroplasty 5 years ago and a total abdominal hysterectomy, remotely. She is independent in all basic and most instrumental activities of daily living. She no longer drives. She resides in a ranch-style home without stairs. She wears glasses for reading. She has no hearing deficits. Her complete review of systems is unremarkable. On examination, she appears well nourished and in no acute distress. Vital signs are as follows: T = 37.0°C, P = 73 beats/minute, RR = 18/minute, and BP = 175/84 mmHg. The patient is edentulous and her HEENT examination shows an early cataract formation on the right. Vision is 20/20 bilaterally. Neck is supple without JVD, adenopathy, or bruits. Lungs are clear. Cardiac examination reveals a normal S1 and S2, no murmurs, and +S4 gallop. Abdomen, skin, and extremity examinations are normal. Muscles are nontender. Neurologic examination reveals intact cranial nerves, symmetric reflexes, and 4/5 strength in all muscle groups. Gait is slow but otherwise normal. Laboratory studies are as follows:

- BUN: 15 mg/dL
- Cr: 0.9 mg/dL
- Na: 138 mEq/L
- K: 4.6 mEq/L
- Cl: 105 mEq/L
- HCO₃⁻: 25 mEq/L
- WBC: 6,000 mm³
- Platelets: 220,000 mm³
- Hgb: 10.8
- TSH: 1.3

In regard to the daughter’s concern of falls, which of the following is the most appropriate next step?

a) Recommend hip protectors at all times
b) Recommend nursing home placement
c) Tai Chi group exercises
d) Increase diltiazem dose
e) Begin bisphosphonate therapy
Answer and Discussion
The answer is c.
Objective: Identify strategies to prevent falls in the elderly.

Falls in the elderly occur commonly and are a major factor threatening the independence of older individuals. Falls usually occur when impairments in multiple domains compromise the compensatory ability of the individual. Multiple preventive intervention studies have been conducted over the past decade. Muscle strengthening and improvement in balance have been shown to reduce falls via a 15-week Tai Chi group exercise program. Eliminating polypharmacy is important, along with home hazard assessment and modification. This patient is already on the appropriate dose of vitamin D and calcium supplementation; both interventions have some evidence for reducing fall risk and minimizing injury. Bisphosphonate therapy has not been evaluated in regard to fall risk, and there is nothing in this case that would trigger this therapy for OP. Hip protectors do not prevent falls, and according to meta-analysis data, they do not significantly reduce complications due to low compliance rates; most fractures in randomized trials occurred when the hip protector was not being used.

Question 121

A 60-year-old man on your inpatient service for 3 days presented with melanotic stools. He has been doing well; his hemoglobin has been stable at 13 mg/dL, and his vital signs have also been stable and normal. He arrived on Friday of a holiday weekend, and you have been unable to schedule an esophagogastroduodenoscopy until the following day. You are paged by his nurse, who reports that he has been restless all afternoon, and now he is demanding and threatening to leave and go home. You immediately go to see the patient, surprised at the behavior described to you by the nurse because he had been very pleasant in the previous 3 days. You look at his vital signs chart outside his room. His BP has been rising over the past 24 hours and is now 170/98 mmHg; on admission, it had been 128/76 mmHg. He has also developed a sinus tachycardia of 118 beats/minute and a temperature of 37.8°C. When you enter the room, he appears agitated and tremulous and is pacing around the room. On seeing you, he states that he must leave. He appears to be watching something in the room and, on inquiry, states that he is watching the little angels who are flying around the room. Which of the following is most likely the cause of this presentation?

a) Alcohol withdrawal
b) Alcohol intoxication
c) Opiate withdrawal
d) Schizophrenia
e) Personality disorder

Answer and Discussion
The answer is a.
Objective: Recognize the features of alcohol withdrawal.

Restlessness, tachycardia, fever, hypertension, and visual hallucinations after 3 days in the hospital are most suggestive of withdrawal from alcohol. Similar presentations may occur with withdrawal from sedative hypnotics. Withdrawal from either alcohol or sedative hypnotics can cause seizures and may be life-threatening. Alcohol intoxication is suggested by the slow or slurred speech, confusion, gait disturbance, and nystagmus. Opiate withdrawal may present with agitation, but other features include dilated pupils, rhinorrhea, nausea, cramps, and restlessness. Schizophrenia does disturb thoughts and behavior and may have features of tactile, auditory, olfactory, and visual hallucinations, but it does not usually present with restlessness, tachycardia, fever, and hypertension. A personality disorder can present with agitated, aggressive, or violent behavior, but it is not usually associated with restlessness, tachycardia, fever, and hypertension.

Question 122

A 74-year-old woman presents to your office with complaints of urinary leakage. She reports urine leakage intermittently throughout the day; leakage is exacerbated by coughing or exertion such as lifting her grandchildren. She denies urgency or nocturia. Her review of systems is negative for constipation, diarrhea, or nocturia. Her past medical history is significant for hypertension, hypothyroidism, and gastroesophageal reflux disease. Her medications include enalapril, levothyroxine, and omeprazole. She does not drink caffeinated or alcoholic beverages. She does not use tobacco. She is married, has 8 children and 17 grandchildren. On examination, her vital signs are as follows: T = 36.6°C, P = 73 beats/minute, RR = 18/minute, and BP = 135/71 mmHg. HEENT examination shows extraocular movements intact and pupils equal, round, reactive to light and accommodation. Neck is supple without JVD, adenopathy, or bruits. Cardiopulmonary examinations are normal. Abdomen is obese, soft, nontender, and without organomegaly. Extremities have no clubbing, cyanosis, or edema. Neurologic examination is normal. Urinalysis is normal. Results of laboratory studies are as follows:

Na: 140 mEq/L
K: 4.0 mEq/L
Cl: 110 mEq/L
HCO₃: 26 mEq/L
Cr: 1.0 mg/dL
BUN: 15 mg/dL
Glucose: 89
Ca: 9.0
Albumin: 4.0
Tbilirubin: 0.7
WBC: 10,000
Hgb: 12.1
Platelets: 185,000
Which of the following is the most appropriate next step to evaluate the cause of her symptoms?

- a) No testing is necessary
- b) Measurement of urine flow rate
- c) Post void residual volumes
- d) Urinary stress test
- e) Urodynamic testing

**Answer and Discussion**

The answer is **d**.

**Objective: Identify the correct diagnostic workup for urinary incontinence.**

Urinary incontinence is an involuntary leakage of urine. There are four major clinical types of urinary incontinence associated with lower urinary tract dysfunction: urge, stress, mixed, and overflow. This patient has features of stress incontinence, which occurs when an increase in intra-abdominal pressure overcomes the sphincter closure mechanisms in the absence of a bladder contraction. The patient denies urgency, which is a sensitive and specific finding for urge and mixed incontinence. In women with stress incontinence symptoms, a clinical stress test is very sensitive for impairment of sphincter tone. In a standing position with a relaxed perineum, the patient should give a single vigorous cough. Leakage instantaneous with the cough suggests impaired sphincter function. Urodynamic testing can be done, but it is invasive and expensive and often not needed with the clinical picture in this case. Urodynamic testing is most useful in patients with mixed symptoms and/or urgency complaints. Post void residuals are helpful in the setting of overflow incontinence.

**Question 124**

The most likely source of CO poisoning in a warehouse operation is:

- a) Malfunctioning central heating unit
- b) Indoor vehicular exhaust
- c) Employee smoking
- d) Ambient (outside) air pollution
- e) Methylene chloride

**Answer and Discussion**

The answer is **b**.

**Objective: Identify the possible sources of CO poisoning.**

Although the central heating unit should always be inspected in any episode of CO poisoning occurring within a building, propane-powered vehicles, such as forklift trucks, are a more likely source of this problem in a warehouse.

Exposure to environmental tobacco smoke and ambient air pollution, although undesirable, are unlikely to result in a clinically significant CO poisoning under usual exposure circumstances.

Methylene chloride is metabolized to CO, but poisoning from this agent occurs during its use as a paint stripper, an unlikely operation to be routinely conducted in a warehouse.

**Question 125**

A 24-year-old male college student presents to the student health center complaining of painful shins. The pain began 1 week ago. His past medical history is generally unremarkable. He takes no prescription medications. He drinks socially on the weekends, and he does not smoke. He is currently a microbiology graduate student and reports spending a great deal of time in the laboratory without much sleep. His review of symptoms is positive for generalized fatigue and malaise, and recently, he has developed loose stools. On examination, his vital signs are as follows: T = 37.9°C, P = 80 beats/minute, RR = 18 breaths/minute, and BP = 128/75 mmHg. Head and neck examination is normal. Oropharynx is clear without erythema. He has no adenopathy. Lungs are clear to auscultation. Cardiac examination reveals normal heart sounds without gallops or murmurs. His shins show discrete painful erythematous nodules bilaterally. Pulses are brisk and symmetric throughout. Neurologic examination is normal. Which of the following tests is most likely to explain the etiology behind the patient’s presentation?

- a) Antistreptolysin-O titer
- b) Angiotensin-converting enzyme level
- c) Tuberculin skin testing
- d) Hemoglobin A1c
- e) Skin biopsy

**Answer and Discussion**

The answer is **a**.

**Objective: Identify common etiologies of erythema nodosum (EN).**

This patient has EN. EN is characterized by red or violet subcutaneous nodules that usually develop in a pretibial...
A 24-year-old woman presents to the student health center with a chief complaint of “hives.” She states that she was in her usual state of good health until yesterday afternoon when she developed a rash on her trunk, which then spread to her face, arms, and legs. The rash is pruritic. She states that the rash seemed to go away last night but returned again this morning. She has no other complaints and is otherwise healthy. Her only medication is a birth control pill (ethinyl estradiol), which she has taken for the past 4 years. She denies over-the-counter medications. She drinks socially and does not smoke. She denies any recent travel. She is currently in veterinary college. She has not had any surgeries, and her family history is significant for rheumatoid arthritis and lupus. On examination, her vital signs are as follows: T = 36.7°C, P = 78 beats/minute, RR = 17 breaths/minute, and BP = 123/79 mmHg. Skin examination reveals diffuse erythematos plaques on the trunk, face, and extremities. The rest of the physical examination is normal. Which of the following is most appropriate next step?

a) Perform a skin biopsy
b) Obtain a complete blood cell count with differential
c) Draw blood for a sedimentation rate, rheumatoid factor, and complement levels
d) Stop the birth control pill
e) Begin hydroxyzine

**Answer and Discussion**

The answer is e.

**Objective:** Identify the correct treatment plan for acute urticaria.

This patient has acute urticaria for which the mainstay of treatment is antihistamine therapy. Acute urticaria is defined as outbreaks of urticarial lesions that do not extend in duration beyond 6 weeks. It is a common condition, affecting up to 20% of the population at some point in their lives. The lesions of acute urticaria are characterized by a rapid onset and resolution within several hours, and they can be recurrent. A presumptive trigger, such as a drug, food ingestion, insect sting, or infection, can occasionally be identified. In patients with acute urticaria who lack any history or physical findings to suggest an underlying disease process, laboratory studies are typically normal and therefore not helpful. Skin biopsy would only be warranted if the urticaria were chronic. Estradiol is not associated with urticaria. Progesterone-containing oral contraceptives, hormone replacement therapy, and even endogenous progesterone may be associated with cyclic urticaria in which lesions appear during the second half of the menstrual cycle and resolve with menstruation.

**Question 127**

A 31-year-old African American man presents to your office very upset. He states that 6 months ago, he noted skin changes on his knees, but he is now getting them on his hands. He is extremely anxious that the lesions will spread to his face. He is otherwise healthy, is not on any medications, and has no other complaints. He is single and works as a building contractor. He does not use tobacco, and drinks socially. His only surgery relates to a fractured humerus as a child. He was adopted, so family history is unknown. On examination, his vital signs are as follows: T = 36.8°C, P = 72 beats/minute, RR = 18 breaths/minute, and BP = 120/83 mmHg. The examination of the skin reveals depigmented lesions on both of his knees, second and third digits of his right hand, and his left elbow. The rest of his physical examination is normal. Which of the following is the most appropriate treatment plan at this time?

a) Observation
b) Topical corticosteroids
c) Photochemotherapy (psoralen plus ultraviolet A)
d) Tacrolimus
e) Hydroquinone

**Answer and Discussion**

The answer is b.

**Objective:** Appropriately treat vitiligo.

This patient has vitiligo, an acquired skin depigmentation that affects all races but is far more disfiguring in blacks. The disease can be devastating psychologically. Topical corticosteroids are frequently the first treatment of choice for patients with limited disease (covering <10% of the body) that does not involve the face. Although vitiligo may spontaneously resolve in 10% to 20% of cases, this patient warrants treatment. Photochemotherapy and topical calcineurin inhibitors have been shown to be effective in clinical studies. Consider recommending depigmentation with hydroquinone if vitiligo affects more than 50% of the face or body and is recalcitrant to therapy. Patients should be advised that depigmentation is permanent, although cases of repigmentation have been reported.

**Question 128**

A 35-year-old man presents to your office stating that he has had the “flu” for weeks with no improvement. “I cannot
work, and I am afraid I am going to lose my job.” For the last month, he has been feeling fatigued, with intermittent nausea, occasional “dizziness,” and severe frontal headaches that occur if he tries to work. He is a forklift operator for a food manufacturing warehouse. He notes that several of his coworkers have had similar symptoms. He denies fever or chills. He is married and has two children. He reports no one at home is ill. He states, “I always feel better after resting at home, but as soon as I get back to work, my head starts pounding before lunch.” He smokes 1 pack of cigarettes daily, and he says he is trying to cut down. He does not take any regular medications but states he has been taking tylenol daily while at work. On examination, his vital signs are as follows: T = 37.0°C, P = 91 beats/minute, RR = 18 breaths/minute, and BP = 154/87 mmHg. HEENT examination is normal, including the fundoscopy. There is no adenopathy. Lungs are clear. Cardiac examination and pulses are normal. Abdomen is nontender without organomegaly. Neurologic and skin examinations are normal. Which of the following is the most appropriate next step?

a) Stress ECG  
b) Monospot test  
c) Carboxyhemoglobin level  
d) MRI of the brain  
e) Lumbar puncture

**Answer and Discussion**

The answer is c.

Objective: Identify the key features and diagnostic workup for carbon dioxide poisoning.

This man has symptoms consistent with CO poisoning. His symptoms worsen or develop predominantly at work, and several coworkers are similarly affected. Propane-powered vehicles, such as forklift trucks, are a likely source of CO poisoning in a warehouse. The earliest symptoms, especially from low-level exposures, are often nonspecific and readily confused with other illnesses, typically flu-like viral syndromes, depression, chronic fatigue syndrome, chest pain, and migraine or other headaches. This often makes the diagnosis of CO poisoning difficult. The clinical manifestations include tachycardia and hypertension, and central nervous system symptoms such as headache, dizziness, confusion, convulsions, and unconsciousness. CO poisoning may also produce myocardial ischemia, atrial fibrillation, pneumonia, pulmonary edema, hyperglycemia, muscle necrosis, acute renal failure, skin lesions, visual and auditory problems, and respiratory arrest. If CO poisoning is suspected, the diagnosis can be confirmed by measurement of blood carboxyhemoglobin.

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**Question 129**

A 42-year-old woman presents to the ED with a 2-hour history of dizziness, blurred vision, and repeated vomiting. Her symptoms began while she was cleaning her bathroom with a household insecticide. Her past medical history is otherwise normal, and she does not take any regular medications. She denies any illicit drug use. Her vital signs are as follows: T = 37.6°C, P = 88 beats/minute, RR = 21 breaths/minute, and BP = 140/82 mmHg. She appears diaphoretic. Pupils are constricted. Lungs are clear to auscultation, and the cardiac examination is normal. Bowel sounds are hyperactive. Reflexes are symmetric, and there is no focal weakness. ECG is normal. Labs are as follows:

- Sodium: 140 mEq/dL
- Potassium: 3.8 mEq/dL
- Chloride: 105 mEq/dL
- CO: 23 mEq/dL
- BUN: 13 mg/dL
- Serum creatinine: 1.0 mg/dL
- INR: 1.1
- AST: 26 U/L
- ALT: 28 U/L
- Plasma pseudocholinesterase: 161 U/L (normal: 350 to 850 U/L)

Which of the following is the most appropriate therapy at this time?

a) Activated charcoal  
b) Atropine  
c) Diazepam  
d) Pralidoxime chloride  
e) Sodium nitrite

**Answer and Discussion**

The answer is d.

Objective: Identify the key features and treatment plan for organophosphate poisoning.

The diagnosis of organophosphate poisoning depends on a history of exposure, the presence of typical signs and symptoms, and laboratory documentation of cholinesterase inhibition. A cholinesterase depression of 25% or more, compared with the pre-exposure baseline, is regarded as evidence of excessive absorption. A reduction of greater than 50% is usually seen with frank poisoning. For relatively mild cases, treatment may consist only of removal from further exposure and decontamination of clothing and skin. Anticholinergic agents such as atropine are used to antagonize cholinergic symptoms and are typically the first agents of choice. Pralidoxime chloride (Protopam) reactivates the enzyme cholinesterase by breaking the acetylcholinesterase–phosphate complex. Its advantages over atropine include its ability to reverse muscle paralysis and possibly central nervous system depression. Activated charcoal is appropriate within 30 minutes of organophosphate ingestion; otherwise, it is of little benefit. Sodium nitrite is used in cyanide poisoning. It has no role in the management of organophosphate toxicity. Diazepam is indicated in organophosphate toxicity that presents with seizures.

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**Question 130**

A 27-year-old obese female patient with history of hypertension presents with complaints of burning pain, numbness, and
tingling over the upper outer thigh. The pain worsens with walking and standing and is relieved with sitting. The patient rubs the outer thigh when describing the symptoms. Which of the following statements regarding her condition is not true?

- a) Sensory loss is seen in a discrete area in the anterolateral thigh.
- b) The straight leg raise is positive.
- c) The deep tendon reflexes and motor strength are normal.
- d) Avoiding tight garments is helpful.
- e) Weight loss will benefit the patient.

**Answer and Discussion**

The answer is b.

**Objective: Recognize different mononeuropathy syndromes.**

Meralgia paresthetica or painful mononeuropathy of the lateral femoral cutaneous nerve occurs when the nerve is trapped as it passes through the inguinal ligament. It is a purely sensory nerve and has no motor component. Hence, neurologic symptoms are limited to sensory changes only, and the neurologic examination is otherwise normal. The straight leg raising test is negative. The deep tendon reflexes are normal, and muscle strength is preserved. There is no evidence of a bone or joint abnormality, and the treatment is reassurance and education. Pregnancy, diabetes, and obesity can predispose to the syndrome. Patients are advised to avoid tight-fitting garments. Physical therapy has not proven to be of any benefit. If symptoms persist, carbamazepine, phenytoin, or gabapentin may be useful.

**Question 131**

You are caring for a 20-year-old woman who was hospitalized for a community-acquired pneumonia. Over the past 3 days, she has had a resolution of her shortness of breath, and she is no longer febrile; you anticipate discharging her today. Her past medical history is significant for schizophrenia for 5 years. Her current medications include ceftriaxone, azithromycin, olanzapine, and acetaminophen as needed. Today her vital signs are: 

- T = 36.8°C, P = 81 beats/minute, RR = 18/minute, BP = 145/88 mmHg, and pulse oximetry = 99% on room air. In general, she appears restless and is unable to sit quietly for a full examination. The nurses comment that she slept little overnight and was frequently in and out of her room. Her lungs are clear to auscultation. She is alert to person, place, and time. Affect is blunted. She denies hallucinations, and she is looking forward to going home. Cogwheeling is present but unchanged from admission. There is no weakness, and gait is normal. Laboratory studies obtained this morning are normal. In addition to converting her IV antibiotics to oral equivalents, which of the following is the most appropriate change in her pharmacotherapy?

- a) Add metoprolol
- b) Change olanzapine to perphenazine
- c) Add haloperidol
- d) Increase her olanzapine dose
- e) Add trihexyphenidyl

**Answer and Discussion**

The answer is a.

**Objective: Recognize akathisia as an adverse effect of antipsychotic medications.**

Akathisia is a subjective sense of restlessness, often accompanied by voluntary movement of the limbs or trunk. It is among the more common movement disorders associated with antipsychotic medications, including the newer agents. Both patients and physicians may mistake akathisia for anxiety, agitation, or insomnia. Akathisia should be suspected in any patient who is unable to sit quietly or who complains of feeling nervous, uncomfortable, or unable to sleep. Treatment options include decreasing antipsychotic medication dose, changing to a different atypical antipsychotic (olanzapine, risperidone, quetiapine, aripiprazole, or clozapine), or adding a β-blocker, antihistamine, benzodiazepine, anticholinergic, or serotonin antagonist. This patient’s BP makes it particularly important to add a β-blocker in this situation.

**Question 132**

A 23-year-old man presents to your office 2 days after an ED visit for chest pain. At that time, his ECG and cardiac biomarkers were normal, and the history was consistent with a panic attack. On patient interview, you note excessive anxiety and worry about a number of events. He reports such symptoms more days than not for as long as he can remember. On review of symptoms, he reports fatigue, diffuse muscle aches, and difficulty sleeping. He has no other past medical history and is on no medications. He received a 2-day supply of alprazolam from the ED, which is now all gone. He states that the medication did help him relax. He denies drinking caffeinated beverages or using illicit drugs, alcohol, or tobacco. He lives with his girlfriend and reports that their relationship is good. He is currently a student in nursing college. His vital signs are as follows:

- T = 36.8°C, P = 84/minute, RR = 20/minute, BP = 125/85 mmHg. HEENT examination is normal. Thyroid is palpable, nonenlarged, and without nodules. The rest of his physical examination is without abnormalities. Laboratory studies reveal a normal complete blood cell count and a normal TSH. In addition to supportive therapy and counseling, which of the following is the most appropriate long-term pharmacotherapy for this patient?

- a) Nortriptyline
- b) Sertraline
- c) Diazepam
- d) Quetiapine
- e) Alprazolam

**Answer and Discussion**

The answer is b.

**Objective: Identify and treat generalized anxiety disorder.**

Generalized anxiety disorder is characterized by excessive worry and anxiety that are difficult to control and that
cause significant distress and impairment. Antidepressant drugs are often the best choice for patients with chronic anxiety disorder. They can be given long term, without risking dependence. SSRIs have fewer side effects than tricyclic antidepressants. Diazepam and alprazolam are excellent choices for short-term treatment but cause too high a risk for dependence when used for an extended period of time. Many patients find it difficult to wean off benzodiazepines once they are started. For acute conditions, benzodiazepine treatment typically lasts up to 6 weeks with tapering and discontinuation over a 2-week period.

**Question 133**

A 45-year-old woman reports being “off-balance” for the past several weeks. She has sustained several falls and was treated at the local urgent care clinic for skin lacerations and mild bruises. She reports no head injury but states that she consumed five cans of beer and enjoyed two to three martinis with dinner, daily for the past 9 years. On review of systems, she complains of chronic abdominal pain. Her past medical history is remarkable for chronic kidney pain. Her past medical history is remarkable for chronic pancreatitis. She has poor dental hygiene, horizontal nystagmus, diplopia, ataxia, and a distended abdomen. A kidney, ureter, and bladder X-ray examination reveals calcifications in the midureteral area. A brain CT reveals cerebral atrophy without evidence of intracranial bleed or masses. Laboratory tests indicate the following:

<table>
<thead>
<tr>
<th>Test</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemoglobin</td>
<td>11.6 g/dL</td>
</tr>
<tr>
<td>WBCs</td>
<td>8,323/mm³ (normal differential)</td>
</tr>
<tr>
<td>Platelets</td>
<td>138,000/μL</td>
</tr>
<tr>
<td>Mean corpuscular volume</td>
<td>107 fL</td>
</tr>
</tbody>
</table>

The most likely explanation of her neurologic symptoms is which of the following?

a) Acute alcohol intoxication  
b) Cocaine overdose  
c) Wernicke encephalopathy  
d) Cerebellar degeneration  
e) Korsakoff psychosis

**Answer and Discussion**

The answer is c.

**Objective: Identify organic causes for symptoms of anxiety before treating with psychiatric medications.**

Symptoms of panic disorder are characterized by discrete attacks of anxiety associated with a sensation of chest pain, palpitations, or nausea. Patients may have multiple ED visits before they are diagnosed. The embarrassment or fear of having panic attacks in public without an easy escape often disrupts social interactions. Alcohol can actually intensify symptoms. Antidepressant drugs are often the best choice for patients with chronic anxiety disorder; however, it is important to rule out other organic causes. Short-term treatment with benzodiazepines is also reasonable, but again, organic pathology should be evaluated first or simultaneously.

**Question 134**

A 28-year-old woman presents to your office with complaints of palpitations for the last 6 months. They are accompanied by light-headedness, chest pressure, and nausea. Initially, they tended to occur only two or three times a day; however, they have now become more frequent. The patient has missed work on several occasions due to the symptoms. She notes that the palpitations are so bothersome that she has stopped socializing with friends except at her own home. Her past medical history is otherwise unremarkable. She does not drink alcohol or abuse drugs. She does not use tobacco and reports that her caffeine intake is limited. Her family history is notable for maternal hypertension; her father suffered a stroke 7 months ago. On examination, she appears well nourished and in no distress. Vital signs are as follows: T = 36.5°C, P = 72/minute, RR = 18/minute, and BP = 120/78 mmHg. HEENT examination is normal. The neck is supple without JVD, adenopathy, or bruits. Lungs are clear to auscultation. Heart tones are normal without murmurs, gallops, or rubs. The rest of her physical examination reveals no abnormalities. Ambulatory ECG monitoring shows occasional premature contractions. Which of the following is the most appropriate next step?

a) Order a transthoracic echocardiogram  
b) Begin antidepressant medication  
c) Check a serum TSH  
d) Recommend a glass of wine nightly with dinner  
e) Prescribe alprazolam

**Answer and Discussion**

The answer is c.

**Objective: Understand the key features of Wernicke encephalopathy.**

Wernicke encephalopathy is caused by thiamine deficiency. Alcoholics are the most commonly affected population in the United States. Patients with significant malnutrition are also at risk. The classic triad is ophthalmoplegia, ataxia, and confusion. Cardiovascular beriberi may coexist. The treatment of choice is parenteral thiamine (50 mg daily until the patient resumes a normal diet, which should begin before starting IV glucose infusion). Korsakoff psychosis is a part of Wernicke disease and may occur together with the other components of the illness. Cocaine inhibits catecholamine reuptake at adrenergic nerve endings, thus potentiating sympathetic nervous system activity. Tachycardia, hypertension, pyrexia, and mood stimulation are seen in cocaine overdose.

**Question 135**

A 56-year-old diabetic woman presents with new-onset diplopia and headache. On examination, she has left eye ptosis,
and her left pupil is dilated and fixed to light. The left eye is deviated laterally and slightly downward. The etiology of these abnormalities is which of the following?

- a) Diabetic third nerve palsy on the left
- b) Diabetic sixth nerve palsy on the right
- c) Left pontine lacunar infarct
- d) Surgical third nerve palsy secondary to an aneurysm of the posterior communicating artery
- e) Migraine attack

**Answer and Discussion**

The objective is d.

**Objective:** Understand the multiple functions of cranial nerve III and resulting pathology.

Total palsy of the third nerve causes ptosis, a dilated pupil, and diplopia. Typically, the eye looks down and out. This occurs when all the nerve fibers are affected, which is the case when a circle of Willis aneurysm causes nerve compression and subsequent injury, especially when such an aneurysm ruptures. Most cases of pupil-sparing oculomotor (third cranial nerve) palsy result from a microvascular infarction of the nerve. This occurs in patients with long-standing diabetes mellitus and hypertension. Spontaneous recovery over a period of months is the rule.

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**Question 136**

A 45-year-old woman presents to your office with complaints of fatigue and lethargy. She reports spending most of the day in bed. Her review of symptoms is positive for difficulty sleeping and loss of appetite. She is a single mother but reports that her only son just recently moved out. Family history is positive for schizophrenia. She does not drink alcohol, smoke, or use illicit drugs. She has worked as a secretary in the past, but she is currently on unemployment benefits. Her only medication is a birth control pill. Her vital signs are as follows: T = 36.7°C, P = 80 beats/minute, RR = 16/minute, and BP = 126/81 mmHg. Physical examination is normal. At the conclusion of the examination, she becomes tearful and states that she is not sure her life is worth living. Which of the following factors increases this patient’s risk for death from suicide?

- a) Age
- b) Gender
- c) Family history
- d) Use of birth control
- e) Marital status

**Answer and Discussion**

The objective is e.

**Objective:** Identify risk factors of suicide.

Suicide among men peaks at age 75 years, and among women, it peaks at 55 years. The predominant age groups for suicide are the elderly (>65 years) and adolescents (15 to 24 years). Women are more likely to attempt suicide (3:1), but men are more likely to complete it (3:1). History of recent loss, such as retirement or bereavement, is a risk factor for suicide. Marital status is important in assessing the suicide risk. Single individuals have a higher suicide risk than those who are divorced. Widowed individuals are at higher risk than those who are married. There is no known relationship between birth control pills and suicidality.

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**Question 137**

You are following a 75-year-old woman in the hospital, who was admitted with a left hip fracture from an innocent fall. She is now postoperative day 3, from open reduction and internal fixation. She has suffered no surgical complications. She is now off narcotics and using acetaminophen around the clock with excellent analgesia. She has been participating in physical therapy, and you are making plans to transfer her to a rehabilitation facility tomorrow. This afternoon, you are paged by her nurse, who reports that she has become very restless, and she is demanding and threatening to leave and go home. You immediately go to see the patient and are surprised at the behavior described to you by the nurse because the patient had been very pleasant the previous 3 days. You look at her vital signs and note that her BP has been rising over the last 24 hours and is now 170/98 mmHg; on admission, it had been 128/76 mmHg. She has also developed a sinus tachycardia of 118 beats/minute and a temperature of 38.3°C. When you enter the room, she appears agitated and tremulous and is trying to climb out of bed. On seeing you, she states that she must leave. She appears to be watching something in the room and, on inquiry, states that she is watching little birds that are flying around the room. Her HEENT examination reveals normal pupil size, reactive to light and accommodation bilaterally. Lungs are clear to auscultation. She is tachycardic, but heart tones are normal. Abdominal examination is normal. Her left hip incision is clean and dry with no drainage. Her IV sites are similarly nonerythematous and nontender. Her current medications include enoxaparin, acetaminophen, synthroid, and lactulose. Laboratory studies from this morning reveal a normal complete blood cell count and normal chemistry panel. Which of the following is most likely causing this presentation?

- a) Urinary tract infection
- b) Opiate withdrawal
- c) Fat embolism to the brain
- d) Alcohol withdrawal
- e) Personality disorder

**Answer and Discussion**

The objective is d.

**Objective:** Recognize alcohol withdrawal as a cause for delirium during a hospitalization.

Restlessness, tachycardia, fever, hypertension, and visual hallucinations after 3 days in the hospital are most suggestive of withdrawal from alcohol. Similar presentations may occur with withdrawal from sedative hypnotics. Withdrawal from
either alcohol or sedative hypnotics can cause seizures and may be life-threatening. Opiate withdrawal may present with agitation, but other features include dilated pupils, rhinorhea, nausea, cramps, and restlessness. Personality disorder can present with an agitated, aggressive, or violent behavior, but usually it is not associated with restlessness, tachycardia, fever, and hypertension. Occult infections can cause altered mental status and somnolence, particularly in patients who are bacteremic. However, infection would not typically cause hypertension and signs of a positive delirium as in this case.

**Question 138**

A 75-year-old woman is brought to the ED because of garbled speech and inability to find words. Her husband states that the symptoms developed suddenly and they have persisted for 1 hour. Her past medical history is significant for hypertension and atrial fibrillation. Her medications include metoprolol, warfarin, and enalapril. She is married and does not drink alcohol or use tobacco. On examination, her vital signs are T = 36.5°C, R = 18/minute, P = 73 beats/minute and irregular, BP = 152/94 mmHg, and pulse oximetry = 93% on room air. Patient is awake and alert. HEENT examination shows mild right facial droop but otherwise is normal. Visual field testing is normal. Neck is supple without carotid bruits. Lungs are clear to auscultation. Abdominal examination is normal. Neurologic examination reveals paraphasic substitutions, an impaired ability to repeat sentences verbatim, and mild weakness of the right side of the face and the right arm; no leg weakness is detected. She is hyperreflexic on the right compared with the left. There is a positive Babinski sign on the right. Which of the following diagnostic tests should be done immediately?

a) CT of the head without contrast  
b) Carotid duplex ultrasonography  
c) Echocardiography  
d) Electroencephalography  
e) MRI/MRA of the brain

**Answer and Discussion**

The answer is **d**.

**Objective:** Identify the correct diagnostic workup for an acute stroke.

This patient presents with a syndrome of aphasia and right hemiparesis that suggests acute stroke in the left middle cerebral artery territory. The patient has presented within the 3-hour window during which IV thrombolytic therapy may be given. Thrombolytic therapy can reverse the neurologic dysfunction in patients with acute ischemic strokes. Thus, it is vital to establish through brain imaging the presence and mechanism of stroke as quickly as possible. CT of the head without radiocontrast is initially indicated for patients with suspected stroke and can reliably distinguish acute intracerebral hemorrhage from ischemia. MRI is also an option for the evaluation of patients with acute stroke; however, it is generally more time-consuming and often less available compared with CT. Acquiring results from MRI should never delay the initiation of thrombolytic therapy in potential candidates. Carotid duplex scanning and echocardiography may be useful for establishing the most likely reason for an ischemic stroke but have little role in the acute management. There is no evidence of seizures in this case, and electroencephalography would not be helpful.

**Question 139**

A 67-year-old man presents to your office concerned about his health. Two of his friends have developed lung diseases from dusts they inhaled in their workplace. He wonders if his lungs are alright since he had worked in several dusty places—the shipyards for 20 years followed by foundry work for another 20 years. He is a prior smoker who is currently asymptomatic. Which of the following statements about the pneumoconioses is most correct?

a) Since he is asymptomatic he does not have a pneumoconiosis.  
b) The most common manifestation of asbestos exposure is a benign asbestos pleural effusion.  
c) The risk of developing asbestosis is increased by smoking.  
d) Complications of silicosis include mycobacterial infections and an increased risk of lung cancer.  
e) Individuals with coal workers’ pneumoconiosis never develop progressive massive fibrosis.

**Answer and Discussion**

The answer is **d**.

**Objective:** Identify the complications of silicosis.

Individuals with silicosis are known to have a higher incidence of mycobacterial infections. All patients with silicosis should receive a standardized intradermal tuberculin skin test. If positive (>10 mm) and there is no sign of an active infection, then treatment for latent tuberculosis should be administered. If there is evidence of active tuberculosis, then a standard treatment regimen including rifampin should be administered. The treatment for nontuberculous mycobacteria is no different in those with silicosis.

Many individuals with silicosis and coal workers’ pneumoconiosis are asymptomatic. The most common manifestation of asbestos exposure is a pleural plaque. There is no increased risk of developing asbestosis in smokers. Individuals with coal workers’ pneumoconiosis may develop progressive massive fibrosis. This more commonly occurs when there is concomitant exposure to silica.

**Question 140**

A 45-year-old woman presents to the ED with frequent falls. On interview, she is confused with disorganized speech. A friend who is with her reports that she has been “off-balance” for the past several weeks. She has sustained several falls in the past month and was treated at the local urgent care clinic for skin lacerations and mild bruises. She apparently has...
suffered no head injury. Her friend confirms that she drinks alcohol regularly, usually finishing a six-pack of beer daily along with two to three martinis with dinner. On review of systems, the patient complains of chronic abdominal pain. Her past medical history is remarkable for hypertension and weekly marijuana use. On examination, she is confused, and her vital signs are as follows: T = 35.4°C, BP = 187/110 mmHg, RR = 20/minute, and P = 78 beats/minute. HEENT examination is significant for poor dental hygiene, horizontal nystagmus, and diplopia. The neck is supple without JVD, adenopathy, or bruits. Lungs are clear to auscultation. Heart tones are normal with a soft 1/6 systolic murmur at the left sternal border. Her abdomen is distended and tender to palpation in the epigastrium. There is no hepatosplenomegaly or dullness to percussion noted. There is no peripheral edema, and pulses are symmetric and brisk throughout. Cranial nerves are grossly intact. On gait testing, she is ataxic. An acute abdominal series is negative for free air but does reveal calcifications in the midepigastric area. Head CT without contrast shows cerebral atrophy without evidence of intracranial bleed or masses. Laboratory tests are as follows:

Hgb: 11.6 g/dL
WBC: 8,323 mm³/dL (normal differential)
Platelets: 138,000/μL
Mean corpuscular volume: 107

Which of the following is the most likely explanation for her neurologic symptoms?

a) Acute alcohol intoxication
b) Wernicke encephalopathy
c) Cocaine overdose
d) Cerebellar degeneration
e) Korsakoff psychosis

Answer and Discussion

The answer is b.

Objective: Identify the key features of Wernicke encephalopathy.

Wernicke encephalopathy is caused by thiamine deficiency. Alcoholics represent the most commonly affected population in the United States. Patients with significant malnutrition are also at risk. The classic triad is ophthalmoplegia, ataxia, and confusion. Cardiovascular beriberi may coexist. The treatment of choice is parenteral thiamine (50 mg daily until the patient resumes a normal diet, which should begin before starting the IV glucose infusion). Korsakoff psychosis is a part of Wernicke disease and may occur together with the other components of the illness. Cocaine inhibits catecholamine reuptake at adrenergic nerve endings, thus potentiating sympathetic nervous system activity. Tachycardia, hypertension, pyrexia, and mood stimulation are seen in cocaine overdose.

Question 141

A 21-year-old male college student who was found confused and disruptive by the dorm security staff is brought to the ED. He states that he has no complaints, is not tired, and is “getting ready to party for 8 more hours.” He denies drinking alcohol. He occasionally smokes cigarettes. On examination, he is agitated, heart rate is 113 beats/minute, BP is 155/96 mmHg, RR is 19, and temperature is 37.1°C. His pupils are dilated. Lungs are clear to auscultation. Heart examination reveals regular tachycardia, with the rest of his physical examination within normal limits. ECG shows sinus tachycardia. Laboratory studies and urine drug screen are pending. Given the history and presentation, which of the following is most likely to be detected by the urine drug screen?

a) Amphetamines
b) Nicotine
c) Cocaine
d) Opiates
e) Hallucinogens

Answer and Discussion

The answer is a.

Objective: Identify key features of amphetamine intoxications.

The use of amphetamines as drugs of abuse has increased markedly since 1975. This use affects a myriad of systems, resulting in a wide range of symptoms that may make it a difficult addiction to recognize. The drug is known to cause a massive release of dopamine in the brain, resulting in agitation, delirium, hallucinations, and death. In addition, it causes a decrease in N-acetylaspartate in the frontal lobes and basal ganglia that may explain the chronic central nervous system side effects, such as the lasting psychosis after the drug is stopped, and the choreoathetoid movements. A high index of suspicion is necessary to make an early diagnosis.

Question 142

A 78-year-old man is evaluated in the ED because of left-sided weakness and visual changes. Six hours earlier, the patient was in bed watching television when he noticed a change in his vision and his left arm felt heavy. He said he got up to go to the bathroom, and he kept falling to his left side. He called a friend who brought him to the ED. His past medical history is significant for hypertension and COPD. His medications include an ipratropium inhaler, diltiazem, hydrochlorothiazide, and albuterol as needed. He is widowed and lives alone. He drinks alcohol occasionally and continues to smoke ½ pack of cigarettes daily with a history of approximately 60 pack-years. On examination, he is awake and alert. Vital signs are as follows: T = 36.9°C, P = 87 beats/minute, RR = 18/minute, and BP = 169/98 mmHg. HEENT examination reveals a left homonymous hemianopia. The neck is supple without JVD, adenopathy, or bruits. Lung sounds are diminished throughout, with scattered rhonchi and no wheezes. Cardiac and abdominal examinations are normal. Neurologic examination confirms severe weakness of the left arm, left leg, and left side
of the face. He has neglect of the left side. Speech is normal and full. Laboratory studies are as follows:

<table>
<thead>
<tr>
<th>Test</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Na</td>
<td>142 mmol/L</td>
</tr>
<tr>
<td>K</td>
<td>4.6 mmol/L</td>
</tr>
<tr>
<td>Cl</td>
<td>100 mmol/L</td>
</tr>
<tr>
<td>HCO₃⁻</td>
<td>29 mmol/L</td>
</tr>
<tr>
<td>Cr</td>
<td>1.2 mg/dL</td>
</tr>
<tr>
<td>BUN</td>
<td>19 mg/dL</td>
</tr>
<tr>
<td>WBC</td>
<td>10,000/μL</td>
</tr>
<tr>
<td>Hgb</td>
<td>12.9 g/dL</td>
</tr>
<tr>
<td>Platelets</td>
<td>183,000/μL</td>
</tr>
<tr>
<td>PT/INR</td>
<td>1.1</td>
</tr>
<tr>
<td>PTT</td>
<td>28 s</td>
</tr>
</tbody>
</table>

ECG shows normal sinus rhythm with voltage criteria for left ventricular hypertrophy. CT scan shows a right middle cerebral artery ischemic stroke. Which of the following is the best immediate treatment?

a) Unfractionated heparin, 18 U/kg/h IV infusion
b) Enoxaparin 1 mg/kg SQ
c) Aspirin 325 mg PO
d) Labetalol 40 mg IV
e) Front-loaded tPA IV

**Answer and Discussion**

The answer is c.

**Objective:** Identify the correct treatment plan for an acute stroke.

This patient has had an acute ischemic stroke of the right middle cerebral artery territory. Aspirin given within 48 hours of stroke onset results in a small but significant reduction in the risk of recurrent stroke during the next 2 weeks and improves the overall outcomes at 6 months. Full weight-adjusted anticoagulation with heparin or LMWH does not help patients with hemispheric ischemic stroke and is associated with an increased risk of hemorrhagic conversion. Fixed doses are appropriate for DVT prophylaxis. Antihypertensives, such as labetalol, are not indicated unless the mean arterial pressure (MAP) is over 140 mmHg. The MAP in this case is approximately 120 to 125 mmHg. Giving labetalol in this circumstance could compromise the cerebral blood flow and extend the infarction. This patient is not eligible for tPA because he could not be treated within 3 hours of symptoms onset.

**Question 143**

A 36-year-old woman presents to your office with complaints of intermittent shortness of breath, cough, and wheeze of 6-month duration. She notes her symptoms are worse during the week than on the weekend and were relieved during a recent vacation. She is a nonsmoker with no prior illnesses who works as a spray-painter in an auto body shop. Which of the following statements about her condition is most true?

a) Very few exposures are known to cause this condition.
b) Diagnosis can only be established by challenge testing.
c) Exposure to latex is the leading cause in health-care workers.
d) Exposure can be allowed to continue as long as treatment is provided.
e) An individual must have a preexisting condition to be affected.

**Answer and Discussion**

The answer is c.

**Objective:** Recognize occupational asthma.

Exposure to latex can act as a sensitizer leading to occupational asthma. It is now the most common cause of occupational asthma in health-care workers. There are over 250 exposures known to cause occupational asthma. The diagnosis requires the presence of asthma (symptoms, pulmonary function testing), the recognition of an exposure (history, skin testing, RAST testing), and a work-related pattern to the symptoms. The cornerstone of therapy is avoidance of the exposure. Preexisting asthma may be made worse by the exposure or asthma can be of new onset related to the exposure of concern.
RAPID BOARD REVIEW—KEY POINTS TO REMEMBER:

**Nongonococcal Urethritis**
- *Chlamydia trachomatis* in 50%, *Ureaplasma urealyticum, Trichomonas vaginalis*, and herpes simplex virus (HSV) in 15%, no etiology in 35% of cases.
- Complications include epididymitis and reactive arthritis.
- Partner notification is important because female sexual partners are at high risk for chlamydial infection.
- Urethritis can be diagnosed
  - on clinical grounds alone when a purulent urethral discharge is present.
  - by \( \geq 5 \) polymorphonuclear leukocytes per oil immersion field on the swab smear.
  - by a positive leukocyte esterase test from a first-void urine specimen with \( \geq 10 \) white blood cells per high-power field. Confirm with Gram stain.
- Submit routinely for the detection of *Neisseria gonorrhoeae* and *Chlamydia trachomatis*.

**Mucopurulent Cervicitis**
- The major infectious include *C. trachomatis*, *N. gonorrhoeae*, and HSV.
- The diagnosis is supported by the visualization of a yellow or green endocervical mucopus on a white swab (positive swab test result).
- Treatment should cover both *C. trachomatis* and *N. gonorrhoeae*.

**C. trachomatis Infection**
- The CDC recommends routine annual screening for *C. trachomatis*
  - in all sexually active adolescents and sexually active women \( \leq 25 \) years.
  - in older women with risk factors (new sexual partner or multiple partners).
- Women with documented chlamydial infections undergo routine rescreening 3 to 12 months after the completion of treatment (CDC).

**Gonorrhea**
- In women, gonococcal infections are often asymptomatic.
- Quinolone use is not recommended because of quinolone-resistant *N. gonorrhoeae*.
- Suspect disseminated gonococcal infection when hemorrhagic pustules, symptoms of tenosynovitis, or oligoarthritis are present.
### Genital Ulceration with Regional Lymphadenopathy

<table>
<thead>
<tr>
<th>GENITAL LESIONS</th>
<th>INCUBATION</th>
<th>TYPE</th>
<th>PAIN</th>
<th>NUMBER</th>
<th>DURATION</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary syphilis (<em>Treponema pallidum</em>)</td>
<td>3–90 days</td>
<td>Clean ulcer, raised</td>
<td>No</td>
<td>Usually single</td>
<td>3–6 weeks</td>
</tr>
<tr>
<td>Primary herpes simplex virus (HSV-1 or -2)</td>
<td>1–26 days</td>
<td>Grouped papules, ulcers, vesicles, pustules, Purulent ulcer, shaggy border</td>
<td>Yes</td>
<td>Often multiple</td>
<td>1–3 weeks</td>
</tr>
<tr>
<td>Chancroid (<em>Haemophilus ducreyi</em>)</td>
<td>1–21 days</td>
<td>Papule, vesicle, ulcer</td>
<td>No</td>
<td>Usually single</td>
<td>Few days</td>
</tr>
<tr>
<td>Lymphogranuloma venereum (<em>Chlamydia trachomatis</em>)</td>
<td>3–21 days</td>
<td>Nodules, coalescing granulomatous ulcers</td>
<td>No</td>
<td>Single or multiple</td>
<td>Progressive</td>
</tr>
<tr>
<td>Granuloma inguinale (<em>Calymmatobacterium granulomatis</em>)</td>
<td>8–80 days</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>INGUINAL ADENOPATHY</th>
<th>ONSET</th>
<th>TYPE</th>
<th>PAIN</th>
<th>FREQUENCY</th>
<th>CONSTITUTIONAL SYMPTOMS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary syphilis</td>
<td>Same time</td>
<td>Firm</td>
<td>No</td>
<td>80%, 70% bilateral</td>
<td>Absent</td>
</tr>
<tr>
<td>Primary herpes simplex virus</td>
<td>Same time</td>
<td>Firm</td>
<td>Yes</td>
<td>80%, usually bilateral</td>
<td>Common</td>
</tr>
<tr>
<td>Chancroid</td>
<td>Same time</td>
<td>Fluctuant, may fistulize</td>
<td>Yes</td>
<td>50–65%, usually unilateral</td>
<td>Uncommon</td>
</tr>
<tr>
<td>Lymphogranuloma venereum</td>
<td>26 weeks later</td>
<td>Indurated, fluctuant, may fistulize</td>
<td>Yes</td>
<td>Unilateral, 1/3 bilateral</td>
<td>Common</td>
</tr>
<tr>
<td>Granuloma inguinale</td>
<td>Variable</td>
<td>Suppurating pseudobubo</td>
<td>10%</td>
<td>15%</td>
<td></td>
</tr>
</tbody>
</table>

HSV, herpes simplex virus.

### Syphilis

**Primary Syphilis**
- The diagnosis should be considered in patients with lesions compatible with a chancre, even if nontreponemal and treponemal tests are negative.
  - *The nontreponemal tests:* Venereal Disease Research Laboratory (VDRL) and rapid plasma reagin are positive in 70% and 80%, respectively, of patients.
  - *The treponemal tests:* Fluorescent treponemal antibody absorption test, microhemagglutination assay for antibody to *T. pallidum*, and *T. pallidum* immobilization test are positive in 85%, 65%, and 50%, respectively, of patients.

**Secondary and Tertiary Syphilis**
- Secondary syphilis may present up to 2 years after the initial infection.
- Common clinical manifestations of secondary syphilis include the skin (rash), mouth and throat, genital lesions, constitutional symptoms, and central nervous system.
  - The nontreponemal and treponemal test results are positive in nearly 100% of patients.
  - In the absence of a specific treatment, patients enter a stage of asymptomatic infection termed *latency*.
  - Tertiary syphilis may produce a cardiac (most common aortitis) or neurologic disease (including meningovascular syphilis, tabes dorsalis, and generalized paresis).

### Genital Warts

- Most visible genital warts are associated with low-risk human papillomavirus (HPV) types (e.g., HPV-6 and -11).
- Patients and their partners should be screened for other STDs.
- The quadrivalent vaccine protects against HPV-6, -8, -16, and -18.
In all 50 states and the District of Columbia, adolescents can receive medical care for sexually transmitted diseases without parental consent.

**SUGGESTED READINGS**

**General**


**Genital Ulcer Disease**


**Herpes Simplex Virus Infection**


**Chancroid**


**Lymphogranuloma Venereum**


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**VAGINAL INFECTIONS**

**CLINICAL MANIFESTATIONS AND DIAGNOSIS**

<table>
<thead>
<tr>
<th></th>
<th>NORMAL VAGINA</th>
<th>YEAST VAGINITIS</th>
<th>TRICHOMONIASIS</th>
<th>BACTERIAL VAGINOSIS</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Etiology</strong></td>
<td>—</td>
<td><em>Candida albicans</em>, other yeasts</td>
<td><em>Trichomonas vaginalis</em></td>
<td><em>Gardnerella vaginalis</em>, mycoplasmas, anaerobes</td>
</tr>
<tr>
<td><strong>Symptoms</strong></td>
<td>—</td>
<td>Itching, irritation, discharge</td>
<td>Malodorous discharge, often profuse</td>
<td>White or gray</td>
</tr>
<tr>
<td><strong>Discharge</strong></td>
<td>Clear or white</td>
<td>White</td>
<td>Yellow</td>
<td>Malodorous discharge</td>
</tr>
<tr>
<td><strong>Color and consistency</strong></td>
<td>Nonhomogeneous, flocular</td>
<td>Clumped, adherent plaques</td>
<td>Thin, homogeneous, frothy</td>
<td>None</td>
</tr>
<tr>
<td><strong>Inflammation of vulva/introitus</strong></td>
<td>—</td>
<td>Vaginal erythema, vulvar dermatitis</td>
<td>Vaginal erythema, strawberry cervix</td>
<td>Homogeneous, coats vaginal mucosa</td>
</tr>
<tr>
<td><strong>pH</strong></td>
<td>&lt;4.5</td>
<td>&lt;4.5</td>
<td>≥4.5</td>
<td>≥4.5</td>
</tr>
<tr>
<td><strong>Ammonia odor with 10% KOH</strong></td>
<td>None</td>
<td>None</td>
<td>Usually present</td>
<td>Present</td>
</tr>
<tr>
<td><strong>Microscopy</strong></td>
<td>Epithelial cells, lactobacilli</td>
<td>Leukocytes, epithelial cells, yeast, mycelia, pseudomycelia in up to 80%</td>
<td>Leukocytes, motile trichomonads in 80–90%</td>
<td>Clue cells, few leukocytes, profuse mixed flora</td>
</tr>
</tbody>
</table>

KOH, potassium hydroxide.
Donovanosis

Syphilis

Urethritis and Cervicitis

Chlamydia Infection

Gonorrhea

Human Papillomavirus Infection

Vaginal Infections
RAPID BOARD REVIEW—KEY POINTS TO REMEMBER:

Acute HIV Infection
- The symptoms of acute HIV infection are self-limited and most likely correlate with viremia.
- Fever (mean, 38.9°C), rash, lymphadenopathy, and non-exudative pharyngitis are each present in >70% of individuals.

Chronic HIV Infection
- Frequently, the initial diagnosis of HIV infection is made when the patient develops an AIDS indicator condition.
- The evaluation of fever of unknown origin or unexplained weight loss should always include an HIV test, even in elderly patients without identified risk factors.
- The Centers for Disease Control and Prevention advocates HIV testing for all individuals ages 13 to 64 years, at least once, with additional annual tests for those with risk behaviors.

Diagnosis
- A positive enzyme-linked immunosorbent assay (ELISA or EIA) is only a presumptive evidence of infection with HIV and must be followed and confirmed by a Western blot.
- False-positive EIAs occur in chronic renal failure, malignancies, severe liver disease, vaccination, or autoreactive antibodies (i.e., ANA).
- Indeterminate assays can also occur in early seroconversion. A repeat assay should be performed within 2 to 4 weeks.

Therapy
- Routine health maintenance care appropriate for the individual's age must not be overlooked, including breast, colon, and prostate cancer screening as per current guidelines.
- If CD4 count <200 cells/mm³, Pneumocystis carinii (now Pneumocystis jirovecii) pneumonia (PCP) prophylaxis should be initiated. The first-line agent is trimethoprim–sulfamethoxazole (TMP–SMX), one double-strength tablet daily.
- If CD4 count <100 cells/mm³, patients with positive Toxoplasma gondii IgG serologies require prophylaxis to prevent reactivation. Daily TMP–SMX is the drug of choice.
- If CD4 count <50 cells/mm³, Mycobacterium avium complex prophylaxis is recommended with azithromycin 1,200 mg/week.

ANTIRETROVIRAL THERAPY
- All patients with symptomatic HIV disease or a CD4 count ≤200 should be offered highly active antiretroviral therapy (HAART). The U.S. Department of Health and Human Services (DHHS) recommends the treatment should be given when CD4 ≤500 cells/mm³.
- First-line regimens include two nucleoside/nucleotide reverse transcriptase inhibitors (NRTIs) and either a non-nucleoside reverse transcriptase inhibitors (NNRTI) or a protease inhibitor PI. DHHS recommends one NNRTI-containing regimen (efavirenz) + tenofovir/emtricitabine, two PI-containing regimens (darunavir + ritonavir or atazanavir + ritonavir) + tenofovir/emtricitabine or an integrase (raltegravir) + tenofovir/emtricitabine.
- Follow the viral load every 4 to 8 weeks, immediately after starting the regimen. The viral load should be undetectable after 16 to 24 weeks of therapy.

Pregnancy
- Cesarean section at 38 weeks is recommended if the viral load >1,000 copies/cc in late pregnancy.
- All HIV-infected women with the viral load >1,000 copies/cc should receive intravenous zidovudine during labor (or as a continuous infusion, beginning with a loading dose prior to the planned cesarean section); the infant should receive zidovudine (for 6 weeks after birth) and nevirapine.

Postexposure Prophylaxis
- A percutaneous exposure through a needlestick injury or intravenous drug use results in transmission 0.4% or 0.67% of the time, respectively.
- Basic regimens contain two NRTIs. The most common are zidovudine/lamivudine or tenofovir/emtricitabine.
Addition of a protease inhibitor is recommended when an expanded regimen is selected. The regimen should be initiated as soon as possible, ideally within 1 hour of the exposure, and continued for 28 days.

**NATIONAL GUIDELINES**

- **UPDATED U.S. PUBLIC HEALTH GUIDELINES FOR MANAGEMENT OF OCCUPATIONAL EXPOSURE TO HIV AND RECOMMENDATIONS FOR POSTEXPOSURE PROPHYLAXIS. MMWR RECOMM REP. 2005;54(RR09):1-17.**

**SUGGESTED READINGS**


Marks G, Crepaz N, Janssen RS. Estimating sexual transmission of HIV from persons aware and unaware that they are infected with virus in the USA. *AIDS*. 2006;20:1447-1450.


RAPID BOARD REVIEW—KEY POINTS TO REMEMBER:

The diagnosis of infective endocarditis (IE) requires a high index of suspicion, as well as the assimilation of clinical, laboratory, electrocardiographic, and echocardiographic data.

MODIFIED DUKE CRITERIA

Major Criteria (M)

Microbiologic
- Typical microorganism isolated from two separate blood cultures (BC)
- Microorganism consistent with IE isolated from persistently positive BC
- Single positive BC for Coxiella burnetii or phase 1 immunoglobulin G antibody titer to C. burnetii > 1:800

Evidence of Endocardial Involvement
- New valvular regurgitation (increase or change in preexisting murmur not sufficient)
- Positive echocardiogram

Minor Criteria (m)
- Predisposition to IE that includes injection drug use and certain cardiac conditions:
  - High risk: previous IE, aortic valve disease, rheumatic heart disease, prosthetic heart valve, coarctation of the aorta, and complex cyanotic congenital heart disease
  - Moderate risk: mitral valve prolapse with regurgitation or leaflet thickening, isolated mitral stenosis, tricuspid valve disease, pulmonary stenosis, and hypertrophic cardiomyopathy
- Fever > 38°C (100.4°F)
- Vascular phenomena (petechiae and splinter hemorrhages are excluded)
- Immunologic phenomena (rheumatoid factor, glomerulonephritis, Osler nodes, or Roth spots)
- Positive BC that do not meet the major criteria (serologic evidence of active infection, single isolates of coagulase-negative staphylococci and organisms rarely causing IE are excluded)

Cases Are Defined Clinically As
- Definite: when 2M, or 1M + 3m, or 5m are present
- Possible: when 1M + 1m, or 3m are present

TREATMENT

Certain principles are important when considering treatment of IE:
- The regimen must be bactericidal and prolonged therapy is often necessary
- Vancomycin is less rapidly bactericidal than semisynthetic penicillins and first-generation cephalosporins
- Skin testing should be performed on patients with a questionable history of immediate hypersensitivity reactions to penicillin

INDICATIONS FOR SURGERY IN PATIENTS WITH INFECTIVE ENDOCARDITIS

- Emergency indication for cardiac surgery (same day):
  - Acute aortic regurgitation (AR) with early closure of mitral valve
  - Rupture of a sinus Valsalva aneurysm into the right heart chamber
  - Rupture into the pericardium
- Urgent indication for cardiac surgery (within 1 to 2 days):
  - Valvular obstruction
  - Unstable prosthesis
  - Acute AR or mitral regurgitation with heart failure, New York Heart Association (NYHA) class III–IV
  - Septal perforation
  - Evidence of annular or aortic abscess, sinus or aortic true or false aneurysm, fistula formation, or new-onset conduction disturbances
  - Major embolism + mobile vegetation > 10 mm + appropriate antibiotic therapy < 7 to 10 days
  - Mobile vegetation > 15 mm + appropriate antibiotic therapy < 7 to 10 days
  - No effective antimicrobial therapy available
Incompletely repaired CHD, with residual defects at the fungal endocarditis caused by a mold or yeast infection with difficult-to-treat organisms.

CHAPTER 15 Infective Endocarditis

Elective indication for cardiac surgery (earlier is usually better)
- Staphylococcal prosthetic valve endocarditis
- Early prosthetic valve endocarditis (≤2 month after surgery)
- Evidence of progressive paravalvular prosthetic leak
- Evidence of valve dysfunction and persistent infection after 7 to 10 days of appropriate antibiotic therapy, as indicated by the presence of fever or bacteremia, provided there are no noncardiac causes for infection
- Fungal endocarditis caused by a mold or yeast
- Infection with difficult-to-treat organisms
- Vegetation growing larger during antibiotic therapy >7 days

PROPHYLAXIS

Recommended when procedures that involve manipulation of gingival tissue or the periapical region of teeth or perforation of the oral mucosa is performed in patients with
- Prosthetic cardiac valve or prosthetic material used for cardiac valve repair
- Previous IE
- Congenital heart disease (CHD):
  - Unrepaired cyanotic CHD
  - Completely repaired CHD, during the first 6 month after the procedure
  - Incompletely repaired CHD, with residual defects at the site or adjacent to the site of a prosthetic patch or device
- Cardiac transplantation with cardiac defects

No longer recommended for genitourinary or gastrointestinal tract procedures.

SUGGESTED READINGS


Roberts GJ. Dentists are innocent! “Everyday” bacteremia is the real culprit: a review and assessment of the evidence that dental sur-

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Pneumonias

Place of Acquisition
- Aspiration or influenza in the nursing home—consider *Staphylococcus aureus*.
- Trip to southwestern United States—consider Coccidioidomycosis.
- Trip to Southeast Asia—consider melioidosis or tuberculosis.
- HIV patient from New York City with cough, fever, and night sweats—consider multidrug-resistant tuberculosis.
- Resident of the desert southwestern United States with exposure to rodent excreta—consider Hantavirus pulmonary syndrome.
- Return from Pacific Northwest, not responding to therapy—consider *Cryptococcus gattii*.

Clinical Presentation
- Acute presentation and localized findings—consider typical pathogens such as *Streptococcus pneumoniae*, *Haemophilus influenzae*, and the enteric gram-negative organisms.
- Subacute presentation and absent or diffuse findings—consider atypical pathogens such as *Mycoplasma*, *Chlamydia*, and viruses.
- Rapid progression—consider *S. pneumoniae* (severe), *Staphylococcus aureus*, or *Legionella*.
- Poor dentition and foul-smelling sputum—consider a polymicrobial lung abscess.
- Bullous myringitis—consider *Mycoplasma pneumoniae*.
- Absent gag reflex or altered sensorium—consider aspiration.
- Encephalitis—consider *M. pneumoniae* or *Legionella pneumophila*.
- Cutaneous manifestations include erythema multiforme (*M. pneumoniae*), erythema nodosum (*Chlamydia pneumoniae* and *Mycoplasma tuberculosis*), or ecthyma gangrenosum (*Pseudomonas aeruginosa*).

**Patient Characteristics**
- Exposure to construction sites or old buildings with accumulations of bat or bird droppings—consider *Histoplasma capsulatum* or *Cryptococcus neoformans*.
- Hunters who skin their own rabbits—consider *Francisella tularensis*.
- Farmers working with stored hay, marijuana smokers—consider *Aspergillus* species.
- Neutropenic patients—consider *Aspergillus* species.
- Immunosuppressive medications—consider various viral, fungal, and mycobacterial agents.
- Alcoholism—consider aspiration pneumonia with mixed flora, as well as tuberculosis.
- Chronic obstructive pulmonary disease (COPD)—consider *Moraxella catarrhalis*, *H. influenzae*, and *S. pneumoniae*.
- Diabetes mellitus—consider *S. aureus*.
- Functional or surgical asplenia—consider *S. pneumoniae* and *H. influenzae*.
- Treatment with tumor necrosis factor inhibitors—consider tuberculosis reactivation and endemic mycoses such as histoplasmosis.

Radiography
- The infiltrate may be absent in the dehydrated patient in the first 24 to 48 hours of rehydration.
- Lobar consolidation or a large pleural effusion suggests a bacterial pathogen.
- Cavitation may be found in gram-negative and staphylococcal bacterial abscesses, as well as mycobacterial, fungal, or nocardial infections.
- A rapidly progressing infiltrate from a single to multiple lobes suggests *L. pneumophila*.
- Aspiration commonly affects the right lung, but both can be affected.
- Diffuse interstitial infiltrates in the absence of fluid overload suggest viruses or *P. jirovecii*.
A sputum specimen reflects lower respiratory secretions when >25 white blood cells and <10 epithelial cells are seen in a low-powered microscopic field.

When a sputum specimen shows a predominant organism, it lends a high positive predictive value for the choice of appropriate antimicrobial therapy.

The protected brush catheter quantitatively distinguishes between tracheobronchial colonizers and pneumonic pathogens. When recovered secretions contain $10^3$ colony-forming units (cfu)/mL of a bacterial pathogen, lower respiratory infection should be suspected.

Thoracoscopic or open-lung biopsy—usually reserved for the deteriorating patient with a pneumonia that defies diagnosis by less invasive techniques.

Blood cultures—indicated in patients with severe pneumonia or immune compromised.

Serologic Testing

Serologic testing for Legionella species, Mycoplasma species, and C. pneumoniae should include sera drawn in both acute and convalescent phases. A fourfold increase in the immunoglobulin G (IgG) titer is suggestive of a recent infection with one of these organisms.

A single IgM titer $\geq 1:16$ is judged to be diagnostic of an acute infection with C. pneumoniae.

Urine antigen tests can be used for the detection of L. pneumophila (does not differentiate between past and current infections), S. pneumoniae, and H. capsulatum.

Serum antigen testing can be used for a suspected cryptococcal infection.

Molecular Techniques

Sputum DNA probes can be used for Legionella species, M. pneumoniae, and M. tuberculosis.

Pharmacologic Treatment

Intravenous antibiotics may be switched to oral ones when the patient is stable and afebrile.

The IDSA/ATS guidelines recommend that antimicrobials be continued for at least 5 days or until the patient has been afebrile and stable for 72 hours.

Health care–associated pneumonias are often adequately treated with an 8-day course of systemic antibiotics.

Certain organisms (e.g., Legionella, S. aureus, Pseudomonas, or C. pneumoniae) may require longer courses.

Patients with comorbidities that compromise local (COPD) or systemic (hematologic malignancy) immunity may take longer to clear their illness.

Suggested readings


RAPID BOARD REVIEW—KEY POINTS TO REMEMBER:

Acute Infectious Diarrhea
- Norovirus is the most common cause of foodborne outbreaks, followed by Salmonella.
- The most common causes of dysentery (grossly bloody stools) in descending frequency are Shigella, Campylobacter, nontyphoid Salmonella, and Shiga toxin–producing Escherichia coli (STEC).
- Indications for stool culture and assay to detect STEC include passage of ≥6 unformed stools/day, persistent diarrhea for ≥1 week, fever, dysentery, and outbreak settings.
- The diagnosis depends on the incubation period, epidemiologic, and clinical clues.
- Rehydration is the most important measure in the management of acute infectious diarrhea (AID).
- A diet of easily digestible food is generally recommended.
- Although many cases of bacterial diarrhea may resolve without a specific antimicrobial therapy, several patient groups who are at risk of systemic complications should receive antimicrobial therapy; the choice of which one depends on the causative pathogen.
- Rifaximin or bismuth subsalicylate reduces the risk of traveler’s diarrhea by about 70%.

Urinary Tract Infections
- Women are at a higher risk for urinary tract infection (UTI) than men. Up to 50% of women have recurrent UTI within 2 years of an initial episode.
- Escherichia coli is the most common causative organism.
- Typical symptoms are sufficient for the diagnosis of acute cystitis, and urinalysis may aid in patients with atypical presentations.
- Routine urine culture is indicated before initiating the treatment for pyelonephritis, complicated UTI, catheter-associated UTI, or prostatitis, but not for a simple cystitis.
- Nitrofurantoin, trimethoprim/sulfamethoxazole (TMP–SMX), TMP, and fosfomycin are the first-line antibiotics for simple cystitis, and TMP–SMX or a quinolone for acute pyelonephritis or prostatitis. Antimicrobial therapy for complicated UTI and catheter-associated UTI should be directed by culture results.
- Screening for and treatment of asymptomatic bacteriuria is indicated in early pregnancy and before urologic procedures in which mucosal bleeding is anticipated.
- Options for recurrent cystitis in women are continuous prophylaxis, postcoital prophylaxis, or self-initiated therapy.
- Topical intravaginal estriol cream in postmenopausal women reduces recurrent UTIs.

Upper Respiratory Tract Infections
- Symptoms such as production of yellow sputum, sore throat, fever, and colored nasal discharge have poor predictive evidence for the efficacy of the prescribed antibiotics.
- A maculopapular rash is noted on presentation in 5% to 10% of infectious mononucleosis cases due to Epstein-Barr virus (EBV), and in up to 95% of patients who receive ampicillin or amoxicillin for presumed group A streptococci (GAS) pharyngitis.
- In patients with mononucleosis due to EBV, lymphocytosis and large, lobulated “atypical” lymphocytes are often seen on peripheral blood smears (sensitivity 75% and specificity 92%).
- Treatment of infectious mononucleosis is supportive; antiviral agents are not recommended.
- Although GAS causes only 10% of pharyngitis cases in adults, about 70% of those presenting with sore throat to primary care physicians receive antibiotics.
- At least 10% of the pharyngitis cases in people aged 15 to 24 years are due to Fusobacterium necrophorum.
- The clinical diagnosis of GAS pharyngitis is not reliable. Thus, throat swab for streptococcal rapid antigen detection test (RADT) using chemiluminescent deoxyribonucleic acid (DNA) probes should be done to guide the antimicrobial therapy (sensitivity 70% to 90% and specificity 95%). A negative RADT should be backed by the culture (90% to 95% sensitive).
- Oral penicillin or amoxicillin for 10 days remains the treatment of choice for GAS pharyngitis. Alternatives include intramuscular benzathine penicillin, oral first-generation
cerebrosporins, oral macrolides, or oral clindamycin. Tetracyclines, sulfonamides, and fluoroquinolones, particularly ciprofloxacin, are not recommended.
- Tonsillectomy to reduce the frequency of GAS pharyngitis is not recommended in adults.
- Majority (90% to 98%) of acute sinusitis cases are due to viruses, with only about 2% to 10% caused by bacteria (Streptococcus pneumoniae 38%, Haemophilus influenzae 36%, Moraxella catarrhalis 16%, Staphylococcus aureus 13%, and Streptococcus pyogenes 4%).
- Purulent nasal drainage and facial pain are the cardinal features of acute sinusitis. Clinical scenarios suggestive of acute bacterial sinusitis include persistence of symptoms without improvement for ≥10 days, severe symptoms (such as fever ≥102°F) lasting 3 to 4 days, or initial improvement followed by a later worsening of symptoms.
- Majority of patients with acute sinusitis do not require imaging studies, culture confirmation by sinus endoscopy, or sinus aspiration. Nasal cultures are not representative.
- Most cases of mild sinusitis improve with topical intranasal steroids and topical or systemic nasal decongestants, without antimicrobial therapy. For patients with features suggestive of acute bacterial rhinosinusitis, amoxicillin–clavulanic acid for 5 to 7 days is the first-line agent, with doxycycline as an alternative choice. Respiratory fluoroquinolones or a combination of an oral third-generation cephalosporin are second-line agents. High doses of amoxicillin–clavulanic are recommended for certain populations. Macrolides, TMP–SMX, and second- or third-generation cephalosporins monotherapy are not recommended.
- Most cases of acute bronchitis are due to viruses. Symptoms last 3 weeks. Treatment is symptomatic.
- Patients with influenza typically present with sudden diffuse or throbbing headache, high fever, severe myalgia, and dry cough.
- Rapid “point of care” influenza tests can rule in, but not rule out the diagnosis. Thus, it should be backed up by a more sensitive PCR test.
- Neuraminidase inhibitors, oseltamivir and zanamivir, shorten the duration of influenza illness by 1 to 2 days, prevent hospitalizations, secondary complications, and death.
- Health care facilities should track influenza vaccination of health-care workers.

**Soft Tissue Infections**

- Purulent cellulitis is mostly due to methicillin-resistant *Staphylococcus aureus* (MRSA) 59% and methicillin-susceptible *Staphylococcus aureus* (MSSA) 17%, while diffuse, nonpurulent/nonculturable cellulitis is mostly due to GAS (70%) and MSSA.
- Empiric oral antimicrobial choices for purulent cellulitis include clindamycin, TMP–SMX, tetracycline, or linezolid, and for nonpurulent cellulitis, dicloxacillin, or cephalaxin.
- Almost all cases of erysipelas are due to GAS. Penicillin is the treatment of choice.
- Most infected bite wounds are polymicrobial. Treat with amoxicillin–clavulanic acid.
- In contrast to paronychia or felon treatment, incision and drainage are contraindicated for herpetic whitlow because this may result in viremia or a secondary bacterial infection.
- Antifungal therapy for onychomycosis takes several weeks, so microbiologic documentation is required.

**SUGGESTED READINGS**


**Acute Infectious Diarrhea**


Urinary Tract Infections


Upper Respiratory Tract Infections


**Soft Tissue Infections**


Cheah AE, Chong AK. Bites to the hand: are they more than we can chew? Singapore Med J. 2011;52(10):715-718, quiz 719.


Hoff NP, Gerber PA. Herpetic whitlow. CMAJ. 2012;184(17):E924.


Question 1

A 19-year-old man has low-grade fever, tender inguinal adenopathy, and grouped vesicles on his penis. He has never had a sexually transmitted disease before, and he has a new female partner. How should this patient be managed?

a) Acyclovir cream applied to the lesions three times daily until resolution
b) No therapy because trials have failed to demonstrate efficacy in this setting
c) Acyclovir, 400 mg orally three times daily
d) Acyclovir, 5 mg/kg intravenously every 8 hours
e) None of the above

Answer and Discussion

The answer is c.

Objective: Identify and manage the genital herpes simplex infection.

The patient has primary herpes simplex virus infection. Topical agents have no role in therapy, and intravenous therapy is reserved for patients who experience complications of primary human immunodeficiency virus (HIV) infection, such as pneumonitis, encephalitis, or hepatitis. The patient should receive some form of treatment because therapy partially relieves symptoms and accelerates healing. Newer antivirals are now available as alternatives to acyclovir. They include famciclovir, 250 mg orally three times daily or valacyclovir, 1 g orally twice daily for 7 days.

Question 2

A 26-year-old man has a penile lesion for several weeks and new swelling in the groins. On examination, a single nontender penile ulcer and bilateral palpable nontender inguinal lymph nodes are present. Rapid plasma reagin test results are negative. The most likely diagnosis is:

a) Lymphogranuloma venereum
b) Chancroid
c) Primary syphilis
d) Variant herpes simplex virus infection
e) Granuloma inguinale

Answer and Discussion

The answer is c.

Objective: Identify limitations of laboratory tests in primary syphilis.

In primary syphilis rapid plasma reagin (RPR) test results are positive in only 70% of the patients. Thus, a negative RPR result does not rule out the diagnosis. The five options listed are part of the differential diagnosis for the syndrome of genital ulcers with regional adenopathy. In the United States, the three most common etiologies for genital ulceration and regional lymphadenopathy are herpes simplex virus (HSV), syphilis, and chancroid. Genital ulcers associated with HSV and chancroid (infection with Haemophilus ducreyi) generally present as multiple, painful ulcers. They generally have painful regional lymphadenopathy as well. Lymphogranuloma venereum (LGV) is an infection with Chlamydia trachomatis (typically serovars L1-3). LGV typically presents with a non-painful ulcer and tender lymphadenopathy or as a painful “buboe” formation (seen also with chancroid). From an epidemiologic standpoint, it is less common than primary syphilis and should be considered after consideration of primary syphilis. Granuloma inguinale is secondary to Klebsiella granulomatis infection and typically presents with a non-painful ulcer. These patients typically do not have lymphadenopathy, but may have painful “buboe.”

Question 3

A 44-year-old man has had a painful penile ulcer and tender inguinal lymph nodes on the right side for several weeks. He had a negative HIV test 1 year before, but had frequent encounters with prostitutes. He saw several physicians, apparently without a diagnosis. On examination, the lymph nodes are fluctuant and have a fistula with pus. Which of the following would be effective treatment?

a) Azithromycin, 1 g orally twice daily for 7 days
b) Ceftriaxone, 250 mg intramuscularly once
c) Ciprofloxacin, 500 mg orally once
d) All of the above
e) None of the above

Answer and Discussion

The answer is b.

Objective: Identify and manage the Haemophilus ducreyi infection (a.k.a. chancroid).

The correct diagnosis is chancroid, an infection with Haemophilus ducreyi. Chancroid typically presents as a painful genital ulcer and tender regional lymphadenopathy. The ulcer usually has clearly demarcated borders and sometimes undermined. A
gray or yellow purulent exudate may be present over the ulcer, with a tendency to bleed when scraped. The inguinal lymphadenitis can sometimes liquefy and present as painful, fluctuant “buboes” that leak frank pus (as was seen in this patient). There is a high rate of co-infection with HIV.

One intramuscular dose of ceftriaxone is the recommended regimen. Azithromycin is another option, but a single dose is sufficient, rather than a 7-day course of therapy. Ciprofloxacin is effective but needs to be given twice daily for 3 days. Finally, erythromycin can be used at a dose of 500 mg orally four times daily for 7 days.

**Question 4**

A 27-year-old woman comes to the office because her boyfriend was recently diagnosed with genital herpes. She is sexually active and does not use condoms. She is asymptomatic and her pelvic examination is normal. She is requesting some type of evaluation for herpes. What is the most appropriate next step?

a) Oral acyclovir for 7 to 10 days  
b) Tzanck smear of the cervix  
c) Glycoprotein G–based herpes simplex virus (HSV) serologies  
d) HSV nucleic acid testing from blood and cervix

**Answer and Discussion**

The answer is **c**.

**Objective: Identify the guidelines on partner testing for genital herpes.**

The Centers for Disease Control and Prevention (CDC) recommended offering testing to those who want to be tested, even if they are not symptomatic. The CDC also recently advocated the use of type-specific glycoprotein G–based serologic tests for the diagnosis of genital herpes in certain circumstances, particularly in suspected cases that are culture negative. A positive herpes simplex virus type 2 antibody test is indicative of an infection with anogenital herpes at some time in the past. The antibody test may be useful in the partner evaluation, although pretest counseling is important. The test is not recommended for routine screening in the population but should be made available to anyone requesting testing.

**Question 5**

A 60-year-old woman is referred for a positive Venereal Disease Research Laboratory (VDRL) test result. She is asymptomatic, except for mild memory loss. She recalls having syphilis as a teenager but never receiving treatment. Cerebrospinal fluid (CSF) examination shows no white blood cells, normal protein, and normal glucose; the CSF VDRL is nonreactive. How should the patient be managed next?

a) Erythromycin, 250 mg orally, four times daily for 2 weeks  
b) Hospitalization and treatment with aqueous crystalline penicillin G at 12 million U intravenously daily for 14 days  
c) Benzathine penicillin G, 2.4 million U intramuscularly (IM) once  
d) Benzathine penicillin G, 2.4 million U IM each week for 3 weeks

**Answer and Discussion**

The answer is **d**.

**Objective: Identify and treat late-latent syphilis.**

The patient has late-latent syphilis. This is evidenced by the fact that the patient has persistently positive nontreponemal tests, representing a previously infected patient without evidence of active disease. The recommended therapy is 3 weekly IM doses of benzathine penicillin G. In penicillin-allergic patients, doxycycline or tetracycline should be given for 4 weeks.

**Question 6**

Which of the following statements about secondary syphilis is false?

a) A rash is the most common clinical manifestation.  
b) Erythromycin is the treatment of choice in penicillin-allergic patients.  
c) Up to 20% of patients have a genital lesion evident.  
d) Nontreponemal test results are almost always positive.

**Answer and Discussion**

The answer is **b**.

**Objective: Identify the important features of secondary syphilis.**

Doxycycline, not erythromycin, is the treatment of choice for secondary syphilis in penicillin-allergic patients. All the other statements are correct. The rash can manifest in many different ways, and by the time it is present, nontreponemal test results are positive almost 100% of the time, making the diagnosis relatively easy, if considered.

**Question 7**

A 19-year-old sexually active man (HIV negative) has dysuria and urethral discharge. He has a new sexual partner. Gram stain of the discharge shows >10 white blood cells per oil immersion field. Which of the following statements is false?

a) He should be specifically tested for *Chlamydia trachomatis*.  
b) He should be specifically tested for *Neisseria gonorrhoeae*.  
c) If the patient is unreliable for follow-up, he should be treated with antibiotics empirically.  
d) This condition could be caused by herpes simplex virus.  
e) Asymptomatic infection is rare.

**Answer and Discussion**

The answer is **e**.

**Objective: Identify the features of infectious urethritis/cervicitis.**

Many men and women with urethritis/mucopurulent cervicitis are minimally symptomatic or asymptomatic. Causative
agents include *N. gonorrhoeae*, *Chlamydia trachomatis*, herpes simplex virus, *Trichomonas vaginalis*, and *Ureaplasma urealyticum*. If a patient is unreliable, he should be treated empirically to help prevent further spread of the infection to other sexual partners.

**Question 8**

A 19-year-old man presents with a painful urethral discharge. He denies any history of prior sexually transmitted diseases. Gram stain of the discharge shows white blood cells with intracellular gram-negative diplococci. The next step is:

- a) No treatment until cultures of the discharge are finalized
- b) Ciprofloxacin, 500 mg orally once
- c) Ceftriaxone, 250 mg intramuscularly (IM) once and azithromycin 1 g orally once
- d) Ceftriaxone, 250 mg IM once
- e) None of the above

**Answer and Discussion**

The answer is c.

**Objective: Identify and manage gonococcal urethritis/cervicitis.**

The patient has gonorrhea. Gram stain is diagnostic, so there is no need to wait for the culture results. Due to the high prevalence of quinolone-resistant *N. gonorrhoeae*, empiric ciprofloxacin use is not appropriate. The lower dose of ceftriaxone is sufficient and empiric therapy for chlamydial infection should always be used concurrently with antimicrobial therapy.

**Question 9**

A 35-year-old woman complains of a several-day history of malodorous vaginal discharge. On pelvic examination, a gray homogeneous discharge is present. Examination of the discharge reveals a pH of 6. Gram stain shows clue cells. The most likely diagnosis is:

- a) Trichomoniasis
- b) *Chlamydia trachomatis* infection
- c) Bacterial vaginosis
- d) Yeast vulvovaginitis
- e) None of the above

**Answer and Discussion**

The answer is c.

**Objective: Identify and manage bacterial vaginosis (BV).**

Gram stain shows clue cells, which are characteristic of bacterial vaginosis. Trichomoniasis can also cause an increased vaginal pH, but does not demonstrate clue cells on the wet-mount preparation. Neither of these findings is present in a vaginal yeast infections or chlamydial cervicitis.

**Question 10**

A 58-year-old woman presents with a 3-week history of nonproductive cough and hoarseness. She reports a temperature of 100.4°F. She is not short of breath and has no chills or sweats. She has a smoking history of 20 packs per year but quit 20 years ago. She lives at home with her husband, who is asymptomatic. She has had several antibiotics in the past week, of which she comments, “I felt a little better after the clarithromycin, but not much, so my doctor changed me to cefuroxime, and I felt worse.” On examination, she appears healthy. She has a low-grade fever of 38°C, her vital signs are otherwise normal. The physical examination is unremarkable. Laboratory evaluation is notable only for a normal white blood cell count with a mild left shift. Chest radiograph reveals a subtle right-sided infiltrate. The most appropriate next step in the care of this patient would be:

- a) Admission for high-dose intravenous erythromycin
- b) Outpatient therapy with oral doxycycline
- c) Admission for intravenous ceftriaxone
- d) Outpatient therapy with oral ciprofloxacin
- e) Home intravenous antibiotic therapy with piperacillin/tazobactam

**Answer and Discussion**

The answer is b.

**Objective: Identify and manage community-acquired pneumonia with features suggesting atypical pathogens.**

The patient presents from community with a subacute, indolent illness and radiographic evidence of pneumonia. No mortality risk factors are present, and admission is probably not warranted. Piperacillin/tazobactam has no activity against common atypical bacterial organisms. Ciprofloxacin has poor activity against gram-positive organisms and should not be used in this setting. Correct therapeutic options include oral tetracyclines, macrolides, levofloxacin, gatifloxacin, or moxifloxacin. In this case, the hoarseness and partial response to clarithromycin raise suspicion for *Chlamydia pneumoniae* as a pathogen. Doxycycline is preferred in this setting.

**Question 11**

A 23-year-old male college student presents in late December with a 5-day history of nonproductive cough and shortness of breath. He notes that a number of his fellow students have had respiratory illnesses over the past 2 months. He has recently tested HIV negative. Physical examination shows that he is in good physical condition. His temperature is 38.3°C, his heart rate is 120 beats per minute, his respiratory rate is 22 breaths per minute, and his blood pressure is 90/60 mmHg. The examination is otherwise remarkable only for a few scattered rales at the lung bases. On laboratory evaluation, he is hypoxemic with a PO2 of 76. The white blood cell count is 14,000/mm3, with a marked left shift. His hemoglobin is 8.3 g/dL, and his peripheral smear shows red blood cell fragments. Chest radiograph reveals bilateral patchy lower lobe infiltrates.

The patient deteriorates soon after admission, requiring mechanical ventilation and vasopressors. Chest radiograph
reveals progression of the infiltrates with involvement of all five lung lobes. A Swan-Ganz catheter is placed, revealing a high systemic vascular resistance and a low cardiac output.

The most appropriate empiric antimicrobial therapy for this patient is:

a) Trimethoprim–sulfamethoxazole 5 mg/kg intravenously (IV) every 6 hours
b) Doxycycline 100 mg IV every 12 hours
c) Piperacillin/tazobactam 3,375 g IV every 6 hours
d) Azithromycin 500 mg intravenously every day plus ceftriaxone 1 g IV every day
e) Clindamycin 900 mg IV every 8 hours

Answer and Discussion
The answer is d.

Objective: Manage community-acquired pneumonia in a severely ill patient.

The patient is acutely and severely ill with a community-acquired process. By IDSA guidelines, the appropriate therapy consists of a combination between a macrolide or fluoroquinolone and ceftriaxone, cefotaxime, or a β-lactam/β-lactamase inhibitor. Because he is HIV negative and acutely ill, trimethoprim–sulfamethoxazole would not provide adequate coverage for either atypical or serious gram-negative pathogens. Likewise, neither piperacillin–tazobactam nor the combination of clindamycin and ceftazidime would cover atypical pathogens. Intravenous doxycycline alone would not cover all likely typical bacterial pathogens. Of the provided answers, only the combination of azithromycin and ceftriaxone would treat severe pneumonia due to both Legionella and typical bacterial pathogens.

This patient presents with several clinical clues to the correct diagnosis. He presents with a nonproductive cough and low-grade fever, suggesting an atypical pathogen. His sputum Gram stain shows no predominant organism, despite a fulminant process. He has evidence of hemolytic anemia and cardiac dysfunction, illustrating the potentially severe complications of an ordinarily indolent pathogen.

Question 12

A 66-year-old man with a history of non-Hodgkin’s lymphoma presents with a 2-week history of dry cough and low-grade fever in January. He has a pet parakeet, and his grandchild has a respiratory illness. His lung examination is remarkable for a few rales at the lung bases. His chest radiograph (X-ray) initially reveals faint infiltrates in both lung bases.

The patient is admitted to the hospital and levofloxacin is administered intravenously. Despite the therapy, the patient’s respiratory status worsens over the first 48 hours of hospitalization. He is admitted to the intensive care unit and requires mechanical ventilation. Subsequent chest x-ray shows reticulonodular infiltrates throughout both lung fields.

Which of the following are causes of therapy failure in community-acquired pneumonia?

a) Wrong diagnosis
b) Empyema
c) Poor adherence to the medical regimen
d) a and c
e) a, b, and c

Answer and Discussion
The answer is e.

Objective: Identify reasons for treatment failure in patients with community-acquired pneumonia.

Several factors can contribute to initial antibiotic therapy failure in community-acquired pneumonia. First, one should consider the correctness of the diagnosis. A number of diagnoses may lead to pulmonary infiltrates, including noninfectious diseases such as heart failure. Host factors such as empyema, immunodeficiency, and bronchial tree obstruction may slow the response to antibiotics. It is also important to consider difficulties with the regimen itself: Is this the wrong drug or dose? Is the patient adhering to the regimen? The clinician must also place less common microbial pathogens in the differential diagnosis, as some pathogens do not respond to standard antibiotic regimens. Finally, certain pathogens, such as Legionella species and Streptococcus pneumoniae, may cause overwhelming infection that may not immediately respond to antibiotics.

In this circumstance, the patient is immunocompromised by virtue of his lymphoma. He has a pet parakeet and might have pneumonia caused by an unusual pathogen, such as Chlamydia psittaci. He has a grandchild with a respiratory illness, but it is January, raising the question of viral pathogens such as influenza, respiratory syncytial virus, adenovirus, parainfluenza virus, and others. Given his rapid decline, bronchoscopy is likely indicated to obtain a specimen for staining and culture for a broad range of pathogens. Serology may be useful to help diagnose infection with Chlamydia species or other atypical pathogens, such as Legionella and Mycoplasma species.

Question 13

A 67-year-old woman with steroid-dependent asthma is admitted to the hospital with fever (temperature 37.9°C), cough, and myalgia. Chest radiography reveals an increase in interstitial markings bilaterally, and the polymerase chain reaction from a nasopharyngeal swab is positive for influenza A. Because of immune suppression, the patient is treated with oseltamivir. The patient experiences resolution of the fever and myalgia and improved cough over the first 2 hospital days, but fever recurs and is accompanied by a productive cough and chills on the third hospital day. On examination, the patient looks acutely ill. Her temperature is 38.5°C, pulse is 126 beats per minute, respiratory rate is 3 breaths per minute, and blood pressure is 90/58 mmHg. There are coarse crackles heard at the left lung base. Chest
radiography now reveals a dense lobar infiltrate at the left base. Which of the following is not an appropriate measure in the care of this patient?

a) Blood cultures
b) Sputum Gram stain and culture
c) Intravenous vancomycin
d) Replace oseltamivir with amantadine
e) Intravenous linezolid

**Answer and Discussion**

The answer is d.

**Objective:** Identify principles of management of acute influenza infections.

This patient, who is seemingly recovering from acute influenza A, suffers a relapse of symptoms with a more acute presentation. The primary concern is for a bacterial superinfection in the lungs. *Staphylococcus aureus* and *Streptococcus pneumoniae* are important pathogens in this setting; community-acquired methicillin-resistant *Staphylococcus aureus* (CA-MRSA) is a concern in this toxic-appearing patient. Blood and sputum studies are clearly indicated to identify a pathogen and direct therapy. Intravenous vancomycin and linezolid are therapeutic options for CA-MRSA. Given the clinical course and radiographic change, it is unlikely that a change in antiviral therapy will have an effect on the patient’s course.

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**Question 14**

A 45-year-old man with Crohn’s disease treated with infliximab presents in December with an increasing nonproductive cough and fever over the past 2 weeks. He denies myalgia but has considerable fatigue. He is prescribed a 5-day course of oral levofloxacin without any improvement. He seeks care again for worsening symptoms. On examination, he looks chronically ill and is actively coughing without sputum production. The patient’s temperature is 37.7°C, and vital signs are otherwise normal. The lung examination is clear. A chest radiograph shows diffusely scattered small nodules.

Which measure is not appropriate in the care of this patient?

a) Protein purified derivative skin testing
b) Bronchoscopy with bronchoalveolar lavage and transbronchial biopsy
c) Fungal complement fixation and immunodiffusion serology battery
d) *Histoplasma* urinary antigen
e) *Streptococcus pneumoniae* urinary antigen

**Answer and Discussion**

The answer is e.

**Objective:** Identify respiratory pathogens in patients receiving tumor necrosis factor (TNF)-α inhibitors.

Therapy with TNF inhibitors such as infliximab has been associated with reactivation of tuberculosis and endemic mycoses such as histoplasmosis. In this setting, protein purified derivative skin testing, *Histoplasma* urinary antigen testing, and fungal serology battery are clearly indicated. Because skin and serologic testing can yield delayed or no diagnosis, bronchoscopy can be critical to obtain diagnostic specimens and direct antimicrobial therapy. The patient’s subacute illness and the radiographic pattern are less consistent with “typical” bacterial pathogens such as *Streptococcus pneumoniae*, and pneumococcal urinary antigen testing is not indicated for this patient.

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**Question 15**

A 30-year-old healthy woman presents with non-bloody diarrhea that has persisted for less than 24 hours. She has nausea and abdominal cramping, but no fever or tenesmus. No recent travel is noted, and her examination is normal. You should

a) Ask her if other family members are affected
b) Check fecal leukocytes by microscopy or lactoferrin
c) Collect stools for bacterial culture and rotavirus polymerase chain reaction
d) Tell her to avoid antidiarrheal agents such as loperamide
e) Start ciprofloxacin empirically

**Answer and Discussion**

The answer is a.

**Objective:** Identify the etiology and management of acute diarrhea.

If acute infectious diarrhea can be linked to the ingestion of a certain meal (for example in a family outbreak setting), the incubation period can be helpful for diagnosis. *Staphylococcus aureus* and *Bacillus cereus* have incubation periods of less than 6 hours, *Clostridium perfringens* and *B. cereus* between 6 and 24 hours, noroviruses, enterotoxigenic *Escherichia coli*, *Vibrio*, *Salmonella*, *Shigella*, *Campylobacter*, *Yersinia*, *Giardia*, *Cyclospora*, *Cryptosporidium* between 16 and 72 hours, respectively. Certain foods are also linked to particular infections: undercooked poultry to campylobacteriosis, undercooked hamburger to shiga toxin-producing *E. coli* (STEC), seafood to *Vibrio* species, improperly refrigerated fried rice to *B. cereus*, fresh soft cheeses to *Listeria monocytogenes*, contaminated eggs to *Salmonella* species, unrefrigerated potato salad to *Staphylococcus aureus* (preformed enterotoxin), and undercooked pork to *Yersinia enterocolitica*.

The most likely cause in this patient is a viral infection. Because the illness is less than 24 hours in duration and is not associated with inflammatory features, the detection of fecal leukocytes and stool cultures are not indicated at this time. Rotavirus polymerase chain reaction should not be used in routine clinical care. Oral rehydration is the appropriate management here. Antimotility agents such as loperamide and diphenoxylate may be used here if needed because the diarrhea is not bloody. Empiric antimicrobials are indicated for moderate to severe travelers’ diarrhea, and febrile, community-acquired, inflammatory diarrhea, particularly in immunocompromised patients, unless STEC is suspected on epidemiologic grounds. Severe nosocomial
diarrhea in patients receiving systemic antibiotics or chemotherapeutic agents should also be treated empirically with metronidazole, pending the results of a *Clostridium difficile* toxin assay. Persistent diarrhea for more than 10 days should raise the concern of protozoal pathogens, such as *Giardia* and *Cryptosporidium*; empiric therapy with metronidazole, pending stool microscopy or immunoassay, is reasonable in this setting.

**Question 16**

A 22-year-old woman presents with dysuria and foul-smelling urine for 24 hours. No fever or suprapubic or flank pain is present. She had a similar episode in the past year. She uses spermicide-coated condoms and diaphragms for contraception. Her examination is normal. You should

a) Collect urine for culture  

b) Order ultrasound of the urinary bladder and kidneys  

c) Prescribe trimethoprim–sulfamethoxazole for 7 days  

d) Advise her to avoid vaginal spermicides  

e) Advise against future self-treatment or prophylaxis

**Answer and Discussion**

**Objective:** Manage acute uncomplicated cystitis.

The microbiology of acute uncomplicated cystitis is women is predictable, so empiric antimicrobial therapy would be appropriate. Collecting urine for culture should be considered if empirical therapy fails. Ultrasound of the urinary bladder may be useful in cases with persistent symptoms to rule out the presence of a stone or diverticulum. Renal ultrasound should be considered if a clinical suspicion for upper UTI is present. First-line treatment for uncomplicated cystitis includes TMP–SMX for 3 days. Extending therapy for 7 days may be considered in patients with persistent symptoms. Other agents that are commonly used in the United States are nitrofurantoin (100 mg twice daily for 5 days) and fosfomycin (3 g in a single dose). Fluoroquinolones and β-lactams are generally efficacious agents, but the most recent Infectious Disease Society of America (IDSA) guidelines recommend against using them as first-line agents given their higher rates of adverse events. The use of vaginal spermicides is a known risk factor for UTI; women with recurrent UTI should be advised to use another form of contraception. Once the diagnosis is established, antimicrobial self-treatment at the onset of dysuria and postcoital prophylaxis are reasonable options for this young woman with recurrent cystitis.

**Question 17**

A 20-year-old college student presents with fever, sore throat, myalgia, splenomegaly, and generalized lymphadenopathy. Which of the following is true?

a) HIV testing should be considered. Treatment is symptomatic.  

b) A vaccine could have prevented this illness. Specific therapy is indicated if presenting within 48 hours.  

c) *Streptococcus pneumoniae* and *Haemophilus influenzae* are likely causes. Amoxicillin remains the first-line agent.  

d) Fever, tonsillar exudate, tender anterior cervical lymphadenopathy, and absence of cough increase the likelihood of group A β-hemolytic streptococcus (GABHS) infection.  

e) Rhinovirus is the most common cause. No diagnostic tests are needed.

**Answer and Discussion**

**Objective:** Identify the differential diagnosis for a mononucleosis-type illness.

In the appropriate setting, patients presenting with a mononucleosis-type illness should be questioned about their sexual practices because the acute retroviral syndrome has a similar presentation. HIV antibody test is usually negative during the acute illness and may require several weeks or months to become positive. An accurate diagnosis requires a plasma HIV RNA test or HIV p24 antigen detection. This has clear clinical and public health implications because a large proportion of HIV-infected people are not aware of their HIV status; thus, they may present at a later stage of disease, while continuing to transmit the infection to others. The CDC currently recommends the “opt-out” HIV screening approach, where assent is inferred unless the patient declines testing. The statement in (b) refers to a patient with influenza, an illness that, unlike infectious mononucleosis, may be preventable with a vaccine and is treatable with specific antiviral agents. The statement in (c) refers to a patient with acute sinusitis, which is not associated with splenomegaly or generalized lymphadenopathy. The statement in (d) refers to a patient with “strep throat,” a form of pharyngitis more common in children than adults and associated with certain clinical features that do not include splenomegaly or generalized lymphadenopathy. The statement in (e) could apply to a patient with nonspecific upper respiratory tract infection (common cold) or bronchitis; these illnesses are gradual in onset and, again, not associated with splenomegaly or generalized lymphadenopathy.

**Question 18**

A 60-year-old diabetic woman with history of varicose veins has mild fever and painful, ill-defined redness around an erosion over her tibia. Which of the following is true?

a) Blood cultures are rarely positive. Penicillin is the drug of choice.  

b) Herpes simplex is in the differential diagnosis. Ask about sexual practices.  

c) Hospital admission for intravenous antibiotics, MRI, and surgical consultation are warranted.  

d) Initiate antimicrobial coverage for streptococci and penicillinase-producing staphylococci.
**Answer and Discussion**

**The answer is d.**

**Objective: Manage a skin and soft tissue infection.**

Risk factors for a soft tissue infection in this woman include the diabetes and varicose veins. The portal of entry for the causative organism is likely the erosion overlying her tibia. The ill-defined redness is more consistent with cellulitis than erysipelas. It is true that blood cultures are usually not positive in most cases of cellulitis, but treatment with penicillin would only be appropriate for erysipelas. Herpes simplex virus infection is not a consideration here, and sexual activity is not a risk factor for cellulitis. Even though one might consider admission to the hospital to initiate intravenous antimicrobial therapy and observe clinical improvement, surgical consultation would only be warranted for this case if necrotizing fasciitis is clinically or radiologically suspected. Topical antifungal therapy may be considered here only if tinea pedis is present.

**Question 19**

A 41-year-old female patient presents to your office for high fevers and general malaise for 1 week duration. Around 6 weeks ago, the patient went camping in Pennsylvania. She reports multiple “bug bites,” but does not recall an obvious tick bite. Over the last week, she has noticed daily fevers to 39°C. She reports some generalized malaise and fatigue, but otherwise no other significant symptoms. She denies any rash. On examination, she has a 39.2°C fever, mild hepatosplenomegaly, but no lymphadenopathy. The peripheral smear reveals direct infection of the red blood cells with a pathogen.

Which of the following is the most likely diagnosis?

a) Histoplasmosis  
b) Borreliosis  
c) Babesiosis  
d) Trypanosomiasis  
e) Ehrlichiosis

**Answer and Discussion**

**The answer is c.**

**Objective: Identify human erythrocyte babesiosis.**

Babesiosis is a protozoal infection with the genus Babesia, leading to a wide range of clinical manifestations, from asymptomatic to severely ill, often depending on the immune status of the host. Babesia directly infects red blood cells (RBCs), where it undergoes asexual reproduction, forming the characteristic tetrad (maltese cross appearance). Risk factors for severe illness include the following: age >50, splenectomy, immunosuppression, TNF-α inhibitor use, and co-infection with HIV. Typically, immunocompetent patients have mild non-specific symptoms, with high fever (up to 40°C) being the hallmark of the disease. Other constitutional symptoms, such as malaise, fatigue, and headache, may be seen. On examination, there can be some mild hepatosplenomegaly, but lymphadenopathy and signs of liver failure are rare. Patients with the above risk factors are prone to a more severe disease, which can manifest as acute respiratory distress syndrome (ARDS), disseminated intravascular coagulopathy (DIC), congestive heart failure, renal failure, and splenic infarcts.

The other conditions listed can often present with similar symptoms. Ehrlichiosis infects granulocytes and monocytes. Histoplasmosis is typically seen in the Ohio River Valley and may be phagocytized by monocytes and granulocytes, but typically does not cause infection of RBCs. Borrelia and trypanosomes may be observed in peripheral blood smears as extracellular organisms, but do not infect RBCs.

**Question 20**

A 19-year-old man is seen in an urgent care center. He reports dysuria for the past 2 days and admits to two sexual partners in the past 3 weeks. Physical examination reveals an otherwise healthy man with a purulent urethral discharge. A Gram-stained smear of the discharge reveals intracellular gram-negative diplococci. Along with appropriate counseling and serologic testing, which of the following would be the most appropriate treatment?

a) A single intramuscular dose of a long-acting antimicrobial, such as benzathine penicillin G combined with a 7-day course of doxycycline  
b) A single intramuscular dose of ceftriaxone, 125 mg  
c) A single oral dose of azithromycin, 1 g and a single intramuscular dose of ceftriaxone, 250 mg  
d) A single oral dose of ciprofloxacin, 500 mg  
e) A single intramuscular dose of cefazolin, 0.5 g, and a 7-day course of doxycycline

**Answer and Discussion**

**The answer is c.**

**Objective: Understand the clinical presentation and treatment of gonorrhea infection.**

This man most likely has gonorrhea. First-generation cephalosporins and long-acting penicillins have no place in the treatment of gonorrhea. Ceftriaxone or ciprofloxacin alone would be inadequate because there is a high incidence of chlamydial infections in patients with gonorrhea. Dual antimicrobial coverage is therefore necessary. Azithromycin is no longer considered appropriate monotherapy as high rates of macrolide resistance have been encountered in the treatment of gonorrhea.

**Question 21**

A 40-year-old man undergoing treatment for lymphoma presents with new-onset vertigo. On further questioning, he also admits to a change in his sense of taste. Along with his prescribed medications, he is also self-medicating with Echinacea. On physical examination, he has a vesicular rash in the right external auditory canal and right-sided facial palsy.
What is the most likely etiology of the new symptoms?

a) Side effect of herbal medication
b) Disseminated malignancy
c) A virus often identified by Tzanck smear
d) Parvovirus infection
e) A virus often identified by heterophile antibody testing

**Answer and Discussion**

The answer is c.

**Objective:** Understand the clinical presentations of herpes zoster infection.

Immunocompromised individuals are particularly susceptible to symptomatic herpes zoster, which can result in Ramsay Hunt syndrome. Pain and vesicles appear in the external auditory canal, and there may be loss of taste sensation in the anterior two-thirds of the tongue. The geniculate ganglion of the sensory branch of the facial nerve is involved.

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**Question 22**

A 41-year-old man reports dull pain over the maxillary areas for the past 10 days and a yellow nasal discharge. He has tried over-the-counter nasal decongestants without relief. Physical examination shows that percussion of the teeth causes pain. You recommend the use of oxymetazoline 0.05% spray and a 10-day course of trimethoprim–sulfamethoxazole. He is seen in routine follow-up 4 months later when he explains that his symptoms did improve for a few days but soon returned. His symptoms are much the same as they were 4 months ago, but he now has a postnasal drip associated with cough. Which of the following statements relating to this patient’s condition is incorrect?

a) Oral amoxicillin for 1 month would be an acceptable next step in management.
b) Computed tomography (CT) is more sensitive than plain radiography.
c) Up to one-third of patients may respond to treatment with an antihistamine and decongestant preparation.
d) A topical corticosteroid is contraindicated.
e) For patients who do not respond to empiric medical therapy, surgical drainage should be considered.

**Answer and Discussion**

The answer is d.

**Objective:** Understand the treatment of chronic bacterial sinusitis.

Symptoms of sinusitis of more than 3 months duration are termed chronic. Sinus drainage obstruction is implicated, leading to a persistent infection. Chronic sinusitis is a clinical diagnosis, but the CT of the sinuses can be helpful in difficult cases. Oral amoxicillin for 1 month is appropriate, and an antihistamine/decongestant may help relieve the cough. A topical corticosteroid may actually accelerate the resolution of symptoms.

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**Question 23**

A 29-year-old woman with a history of recurrent sinus infections is seen in the outpatient department with a dry cough, dyspnea, and headache for 2 weeks. A physician gave her a 5-day course of clarithromycin, with no clinical improvement. She is not taking any medications at the moment, does not smoke, and has not traveled outside the country. Symptoms of fatigue since she returned from a field trip to Arizona 3 weeks ago have caused her to miss several days from work. On examination, a nonspecific maculopapular erythematous rash is noted. A chest radiograph demonstrates a focal upper lobe infiltrate and hilar adenopathy. Biopsy of the rash shows eosinophilic infiltrates. Which is the most likely cause of this presentation?

a) Mycoplasma pneumonia
b) Lyme borreliosis
c) Varicella pneumonia
d) Coccidioidal pneumonia (valley fever)
e) Streptococcal pneumonia

**Answer and Discussion**

The answer is d.

**Objective:** Understand the clinical presentation of coccidioidal pneumonia.

The presentation is typical for coccidioidal infection. Coccidioidomycosis is a fungal infection acquired by inhalation of fungal arthrospores. The disease is endemic in south central California, southern Arizona, Nevada, New Mexico, and parts of Texas. Many cases elude diagnosis because symptoms may be mild and nonspecific. Cutaneous lesions may be present in as many as 25% of the patients. Chest radiology most commonly shows a single focal infiltrate. Laboratory studies typically show eosinophilia. Mild elevation of alanine transaminase may also be present. A common clue to the diagnosis is nonresolution of the symptoms when treatment is directed toward the bacterial pneumonia.

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**Question 24**

Which of the following statements regarding hepatitis C is false?

a) In patients with chronic infection with hepatitis C virus, hepatitis A virus immunization is indicated if patients have not previously been exposed.
b) Chronic infection develops in approximately 20% of patients.
c) Cirrhosis develops in 20% of the infected patients.
d) Can be associated with cryoglobulinemia.
e) Of patients with hepatitis C, 30% to 40% have no identifiable risk factors for acquiring the infection.

**Answer and Discussion**

The answer is b.

**Objective:** Understand the natural history of hepatitis C virus infection.
The most common presentation of hepatitis C is a chronic asymptomatic elevation of hepatic transaminases. A state of chronic infection occurs in at least 50% of the patients, and in those in whom cirrhosis develops, an increased risk of hepatic malignancy is present.

**Question 25**

A 35-year-old woman reports dysuria. Other than a minor back pain, for which she is taking ibuprofen, she has generally been healthy. Her vital signs and physical examination are normal. A urine dipstick test reveals 2+ leukocyte esterase. Urine is immediately sent to the laboratory for culture and sensitivity. She is told that she has a urinary tract infection and is given a prescription for trimethoprim–sulfamethoxazole. Two days later, the urine culture report indicates no bacterial growth. In interpreting this report, you consider:

a) Sterile pyuria may occur in the presence of urinary tract infection if this patient had been self-medicating with an antibiotic.
b) Sterile pyuria may be caused by an atypical organism such as Chlamydia trachomatis, U. urealyticum, or Mycobacterium tuberculosis.
c) Obtain further history regarding her analgesic intake and consider chronic interstitial nephritis in the differential.
d) Repeat the urine dipstick because vaginal leukocytes may have contaminated the original urine sample.
e) All of the above.

**Answer and Discussion**

The answer is e.

**Obstructive: Understand the role of urinalysis in the diagnostic evaluation of a urinary tract infection.**

A true infection without pyuria is rare, but pyuria in the absence of infection does occur. This woman may have had a urinary tract infection that has been partially treated with an antibiotic. In addition, vaginal leukocytes may have contaminated the original urine specimen. Atypical organisms, such as Chlamydia trachomatis, U. urealyticum, or Mycobacterium tuberculosis, may not grow in standard cultures, and thus patients who have symptoms of a urinary tract infection with a negative culture result should be tested for these organisms. Other important causes of sterile pyuria include chronic interstitial nephritis (hence the questioning regarding analgesic use), urothelial tumors, and nephrolithiasis. Nevertheless, the presence of leukocyte esterase and nitrite on urine dipstick has 95% sensitivity and 75% specificity for the diagnosis of a bacterial urinary tract infection.

**Question 26**

A 25-year-old man presents to the emergency department with fever, chills, cough, and dyspnea on exertion. He is reluctant to give any further history. On examination, he is febrile, tachypneic, tachycardic, and normotensive. He appears to have significant muscle wasting. The physical examination is notable for the presence of an oral thrush, poor dentition, normal lung examination, and rapid but regular heart sounds without the evidence of a murmur. Further laboratory testing and radiologic examinations are done. Meanwhile, a friend mentions that the patient was diagnosed with HIV infection 9 years ago and last saw his physician 3 months ago. Which of the following findings or additional history would be least supportive of the diagnosis of Pneumocystis jiroveci pneumonia?

a) The CD4 count is 600/mm³.
b) The patient has been treated with aerosolized pentamidine monthly.
c) Arterial blood gas readings taken while breathing room air are pH 7.43, PCO₂ 36 mmHg, PO₂ 64 mmHg, HCO₃⁻ 28 mEq/L, and SaO₂ 93%.
d) Chest plain film reveals a right lower lobe consolidation.
e) Lactate dehydrogenase level is 550 U/L.

**Answer and Discussion**

The answer is a.

**Objective: Understand the clinical and laboratory features of Pneumocystis jiroveci pneumonia.**

The two most common laboratory abnormalities in HIV patients with Pneumocystis jiroveci pneumonia include a decreased CD4 cell count <200/mm³ and an elevated lactate dehydrogenase level. Although possible, it is unlikely that Pneumocystis jiroveci pneumonia develops in patients with CD4 counts >200/mm³.

**Question 27**

The following are true in regard to screening for sexually transmitted diseases (STDs) except:

a) All patients being evaluated for STDs should be offered counseling and testing for HIV.
b) Asymptomatic women with risk factors for STDs should be screened for gonococcal or chlamydial infections during their annual pelvic examination.
c) HIV-infected patients should be screened annually for N. gonorrhoeae.
d) Pregnant women should be screened for Chlamydia trachomatis.
e) All sexually active women and pregnant women need to be screened for herpes infections.

**Answer and Discussion**

The answer is e.

**Objective: Understand the sexually transmitted disease screening guidelines.**

According to the 2010 CDC treatment guidelines for STDs, all patients being evaluated for STDs should be offered testing for HIV. All women with risk factors for STDs should be screened for a gonococcal or chlamydial infection annually and offered human papillomavirus vaccination if cervical cytology is normal. Hepatitis B screening should be...
offered to men who have sex with men (MSM), patients with a history of multiple sex partners, or intravenous drug abuse. It is recommended that sexually active MSM undergo annual testing for N. gonorrhoeae, Chlamydia trachomatis, HIV, and syphilis. Pregnant women should be screened for Chlamydia trachomatis, HIV, hepatitis B, and syphilis infections. Patients with HIV should be screened annually for N. gonorrhoeae, Chlamydia trachomatis, syphilis, hepatitis B, and hepatitis C. Local and state public health departments should be kept informed of chancreoid, Chlamydia trachomatis, N. gonorrhoeae, acute hepatitis B and C, HIV, and syphilis. The U.S. Preventive Services Task Force (USPSTF) recommends against routine serologic screening for herpes simplex virus (HSV) in asymptomatic pregnant women at any time during pregnancy to prevent neonatal HSV infection and in asymptomatic adolescents and adults.

Question 28

A 25-year-old heterosexual man with a single sex partner presents to his primary care physician requesting an HIV test. Which of the following would be the most correct statement?

a) Testing should not be done because he has no risk factors.
b) A positive enzyme immunoassay test would need confirmation with a Western blot to lessen the likelihood of a false-positive test result.
c) The false-positive and false-negative rates of the enzyme immunoassay and Western blot tests are related to the prevalence of HIV in the population being tested.
d) b and c
e) None of the above

Answer and Discussion

The answer is d.

Objective: Understand the diagnostic evaluation of HIV infection.

This man should be tested because he is requesting it. To diminish the chances of a false-positive result, a Western blot should be performed to confirm a positive enzyme immunoassay. Unlike sensitivity and specificity, the false-positive and false-negative rates are directly related to the prevalence of disease in the population. For example, the higher the prevalence of disease, the higher the false-negative rate will be; the lower the prevalence of disease, the higher the false-positive rate will be.

Question 29

A 35-year-old sexually active woman traveling to Africa 2 weeks later, presents to her local physician. She was told in the past her ECG was not entirely normal. She is otherwise healthy and takes no medications. Which of the following statements is most accurate?

a) Malaria prophylaxis with chloroquine is recommended because traveling to sub-Saharan Africa does not increase her chance of chloroquine-resistant Plasmodium falciparum exposure.
b) Mefloquine is the drug of choice in most chloroquine-resistant areas and is effective against all strains of Plasmodium falciparum.
c) Mefloquine should not be prescribed for individuals with cardiac conduction abnormalities because of the association with sinus bradycardia and a prolonged QT interval.
d) If this patient is pregnant and travel cannot be deferred, she should be given doxycycline because chloroquine and mefloquine have been shown to be teratogenic.
e) None of the above

Answer and Discussion

The answer is c.

Objective: Understand the prevention of malaria in travelers to endemic regions.

Malaria leads to 1 million deaths out of 200 million cases worldwide each year. Of Plasmodium falciparum, Plasmodium vivax, Plasmodium ovale, and Plasmodium malariae, Plasmodium falciparum can rapidly progress to coma and death. Travel to sub-Saharan Africa poses the greatest risk for acquisition of Plasmodium falciparum for American travelers. Strains of Plasmodium falciparum are increasingly becoming more resistant to chloroquine; thus, mefloquine is the chemoprophylactic agent of choice in areas where chloroquine resistance prevails. Adverse effects associated with mefloquine include nausea, dizziness, and vertigo. Mefloquine has been associated with neuropsychiatric effects, including inability to concentrate, bad dreams, paranoid ideation, seizures, and psychosis, as well as cardiac conduction abnormalities leading to sinus bradycardia and a prolonged QT interval. Pregnancy should not be a contraindication to chemoprophylaxis if travel cannot be postponed. Chloroquine is without any established teratogenicity, and mefloquine seems to be safe, as well. However, a tetracycline such as doxycycline should not be prescribed because of harmful effects on the fetus (dental discoloration and dysplasia and inhibition of bone growth).

Question 30

A 35-year-old man presents to the emergency department with abdominal cramping, tenesmus, and sudden onset of bloody diarrhea. On examination, he is toxic-appearing, with a temperature of 40°C and normal blood pressure and respiratory rate. He is mildly tachycardic and slightly tender in the right lower quadrant. A presumptive diagnosis is made after examining the stool for fecal leukocytes and is confirmed by culture of rectal swab. All the following regarding this diagnosis are true, except

a) Stool examination would reveal polymorphonuclear leukocytes on methylene blue stain.
b) Blood cultures would likely reveal the causative organism.
c) In general, antibiotics are not essential for the treatment because this illness is generally self-limited in duration, averaging approximately 7 days.
d) Antibiotic treatment in infected patients can reduce the transmission of this organism to other individuals.

e) The development of bacteremia in this condition is more common in children than adults.

Answer and Discussion
The answer is b.

Objective: Understand the diagnostic evaluation of infectious diarrhea.

Acute-onset bloody diarrhea, high fever, and crampy abdominal pain with tenesmus typically characterize Shigella gastroenteritis. Initial diagnostic tests may include an examination of the stool stained with methylene blue to look for polymorphonuclear leukocytes. Fecal leukocytes may occur in other bacterial diarrheas and are not specific for Shigella. The presence of fecal leukocytes suggests a bacterial etiology. Culture of the stool or rectal swab can confirm the diagnosis. Blood cultures are rarely helpful, as bacteremia is rare, occurring in approximately 7% of children but few adults. Patients at risk for bacteremia include those who are elderly, HIV infected, or malnourished, or those who have underlying diseases, such as diabetes mellitus (DM). Untreated, shigellosis is highly contagious and is generally a self-limited illness with an average duration of 7 days. The organism can be shed in the stool for up to 6 weeks. For this reason, food handlers, day-care workers, and health-care workers should be treated, along with anyone with bacteremia. Treatment in the United States should start with trimethoprim–sulfamethoxazole. Healthy adults with mild diseases can alternatively be treated with norfloxacin. Ampicillin should not be used because of developing resistance. Treatment outside the United States generally consists of a quinolone.

Question 31

A 35-year-old woman who was diagnosed with HIV infection 9 years ago and has been reluctant to start treatment now presents to you for advice. You obtain her CD4 cell count, which is 200/mm³, and her viral load (RNA-polymerase chain reaction), which is 30,000 copies/mL. In addition, a pregnancy test is negative. Of the following options, which would you recommend as the most appropriate initial therapy for this patient?

a) No treatment because she does not meet criteria for drug therapy
b) Didanosine, zalcitabine, and indinavir
c) Zidovudine
d) Zidovudine, didanosine, and nevirapine
e) Zidovudine and didanosine

Answer and Discussion
The answer is d.

Objective: Understand the indications for initiating therapy for HIV infection.

The criteria for the initiation of therapy in HIV-infected patients include acute HIV infection or, within the first 6 months of seroconversion, symptomatic HIV infection, or asymptomatic infection with a CD4 cell count <500/mm³ or viral load (RNA-polymerase chain reaction) >20,000 copies/mL. Recommended initial therapy in these patients includes the combination of two nucleoside reverse transcriptase inhibitors (zidovudine, lamivudine, zalcitabine, or didanosine) and a protease inhibitor (indinavir, saquinavir, ritonavir, or nelfinavir). Therefore, choice b would be correct, but the combination of zalcitabine and didanosine should be avoided because of possible toxicity. Alternately, one can use two nucleoside reverse transcriptase inhibitors and a nonnucleoside reverse transcriptase inhibitor (nevirapine, delavirdine, or efavirenz). Therefore, choice d would be the best choice. Combination therapy with two nucleoside reverse transcriptase inhibitors or monotherapy is not recommended. In the case of a pregnant woman, however, in the absence of the indications mentioned previously, monotherapy with zidovudine is indicated in the second and third trimesters to reduce the risk of fetal transmission.

A 28-year-old man medical assistant is seen in occupational health for pre-employment screening. He is asymptomatic, and his physical examination is normal. He undergoes drug screening and is offered hepatitis immunization. He explains that a physician at his previous place of employment told him that he does not need hepatitis B immunization. You take samples for hepatitis B virus serology and ask him to return in 2 days to discuss the results. The following results are reported.

<table>
<thead>
<tr>
<th>Antigen</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>HBsAg</td>
<td>Negative</td>
</tr>
<tr>
<td>Anti-HBs</td>
<td>Positive</td>
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<tr>
<td>HBeAg</td>
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<td>HBeAg</td>
<td>Negative</td>
</tr>
<tr>
<td>Anti-HBe</td>
<td>Negative</td>
</tr>
</tbody>
</table>

What would be the most accurate advice for this patient?

a) He has a high level of infectivity and should not be employed under federal guidelines.
b) He has a low level of infectivity and can be employed as long as universal precautions are followed.
c) He most likely has chronic hepatitis B virus infection and should have liver function testing.
d) All his sexual partners must be advised to undergo testing.
e) None of the above

Answer and Discussion
The answer is e.

Objective: Understand the common serologic patterns related to hepatitis B virus infection.

This patient is positive only for hepatitis B surface antibody, which is consistent with prior immunization or past exposure. Hepatitis B “e” antigen is correlated with high infectivity, and its disappearance (appearance of anti-HBe)
in infected patients heralds lower infectivity. Patients with chronic infection would be positive for hepatitis B surface antigen.

**Question 33**

A 59-year-old diabetic man is seen in the outpatient clinic. He reports left side ear pain for the past 2 weeks and a greenish discharge from the ear canal. His diabetes is well controlled and he is known to be compliant with your recommendations. His medications include an oral hypoglycemic agent. He does not have any allergies. In order to get to sleep without discomfort, he has self-medicated with tramadol that was prescribed for his wife. He appears comfortable but is noted to have a temperature of 39.1°C. On examination, the external auditory meatus is exquisitely tender, and you note some friable reddish tissue. What would be the most appropriate next step in management?

- a) Recommend instillation of a suspension of polymyxin B/neomycin/hydrocortisone four times daily for 7 days, with a scheduled return outpatient visit every 7 days until cure is achieved.
- b) Prescribe clotrimazole 1% solution, three drops twice daily for 14 days.
- c) Prescribe clotrimazole 1% solution, three drops twice daily for 14 days in combination with a topical steroid cream.
- d) Prescribe clotrimazole 1% solution applied to a wick left in the ear canal and recommend avoidance of moisture entering the ear canal when he is bathing by use of cotton wool for plugging.
- e) Admit him for intravenous antibiotics and possible debridement.

**Answer and Discussion**

The answer is e.

**Objective:** Understand the treatment of otitis externa.

Otitis externa is also termed swimmer’s ear. Maceration of the skin of the external auditory canal is present, and there may be impairment of hearing as debris obstructs the canal. A greenish exudate suggests *Pseudomonas* infection. In uncomplicated cases, debris should be removed and a topical antibiotic applied. If bacterial infection is suspected, an antibacterial steroid solution is appropriate. A fungal infection is treated with clotrimazole solution applied locally for 14 days. Malignant otitis externa is more common in diabetics and is characterized by severe pain and fever. In this situation, there may be rapid spread of infection to local skin and bone, and immediate hospital admission for intravenous antibiotics is indicated.

**Question 34**

A 28-year-old male visiting student from India is seen in an urgent care facility. He reports that his friend’s dog bit his hand 1 hour ago. The dog is apparently in good health. Examination of the affected hand reveals small, superficial puncture wounds. He does not have any allergies. He does not recall any childhood immunizations. What is the most appropriate management for this patient?

- a) Thorough cleansing of the wound with soap and water only
- b) Wound irrigation and a 7-day course of antibiotics, with observation of the dog for 10 days
- c) Wound irrigation and tetanus and diphtheria toxoid immunization, with destruction of the dog
- d) Irrigation, 7 days of antibiotics, tetanus and diphtheria toxoid immunization, tetanus immunoglobulin, and observation of the dog for 10 days, with repeat tetanus and diphtheria immunizations in 1 and 6 months
- e) Irrigation, tetanus and diphtheria toxoid immunization, tetanus immunoglobulin, and observation of the dog for 10 days, with repeat tetanus and diphtheria immunizations in 1 and 6 months

**Answer and Discussion**

The answer is d.

**Objective:** Understand the clinical evaluation and treatment of animal bites.

The appropriate treatment for animal bites before the appearance of local infection is of paramount importance. Appropriate prophylaxis for tetanus is necessary. It is uncertain whether this patient previously received tetanus immunization, and he should therefore receive tetanus immunoglobulin and a primary series of immunizations. Dog bites can cause local infection with multiple organisms and always raise a concern about rabies. Precautions for rabies involve observing the dog for 10 days by quarantine, if necessary. If the dog cannot be observed, then human rabies immune globulin and diploid vaccine should be administered to the patient. Minor abrasions should be cleaned thoroughly and puncture wounds irrigated. Antibiotic use is necessary if bites involve the hand or face, or if there is any sign of infection.

**Question 35**

A 22-year-old woman nurse has mild discomfort and tearing of her right eye. She is afebrile. On examination, no purulent drainage is present, but there is hyperemia of the conjunctiva. Preauricular adenopathy is also noted. Which of the following is the most important recommendation?

- a) Topical vasoconstrictive drops and cold compress alone
- b) Oral tetracycline, 250 mg four times daily for 21 days
- c) No specific medication, but a request for her to use thorough hand washing, not to share towels, and to remain away from work until her tearing has settled down
- d) Cold compress for symptomatic relief alone
- e) Gentamicin solution, one or two drops every 4 hours

**Answer and Discussion**

The answer is c.

**Objective:** Understand the clinical features and treatment of viral conjunctivitis.

This woman has viral conjunctivitis. Preauricular adenopathy is a characteristic feature, but it is not always found. The
infection is highly contagious, and patients should be cautioned to use strict hygiene. If the patient is in an occupation that may pose the risk of spread, time off work may be prudent. Symptomatic treatment can be helpful, but hygiene advice takes priority. Oral tetracycline is used in inclusion conjunctivitis to treat chlamydial infection. Gentamicin drops are indicated in chronic bacterial conjunctivitis.

**Question 36**

A 45-year-old African American woman presents to the emergency department with fever, cough productive of reddish sputum, shortness of breath, and dyspnea on exertion. She was well until approximately 5 days ago. She denies any chest pain, palpitations, abdominal pain, diarrhea, or neurologic symptoms. Her vital signs reveal that she is febrile, normotensive, and tachycardic. On examination, she appears in mild respiratory distress. She has a normal head, eyes, ears, nose, and throat examination. Her neck is supple without any lymphadenopathy. On examination of her lungs, decreased breath sounds and egophony are heard in the left lower base, and dullness to percussion is present in the same region. Cardiovascular, abdominal, and neurologic examinations are unremarkable. All the following regarding the diagnosis of community-acquired pneumonia in this patient are true, except:

a) The clinical presentation of an abrupt illness with fever, chills, cough, and pleuritic pain is compatible with a *Streptococcus pneumoniae* infection.

b) *Streptococcus pneumoniae* is the most common pathogen responsible for community-acquired pneumonia, in all age groups.

c) *Streptococcus pneumoniae* is acquired through the nasopharynx and is carried asymptptomatically by 50% of people at some point in their lives.

d) If this patient has *Streptococcus pneumoniae* infection, sputum culture will grow the organism in more than 80% of cases.

e) Overall, *Streptococcus pneumoniae* infection associated mortality is low but intensive care unit patients can have a mortality of up to 25%.

**Answer and Discussion**

The answer is e.

**Objective:** Recognize the most common community-acquired pneumonia pathogen and its sequelae.

*Streptococcus pneumoniae* is the most common pathogen associated with community-acquired pneumonia and accounts for up to 66% of bacterial pneumonia in some series in which serologic techniques were used. Nevertheless, the organism is isolated in only 5% to 18% of the cases. In fact, the sputum culture is negative in 50% of patients with bacteremic pneumococcal pneumonia. Fever, chills, cough with rusty-colored sputum, and abrupt-onset pleuritic pain are the symptoms often ascribed to pneumococcal pneumonia. Rales and tubular sounds are often heard over the affected lobe. Most cases are uncomplicated, but among patients in the ICU mortality can reach 25%. Risk factors for the development of complications include age, pre-existent lung disease, AIDS or other forms of immunodeficiency, or nosocomial acquisition.

Abscesses are usually culture-positive and respond rapidly to drainage. Parapneumonic effusions are associated with concurrent bacteremia with penicillin-resistant pneumococci. Finally, the most serious complication, bacteremia, occurs in 25% of patients. This complication is increased in splanchnectomized patients. The use of the sputum Gram stain and sputum culture in the diagnosis of *Streptococcus pneumoniae* infection is debated, but these tests may sometimes aid in choosing the optimal antimicrobial regimen. Penicillin covers the majority of cases, but increasing resistance to penicillin is occurring, thus necessitating use of a cephalosporin or, in some cases with significant resistance, vancomycin.

**Question 37**

A 42-year-old Boy Scouts scoutmaster presents with a painful violet pustule on the dorsum of his right hand that appeared 2 weeks after returning from a fishing trip. A crusted ulcer is seen in the midportion of the pustule. He denies any constitutional symptoms. The most likely cause of this infection is:

a) *Mycobacterium leprae*

b) *Pseudomonas aeruginosa*

c) *Sporothrix schenckii*

d) *Rickettsia rickettsii*

e) *Mycobacterium marinum*

**Answer and Discussion**

The answer is e.

**Objective:** Recognize soft tissue infections caused by *Mycobacterium marinum*.

Swimming pool and fish tank granulomas are caused by *Mycobacterium marinum*. A small violet nodule or pustule appears at a skin surface exposed to contaminated water. A crusted ulcer or a small abscess evolves thereafter. The incubation period is 1 to 8 weeks after exposure. *Mycobacterium leprae* is the causative agent of leprosy. The incidence of leprosy in the United States has fallen to an average of 150 cases/year. The incubation period ranges between 3 and 5 years. *Pseudomonas aeruginosa* bacteremia may be associated with ecthyma gangrenosum, which is characterized by central necrosis surrounded by violaceous ecchymotic areas. Lymphangitic sporotrichosis is the most common manifestation of *Sporothrix schenckii* infection. A painless, red nodule forms at the site of inoculation, followed by several nodules along the lymphatic channels over the next few weeks. *Rickettsia rickettsii* causes Rocky Mountain spotted fever, a tickborne disease. This is a systemic disease with skin rash that manifests as macules, up to 5 mm in diameter, on the wrists and ankles.

**Question 38**

A 68-year-old man was brought by his family to the emergency room (ER) after being found confused and complaining of headache. He lives alone, and his family is unaware of
the duration of his symptoms. Medical history is significant for hypertension (HTN) that is well controlled by lisinopril 40 mg daily and hyperlipidemia for which he takes atorvastatin 20 mg daily. He is a car salesman and has had sexual male partners in the past but has not had any sexual activity since 15 years ago.

On admission, his blood pressure is 100/60, HR = 80, temperature = 36.7°C, and RR = 20. A lumbar puncture was performed in the ER. CSF analysis showed RBC = 0, WBC = 201, 75% neutrophils, 12% lymphocytes, glucose = 18, and protein = 70. He was started on vancomycin and ceftriaxone. CSF Gram stain showed many polymorphonuclear leukocytes, few mononuclear cells, and no organisms. HIV test was performed and came back positive. CD4 count was 46. Preliminary CSF culture results show yeast.

Which of the following is the most appropriate therapy?

a) Amphotericin B 0.7 mg/kg IV q 24 hours  
b) Caspofungin 50 mg IV q 24 hours  
c) Fluconazole 400 mg PO q 24 hours  
d) Fluconazole 200 mg IV q 24 hours

**Answer and Discussion**

The answer is a.

**Objective:** Understand the diagnosis and treatment of cryptococcal meningitis.

The patient has AIDS and likely has cryptococcal meningitis based on the CSF findings and culture. Cryptococcal infection is usually associated with CD4 counts that are ≤100. Amphotericin B 0.7 mg/kg/d is the standard of therapy for cryptococcal meningitis. Flucytosine is usually used in combination with amphotericin B for at least 2 weeks. Flucytosine targets pyrimidine biosynthesis and is not used as sole therapy because strains frequently become resistant. Fluconazole has good CSF penetration but is fungistatic. With clinical improvement, the amphotericin B and flucytosine are switched to fluconazole 400 to 800 mg for several weeks, followed by lifelong suppressive therapy with fluconazole 200 mg PO daily to prevent infection relapse. Echinocandins, such as caspofungin, have no activity against *Cryptococcus neoformans*.

### Question 39

A 35-year-old man is seen by a primary care physician for a physical examination. He has just moved from Tennessee and wants to establish care. He states that he has been healthy except for having a bout of pneumonia a year ago and an abnormal taste in his mouth for several months. His medications include vitamin E, Flonase, and occasional ibuprofen for muscle aches. He is a restaurant manager and is married with no children. He has no known allergies.

His physical examination reveals no abnormalities. His primary care doctor orders labs for him, including an HIV test, which comes back positive. He is seen back in clinic and undergoes counseling regarding his diagnosis. More tests are ordered. His CD4 count is 125, and viral load is 36,000; he is *Toxoplasma gondii* IgG positive. His hepatitis panel shows hepatitis B surface antibody positive and hepatitis C antibody negative. His G6PD screen is negative. He had a tuberculin skin test reaction measuring 5 mm. He is referred to an infectious disease specialist and is waiting for an appointment.

Which of the following prophylaxis treatments for opportunistic infections should you offer?

a) TMP–SMX for *Pneumocystis jiroveci* prophylaxis  
b) TMP–SMX for *Pneumocystis jiroveci* prophylaxis and azithromycin for *Mycobacterium avium* complex  
c) TMP–SMX for *Pneumocystis jiroveci*, azithromycin for *Mycobacterium avium* complex, and dapsone for *T. gondii*  
d) TMP–SMX for *Pneumocystis jiroveci* and isoniazid (INH) for latent tuberculosis

**Answer and Discussion**

The answer is d.

**Objective:** Select the appropriate antibiotic prophylaxis for opportunistic infections in HIV/AIDS.

HIV-infected patients are at risk for various opportunistic pathogens. Prophylaxis is based on the history and CD4 count. Current standard of care recommends prophylaxis for *Pneumocystis jiroveci* pneumonia (PCP) with TMP–SMX double-strength, 1 tablet daily when CD4 is <200. Dapsone is an alternative regimen for PCP if TMP–SMX is not tolerated (dapsone 100 mg PO daily or 50 mg PO BID). *Toxoplasma gondii* prophylaxis is indicated if the patient is IgG positive and CD4 count is <100 and should consist of TMP–SMX double-strength 1 tablet daily. Prophylaxis for *Mycobacterium avium* complex is initiated if CD4 count is <50 and consists of azithromycin 1,200 mg PO weekly or clarithromycin 500 mg PO BID. If an HIV-infected patient has a tuberculin skin test ≥5 mm or a history of untreated positive tuberculin skin test or exposure to someone with active tuberculosis (whether or not the patient had a positive tuberculin skin test), prophylaxis with INH 300 mg PO daily and vitamin B6 50 mg PO daily for 9 months is recommended. Primary prophylaxis can generally be discontinued once particular pathogen CD4 threshold is exceeded for at least 3 months. Primary prophylaxis should be restarted if the CD4 count again drops below treatment thresholds.

### Question 40

A 26-year-old man is seen at the clinic because he was informed that one of his previous female partners was diagnosed with gonorrhea. He denies any present complaints and denies any medical problems. He is not on any medication. He has had three new partners in the past 2 months and does not use condoms consistently. His last sexual activity was 2 weeks ago.

On examination, he has small bilateral inguinal nodes that are nontender and purulent urethral discharge. He is also found to have flat-topped lesions in his perianal area and whitish plaques on his tongue. Urethral Gram stain is not available, but the urine and blood tests are sent to the lab.
Which of the following should the patient receive for therapy?

a) Benzathine PCN IM  

b) Benzathine PCN IM and ceftriaxone IM  

c) Benzathine PCN IM, ceftriaxone IM, and doxycycline PO  

d) Ceftriaxone IM and doxycycline PO

**Answer and Discussion**

The answer is c.

**Objective:** Identify the correct treatment regimen for sexually transmitted diseases.

The patient is a known contact to a partner with gonorrhea and should be treated with ceftriaxone IM. It is important to know that a single 250 mg injection of ceftriaxone is effective in treating gonorrhea at all anatomic sites. There are no clinical data to support the use of higher doses of ceftriaxone. In 2007, emergence of fluoroquinolone-resistant *N. gonorrhoeae* in the United States prompted CDC to no longer recommend fluoroquinolones for the treatment of gonorrhea, leaving cephalosporins as the only remaining recommended antimicrobial class. He has urethral discharge on examination, and nongonococcal urethritis cannot be excluded. Patients being treated for *N. gonorrhoeae* should also be treated for concomitant nongonococcal urethritis since symptoms are often subtle and easily missed. Therefore, he should be treated with azithromycin 1 g orally in a single dose or doxycycline 100 mg PO BID for 1 week. His examination, however, reveals signs of secondary syphilis, and he should be treated with benzathine PCN as well. While secondary disease is known for the many different ways it can manifest, symptoms most commonly involve the skin, mucous membranes and lymph nodes. There may be a symmetrical, reddish-pink, non-itchy rash on the trunk and extremities, including the palms and soles. The rash may become maculopapular or pustular. It may form flat, broad, whitish, wart-like lesions known as *condyloma lata* on mucous membranes. All of these lesions harbor spirochetes and are infectious. These lesions are called mucous patches when found on mucous membranes such as the mouth, vulva, and glans penis. Other manifestations include constitutional symptoms such as fever, malaise, and pharyngitis.

**Question 41**

A 48-year-old woman with myelofibrosis underwent allogeneic bone marrow transplantation (CMV recipient negative and donor positive). She had a complicated posttransplant course, including severe mucositis, esophagitis, and neutropenic fevers. She was eventually discharged home but later developed extensive graft-versus-host disease (GVHD) and was placed on high-dose prednisone and tacrolimus at home. She has been on prophylactic TMP–SMX. A few weeks later, she is seen urgently at her primary care doctor’s office with complaints of cough and shortness of breath. A CT chest was negative for pulmonary embolism. The CT is shown:

Which of the following organisms is most likely responsible?

a) *Aspergillus fumigatus*  
b) *Pneumocystis jiroveci*  
c) Epstein-Barr virus  
d) Cytomegalovirus

**Answer and Discussion**

The answer is a.

**Objective:** Identify possible etiologies for pulmonary nodules in immunosuppressed patients.

The patient has undergone bone marrow transplantation and is on tacrolimus and high-dose steroids for GVHD. She is especially at risk for fungal infections, particularly aspergillosis. Her chest CT shows the typical “halo sign” (lung nodule with surrounding ground-glass appearance) that is seen in early pulmonary aspergillosis. The chest CT is not typical for *Pneumocystis jiroveci*, which usually would show diffuse or patchy ground-glass opacities, rarely nodules. It is also less likely given that she has been taking TMP–SMX prophylaxis. Patients with acute EBV may show lymphadenopa-
thy on chest CT, but it is rare to find pulmonary manifestations. CMV pneumonitis may show ground-glass opacities or multiple small nodules.

**Question 42**

A 56-year-old woman was seen for intermittent arthritis symptoms lasting for 2 weeks. She described episodes of right knee swelling and pain that started around 3 months after returning from a trip to Connecticut where she visited her daughter and her family. She did a lot of outdoor activity in Connecticut, including camping trips with her grandchildren. She recalls catching the flu from her grandson a few days prior to returning to Michigan. She does not recall a tick bite, but she did have a rash at that time, which resolved after a few weeks. She saw a physician briefly and was given doxycycline, but she admits to having forgotten it in Connecticut on her trip back to Michigan. On examination, her right knee is warm and swollen, with no surrounding erythema. Her neurologic examination is normal. Lyme IgG was positive (ELISA and Western immunoblot). Knee synovial fluid demonstrates 14,000 WBC/mm³ with 86% neutrophils, no crystals, and negative cultures. What is the best therapeutic option for this patient?

- **a)** No therapy; symptoms will resolve
- **b)** Doxycycline 100 mg PO BID
- **c)** Penicillin G 24 million units IV q4 hours
- **d)** Ceftriaxone 2 g IV q24 hours

**Answer and Discussion**

The answer is **b**.

**Objective:** Diagnose and treat Lyme arthritis.

This patient has the arthritic manifestations of late Lyme disease. Lyme disease is diagnosed clinically based on symptoms, objective physical findings, or a history of possible exposure to infected ticks, as well as serologic blood tests. A two-tiered protocol is recommended by the CDC for serologic testing: the sensitive ELISA test is performed first, and if it is positive or equivocal, then the more specific Western blot is run. The reliability of testing in diagnosis remains controversial. Studies show the Western blot IgM has a specificity of 94% to 96% for patients with clinical symptoms of early Lyme disease. The initial ELISA test has a sensitivity of about 70%, and in two-tiered testing, the overall sensitivity is only 64%, although this rises to 100% in the subset of people with disseminated symptoms, such as arthritis. She has a history of travel to an endemic area (Connecticut) with history of flu-like symptoms and rash, which was likely erythema chronicum migrans. She did not take therapy at that time. Late Lyme disease can present as an arthritis, which can be intermittent or chronic, a neurologic disease, which can affect the central or peripheral nervous system, or as acrodermatitis chronica atrophicans (bluish-red skin lesions that become atrophic).

Lyme arthritis can be treated with oral agents, particularly doxycycline, amoxicillin, or cefuroxime axetil for 4 weeks if patients do not have any neurologic disease. Patients with Lyme arthritis and neurologic involvement should be treated intravenously, preferably with ceftriaxone. Penicillin G is an alternative parenteral therapy.

**Question 43**

A 70-year-old man was brought to the ER after being found unresponsive by his wife. His past medical history is significant for HTN, coronary artery disease, ischemic cardiomyopathy, and arthritis. He had recently been seen by his primary care physician for some weight loss and diarrhea. His wife says that the diarrhea has been on and off now for several months. At the ER, his blood pressure is 75/40, HR is 120, temperature is 39°C, and RR is 24. He was brought to the ICU and started on broad-spectrum antibiotics for presumed sepsis. Blood cultures drawn in the ER grew *Clostridium septicum*. The patient was eventually stabilized and transferred to the regular nursing floor. What will you recommend to complete this patient’s workup?

- **a)** Send stool for *Clostridium difficile*
- **b)** Repeat blood cultures in 2 weeks after finishing therapy
- **c)** CT abdomen and pelvis
- **d)** Send stool for ova and parasites

**Answer and Discussion**

The answer is **c**.

**Objective:** Identify the proper work-up for *Clostridium septicum* species bacteremia.

*Clostridium septicum* bacteremia is associated with malignancies, especially relapsed leukemia or colon cancer, in 70% to 80% of cases. The reason for this association is not fully understood, but may be attributed to the presence of *Clostridium septicum* species proteins that bind to ligands that are overexpressed in colonic neoplasms. Identification of *Clostridium septicum* infection should prompt evaluation for colonic carcinoma because bacteremia has preceded the diagnosis of cancer in some cases. Another common pathogen associated with colonic carcinoma is *Streptococcus galolyticus* subspecies (*Streptococcus bovis* biotype 1) infections. Colonic neoplasia has been observed in the setting of *Streptococcus bovis* infection at multiple sites, but is most common in *Streptococcus bovis* infective endocarditis.

**Question 44**

A 43-year-old man has a history of allogeneic bone marrow transplant 10 years ago for follicular lymphoma. The medical course was complicated by chronic GVHD. The patient also has a history of CMV viremia. He is now admitted with chest pain and increasing shortness of breath for about a month. He was seen by his primary care physician a week before, diagnosed with pneumonia and prescribed levofloxacin. However, patient’s symptoms persisted and were eventually admitted to the hospital. His blood pressure was 110/60, heart rate 88, temperature 37.2°C, and respiratory rate 22. His oxygen saturation was 92% on 3L nasal cannula. CT of
the chest showed cavitary nodules in the right upper lobe. The patient became disoriented, and the MRI of the brain showed a focal, enhancing solid cystic mass in the right frontal lobe. Bronchoscopy was performed, and the bronchoalveolar lavage showed partially acid-fast thin branched filaments. Blood cultures grew the same organism.

What is the most likely diagnosis in this patient?

a) Disseminated tuberculosis  
b) Nocardiosis  
c) Disseminated MAI  
d) Actinomycosis

**Answer and Discussion**

**Objective:** Identify common features of *Nocardia* infection in immunosuppressed patients.

Microscopically *Nocardia* is seen as a partially acid-fast, filamentous, branching, gram-positive rod. Polymerase chain reaction (PCR) provides a more accurate and rapid result for the diagnosis of nocardiosis than the conventional methods but is not available in most clinical laboratories. Nocardiosis is an opportunistic infection but can also occur in immunocompetent patients. The most common disease sites are the lung, central nervous system (CNS), and skin, but *Nocardia* can disseminate to virtually any organ. There are no pathognomonic signs or symptoms for nocardiosis. It should be suspected in any patient who presents with brain, soft tissue, or cutaneous lesions, and a concurrent or recent pulmonary process. CNS nocardiosis presents as a parenchymal abscess, and CNS involvement occurs in 20% of cases overall. The acid-fast staining differentiates *Nocardia* from *Actinomyces, Mycobacterium tuberculosis* and *Mycobacterium avium* complex are acid fast but will not appear filamentous or branching.

However, his arm has gotten worse. He is otherwise healthy, although he admits to occasionally using cocaine. He denies intravenous drug use. On physical examination, his upper arm is markedly edematous, with erythema and severe tenderness. MRI of the right upper extremity shows a large area of edema and cellulitis along the medial aspect of the arm with a discrete abscess in the soft tissues at the mid arm. The patient is admitted and undergoes incision and drainage. Cultures grow methicillin-resistant *Staphylococcus aureus*. Which of the following is correct about community-acquired MRSA?

a) It is usually resistant to β-lactams and clindamycin.

b) It usually only causes invasive disease in immunocompromised patients, such as HIV and transplantation patients.

c) Linezolid has good activity against community-acquired MRSA.

d) It has been shown to cause severe necrotizing pneumonia.

**Answer and Discussion**

**Objective:** Identify common features of community-acquired MRSA.

CA-MRSA is defined as MRSA infection that occurs in the absence of health-care exposure. CA-MRSA is most often associated with skin and soft tissue infections in young, otherwise healthy individuals. Community-acquired MRSA (CA-MRSA) and hospital-acquired MRSA differ in their molecular characteristics and antimicrobial susceptibilities. CA-MRSA is usually resistant to β-lactam antibiotics but is usually susceptible to TMP–SMX and clindamycin. A multidrug-resistant isolate has been described among men who have sex with men. It has been shown to cause severe pneumonia and skin and soft tissue infections even in immunocompetent individuals. CA-MRSA strains are also more likely to produce Panton-Valentine leukocidin (PVL) virulence factor, a cytoxin that causes leukocyte destruction and tissue necrosis. Linezolid has activity for CA-MRSA and is FDA approved for complicated skin and soft tissue infections and hospital-acquired pneumonia. Patients with MRSA infections due to “community-associated” strains have also been observed with increasing frequency among patients in hospital settings. CA-MRSA strains may also cause hospital-onset, health-care–associated infections, since patients who become colonized with CA-MRSA strains in the community may require hospitalization and either transmit such strains to other hospitalized patients or develop infection while hospitalized (e.g., following surgery or insertion of an invasive device).

**Question 46**

A 25-year-old male medical student traveled to India for a vacation to visit his family for 2 weeks. Five days after returning to the United States, he started having watery, nonbloody diarrhea, around three to five times per day with abdominal cramping for 2 days. He has no fever and no nausea or vomiting. He traveled with his wife who is doing fine. He says he only...
drank bottled water and ate only food prepared by his family. He stayed mainly in the city area but did buy food occasionally from street vendors. On examination, his blood pressure is 110/60, HR is 92 bpm, RR is 20, and temperature is 37.1°C. His abdomen is nontender. His white cell count is 7,000. His rectal examination shows brown stool in the rectal vault. What is the next appropriate step in management of this patient?

a) TMP–SMX DS 1 tablet BID for 5 days
b) Order stool cultures
c) Fluid replacement
d) Order stool for *Clostridium difficile*

**Answer and Discussion**

**Objective:** Identify and treat traveler’s diarrhea.

Fluid hydration is the most appropriate management at this time. Traveler’s diarrhea is a common illness, particularly in travelers from industrialized nations to developing countries. It is usually self-limited. Bacteria, viruses, and parasites can cause traveler’s diarrhea, but approximately 80% is of bacterial etiology. There is no need to order stool studies, unless the diarrhea is prolonged (>10 to 14 days) or accompanied by fever and colitis or the traveler is immunosuppressed. Travelers should be given a prescription for antibiotics for empiric self-treatment if diarrhea develops abroad. Ciprofloxacin, levofloxacin, ofloxacin, norfloxacin, and azithromycin are some of the oral agents that are recommended. Usually the antibiotic is prescribed for 3 days. Due to high levels of resistance, TMP–SMX is no longer recommended.

**Question 47**

A 75-year-old man with a history of DM and HTN was brought in by his family for a 3-day history of fever and generalized headaches. He also complained of neck pain in the past 24 hours. On examination, temperature was 38.8°C, HR was 102 bpm, and RR was 18. He was mildly lethargic, but oriented to time, place, and person. Nuchal rigidity was present. The rest of his neurologic examination was nonfocal. A lumbar puncture was performed and CSF fluid analysis showed 320 WBCs with 80% neutrophils, proteins 140 mg/dL, and glucose 20 mg/dL. What treatment is appropriate at this time?

a) Hold antibiotics until CSF Gram stain and culture results are able to direct antibiotic therapy
b) Cefotaxime
c) Ceftriaxone plus vancomycin
d) Ceftriaxone, vancomycin, and ampicillin

**Answer and Discussion**

**Objective:** Identify the empiric treatment regimens for acute bacterial meningitis.

This patient presents with acute bacterial meningitis and empiric antibiotic therapy should be initiated as soon as possible to improve the associated morbidity and mortality. The empiric approach to antibiotic selection in patients with suspected bacterial meningitis is directed at the most likely bacteria based on the patient’s age and underlying disease status. Selected third-generation cephalosporins, such as cefotaxime and ceftriaxone, are the β-lactams of choice in the empiric treatment of meningitis. They are active against *Streptococcus pneumoniae*, *Haemophilus influenzae*, and *Neisseria meningitidis*. These drugs have consistent CSF penetration and potent activity against the major pathogens of bacterial meningitis, with the notable exceptions of *Listeria monocytogenes* and some penicillin-resistant strains of *Streptococcus pneumoniae*. With the worldwide increase in the prevalence of penicillin-resistant pneumococci, vancomycin should be added to cefotaxime or ceftriaxone as empiric treatment until culture and susceptibility results are available. Ceftazidime, a third-generation cephalosporin with broad in vitro activity against gram-negative bacteria including *Pseudomonas aeruginosa*, is much less active against penicillin-resistant pneumococci than cefotaxime and ceftriaxone. However, a fourth-generation cephalosporin, cefepime, has been shown to be safe and therapeutically equivalent to cefotaxime for the treatment of bacterial meningitis and can be considered a suitable alternative to cefotaxime or ceftriaxone when broad activity against both the pneumococcus and gram-negative bacteria, such as *Pseudomonas aeruginosa*, is necessary. Among patients over the age of 50, or with impaired cell-mediated immunity (due, for example, to lymphoma, cytotoxic chemotherapy, or highdose glucocorticoids), coverage must be directed against *Listeria monocytogenes*. Empiric coverage for this pathogen is ampicillin.

**Question 48**

A 32-year-old woman, previously healthy, is admitted to the hospital 2 weeks after traveling on a cruise ship. For the past 4 days, she has been having fever, progressive cough, and dyspnea. She has also noted some diarrhea with intermittent abdominal pain. On admission, her temperature is 40°C, BP is 90/60, HR is 100 bpm, RR is 22, and saturation is 89% on room air. On examination, she is found to be confused and lethargic. Her chest examination shows rales on auscultation of the right lower lobe. Heart sounds are regular, and there are no murmurs. Abdominal examination shows good bowel sounds with a nondistended, nontender abdomen. She has no edema. Labs are as follows:

- WBC: 12,000/µL
- Hb: 12 g/dL
- Platelets: 100,000/µL
- Na: 129 mmol/L
- K: 3.8 mmol/L
- Cl: 98 mmol/L
- HCO₃⁻: 24 mmol/L
- BUN: 20 mg/dL
- Creatinine: 1.0 mg/dL

Chest x-ray shows right lower lobe consolidation.
Which organism is the most likely etiologic agent?

a) Streptococcus pneumoniae  
b) Legionella pneumophila  
c) Chlamydia pneumoniae  
d) Histoplasma capsulatum

**Answer and Discussion**

The answer is b.

**Objective:** Understand the common features of Legionnaire’s disease.

Patients with pneumonia secondary to Legionella commonly present with high fever and gastrointestinal symptoms including diarrhea, nausea, and vomiting. Headaches and mental status changes may be seen, as well as electrolyte disturbances, particularly hyponatremia. Pneumonia is the predominant clinical manifestation of Legionella infection. In epidemiologic studies, Legionella is consistently reported among the top three or four most commonly identified pathogens in community-acquired pneumonia in immunocompetent patients and is also a common cause of hospital-acquired pneumonia. Eight cases of Legionnaire’s disease associated with cruise ship travel were reported to the CDC in November 2003 to May 2004. This diagnosis should be highly entertained among patients with the typical clinical manifestations of the illness, especially in the setting of a history of recent travel. Culture for Legionella species is the single most important laboratory test. Urinary antigen testing is rapid, sensitive, specific, and not costly, but is only useful for the diagnosis of Legionella pneumophila type 1 infection (which accounts for 90% of community-acquired Legionella infections in the United States).

**Question 49**

A 58-year-old man with myasthenia gravis well controlled with pyridostigmine and mitral valve replacement with a St. Jude’s valve 6 months prior is admitted to the hospital for low-grade fever and generalized malaise. Two blood culture sets taken in the ER are found to be growing gram-positive cocci in clusters. Within an hour of starting the IV infusion, the patient develops respiratory failure and needs to be brought to the ICU for intubation. He is found to have flaccid paralysis, dilated pupils, and hypoactive reflexes. What is the most appropriate next step?

a) Infuse vancomycin at a much slower rate  
b) Stop gentamicin infusion and give calcium gluconate with neostigmine  
c) Do an MRI of the brain  
d) Do a stat transesophageal echo (TEE) to rule out an abscess and a conduction abnormality causing his respiratory failure  
e) Administer naltrexone immediately

**Answer and Discussion**

The answer is b.

**Objective:** Identify an acute neuromuscular blockade in a patient with neuromuscular disease given an aminoglycoside.

Neuromuscular blockade after aminoglycoside administration is rare but potentially life threatening. This has been reported among patients given gentamicin, neomycin, streptomycin, kanamycin, tobramycin, or amikacin. Certain factors such as renal insufficiency, neuromuscular disease, botulism, hypocalcemia, and coadministration of succinylcholine and tubocurarine have been associated with this serious side effect. Calcium gluconate and neostigmine may reverse the respiratory depression and apnea.

Infusing vancomycin rapidly is not reported to be associated with neuromuscular blockade, and thus slowing its infusion rate will not reverse the patient’s respiratory failure. A brain MRI will not be diagnostic in this case given that the patient’s presentation is more consistent with a neuromuscular junction problem rather than a CNS lesion. The patient’s presentation is not consistent with respiratory failure caused by a conduction disturbance, and thus, doing a stat TEE may not be helpful at this time. There is no report of opioids administration, therefore administering naltrexone, an opioid antagonist, is not indicated.

**Question 50**

A 34-year-old man comes to the ER with a 4-day history of generalized malaise, low-grade fevers, chills, and myalgias. He works at a textile mill, and he states that he had to stay off work for the past few days because he felt like he had the flu. His temperature on admission is 39°C, BP is 120/72, RR is 18, and saturation is 96% on room air. He is admitted for further workup. Ceftriaxone and azithromycin are started empirically for a possible community-acquired pneumonia. The next day, the patient deteriorates rapidly, becomes hypotensive, and is saturating only 86% on room air. He is visibly dyspneic, and has a stridor on the physical examination. A chest x-ray is shown here.
**Question 51**

A 20-year-old man who is HIV positive (last CD4 count = 180; undetectable viral load), on HAART therapy, comes to your office for a routine health maintenance screening in late October. He has a history of *Candida* esophagitis 2 years ago and no other opportunistic infections. He is sexually active with male partners only. He tells you he cannot recall having received any immunizations in the recent past. He has no history of chickenpox as a child. What vaccines would you consider giving him for preventive care?

- a) Hepatitis A vaccine, hepatitis B vaccine, influenza, Pneumovax, Tdap
- b) Hepatitis A vaccine, hepatitis B vaccine, influenza, Pneumovax, Tdap, varicella
- c) Hepatitis A vaccine, hepatitis B vaccine, influenza, Pneumovax, Tdap, meningococcal vaccine, *Haemophilus influenzae* vaccine
- d) Hepatitis B vaccine, influenza, Pneumovax, Tdap

**Answer and Discussion**

The answer is a.

**Objective:** Identify safe and appropriate vaccines in HIV patients.

The vaccines recommended for HIV patients include hepatitis B, influenza, pneumonia, and Tdap. Immunization for hepatitis A is also recommended among HIV patients with the following risk factors for acquiring the disease: men who have sex with men, patients with hepatitis C, and IV drug abusers.

The varicella vaccine, being a live vaccine, is contraindicated among immunosuppressed patients, including those with HIV. Both meningococcal and *Haemophilus influenzae* vaccines are not routinely recommended in HIV patients. One can consider meningococcal vaccination among those who will be traveling to endemic areas, military recruits, dormitory residents, or those with functional or anatomic asplenia. *Haemophilus influenzae* vaccination is not recommended because the vaccine is not protective for most infecting strains in HIV patients.

**Question 52**

A 19-year-old man is referred to you for a tuberculin skin test of a 7 mm induration. He states that he was born and raised in the United States and that he has no history of prior BCG vaccination. However, he had been exposed to his mother who had active pulmonary tuberculosis 6 months ago. He still lives with both parents at home. A chest x-ray (CXR) done today is normal, and he feels well. What is the best option among the choices below?

- a) Observe and repeat the tuberculin skin test in a year
- b) Repeat a tuberculin skin test (TST) in 8 to 10 weeks and measure the difference
- c) Take INH daily for 9 months
- d) Take rifampin daily for 6 months

**Answer and Discussion**

The answer is c.

**Objective:** Interpret a PPD and correctly treat latent TB.

Take INH daily for 9 months is the best answer among the choices. The patient has had a previous recent exposure to
active tuberculosis from a close contact, which puts him at high risk for developing active tuberculosis. His PPD is thus considered positive for latent infection since it is ≥ 5 mm, with negative symptoms and a negative CXR. It is highly recommended that he receives therapy. The preferred regimen is isoniazid INH daily for 9 months. Other alternative regimens include either INH daily for 6 months or rifampin daily for 4 months.

**Question 53**

A 55-year-old woman with DM and chronic kidney disease presents to your clinic for worsening cough and dyspnea associated with low-grade fevers for the past 3 weeks. She initially presented to a local doctor 1 week ago and was prescribed doxycycline for 5 days. Despite this, she remains symptomatic, with worsening shortness of breath and persistent fevers.

Her vital signs at your office are as follows: temperature = 38°C, HR = 82, BP = 123/72, RR = 18, saturation = 97% on room air. She looks comfortable at rest and is alert and oriented. Her head and neck examination are unremarkable. Chest auscultation reveals decreased breath sounds over the right middle lung field with increased tactile fremitus. Heart sounds are regular without murmurs. The rest of the physical examination is normal. Labs done reveal the following: WBC = 11,000/µL, Hb = 11.8 g/dL, platelets = 250,000/µL, Na = 135 mmol/L, K = 4.0 mmol/L, Cl = 100 mmol/L, HCO₃⁻ = 24 mmol/L, BUN = 10 mg/dL, and Creatinine (Cr) = 1.6 mg/dL. Chest x-ray reveals right middle lobe consolidation. She lives in an active lifestyle and is single but has family who live close by. She has no drug allergies. What is your next step in the management of this patient?

a) Admit patient for treatment of pneumonia with IV antibiotics given that she failed previous oral therapy
b) Switch to amoxicillin–clavulanate plus azithromycin and ask her to follow up with you in 5 days
c) Switch to azithromycin for 5 days and ask her to follow up with you in 5 days
d) Continue doxycycline to complete regimen for 10 days to see its maximal effect

**Answer and Discussion**

The answer is **b**.

**Objective: Risk stratify and treat community-acquired pneumonia.**

The first decision to make when faced with a patient with community-acquired pneumonia is whether or not hospital admission is necessary. Based on the CURB-65 score, which is one of the two main severity scoring systems recommended for use in determining the need for hospitalization, she does not qualify for hospital admission. CURB-65 score consists of C–confusion, U–BUN >20 mg/dL, R–respirations >30, B–blood pressure (systolic <90 and diastolic <60), and >65 years of age. The score is predictive for a high 30-day mortality if any one of the criteria is fulfilled. The second severity index that may be used for this purpose is the Pneumonia Severity Index (PSI), which is more complex in terms of parameters and patient evaluation.

Once the decision for outpatient management has been made, the choice of the empiric antibiotic regimen to be administered needs to be made. There are several risk factors in this case for drug-resistant pathogens (particularly Streptococcus pneumoniae) causing pneumonia, including DM and chronic kidney disease, as well as previous antimicrobial use. Thus, it is necessary to broaden coverage by using amoxicillin–clavulanate, which is more active against penicillin-resistant Streptococcus pneumoniae than doxycycline. The addition of azithromycin is necessary to cover for atypical microorganisms as well. Another alternative would be a respiratory fluoroquinolone such as moxifloxacin or levofloxacin.

**Question 54**

A 42-year-old woman comes to your clinic in July complaining of headaches, malaise, and generalized arthralgias 2 weeks after arriving from a summer trip in Arkansas. One week ago, she noted the onset of intermittent fevers and chills. No one else is sick at home. On examination, temperature is 38.2°C, HR is 84 bpm, RR is 16, and saturation is 98% on room air. Her chest is clear, and her heart examination unremarkable. She has no rash. Neurologic examination is nonfocal, and her neck is supple. Joints examination shows no synovitis or swelling. Labs are as follows: WBC = 2,500/µL, Hb = 11.0 g/dL, platelets = 85,000/µL, Na = 135 mmol/L, K = 3.5 mmol/L, AST = 80 U/L, ALT = 72 U/L, ALP = 110 U/L, BUN = 20 mg/dL, Creatinine (Cr) = 0.9 mg/dL, and LDH = 280. What is the most appropriate treatment for this patient?

a) Check ANA and rheumatoid factor
b) Tell her that this is likely a summer viral illness that will go away on its own
c) Schedule a hematology consult for bone marrow biopsy
d) Start doxycycline 100 mg orally BID

**Answer and Discussion**

The answer is **d**.

**Objective: Identify and treat ehrlichiosis.**

The best answer is to start doxycycline 100 mg orally BID. This patient most likely has ehrlichiosis, based on her exposure to an endemic area during the summer season, her symptoms associated with pancytopenia, and the lack of a rash.

Ehrlichia infections have been called “spotless Rocky Mountain fever.” The two most important human ehrlichial diseases are human monocytic ehrlichiosis (HME), which is caused by *Ehrlichia chaffeensis*, and human granulocytic anaplasmosis (HGA), which is caused by *Anaplasma phagocytophilum*. Most cases occur in the spring and summer, and in the United States, cases of HGA outnumber HME. The principal vector of *E. chaffeensis* (agent of HME) is the Lone Star tick (*Amblyomma americanum*). The vectors of *Anaplasma phagocytophilum* (agent of HGA) are *Ixodes* tick. The organism affects the monocytes or neutrophils, and patients typi-
A 62-year-old man with end-stage renal disease (ESRD) on hemodialysis, DM, and HTN is admitted for low-grade fevers and chills for the past 3 days occurring especially during dialysis. He has no other symptoms except for generalized weakness. His admitting vital signs include a temperature of 38.0°C, BP of 140/87, HR of 92 bpm, RR of 18, and saturation of 97% on room air. On physical examination, he is alert and oriented and looks well. He has anicteric sclerae without conjunctival hemorrhages, good dentition, a clear chest on auscultation, and a regular heart rhythm without murmurs or ectopy. Abdominal examination is benign, and on his extremities, there are no stigmata of endocarditis. He has a hemodialysis catheter on his right chest wall, which appears clean and nontender. The patient states that this is his third catheter in the past 2 years given his previous history of line-related bloodstream infections. His labs are as follows: WBC = 18,000/µL, Hb = 10 g/dL, platelets = 156,000/µL, Na = 137 mmol/L, K = 5.0 mmol/L, Cl = 100 mmol/L, HCO₃⁻ = 24 mmol/L, Creatinine (Cr) = 6.2 mg/dL, and BUN = 45 mg/dL. Two out of two blood cultures drawn at the ER are growing gram-positive cocci (GPC) in clusters. Which of the following statements concerning this case is the most accurate?

a) Await identification of the GPCs before deciding on the antibiotic course. It may be possible to salvage the catheter.

b) This is a bacteremia secondary to the hemodialysis catheter. The catheter must be pulled out as soon as possible.

c) In a line-related bacteremia secondary to *Enterococcus*, an attempt should be made at salvaging the catheter as long as the patient is doing well without any metastatic sites of infection.

d) *Nafcillin* is the first drug of choice for empiric therapy in this case, pending identification and susceptibilities.

**Answer and Discussion**

The answer is **a**.

**Objective:** Identify the appropriate management of central-line associated bloodstream infections.

In this patient, the most likely source for fevers is a catheter-related bacteremia. Based on current guidelines regarding the management of line-related infections, an attempt to salvage this hemodialysis catheter may be made depending on several factors, including stable clinical status, absence of tunnel or site infection, and the microorganism causing the bacteremia. GPC in clusters will most commonly yield either *Staphylococcus aureus* or *Staphylococcus epidermidis*. If the latter is identified, then it is reasonable to leave the catheter in place. In this case, given that the patient is nontoxic, the line looks clean and is functioning, and this is the third catheter in the past 2 years, the catheter does not have to be removed before getting the final result of the culture. It has to be removed however if *Staphylococcus aureus* is found to be the infecting organism, given its virulence and propensity for adherence to catheters and endovascular structures.

In case of *Enterococcus* being the infecting organism, similarly with the *Staphylococcus aureus*, the catheter would need to be pulled out as well because of this organism’s highly adherent property. Vancomycin is the first drug of choice for empiric therapy, anticipating a high likelihood for methicillin-resistant *Staphylococcus aureus* (MRSA) in a dialysis patient exposed to multiple health-care settings.
c) Vancomycin is the drug of choice for this patient given the convenience of giving it with dialysis for the next 2 weeks.

d) Adding gentamicin to vancomycin or nafcillin for 2 weeks is synergistic and will give the best outcomes in treatment of MSSA line-related bacteremia.

Answer and Discussion

The answer is b.

Objective: Identify appropriate management of central line-associated bloodstream infections.

β-Lactam agents such as nafcillin or oxacillin, as well as first-generation cephalosporins such as cefazolin, are bactericidal against MSSA and are thus the antibiotics of choice for the treatment of MSSA bacteremia. It has been found in multiple studies involving both human and animal models that vancomycin is significantly inferior in the treatment of MSSA bacteremia.

Regarding a catheter-related MSSA bacteremia without complications or metastatic foci of infection such as endocarditis, there are no data suggesting that adding aminoglycosides to the regimen will improve the outcome. This patient cleared the MSSA quickly and had a negative echo. Adding gentamicin and continuing for 2 weeks is not indicated in this case.
POINTS TO REMEMBER:

Superior Vena Cava Syndrome
- The key to managing superior vena cava (SVC) syndrome is to effectively treat the underlying cause; more than 60% of the cases are due to intrathoracic tumors.
- Chest computed tomography (CT), ideally contrast-enhanced, is a crucial diagnostic tool in patients with suspected SVC syndrome.
- Endovascular stenting is indicated in patients with severe symptoms or anticipated poor response to treatment.

Pericardial Tamponade
- Pericardial tamponade with hemodynamic compromise from a malignant pericardial effusion warrants emergent intervention, with percutaneous pericardial drainage with intrapericardial sclerosis as the procedure of choice.
- The presence of a hemorrhagic effusion without history of antecedent trauma increases the risk of malignancy.
- Pericardial fluid should be sent for cytology and/or flow cytometry when a malignant effusion is suspected.
- Surgical pericardiotomy or pericardiectomy is considered in recurrent pericardial effusion or if pericardial biopsy is needed for diagnosis.

Epidural Spinal Cord Compression
- The diagnosis of spinal cord compression must be anticipated; once neurologic dysfunction develops, it is rarely reversible.
- Back pain presenting in any patient with a current or past history of malignancy warrants further evaluation and documentation of a complete neurologic exam.
- MRI of the entire spine axis is the gold standard imaging modality.
- The most common location for epidural spinal cord compression is in the thoracic spine (60%).
- Intravenous corticosteroids should be the initial treatment for SCCS until definitive treatment is possible.
- Urgent surgery is indicated in patients with spinal instability, but radiation is the mainstay for most patients.

Tumor Lysis Syndrome
- Rapid cell death results in a number of metabolic disturbances that define the syndrome of tumor lysis syndrome, including hyperkalemia, hyperuricemia, hyperphosphatemia, and hypocalcemia (due to precipitation of calcium phosphate).
- Aggressive IV hydration and management of electrolyte abnormalities are the key initial management.
- Hemodialysis is an effective last resource.

Hypercalcemia of Malignancy
- Symptomatic hypercalcemia of malignancy or asymptomatic serum calcium concentration >14 mg/dL (3.5 mmol/L) warrants urgent intervention.
- Aggressive IV hydration and diuretics are the initial management followed by bisphosphonates.
- Hemodialysis can be considered in patients not responding to conservative treatment.

SUGGESTED READINGS


POINTS TO REMEMBER:

- Human papillomavirus testing in addition to the Papanicolaou smear is an acceptable method for cervical cancer screening in women older than 30 years.
- Primary prevention of cervical cancer through the use of the HPV vaccine would have a far greater impact worldwide than screening alone. Vaccination for females is currently recommended between the ages of 9 and 26.
- Uterine cancer is the most common gynecologic cancer, causing approximately 6% of all malignancies and accounting for 3% of all cancer deaths in women.
- Most women with endometrial cancer are diagnosed at an early stage and are often cured by surgery with or without radiation therapy.
- Type II endometrial cancers consisting of clear cell and papillary serous types are higher risk and are often treated with multiple modalities including surgery, chemotherapy, and radiation.
- Intraperitoneal chemotherapy with cisplatin and paclitaxel was shown to improve overall survival by 16 months when compared to intravenous administration in women with optimally debulked ovarian cancer.
- To date, most patients with newly diagnosed prostate cancer present with organ-confined disease as a result of a positive screening test.
- To date, there is no randomized prospective evidence to suggest that one modality of local definitive treatment for localized prostate cancer is superior to the other one (i.e., surgery versus radiation).
- Although chemotherapy confers a high cure rate for testicular cancer (more than 80% for good and intermediate-risk patients), patients live long enough to experience late toxicities.

SUGGESTED READINGS

Gynecologic Cancers


Male Genitourinary Cancers
POINTS TO REMEMBER:

- Chronic lymphocytic leukemia (CLL) is the most common leukemia in the Western hemisphere and may be complicated in several important ways:
  1. Infection. Patients with CLL are predisposed to a variety of infections.
  2. Autoimmune phenomena. These usually manifest as cytopenias (idiopathic thrombocytopenic purpura and autoimmune hemolytic anemia).
- Smudge cells may be seen on peripheral blood smear in CLL. Hypogammaglobulinemia is a hallmark of CLL.
- Chronic myelogenous leukemia (CML) is characterized by BCR/ABL fusion [translocation of chromosomes 9 and 22 t(9;22)], also known as the Philadelphia chromosome.
- Imatinib mesylate was developed as a specific inhibitor of the BCR/ABL tyrosine kinase. In patients refractory to, or intolerant of, interferon, imatinib results in a near 100% hematologic remission and at least a 50% cytogenetic remission. Second- and third-generation tyrosine kinase inhibitors are now available as well.
- Patients who present with the clinical features of CML, but lack detectable BCR/ABL, often have another myeloproliferative disorder, such as myelofibrosis or chronic myelomonocytic leukemia.
- Acute myeloid leukemia (AML) is defined by the presence of ≥20% myeloblasts in the peripheral blood or bone marrow. Most important prognostic indicators include age, cytogenetics, and molecular genetics.
- Treatment of AML remains 3 days of an anthracycline and 7 days of cytarabine. Consolidation chemotherapy is indicated in good-risk cytogenetics. However, allogeneic stem cell transplantation has benefit in those with poor-risk cytogenetics.
- Elderly AML patients receive dose-reduced chemotherapy regimens.
- Acute promyelocytic leukemia (APL) is a unique subtype of AML. It is characterized by coagulopathy in the form of disseminated intravascular coagulation.
- APL is extremely sensitive to all-trans retinoic acid (ATRA), anthracycline, and arsenic trioxide. Cure rates are high in APL.
- The treatment of Hodgkin’s disease often uses alkylating agents. Myelodysplastic syndromes (MDS) and AML are the most common secondary malignancies associated with the treatment of Hodgkin’s disease.
- MDS are characterized by ineffective hematopoiesis, bone marrow failure, peripheral blood cytopenias, and reduced survival. Increased age and exposure to alkylating agents/topoisomerase II inhibitors, and ionizing radiation are risk factors for MDS.
- MDS may be classified as indolent or aggressive (lower or higher risk). Allogeneic stem cell transplant, the only potentially curative approach to MDS, is a realistic option for only about 5% to 10% of patients.
- Acute lymphoblastic leukemia (ALL) is divided into two major categories: precursor lymphoid neoplasms and mature lymphoid neoplasms. Most ALL treatment for adults follows the basic strategy of induction, consolidation—intensification, CNS prophylaxis, and maintenance therapy. Successful adult chemotherapy regimens have been modeled after pediatric regimens.
- The incidence of infection increases with more profound and prolonged neutropenia, particularly as the absolute neutrophil count falls to <500/μL.
- In febrile neutropenia, prompt antibiotic administration is critical. The initial empiric antibiotic should be broad-spectrum enough to cover a wide variety of organisms, including *Pseudomonas aeruginosa*.
- Tumor lysis syndrome (TLS) occurs when blasts are broken down rapidly into the bloodstream, either spontaneously or following antineoplastic therapy—most common in rapidly proliferative hematologic malignancies, such as AML, ALL, and Burkitt’s lymphoma.
- TLS is associated with sudden development of hyperkalemia, hyperuricemia, hyperphosphatemia, hypocalcemia, and increased serum lactate dehydrogenase levels. Patients should be started on allopurinol and hydration with intravenous fluids.
SUGGESTED READINGS


**POINTS TO REMEMBER:**

- The **activated partial thromboplastin time (aPTT)** is a clot-based test that measures the time for recalcified plasma to clot in the presence of anionic phospholipids and an activator of the contact system. It assesses the integrity of the so-called intrinsic and common pathways (factors XI, X, IX, VIII, V, and II, and fibrinogen), as well as the contact pathway (factors XII, prekallikrein, and high-molecular-weight kininogen).

- The **prothrombin time (PT)** measures the ability of recalcified plasma to clot in the presence of anionic phospholipids and tissue factor. It is primarily sensitive to deficiency of the vitamin K–dependent factor VII and is widely employed to monitor the oral anticoagulant warfarin.

- Any abnormality of aPTT or PT warrants further investigation.

- The first step in evaluating a prolonged PT or PTT is a mixing study in which patient plasma is mixed 1:1 with pooled normal plasma. Complete correction of the PT or PTT indicates a factor deficiency whereas persistent prolongation or only partial correction indicates a circulating factor inhibitor or lupus anticoagulant.

- An initial panel of tests is advised to evaluate a bleeding diathesis, which includes: a complete blood count with differential, an examination of the peripheral blood smear cells, and a PT and aPTT to evaluate the coagulation cascade.

- **von Willebrand disease (vWD)** is the most common inherited bleeding disorder of primary hemostasis, affecting up to 1% of the general population. It is caused by quantitative or qualitative abnormalities in von Willebrand factor (vWF).

- Platelet dysfunction is a common complication of a wide variety of conditions, especially *uremia*, which can alter prostaglandin metabolism, induce a storage pool-like platelet defect, and induce abnormalities in the interaction between vWF and platelet receptors.

- The approach to the hypercoagulable patient should include a comprehensive clinical evaluation to guide management of the acute thrombosis, age-appropriate screening for an underlying malignancy, and selection of patients for further special coagulation testing.

**SUGGESTED READINGS**


Anemia

Alan E. Lichtin

POINTS TO REMEMBER:

- **Anemia** is defined as a reduction in the RBC mass as measured by either the hematocrit or the hemoglobin concentration.
- If severe enough, all anemias result in symptoms of tissue hypoxia (i.e., the consequence of a low oxygen-carrying capacity of the blood) including weakness, headache, feeling “cold,” and exertional dyspnea.
- Acquired anemia is a symptom and not a disease. Complete investigation for the underlying pathology is imperative.
- When anemia is detected, the first step in evaluation is always to exclude acute blood loss by history and physical examination, including stool guaiac for occult blood loss.
- The size of the red cells, or mean corpuscular volume (MCV), is an important tool to help determine the cause of the anemia.
- The corrected reticulocyte count is a useful test because it serves to divide anemias into two major categories:
  - **Hyperproliferative anemias**, resulting from the loss or destruction of RBCs, with an associated increased bone marrow activity.
  - **Hypoproliferative anemias**, resulting from decreased bone marrow production.
- A peripheral blood smear (PBS) should be ordered on all patients as part of the initial anemia evaluation.
- Common lab findings that suggest the presence of a hemolytic anemia include: indirect hyperbilirubinemia, reticulocytosis, hemoglobinemia, low haptoglobin levels, and possibly hemoglobinuria.
- The two broad categories of immune hemolytic anemias include: indirect hyperbilirubinemia, reticulocytosis, hemoglobinemia, low haptoglobin levels, and possibly hemoglobinuria.
- The two broad categories of immune hemolytic anemias include: indirect hyperbilirubinemia, reticulocytosis, hemoglobinemia, low haptoglobin levels, and possibly hemoglobinuria.
- A positive direct Coombs’ test identifies antibodies present on a patient’s circulating red blood cells, and an indirect Coombs’ test identifies antibodies present in a patient’s serum capable of reacting with red blood cells.
- The presence of hyersegmented neutrophils on PBS in the setting of a macrocytic anemia indicates the presence of a megaloblastic process, that is, vitamin B₁₂ or folate deficiency and can help to differentiate the megaloblastic macrocytic anemias from other macrocytic processes.
- Vitamin B₁₂ deficiency generally takes years to develop since the body maintains a storage pool in the liver; folate deficiency, however, can develop over weeks to months.
- Vitamin B₉ deficiency alone can be associated with neurologic and neuropsychiatric symptoms, and often presents with profound fatigue.
- Anemia of chronic disease can be normocytic or microcytic. Typical laboratory findings include low serum iron, low total iron-binding capacity (transferrin), and a low percent of transferrin saturation, often with an elevated serum ferritin.
- Certain clinical examination findings suggestive of iron deficiency include glossitis, stomatitis, and fingernail changes (koilonychia or “spoon nail”); Pica, the craving of nonnutritional substances, that is, ice chips, is a unique symptom also suggestive of underlying iron deficiency.
- The exogenous dosing of erythropoietin to treat anemia has come under increasing scrutiny, and new Food and Drug Administration (FDA) black box warnings since 2007 have led to less use.

SUGGESTED READINGS


POINTS TO REMEMBER:

- The estimated annual incidence of invasive breast cancer in the United States is in the range of 200,000 per year, and the death rate, although improving, remains close to 40,000 per year in this country.
- For a woman, the estimated lifetime risk of being diagnosed with breast cancer is approximately 1 in 8.
- Traditional breast cancer risk factors include female gender, increasing age, prolonged cyclic estrogen exposure, and history of chest wall irradiation.
- Newer recognized breast cancer risk factors include: dense breast tissue on mammography, alcohol consumption, certain histologies identified on biopsy including lobular carcinoma in situ (LCIS) and atypical hyperplasia, and combination estrogen–progesterone postmenopausal hormone replacement therapy.
- Familial breast cancer syndromes account for a minority of breast cancer cases.
- Pathological mutations in BRCA-1 and BRCA-2 are estimated to be present in less than a half a percent (0.5%) of the general population, but the frequency of mutations is higher in some groups such as the Ashkenazi Jewish population. Individuals with BRCA-1 or BRCA-2 mutations may have a >80% risk of developing breast cancer by age 70 years, particularly in families in which the penetrance of the gene is high.
- Other familial syndromes that account for a smaller proportion of inherited breast cancer include: the Li-Fraumeni syndrome resulting from an inherited p53 mutation, Cowden syndrome, Muir-Torre syndrome, Peutz-Jeghers syndrome, and heterozygosity for the ataxia-telangiectasia gene.
- Screening mammography reduces the risk of breast cancer death, particularly for women between the ages of 50 and 69.
- Tissue biopsy is required for breast cancer diagnosis and may consist of fine-needle aspiration, core biopsy, or excisional biopsy.
- The most common histologic types of invasive breast cancer are infiltrating ductal carcinoma and infiltrating lobular carcinoma.
- Ductal carcinoma in situ (DCIS) is an early noninvasive form of breast cancer that should not have the ability to metastasize.
- Lobular carcinoma in situ (LCIS) is not a true cancer associated with increased breast cancer risk; excision of LCIS does not alter subsequent cancer risk.
- Breast cancer is staged using the TNM system. Stages I, II, and III are referred to as early breast cancer and stages IIIB and IIIC are locally advanced breast cancer; Stage IV is characterized by distant metastatic disease.
- Standard surgical treatment for invasive breast cancer includes either mastectomy (removal of the entire breast) or excision of the tumor (lumpectomy or partial mastectomy). In addition, evaluation of axillary lymph nodes with either an axillary dissection or a sentinel lymph node biopsy (SLNB) is usually performed.
- Radiation treatment to the breast, chest wall, and/or regional lymph node regions reduces risk for local recurrence.
- Adjuvant systemic treatments including chemotherapy, hormonal therapy, and biologic therapy are given to reduce the risk of developing metastatic disease by eradicating occult micrometastases.
- The prognosis of metastatic breast cancer is widely variable, but life expectancy is usually measured in years.
- Treatment of metastatic disease is aimed at reducing cancer-related symptoms and prolonging survival.

SUGGESTED READINGS


POINTS TO REMEMBER:
- The diagnosis of lymphoma requires a tissue biopsy.
- Fine-needle aspiration is an inadequate biopsy technique to diagnose lymphoma; excisional lymph node biopsy is preferred, although in certain instances a core needle biopsy can be adequate.

Hodgkin Lymphoma
- Two major types of Hodgkin lymphoma are recognized: classical (which includes the nodular sclerosis, mixed cellularity, lymphocyte-rich, and lymphocyte-depleted subtypes) and nodular lymphocyte predominant.
- Patients with a history of mononucleosis, autoimmune disease, or immunodeficiency, including HIV infection, have an increased incidence of Hodgkin lymphoma.
- Only one-third of patients with Hodgkin lymphoma present with B symptoms.
- Hodgkin lymphoma is highly curable.
- Hodgkin lymphoma survivors are at increased risk for certain infections, hypothyroidism, benign or malignant thyroid tumors, and development of other solid tumors (in 10% to 20% of cases).

Non-Hodgkin Lymphoma
- Patients with inherited and acquired immunodeficiencies have a significantly increased risk of developing non-Hodgkin lymphoma (NHL).
- Because NHL may involve any lymphatic or extralymphatic tissue, virtually any presenting symptom is possible; most patients complain of painless enlargement of one or more superficial lymph nodes.
- NHL can be divided into two broad categories: indolent and aggressive.
- Gastric mucosa-associated lymphoid tissue (MALT) lymphoma is a unique and uncommon variant of extranodal marginal zone B-cell lymphoma of MALT, which involves the stomach, and approximately 90% of cases are caused by Helicobacter pylori.
- The addition of rituximab immunotherapy to conventional chemotherapy has led to improved survival in patients with several types of B-cell NHL.

SUGGESTED READINGS
**POINTS TO REMEMBER:**

- The terms “plasma cell disorders” or “plasma cell dyscrasias” are used interchangeably for a group of diseases characterized by transformation and monoclonal expansion of plasma cells, that, in the majority of cases, secrete a product called the M-protein or paraprotein.
- Unexplained bone pain, spontaneous fractures, elevated serum total protein, renal insufficiency, proteinuria, neuropathy, recurrent infections, and anemia should prompt investigation for plasma cell dyscrasia.
- Baseline assessment of any plasma cell disorder includes quantification of the clonal protein by serum protein electrophoresis, serum-free light chain assay, and since urine protein excretion varies during the day, 24-hour urine collection for urine protein electrophoresis.
- The combination of serum immunofixation, urine immunofixation, and serum-free light chain assay will reliably rule out secretory plasma cell disorders if negative (no monoclonal band on immunofixation and normal serum-free kappa/lambda ratio) but, if multiple myeloma is strongly suspected, a bone marrow examination is indicated to rule out nonsecretory myeloma.
- Skeletal survey (plain X-rays from skull to ankles) remains a standard test to evaluate for lytic bone disease in all plasma cell disorders but patients with otherwise asymptomatic myeloma should undergo additional imaging (PET/CT or whole-body MRI) to rule out early myeloma-related bone disease.
- Multiple myeloma (MM) is the second most frequent hematologic malignancy with an incidence of 6 to 7 cases per 100,000 per year.
- Both monoclonal gammopathy of undetermined significance (MGUS) and MM affect African Americans more frequently than Caucasians, and in all races are more common in men.
- Symptomatic multiple myeloma (sMM) differs from asymptomatic multiple myeloma (aMM) and MGUS by the presence of significant organ dysfunction, now called myeloma-defining events (MDEs).
- Myeloma-defining events include plasma cell disorder–related hypercalcemia, renal insufficiency, anemia, bone lesions (CRAB symptoms), and hyperviscosity.
- The quantity of monoclonal protein and/or bone marrow plasma cells differentiates MGUS from aMM. Both conditions require the absence of significant clonal plasma cell–related organ dysfunction.
- In contrast to MGUS, clonal plasma cells have to be documented for the diagnosis of sMM, and often 10% bone marrow plasma cells are needed to demonstrate definite kappa or lambda restriction.
- Treatment for sMM is not curative but prolongs life, which has not been shown for MGUS, and has not yet been convincingly demonstrated for aMM.
- MGUS and aMM carry an unrelenting risk for progression to sMM, and patients must be followed lifelong with a goal to detect progression to sMM before it causes serious complications.
- Plasma cell disorder–related emergencies include hypercalcemia, cast nephropathy, and cord compression.
- Amyloidosis is characterized by extracellular deposition of pathological insoluble fibrillar proteins in organs and tissues and can be separated into localized disease or secondary disease.
- Waldenström’s macroglobulinemia (WM) is an uncommon disease resulting from the clonal proliferation of lymphoplasmacytic cells that produce monoclonal immunoglobulin M (IgM). However, the presence of a monoclonal IgM is not synonymous with WM and may be seen in other lymphoproliferative disorders.

**SUGGESTED READINGS**


POINTS TO REMEMBER:

Peripheral blood smear morphology should be interpreted in the context of clinical features. Review of the peripheral blood smear can clarify spurious results in a complete blood count. Acute promyelocytic leukemia frequently presents with a normal or low white blood cell count and evidence of a consumptive coagulopathy. Consider thrombotic thrombocytopenic purpura in the differential diagnosis whenever there is microangiopathic hemolytic anemia with thrombocytopenia.

Platelet satellitosis or platelet clumping may result in spurious thrombocytopenia due to an EDTA (ethylenediaminetetraacetic acid)-related phenomenon.

SUGGESTED READINGS

Funding mechanisms

Goals of care
A morphine infusion is inappropriate care for many dying patients. Palliative medicine is not limited in this way and may actively attempt to prolong life if consistent with the goals and values of the patient and family.

Funding mechanisms: Hospice care is a specific capped benefit, whereas there is no specialized funding mechanism for palliative care.

Studies have shown that end-stage cardiac and pulmonary patients are as symptomatic as cancer patients, but there are few studies on specific symptom management.

A morphine infusion is inappropriate care for many dying patients. It should not be used for sedation.

Palliative sedation, the conscious choice to decrease the level of consciousness of a patient is a procedure that requires patient and/or family consent.

SUGGESTED READINGS


CHAPTER 27  Palliative Medicine: What Every Internist Ought to Know  


Navigante AH, Castro MA, Cerchietti LC. Morphine versus midazolam as upfront therapy to control dyspnea perception in cancer patients while its underlying cause is sought or treated. *J Pain Symptom Manage.* 2010;39(5):820-830.


Question 1

A 19-year-old African American man presents to the emergency department with severe abdominal pain and jaundice. His past medical history is unremarkable, although his mother reports “growing pains” as a child. Further questioning reveals that the patient is adopted. He is febrile and tachycardic. The abdomen is diffusely tender. No rebound is present, and bowel sounds are present throughout. A small skin ulcer is noted on his left lower extremity. Complete blood cell count shows white blood cells at 17 K/μL, hemoglobin at 6.3 g/dL, and mean corpuscular volume at 89 μm³. Aspartate transaminase and alanine transaminase values are normal. Indirect bilirubin is 3.6 mg/dL. A peripheral smear was performed and displays crescent-shaped RBCs. Which of the following statements regarding this patient’s condition is true?

a) Sepsis is the most common cause of death in adults.
b) In the United States, few patients survive beyond the fifth decade.
c) A selective advantage against Plasmodium vivax malaria is present.
d) Transmission is autosomal dominant with variable penetrance.
e) Symptoms do not develop until the patient is older than 6 months.

Answer and Discussion

The answer is e.

Objective: Identify important epidemiologic and prognostic facts in sickle cell anemia.

This patient has sickle cell anemia (SSA), the most common heritable hematologic disease affecting humans. Inheritance is autosomal recessive, and among African American adults, SSA has a prevalence of 1 in 500, with 10% being carriers of the sickle trait. Patients have an electrophoretically abnormal hemoglobin (HgbS) that differs from HgbA by substitution of valine for glutamic acid at the sixth position of the β chain. On deoxygenation, HgbS begins to polymerize and changes the RBC from a biconcave disk to an elongated sickle shape. Patients with SSA have a selective advantage against Plasmodium falciparum malaria, with preferential sickling of parasitized cells. The rate of polymerization depends on the concentration of HgbS and the extent of deoxygenation. The sickling may be irreversible if enough cell damage occurs. Fetal hemoglobin (HgbF) is protective against polymerization and varies in its distribution among RBCs in patients with SSA. Signs and symptoms of the disease do not usually appear until the sixth month of life, at which time most HgbF has been replaced by HgbS. The most common cause of death in adult patients with SSA is from acute chest syndrome. Worldwide, approximately 120,000 babies with SSA are born each year, but <2% survive to the age of 5 years. In the United States and other developed countries, SSA patients often survive into their fifth or sixth decade.

Question 2

The patient proves to have squamous cell carcinoma of the lung and receives a course of mediastinal radiation therapy. The patient does quite well, noting rapid improvement in both the symptoms and signs of her superior vena cava obstruction. A staging workup subsequently demonstrates evidence of asymptomatic bone metastases in rib, femur, and multiple vertebral bodies. Because the patient is feeling well, she declines any discussion of chemotherapy and is followed in your office. Four months later, the patient calls you with the complaint of a 2-week history of increasing mid-back pain. The patient is fully ambulatory, but the pain is causing difficulty sleeping. The patient specifically denies any weakness in the lower extremities, radicular pain, or incontinence. You would do which of the following?

a) Suggest a course of acetaminophen with codeine
b) Order an elective bone scan
c) Refer the patient for radiation therapy to the spine
d) Order an MRI of the entire spine

Answer and Discussion

The answer is d.

Objective: Recognize symptoms of cord compression.

Spinal metastases have already been demonstrated in this patient. The new development of pain suggests the possibility of spinal cord compression and mandates the performance of a whole spine MRI. While it is important to identify focal neurologic complaints and serial neurologic examinations are necessary, they are not essential to the diagnosis of cord compression. Cord compression is an oncologic emergency, and symptomatic relief without further workup is not recommended. The imaging modality of choice is an MRI of the whole spine. While a nuclear medicine bone scan may identify lytic lesions in the spine, it does not have adequate...
sensitivity or specificity to identify cord compression. The treatment of choice depends on the MRI, and depending on the severity, may require urgent neurosurgical evaluation.

**Question 3**

In the office, you perform a 1-L thoracentesis for slightly bloody fluid, which on analysis proves exudative. Cultures are negative, and cytologies are not diagnostic. The patient feels immediately better after the thoracentesis but returns to the office 3 days later with increasing dyspnea and recurrence of this effusion. Your next step is which of the following?

a) Repeat the thoracentesis with cytology
b) Repeat the thoracentesis with cytology and perform a closed pleural biopsy
c) Refer the patient for thoracoscopy
d) Refer the patient for chest tube drainage and pleural sclerosis

**Answer and Discussion**

The answer is d.

**Objective:** Identify therapeutic strategies for likely recurrent malignant effusion.

In a patient with a diagnosed malignancy and recurrent pleural effusions, the pre-test probability of a malignant effusion is fairly high. Attempts to confirm the diagnosis may be difficult due to the low sensitivity of pleural fluid cytology. In a patient this sick with recurrent symptomatic effusions, it may be most prudent to forego further aggressive attempts to confirm the likely diagnosis of a malignant pleural effusion and to proceed directly to appropriate management. Repeat thoracentesis will provide temporary symptomatic relief, but will need to be repeated frequently. Thoracoscopy is a diagnostic maneuver and will offer no significant therapeutic benefit. Chest tube drainage followed by pleural sclerosis is the most likely definitive management for this patient’s recurrent effusions.

**Question 4**

You are following a 65-year-old man with a recently diagnosed acute myeloid leukemia initiated on induction chemotherapy. The patient has onset of heart palpitations, numbness and tingling in his hands and feet, and severe pain in his right big toe. You are concerned about tumor lysis syndrome. Tumor lysis syndrome is associated with all the following, except

a) Hypercalcemia
b) Hyperkalemia
c) Hyperphosphatemia
d) Hyperuricemia

**Answer and Discussion**

The answer is a.

**Objective:** Identify lab abnormalities in tumor lysis syndrome.

Tumor lysis syndrome (TLS) is a known and often profound complication of any malignancy, but is most often seen in acute hematologic malignancies after initiation of cytotoxic chemotherapy. Some of the other risk factors associated with TLS are high tumor cell proliferation rate, large tumor burden, and chemosensitivity of the malignancy. Laboratory abnormalities of TLS center around release of intracellular products, leading to hyperuricemia, hyperkalemia, and hyperphosphatemia among others. Hyperphosphatemia can then lead to a secondary hypocalcemia with precipitation of calcium phosphate, which can lead to deposition in renal tubules leading to rapidly progressive renal failure. Symptoms of TLS center around these electrolyte abnormalities, and lead to a very heterogeneous presentation.

**Question 5**

A 24-year-old woman presents for an annual gynecologic examination. She has never had a Papanicolaou (Pap) smear and has been sexually active since age 19 years with five lifetime partners to date. She has not had any pregnancies or sexually transmitted diseases. What do you recommend regarding her gynecologic screening and care?

a) No screening currently necessary
b) Pap smear alone
c) Pap smear and human papillomavirus (HPV) testing
d) Pap smear and HPV vaccine
e) None of the above

**Answer and Discussion**

The answer is d.

**Objective:** Identify indications for cervical cancer screening and HPV vaccination.

According to the United States Preventative Services Task Force (USPSTF) update in 2012, cervical cancer screening should begin at age 21 years for all patients with Papanicolaou (Pap) smear screening. The recommendation for screening women between 21 and 65 years of age for cervical cancer is cytology testing every 3 years with reflexive HPV testing. In women older than 30 years, concurrent Pap and HPV testing every 5 years can replace cytology testing with Pap smear alone every 3 years. By the age of 30, most transient HPV infections have cleared. However, current recommendations are to vaccinate all women aged 11 to 12 years, catch up vaccination for women aged 13 to 26 years, and consideration for vaccination of girls aged 9 to 10 years.

**Question 6**

A 56-year-old woman had a recent diagnosis of breast cancer. She underwent breast lumpectomy with negative lymph nodes and negative margins, breast irradiation, and is now on tamoxifen. Due to the increased risk of endometrial cancer with tamoxifen use, you recommend

a) Hysterectomy ± bilateral salpingo-oophorectomy
b) An endometrial biopsy at least every 6 months while on tamoxifen therapy
c) Annual ultrasound screening while on tamoxifen therapy
d) Evaluation only if symptoms arise
e) Oral progesterone therapy
Answer and Discussion
The answer is d.
Objective: Identify risk of endometrial cancer and recommended screening in women taking tamoxifen.
Tamoxifen is associated with an increased risk of endometrial cancer (estimated ∼ 1 in 500). However, studies have not shown any benefit to screening women taking tamoxifen with either ultrasound or biopsy. Symptoms should drive any additional workup for identifying potential endometrial cancer in women taking tamoxifen. Common symptoms include vaginal bleeding or discharge. Evaluation should include ultrasound measurement of endometrial thickness and hysteroscopy with biopsy.

Question 7
A 74-year-old obese white woman presents with vaginal bleeding. You do an endometrial biopsy and find a grade 1 endometrial carcinoma. She asks about her primary mode for therapy, and you tell her
a) Whole pelvic radiation is the primary treatment modality in women older than 70 years
b) Hysterectomy, oophorectomy, and staging are the best initial approaches
c) A trial of progesterone and repeat biopsy in 3 months would have high cure rates
d) Concomitant chemoradiation has been shown to improve survival in locally advanced endometrial cancer
e) None of the above

Answer and Discussion
The answer is b.
Objective: Identify treatment modality for endometrial cancer.
Current standard of care for women with endometrial cancer is surgical staging with hysterectomy, salpingo-oophorectomy, and staging lymph node sampling. Radiation can be used as primary therapy in medically inoperable patients, and hormonal therapy can be used cautiously in young women who want to preserve their fertility. There are currently no data to support chemoradiation in endometrial cancer.

Question 8
A healthy 42-year-old female patient asks about screening for ovarian cancer. She has no symptoms suggestive of the disease, and the results of her physical examination are normal. You should
a) Ask about her family history of ovarian and breast cancers
b) Strongly recommend yearly screening until at least age 70 years
c) Recommend a CA-125 blood test and transvaginal ultrasonography
d) Recommend consultation for prophylactic oophorectomy
e) None of the above

Answer and Discussion
The answer is d.
Objective: Identify appropriate therapy for metastatic ovarian cancer.
The standard treatment for advanced ovarian cancer is surgical debulking, followed by cisplatin or carboplatin, plus paclitaxel chemotherapy regimen. No evidence suggests that neoadjuvant chemotherapy or chemotherapy alone is more beneficial than the surgery plus chemotherapy. Given the overwhelming evidence for a primary ovarian cancer, additional diagnostic testing for another primary malignancy, including colonoscopy and esophagogastroduodenoscopy, would not be appropriate.

Question 9
A 53-year-old female patient with abdominal bloating and a large pelvic mass, carcinomatosis, and CA-125 of 1,340 U/mL presents to discuss paracentesis results showing adenocarcinoma. She asks for your recommendation regarding treatment. Which one of the following would be the best recommendation in this setting?

a) Refer for colonoscopy and esophagogastroduodenoscopy
b) Begin neoadjuvant chemotherapy while awaiting surgical consultation
c) Give six cycles of cisplatin or carboplatin plus paclitaxel, and then repeat abdominal imaging to assess response
d) Referral for surgical tumor resection followed by cisplatin or carboplatin plus A taxane
e) None of the above

Answer and Discussion
The answer is d.
Objective: Identify screening strategies for ovarian cancer.
Currently, no evidence suggests that screening for ovarian cancer reduces mortality from this malignancy. If there are multiple women with breast or ovarian cancer, particularly at young ages, these women should be referred for genetic counseling and testing. High-risk patients can then be offered screening. However, it can certainly be argued that screening at least has the potential for detecting the disease at an earlier point in time when therapy may be more effective. A woman undergoing such screening must be informed of the limited data supporting this therapeutic strategy.

Question 10
A 67-year-old man, 4 years status post prostatectomy presents with low back pain and tenderness. His prostate-specific antigen is 185, and a bone scan is positive in multiple areas. The most appropriate treatment is

a) Orchiectomy
b) Radiation therapy to the prostate bed followed by orchiectomy
c) Chemotherapy with docetaxel
d) Bicalutamide (Casodex) followed by goserelin (Zoladex) subcutaneously every 3 months

e) a or d

**Answer and Discussion**

The answer is e.

**Objective:** Identify appropriate therapeutic strategy for recurrent, metastatic prostate cancer.

Orchiectomy (a) or bicalutamide followed by goserelin (d) represents appropriate initial hormone therapy for patients with systemic disease from metastatic prostate cancer. Bicalutamide is given before goserelin for approximately 10 days to prevent the stimulation of prostate cancer growth that accompanies the transient surge in testosterone production that occurs shortly after the initiation of luteinizing hormone–releasing hormone agonists (goserelin or leuprolide). The great majority of men have rapid systematic relief, with a radiographic response as well. Radiation to the prostate bed (b) has no role for a patient with metastatic cancer and, therefore, would be performed prior to orchiectomy. Chemotherapy (c) is appropriate for the patient whose disease progresses on hormone therapy.

**Question 11**

A 28-year-old male baseball star presents with a painless left testicular mass. Physical examination is otherwise normal. α-Fetoprotein is >400. The most appropriate next step is

a) Testicular ultrasound
b) Ultrasound-guided transcrotal testicular biopsy
c) Inguinal orchiectomy
d) Trial of antibiotics
e) Whole body positron emission tomography scan

**Answer and Discussion**

The answer is a.

**Objective:** Identify diagnostic strategy for suspected testicular cancer.

Testicular ultrasound (a) is the initial diagnostic test of choice for any patient who presents with a testicular mass. Although one might argue that an α-fetoprotein level of 400 in a young man with a testicular mass is essentially diagnostic of testicular cancer, an ultrasound is still an important first step followed by radical inguinal orchiectomy (c). A transscrotal testicular biopsy (b) is contraindicated due to the violation of tissue planes, which allows alternate lymphatic avenues of metastasis. A trial of antibiotics (d) is not warranted in a patient who has a painless left testicular mass and no testicular tenderness to suggest epididymitis or some other infectious etiology. A whole body positron emission tomography scan (e) is not a staging procedure at the initial diagnosis of testicular cancer. CT scanning of the chest, abdomen, and pelvis is the standard staging workup, but would not be pursued before a diagnosis has been confirmed.

**Question 12**

A 22-year-old man with testicular cancer comes back to your office 5 months after a radical inguinal orchiectomy and chemotherapy for nonseminomatous germ cell tumor. The patient feels well and has no complaints. His markers (α-fetoprotein, β-HCG, and LDH) normalized with treatment and remain normal. A mass is palpated in the left midabdomen. This mass is most likely

a) A mature teratoma, best treated with surgical resection
b) Recurrent testicular cancer, best treated with high-dose chemotherapy and autologous stem cell rescue
c) Seminoma, best treated with radiation therapy
d) Chemotherapy-induced chloroma (solid tumor manifestation of acute leukemia), best treated with radiation and chemotherapy

e) A 28-year-old male baseball star presents with a painless left testicular mass. Physical examination is otherwise normal. α-Fetoprotein is >400. The most appropriate next step is

**Answer and Discussion**

The answer is a.

**Objective:** Diagnose and treat a mature teratoma after therapy for nonseminomatous germ cell tumor.

Mature teratoma (a) is a well-known phenomenon that can occur after the successful treatment of nonseminomas, particularly those that contain a component of teratoma. Such a mass is generally curable with surgical resection. Left untreated, these masses can degenerate into malignant teratomas that are not curable. Recurrent testicular cancer (b) can certainly occur but is an unusual phenomenon and, in the setting of tumor markers that remain normal, would be highly unlikely. Seminoma (c) would similarly be extremely unusual after chemotherapy for a nonseminoma. Chemotherapy-induced acute leukemia (d) is a well-described complication of chemotherapy but occurs with a latency of 2 to 9 years. In addition, a patient with acute leukemia and tumor bulk consisting of a chloroma would not generally be asymptomatic.

**Question 13**

A 35-year-old woman presents to the emergency room with 24 hours of fever and chills. In addition, she complains of increasing fatigue, dyspnea on exertion, and spontaneous bruising.

On physical examination, she appears ill; her vitals are temperature 39.5°C, blood pressure 80/40 mmHg, pulse 140 beats/minute, respiration rate 22 breaths/minute, petechiae on soft palate, no lymphadenopathy, clear lungs, tachycardia, I/VI systolic ejection murmur, no abdominal mass or hepatosplenomegaly, and scattered petechiae, especially on lower extremities.

Her laboratory values are hemoglobin, 8.7; platelets, 14,000; white blood cells, 3,000, with 2% neutrophils, 45% lymphocytes, and 53% blasts; international normalized ratio, 1.1; partial thromboplastin time, 23; and fibrinogen, 345.
Her peripheral blood smear shows normochromic, normocytic anemia; thrombocytopenia; rare neutrophils; and many blasts.

The best course of action is to immediately
a) Withhold antibiotics until the source of infection is identified
b) Fluid resuscitate and start piperacillin and gentamicin
c) Fluid resuscitate and give granulocyte transfusion
d) Perform bone marrow aspirate and biopsy

**Answer and Discussion**

The answer is b.

**Objective: Treat life-threatening sepsis in a neutropenic patient.**

This patient has life-threatening sepsis and must be admitted for fluid resuscitation; a quick evaluation including blood cultures; and the administration of empiric, broad-spectrum intravenous antibiotics. Broad-spectrum antibiotics should specifically target gram-negative bacilli, as this is the predominant group of pathogens involved in neutropenic patients. Empiric coverage of gram-positive agents in this patient would not be inappropriate, but should not supersede coverage of gram-negative agents. While every attempt to obtain cultures prior to initiation of antibiotics should be made, antibiotics should not be withheld to identify a source, as time to antibiotic initiation has been shown to directly correlate with mortality. She is anemic, thrombocytopenic, has spontaneous bruising, and is at risk for life-threatening hemorrhage. She will likely need transfusion with RBCs and platelets. However, there is no clear role for granulocyte transfusions. Bone marrow aspirate and biopsy may be needed in the future to diagnose etiology of her neutropenia, but are not indicated at this time.

**Question 14**

A 25-year-old man presents to the emergency room complaining of dyspnea on exertion for several days. Recently, he has noted frequent nasal congestion and occasional epistaxis. He denies fevers, night sweats, and weight loss, and has noted a rash on his legs. He denies any hospitalizations or history of transfusions.

On physical examination, you find a well-developed man in no acute distress; temperature 36.8°C, blood pressure 126/74 mmHg, respiration rate 20 breaths/minute; his oral mucosa has a few petechial hemorrhages, the skin of the pretibial area is covered with petechial hemorrhages, and no palpable lymphadenopathy or splenomegaly is present; he is otherwise normal.

His laboratory values are hemoglobin, 8.3; platelets, 32,000; white blood cells, 1,100, with 1% neutrophils, 73% lymphocytes, 13% monocytes, and 13% blasts; prothrombin time, 20; international normalized ratio (INR), 2.1; partial thromboplastin time, 40; and fibrinogen, 90.

His peripheral smear shows pancytopenia, circulating blasts with Auer rods, and occasional schistocytes. A bone marrow aspirate and biopsy is hypercellular with 85% blasts and immature granulocytes.

The most important next step is to
a) Confirm the diagnosis with cytogenetic analysis
b) Start piperacillin and gentamicin
c) Transfuse platelets and fresh-frozen plasma
d) Start chemotherapy

**Answer and Discussion**

The answer is d.

**Objective: Diagnose and treat acute promyelocytic leukemia.**

This patient probably has acute promyelocytic leukemia, given the obvious Auer rods and evidence of a significant coagulopathy, likely disseminated intravascular coagulopathy (DIC) as evidenced by anemia, thrombocytopenia, elevated INR, and low fibrinogen. Both plasma and platelets are needed to reduce the incidence of fatal hemorrhage. In the absence of fever or other signs of infection, antibiotics are not recommended for neutropenia. Prophylactic antibiotics are controversial but have not consistently been shown to improve survival. Urgent therapy is needed, but chemotherapy may precipitate a worsening of the coagulopathy. All-trans retinoic acid is usually started before chemotherapy in order to reduce the incidence of severe bleeding.

**Question 15**

A 29-year-old woman presents to your office for a Papanicolaou smear. She is asymptomatic and has a normal physical examination except for a moderately enlarged spleen.

Her laboratory values are hemoglobin, 11.9; platelets, 671,000; and white blood cells, 227,000, with 55% neutrophils, 7% metamyelocytes, 19% myelocytes, 2% promyelocytes, 2% blasts, 1% eosinophils, 7% basophils, and 3% lymphocytes. A bone marrow chromosome analysis shows 46,XX, t(9;22).

The most important next step is to
a) Immediately hospitalize
b) Start chemotherapy
c) Tissue-type the patient and her siblings to consider bone marrow transplantation
d) Start imatinib

**Answer and Discussion**

The answer is d.

**Objective: Diagnose and treat chronic myelogenous leukemia (CML).**

This patient’s signs, symptoms, complete blood count, and bone marrow are characteristic of CML. The t(9;22) is the Philadelphia chromosome, which secures the diagnosis. The high white blood cell count requires neither leukapheresis nor hospitalization. Unlike a high blast count, a high neutrophil count does not increase the risk of leukostasis and hyperviscosity syndrome. Hydroxyurea, and other chemotherapeutic agents, will not prevent the progression of CML to blast crisis. The only known curative therapy is bone marrow transplant,
but this procedure carries a significant risk of early mortality. Because imatinib induces long-lasting remissions in the majority of patients, transplant is usually deferred until the time imatinib and other tyrosine kinase inhibitors fail.

**Question 16**

A 35-year-old man with acute myelogenous leukemia has been severely neutropenic for 10 days and has been febrile with temperatures >38.5°C for the past 5 days. He has been on piperacillin, gentamicin, and vancomycin for 8 days. No localizing signs of infection are present on examination, and all cultures are negative to date. The most appropriate course of action would be to

a) Continue current antibiotics
b) Change antibiotics to imipenem
c) Add voriconazole
d) Draw fungal cultures and continue current antibiotics

**Answer and Discussion**

The answer is c.

**Objective: Identify risk of fungal infections in a neutropenic patient.**

As the duration of neutropenia increases, the risk of fungal infection increases. This is particularly true in the setting of broad-spectrum antibacterials. This patient is at high risk for fungal infection. The current antibiotics are failing; thus continuing them with no other changes is inappropriate. A change to imipenem might cover additional bacterial pathogens, but does not address the risk of fungal infection. Fungal infections are difficult to isolate. Clinical studies have clearly demonstrated the importance of *empiric* antifungal therapy. Thus, voriconazole is the correct choice.

**Question 17**

A 75-year-old man with a 5-year history of untreated, chronic lymphocytic leukemia presents with fatigue and a peculiar craving for ice. Examination reveals generalized, but small peripheral lymphadenopathy and a barely palpable spleen tip. His laboratory values are white blood cells, 34,000; hemoglobin, 5.2; and platelets, 133,000; reticulocytes 2%; direct Coombs’ test negative; and lactate dehydrogenase and bilirubin normal. The peripheral blood smear demonstrates normocytic red cells and no polychromasia. The most likely cause of anemia in this patient is

a) Pure red cell aplasia
b) Autoimmune hemolytic anemia
c) Bone marrow infiltration with leukemia
d) Gastrointestinal bleeding

**Answer and Discussion**

The answer is d.

**Objective: Identify causes of anemia in patients with chronic lymphocytic leukemia (CLL).**

CLL is a fairly common lymphoproliferative disorder in the older patient population. Although CLL may be the direct cause of anemia in some patients, it is important to remember that these patients are also at risk for other problems as well. This particular patient has pica, a very specific symptom of iron deficiency anemia. Even though the red cells are not microcytic, iron deficiency anemia is still possible, especially if the onset is relatively rapid. Pure red cell aplasia is another possibility, but less likely given the indolent nature of the patient’s leukemia and the presence of pica. Similarly, infiltration of the marrow with leukemia in an untreated patient would not likely be enough to induce this degree of anemia given the nonbulky lymph nodes, modest splenomegaly, and modest leukocytosis. The absence of microspherocytes, reticulocytosis, and a negative Coombs’ test make autoimmune hemolytic anemia (AIHA) the least likely cause of anemia in this patient, but AIHA is a common cause of anemia in patients with CLL.

**Question 18**

At 2:00 AM, a young woman presents to the emergency department of a small rural community hospital complaining of headache and fever. Except for some pallor, mild scleral icterus, and sleepiness, the physical examination is normal. The complete blood count report comes back with “low platelets” and a hematocrit of 28%. The prothrombin time/activated partial thromboplastin time and electrolytes are normal. The lab sends down the peripheral smear, which you examine under the microscope.

The next best step is

a) Immediate broad-spectrum antibiotics for probable meningococcal sepsis
b) Platelet transfusions to control a probable intracerebral bleed
c) High-dose steroids for probable autoimmune thrombocytopenia with autoimmune hemolytic anemia (Evan’s syndrome)
d) Immediate transfusions of fresh-frozen plasma
Answer and Discussion
The answer is d.

Objective: Diagnose and treat thrombotic thrombocytopenic purpura (TTP).

The diagnosis of TTP is easily made given the clear evidence of microangiopathic hemolysis (arrows show schistocytes on blood smear) associated with thrombocytopenia, fever, and neurologic signs/symptoms. With this degree of thrombocytopenia and hemolysis, a normal prothrombin time/activated partial thromboplastin time effectively rules out disseminated intravascular coagulation, thus making sepsis unlikely. Autoimmune hemolytic anemia does not produce schistocytes, but rather produces spherocytes. Platelet transfusions are relatively contraindicated in TTP because of their potential to aggravate thrombosis. Ideally, the patient should receive plasmapheresis with fresh-frozen plasma (FFP) replacement; however, in the emergency setting in a rural emergency department, the first available treatment is transfusion with large volumes of FFP while making arrangements for transfer to an institution that can perform apheresis.

Question 19

An asymptomatic 59-year-old woman was referred to you for preoperative clearance for a planned open colectomy. The routine laboratory examinations were all normal except for an elevated activated partial thromboplastin time (aPTT) of 57 seconds. She denied any history of excess bleeding or bruising. The lab calls you the next day to inform you that when they mixed her plasma 1:1 with pooled normal plasma, the aPTT was 43 seconds, normal being <31 seconds. Which of the following is most likely true?

a) The story is most consistent with mild von Willebrand disease, and the patient should be treated preoperatively with DDAVP (desmopressin).

b) The most likely diagnosis is “lupus anticoagulant,” and the patient needs to receive perioperative thromboprophylactic therapy because of the increased risk of venous thromboembolism.

c) The woman likely has congenital factor XI deficiency and needs to have fresh-frozen plasma administered prior to surgery.

d) The woman most likely has an acquired, autoimmune factor VIII inhibitor and needs aggressive immune suppressive therapy prior to surgery.

Answer and Discussion
The answer is b.

Objective: Identify causes of elevated coagulation studies.

The aPTT would correct to normal if the patient had von Willebrand disease or congenital factor XI deficiency because the aPTT prolongs only if factor levels drop below ~40% of normal. Acquired factor VIII inhibitors are almost always associated with severe bleeding and bruising. Thus, the likely scenario here is lupus anticoagulant, a finding seen with the antiphospholipid syndrome. This is a significant risk factor for thrombosis, and the additional prothrombotic stress of general surgery mandates thromboprophylaxis.

Question 20

Mr. Jones is a 77-year-old retired steel worker who is widowed and lives alone in a two-story house. He was brought to the emergency room (ER) by his daughter because of an extremely painful, swollen, red right leg. He believed that maybe he twisted his knee while walking down the stairs in his home, but when the pain and swelling did not improve after 24 hours and the swelling extended up into his thigh, he called his daughter who immediately brought him to the ER. A physical examination revealed normal vital signs; mild degenerative joint disease; and a swollen, erythematous right leg. A duplex Doppler was performed and revealed a large occlusive thrombus extending from the popliteal vein to the iliofemoral system. Chest x-ray and ECG were normal, and the physician in the infirmary gave him a prescription for enoxaparin and warfarin and referred him to your office. You saw him 3 days later, at which time his international normalized ratio was 2.8. You take a detailed history and discover that he has been feeling “poorly” for about 2 months. He notices a definite loss of energy, decreased appetite, and constipation. Physical examination reveals a rather frail elderly man with muscle wasting in the temporal region. Prostate is 3+ enlarged but without nodules. Stool is negative for occult blood. The remainder of the examination is negative except for the right leg, which is still swollen and tender, although no longer red. The most appropriate course of action at this point is to

a) Obtain colonoscopy
b) Stop the enoxaparin because his international normalized ratio is now therapeutic
c) Obtain thrombophilia panel, including factor V Leiden assay, to guide decision on duration of anticoagulation
d) Obtain plasma anti-Xa assay to assess enoxaparin dosing because his leg is still swollen and tender

Answer and Discussion
The answer is a.

Objective: Identify deep venous thrombosis as a potential complication of malignancy.

An underlying malignancy is the most likely etiology of his thrombophilia, and the presence of an inherited or other acquired thrombophilia is not likely to influence therapeutic decisions. Randomized trials showed that heparin therapy should always be extended for at least 5 days in patients with venous thromboembolism, even if the international normalized ratio (INR) is therapeutic. In fact, newer studies suggest that low molecular weight heparins are more effective than warfarin in long-term treatment of cancer-associated venous thrombosis. In this case, the rapid INR response is probably due to underlying vitamin K deficiency from malnutrition. Resolution of symptoms from severe deep vein thrombosis...
can take many days; persistent swelling at day 3 is not an indication of inadequate heparin effect.

**Question 21**
Which of the following bleeding disorders can be present despite normal screening coagulation studies (PT, aPTT, and PFA-100)?

a) Mild von Willebrand disease  
b) Mild hemophilia  
c) Factor XIII deficiency  
d) α-Antiplasmin deficiency  
e) All of the above

**Answer and Discussion**  
The answer is e.  
**Objective:** Identify role of coagulation studies in bleeding disorders.  
Mild coagulation factor deficiencies can be difficult to diagnosis because the screening assays are sensitive only to levels below 30% to 40% of normal. Disorders of clot stability, including fibrinolysis defects (e.g., α2-antiplasmin deficiency) and abnormal fibrin clot cross-linking (factor XIII deficiency), will not affect prothrombin time or activated partial thromboplastin time. von Willebrand factor levels fluctuate greatly and are sensitive to estrogen levels and acute inflammation so that platelet screening tests can be normal in patients with mild von Willebrand disease.

**Question 22**
A 56-year-old man has an uneventful mitral valve replacement surgery. Heparin was given during the procedure and continued postoperatively. On the eighth postoperative day, he develops a painful, cold, pulseless leg. His activated partial thromboplastin time is subtherapeutic at 39 seconds. His platelet count is 55,000/μL (112,000 on postop day 1). The most important next step in his management is to

a) Obtain a vascular surgery consultation for revascularization  
b) Increase the dose of heparin to obtain a therapeutic-activated partial thromboplastin time  
c) Perform platelet transfusion to increase count to >100,000/μL  
d) Discontinue all heparin immediately  
e) Begin warfarin and order anti-PF4 antibody test so that heparin can be safely stopped if the test is positive

**Answer and Discussion**  
The answer is d.  
**Objective:** Identify appropriate therapeutic strategy for presumed heparin-induced thrombocytopenia (HIT).  
If HIT is suspected, as it should be in this case of acute thrombosis in the setting of a 50% drop in platelet count, then it is critical to stop all heparin (including catheter flushes immediately) and initiate therapy with a direct thrombin inhibitor. Giving more heparin or infusing platelets are associated with worse outcomes. Vascular surgery may be helpful, but not before stopping the heparin. Warfarin has been associated with cutaneous thrombosis and necrosis in the setting of HIT and should not be used acutely.

**Question 23**
Which of the following is true of DDAVP (desmopressin)?

a) Is an analog of vasopressin and can cause hypernatremia  
b) Should not be given chronically to prevent bleeding in patients with moderate von Willebrand disease (vWD)  
c) Does not have efficacy in several mild platelet disorders, such as storage pool defect  
d) Can be used in all causes of vWD

**Answer and Discussion**  
The answer is b.  
**Objective:** Identify indications for DDAVP (desmopressin).  
DDAVP is an analog of vasopressin and therefore can cause hyponatremia by increasing the activity of the ADH axis. It also has been shown to stimulate the release of von Willebrand factor from endothelial cells. However, tachyphylaxis occurs with this drug so that efficacy typically disappears after two or three sequential doses. Thus, it cannot be given chronically. Type IIB vWD is associated with a gain-of-function mutation such that when von Willebrand factor binds to glycoprotein 1, it leads to increased clearance of platelets. DDAVP, which stimulates release of von Willebrand factor, can cause thrombosis and/or severe thrombocytopenia in patients with type IIB vWD and, thus, should not be used in that setting.

**Question 24**
A 22-year-old sexually active female college student is referred to you from the Student Health Service because of a low platelet count (18,000/μL) that was discovered when a complete blood count (CBC) was obtained to evaluate a rash on her lower extremities. She has been feeling otherwise well, but has noted some gum bleeding when she brushes her teeth over the past few days. She takes no medications other than a multivitamin. She had a normal CBC at the time of her college physical. The following would be an appropriate next step:

a) Immediately obtain bone marrow aspirate  
b) Begin therapy with intravenous immunoglobulin G because her platelet count is so low  
c) Send out tests for hepatitis C and HIV  
d) Send out tests to rule out systemic lupus erythematosus

**Answer and Discussion**  
The answer is c.  
**Objective:** Identify risk factors for ITP.  
The most likely diagnosis is idiopathic/immune-mediated thrombocytopenic purpura (ITP), and in a young woman...
with no other likely cause of thrombocytopenia, a bone marrow aspirate is not necessary. Intravenous immunoglobulin is not considered first-line therapy in the absence of major bleeding; rather, prednisone at 1 mg/kg/day would be the preferred medical therapy. Although lupus is associated with ITP, finding a positive ANA or anti-DNA would not change management. HIV and hepatitis C are not uncommon causes of ITP in young, sexually active patients and should always be ruled out.

**Question 25**

You are called to the surgical intensive care unit to consult on a case of a 60-year-old 75 kg male chronic alcoholic who was admitted with a severe gastrointestinal bleed. After resuscitation with 4 units of packed RBCs, he was noted to have a hemoglobin of 11 g/dL, an activated partial thromboplastin time (aPTT) of 90 seconds, a prothrombin time (PT) of 24 seconds, a platelet count of 90,000, and a bilirubin of 12. The lab reported that a 50:50 mix of his plasma with pooled normal plasma corrected both the aPTT and PT to normal. Appropriate therapeutic interventions include

- Transfuse 2 units of fresh-frozen plasma now and repeat every 8 hours
- Administer low-dose heparin to stop the DIC process
- Administer high-dose steroids to raise the platelet count
- None of the above

**Answer and Discussion**

The answer is d.

**Objective: Identify expected correction of coagulopathy with transfusion.**

This patient has a profound coagulopathy, likely due to hepatic failure, although a component of vitamin K deficiency could also be present. There is no evidence to support disseminated intravascular coagulation. The modest thrombocytopenia is probably multifactorial in origin, including splenomegaly from portal hypertension and alcohol-related marrow toxicity; high-dose steroids are not likely to have a significant effect. The appropriate treatment is transfusion of fresh-frozen plasma, but he will need far more than 2 units to correct his severe factor deficiency, and dosing every 8 hours will not be adequate. While every patient responds differently to fresh-frozen plasma, current thought is that 10% increase in coagulation factors is the minimum required to see any clinical response. In an average 70 kg patient, 4 units of fresh frozen plasma would achieve ~10% increase in coagulation factors.

**Question 26**

Ms. Smith is an 82-year-old widow who lives alone and has been brought to your emergency department by her niece who notes that her aunt has been “failing” for the past 2 to 3 months. Other than long-standing hypertension, the medical history is noncontributory. Physical examination reveals a sleepy, thin elderly woman with pedal edema, blood pressure of 190/110 mmHg, and S3 gallop. Laboratory values are remarkable for hemoglobin of 7 g/dL, creatinine of 9.2, and blood urea nitrogen of 123. That evening, she develops a severe nose bleed that requires packing by the ear/nose/throat service and also notices bleeding external hemorrhoids. Which of the following can be used to improve her hemostasis?

- a) Aggressive dialysis to resolve her uremic state
- b) Packed RBC transfusion and erythropoietin to bring her hemoglobin to >10 g/dL
- c) Intravenous desmopressin
- d) High doses of estrogen
- e) All of the above

**Answer and Discussion**

The answer is e.

**Objective: Identify therapeutic strategies for uremic platelet dysfunction.**

Uremia is associated with a moderate to severe multifactorial bleeding diathesis that can be improved with dialysis and that responds partially to pharmacologic intervention with DDAVP (desmopressin) (can only be used acutely) or estrogen (can be used more chronically). One function of RBCs is to “push” platelets to the outer edge of the column of flowing blood, maximizing their interaction with the vascular wall. Thus, the bleeding time is negatively influenced by severe anemia and can be improved by treating the anemia.
Question 28

A 31-year-old woman presents with complaints of fatigue, dyspnea on exertion, and tinnitus. The symptoms started 1 month ago. She had previously been in "perfect health." She has had three normal pregnancies. Her physical examination is remarkable for pallor. The hemoglobin concentration is 7.5 g/dL, the white blood cell count is 6,200, and her platelet count is 550,000/μL. After her last pregnancy 2 years ago, her hemoglobin was normal. Which of the following tests is the most appropriate first test in the initial evaluation of this patient's anemia?

a) Serum folate and vitamin B₁₂ level  
b) Review of the peripheral blood smear  
c) Serum ferritin determination  
d) Haptoglobin level  
e) Coombs’ direct and indirect tests

Answer and Discussion

The answer is b.

Objective: Identify initial workup of new anemia.

A review of the peripheral blood smear (PBS) is the single most valuable first step in evaluating an acute anemia. The morphology of the RBCs, the presence of polychromasia (reticulocytes), and platelet morphology can help focus the differential diagnosis and evaluation immediately. The differential diagnosis for this patient’s acute or subacute anemia is broad and includes both gastrointestinal blood loss and diverse causes of hemolysis. The iron studies, folate and B₁₂ levels, haptoglobin, and Coombs’ test are premature and should be ordered according to results of the PBS review and reticulocyte count.

Question 29

A 24-year-old Lebanese male exchange student comes to the college infirmary with a 3-day history of upper respiratory infection symptoms, cough, purulent sputum, and a low-grade fever. His chest examination is clear, and he is given available trimethoprim-sulfamethoxazole (Bactrim) samples for clinical bronchitis. The following day, he returns with shortness of breath, severe abdominal pain, a high spiking fever, and dark urine. A complete blood count reveals a hemoglobin of 7 g/dL and a white blood cell count of 12,500. Peripheral blood smear has fragmented RBCs, and distinct “bite cells” are present. The chest radiograph is normal. The patient is admitted to the hospital. Which of the following statements is true?

a) The Coombs’ direct test will be positive  
b) The haptoglobin will be undetectable  
c) A sickle prep screen would be positive  
d) All of the above

Answer and Discussion

The answer is b.

Objective: Identify glucose-6-phosphate dehydrogenase (G6PD) deficiency as a cause of acute anemia.

This patient has clinical G6PD deficiency with acute hemolysis, as manifested by the acute drop in hemoglobin, dark urine, and fragmentation on the peripheral blood smear. People of Mediterranean descent are more susceptible to rapid severe hemolysis, in contrast to people of African descent. The “bite cells” on the smear are pathognomonic for this condition, which was triggered by the oxidative stress of the sulfa drugs. The precipitating hemoglobin results in RBC stromal damage and acute hemolysis. The haptoglobin level will be low if not undetectable because of its binding to free hemoglobin and removal by the liver. The Coombs’ tests, both direct and indirect, are negative because antibodies are not involved in this physical form of hemolysis. Although many antibiotics might produce immune hemolysis, the time course of acute onset within 24 hours goes against any immune process. The sickle preparation will be negative because the precipitation of hemoglobin results in inclusion bodies but not in polymerization with deformity of the RBC architecture. Sickle cells will not be seen unless this patient also has a hemoglobinopathy.

If the G6PD enzyme levels were measured, they would be near normal in the remaining young cells that survived and were not hemolyzed. As these cells age, the enzyme decays, and the enzyme levels drop, thus making these cells vulnerable to stress hemolysis. After acute hemolysis, however, the surviving cells usually have normal levels of enzyme.

Question 30

A 48-year-old man presents with fatigue, weakness, diffuse non-localizing abdominal complaints, loss of libido, “funny sensations” in his arms and legs, and depression. He has attempted to medicate himself with “megadose” of B-complex vitamins as well as vitamin E and α-carotene. He denies any recent alcohol consumption and has had no diarrhea or steatorrhea. He has never had surgery. Physical examination is remarkable for a chronically ill-appearing middle-age man. The only objective abnormalities include decreased sensation in the legs and decreased proprioception. Initial workup includes a complete blood count with a hemoglobin of 13 g/dL, mean corpuscular volume of 120, and white blood cell count of 4,500. Platelets were 220,000. The peripheral blood smear confirms macrocytosis and rare hypersegmented polys. Reticulocyte count is 0.5%. You measure serum B₁₂ and folate levels because of the macrocytosis. Folate is >14 (normal > 2.0) and B₁₂ is 20 (normal > 100). Which of the following statements is false?

a) Administration of folate can correct the anemia of B₁₂ deficiency  
b) With severe vitamin B₁₂ deficiency, pancytopenia can result  
c) Folate administration cannot correct the myelin production defects and neurologic deficits  
d) An oral vitamin B₁₂ preparation (Geritol) would have been likely to prevent the patient’s neurologic deficits

Answer and Discussion

The answer is d.

Objective: Identify pernicious anemia.

This patient most likely has pernicious anemia, an autoimmune disease directed against the intrinsic factor.
producing parietal cells of the gastric antrum. Almost all vitamin B\textsubscript{12} deficiency is the result of malabsorption, either because of a lack of intrinsic factor (pernicious anemia) or because of a defective small bowel. Dietary deficiency is very rare and occurs almost exclusively in strict ovo-lacto vegetarians who consume no animal products (vegan). Oral vitamin B\textsubscript{12} administration cannot overcome the deficit in malabsorption. Schilling’s test, which measures the absorption of oral vitamin B\textsubscript{12} in the presence of exogenous intrinsic factor, can distinguish the etiology of the malabsorption.

Folate administration circumvents the B\textsubscript{12} defect, in the production of thymidine and DNA synthesis. Therefore, anemia may be ameliorated, and only macrocytosis may exist. Folate does not correct the defect in myelin production, however, so neurologic deficits may exist without hematologic abnormalities.

**Question 31**

A 40-year-old premenopausal woman treated with chemotherapy alone for early-stage hormone receptor–positive breast cancer 3 years ago develops diffuse bone pain and is found to have multiple lytic bone metastases. Appropriate management for this patient is:

a) Refer to radiation therapy  
b) Begin a selective aromatase inhibitor  
c) Initiate trastuzumab in combination with taxane chemotherapy  
d) Recommend bilateral oophorectomy, tamoxifen, and monthly zoledronate  
e) Proceed with high-dose chemotherapy and stem cell transplant

**Answer and Discussion**

The answer is d.

**Objective: Identify therapeutic strategy for metastatic hormone receptor–positive breast cancer.**

Appropriate first-line hormonal therapy for a premenopausal woman with osseous metastatic breast cancer includes ovarian ablation, tamoxifen, or both. An aromatase inhibitor in combination with ovarian ablation would also be reasonable, but is not listed as an option. The addition of a bisphosphonate decreases the risk of fracture and other complications of lytic bone metastases.

**Question 32**

Which of the following factors in metastatic breast cancer predicts for response to hormonal therapy?

a) Prior response to tamoxifen  
b) Young age  
c) Hepatic involvement of breast cancer  
d) Persistence of menses following adjuvant breast cancer therapy

**Answer and Discussion**

The answer is a.

**Objective: Identify predictors of response to hormone therapy for metastatic breast cancer.**

Response to hormonal therapy for metastatic disease is more likely with estrogen receptor/progesterone receptor–positive disease; long disease-free intervals; older age; disease that is limited to bone, soft tissues, and pleura; and disease that has previously responded to hormonal therapy.

**Question 33**

Which of the following most clearly improves the cure rate for a 75-year-old woman who has undergone excision of a 2 cm estrogen receptor–positive left breast cancer?

a) Left axillary dissection or sentinel lymph node procedure  
b) Bilateral mastectomy  
c) Anastrozole 1 mg daily for 5 years  
d) CMF (cyclophosphamide, methotrexate, and 5-fluorouracil) chemotherapy for 6 months

**Answer and Discussion**

The answer is c.

**Objective: Identify prognostic markers for hormone receptor–positive breast cancer.**

Although an axillary node dissection or sentinel lymph node procedure is appropriate for the staging of breast cancer, a survival advantage to such procedures has not been established. Similarly, neither mastectomy nor bilateral mastectomy has demonstrated a survival benefit over breast-conserving surgery. The benefit of chemotherapy in women older than the age of 70 years with low-risk disease is unclear; however, a clear benefit in both survival and recurrence-free survival persists with endocrine therapy such as anastrozole.

**Questions 34 to 39**

For each of the following treatments used in patients with early breast cancer, match the associated potential long-term toxicity:

1. Tamoxifen  
2. Anastrozole  
3. Doxorubicin  
4. Cyclophosphamide  
5. Paclitaxel  
6. Chest wall and axillary radiation therapy

a) Congestive heart failure  
b) Premature menopause  
c) Uterine cancer  
d) Neuropathy  
e) Lymphedema  
f) Osteoporosis
Answers and Discussion

Question 34
The answer is c.
Objective: Identify common side effects of tamoxifen.
Tamoxifen is approved currently as adjuvant hormone therapy for hormone receptor-positive breast cancer. It works by competitively binding at the estrogen receptor. Tamoxifen has estrogen-like effects on the endometrium and, like estrogen, increases the risk of uterine cancer. The risk of endometrial cancer is ~1 in 500 patients, and currently there are no data suggesting routine screening for endometrial cancer while on tamoxifen. While relatively safe, tamoxifen is also associated with cardiovascular events, thromboembolic events, and hot flashes.

Question 35
The answer is f.
Objective: Identify common side effects of aromatase inhibitors, such as anastrozole.
Aromatase inhibitors work by directly inhibiting peripheral conversion of androstenedione to estrone and testosterone to estrogen, decreasing the estrogen levels peripherally. Because of profound lowering of estrogen levels, the aromatase inhibitors can result in premature menopause, and the associated complications and symptoms. This is most notably increased bone density loss, increasing the risk of osteoporosis and fracture.

Question 36
The answer is a.
Objective: Identify common side effects of doxorubicin.
Doxorubicin belongs to the class of chemotherapeutic agents known as anthracyclines. These cytotoxic agents work by inhibiting topoisomerase II leading to inhibition of DNA and RNA synthesis. The two main toxicities identified include marrow suppression and cardiotoxicity. Cardiotoxicity associated with doxorubicin is categorized as acute versus chronic. Acute cardiotoxicity usually occurs within 2 to 3 days of exposure. The incidence of acute cardiotoxicity is ~11%, and typically presents as chest pain due to myocarditis or arrhythmias. Acute LV dysfunction is a rare manifestation of acute cardiotoxicity. Chronic cardiotoxicity is generally less common and is related to total (lifetime) dose of doxorubicin. It is typically seen ~30 days post exposure, but has been seen much later as well (as far out as 10 years). Doxorubicin cardiotoxicity is presumed secondary to increased oxidative stress leading to a dilated cardiomyopathy, which unfortunately is often not reversible. Management of doxorubicin cardiomyopathy is similar to other forms of dilated cardiomyopathy, and prevention is often the best strategy.

Question 37
The answer is b.
Objective: Identify side effects of cyclophosphamide.
Cyclophosphamide is an alkylating agent and works by preventing cell division leading to decreased DNA synthesis. Alkylating agents, including cyclophosphamide, can cause ovarian failure. The risk is increased with higher patient age and higher cumulative drug dose.

Question 38
The answer is d.
Objective: Identify side effects with Paclitaxel.
Paclitaxel belongs to the taxane group of anti-neoplastics and inhibits cell replication by inhibiting mitosis by promoting microtubule assembly. The side effect profile of Paclitaxel is centered around predominantly hematologic and neurologic manifestations. Paclitaxel is associated with a peripheral neuropathy that preferentially affects the long nerves. This effect is usually reversible but may persist in some patients.

Question 39
The answer is e.
Objective: Identify side effects of radiation therapy for breast cancer.
Local-regional radiation therapy is associated with an increased risk of lymphedema in the affected arm. The risk is increased with axillary radiation and with prior axillary dissection.

Question 40 to 42
A 20-year-old woman presents with night sweats, 15-lb weight loss, and painless left neck lumps. Physical examination is remarkable only for multiple, nontender, rubbery, mobile, 1- to 2-cm left cervical lymph nodes. Laboratory studies reveal normocytic, normochromic anemia. CT of the neck confirms the presence of left cervical and supraclavicular lymphadenopathy.

Which procedure has the highest diagnostic yield?
a) Fine-needle aspiration of an enlarged lymph node
b) Core needle biopsy of an enlarged lymph node
c) Excisional biopsy of an enlarged lymph node
d) CBC w/ differential

Answer and Discussion
The answer is c.
Objective: Identify diagnostic techniques for lymphadenopathy.
The diagnosis of lymphoma requires histologic examination of a lymph node or involved tissue. The cytoclogic specimen provided by a fine-needle aspiration is usually inadequate to
make a diagnosis of lymphoma, let alone determine the specific subtype. An excisional lymph node biopsy provides the most tissue for the pathologist to evaluate the lymph node and perform any indicated ancillary diagnostic studies. CBC while helpful in hematologic malignancies can often be nondiagnostic when concerned about lymphoma.

Question 41

Biopsy reveals classical Hodgkin lymphoma. CT of the chest, abdomen, and pelvis demonstrates thoracic lymphadenopathy and splenic lesions. What is the correct stage?

a) Stage IIA  
b) Stage IIB  
c) Stage IIIA  
d) Stage IIIB

Answer and Discussion

The answer is d.

Objective: Correctly stage Hodgkin lymphoma.

Staging of Hodgkin lymphoma involves two components: location of lymph node involvement and presence of B symptoms. Involvement of lymphoid tissue above and below the diaphragm indicates at least stage III. Both lymph nodes and spleen are considered lymphoid tissue. The presence of night sweats and weight loss (i.e., B symptoms) adds the letter B.

Question 42

Which feature predicts a good prognosis?

a) Age 20 years  
b) Female sex  
c) Both age 20 years and female sex  
d) Peripheral leukocytosis

Answer and Discussion

The answer is c.

Objective: Identify prognostic factors for Hodgkin lymphoma.

The International Prognostic Factors Project identified seven independent poor prognostic features among patients with newly diagnosed, advanced stage Hodgkin lymphoma: hypoalbuminemia, anemia, male sex, stage IV, age 45 years or older, leukocytosis, and lymphopenia.

Question 43

A 78-year-old man complains of dyspepsia and 10-lb weight loss during the past several months. Eight years earlier, he had a gastrointestinal bleed that was attributed to ibuprofen-induced gastritis. His only medication is a baby aspirin. Physical examination is unremarkable. Laboratory studies are normal. Esophagogastroduodenoscopy shows erythema and ulcerations “consistent with medication-induced gastropathy.” Biopsies unexpectedly reveal extranodal marginal zone B-cell lymphoma of mucosa-associated lymphoid tissue. Complete staging evaluation demonstrates no other evidence of lymphoma.

Which of the following statements is correct?

a) Helicobacter pylori is probably involved in the development of this patient’s lymphoma
b) H. pylori eradication may help his gastritis, but not his lymphoma

c) H. pylori is the only infectious agent implicated in lymphomagenesis

Answer and Discussion

The answer is a.

Objective: Identify role of H. pylori in gastric MALT lymphoma.

H. pylori is demonstrable in 90% or more of patients with gastric mucosa-associated lymphoid tissue (MALT) lymphoma. The majority of patients with localized gastric MALT lymphoma respond to eradication of these bacteria. Other infectious agents (e.g., Epstein-Barr virus) have been implicated in the pathogenesis of several other types of lymphoma.

Question 44

A 70-year-old woman complains of fatigue and progressive abdominal discomfort during the past 2 months and a “bulk” in her left abdomen during the past week. Her performance status is 1. Physical examination reveals a few 1 cm right axillary lymph nodes and a huge left lower quadrant mass. Laboratory studies include a white blood cell count of 15.4 with a normal differential, hemoglobin of 10.0, platelets of 370, and lactate dehydrogenase of 897 (normal, 100 to 220). CT of the chest, abdomen, and pelvis shows a few slightly enlarged right axillary lymph nodes and massive retroperitoneal and mesenteric lymphadenopathy. CT-guided core needle biopsy demonstrates diffuse large B-cell lymphoma. Bone marrow biopsy shows no evidence of lymphoma.

Which of this patient’s presenting features predicts a good prognosis?

a) Age 70 years  
b) Stage III  
c) Elevated lactate dehydrogenase  
d) Good performance status

Answer and Discussion

The answer is d.

Objective: Identify prognostic factors for non-Hodgkin lymphoma.

The International Non-Hodgkin Lymphoma Prognostic Factors Project identified five independent poor-risk features among patients with newly diagnosed, advanced stage, aggressive non-Hodgkin lymphoma: age older than 60 years, performance status 2 to 4, stage III or IV, elevated lactate dehydrogenase, and two or more extranodal sites of involvement.
Question 45

A 68-year-old man is noted to have an elevated total protein level on a routine laboratory test done by his primary care physician. He is asymptomatic, has a normal complete blood count, serum creatinine AST/ALT, and calcium levels. A serum protein electrophoresis is ordered and reveals a monoclonal protein immunoglobulin G kappa measuring 0.5 g/dL. A skeletal survey is without evidence of lytic lesions. What should you recommend to this patient?

a) Bone scan
b) Observation
c) Treatment with thalidomide and dexamethasone
d) MRI of the spine
e) None of the above

Answer and Discussion

The answer is b.

Objective: Identify and treat monoclonal gammopathy of unknown significance (MGUS).

The abnormal serum protein electrophoresis (SPEP) with monoclonal protein in an asymptomatic patient with normal creatinine, calcium, and hemoglobin is suggestive of MGUS. A bone marrow biopsy is not necessary in this patient because it is unlikely to diagnose multiple myeloma (MM).

Patients with MGUS are at risk of developing myeloma or a lymphoid neoplasm, with the risk of progression being about 1% a year, and hence, close observation with complete blood count, serum creatinine, calcium, and SPEP and urine protein electrophoresis is recommended every 6 months, or if there is a change in symptoms.

Treatment with agents used in myeloma is not recommended in MGUS. An MRI of the spine is not recommended in this patient in the absence of bone/back pain. A bone scan is not usually helpful in MM because bone lesions are frequently purely lytic.

Question 46

The previous patient is managed conservatively. Six years later, he is noted to have an elevation in his M protein, a mild increase in his serum creatinine and calcium, and back pain. A bone marrow biopsy reveals 14% monoclonal plasma cells, and a skeletal survey reveals multiple punched-out lesions (lytic lesions) in the skull and thoracic spine. An MRI of the spine does not reveal any cord compression. What should you do next?

a) Continue monitoring of his monoclonal gammopathy
b) Start monthly intravenous bisphosphonate therapy
c) Start therapy with melphalan and prednisone
d) Prescribe ibuprofen for his bone pain
e) Start therapy with melphalan, prednisone, and thalidomide, along with monthly intravenous pamidronate

Answer and Discussion

The answer is d.

Objective: Identify osteonecrosis of the jaw secondary to bisphosphonate.

A 65-year-old man is diagnosed with multiple myeloma (MM). He had been planning dental extractions, but because of his new diagnosis decides to postpone the visit to the dentist. He receives intravenous pamidronate for MM. Nine months later, his tooth pain gets worse, and he has a tooth extraction done. He presents 1 month later again to his dentist with complaints of pain, swelling, and feelings of numbness of the jaw. Infection is suspected, and the patient is treated with antibiotics. The problem persists, and 3 weeks later, he has exposed bone at the site. What are the recommendations relevant to this condition?

a) Dental extractions should have been done prior to starting pamidronate
b) Endodontic (root canal) therapy is preferable to extractions once a patient is on bisphosphonates
c) Referral to oral maxillofacial surgeon or dental oncologist is recommended once the condition develops
d) All of the above

Answer and Discussion

The answer is d.

Objective: Identify osteonecrosis of the jaw secondary to bisphosphonate.

The condition described is osteonecrosis of the jaw. The majority of reported cases of bisphosphonate-associated osteonecrosis of the jaw (BON) with the use of zoledronic acid and pamidronate have been associated with dental procedures such as tooth extraction; however, less commonly, BON appears to occur spontaneously in patients taking these drugs.
The risk for developing BON is much higher for cancer patients on intravenous bisphosphonate therapy than the risk for patients on oral bisphosphonate therapy. It is recommended that cancer patients
- Receive a dental examination prior to initiating therapy with intravenous bisphosphonates
- Avoid invasive dental procedures while receiving bisphosphonate treatment. For patients who develop osteonecrosis of the jaw while on bisphosphonate therapy, dental surgery may exacerbate the condition
- Dental infections should be managed aggressively and nonsurgically (when possible)
- Endodontic therapy is preferable to extractions, and, when necessary, coronal amputation with root canal therapy on retained roots to avoid the need for extraction

**Question 48**

A 69-year-old man presents to his primary care physician with nonspecific complaints of fatigue and malaise. The symptoms are believed to be due to depression. He presents 3 months later with worsening fatigue, diarrhea, shortness of breath, and lower extremity edema. The chest x-ray is consistent with congestive heart failure. Laboratory evaluation includes a hemoglobin of 10 g/dL, creatinine of 2.2 g/dL, serum albumin of 2.9 g/dL, and 4 g of albuminuria per 24 hours. An echocardiogram reveals concentrically thickened ventricles with a starry sky appearance. Which of the following is true about his potential diagnosis?

a) Macroglossia can be seen in about 20% of the patients
b) A subcutaneous fat pad aspirate stained with Congo red will be positive in about 85% of patients
c) A cardiac biopsy is likely to be diagnostic
d) All of the above

**Answer and Discussion**

The objective is to identify diagnostic strategies for amyloidosis.

The patient's signs and symptoms are suggestive of amyloidosis. The diagnosis of amyloidosis is frequently missed initially. Initial symptoms tend to be nonspecific with fatigue, malaise, and weight loss. The kidney and heart are most commonly involved. The elevated serum globulin, abnormal hemoglobin and creatinine, and the echocardiogram findings are suggestive. Biopsy of involved organ will confirm the diagnosis. A less invasive option is subcutaneous fat aspirate or rectal biopsy stained with Congo red.

**Question 49**

A 62-year-old man with history of multiple myeloma, hypertension, and benign prostatic hypertrophy undergoing treatment with thalidomide presents to his internist with complaints of low back pain and tingling and numbness in his feet after lifting his 30-lb dog. He also complains of difficulty urinating and believes that his dose of doxazosin needs to be readjusted. The next step should be

a) Give him a prescription for ibuprofen and a muscle relaxant
b) Perform a urinalysis and increase the dose of doxazosin
c) Reassure him that it is probably a strain and that a few days rest will take care of the problem
d) Perform an immediate MRI of the spine
e) Discontinue thalidomide

**Answer and Discussion**

The objective is to identify cord compression.

Cord compression is a real and devastating consequence of multiple myeloma. The threshold of suspicion should be low and, in the presence of signs and symptoms of potential cord involvement and a change in character of back pain, should warrant an MRI of the spine. Studies indicate that the eventual neurologic outcome depends on the speed of intervention. Once neurologic impairment sets in, the chances of full recovery diminish. Cord compression is an oncologic emergency, and a prompt radiologic evaluation and neurosurgical consultation are needed.

Although thalidomide can cause peripheral neuropathy, it should not result in exacerbation of back pain or urinary symptoms. Thus, discontinuing thalidomide should not result in improvement in his symptoms.

**Question 50**

A 19-year-old African American man presents to your office with generalized fatigue and frequent sinus infections. The patient has never seen a physician before and denies any previous history. He is adopted and does not know anything regarding his family history. When he gets recurrent sinus infections, he has been taken to urgent care settings, where he gets antibiotics and starts feeling better. He is generally asymptomatic, except for some occasional sinus infections, he has been taken to urgent care settings, where he gets antibiotics and starts feeling better. He is generally not active and has frequent joint pains. You get a CBC, which shows some mild anemia with a Hgb of 9 gm/dL, and is otherwise unremarkable. Among other testing, you get a peripheral smear which shows Howell-Jolly bodies. The most likely diagnosis is:

a) Sickle cell anemia
b) Sickle cell trait
c) Hemoglobin S-hereditary persistence of fetal hemoglobin
d) Hemoglobin C trait
e) Hemoglobin C disease

**Answer and Discussion**

The objective is to identify signs and symptoms of functional asplenia.

This patient has both symptoms and laboratory findings consistent with asplenia. Howell-Jolly bodies are evidence of functional asplenia or postsplenectomy state, as is recurrent
infections with encapsulated organisms. Patients with sickle cell anemia undergo autosplenectomy due to vascular occlusion by sickled cells. None of the other conditions listed is associated with functional asplenia.

Question 51

A 25-year-old female student presents to the emergency room complaining of frequent nasal congestion and occasional epistaxis. She denies fevers, night sweats, and weight loss, and has noted a rash on his legs.

On physical examination, you find a well-developed woman in no acute distress; temperature 36.8°C, blood pressure 126/74 mmHg, respiration rate 20 breaths/minute; her oral mucosa has a few petechial hemorrhages and no palpable lymphadenopathy or splenomegaly is present. You get a peripheral smear, which is shown here.

Answer and Discussion

The answer is d.

Objective: Identify indications for an inferior vena cava (IVC) filter.

IVC filters do not prevent deep vein thrombosis (DVT); in fact, they may promote the formation of DVT. IVC filters can prevent pulmonary embolism in perioperative setting, but the use of permanent filters in this setting would inappropriately place patients at risk for future DVT and the post-thrombotic syndrome. Retrievable filters offer a potential option for high-risk perioperative patients, but this approach is experimental right now.

Question 53

A 78-year-old man with prostate cancer presents to the emergency department with an acute left superficial femoral deep vein thrombosis. His daughter is a nurse and lives with her father. He is 90 kg, and his creatinine is 3.2 mg/dL. Which of the following is the most appropriate treatment plan?

a) Outpatient enoxaparin 1 mg/kg subcutaneously every 12 hours with a 4-day minimum overlap of warfarin until a stable international normalized ratio (INR) of 2 to 3 is reached
b) Inpatient tinzaparin 175 U/kg subcutaneously daily with a 4-day minimum overlap of warfarin until a stable INR of 2 to 3 is reached
c) Inpatient intravenous activated partial thromboplastin time–adjusted unfractionated heparin with a 5-day minimum overlap of warfarin until a stable INR of 2 to 3 is reached
d) Outpatient fondaparinux 5.0 mg subcutaneously daily for 3 to 6 months before overlapping with warfarin
e) Outpatient enoxaparin 1 mg/kg subcutaneously daily for 3 to 6 months before overlapping with warfarin

Answer and Discussion

The answer is e.

Objective: Identify treatment strategy for acute DVT in the setting of malignancy and chronic renal insufficiency.

This patient has evidence of acute myelogenous leukemia with a peripheral smear showing Auer rods. Auer rods are typically observed in myeloid blasts and are characteristically present in bundles in acute promyelocytic leukemia. Acute promyelocytic leukemia specifically has a high association with disseminated intravascular coagulopathy (DIC) and is treated with all-trans retinoic acid. None of the other conditions listed is an acute myeloid leukemia or high-grade myelodysplastic syndrome and do not typically have Auer rods on peripheral smear.

Answer and Discussion

The answer is e.

Objective: Identify treatment strategy for acute DVT in the setting of malignancy and chronic renal insufficiency.

This patient has deep vein thrombosis in the setting of active cancer. According to the American College of Chest Physicians, weight-adjusted dose low molecular weight heparin
Objective: Understand the treatment of myeloma kidney.

Renal failure is a fairly common problem in patients with multiple myeloma, with approximately 20% presenting with a plasma creatinine ≥2 mg/dL (176 μmol/L) at presentation. The diagnosis can be made clinically in a patient older than 40 years who has unexplained renal failure and elevated quantities of monoclonal free light chains in both the plasma and urine. However, definitive diagnosis is by a kidney biopsy. Biopsy is recommended when the history or clinical features are atypical for myeloma cast nephropathy (e.g., significant proteinuria, active urinary sediment, nephrotoxic drugs). Common causes of acute renal failure in multiple myeloma are cast myeloma kidney, hypercalcemia, and volume depletion. Patients with myeloma kidney should receive dexamethasone-based chemotherapy as rapidly as possible to decrease light chain formation. Intravenous fluids are given to treat volume depletion, hypercalcemia, and hyperuricemia and to produce a high urine flow rate to minimize light chain precipitation. Loop diuretics should be used cautiously as they may promote cast formation. If the initial corrected serum calcium concentration is <14 mg/dL (4 mmol/L), fluid therapy is instituted for up to 12 hours, and then intravenous bisphosphonate is administered if there is no response. If the corrected serum calcium concentration is ≥14 mg/dL (4 mmol/L), bisphosphonates should be administered immediately, along with intravenous fluids. The evidence evaluating the effectiveness of plasmapheresis is conflicting and is not advocated as the first-line therapy.

**Question 54**

A 55-year-old man with a history of polycythemia vera sees his family physician for routine follow-up. A hematocrit drawn at the visit is 48%. Which of the following is most likely?

a) The iron stores in his bone marrow would be increased
b) He has decreased cerebral blood flow and is at increased risk of thrombotic complications
c) His bone marrow will be hypocellular, except for hyperplasia of red cell progenitors
d) An increased level of circulating erythropoietin is present in his plasma
e) He does not have an increased bleeding tendency due to preservation of platelet function

**Answer and Discussion**

**The answer is e.**

Objective: Understand the complications of polycythemia vera.

Patients with polycythemia vera who have a hematocrit >45% usually have decreased cerebral blood flow and an increased thrombotic tendency. The bone marrow is usually hypercellular, with hyperplasia of all bone marrow elements. Iron stores are not increased, and patients may actually be iron deficient due to an increased tendency for gastrointestinal blood loss because of dysfunctional platelets. Finally, a characteristic finding in polycythemia vera is a decreased erythropoietin level due to feedback inhibition (i.e., the proliferation of marrow elements occurs independently of erythropoietin stimulation).

**Question 56**

A 60-year-old man reports generalized fatigue. He has been having red urine for the past few days and tarry stools for the past month. He has a history of severe arthritis for which he has been taking over-the-counter ibuprofen. Vital signs and physical examination are normal, but an initial complete blood count revealed a leukocyte count of 7,000/mm³, hemoglobin of 7 mg/dL, hematocrit of 20%, and platelet count of 600,000 μL. The mean cell volume (MCV) is 62 fl, and MCH is 29 pg. He is hemodynamically stable. His stool for occult blood is positive. The most appropriate next step in this patient’s management is which of the following?

a) Serum haptoglobin
b) Esophagogastroduodenoscopy
c) Colonoscopy
d) Cystoscopy
e) Iron tablets
Answer and Discussion

The answer is b.

Objective: Understand the features and evaluation of iron deficiency anemia.

The low MCV and guaiac-positive stools point toward iron deficiency anemia. The red-colored urine is due to beeturia, which is an infrequent manifestation of iron deficiency in which the eating of beets leads to the formation of red urine. This is due to increased intestinal absorption and excretion in the urine of the reddish pigment betalaine. Betalaine is decolorized by ferric ions. This most likely explains the predisposition in iron deficiency to beeturia. The laboratory values in iron deficiency are microcytosis, hypochromia, a low serum iron, an increased total iron binding capacity (transferrin), a reduced transferrin saturation, and a reduced ferritin. The test with the highest sensitivity and specificity for the diagnosis of iron deficiency is serum ferritin. Iron deficiency anemia is most often associated with blood loss. To find the cause, the first step is esophagogastroduodenoscopy (EGD) followed by a colonoscopy if the EGD is non-diagnostic. In this patient, iron deficiency anemia is most likely secondary to peptic ulcer disease caused by excessive use of nonsteroidal anti-inflammatory drugs for his severe arthritis.

Question 57

A 30-year-old physically fit man presents with deep vein thrombosis (DVT). He has a history of allergic rhinitis each summer. He has had no recent trauma or surgery and has not traveled in the past 6 months. He is adopted and does not have any medical family history. What is the most common underlying cause of DVT?

a) Factor V Leiden, activated protein C resistance
b) Protein C deficiency
c) Protein S deficiency
d) Antithrombin III deficiency
e) Dysfibrinogenemia

Answer and Discussion

The answer is a.

Objective: Understand the etiologies of unprovoked venous thrombosis.

Inherited thrombophilia is associated with a genetically increased risk for venous thromboembolism. Factor V Leiden mutation accounts for 40% to 50% of cases. Protein C, protein S, and antithrombin III deficiencies and dysfibrinogenemia are all causes of inherited thrombophilia, but they are less common.

Question 58

A 65-year-old man reports back pain. In review of his chart, you note a hemoglobin level of 10 mg/dL and an elevated total protein. You entertain the diagnosis of multiple myeloma. Which of the following statements is true?

a) Among neurologic manifestations of myeloma, 5% to 10% of patients have extramedullary plasmacytomas leading to cord compression, although peripheral neuropathy is more common
b) The anemia is most likely microcytic and hypochromic and occurs in a majority of patients with multiple myeloma
c) Hypercalcemia is common, occurring in more than 50% of patients with multiple myeloma
d) The two major causes of renal failure in these patients include cast nephropathy and hypercalcemia
e) In myeloma kidney, casts accumulate in the loop of Henle. These casts are composed of precipitated monoclonal light chains that interact with Tamm-Horsfall mucoprotein synthesized by the tubular cells in the ascending limb of the loop of Henle

Answer and Discussion

The answer is d.

Objective: Understand the clinical features of multiple myeloma.

More than two-thirds of patients with multiple myeloma have a normocytic and normochromic anemia during their illnesses; 50% have rouleaux formation, and only approximately 15% have hypercalcemia. The most common neurologic manifestations are thoracic or lumbosacral radiculopathy, with a cord compression secondary to extramedullary plasmacytomas developing in 5% to 10% of patients. Peripheral neuropathy is rare. The major causes of renal failure in these patients are cast nephropathy and hypercalcemia. In myeloma kidney, casts formed by precipitating monoclonal light chains that interact with the Tamm-Horsfall mucoprotein (synthesized by the tubular cells in the ascending limb of the loop of Henle) accumulate in the distal and collecting tubules.

Question 59

A 21-year-old woman with a history of sickle cell disease is admitted to the hospital with a pain crisis. This is her sixth admission in the past 4 years. She has been on folate and hydroxyurea therapy as an outpatient. On the day of admission, her temperature is 39°C, blood pressure 130/90 mmHg, pulse 120 beats/minute, and respiratory rate 12 breaths/minute. Her physical examination reveals that she is in moderate distress. Her head, eyes, ears, nose, and throat examination is unremarkable, as are her pulmonary and cardiovascular examinations, except for tachycardia. The abdomen is soft and nontender, with normal bowel sounds. Examination of her extremities does not demonstrate any edema. Initial laboratory tests show a normal chemistry profile. Complete blood count (CBC) shows that her white cell count is 15,000/mm³, hemoglobin level is 7.5 mg/dL, and hematocrit
is 20%. Which of the following is least appropriate in the initial management of this patient?

a) Continuous intravenous fluids: dextrose water with potassium chloride at 200 mL/hr
b) A narcotic analgesic given for adequate pain control
c) Packed RBC transfusion, 2 U, each over 4 hours
d) Cultures of blood and urine, chest radiograph, and careful examination of the skin for a potential source of fever and infection
e) Reticulocyte count

Answer and Discussion
The answer is c.

Objective: Understand the treatment of sickle cell crisis.

Packed RBC transfusions are the least appropriate choice for a patient with sickle cell anemia. The reticulocyte count is essential in ruling out the possibility of an aplastic crisis. Cultures of the blood and urine, along with chest radiography, help rule out infection. Pain control and intravenous hydration are the mainstays of therapy for patients with a sickle cell crisis.

Question 60
The following are all risk factors for the development of carcinoma of the bladder, except

a) Cyclophosphamide use
b) Family history
c) Tobacco smoke exposure
d) Schistosoma haematobium infestation
e) Recurrent stones

Answer and Discussion
The answer is b.

Objective: Understand the risk factors for developing bladder cancer.

Transitional cell carcinoma of the bladder is more common than either squamous cell carcinoma or adenocarcinoma and has a more favorable prognosis. A risk factor for the squamous subtype includes schistosomal infestations. Other risk factors include aromatic amines present in the products of chemical dyes and cigarette smoke, recurrent stones or infection, and use of cyclophosphamide. Family history is not a risk factor for bladder carcinoma; it is a risk factor for renal cell carcinoma.

Question 61
A 26-year-old woman is undergoing autologous bone marrow transplantation for non-Hodgkin's lymphoma. On the third day of her admission, she is found to have a temperature of 39°C. She feels well, and the examination does not reveal any localizing signs of infection. Laboratory studies show an absolute neutrophil count of 420/mm³. What would now be the most appropriate management for this patient?

a) Close observation only
b) Blood cultures
c) Blood cultures and empiric treatment with piperacillin-tazobactam
d) Blood cultures and empiric treatment with an aminoglycoside only
e) Blood cultures and empiric treatment with vancomycin and an aminoglycoside

Answer and Discussion
The answer is c.

Objective: Understand the management of neutropenic fever.

This woman has neutropenic fever. Neutropenia is defined as an absolute neutrophil count <500/mm³. Patients with an absolute neutrophil count <500/mm³ due to chemotherapy or marrow failure are at high risk for overwhelming bacterial infection. Blood cultures are indicated, and antibiotics should be commenced as soon as possible. Most antibiotic regimens target gram-negative bacilli. The choice of monotherapy with an anti-pseudomonal beta-lactam or carbapenem is appropriate. Vancomycin should be added only if the patient has signs of cardiovascular compromise, positive blood cultures for gram-positive cocci before final identification of the organism, recent quinolone prophylaxis, patients receiving intensive chemotherapy causing substantial mucosal damage, or if methicillin-resistant Staphylococcus aureus or penicillin resistance is suspected.

Question 62
All the following statements regarding chronic myelogenous leukemia (CML) are true, except

a) It is genetically characterized by the Philadelphia chromosome, a reciprocal translocation between chromosomes 9 and 22, t(9;22)
b) The translocation that accounts for the Philadelphia chromosome is most commonly found in all hematopoietic cell lines but not nonhematopoietic cell lines
c) The translocation seen in CML is also seen in other myeloproliferative disorders, such as polycythemia vera and idiopathic myelofibrosis
d) The propensity of CML to progress to acute transformation is approximately 90%, much higher than that seen for other myeloproliferative disorders
e) Patients often present with a palpable spleen and have an elevated leukocyte count, often >200,000/mm³

Answer and Discussion
The answer is c.

Objective: Understand the features and natural history of chronic myelogenous leukemia (CML).

CML is the only myeloproliferative disorder characterized by the Philadelphia chromosome, a reciprocal translocation between chromosomes 9 and 22. This translocation is
commonly found in all hematopoietic cell lines, but not in nonhematopoietic cell lines. The propensity of the myelo-proliferative disorders to progress to acute transformation is highest in CML (approximately 90%) and lowest for essential thrombocytopenia (<5%).

**Question 63**

A 25-year-old woman is noted on preoperative laboratory testing to have an abnormal complete blood count. She is otherwise well and awaiting a laparoscopy for chronic abdominal pain. Leukocyte count is 5,000/mm$^3$, hemoglobin level is 12 mg/dL, hematocrit is 36%, and platelet count is 14,000/mm$^3$; chemistry profile and serum creatinine are normal. On further questioning, she admits to easy bruising and heavy menses. Further testing is done. An antinuclear antibody test result is negative. Which of the following diagnoses is most consistent with these findings?

a) Splenic sequestration  
b) Idiopathic thrombocytic purpura  
c) Thrombocytopenia purpura  
d) Heparin-induced thrombocytopenia  
e) Systemic lupus erythematosus

**Answer and Discussion**

The answer is b.

**Objective: Recognize common features of idiopathic thrombocytic purpura.**

Idiopathic thrombocytic purpura (ITP) in adults normally presents as chronic idiopathic thrombocytic purpura, a more indolent form. Patients are more often women (3:1) 20 to 40 years of age and have a history of easy bruising and menometrorraghia. Some cases of ITP are associated with a preceding viral infection. Alterations in the immune response might induce loss of peripheral tolerance and promote the development of self-reactive antibodies. There is marked variability in the clinical presentation of ITP. Although the onset of ITP may be acute and abrupt, it is more often insidious. Similarly, bleeding in symptomatic patients can range from petechiae and easy bruising to a severe bleeding diathesis. Because a low platelet count may be seen in systemic lupus erythema-tosus, antinuclear antibody testing and bone marrow biopsies are often required to rule out other causes. Thrombotic thrombocytic purpura (TTP) is an acute syndrome with abnormalities in multiple organ systems. Clinical presentation often occurs in a pentad of symptoms: fever, microangiopathic hemolytic anemia, thrombocytopenia, renal dysfunction, and acute neurologic alterations. With otherwise normal blood count, and lack of other associated symptoms, this would be unlikely. There is no history of heparin exposure which makes heparin-induced thrombocytopenia unlikely.

**Question 64**

A 45-year-old man undergoing rehabilitation after hip surgery as a result of a motor vehicle accident is noted on a routine complete blood count to have a platelet count of 55,000/mm$^3$; at hospital discharge 3 weeks ago, it was 200,000/mm$^3$. He has been taking a narcotic analgesic and lorazepam, as well as subcutaneous heparin injections, since admission to the rehabilitation center. Heparin has been stopped. Peripheral blood smear is unremarkable, except for thrombocytopenia. Which of the following diagnoses is most consistent with these findings?

a) Splenic sequestration  
b) Idiopathic thrombocytic purpura  
c) Thrombocytopenia purpura  
d) Heparin-induced thrombocytopenia  
e) Systemic lupus erythematosus

**Answer and Discussion**

The answer is d.

**Objective: Recognize common features of heparin-induced thrombocytopenia.**

This man has been receiving heparin subcutaneously since his surgery. The development of heparin-induced thrombocytopenia may occur from 5 to 10 days after the initiation of therapy. A nonimmunogenic thrombocytopenia (type 1) may occur in 10% to 20% of patients on heparin. It is characterized by a decrease in the platelet count in the initial days of therapy, with a return to normal range with continued therapy, and poses no clinical risk. Immunogenic thrombocytopenia (type 2) may occur in 2% to 3% of patients on heparin; however, it is characterized by a progressive decrease in platelet count, along with an increased risk of both venous and arterial thrombosis. The antigen is believed to be a heparin–platelet factor IV complex in most patients. Treatment is immediate discontinuation of heparin therapy. The diagnosis of heparin-induced thrombocytopenia must be made clinically, although better assays are becoming available to detect the presence of heparin-induced platelet antibodies. A pretest clinical scoring system (“4T’s”) has been validated. It includes degree of thrombocytopenia, timing of the decreased counts in relation to heparin exposure, presence of thrombosis or other sequelae, and other possible explanations for the thrombocytopenia.

A 55-year-old man presents with confusion and fever. He presented with an acute inferoposterior myocardial infarction 1 week prior and underwent coronary angioplasty with stent placement to the right coronary artery. He has been receiving aspirin, metoprolol, and clopidogrel since the procedure. On physical examination, he is febrile (38.4°C), disoriented to place and time, his heart rate is 85 beats/minute, and his blood pressure is 95/73 mmHg. The medical resident witnesses a short-lived tonic-clonic seizure while examining the patient. Although his postictal state lasts an hour, no focal neurologic abnormalities are detected on repeated neu-
logic examinations. A brain CT is unremarkable. Laboratory studies reveal the following:

<table>
<thead>
<tr>
<th></th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hematocrit</td>
<td>24%</td>
</tr>
<tr>
<td>White blood cells</td>
<td>7,100/mm³</td>
</tr>
<tr>
<td>Platelets</td>
<td>11,000/mm³</td>
</tr>
<tr>
<td>Prothrombin time</td>
<td>12 seconds</td>
</tr>
<tr>
<td>Partial thromboplastin time</td>
<td>31 seconds</td>
</tr>
<tr>
<td>Blood urea nitrogen</td>
<td>21 mg/dL</td>
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<tr>
<td>Serum creatinine</td>
<td>2.9 mg/dL</td>
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<tr>
<td>Lactate dehydrogenase</td>
<td>900 U/L</td>
</tr>
<tr>
<td>Direct Coombs’ test</td>
<td>Negative</td>
</tr>
</tbody>
</table>

The next step in the management of this patient at this time is

a) Pulmonary artery catheterization placement for hemodynamic guided management
b) Intravenous fluid resuscitation and positive inotropic agents
c) Broad-spectrum intravenous antibiotics and cerebrospinal fluid analysis
d) Transthoracic echocardiography
e) Peripheral blood smear review

**Answer and Discussion**

**The answer is e.**

**Objective: Recognize the common features of thrombotic thrombocytopenic purpura (TTP).**

TTP is an acute syndrome that affects myriad systems. The classic pentad of clinical features includes thrombocytopenia, microangiopathic hemolytic anemia, neurologic changes, renal function abnormalities, and fever. Because of the association between ticlopidine use and TTP, clopidogrel, a newer thienopyridine derivative whose mechanism of action and chemical structure are similar to those of ticlopidine, has largely replaced ticlopidine in clinical practice. Several reports showed, however, that TTP could also occur after the initiation of clopidogrel therapy, often within the first 2 weeks of treatment. Although TTP remains an extremely rare complication of clopidogrel, physicians should be aware of the possibility of this potentially life-threatening syndrome when initiating clopidogrel treatment.

**Question 66**

A 53-year-old white woman presents to your office because of a fever and newly developing painful rash. She states that she has not felt well for over 2 weeks and has noted daily temperatures of over 38.5°C. Her rash developed in the last 48 hours on her neck and face. The rash is painful and does not itch. She has no shortness of breath or cough. She states that her knees and hips have been sore, but otherwise, she does not have any localized pain or other symptoms. She reports fatigue and generalized malaise during the episodes of fever. Her past medical history is significant for hyperlipidemia, and she takes a baby aspirin and simvastatin daily. She does not smoke or drink alcohol. She is married and works as an accountant. She has no pets, drinks city water, and denies any recent travel outside of the United States. Her family history is notable for cardiovascular disease. On examination, her vital signs are: T = 38.3°C; P = 90 beats/minute; RR = 18 breaths/minute; and BP = 116/73 mmHg. HEENT examination reveals erythematous annular plaque lesions on the neck and left cheek. Extraocular muscles are intact, and pupils are equal, round, and reactive to light. The neck is supple without jugular venous distention, adenopathy, or bruits. Her lungs are clear to auscultation. Cardiac examination reveals normal heart sounds without murmurs or gallops. Her abdomen is soft and nontender. There is no organomegaly, distention, or rebound. Other than the lesions on the neck and face, the skin examination is normal. She is generalized weak, but her neurologic examination is nonfocal. Laboratory studies are as follows:

- Sodium: 144 mEq/dL
- Potassium: 4.1 mEq/dL
- Chloride: 100 mEq/dL
- CO₂: 27 mEq/dL
- Blood urea nitrogen: 23 mg/dL
- Serum creatinine: 1.2 mg/dL
- Leukocyte count: 18,300 μL
- Hemoglobin: 14.1 g/dL
- Hematocrit: 40%
- Platelets: 550,000 μL
- MCV: 83 fl
- Differential: 95% bands

A skin biopsy of the plaque is taken. Which of the following is the most likely biopsy result?

a) Dermal inflammatory neutrophilic infiltrate without vasculitis
b) Intraepithelial acantholysis without disruption of the basement membrane
c) Atypical mononuclear cells in the epidermis and upper dermis with Pautrier microabscesses
d) Leukocytoclastic vasculitis
e) Noncaseating granulomas

**Answer and Discussion**

**The answer is a.**

**Objective: Recognize the common features of Sweet’s syndrome.**

This patient has peripheral neutrophilia, fever, and painful erythematous plaques. This is consistent with Sweet’s syndrome or acute febrile neutrophilic dermatosis. The syndrome is associated with acute leukemia in about 20% of patients. Intraepithelial acantholysis is consistent with pemphigus. An atypical mononuclear infiltrate with Pautrier microabscesses is seen in mycosis fungoides. Lesions are typically pruritic and resemble common dermatoses until skin changes evolve. Leukocytoclastic vasculitis is a nonspecific skin biopsy finding
but may be seen in urticaria, drug reactions, and serum sickness. Noncaseating granulomas are a feature of sarcoid.

**Question 67**

A 42-year-old white man presents to your office for routine follow-up. He has a past medical history of hypertension and currently takes enalapril daily. He reports that he is feeling well, and his review of systems is negative. He is married and works as a construction manager. He does not smoke, and he drinks alcohol occasionally. His past surgeries include an appendectomy as a teenager and two knee arthroscopies on the left knee. He is an active tennis player and reports no changes in his exercise tolerance. On examination, his vital signs are: T = 37.1°C; P = 69 beats/minute; RR = 18 breath/minute; and BP = 128/82 mmHg. HEENT is normal. The neck is supple without jugular venous distention, adenopathy, or bruises. His lungs are clear to auscultation. Cardiac examination reveals normal heart sounds without murmurs or gallops. His abdomen is soft and nontender. There is no organomegaly, distention, or rebound. Skin examination reveals multiple moles and freckles across his shoulders and over his back. He has an asymmetric, dark brown-black, 7 mm lesion over his right scapula. Neurologic examination is normal. Skin biopsy of the lesion confirms melanoma that is nonulcerated with 3 mm depth of invasion. Chest radiograph is normal. Laboratory studies are as follows:

- Sodium: 140 mEq/dL
- Potassium: 4.0 mEq/dL
- Chloride: 107 mEq/dL
- CO2: 26 mEq/dL
- Blood urea nitrogen: 10 mg/dL
- Serum creatinine: 0.7 mg/dL
- LDH: 145 mg/dL
- Alkaline phosphatase: 28 mg/dL
- Leukocyte count: 5,200 μL
- Neutrophils: 80%
- Platelet count: 251,000/μL
- Hemoglobin: 14.1 g/dL
- Hematocrit: 40%
- Reticulocyte count: 7%

Which of the following is the most appropriate next step?

a) CT of the chest, abdomen, and pelvis  
b) PET scan  
c) MRI of the brain with gadolinium  
d) Sentinel lymph node biopsy  
e) Recombinant interferon α-2b

**Answer and Discussion**

**Objective:** Diagnose and treat cutaneous melanoma.

This patient has cutaneous melanoma, and surgical excision is the preferred treatment for melanoma. Although resection usually controls the primary lesion, melanoma often metastasizes through lymphatic channels to regional lymph nodes. Accurate staging at diagnosis is important to assess the prognosis and determine whether the patient is eligible for clinical trials of adjuvant therapies. Lymphatic mapping is based on the concept that sites of cutaneous melanoma have specific patterns of lymphatic spread and that one or more nodes are the first to be involved with metastatic disease within a given lymph node basin. If the sentinel lymph nodes are not involved, the entire basin should be free of tumor. Interferon is reserved for patients with high-risk tumors such as those with documented lymphatic involvement or those with >4 mm depth of invasion. Radiographic studies in asymptomatic patients rarely identify metastatic lesions and are not recommended.

**Question 68**

A 19-year-old African American man with homozygous (SS) sickle cell disease is admitted to the hospital for pain in the lower extremities. He has been admitted three times in the preceding year for similar symptoms, diagnosed with acute vaso-occlusive (pain) crises, and treated with analgesics and intravenous hydration. He reports neither fever nor cough and states that his pain resembles that of the prior three episodes but is slightly worse.

On physical examination, vital signs show a heart rate of 104 beats/minute, normal blood pressure and respiratory rate, and temperature of 37.3°C. He is oriented and alert and appears uncomfortable. Scleral icterus is noted. Physical examination is otherwise unremarkable. Chest x-ray is normal. Abdominal ultrasound notes absence of the spleen and gallstones. Laboratory studies are as follows:

- WBC: 9,600/μL  
- Hgb: 8.6 g/dL (patient baseline: 9.4 g/dL)  
- Platelet count: 156,000/μL  
- Total bilirubin: 5.4 mg/dL  
- Creatinine: 1.2 mg/dL

Which of the following treatment approaches is indicated for this patient?

a) Transfusion of RBCs is indicated in this case but only using a partial exchange technique (phlebotomy interchanged with administration of normal saline and packed RBCs).

b) Analgesia and intravenous fluids should be given, whereas packed RBC transfusion is not indicated in this patient.

c) In addition to administration of analgesia and intravenous fluids, transfusion of packed RBCs should be undertaken to achieve a hemoglobin concentration of over 12 mg/dL.

**Answer and Discussion**

**Objective:** Identify correct treatment for sickle cell vaso-occlusive crisis.

The clinical findings in this case point to a pain crises, also known as a “vaso-occlusive crisis” or “painful episode.” Although
pain may also be associated with infection, further infectious workup and empiric antibiotics use are necessary only in the presence of fever or signs of infection on physical examination.

Painful episodes may occur more frequently in patients with a hemoglobin level exceeding 8.5 mg/dL. Analgesia using parenteral opioids and judicious use of nonsteroidal anti-inflammatory drugs are the mainstay of care and should be undertaken promptly. Patient-controlled analgesia (PCA) is often useful, although avoidance of oversedation—with development of respiratory acidosis and hypoxia—is key to avoid exacerbation of sickling of RBCs. In addition, especially in patients without evidence of systolic cardiac dysfunction, aggressive volume expansion is recommended.

RBC transfusion is not indicated in the management of pain crises. Aplastic crisis, acute splenic sequestration, cerebrovascular accident, and acute chest syndrome are indications for RBC transfusion. Risks of transfusion include elevation of blood viscosity and worsening of vaso-occlusion, alloimmunization, iron overload, and transmission of viral infections.

Simple transfusion of packed RBCs to achieve a hemoglobin concentration of >12 mg/dL may cause harm due to an increase in blood viscosity. Indications for simple transfusion include aplastic crisis or acute splenic sequestration. There is no evidence for aplastic crisis given the elevated reticulocyte count and hemoglobin level that is only slightly lower than baseline. Similarly, acute splenic sequestration is unlikely; this patient has undergone involution of the spleen (“auto-splenectomy”), a common event early in life for sickle cell patients. The pooling and vaso-occlusion that characterize splenic sequestration, accompanied by a marked drop in hemoglobin and splenic engorgement, do not occur in these patients.

Partial exchange transfusion is useful as acute therapy of a cerebrovascular accident, priapism, acute chest syndrome, multiorgan failure, and in the perioperative setting. This approach reduces the proportion of sickled RBCs and favorably impacts blood viscosity compared with simple transfusion. In patients receiving chronic red cell transfusions, this approach will reduce transfusional iron overload.

Referral to a surgeon for urgent cholecystectomy is not indicated. No evidence of cholecystitis or choledochothiasis is present. This patient’s elevated bilirubin is likely due to ongoing, chronic hemolysis. Such patients almost universally have gallstones due to increased turnover of RBC and heme pigment.

**REFERENCE**


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**Question 69**

A 35-year-old woman is referred to your clinic for establishment of care including routine health maintenance. She is a nonsmoker and a vegetarian (who consumes dairy products) and is training for a triathlon by exercising strenuously at least four times a week. Her past medical history is significant only for a breast biopsy showing fibrocystic change at age 27. On review of her family history, she reveals that a maternal aunt developed breast and ovarian cancer in her fifties and that her only sister has recently been diagnosed with breast cancer at age 43. She has never been pregnant and experienced menarche at age 16. She is concerned that she may be at risk for breast cancer and wants to do everything she can to characterize this risk. Which of the following is true regarding her risk of developing breast cancer?

a) This patient has no risk factors for developing breast cancer, and she should begin screening mammography at age 50.

b) She is at increased risk for developing breast cancer, and genetic testing for *BRCA* mutations is indicated.

c) Due to her age of menarche and history of fibrocystic change on prior biopsy, she is at increased risk for developing breast cancer.

d) Physical activity to this degree has been shown to promote development of breast cancer through an effect on ovulation.

**Answer and Discussion**

The answer is b.

**Objective: Identify the indications for genetic cancer testing.**

The presence of a second-degree relative (the patient’s maternal aunt) with both breast and ovarian cancer constitutes grounds for testing for known mutations of the *BRCA* gene. In addition, the diagnosis of breast cancer in her only sister raises the question of a hereditary breast cancer syndrome, although without the complete family history including her aunt’s diagnosis, this would not necessarily indicate genetic testing. A number of decision analyses and guidelines have been established for selecting patients for genetic testing. A useful summary is available from the U.S. Preventive Services Task Force.

Importantly, the decision to undertake genetic testing also must consider how test results would influence the management of a particular patient. Discovery of a *BRCA1* mutation, for example, confers a lifetime risk of over 50% for developing breast cancer and would require consideration of prophylactic mastectomy, chemoprevention (e.g., with tamoxifen), or increased intensity surveillance. If the patient is a candidate for one or more of these approaches, such testing should be considered in conjunction with pre- and post-test genetic counseling. Many centers employ specialists in these fields, and referral to such a specialist is indicated in this case.

Independent of her *BRCA* status (even if negative), her risk for breast cancer is increased by having an affected first-degree relative. Nulliparity is also a risk factor for breast cancer. In addition, while a reduction in breast cancer mortality from
mammographic screening has been more clearly demonstrated in patients over age 50, there is also evidence pointing to such a benefit starting at age 40. This evidence forms the basis for recommendations of a number of groups, including the U.S. Preventive Services Task Force, that recommend screening mammography, with or without clinical breast examination (CBE), every 1 to 2 years for women aged 40 and older (B recommendation). At the very least, in patients at average risk, a decision to institute screening at 40 should be made with respect to individual patient wishes and after a discussion of the risk of false-positive results, which may require further invasive testing.

Later age at menarche is associated with a reduced risk of developing breast cancer. Fibrocystic change is considered a benign breast lesion, and it is not associated with any increase in breast cancer risk. The effect of regular physical exercise on the risk of developing breast cancer is unclear, especially in premenopausal women, but if anything, it is likely protective. A decreased risk in cases of exercise-induced anovulation has been postulated and is related to decreased exposure to (endogenous) estrogen.

**REFERENCE**


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**Question 70**

A 44-year-old previously healthy woman is seen in your office for evaluation of a right-sided breast lump noted on breast self-examination. She reports first noticing a “lump” in the right upper breast during breast self-examination 2 weeks prior, which she says has not increased in size and is associated with no skin changes. She denies nipple discharge and states that the mass has not changed in size. She has not yet had her first mammogram. Family history includes a maternal grandmother who died of breast cancer at age 73. She has had four children and has never used exogenous estrogen. A coworker has recently been diagnosed with breast cancer, and the patient wants to do “everything” to evaluate her condition.

On physical examination, the patient appears well although somewhat anxious and has normal vital signs. There is no palpable lymphadenopathy. On breast examination, the skin appears normal and the breasts are symmetric. There is a palpable 2.5-cm nodule that is nontender, feels cystic, and is mobile; it is located the right upper outer breast quadrant. The physical examination is otherwise normal.

Which of the following represents the best approach in this case?

a) Provide reassurance and establish a plan for reevaluation with history and physical examination in 6 months

b) Mammography; if negative, provide reassurance and plan for reevaluation in 6 months

c) Order an ultrasound; if a simple cyst is seen, refer the patient for fine-needle aspiration (FNA) biopsy

d) Order an ultrasound; if a simple cyst is seen, no biopsy is needed

**Answer and Discussion**

**Objective: Understand the diagnostic algorithm for breast mass.**

Several diagnostic algorithms have been proposed for the evaluation of a breast mass. All indicate that a distinct mass found on physical examination requires further workup with ultrasound and/or biopsy. Physical findings are not accurate enough to rule out cancer and should not comprise the sole diagnostic test in this case. Although some qualities of this patient’s breast mass (cystic, mobile) do not raise immediate concern for malignancy, and she lacks obvious risk factors for breast cancer based on her history, her age and the lesion size of over 2 cm make breast cancer more likely.

Ultrasound is a reasonable first diagnostic step, although initial fine-needle aspiration is also acceptable. Demonstration of a simple cyst requires no further immediate action, whereas a solid lesion or complex cyst calls for biopsy (either needle biopsy or excision of the lesion).

Mammography can be performed in conjunction with ultrasound in this patient, although it is less useful in patients under age 35 given increased density of normal breast tissue. It may detect other (including contralateral) breast lesions. Nonetheless, mammography is known to miss a large proportion (up to 20%) of clinically palpable breast cancers, so evaluation should not stop with a negative mammogram. At any rate, a mammographically “nonsuspicious” finding in the setting of a palpable breast mass will bolster the negative predictive value of the ultrasound.

Ultrasoundographic findings of a simple cyst provide a high negative predictive value for malignancy in this setting and make biopsy unnecessary. Any other finding should prompt FNA biopsy, which is a safe, office-based procedure.

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**Question 71**

A 52-year-old man with hypertension and dyslipidemia presents to your office for follow-up and routine health maintenance. He takes a thiazide diuretic and a statin. Past medical and surgical history are otherwise unremarkable. He is a college professor who drinks two glasses of wine per night with dinner and never smoked tobacco.

He has an older brother who was diagnosed with early-stage colon cancer last year at age 57, but otherwise, there is no family history of malignancy. He would like to know whether he should be evaluated for colon cancer and what test he should undergo.

What strategy should be recommended for colon cancer screening for this patient?

a) Refer for colonoscopy starting at age 60, with further testing depending on the findings

b) Refer for colonoscopy now and arrange further evaluation and screening based on the results
c) Initiate fecal occult blood testing, with plans to repeat this test on an annual basis
d) Recommend sigmoidoscopy be performed now and repeated at 5-year intervals

Answer and Discussion
The answer is b.

Objective: Identify appropriate colon cancer screening based on risk factors.

Because of his brother’s diagnosis of colon cancer under age 60, this patient is considered at high risk for development of colon cancer. Guidelines point for early initiation of colonoscopic screening in such patients, generally beginning at age 40 or at 10 years prior to the age of the affected relative’s diagnosis (whichever is earlier). Depending on the findings during initial colonoscopy, a future screening schedule will be determined. For example, finding of more than three adenomatous polyps would require repeat colonoscopy in 3 years, whereas patients with one or two tubular adenomas can be screened again 5 years later. In this high-risk patient, a colonoscopy will need to be repeated at least every 5 years.

Colonoscopy is also the recommended screening method for other high-risk patients, such as those with a personal history of colon cancer or inflammatory bowel disease or a family history of hereditary nonpolyposis colorectal cancer (HNPCC). Annual fecal occult blood testing (FOBT) and sigmoidoscopy at 5-year intervals are acceptable alternatives to colonoscopy in average-risk patients beginning at age 50. Annual FOBT is often recommended in conjunction with sigmoidoscopy every 5 years because the combined approach has been shown to increase yield over FOBT alone (although long-term survival has not been proven to be superior). Other options for average-risk patients include double-contrast barium enema and colonoscopy every 10 years. Regardless of the technique, screening should be initiated for all patients by age 50.

Notably, a family history of a single first-degree relative of any age with colon cancer, or even an adenomatous polyp, constitutes grounds for initiation of earlier screening (starting at age 40, with any standard screening technique noted above) according to 2003 American Gastroenterological Association guidelines. The magnitude of increased risk of developing colon cancer is smaller for these patients compared with patients with siblings developing colon cancer at <60 years old, but is still higher than the general population.

REFERENCE


Question 72

A 26-year-old male graduate student with no prior medical history is referred to you while visiting his parents during the holidays. He has noticed some rectal bleeding, occurring sporadically, over the preceding 3 years but has never sought medical care. He does so now at the urging of his family.

He gives a history only of occasional rectal bleeding and denies abdominal pain, constipation, frequent or loose stools, passage of mucus, or fever. The bleeding occurs on initiation of occasional bowel movements and colors the toilet water red. He denies black-colored stools.

His parents and two brothers (ages 29 and 34 years) are healthy. He takes no medications.

On physical examination, he appears well, and vital signs are normal. He has a number of epidermoid cysts on the legs and two on the face. Rectal examination is significant for a number of palpable polyps and a small amount of bright red blood, with no hemorrhoids. Physical examination is otherwise unremarkable.

Your counseling of this patient should most closely resemble which of the following?
a) These findings are suggestive of ulcerative colitis, and 5-aminosalicylate suppositories will alleviate his symptoms.
b) Due to concern of a mutation in the adenomatous polyposis coli (APC) gene, referral for endoscopic evaluation is indicated.
c) There is no need for concern; the bleeding is due to small polyps, which in a young man can cause occasional rectal bleeding and will resolve spontaneously.
d) The absence of a family history of colon cancer rules out the possibility of a genetic lesion causing polyposis.

Answer and Discussion
The answer is b.

Objective: Identify common features of familial adenomatous polyposis.

The history and physical findings in this patient are consistent with an APC gene mutation causing colonic polyposis. The history does not suggest inflammatory bowel disease (absence of pain or change in stool frequency and consistency), and the physical finding of polyps requires further investigation via endoscopy. If the characteristic finding of more than 100 colonic polyps is made, then the diagnosis of familial adenomatous polyposis (FAP) is secure. One-third of patients with a new diagnosis of FAP lack a family history of colonic polyposis or cancer. Gardner’s syndrome refers to FAP accompanied by extracolonic manifestations such as cutaneous cysts, dental abnormalities, desmoid tumors, polyps elsewhere in the gastrointestinal tract, and other malignancies (e.g., thyroid, liver, central nervous system).

In this patient, if FAP is found on endoscopy, genetic testing for an APC gene mutation in this patient should be undertaken. If a mutation of the APC gene (on chromosome 5q21) is identified, genetic testing of first-degree family members may be informative of their risk as well. (If the gene test is uninformative, endoscopic screening for first-degree relatives should be recommended.)
Although FAP accounts for less than 1% of the total colon cancer risk in the United States, the risk of colorectal cancer approximates 100% by age 45 in affected patients. Therefore, colectomy is recommended as the primary mode for prevention of colorectal cancer.

Distal (rectal) polyps in a young man should prompt further evaluation, given the possibility of FAP, and the natural history of colorectal polyps is not of spontaneous resolution. In addition, as noted, this patient lacks symptoms of inflammatory bowel disease, which would, at any rate, require further testing (including endoscopy and biopsy) before initiating treatment.

Question 73
A 26-year-old woman is hospitalized for parenteral antibiotics for treatment of pelvic inflammatory disease complicated by vomiting and severe abdominal pain. On admission, pregnancy test is negative, and Chlamydia trachomatis infection is diagnosed. After 24 hours of intravenous antibiotics, she has defervesced and, on hospital day 3, is without complaints and tolerating a regular diet. She is ready for discharge, and treatment with antibiotics is arranged to complete a total of 14 days of therapy.

Later she presents to your clinic for follow-up, having completed her course of antibiotics. She is feeling well and has returned to her job and resumed her prior smoking habit. In addition to scheduling evaluation of her sexual partner (for examination and treatment for Chlamydia), you appropriately perform testing for syphilis and hepatitis B and C.

She declines an HIV test. She complains of ongoing vaginal discharge and some bleeding and has never undergone conventional cervical cytologic testing (a Papanicolaou smear). A pelvic examination and HPV testing are performed, and an area of cervical ulceration is visible on physical examination.

What is the appropriate next step in your management?

a) Prescribe an additional course of antibiotics for treatment of cervicitis
b) No further treatment is needed; reassure her that her symptoms will resolve
c) Arrange for a punch biopsy of the ulcerated area
d) Refer for a loop electrosurgical excision procedure (LEEP)

Answer and Discussion
The answer is c.

Objective: Identify appropriate diagnostic workup of cervical lesion.

This patient has a visible cervical lesion and risk factors for development of cervical cancer. Known risks in this case include recent diagnoses of Chlamydia, a sexually transmitted disease, and cigarette smoking. Other risk factors include early onset of sexual activity, immunosuppression, prolonged use of oral contraceptives, and high parity.

Even in absence of known risk factors in this patient, biopsy of a lesion visible on cervical examination is necessary. Squamous cell carcinoma of the cervix can present as a superficial ulceration or an exophytic tumor. Punch biopsy will allow diagnosis of dysplasia or frank carcinoma and will guide the next stage of evaluation. Staging techniques for cervical cancer rely on a pelvic examination by an experienced examiner and information gained by further surgical techniques such as colposcopy or conization (including loop electrosurgical excision). The commonly used Federation of Gynecologists and Obstetricians (FIGO) staging system relies heavily on the pelvic examination and does not incorporate information gained from computed tomography of magnetic resonance imaging.

Cervicitis can be a cause of vaginal discharge; however, it can also accompany malignancy and cannot explain the ulceration seen on physical examination. Loop electrosurgical excision procedure is a type of conization procedure (cone-shaped biopsy) performed for treatment of known dysplasia or in patients with superficial cervical cancer (<3 mm depth of penetration) who desire future pregnancy. Its use is based on prior tissue diagnoses of cancer or dysplasia based on pathologic evaluation.

Question 74
An 81-year-old man with hypertension, dyslipidemia, and longstanding urinary obstruction due to benign prostatic hyperplasia (BPH) presents for a scheduled office visit. He has recently been on a cruise to the Bahamas and remains physically active.

In the past, he experienced nocturia two times per night and urinary hesitancy but has no dysuria, urgency, or frequency. Also in the past, he changed his lifestyle practices, especially by reducing caffeine and alcohol intake, with a positive effect on his BPH symptoms. However, he points out that over the past year, his urinary stream is becoming weaker, his nocturia is more severe, and it is harder to initiate urination. He states that these symptoms are impairing his quality of life. On review of systems, he notes chronic mid-back pain for the past 3 months, which he attributes to muscle strain; the pain is better when he lies flat and is relieved by acetaminophen.

Physical examination shows a well-appearing man, with normal vital signs and normal cardiac, pulmonary, and abdominal findings. Prostate examination shows no nodules, induration, or asymmetry, although the prostate is enlarged. Rectal sphincter tone is normal. Neurologic and musculoskeletal examinations are also normal.

Complete blood count (CBC) shows a mild normocytic anemia with a hemoglobin of 13.0 g/dL; CBC and serum chemistries, including renal function, are otherwise unremarkable.

Which of the following represents the best approach to his increasing obstructive urinary symptoms?

a) Start an α-adrenergic antagonist, given the worsening of obstructive urinary symptoms despite lifestyle changes
b) Perform a serum prostate-specific antigen (PSA) test, since identification of cancer would improve this patient’s longevity
c) Perform a bone scan to rule out vertebral metastases from prostate cancer
d) Order an ultrasound of the kidneys to rule out hydronephrosis

**Answer and Discussion**

**The answer is a.**

**Objective: Diagnose and treat benign prostatic hyperplasia.**

Prostatic adenocarcinoma tends to arise in the periphery of the prostate, where it is less likely to compress the prostatic urethra; for this reason, cancer need not be invoked as a culprit for worsening BPH symptoms. The absence of suspicious physical findings (which would require referral for biopsy) and the possibility for transient elevation of PSA after prostatic examination are further reasons not to perform PSA testing. Worsening of BPH symptoms is not unexpected over time and portends little regarding his prostate cancer risk and any benefit achievable by screening. Initiation of an alpha-adrenergic antagonist or a 5-α-reductase inhibitor is reasonable in this patient.

PSA screening for prostate cancer has not been prospectively proven to prolong survival. Even though prostate cancer is more common in older men, “overdiagnosis” of indolent cases of prostate cancer may expose patients to unnecessary risks of therapy (radical prostatectomy or radiation). In this context, overdiagnosis can be thought of as an extreme form of length-time bias, occurring when outcomes of patients with early, indolent tumors found by PSA screening are averaged in with all other cases, resulting in better outcomes misattributed to screening and early treatment. Rather, the discovery of biologically indolent cases using PSA screening dilutes the “pool” of all prostate cancers’ severity, and outcomes appear better regardless of the intervention. Epidemiologic and retrospective data are highly susceptible to the effect of length-time bias. Until an overall survival benefit to PSA screening is proven with prospective studies, its use in screening cannot be routinely recommended.

A radionuclide bone scan is sometimes used in staging known prostate cancer, although is not indicated in all cases (low Gleason score, relatively low PSA level, nonpalpable tumors on examination). Abnormal bone scan results frequently require corroboration with plain radiographs, since they can be associated with a high rate of false positives. Finally, in absence of elevated serum creatinine, ultrasound for evaluation of hydronephrosis is not indicated.

**Question 75**

A 75-year-old man with a history of recently diagnosed squamous cell lung cancer is brought to the emergency room for a 2-day history of worsening confusion and weakness. He has to be helped from a wheelchair to the bed due to weakness and disorientation. It is difficult to obtain a history from the patient, but his son suggests that his only other symptom is constipation. He has not yet received treatment for his lung cancer, and you are told that it is only in the lung. On examination, the patient is only able to tell you his name. This temperature is 37.2°C, blood pressure is 122/75 mmHg, pulse is 110 beats/minute, respiratory rate is 12/min, and oxygen saturation is 95% on room air. His labs reveal a serum calcium of 13.2 mg/dL, and his EKG shows shortening of the QT interval.

The patient is admitted to the hospital for further evaluation and management of his hypercalcemia. Other than lung cancer, his only significant medical history includes hypertension and diabetes, which are both well controlled. Upon admission, he remains confused. The remainder of his labs shows the following: sodium = 135 mmol/L, potassium = 3.8 mmol/L, chloride = 102 mmol/L, bicarbonate = 24 mmol/L, blood urea nitrogen = 12 mg/dL, and creatinine = 1.1 mg/dL. What is true about the most initial treatment for this patient?

a) Patient should initially receive furosemide 80 mg IV every 6 hours to increase calcium excretion.
b) The patient should receive normal saline at 200 mL/hr for hydration.
c) The patient should initially receive zoledronic acid IV to rapidly decrease calcium resorption from the bone.
d) Calcitonin should be given after zoledronic acid due to development of tachyphylaxis.

**Answer and Discussion**

**The answer is b.**

**Objective: Understand the management of hypercalcemia.**

The correct management of hypercalcemia of malignancy requires decreasing the concentration of calcium in the serum and correcting the underlying cause. The most important initial therapy to reduce the concentration of calcium is hydration. Patients should be hydrated to maintain a urine output of 100 to 150 mL/hr. Aggressive hydration is usually required since most patients will be volume depleted on presentation. Hydration should be carefully monitored due to possible renal insufficiency associated with hypercalcemia and the likelihood of heart failure in patients in this population. It is inappropriate to give diuretics initially. Loop diuretics increase calcium excretion by inhibiting the reabsorption of calcium in the loop of Henle. As discussed, these patients are often volume depleted, and the benefit from increasing calcium excretion would be offset by the worsening of volume depletion by the diuretic effect of these agents. These agents are most useful for treating any fluid overload that results from the hydration, not as an initial treatment. Although zoledronic acid should be given to patients to decrease the resorption of calcium from the bones, this is not an immediate effect. Although zoledronic acid is often used instead of pamidronate due to increased potency and a more rapid infusion rate, the maximum effect of these agents occurs in 2 to 4 days. Patients with hypercalcemia of malignancy should receive a bisphosphonate as part of their treatment and often continue to receive these agents after resolution of their hypercalcemia, but these agents are not given for an immediate effect. By comparison,
calcitonin has a very rapid onset of action with a maximum effect in 4 to 6 hours. Patients with severe or symptomatic hypercalcemia should be given calcitonin with additional doses given to patients with calcitonin-sensitive hypercalcemia. The efficacy of calcitonin is limited by development of tachyphylaxis, whereby a rapid tolerance develops within 48 hours. The use of calcitonin does not affect the efficacy of bisphosphonates. Therefore, it is not accurate that calcitonin should be given after bisphosphonates.

Question 76
A 23-year-old man with newly diagnosed Burkitt lymphoma is transferred for treatment. He presented to an outside hospital with abdominal pain and distention and was found to have a large right lower quadrant mass causing partial small bowel obstruction. The biopsy of this mass was positive for Burkitt lymphoma. Further evaluation reveals bulky abdominal adenopathy and involvement of the bone marrow. On examination, he is in no distress with a temperature of 37.4°C, blood pressure of 130/78 mmHg, pulse of 90 beats/minute, respiratory rate of 12/min, and oxygen saturation of 98% on room air. His examination is only notable for some diffuse abdominal tenderness. His CBC shows a WBC of 10,600/μL, hemoglobin 9.5 of g/dL, and platelets of 550,000/μL. Serum chemistries include potassium of 3.5 mmol/L, creatinine of 1.0 mg/dL, uric acid of 6.6 mg/dL, phosphorus of 3 mg/dL, calcium of 8 mg/dL, and LDH of 300 U/L. Which of the follow best describes the proper management of this patient prior to administering chemotherapy?

a) The patient should be given potassium supplements to prevent the hypokalemia associated with beginning treatment.
b) The patient should receive diuretics prior to treatment to increase the excretion of uric acid.
c) The patient should receive allopurinol and normal saline for hydration to prevent uric acid nephropathy.
d) There is no need to hydrate or give allopurinol since there are currently no electrolyte abnormalities.

Answer and Discussion
The answer is c.

Objective: Diagnose and treat tumor lysis syndrome.
The key to successful management of this patient is to recognize the risk for developing tumor lysis syndrome and preventing it. Tumors that are commonly associated with tumor lysis syndrome include poorly differentiated lymphoma, such as Burkitt lymphoma, and acute lymphoblastic leukemia. Other risk factors include renal dysfunction, elevated uric acid, volume depletion, chemotherapy-sensitive tumors, and a large tumor burden. Because of the increased risk for tumor lysis syndrome associated with both hyperuricemia and volume depletion, diuretics should not be administered in anticipation of chemotherapy. Diuretics can worsen both volume depletion and uric acid excretion, worsening the renal failure associated with tumor lysis syndrome. Since tumor lysis syndrome is due to treatment, the electrolyte status of the patient prior to treatment should not influence whether steps should be taken to prevent developing this complication. Upon treatment with chemotherapy, destruction of the tumor cells can lead to the hyperkalemia, hyperuricemia, hyperphosphatemia, and hypocalcemia that are associated with tumor lysis syndrome. The likelihood of developing tumor lysis syndrome should guide the use of allopurinol and how aggressively to hydrate prior to therapy. One of the common laboratory abnormalities associated with tumor lysis syndrome is hyperkalemia. Although this patient’s potassium is 3.5 mmol/L, he will likely have an increase, not a decrease, in his potassium with therapy due to release of intracellular potassium from the tumor cells. He should, therefore, not receive supplemental potassium.

Question 77
A 58-year-old man comes to the emergency room after developing a fever of 38.8°C and shaking chills. The patient has metastatic colon cancer and received his third cycle of chemotherapy last week. He had a fever with his previous cycle of chemotherapy. On examination, his temperature is 39°C, blood pressure is 115/75 mmHg, pulse is 115 beats/minute, respiratory rate is 18/min, and oxygen saturation is 96% on room air. His labs are significant for a WBC of 900/μL, hemoglobin of 9 g/dL, and platelets of 85,000/μL with an absolute neutrophil count of 220/μL. A chest x-ray is without evidence of pneumonia, and blood cultures are pending. Which of the following is most accurate about this patient’s neutropenic fever?

a) The fever is likely a physiologic response to repeated bone marrow suppression, and antibiotics should only be given if cultures are positive.
b) Neutropenic fever is often from enteric gram-negative organisms, and patients should immediately receive antibiotics to cover these organisms.
c) Due to the severity of the neutropenia, the fever is likely from a fungal infection, and antifungal therapy should be started immediately.
d) Neutropenic fever is rarely from gram-positive organisms, and vancomycin should only be started if skin lesions with erythema or purulent discharge are present.

Answer and Discussion
The answer is b.

Objective: Diagnose and treat febrile neutropenia.
One of the most common causes of neutropenia is gram-negative bacteria from the gastrointestinal tract, thought to be due to bacterial translocation. These infections are also the ones that frequently lead to the more serious complications of neutropenia with development of hypotension and septic shock. As a result, it is critical that patients who have received chemotherapy have their CBC checked promptly if they develop a fever and that they are quickly treated with antibiotics that cover gram-negative organisms. Patients
who develop neutropenia following chemotherapy must be treated with antibiotics empirically prior to the results of any cultures. Fever is not an expected response inherent to suppression of the bone marrow, so any fever in this setting must be considered an infection. Furthermore, many patients who present with neutropenic fever receive empiric antibiotics, and an organism is never identified. The etiology of neutropenic fever in most patients is bacterial, and initial treatment is directed toward gram-negative organisms with inclusion of gram-positive coverage, if appropriate. If after a few days, the fever has not resolved, antifungal coverage should be added at that time. There is not a correlation between the severity of neutropenia and the etiology of the fever, although the risk of infection does correlate with the duration of neutropenia. In most cases, fungal coverage is empiric and does not need to be started urgently. Gram-positive organisms do cause a significant number of neutropenic fevers. In the absence of neutrophils, skin infections will commonly not show the typical erythema or purulence, so this is not a good basis for making clinical judgments. Indications for adding vancomycin to the treatment regimen for neutropenic fever include clinical suspicion for a catheter-related infection, known colonization with gram-positive organisms resistant to cephalosporins or penicillins, positive blood cultures for a gram-positive organism, and hypotension.

**Question 78**

A 62-year-old previously healthy man is admitted to the hospital from the emergency room at 2:00 AM after developing a cough and progressive shortness of breath over the past 2 days. He denies fever and chills and has no sick contacts. On examination, he is in moderate distress from his dyspnea. His temperature is 37.0°C, blood pressure is 125/75 mmHg, pulse is 110 beats/minute, respiratory rate is 18/min, and oxygen saturation is 95% on room air. He has distended jugular veins and edema of his face and arms, and his lungs are clear to auscultation. The chest x-ray in the emergency room shows a widened mediastinum. His social history is positive for a 40 pack-year smoking history. You are told that he is being admitted for treatment of superior vena cava syndrome. Although considered an oncologic emergency, it is important to treat the patient’s symptoms while diligently trying to make a diagnosis, particularly in a patient without a known malignancy. Although diagnostic tests and treatment will ultimately be needed, this patient, who was admitted in the middle of the night, should have the head of the bed elevated for comfort and diuretics for intravascular volume reduction to relieve symptoms. He is hemodynamically stable and there is no need for any urgent intervention at this time. Although a CT of the chest will likely be required to guide the diagnosis, this does not have to be done urgently, and relief of symptoms should supersede the imaging test. Similarly, until a diagnosis of superior vena cava syndrome is made and there is pathology available from the tumor, the appropriate course of radiation therapy cannot be planned. Although this patient has a widened mediastinum on chest x-ray, the clinical history and physical examination do not support a diagnosis of inhalational anthrax. While corticosteroids may decrease the tumor burden and relieve symptoms, it may also cause difficulties in obtaining appropriate histologic diagnosis of the tumor.

**Question 79**

A 68-year-old woman with a history of breast cancer comes to your office for a routine physical examination. During the review of systems, she complains of back pain that has developed in the past month with progressive numbness and weakness in her legs over the last week. She denies any bowel or bladder dysfunction. On examination, she has no pain to palpation over the spine but some loss of sensation in both feet and 4/5 strength in the lower extremities bilaterally. You are concerned about spinal cord compression due to metastatic breast cancer and obtain an MRI that shows moderate cord compression in the lumbar spine. Which of the following statements about spinal cord compression is true?

- **a)** A recent study has shown that radiation therapy is superior to surgery for most patients with spinal cord compression.
- **b)** An x-ray of the lumbar or thoracic spine has a greater specificity and is more cost-effective than an MRI for diagnosing spinal cord compression.
- **c)** The patient’s symptoms at the time of diagnosis with spinal cord compression are more predictive than the size of the lesion for determining the patient’s outcome following therapy for spinal cord compression.
- **d)** Nearly all patients will have neurologic symptoms at the time of diagnosis of spinal cord compression.

**Answer and Discussion**

The answer is **c**.

**Objective: Understand key features of spinal cord compression.**

The patient has a history of breast cancer and developed back pain followed by neurologic symptoms in her legs. Unfortunately, the neurologic compromise that comes from injury.
to the spinal cord in a patient with cord compression is often irreversible. Surgery or radiation therapy for cord compression will palliate symptoms and stop further progression of neurologic compromise but will usually not reverse any deficits. Therefore, the outcome is dependent on the presenting symptoms, not the tumor type, size of the lesion, or type of therapy. Therefore, it is important to have a low threshold for detecting cord compression. Many patients with cord compression have back pain as their initial complaint but are not imaged until neurologic deficits occur. With a low threshold for imaging patients for back pain with cancers that are likely to cause cord compression, many patients could be treated before they develop neurologic symptoms. The best test for spinal cord compression is an MRI. An x-ray can show abnormalities in the vertebrae from cord compression but cannot show the cord and impingement on the cord by soft tissue masses or from bone fragments. A noncontrast MRI is appropriate for most patients with suspected cord compression, although an MRI with contrast is required if there is concern for leptomeningeal disease that may be affecting the spinal cord. The treatment for cord compression is surgery, radiation therapy, or chemotherapy for sensitive tumors. Although an area of controversy in the past, current studies suggest that surgery followed by radiation is the best approach to therapy for patients with limited-extent disease and a favorable prognosis. Poor surgical candidates or patients with more extensive disease may benefit from palliative radiation therapy. Patients with chemotherapy-sensitive tumors, such as germ cell tumors, lymphoma, breast cancer, or prostate cancer, may benefit from systemic chemotherapy.
RAPID BOARD REVIEW—KEY POINTS TO REMEMBER:

- The distinction between crystal-induced and bacterial arthritis cannot be made reliably with studies from peripheral blood or from clinical presentation alone. Synovial fluid analysis, with cell count, polarized microscopy, and culture, is the gold standard diagnostic test.

Gouty Arthritis

- Attacks of acute gout can be elicited by abrupt changes in serum urate levels, whether up or down. Serum urate may be normal at the time of an attack, but if checked repeatedly, in the absence of hypouricemic therapy, chronic gout patients will almost invariably have serum levels >6.7 mg/dL, the saturation point for urate.

Non-urate Crystalline Arthritis

- Calcium pyrophosphate crystals can cause attacks that totally mimic gout (pseudogout), but they can also cause chronic arthritis syndromes. Radiographic finding of calcium deposition within menisci and other intra-articular cartilage has been termed chondrocalcinosis and may be asymptomatic or associated with inflammatory arthritis. Systemic diseases associated include hyperparathyroidism, hypothyroidism, hypophosphatasia, hypomagnesemia, gout, amyloidosis, prior joint trauma or surgery, hemochromatosis.

- Oxalate-induced arthritis, in patients on dialysis.
- Hydroxyapatite-induced arthritis, in patients with Milwaukee shoulder.

Treatment of Crystalline Arthritis

- Hyperuricemia develops in the overwhelming majority of patients because of insufficient renal excretion rather than overproduction. Therapy includes xanthine oxidase inhibitors, such as allopurinol, and uricosuric agents, such as probenecid.

- Colchicine or NSAIDs should be used as initial simultaneous prophylactic antiinflammatory medications because drug-induced hypouricemia frequently precipitates an attack of gout.

- Acute attacks can be treated with NSAIDs at high doses (not aspirin), corticosteroids, ACTH, intra-articular corticosteroids, IL1 antagonists (off label), or colchicine.

Septic Arthritis

- Septic arthritis may be the initial manifestation of systemic bacterial infection and is associated with a >10% mortality.

- The culture of synovial fluid confirms the diagnosis. A negative Gram stain does not exclude the possibility of infection.

- Staphylococci and streptococci are the most common organisms. Fibrocartilage joints (sternoclavicular, sacroiliac, acromioclavicular) are prone to infection after persistent bacteremia, particularly with gram-negative organisms.

- The treatment of suspected septic arthritis should not be delayed until culture results are available. Treatment includes parenteral systemic antibiotics and adequate local drainage.

Culture-Negative and Crystal-Negative Acute Arthritis

Disseminated Gonococcal Infection

- The arthritis often follows a syndrome of migratory myalgia and arthralgia.

- Produces skin lesions and tenosynovitis more commonly than other infections.
The absence of pelvic symptoms (or physical findings) in no way excludes the disease.

Evaluation includes blood, joint fluid, cervical, vaginal, rectal, and pharyngeal cultures.

**Lyme disease**
(tick-transmission of the spirochete *Borrelia burgdorferi*).

- History of an initial characteristic rash, erythema chronium migrans, followed by fluctuating neurologic syndromes and cardiac conduction defects.
- The joint involvement is a monoarticular or oligoarticular, remittent or intermittent, large joint arthritis.
- The provisional diagnosis of Lyme disease must include the following factors:
  - Opportunity for exposure to a suitable tick vector
  - Clinical pattern of symptoms consistent with described disease manifestations
  - Positive ELISA supported by a positive Western blot test result (seronegative Lyme disease is extremely uncommon, and this diagnosis should be entertained only with a great deal of caution).

**Reactive Arthritis**

- Organisms associated include *Chlamydia, Salmonella, Clostridium difficile,* and *Yersinia*.
- Features include mild conjunctivitis or uveitis, allergic or infectious urethritis, balanitis, psoriasiform skin lesions, or oral ulcerations. Sausage digits, enthesitis, and asymmetric sacroiliac involvement may also occur.

**SUGGESTED READINGS**


RAPID BOARD REVIEW—KEY POINTS TO REMEMBER:

**Chronic Noninflammatory Arthritis**

**Osteoarthritis**
- The affected joints are more painful with use and improve with rest. Some stiffness on arising in the morning, but usually <30 minutes. *Gelling*, or a stiffening of the joints during periods of rest, is mild. No systemic symptoms, and absent local signs of inflammation.
- The physical examination reveals bony osteophytes on the margins of the joints, joint area may be tender on palpation, the overlying synovium is not usually thickened or inflamed and joint effusions may be present. Crepitus, a sensation of friction within the joint, may be felt.
- Over time, the range of motion of the joint is diminished, and angulation deformities may be apparent, especially at the distal interphalangeal (DIP) and proximal interphalangeal (PIP) joints of the fingers, the first metacarpal phalangeal (MTP) joint, and the knees.
- Radiographs show an asymmetric loss of joint space, subchondral sclerosis, marginal osteophytes, and subchondral cysts.
- Secondary OA is suspected when a joint that is not commonly involved by primary OA shows evidence of OA on physical examination and radiographs.

**Chronic Inflammatory Arthritis**
- Joint pain, morning stiffness that typically last >1 hour. The joints feel better with use, and the worst periods are during the night and on arising in the morning. Gelling is prominent. Systemic symptoms and extraarticular organ manifestations can be present.
- An examination of the joint will reveal warmth, tenderness, joint swelling (a mixture of synovial thickening and joint effusion), loss of function, and, occasionally, erythema.

**Rheumatoid Arthritis**
- Usually a symmetric, polyarticular arthritis. Small joints of hands and feet are classic: PIP, MCP, wrist, ankle, MTP (however typically spares DIPS); but almost any joint can be involved: TMJ, elbow, shoulder, C-spine, hip, knee.
- With progression: swan neck and boutonniere deformities of the fingers, volar subluxation of the carpus, loss of full extension of the elbows and full abduction of the shoulders, valgus angulation at the knees and ankles, and pes planus.
- The serum rheumatoid factor (RF) has 70% to 80% sensitivity and 80% specificity. Antibodies to cyclic citrullinated peptide (anti-CCP) are highly specific for RA (95%), with a sensitivity of about 70%.
- Radiographs initially show periarticular osteopenia and soft tissue swelling. As the disease progresses, a symmetric loss of joint space and periarticular marginal erosions appear.
- Patients should be started on disease-modifying antirheumatic drugs (DMARDs).

**Spondyloarthritides**
- Common features include the following:
  - Inflammatory spinal disease and sacroiliitis
  - Peripheral arthritis (asymmetric, lower extremities, oligoarticular)
  - Enthesopathy: inflammation of tendon insertion
  - Extra-articular manifestations (e.g., anterior uveitis, iritis, colitis)
  - Genetics (association with HLA-B27, significant familial aggregation)
  - Seronegative (absence of rheumatoid factor)

**Ankylosing Spondylitis**
- Typically present with chronic (>3 months) inflammatory back pain: age of onset <40 years, insidious onset, improvement with exercise but not with rest, pain at night.

**Psoriatic Arthritis**
- Cutaneous psoriasis + signs and symptoms of an inflammatory arthritis.

**Reactive Arthritis (Reiter’s Syndrome)**
- Immune-mediated arthritic process following an infectious process, after 2 to 4 weeks.
Spondyloarthritis of Inflammatory Bowel Disease
- Arthritis can occur in association with either ulcerative colitis or Crohn’s disease.

Viral Arthritis
- Arthralgias and arthritis can be seen with a number of viruses, including parvovirus B19, acute hepatitis B, chronic hepatitis C, rubella (infection and vaccination), and alphaviruses.

Sarcoid Arthritis
- Multisystem disorder of unknown etiology characterized by noncaseating granulomas in the affected tissues. Arthritis is seen in approximately 25% of sarcoidosis patients.
- Lofgren’s syndrome = acute arthritis + bilateral hilar adenopathy + erythema nodosum.

Adult-Onset Still’s Disease
- Systemic, inflammatory, multisystem disease with fever, arthritis, and skin rash.

Rheumatic Fever
- 2 major, or 1 major + 2 minor criteria + evidence of a previous streptococcal infection.
- Major criteria: carditis, polyarthritis, chorea, erythema marginatum, subcutaneous nodules
- Minor criteria: arthralgia, fever, ↑ ESR, ↑ C-reactive protein, ↑ PR interval

Medications
- Cyclooxygenase 2–selective nonsteroidal antiinflammatory drugs (NSAIDs) are less likely to cause gastric bleeding, but are otherwise not preferable to nonselective NSAIDs.
- Patients receiving antitumor necrosis factor therapies are at increased risk for infections, including the reactivation of latent mycobacterial infections.

SUGGESTED READINGS


RAPID BOARD REVIEW—KEY POINTS TO REMEMBER:

Systemic Lupus Erythematosus
- Complex autoimmune inflammatory disease that can affect virtually any organ system in the body, and the presentation can vary considerably from patient to patient.
- A patient is said to have a high likelihood of having systemic lupus erythematosus (SLE) if that person exhibits 4 of the following 11 features:
  - Malar rash
  - Discoid rash
  - Photosensitivity
  - Oral ulcers
  - Serositis
  - Arthritis
  - Renal involvement
  - Neurologic involvement
  - Hematologic abnormalities
  - Positive antinuclear antibodies (ANAs)
    - ANA is present in 97% to 100% of patients with lupus.
    - ANA is lacking in specificity because it is found in many other disease states. Healthy individuals may also have a positive ANA, with a prevalence of 5% to 7%.
  - Evidence of immunologic dysfunction as revealed by:
    - false-positive VDRL (Venereal Disease Research Laboratory) test,
    - positive anti-double-stranded DNA antibody,
    - positive anti-Sm (Smith) antibody (greatest specificity, sensitivity only 30% to 40%), or
    - presence of an antiphospholipid antibody
- Coronary artery disease is a leading cause of premature death in SLE. In young women with SLE, the risk of myocardial infarction is increased 50-fold.
- Drug-induced lupus is a syndrome of lupus-like illness associated with the ingestion of certain medications (procainamide, hydralazine, α-methyldopa, isoniazid, quinidine).
  - ANA is required for the firm diagnosis.
  - Antibodies to histone do not have a discriminatory value.
  - Anti-double-stranded DNA antibodies are generally not found in drug-induced lupus.

Antiphospholipid Antibody Syndrome
- Syndrome characterized by recurrent arterial and/or venous thromboses, recurrent fetal loss, and thrombocytopenia in association with sustained elevated titers of antiphospholipid antibodies.
- The initial testing consists of a lupus anticoagulant assay (usually the aPTT) plus an anticardiolipin ELISA. If negative or equivocal, further testing with other coagulation tests (i.e., DRVVT, β2GP-I ELISA, or assays for other phospholipids) can be pursued.

Scleroderma (Progressive Systemic Sclerosis)
- The onset is typically heralded by Raynaud’s phenomenon, with the later development of sclerodactyly and skin thickening and fibrosis over the hands, arms, legs, face, and trunk.
- Late complications of the musculoskeletal disease include joint contractures, muscle atrophy, and skin ulceration over the contracted joints.
- Internal organ involvement includes interstitial lung disease, cardiac arrhythmias, rapidly progressive renal failure, esophageal dysmotility, and gut hypomotility.
- Antibodies to topoisomerase I (anti-Scl-70)—70% of patients with diffuse scleroderma.
- Limited scleroderma, including CREST (Calcinosis cutis, Raynaud’s phenomenon, Esophageal dysmotility, Sclerodactyly, Telangiectasia) syndrome, is characterized by a more restricted cutaneous disease.
- Anticentromere antibodies—95% of patients with CREST.
- Scleroderma renal crisis is a form of rapidly progressive renal insufficiency that can affect patients with diffuse scleroderma.
  - The prior use of systemic corticosteroids—a risk factor for the development of scleroderma renal crisis, so steroid use should be minimized in patients with scleroderma.
  - The prompt initiation of ACE inhibitors at the diagnosis of renal crisis is associated with a dramatically enhanced renal and patient survival.

Sjögren’s Syndrome
- Chronic autoimmune exocrinopathy with “sicca complex”: dry mouth (xerostomia), dry eyes (xerophthalmia),
and often salivary gland (parotid and/or submandibular gland) enlargement.

- Patients can develop dryness of the throat (xerostomia), dry skin, vaginal dryness, and other symptoms from exocrine gland inflammation.

**Idiopathic Inflammatory Myopathies**

- The idiopathic inflammatory myopathies include seven disorders:
  - Polymyositis (PM)
  - Dermatomyositis (DM)
  - Inclusion body myositis
  - Idiopathic inflammatory myopathy associated with malignancy
  - Childhood PM/DM
  - Amyopathic dermatomyositis
  - Overlap syndromes with other collagen vascular diseases

- These disorders share several clinical features, including a gradually progressive proximal muscle weakness that is usually painless.

- The periorbital edema and heliotrope rash over the eyelids are typical of DM. Gottron’s papules are pathognomonic for DM.

- The laboratory hallmark of PM and DM is a striking elevation of CPK, and CPK-MB. Anti-Jo-1 antibodies are found in 20% of patients with polymyositis.

- EMG—characteristic abnormalities

- Histology—variable degrees of mononuclear cell infiltrates.

**Steroid myopathy**

- Mimics PM/DM clinically—proximal muscles are more affected than the distal muscles.

- Has normal CPK and other enzyme levels.

**SUGGESTED READINGS**

**Systemic Lupus Erythematosus**


**Antiphospholipid Antibody Syndrome**


**Scleroderma**


**Sjögren’s Syndrome**


**Idiopathic Inflammatory Myopathy**


RAPID BOARD REVIEW—KEY POINTS TO REMEMBER:

- Vasculitis is defined by the presence of blood vessel inflammation. It is a histologic feature shared by a diverse range of diseases that may be characterized by differing patterns of organ involvement, severity, treatment, and outcome.
- The signs and symptoms of vasculitis can be nonspecific, related to organ and tissue ischemia, and/or reflective of generalized inflammation, which is influenced by the underlying diagnostic cause.
- Antineutrophil cytoplasmic antibodies (ANCAs) have not been found to be a reliable measure of disease activity, and changes in ANCA level alone should not be used to guide treatment decisions.
- The therapy of systemic vasculitis varies depending on the type of vasculitis, site of organ involvement, and severity. Certain types of vasculitis may be self-limiting and merely require careful monitoring, while others necessitate aggressive immunosuppressive treatment.

Giant Cell Arteritis

- Large + medium-vessel (predominantly cranial) granulomatous arteritis
- Almost exclusively >50 years, more common in women, rarely in African Americans
- Diagnosis = clinical features + elevated ESR + positive temporal artery biopsy
- Glucocorticoid therapy should be started immediately in order to protect vision.
- Aspirin 81 mg daily may reduce cranial ischemic complications.

Takayasu Arteritis

- Large-vessel granulomatous arteritis (aorta, its main branches, pulmonary arteries)
- Predominantly in young women
- Diagnosis = clinical features + arteriographic imaging (MRA, CT arteriography, or catheter-directed dye arteriography) revealing aneurysm formation (aortic root with aortic regurgitation) or stenosis (especially abdominal aorta)
- Glucocorticoids, methotrexate, infliximab

Polyarteritis Nodosa

- Small- and medium-sized muscular arteries vasculitis (not capillaries, or venules)
- Men:women ~2:1, typically between 40 and 60 years
- Diagnosis = clinical features (NOT glomerulonephritis (GN) or pulmonary hemorrhage) + arteriographic findings or biopsy-proven vasculitis (multiple microaneurysms)
- Prednisone and cyclophosphamide for life-threatening cases

Wegener’s Granulomatosis

- Granulomatous inflammation ± small vessel vasculitis
- Diagnosis = involvement of the upper and lower respiratory tract and kidneys + biopsy
- ANCA positive 80% to 100% patients—80% to 95% against proteinase-3 (PR-3) (i.e., cANCA)
- High-dose prednisone + cyclophosphamide (CYC) or rituximab in severe cases. After 3 to 6 months switch to methotrexate or azathioprine for remission maintenance
- Trimethoprim–sulfamethoxazole decreases the rate of upper respiratory flares

Microscopic Polyangiitis

- Small ± medium-vessel nongranulomatous vasculitis
- Diagnosis = pulmonary (alveolar hemorrhage) and renal involvement (rapidly progressive GN) + biopsy
- pANCA directed against myeloperoxidase (MPO) 50% to 80% positive
- Treatment similar to the one for GPA

Eosinophilic Granulomatosis with Polyangiitis (Churg-Strauss Syndrome)

- Small- to medium-size vessel necrotizing vasculitis, with eosinophils, and granulomas
- Diagnosis = asthma + clinical features of vasculitis (palpable purpura or skin infarction and other organ involvement) + eosinophilia (>1,500 cells/mm³)
- ANCA positive <40% of patients and are typically anti-MPO-ANCA
- High-dose glucocorticoids. CYC for refractory or life-threatening cases
IgA Vasculitis (Henoch-Schönlein Purpura)

- Leukocytoclastic vasculitis and often IgA deposition on skin biopsies
- A disease of children, rarely of adults
- Palpable purpura + varying degrees of polyarthralgia, arthritis, myalgia, GI ischemia (including intussusception), and glomerulonephritis
- In ~60% of cases, patients describe a preceding infection with streptococci, mycoplasma pneumonia, *Yersinia, Legionella, Helicobacter pylori*, Epstein-Barr virus, Hepatitis B virus (HBV), varicella, adenovirus, cytomegalovirus, or parvovirus B19
- Glucocorticoids for life-threatening visceral disease, cytotoxic drugs

Cryoglobulinemic Vasculitis

- Type I: monoclonal Ig often in lymphoproliferative diseases such as B-cell malignancies
- Type II: mixed monoclonal + polyclonal Ig, often associated with HCV
- Type III: mixed polyclonal Ig
- Antiviral therapy ± Rituximab in HCV-associated cryoglobulinemia

Cutaneous Vasculitis

- Small-vessel (capillaries and venules) inflammation, with leukocytoclasia
- Palpable purpura and maculopapular lesions, sometimes nodules and ulcerations
- In >70% of cases, it is secondary to drugs, infections, malignancies, primary systemic vasculitis, cryoglobulinemia, connective tissue diseases, urticarial; in 30% it is idiopathic.
- Symptomatic patients need antihistamines, colchicine, dapsone, or glucocorticoids; methotrexate or azathioprine for severe cases.

SUGGESTED READINGS

Nueninghoff DM, Hunder GG, Christianson TJ, et al. Incidence and predictors of large-artery complication (aortic aneurysm,


**Rapid Board Review—Key Points to Remember:**

- Eliciting tenderness that does not mimic the patient’s pain syndrome is not diagnostic.

**Hip Girdle**

- **Hip Joint Pathology**—pain deep to the inguinal crease, elicited by passive motion of the hip, but not reproduced by palpation.
- **Trochanteric Bursitis**—pain reproduced by palpation of the superficial trochanteric bursa, over the trochanteric prominence, or deep trochanteric bursa, in a deep groove, proximal and slightly posterior.
- **Ischial Bursitis**—tenderness along the ischial prominence.
- **Gluteal Bursitis**—pain elicited by deep palpation along the gluteal muscles.
- **Piriform Syndrome**—pain by deep palpation of the piriformis muscle in the lateral upper quadrant of the buttock area, or, more specifically, by rectal wall examination.
- **Meralgia Paresthetica**—area of intense dysesthesia, often with numbness on careful pinprick examination in a patch of skin on the anterior thigh.

**Knee**

- Pain surrounding the knee is frequently attributed to osteoarthritis of the knee, especially in the elderly. However, pain in the knee area can be referred from the hip joint, the lumbar spine, and (rarely) from the foot in patients with significant pes planus and tightened calf muscles.
- **Pes-Anserine Bursitis**—pain elicited by gentle palpation approximately 1 cm below the joint line on the medial aspect of the leg.
- **Prepatellar Bursitis**—area of swelling immediately anterior to the patella.

**Elbow**

- **Olecranon Bursitis**—swelling over the olecranon process.
- **Lateral and Medial Epicondylitis**—pain reproduced by palpation of the specific area surrounding the epicondyle; in lateral epicondylitis, pain can be elicited by resisted, active extension of the middle finger.

**Hand**

- **Carpal Tunnel Syndrome**—reproduction of dysesthesias in the appropriate distribution by pressure over the carpal canal; Tinel’s sign; Phalen’s maneuver.
- **De Quervain’s Tenosynovitis**—pain elicited over the radial styloid by resisted abduction of the thumb, or with passive movement of the fist in an ulnar direction while patient places the thumb inside a closed fist.

**Shoulder**

- Acute shoulder pain in the absence of trauma is most frequently caused by rotator cuff disease (periartritis) rather than true shoulder joint disease.
- Shoulder pain not reproduced by shoulder motion suggests referred pain.
- Sharp pain with abduction or full arm motion is termed impingement.
- **Supraspinatus Tendonitis**—pain referred to the deltoid and upper arm region when patient elevates an arm with the thumb pointed toward the ground and the examiner applies downward pressure.
- **Acromioclavicular Osteoarthritis**—pain when the patient reaches across his or her body in the anterior plane or reaches far behind his or her back.
Lumbar Canal Stenosis—pseudoclaudication of calves or thighs that is reduced when the patient bends forward. It can mimic vascular ischemia.

FIBROMYALGIA

Generalized pain syndrome with no objective neurologic or inflammatory markers abnormalities; the presence of multiple discrete myofascial tender points on examination is characteristic, but not required for diagnosis.

POLYMYALGIA RHEUMATICA

Diagnosis suggested by the presence of bilateral periarthritis in patients older than 60, without an obvious inciting event.

SUGGESTED READINGS


**Question 1**

Sweet's syndrome is often associated with which of the following?

a) Adenocarcinoma of the breast
b) Adenocarcinoma of the gastrointestinal tract
c) Pulmonary disease
d) Myocarditis
e) Leukemia

**Answer and Discussion**

The answer is e.

**Objective:** Identify the association between Sweet’s syndrome and malignancy.

Sweet's syndrome (a.k.a. febrile neutropenic dermatosis) is a rare autoimmune condition with hallmark features of high fever, tender and erythematous skin lesions (can be papules, nodules, or plaques), and the biopsy showing a neutrophilic infiltration. Peripheral neutrophilia may also be seen at times, but is not necessary for diagnosis. It is most commonly seen in female between the ages of 30 and 60 (although it has been seen in younger patients as well). The pathophysiology of Sweet's syndrome is not completely understood, but it has been associated with some medications (most commonly the granulocyte colony–stimulating factor, but case reports with antihypertensives, antineoplastic, antibiotics, and antiepileptics, among others have been also reported), acute viral gastrointestinal or upper respiratory infections, inflammatory bowel disease, pregnancy, and some malignancies. Sweet's syndrome is strongly associated with myelocytic or myelomonocytic leukemia. The cornerstone of therapy includes either topical, intralesional, or systemic corticosteroids.

**Question 2**

A 56-year-old man presents to the emergency department with a 2-day history of increasing right wrist pain and associated swelling. He denies a history of prior episodes of arthritis or any antecedent trauma. His only medication is a diuretic for the treatment of hypertension. He was recently hospitalized for a transurethral prostate resection for benign prostatic hypertrophy. His older brother has been diagnosed with gout. The most useful diagnostic tests for this patient include

a) Radiography of the wrist
b) Serum urate level
c) Complete blood cell count with differential and erythrocyte sedimentation rate
d) b and c
e) None is particularly useful

**Answer and Discussion**

The answer is e.

**Objective:** Identify the appropriate diagnostic maneuvers for an acute monoarticular arthritis.

The major differential diagnosis for an acute monoarticular arthritis includes acute crystal disease and infection. The synovial fluid analysis with crystal analysis, gram stain, and culture are crucial for differentiating these two conditions, as their treatment is divergent. Both will have an inflammatory pattern with high polymorphonuclear leukocytes on the synovial fluid analysis; however, the acute crystal disease should have either negatively birefringent crystals (urate) or rhomboid weakly positively birefringent crystal (CPPD) on analysis. Diagnosing acute septic arthritis necessitates gram stain and culture. Radiograph of the wrist is often non-diagnostic. Elevated serum urate levels are associated with gout, but as a diagnostic test for an acute gouty arthritis, it lacks both sensitivity and specificity. Complete blood counts and inflammatory markers are nonspecific for either of these conditions.

**Question 3**

A 26-year-old African American woman presents with a chief complaint of foot pain. Examination reveals ankle joint arthritis. She is afebrile and otherwise symptom free. She has a documented history of sickle cell anemia. The synovial fluid reveals a white blood cell count of 18,000/mm³, with 86% neutrophils. No crystals are seen. She is treated with a broad-spectrum antibiotic but experiences only minimal improvement after 3 days. Synovial cultures after 72 hours are negative. The presumptive diagnosis is

a) Gout
b) Salmonella arthritis
c) Avascular necrosis
d) Gonococcal arthritis
e) Reactive arthritis

**Answer and Discussion**

The answer is d.

**Objective:** Identify the diagnostic limitations of acute gonococcal arthritis.

Seventy-two hours is not always sufficient time to observe a dramatic response to antibiotics. Whereas salmonella or
other routine bacterial infections are expected to be recognized in bacterial cultures, gonococcus is often not isolated from the joint fluid. Gout is more common in sickle cell patients, but the diagnosis of gout should not be made in this setting in the absence of visualized crystals. Avascular necrosis is commonly associated with sickle cell anemia, but does not elicit an inflammatory synovial fluid response.

**Question 4**

A 32-year-old man reports pain in the joints and dysuria. The right fourth toe is diffusely swollen, and the right ankle and left knee are warm, with pain on range of motion. The left eye is red. Urinalysis shows 25 to 30 white blood cells/hpf and 1 to 2 red blood cells/hpf. Urine culture and urethral swab for gonococcal infection are both negative. What is the diagnosis?

a) Acute gout  
b) Adult-onset Still’s disease  
c) Reactive arthritis (a.k.a. Reiter’s syndrome)  
d) Polymyalgia rheumatica  
e) Acute rheumatic fever

**Answer and Discussion**

The answer is c.

**Objective:** Identify the clinical manifestations of acute reactive arthritis (a.k.a. Reiter’s syndrome).

The diffusely swollen toe likely represents a sausage digit, suggesting that the illness is likely to be a spondyloarthropathy. The triad of arthritis, conjunctivitis, and sterile urethritis is diagnostic of reactive arthritis (a.k.a. Reiter’s syndrome). The treating physicians wisely did appropriate cultures to rule out a disseminated gonococcal infection, which can also cause arthritis, urethritis, and conjunctivitis. Reactive arthritis is classically a post-infectious complication, most commonly after acute infectious gastroenteritis or colitis.

**Question 5**

A 67-year-old man complains of gradually worsening knee pain for 5 years. He now can walk only 50 m before stopping, due to the pain. Morning stiffness is 20 minutes. The right knee is cool with moderate crepitus, a small effusion, and range of motion from 5 to 90 degrees. On weight bearing, he has a moderate varus deformity. What is your plan?

a) Check baseline hepatic transaminases and start methotrexate  
b) Administer a trial of prednisone 20 mg/day for 1 week  
c) Check erythrocyte sedimentation rate and serum rheumatoid factor  
d) Arthrocentesis to rule out gout  
e) Order radiographs and refer to orthopedics

**Answer and Discussion**

The answer is e.

**Objective:** Identify the appropriate workup and management for osteoarthritis.

The history and examination suggest a gradual deterioration of the knee without the signs and symptoms of an inflammatory process. The typical history and physical examination are seen, notable for gradually worsening of knee pain, minimal morning stiffness, non-inflammatory joint examination, with crepitus, varus deformity on weight bearing, and limited range of motion. This is sufficient to make a diagnosis of osteoarthritis (OA). No further diagnostic workup is necessary given the chronicity of a monoarticular arthritis makes an acute inflammatory arthropathy, such as gout or RA, unlikely. Because the patient can only walk 50 m at a time and has a marked loss of the knee range of motion, one can conclude that the OA is rather advanced and the quality of life significantly diminished. OA is a progressive condition, and while systemic anti-inflammatories and intra-articular corticosteroids may be helpful initially, surgery is probably inevitable. It would be reasonable to proceed with the orthopedic consultation.

**Question 6**

A 35-year-old woman is admitted for dyspnea. On examination, she has decreased breath sounds at the left lung base, and synovial thickening in her metacarpal phalanges, proximal interphalangeals, wrists, and ankles. The olecranon bursa is diffusely swollen with embedded nodules. Her laboratory results are hemoglobin 11.2 g/dL, platelets $545 \times 10^9$/L, erythrocyte sedimentation rate 102 mm/hr C-reactive protein 7.4, antinuclear antibodies + 1:160, and rheumatoid factor 168 IU/mL (normal 0 to 20). A chest radiograph shows left pleural effusion. The thoracentesis reveals an exudative fluid, with pH 7.38, and glucose 24 mg/dL. What is the most likely diagnosis?

a) Systemic lupus erythematosus  
b) Bacterial endocarditis with empyema  
c) Adult-onset Still’s disease  
d) Lyme carditis  
e) Rheumatoid arthritis

**Answer and Discussion**

The answer is e.

**Objective:** Identify the extra-articular manifestations of rheumatoid arthritis.

The joint examination suggests a polyarticular inflammatory arthritis. The swollen olecranon bursa with embedded nodules is typical of rheumatoid arthritis (RA). Gout can cause olecranon bursitis with embedded tophi, but polyarticular tophaceous gout would be uncommon in a 35-year-old woman. Evidence suggests an acute phase response, further suggesting the presence of a systemic inflammatory disease. Patients with seropositive RA are at risk for extra-articular manifestations of the disease, including rheumatoid nodules and pleuropericarditis. A positive antinuclear antibody test is not unusual in RA and does not, by itself, suggest the presence of lupus. The exudative pleural effusion with a low glucose is typical of RA. Although bacterial endocarditis can present as a systemic inflammatory illness with arthritis and a positive rheumatoid factor, the normal pH of the pleural fluid suggests that the low glucose is not caused by an empyema.
Question 7

A 58-year-old diabetic woman reports pain with the use of the hands. Examination reveals bony enlargement of the metacarpophalangeal (MCP) joints but no synovial thickening. Laboratory evaluation reveals an erythrocyte sedimentation rate of 22 mm/hour. Radiographs reveal joint space narrowing at the MCP and proximal interphalangeal joints, with osteophytes on the radial aspect of the metacarpal heads. Patient is also noted to have elevated hepatic transaminases on labs. What is the most likely diagnosis?

a) Primary osteoarthritis  
b) Hemochromatosis  
c) Rheumatoid arthritis  
d) Hepatitis C with cryoglobulinemia  
e) Sarcoidosis

Answer and Discussion

The answer is b.

Objective: Identify secondary osteoarthritis secondary to hemochromatosis.

The physical examination and radiographs suggest osteoarthritis of the MCP joints, where cartilage loss from aging alone would be unusual. Typically, patients suffering from primary osteoarthritis with MCP and PIP involvement have other joint involvement as well. The radiographic findings are typical of hemochromatosis. The diabetes mellitus and elevated transaminases may be other manifestations of hemochromatosis.

Question 8

A 28-year-old woman presents with a 3-month history of fatigue; patchy hair loss; Raynaud’s phenomenon; and joint stiffness, pain, and swelling in the small joints of the hands, wrists, elbows, and knees. Your examination reveals normal vital signs, several shallow oral ulcers, frontal hair loss, and synovitis at the proximal interphalangeals, metacarpal phalangeals, and wrist joints. The most important test to obtain at this point is

a) Anti–double-stranded DNA antibodies  
b) Anti–single-stranded DNA antibodies  
c) Anti-Smith antibody  
d) Microscopic examination of the urinalysis  
e) Rheumatoid factor

Answer and Discussion

The answer is d.

Objective: Identify the urgent workup in a patient with acute inflammatory arthropathy.

This patient has nonspecific symptoms with Raynaud’s phenomenon, inflammatory arthropathy, alopecia, and oral ulcers. This is concerning for an acute systemic vasculitis. Diagnosing the condition, while important, will not change the management acutely. The most important test would involve looking for acute glomerulonephritis, which would necessitate urgent admission and immunosuppression to preserve the renal function.

Question 9

A 48-year-old man has been followed for gradually progressive skin thickening, which began in the hands and spread centrally to now extend to the upper arms, trunk, and face. He has been maintained on calcium channel blockers for Raynaud’s phenomenon, although his borderline low blood pressure has not allowed optimal dosing of the medicine for the vasospasm. He presents for a routine visit with increasing fatigue, some exertional shortness of breath, and a blood pressure of 160/100 mmHg. Your first action is

a) Arrange for pulmonary function testing to be done  
b) Increase the calcium channel blocker  
c) Order complete blood count (CBC) with peripheral smear and serum creatinine, and institute treatment with an angiotensin-converting enzyme inhibitor  
d) Order CBC with peripheral smear and serum creatinine, and institute treatment with D-penicillamine

Answer and Discussion

The answer is c.

Objective: Identify the management of scleroderma renal crisis.

This is scleroderma renal crisis, a true medical emergency. Patient has evidence of underlying systemic sclerosis, with skin thickening and Raynaud’s phenomenon. Scleroderma renal crisis is evidenced by the hypertension and progressively worsening renal function. Symptoms often include exertional dyspnea and worsening fatigue. Management of scleroderma renal crisis is centered around timely administration of an angiotensin-converting enzyme inhibitor (ACEI).

Question 10

Measures of lupus disease activity include all but

a) Anti–double-stranded DNA antibody levels  
b) Antinuclear antibody levels  
c) C3 (third component of complement)  
d) C4 (fourth component of complement)

Answer and Discussion

The answer is b.

Objective: Identify the role of laboratory tests in systemic lupus erythematosus (SLE).

Antibody testing is a large part of both the diagnosis and the prognosis of systemic lupus. Antinuclear antibody is a highly sensitive test for the diagnosis of SLE. The antinuclear antibody, however, does not reliably fluctuate with disease activity. Anti–double-stranded DNA antibody level is both a highly sensitive test for the diagnosis of SLE and also directly related to disease activity. SLE is a complement deposition disease, and C3 and C4 are inversely related to the disease activity of SLE.
CASE PRESENTATION
FOR QUESTIONS 11 TO 14

A 39-year-old woman presents to your office with concerns that she may have systemic lupus erythematosus (SLE) because her younger sister has been recently diagnosed with the condition by another physician. Your patient describes fatigue, hair loss in the comb but no patchy “bald spots,” a weight gain of 20 lb in the past 6 months, and achy joints and muscles. She feels weak and reports shortness of breath with minimal exertion (after climbing one flight of stairs). Her past medical history reveals Hashimoto’s thyroiditis diagnosed 6 years ago, and she has been on thyroxine since then, although she has not had follow-up for that condition in more than a year. She also has hypercholesterolemia and takes pravastatin. Her social history reveals cigarette smoking, one pack per day, which she explains helps her defray the stress of her job (she works full time in a family-owned restaurant as the business manager, shopper, and part-time cook). The family history is notable for her father having committed suicide after a long struggle with depression. Her mother has thyroid disease and rheumatoid arthritis; her sister has recently diagnosed SLE, and her twin teenage sons are healthy, but have recently been on a brief detention from school after being caught drinking alcohol on the school premises. On review of systems, she denies Raynaud’s phenomenon, hematuria, or pleurisy, but reports occasional painful mouth ulcers, dry mouth and dry eyes, trouble sleeping, and irregular and heavy menses.

Your examination reveals a blood pressure of 135/85 mmHg, a regular pulse of 90 beats/minute, and no fever. Weight is 100 kg. Skin examination shows mild eczema on the hands, with dry skin. The oral mucosa and hair density on the scalp both appear unremarkable. The eyes are moist, and Schirmer’s test documents 14 mm wetting in both eyes. No enlargement of the thyroid, cervical lymph nodes, or major salivary glands is present. The chest and abdominal examinations are normal. The musculoskeletal examination reveals full strength in the distal muscle groups, but “breakaway” weakness proximally, with the patient complaining of soreness in the muscles on manual resistive testing. Tenderness is noted on palpation of the proximal interphalangeals, metacarpal phalangeals, and wrist joints, without distinct synovitis. The articular range of motion is normal throughout, with the patient stating that the shoulders, neck, and hips feel achy during these maneuvers. The patient has tenderness to soft tissue palpation at 12 tender points.

**Question 11**
Which of the following statements is true?

a) Stress may be playing a significant role in this patient’s presenting complaints.

b) A positive antinuclear antibody test will help establish a diagnosis of system lupus erythematosus in this patient.

c) Antibodies to SSA (Ro) and SSB (La) are likely to be present.

d) A normal creatine phosphokinase test would rule out statin-related myopathy.

**Answer and Discussion**

The answer is a.

**Objective: Differentiate historical and physical examination findings of SLE and fibromyalgia.**

This patient presents, as many do, with nonspecific complaints and few objective findings. Even the manual resistive testing results are subjective to a degree because they depend on the patient effort, which is determined in part by patient pain. The physician must consider a differential diagnosis that includes anemia (from heavy menses), hypothyroidism, statin-induced myopathy (which may occur with a normal creatine phosphokinase test), and fibromyalgia (as suggested by the poor sleep, tender points, and stressful family/social situation). Other etiologies to consider include depression, smoking-related pulmonary disease, idiopathic inflammatory myopathies, and other disorders, the workup for which will be guided by the first battery of test results.

**Question 12**

The least useful test on this visit would be

a) Thyroid-stimulating hormone

b) Creatine phosphokinase

c) Complete blood count

d) Antinuclear antibody

**Answer and Discussion**

The answer is d.

**Objective: Identify the role of laboratory tests in diagnosing systemic lupus erythematosus (SLE).**

Although the patient is naturally concerned about SLE, she does not display any objective findings that would suggest this illness. An antinuclear antibody (ANA) test will not be helpful at this time because the patient might well have a positive ANA related to her Hashimoto’s thyroiditis and as a relative of someone with SLE. The diagnosis of SLE is made based on the combination of laboratory work and history and physical examination (PE) findings. With the lack of historical and PE findings, the patient is more likely to have a false-positive elevation of anti-nuclear antibody than a real elevation of anti-nuclear antibody associated with SLE. Likewise, with the lack of objective findings, SSA and SSB autoantibodies are unlikely to be positive.

**Question 13**

A treatment plan at the end of the first visit (before laboratory data are available) would reasonably include which of the following?

a) Addition of prednisone, 5 to 10 mg/day

b) Discontinuation of pravastatin

c) Decrease in thyroxine dose

d) Addition of hydroxychloroquine, 200 mg twice a day

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**Answer and Discussion**
The answer is b.

**Objective: Manage nonspecific complaints associated with myalgias.**

Treating a patient with multiple nonspecific complaints requires a graded approach with frequent follow-up to gauge the effectiveness of interventions. On the initial visit, counseling for stress reduction, smoking cessation, and weight loss would be in order. A pravastatin “drug holiday” would determine whether the myalgias and weakness are related to a statin side effect. After these interventions, one would consider additional testing or medications. There is no role for decreasing the thyroxine dosing without an objective evidence of hyperthyroidism. There is no immediate indication for corticosteroids or hydroxychloroquine as well.

**Question 14**

Symptoms and signs that should lead to consideration of an underlying systemic vasculitis include

a) Mononeuritis multiplex
b) Fever of unknown origin
c) Digital ischemia
d) Red blood cell casts in the urine
e) All of the above

**Answer and Discussion**
The answer is e.

**Objective: Identify common clinical features of systemic vasculitis.**

The diagnosis of vasculitis begins with a clinical suspicion. There are relatively few findings of high diagnostic specificity for systemic vasculitis, but suspicion should mount in the presence of presumptive signs or “red flags” for vasculitis. These include fever of unknown origin with constitutional symptoms; unexplained multisystem organ disease; unexplained inflammatory arthritis; unexplained myalgias; a suspicious rash, in particular palpable purpura; peripheral neuropathies, especially mononeuritis multiplex; unexplained end-organ ischemia, including cardiac, central nervous system, and gastrointestinal; and glomerulonephritis. Although none of these findings is specific for systemic vasculitis, the presence of any one or more should lead to an increasing suspicion of the disease.

**Question 15**

A 50-year-old man was admitted with a 3-month history of fever, weight loss, abdominal pain, and hypertension. A detailed workup for fever of unknown origin was unrevealing. Pertinent physical findings included a blood pressure of 220/120 mmHg, livedo reticularis on the legs, foot drop on the left, and absent pin-prick sensation in the lower legs. Laboratory study results included an erythrocyte sedimentation rate of 100 mm/hour, a creatinine level 2.2 mg/dL, microscopic hematuria, and an aspartate transaminase level twice the upper limit of normal.

Polyarteritis nodosa is suspected. After consideration of the diagnostic yield and risks, the logical next step would be

a) Skin biopsy
b) Percutaneous renal biopsy to demonstrate vasculitis of extraglomerular vessels
c) Abdominal angiography
d) Sural nerve biopsy

**Answer and Discussion**
The answer is d.

**Objective: Identify the diagnostic workup for polyarteritis nodosa.**

This patient presents with a clinical picture highly suspicious for systemic vasculitis, in particular, polyarteritis nodosa (PAN). Each diagnostic test outlined in the question should be considered in terms of sensitivity, specificity, and risk. A skin biopsy is sensitive but nonspecific because vasculitis of the skin can be caused by so many different conditions. On occasion, a nodular subcutaneous lesion may have characteristic features. Palpable purpura is less specific, and leukocytoclastic vasculitis may occur in many conditions. Percutaneous renal biopsy in this setting is insensitive for demonstrating vasculitis of the extraglomerular vessels and may be risky because PAN can cause microaneurysm formation. Abdominal angiography has increased sensitivity, but in the presence of severe hypertension and azotemia, it carries unacceptable risks. The sural nerve biopsy, although somewhat morbid and invasive, has an increasing diagnostic yield (>60%), particularly in the presence of objective neurologic signs and symptoms.
The differential diagnosis for the rash shown includes:

- a) Drug-associated vasculitis
- b) Vasculitis with malignancy
- c) Henoch-Schönlein purpura
- d) Subacute bacterial endocarditis
- e) a and b
- f) All of the above

**Answer and Discussion**

The answer is f.

**Objective:** Identify the differential diagnosis for a palpable purpura.

The rash shown is a palpable purpura. It is highly specific for small-vessel cutaneous vasculitis but is unrevealing of an underlying nosologic diagnosis. Drug-associated vasculitis is an extremely common cause of small-vessel vasculitis. Vasculitis associated with malignancies is most frequently found in the setting of an underlying lymphoproliferative disease. A small-vessel vasculitis such as this would be characteristic. Henoch-Schönlein purpura is characterized not only by such a rash but also by the presence of abdominal pain and glomerulonephritis. It is most frequently seen in children but may also be seen in adults. Subacute bacterial endocarditis has a variety of extracardiac complications, the majority of which are mediated by immune complexes. A small-vessel vasculitis would not be unusual in subacute bacterial endocarditis, although it is rare for this to be the dominant and presenting finding of the disorder. Many other conditions can be seen with this type of rash, including a variety of connective tissue diseases (e.g., rheumatoid arthritis, systemic lupus erythematosus), other types of infections, cryoglobulinemia secondary to hepatitis C virus infection, and a variety of miscellaneous systemic diseases.

**Question 17**

The following is true about the antineutrophil cytoplasmic antibody (ANCA) test:

- a) cANCA representing antibodies to PR-3 is highly correlated with a diagnosis of Wegener’s granulomatosis (WG)
- b) pANCA by immunofluorescence is sufficient for a diagnosis of WG or microscopic polyangiitis
- c) A rise in ANCA titers alone should prompt an escalation of immunosuppressive therapy
- d) a and b
- e) a, b, and c

**Answer and Discussion**

The answer is a.

**Objective:** Identify the role of ANCA testing in the diagnosis and prognosis of systemic vasculitis.

ANCA testing has been a step forward in the diagnostic process for certain forms of systemic vasculitis. The test is generally performed by immunofluorescence, but should also be confirmed by antigen-specific assays. In the majority of cases, an immunofluorescent pattern of cANCA is associated with antibodies to the neutrophil enzyme PR-3. It is highly correlated with the diagnosis of WG, being more than 80% sensitive and more than 95% specific, in the presence of an active, untreated, and widespread disease. pANCA by immunofluorescence, however, is not only less sensitive for the diagnosis of WG (present in only a small percentage of cases) but also relatively nonspecific. The pANCA pattern can be mimicked by a variety of antibodies, including ANA. The antibodies of interest in the diagnosis of systemic vasculitis responsible for the pANCA pattern of immunofluorescence are those directed against myeloperoxidase, another neutrophil enzyme. ANCA test results by immunofluorescence should always be confirmed by an antigen-specific assay. Finally, although some studies have suggested that ANCA levels are higher in those patients with active disease, this is not useful at the level of the individual patient. ANCA titers alone are not useful to assess disease activity and should not be used as a justification for the modification of therapy. A clinical evaluation of end-organ damage is still the "gold standard" for determining modifications of therapy.

**Question 18**

Which of the following statements about cryoglobulinemic vasculitis is correct?

- a) The most common clinical finding is a vasculitic rash.
- b) If the cryoglobulin is composed only of a monoclonal immunoglobulin, it is generally associated with an underlying malignancy.
- c) The most common associated condition is an underlying infection with hepatitis B virus.
- d) a and b
- e) a, b, and c

**Answer and Discussion**

The answer is d.

**Objective:** Identify the clinical features of cryoglobulinemic vasculitis.

Cryoglobulinemia and cryoglobulinemic vasculitis result from immunoglobulins and other proteins that precipitate from serum at temperatures lower than 37°C. Cryoglobulins are characterized on the basis of their content as type I (monoclonal), type II (mixed or monoclonal), or type III (polyclonal). The vast majority of cases of mixed cryoglobulinemia are associated with an underlying hepatitis C virus infection. Patients with cryoglobulinemia from any underlying cause may have a variety of end-organ manifestations. A small-vessel vasculitis, most often manifesting as a palpable purpura, is the most frequent finding. Arthralgia and arthritis are also common. With considerable frequency, patients
also have glomerulonephritis, peripheral neuropathy, and a variety of other complications.

**Question 19**

A 56-year-old overweight woman with radiographic osteoarthritis of the right knee presents with the chief complaint of increasing, limiting knee pain, most notable when rising from a chair or toilet, while walking up stairs, and in bed at night. Examination reveals valgus deformity with walking, minimal cool-knee effusions, and tenderness to palpation (which mimics the pain) at the medial aspect of the joint, approximately 2 inches distal to the joint line. You suggest

a) Full-dose nonsteroidal anti-inflammatory drug trial (patient has been using over-the-counter preparations)
b) Quadriceps-focused strengthening regimen
c) Intra-articular steroid injection
d) Steroid injection of anserine bursa
e) a and b

**Answer and Discussion**

The answer is d.

**Objective: Identify anserine bursitis in a patient with osteoarthritis.**

The pes anserine bursitis should be treated. Patients with osteoarthritis of the knee have many causes of pain. Anserine bursitis is one of the most common nonarticular one. It is particularly common in overweight patients with valgus deformity. Pain is reproduced by local pressure. It often does not respond to nonsteroidal anti-inflammatory drugs but does respond to local injections. Osteoarthritis is not usually a cause of nocturnal pain in bed; however, patients with anserine bursitis get relief by relieving the pressure of their legs touching, by sleeping with a pillow between their knees.

**Question 20**

A 42-year-old woman, with a diagnosis of rheumatoid arthritis for 2 years (fairly well controlled on hydroxychloroquine, nabumetone, and 2.5 mg prednisone daily), 8 months after the birth of a healthy boy, presents for a routine visit complaining of increasing “pain all over.” She describes increase morning stiffness in her back, neck, and hands; trouble sleeping; and painful flares after physical exertion. The erythrocyte sedimentation rate is 22 mm/hour, and the rheumatoid factor is present in a high titer. Joint examination shows multiple tender, nonswollen joints; normal grip strength; bilateral trochanteric bursitis, gluteal tenderness, and costochondritis; and anserine bursitis. The course of action should be to

a) Increase prednisone for 10 days and then taper
b) Add methotrexate
c) Add a tricyclic plus physical therapy
d) b and c

e) Additional options that may be considered include:
a) Early-onset hip arthritis (limited internal rotation)
b) Multiple sclerosis
c) Lumbar disc herniation (decreased knee reflex, posterior quadriceps weakness)
d) Lateral cutaneous nerve syndrome
e) Trochanteric bursitis

**Answer and Discussion**

The answer is c.

**Objective: Understand the clinical features of lateral cutaneous nerve syndrome.**

Entrapment of the lateral cutaneous nerve is characterized by pain, dysesthesia, or hypesthesia at the lateral thigh. Repetitive exercises, particularly extending the hips while doing the splits, could be a factor in this woman. Tight clothing, obesity, and trauma have also been implicated in causing irritation to the lateral cutaneous nerve, particularly in its path adjacent to the anterosuperior iliac spine. Hip arthritis would be expected to demonstrate a limited internal rotation. The diagnosis of multiple sclerosis requires documentation of neurologic events over time at different sites of the neuraxis. Normal knee reflexes are less likely with a lumbar disc herniation, which can also affect quadriceps strength. Tenderness would be expected on physical examination in trochanteric bursitis.

**Question 22**

A 17-year-old woman reports aching in the groin area. She is athletic, jogs several miles a day, and is a member of a cheerleading team. She describes an abnormal sensation over the anterolateral thigh. On occasion, she has noticed an “electric jab”–type sensation on extending the knee and has curtailed her running. Her past medical history is noncontributory, and she feels well otherwise. You observed her gait to be normal when she entered the office. A normal range of movement is present on examination and reflexes in the lower extremities are symmetric. Tenderness is not elicited. What is the most likely diagnosis?

a) Early-onset hip arthritis (limited internal rotation)
b) Multiple sclerosis
c) Lumbar disc herniation (decreased knee reflex, posterior quadriceps weakness)
d) Lateral cutaneous nerve syndrome
e) Trochanteric bursitis

**Answer and Discussion**

The answer is d.

**Objective: Understand the clinical features of lateral cutaneous nerve syndrome.**

The patient has fibromyalgia. The diagnosis is most likely secondary fibromyalgia, perhaps precipitated by the stress of a newborn child in the house. The symptoms will not respond to intensified therapy for the rheumatoid arthritis. A detailed examination will likely reveal additional myofascial trigger points. Education is another key element of the therapy.

A 64-year-old diabetic woman is hospitalized with the diagnosis of myocardial infarction. During hospitalization, she undergoes coronary angiography and is discharged on the
sixth day. You see her in follow-up 8 weeks later, and she explains that she has right-side shoulder discomfort. She also reports some stiffness in the fingers of her right hand. She explains the pain has come on gradually and is not related to ambulation. The use of the upper extremity on her dominant left side is without pain. She explains that after her hospitalization, she felt low in her mood, and a psychiatrist told her that she was depressed. Physical examination reveals a significant reduction in both the active and passive range of motion of the right shoulder compared with the left side. Movement of the right shoulder is painful. Tenderness to palpation is also present. Plain radiographs of the shoulder are reported as normal. Which is the most likely cause of her shoulder pain?

a) Adhesive capsulitis
b) Impingement syndrome
c) Angina
d) Rotator cuff tear
e) Fibromyalgia

Answer and Discussion

The answer is a.

Objective: Understand the clinical features of adhesive capsulitis.

Adhesive capsulitis is characterized by a gradual onset of symptoms, with pain and progressive reduction in the active and passive range of motion. Patients often have a recent history of immobilization in a hospital bed. Diabetic patients are known to have an increased risk of capsulitis that is particularly resistant to treatment. Hypothyroidism and Parkinson’s disease are also associated with adhesive capsulitis. Patients with impingement syndrome usually have a good range of motion, and osteoarthritis would be seen on radiography. The examination in a rotator cuff tear would show a normal passive range of movement. Fibromyalgia is associated with depression, but this patient does not meet other criteria for this diagnosis. The tenderness to palpation in this patient is not consistent with angina.

Question 23

A 27-year-old man, a concert pianist, reports a gradually worsening back pain and stiffness, for 6 months. He describes the pain as being worst on waking and located in the lumbar and gluteal region. He recalls being awakened by the pain on a number of occasions, and he has arisen and stretched his back to relieve the discomfort. Taking a warm shower helps alleviate the stiffness, and sitting for prolonged periods exacerbates it. The Schober test demonstrates a separation of 3 cm. Which of the following is most compatible with this patient’s illness?

a) Occupation-related illness
b) Finding of an early diastolic murmur
c) Positive antinuclear antibody test
d) Disease moderately responsive to systemic glucocorticoids
e) Dry mouth and eyes

Answer and Discussion

The answer is b.

Objective: Understand the clinical features of ankylosing spondylitis.

The insidious onset, morning stiffness, and symptom duration of longer than 3 months suggest that the most likely cause of the man’s back pain is inflammatory. Limitation of the spinal movement demonstrated by the Schober test suggests the diagnosis of ankylosing spondylitis. Aortic insufficiency is an association, as are inflammatory bowel disease and iritis. A positive antinuclear antibody test is not a feature of the illness, although up to 90% of patients carry the HLA-B27 gene. Glucocorticoids have not been found to be helpful in the management of the disease. Sitting with a poor posture for prolonged periods may be implicated in the back pain, as could be suspected in a pianist, but it would not explain the morning stiffness. Dry mouth and eyes are features of Sjögren’s syndrome.

Question 24

A 45-year-old man has recently moved into the area and has been renovating his home. He reports severe pain over the right elbow and back of the forearm. Examination reveals pain to pressure over the wrist extensor muscles, 1 cm below the lateral epicondyle. Strength is preserved. Which of the following is the most likely cause of his pain?

a) Tennis elbow
b) Radial nerve entrapment
c) Olecranon bursitis
d) Ruptured biceps tendon
e) Golfer’s elbow

Answer and Discussion

The answer is a.

Objective: Understand the clinical features and examination findings of lateral epicondylitis.

Repetitive overuse of the forearm muscles can result in lateral epicondylitis or tennis elbow. The description given is most suggestive of this process. Golfer’s elbow is also associated with overuse of the forearm but involves the medial epicondyle. Ruptured biceps tendon results in weakness, and olecranon bursitis most often manifests with posterior elbow pain. Radial nerve entrapment is rare and, therefore, not the most likely cause of pain.

Question 25

A 52-year-old man reports bilateral ear pain. He describes no change in his hearing or any febrile episodes. His past medical history is notable for a history of episcleritis, and he has stiffness and pain in both upper extremities, which have been bothering him intermittently over the past 6 months. He had some epistaxis after taking ibuprofen for the stiffness and was advised to discontinue it by a pharmacist. On
examination, tenderness and swelling of the cartilaginous portion of the ears are present. You have to talk loudly to be understood, and you note that the patient’s voice is hoarse. What is the most appropriate initial management for this patient?

a) Start oral prednisone, 40 mg daily
b) Prescribe a mild topical corticosteroid to be applied to the ears twice daily
c) Prescribe a nasal decongestant for 2 weeks
d) Request antinuclear antibody studies
e) Restart ibuprofen

**Answer and Discussion**

The answer is a.

**Objective:** Understand the clinical features and examination findings of relapsing polychondritis.

This man has the typical features of relapsing polychondritis. Disease activity can be suppressed with oral glucocorticoids. Nonsteroidal anti-inflammatory drugs, topical steroids, and decongestants are unlikely to affect the disease course. Anemia of chronic disease and an elevated erythrocyte sedimentation rate can be seen. Although the rheumatoid factor and antinuclear antibody may be positive, they do not contribute to the diagnosis in this case.

**Question 26**

An 82-year-old white man with past medical history of hypertension, coronary artery disease, cerebrovascular accident, T12 compression fracture, and asthma presents with malaise; anorexia; hip and shoulder pain and stiffness; and an inability to rise from chair, walk, and care for himself. On further questioning, he reports a 3-month history of fatigue, weight loss, and bilateral shoulder and hip stiffness. He recalls feeling relief from his symptoms after self-administration of tapered corticosteroid doses taken during episodes of asthma exacerbation. On examination, he is afebrile, has limited range of motion of the hips and shoulders, and is unable to raise the right arm laterally above 30 degrees. Point tenderness at the subacromial bursa is noted. His examination is otherwise unremarkable. A brain CT shows no evidence of an intracranial hemorrhage or recent infarct. Laboratory tests indicate the following:

<table>
<thead>
<tr>
<th>Test</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Na⁺</td>
<td>135 mEq/dL</td>
</tr>
<tr>
<td>K⁺</td>
<td>4.1 mEq/dL</td>
</tr>
<tr>
<td>Blood urea nitrogen</td>
<td>21 mg/dL</td>
</tr>
<tr>
<td>Creatinine</td>
<td>1.1 mg/dL</td>
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<tr>
<td>HCO₃⁻</td>
<td>23 mEq/dL</td>
</tr>
<tr>
<td>White blood cells</td>
<td>5,300/mm³</td>
</tr>
<tr>
<td>Hemoglobin</td>
<td>10.0 g/dL</td>
</tr>
<tr>
<td>Platelets</td>
<td>389,000/μL</td>
</tr>
<tr>
<td>Westergren sedimentation rate</td>
<td>99 mm/hour</td>
</tr>
<tr>
<td>C-reactive protein</td>
<td>6.6 mg/L</td>
</tr>
<tr>
<td>Creatine phosphokinase</td>
<td>241 U/L</td>
</tr>
</tbody>
</table>

He receives prednisone (20 mg/day) and exhibits a dramatic subjective and objective improvement after 24 hours. Ten days after the initiation of prednisone, he has no further complaints, and his Westergren sedimentation rate and C-reactive protein levels have decreased to 22 mm/hour and 0.3 mg/L, respectively; his Hgb level has increased to 12.3 g/dL. The most likely cause of this patient’s musculoskeletal symptoms is

a) Inflammatory polymyositis
b) Fibromyalgia
c) Pseudo-osteoarthritis
d) Inclusion body myositis
e) Polymyalgia rheumatica

**Answer and Discussion**

The answer is e.

**Objective:** Diagnose and treat polymyalgia rheumatica.

Although this patient has several medical problems, note that the examiner is interested in the most likely cause of his musculoskeletal problems. Polymyalgia rheumatica is the leading diagnosis when an elderly patient presents with girdle pain and stiffness, increased acute-phase reactants, and anemia, especially when the symptoms improve with systemic glucocorticoids.

Polymyositis is less likely in the absence of an elevated creatine phosphokinase and presence of muscle pain. Fibromyalgia does not cause the laboratory abnormalities described in this case. Pseudo-osteoarthritis is a condition that describes the progression of calcium pyrophosphate dihydrate crystal deposition disease to joint degeneration. Multiple joints are usually involved, but the most commonly affected joints are the knees, followed by the wrists and metacarpophalangeal joints. Inclusion body myositis is an idiopathic inflammatory myopathy that presents with the insidious onset of weakness over several years. Symmetric proximal lower extremity weakness is usually the first sign. Myalgias are encountered in approximately 40% of cases.

**Question 27**

A 67-year-old woman presents to your office complaining of headache and double vision. For the past 2 days, she has had difficulty seeing clearly, and occasional double vision. This morning, she reports a dramatic decrease in her vision on the right. She has not felt well for 2 weeks, complaining of intermittent headaches, muscle aches, and pain in her hips, shoulders, and upper back. She admits to weight loss, although she states, “I know I am not eating as much as usual because my jaw hurts too much to chew my food!” She also notes that she cannot get the right temperature in her house, reporting that she is either too cold or too hot. Her past medical history is unremarkable, except for a hysterectomy, remotely. She has been taking acetaminophen for her muscle aches, without much relief. She is not on any prescription medications. She is married and lives with her...
husband. She does not drink or smoke. She has two children that are grown, without medical problems. On examination, her vital signs are: \( T = 38.2^\circ C; P = 87 \text{ beats/minute}; \text{ RR} = 20 \text{ breaths/minute}; \text{ and BP} = 122/75 \text{ mmHg}. \) HEENT examination shows that her extraocular muscles are grossly intact and her pupils are reactive to light. Funduscopic examination on the right is shown.

There is no pain on the palpation of the face. She has decreased range of motion of her neck. There is no jugular venous distention or adenopathy. There is a mild carotid bruit on the right. Lungs are clear, and the cardiac and abdominal examinations are normal. Pulses are diminished but symmetric throughout. There is a positive subclavian bruit on the left. The shoulders’ and hips’ active range of motion is limited due to pain. Basic laboratory studies are obtained in your office and are as follows:

- Sodium: 143 mEq/dL
- Potassium: 4.5 mEq/dL
- Chloride: 105 mEq/dL
- \( \text{CO}_2: 22 \text{ mEq/dL} \)
- Blood urea nitrogen: 13 mg/dL
- Serum creatinine: 0.7 mg/dL
- Leukocyte count: 5,600 \( \mu L \)
- Hemoglobin: 9.3 g/dL
- Hematocrit: 32%
- Platelets: 423,000 \( \mu L \)
- MCV: 83 fL

Which of the following is the most appropriate next step in the management of this patient?

a) Temporal artery biopsy  
b) Systemic glucocorticoids  
c) MRI of the brain  
d) Aspirin  
e) Packed erythrocyte transfusion

**Answer and Discussion**

**Objective:** Identify and treat giant cell arteritis with eye involvement.

This patient has giant cell arteritis (GCA). GCA is a systemic vasculitis that affects people over 60 years of age. GCA may present with the onset of sudden loss of visual acuity in one or both eyes and diplopia. Systemic symptoms such as headache, arthralgias, myalgias, fever, weight loss, anemia, and jaw claudication may be present. Glucocorticoid treatment should be instituted promptly once the diagnosis of GCA is strongly suspected, often even before it is confirmed. For patients in whom the diagnostic suspicion of GCA is high, especially those with recent or threatened vascular complications such as visual loss, therapy should be started immediately. A temporal artery biopsy should be obtained as soon as possible, but treatment should not be withheld while awaiting the performance or the results of the biopsy.

**Question 28**

A 48-year-old man presents with generalized weakness, oliguria, and hypertension. Six months ago, he developed a left-side Bell’s palsy. This was followed by a left-side foot drop 3 months ago. His physical examination reveals BP of 180/100 mmHg, pulse of 90 beats/minute, and RR of 20 breaths/minute. Examination of the HEENT reveals some maxillary sinus tenderness. The respiratory examination reveals some scattered harsh breath sounds. Neurologically, he is alert and oriented, with left-side Bell’s palsy and left-side foot drop. Labs are significant for Hgb of 10.9 g/dL, normal WBC, and normal platelet count. BUN is 40 mg/dL, and serum creatinine is 3.5 g/dL. Urine sediment shows evidence of proteinuria and red cell casts. CT of the brain is normal except for evidence of sinusitis. X-ray of the chest shows nodular opacities in both lungs. What is the most likely diagnosis?

a) Goodpasture’s syndrome  
b) Thrombotic thrombocytopenic purpura  
c) Granulomatosis with polyangiitis (GPA)  
d) Microscopic polyangiitis  
e) SLE with lupus nephritis

**Answer and Discussion**

**Objective:** Identify the common features of granulomatosis with polyangiitis (Wegener’s).

This patient’s clinical presentation has the of upper and lower respiratory tract and renal involvement consistent with granulomatosis with polyangiitis (Wegener’s). GPA is characterized by necrotizing granulomatous inflammation of the small-sized vessels in various organs. Although the three sites mentioned earlier are commonly affected,
A 65-year-old woman presents with a skin rash over her upper trunk and associated muscle weakness. The rash is worst over the neck, shoulders, and upper part of the chest. Physical examination reveals periorbital edema with a purplish scaly rash on the upper eyelids and also over the knuckles and proximal interphalangeal joints. She also has weakness in her shoulders and hips. This has been getting progressively worse over time. She also feels generally unwell. She has difficulty getting up from the chair without support and cannot raise her arms above shoulder level. Her laboratory tests show normal CBC, with elevated AST of 700 U/L and elevated CPK of 1,000 U/L. Muscle biopsy shows perivascular and interstitial inflammatory infiltrates with groups of muscle fiber degeneration and regeneration. Which of the following statements is not true about this condition?

a) This condition can be associated with an underlying malignancy in patients above the age of 40 years.
b) Treatment includes glucocorticoids and immunosuppression.
c) Subcutaneous calcium deposits may be seen in these patients.
d) Pulmonary involvement is not seen in this condition.
e) This disease may occur in children as well.

**Answer and Discussion**

The answer is e.

**Objective:** Identify common features of dermatomyositis.

This patient has dermatomyositis (DM). She has a characteristic distribution of the rash, muscle weakness with presence of Gottron’s papules on the knuckles, and a heliotrope rash on the upper eyelids. The Bohan and Peter classification includes five subsets of myositis: DM, polymyositis (PM), myositis associated with malignancy, childhood DM/PM, and myositis overlapping with other collagen vascular disorders. Approximately 25% of patients with DM have an underlying malignancy—the most common being ovarian, lung, pancreatic, stomach, colorectal cancer, and non-Hodgkin’s lymphoma. The myositis may follow the course of the malignancy or run its own independent course. Malignancy is more common in patients with DM above 40 years of age. Pulmonary disease in the form of interstitial pneumonitis occurs in DM and PM in approximately 15% to 63% of patients. DM may be part of the antisynthetase syndrome, which presents as interstitial lung disease (ILD), inflammatory muscle disease, fever, polyarthritis, Raynaud’s phenomenon, and thick cracked skin on the fingers (mechanic’s hands). Dermatomyositis-sine myositis, also known as amyopathic DM, is diagnosed in patients with a typical cutaneous disease in whom there is no evidence of muscle weakness and who repeatedly have normal serum enzyme levels. Immunosuppression with glucocorticoids with or without intravenous immunoglobulin (IVIG), tacrolimus, cyclosporin, cyclophosphamide, and azathioprine may be needed. Calcium deposits (calcinosis) in the skin or muscle is unusual in adults but may occur in approximately 40% of children or adolescents with DM. Calcinosis cutis presents as firm, yellow, or flesh-colored nodules, often over bony prominences. These nodules can extrude through the skin surface, and secondary infection may occur. DM is well described in children and adolescents.

**Question 30**

A 20-year-old man presents with complaints of low back pain and fatigue for 6 months. His symptoms are worse in the morning, with associated stiffness lasting 1.5 hours. His symptoms improve with exercise. He denies any trauma, radiation of the pain, and bladder or bowel symptoms. He has no pain in any other joints. On examination, there is tenderness over the lumbar spine and sacroiliac joints. On bending forward, he has restricted range of motion in the lumbar spine. X-rays of the lumbar spine and sacroiliac joints show evidence of spondillitis. The presence of HLA-B27 in this patient increases his risk for which of the following?

a) Chorioretinitis and posterior uveitis
b) Psoriasis
c) Celiac sprue
d) Aortitis and conduction system disease

**Answer and Discussion**

The answer is d.

**Objective:** Identify key features of ankylosing spondylitis.

This young gentleman has ankylosing spondylitis (AS). AS is an inflammatory disorder that belongs to the family of disorders referred to as spondyloarthropathies. It characteristically affects young men and predominantly involves the axial skeleton, although peripheral joints may be involved as well. Progressive inflammation of the entheses (sites of ligamentous attachment to bone) and ankylosis (fibrotic and bony) lead to transformation of the spine into a rigid structure with severe restriction of mobility (“bamboo spine”). AS shows a
marked correlation with the presence of HLA-B27 antigen (>90% of Caucasian patients with AS will be HLA-B27 positive). In this patient, HLA-B27 does not change the post-test probability of the disease because the pre-test probability is very high for AS. HLA-B27 testing per se should not generally be used for the diagnosis of spondyloarthopathies; only a minority of patients with HLA-B27 develop AS. HLA-B27 does not increase the risk for panuveitis in patients with AS; it is associated with iritis.

**Question 31**

A 48-year-old man presents with generalized weakness, oliguria, and hypertension. Six months ago, he developed left-side Bell’s palsy. This was followed by a left-side foot drop 3 months ago. His physical examination reveals a BP of 180/100 mmHg, pulse of 90 beats/minute, and RR of 20 breaths/minute. Examination of the HEENT reveals some scattered sinusal tenderness. Respiratory examination reveals some scattered harsh breath sounds. Neurologically, he is alert and oriented, with a left-side Bell’s palsy and left-side foot drop. Labs are significant for Hgb of 10.9 g/dL, normal WBC, and normal platelet count. BUN is 40 mg/dL, and serum creatinine is 3.5 g/dL. Urine sediment shows evidence of proteinuria and red cell casts. CT of the brain is normal except for evidence of sinusitis. X-ray of the chest shows nodular opacities in both lungs. A kidney biopsy is performed. Which of the following pathologic findings do you expect to find?

a) Membranoproliferative GN, diffuse immune deposits  
b) Crescentic GN, linear immune deposits  
c) Crescentic glomerulonephritis (GN), no immune deposits on immunofluorescence  
d) Microvascular thrombosis

**Answer and Discussion**

**Objective:** Identify the kidney biopsy pattern in granulomatosis with polyangiitis.

Renal involvement occurs in about 18% of the patients at the onset and 77% throughout the course of granulomatosis with polyangiitis (GPA). Left untreated, it directly or indirectly results in mortality in GPA. Once clinically detectable renal dysfunction sets in, it has a rapid downhill course if not appropriately treated. The histopathology of renal biopsy in GPA varies from a focal segmental necrotizing glomerulonephritis (GN) to crescentic GN, but classically without any evidence of immune deposits (pauci-immune) on immunofluorescence. The presence of immune deposits would favor an immune complex–mediated disease such as lupus nephritis. Linear deposits of immune complexes on the basement membrane due to an antibody to the noncollagenous domain of type IV collagen would be characteristic of anti-glomerular basement membrane syndrome. Microvascular thrombosis would be consistent with thrombotic thrombocytopenic purpura or another hypercoagulable state.

**Question 32**

A 70-year-old woman presents for mid-back pain. This pain started suddenly when she woke up 3 days ago. She denies any preceding trauma. She gives a history of right ankle fracture from missing a step when going downstairs in her apartment last year. On examination, she is a thin lady who is hemodynamically stable and weighs 115 lb. The examination is normal except for focal tenderness over the spine in the T10 region. An x-ray shows a wedge compression fracture of the T10 vertebra. Her laboratory tests are normal. A bone mineral density scan reveals a T score of –1.6 at the lumbar spine and –1.7 at the right hip. What should be the next course of treatment?

a) She has osteopenia; treat with vitamin D 800 units and calcium 1,200 mg/d.  
b) She has osteopenia; check vitamin D levels, treat with vitamin D 800 units and calcium 1,200 mg/d, and repeat BMD in 1 year.  
c) She has osteoporosis; treat with high-dose vitamin D (50,000 units weekly) and calcium (1,200 mg/d).  
d) She has osteoporosis; treat with bisphosphonates, vitamin D, and calcium.

**Answer and Discussion**

**Objective:** Diagnose and treat osteoporosis in a patient with a fragility fracture.

This elderly lady has presented with fractures involving her spine and previously her ankle. Osteoporosis is a clinically significant problem, especially in the elderly population. Osteoporosis is caused by an imbalance in the osteoclastic and osteoblastic activities in the bone, which is an extremely metabolically active tissue. Bone mineral density testing using dual x-ray absorptiometry (DEXA) is commonly used to diagnose osteoporosis. The T-score compares current bone mass with peak bone mass. According to the WHO definition, a T-score of <-1.0 is normal bone density, -1.0 to -2.5 is osteopenia, and >=-2.5 is osteoporosis. Based on this scoring system, this lady has osteopenia, but she should be diagnosed as having osteoporosis because she has a history of fragility fractures [fractures caused by trauma equivalent to that sustained as a result of a fall from standing height or less (a fracture from minimal or no trauma)]. Therefore, she should be treated with bisphosphonates, approximately 1,500 mg calcium a day, and approximately 600 to 800 IU of vitamin D, a day. The importance of exercise, diet, smoking cessation, and fall prevention cannot be overemphasized. Workup for secondary disorders may be necessary when indicated.

**Question 33**

A 40-year-old overweight woman presents to your office for right hip pain. The pain is worse with activity, especially climbing stairs. It started 3 months ago. She denies any trauma. She has difficulty sleeping on her right side due to
the pain. She has tried some nonsteroidal anti-inflammatory drugs (NSAIDs) that provided temporary relief. Upon asking about the exact location of the pain, she points to the upper lateral aspect of the thigh. Physical examination does not elicit pain on passive movement, and there is no limitation of motion at the right hip. Palpation over the painful site (upper lateral aspect of the thigh) elicits tenderness. No other tender points are elicited. What is the diagnosis, and what should be done next?

a) She has trochanteric bursitis; advise conservative management, local steroid injection, and limiting certain activities.
b) She has degenerative arthritis; continue NSAIDs.
c) She has meralgia paresthetica; advise surgical decompression of the entrapped nerve if symptoms persist more than 6 weeks.
d) She has fibromyalgia; treat with aerobic exercise and selective serotonin reuptake inhibitors (SSRIs).

**Answer and Discussion**

**The answer is a.**

**Objective: Diagnose and treat trochanteric bursitis.**

This clinical picture is highly consistent with trochanteric bursitis. Trochanteric bursitis is more common in obese women and presents as a deep aching pain on the lateral aspect of the hip that is made worse by exercise, often worse at night, and relieved by rest. Physical examination reveals tenderness over the greater trochanter of the femur. Rest, NSAIDs, local ultrasound, and physical therapy can help, but local steroid injection provides diagnostic information as well as therapeutic relief for symptoms. True hip pain, as would be seen with OA, is typically felt in the groin area. Meralgia paresthetica results from entrapment of the lateral femoral cutaneous nerve and is felt along the course of the nerve on the anterolateral part of the thigh; surgery is virtually never necessary. She does not fulfill criteria for fibromyalgia; fibromyalgia is not a regional pain syndrome.

**Question 34**

A 45-year-old woman with a history of polymyositis for the last 8 years presents with increasing difficulty climbing stairs for the last 3 to 4 months due to leg heaviness. She denies any muscle soreness. She otherwise feels well. She has no difficulty holding on to her footwear or gripping objects. She denies any shortness of breath as limiting her mobility. She has been on prednisone (60 mg/d initially, now 40 mg/d) since the onset of her illness. On examination, she is overweight, with a buffalo hump and striae over her abdomen. There is no muscle tenderness. Hip and shoulder joints have good range of motion. Motor examination reveals a power of 3/5 at the proximal muscles (shoulder and hip) and 5/5 distally. Reflexes and sensation are normal. Her laboratory tests show normal CBC, normal electrolytes, normal thyroid function, normal erythrocyte sedimentation rate and C-reactive protein, and normal CPK levels. What should be the next step in management?

a) Muscle biopsy
b) Electromyography
c) Taper steroids; refer to physical therapy
d) Increase the dose of steroids; see the patient back in 2 months

**Answer and Discussion**

**The answer is c.**

**Objective: Recognize steroid myopathy as a cause for muscle weakness, with prolonged steroid use.**

This patient has been on steroid therapy for a prolonged period of time. Steroid myopathy should always be suspected in patients on long-term steroid therapy. It also presents as proximal muscle weakness. Reflexes and sensation are characteristically normal. In this patient with polymyositis (PM), steroid myopathy should be diagnosed because she seems to be in clinical remission for polymyositis and has normal muscle enzymes, as inflammatory markers. Increasing the dose of steroids is not indicated because there is no clinical or laboratory evidence of worsening disease. Muscle biopsy typically shows type II fiber (type IIb) atrophy, but this is not needed in most cases where the diagnosis is clear. Aerobic and muscle strengthening exercises are helpful.

**Question 35**

A 20-year-old woman presents to you for knee pain. She started having right knee pain 6 months ago, and now she notices that the knee occasionally swells up. Her left knee and right ankle are also similarly affected intermittently. She has not had much back pain or problems with red painful eyes. Over the last year, she has had episodic bouts of loose stools, some containing blood. She states that she felt generally sick during those times and her joints also hurt the worst. The colonoscopy showed uniform involvement of the colonic mucosa with friable areas. On physical examination, she is a thin lady with a normal physical examination except some tenderness on passive and active movement of her right knee. There is also a small joint effusion. Which of the following statements is true about this joint disease process?

a) The joint problem is related to her GI tract pathology, and its activity parallels the GI disease activity.
b) The joint problem is not related to her GI tract pathology.
c) The joint problem is related to her GI tract pathology, but its course does not parallel the GI disease activity.
d) The joint disease and GI disease both respond to mesalamine therapy.

**Answer and Discussion**

**The answer is a.**

**Objective: Recognize enteropathic arthritis associated with inflammatory bowel disease.**

This young woman has probable ulcerative colitis. Peripheral arthritis occurs in 10% to 20% of patients with Crohn's disease.
disease or ulcerative colitis. It may even be the first symptom of inflammatory bowel disease (IBD). The pattern of arthritis may be migratory or additive. Knees, ankles, and feet are most commonly affected. Large effusions may occur in the knee. Deformities are rare, and erosive changes on x-rays are very unusual. The peripheral joint symptoms often parallel the bowel disease activity; surgical colectomy may result in permanent remission of the joint disease. The other skeletal involvement affecting the spine (axial arthropathy) occurs in about 10% of the patients, is more common in men, and runs a course independent of the bowel disease.

Question 36
A 40-year-old man known to be HIV positive (on HAART for 9 months) presents for right knee pain and swelling. His symptoms started a week ago and are now getting better. On questioning, he gives a history of a self-limiting, nonbloody diarrhea 3 weeks ago. Two weeks ago, his right eye was painful and red; it spontaneously resolved in 3 to 4 days. He denies any genital rash or scaling rash on his feet. On examination, the eye examination is normal. The right knee is slightly swollen. It is warm to touch and minimally tender on movement and palpation. Joint aspirate demonstrates 10,000 WBC with 80% neutrophils and no crystals. What is the diagnosis and management?

a) He has an opportunistic infection; treat with empiric antibiotics.
b) He has reactive arthritis; treatment with nonsteroidal anti-inflammatory drugs (NSAIDs); administer steroids if refractory.
c) He probably has gout; treat with colchicine.
d) He has acute articular syndrome; treat with NSAIDs.

Answer and Discussion
The answer is b.

Objective: Diagnose and treat reactive arthritis.

This man presents with a classic clinical picture of reactive arthritis (ReA). Reactive arthritis typically follows a gastrointestinal or genitourinary infection. It is more common in men (M:F = 9:1) and is associated with the HLA-B27 antigen (~80%). ReA clinically manifests as an asymmetric, additive, oligoarticular arthritis, more commonly involving the lower extremities. Heel pain may occur due to enthesopathy of the Achilles tendon. Uveitis occurs in 12% of cases. HIV infection is associated with ReA indirectly through other sexually transmitted diseases. ReA in patients with HIV tends to be more severe. The initial treatment is with NSAIDs; further immunosuppression with drugs such as sulfasalazine, methotrexate, or anti-TNF therapy may be warranted in resistant cases. This patient does not have gout because the joint fluid is negative for crystals. Acute articular syndrome is also seen in patients with HIV and usually causes acute joint and bone pain but is usually self-limiting and lasts for several days. Septic arthritis is unlikely given that he is clinically improving; the patient’s clinical picture is very consistent with ReA.

Question 37
A 42-year-old man presents for bilateral ankle pain and swelling. His symptoms started a month ago and have been getting steadily worse. There is an associated dry cough. He denies any fever or weight loss. He has not traveled recently. On physical examination, he is afebrile. A reddish-purple, tender, raised nodular rash is noted over the shins. His physical examination is otherwise unremarkable. His laboratory tests are normal. Chest x-ray shows bilateral hilar lymphadenopathy and an infiltrate in the right lower lobe. PPD is negative. A transbronchial lung biopsy shows epithelioid cells and noncaseating granulomas. Which of the following is true of this illness?

a) It is usually confined to the lungs and lymph nodes.
b) Glucocorticoids are the treatment of choice and usually produce rapid benefit.
c) It is more common in Caucasians.
d) An elevated ACE level is present in most cases and diagnostic of this condition.

Answer and Discussion
The answer is b.

Objective: Identify key features of sarcoidosis.

This patient most likely has sarcoidosis. Several clinical features of this disease are present: dry cough, erythema nodosum, bilateral hilar adenopathy, and the infiltrate on the CXR. Sarcoidosis is an inflammatory disorder of unknown etiology characterized by granulomatous involvement of various tissues. Tissue biopsy shows noncaseating epithelioid granulomas. Sarcoidosis can involve virtually any organ system, although the lungs are most classically involved (90% will have an abnormal CXR). Rheumatologic involvement may occur as arthritis (15%), uveitis (20%), or myositis (4%). Heel pain and ankle involvement are common. Acute arthritis can occur as a component of Lofgren’s syndrome (acute presentation of sarcoidosis characterized by erythema nodosum, hilar lymphadenopathy, fever, and polyarthritis). The prevalence in African Americans is much higher than in Caucasian Americans (8:1). Elevated ACE levels may be seen but may occur with other conditions such as active histoplasmosis, amyloidosis, diabetes, berylliosis, primary biliary cirrhosis, and hyperthyroidism. Glucocorticoids are used for severe lung disease, uveitis, hypercalcemia, cardiac involvement, neurosarcoidosis, or other severe organ involvement. Other immunosuppressants such as methotrexate or anti-TNF therapy have been used as steroid-sparing agents with variable efficacy. Histoplasmosis can mimic Lofgren’s syndrome and should be excluded, especially in the presence of a lung infiltrate (like this case).

Question 38
A 75-year-old Caucasian woman presents for neck and shoulder pain that started about 2 months ago. She has associated stiffness that is worst in the morning and lasts about 2 hours.
She denies any weakness in the shoulders. Recently, she has been noticing some pain and stiffness in her hips as well. She denies any headache, scalp tenderness, jaw claudication, or visual disturbances. Physical examination is unrevealing except for pain when she actively moves her shoulders. Her laboratory tests show: Hgb = 11 g/dL, normal WBC, and platelet count of 55,000/μL. Alkaline phosphatase is 150 U/L. Hepatic panel is otherwise normal. Erythrocyte sedimentation rate (ESR) is 70 mm/hour, and C-reactive protein (CRP) is elevated at 3.0 mg/L. What is the correct treatment for this condition?

a) This condition characteristically responds rapidly to low-dose steroids.  
b) This condition should be treated aggressively with high-dose prednisone.  
c) This is a benign condition that does not need monitoring and follow-up after it resolves.  
d) Treatment for 2 to 3 months is usually sufficient.

**Answer and Discussion**

**Objective: Diagnose and treat polymyalgia rheumatica.**

This patient's presentation is consistent with polymyalgia rheumatica (PMR). PMR is most commonly diagnosed in women older than 50 years of age presenting with pain and stiffness of the neck, shoulder, and pelvic girdle muscles lasting more than 4 weeks. It is often accompanied by systemic symptoms of malaise, weight loss, and low-grade fever. Acute-phase reactants such as ESR and CRP are elevated. This lady has no symptoms (i.e., jaw claudication, temporal headache, temporal artery tenderness, visual changes) of giant cell arteritis (GCA), which is believed to be the other end of the PMR spectrum and is characterized by vascular inflammation. PMR is exquisitely steroid sensitive and responds well to low-dose prednisone (10 to 20 mg/d). PMR warrants close clinical and laboratory monitoring with observation for symptoms of GCA. Treatment of PMR may be for 2 to 3 years (and even longer), with slow taper of prednisone to the lowest dose required to control inflammation. High-dose prednisone (60 mg/d or 1 mg/kg/d) is typically used for the treatment of GCA.

**Question 39**

A 34-year-old Hispanic man with history of scleroderma presents to the ER with malaise, weight loss, and diffuse pain with weakness for about 3 months. He has a history of hypertension, and his blood pressure on hydrochlorothiazide 12.5 mg/d and diltiazem 30 mg/d had been well controlled. On examination, the patient is alert, with temperature of 36.6°C, BP of 194/97 mmHg, pulse of 91 beats/minute, and oxygen saturation of 96% on room air. Both heart sounds are heard, with no murmurs or rubs, lungs are clear on auscultation, and funduscopic examination shows grade III retinopathy. He has thickened skin diffusely, telangiectasias on the face, tendon friction rubs, sclerodactyly, and difficulty forming a grip.

His laboratory workup shows proteinuria of 100 mg/dL, ANA positive, nucleolar, with a titer of 1:160, hemoglobin of 12.0 mg/dL, platelet count of 400,000/μL, CK of 257 U/L with MB of 4%, erythrocyte sedimentation rate of 11 mm/hour, BUN of 37 mg/dL, and Cr of 1.5 mg/dL.

What would be the best initial treatment for this patient?

a) Increase the dose of diltiazem and hydrochlorothiazide  
b) Start prednisone 40 mg/d  
c) Start captopril 6.25 mg PO TID and titrate up  
d) Start metoprolol 25 mg PO BID and titrate up as needed

**Answer and Discussion**

**Objective: Identify and treat scleroderma renal crisis.**

This patient has diffuse systemic sclerosis (SSc) and has developed renal crisis, which is characterized by the abrupt onset of hypertension, grade III or IV retinopathy, and rapid deterioration of renal function. Abnormal laboratory tests include proteinuria, microscopic hematuria, and elevated creatinine level. In severe cases, patients may develop thrombocytopenia and anemia secondary to a microangiopathic process.

The use of high-dose glucocorticoids increases the risk of renal crisis. The use of angiotensin-converting enzyme inhibitors has improved the outcome of renal crisis, and 1-year survival has increased from 15% to 76%. It is believed that blockade of angiotensin is the most effective way to manage this complication. The need for dialysis in this setting may be reversible. Other antihypertensives are less effective in this condition.

**Question 40**

An 89-year-old white woman is having pain and stiffness in the neck and shoulders, with fatigue for 2 months. The symptoms started acutely and are gradually worsening. She has pain at night with difficulty arising. She has difficulty with dressing herself in the morning. She denies any night sweats, significant weight loss, loss of appetite, and headaches. On examination, she is alert with a temperature of 36.6°C, pulse of 80 beats/minute, and blood pressure of 130/80 mmHg. She has painful lateral rotation of neck and painful abduction of shoulders. She has no objective weakness or joint swelling. Her blood work shows erythrocyte sedimentation rate of 83 mm/hour, C-reactive protein of 9.3 mg/L, hematocrit of 37%, platelet count of 560,000/μL, and CPK of 450 U/L (normal). Colonoscopy done 6 months ago was normal. She is up to date on her mammogram, Pap test, and routine screening exams. What is the next step in management?

a) Get x-ray of cervical spine  
b) Start on prednisone 20 mg/d  
c) Start on prednisone 60 mg/d  
d) Start on nonsteroidal anti-inflammatory medications
Answer and Discussion

The answer is b.

Objective: Diagnose and treat polymyalgia rheumatica.

This patient most likely has polymyalgia rheumatica (PMR). It is a symptom complex characterized by pain and stiffness of at least 4 weeks duration, in the muscles of the neck, shoulder, and pelvic girdle. The myalgias are sometimes combined with symptoms of systemic inflammation, like malaise, weight loss, and night sweats. Laboratory abnormalities include an elevated sedimentation rate, elevated C-reactive protein, and anemia. There is no pathognomonic test for PMR, and it is critical to consider an underlying infection or occult malignancy.

PMR is usually exquisitely sensitive to glucocorticoid therapy. Most patients show a dramatic improvement in their symptoms when treated with prednisone 20 mg/d or even a lower dose. Occasionally, patients may need higher doses of prednisone, but this should prompt vigilance for an alternative disease. Dose adjustment should be based mainly on clinical symptoms and not exclusively on laboratory abnormalities.

Objective: Diagnose patellofemoral pain syndrome.

This patient has patellofemoral pain syndrome (chondromalacia patellae), which occurs in young age groups and often involves both knees. Patients have pain and crepitus in the patellar region that is aggravated by overactivity involving knee flexion, particularly climbing or going down the stairs. On examination, she has small effusions in both knees and pain with patellar movements. What is the most likely diagnosis?

a) Patellar tendonitis
b) Osgood-Schlatter syndrome
c) Prepatellar bursitis
d) Chondromalacia patellae

Answer and Discussion

The answer is d.

Objective: Identify the appropriate prophylactic regimen in a patient receiving high-dose steroids and cytotoxic agents.

The combination of glucocorticoids and cytotoxic drugs results in lymphocytopenia, which in turn is a risk factor for Pneumocystis jiroveci pneumonia (PCP). The incidence of PCP in GPA is reported as 6%. Hence, all patients with GPA who are not allergic to sulfas and are receiving glucocorticoids in combination with a cytotoxic therapy should receive TMP–SMX (three times weekly) as prophylaxis. For patients who are allergic to TMP–SMX, alternative regimens include aerosolized pentamidine, atovaquone, or dapsone alone or in combination with pyrimethamine.

One of the major side effects of corticosteroid (CS) therapy is osteoporosis and increased fracture risk. CS therapy increases bone resorption and decreases bone formation. It enhances the apoptosis of osteoblasts and increases the survival of osteoclasts. The cumulative steroid dose is the primary predictor of bone loss. Bisphosphonate therapy along with calcium and vitamin D is recommended for the prevention of osteoporosis if a patient is anticipated to take CS for more than 3 months. However, bisphosphonate therapy is not recommended for use in patients with Clcr < 35 mL/min.
Since this patient has an elevated creatinine, only calcium and vitamin D should be used for osteoporosis prevention.

**Question 43**

A 26-year-old woman with a history of granulomatosis with polyangiitis (GPA) in remission, on weekly methotrexate 15 mg and low-dose prednisone 10 mg/d is admitted with fever and cough. The cough started about a month ago and has progressively worsened, and 2 days ago, she noticed the fever.

She has also been having blood-stained nasal discharge for the last 2 weeks and is taking amoxicillin. She does not have any skin rash, joint pain, shortness of breath, hemoptysis, hoarseness, numbness, or tingling. She complains of night sweats and fatigue but no weight loss. On physical examination, she has a cushingoid facies with saddle-nose deformity, temperature of 101.2°F, pulse of 90 beats/minute, and BP of 100/60 mmHg. She has diffuse bilateral rales on the lung examination. Her laboratory tests show a white blood cell count of 15,800/μL, hemoglobin of 9.8 g/dL, and platelet count of 544,000/μL. The ANCA titer is rising. Her urinalysis is normal, and creatinine is 0.7 mg/dL. Blood cultures are negative. CT scan of her chest, as shown, shows a large, thick-walled cavity with irregular margins.

Air bronchograms are seen in the periphery of the lesion. What would be the next step in the management of the patient?

a) Hold prednisone and methotrexate and start on antibiotics
b) Increase the dose of prednisone
c) Schedule bronchoscopy
d) Add cyclophosphamide

**Answer and Discussion**

The answer is c.

**Objective:** Recognize the etiology of cavitary lung lesions in granulomatosis with polyangiitis.

This patient with GPA is either having a flare of her underlying disease or an infectious complication. The cavitary lesion seen on the CT scan of the chest can be seen in granulomatosis with polyangiitis or could be secondary to opportunistic infections like nocardiosis, histoplasmosis, tuberculosis, or aspergillosis. Serious infections are a major concern in patients with GPA who are immunosuppressed. The determination of relapse should be based on objective evidence of disease activity, but infections complications can mimic a disease flare. Hence, a bronchoscopy should be done to rule out an infection; of note, the bronchoscopy may not confirm active GPA but is done to rule out an infection. Rising ANCA titer alone cannot be used for predicting a flare of GPA.

**Question 44**

A 44-year-old man with a past history of previously documented gout in his knee is admitted with pain and swelling in the left elbow for about 10 days. He has no other joint involvement. One month previously, he had been hospitalized for urinary obstruction due to an enlarged prostate with a urinary tract infection. On physical examination, he is febrile with temperature of 102°F, pulse of 100 beats/minute, and BP of 124/78 mmHg. Joint examination reveals a hot and swollen left elbow with limited range of motion. He also has multiple nontender nodules on his metacarpophalangeal and proximal interphalangeal joints, as shown in the figure.

His laboratory tests show a white blood cell count of 12,200/μL, sedimentation rate of 124 mm/hour, and C-reactive protein of 17.3 mg/L; uric acid is 9.1 mg/dL, and Cr is 1.6 mg/dL. The left elbow is aspirated and shows 50,000 WBC with 80% neutrophils. Gram stain shows many polymorphonuclear cells, and the culture is pending. Polarizing microscopy shows negatively birefringent intracellular crystals. What is the next step in the management of this patient?

a) Start on nonsteroidal anti-inflammatory drug
b) Start on prednisone
c) Start on colchicine and allopurinol
d) Start on intravenous antibiotics

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Answer and Discussion
The answer is d.
Objective: Diagnose and treat acute monoarticular arthritis.
This patient has tophaceous gout and is currently having an acute inflammatory monoarthritis in the left elbow. The possibilities include acute gout versus infection. Presence of monosodium crystals in the joint fluid does not rule out gout with a coexistent infection. Erythrocyte sedimentation rate and C-reactive protein, which are markers of inflammation, can be elevated both in gout and in infection. A very high synovial cell count is compatible with either gout or infection. The prolonged symptoms and history of recent infection warrant treatment for a possible infection until the culture results return. Hence, the patient should be started on intravenous antibiotics while awaiting the culture results.

Question 45
A 24-year-old woman presents with fatigue, joint and muscle pain, and low-grade fever for the last 6 weeks. She has been taking minocycline for about 6 months for severe facial and truncal acne. She has no history of recent travel or immunizations. She denies any dysuria, painful red eyes, or diarrhea. On physical examination, she has a temperature of 100°F, pulse of 80 beats/minute, and no joint swelling. She has normal heart and lung exams. She is ANA positive and anti-histone antibody negative. Parvovirus B19 IgM and IgG antibodies are negative. What is the next step in the management of this patient?

a) Discontinue minocycline
b) Start on hydroxychloroquine
c) Start on a nonsteroidal anti-inflammatory drug
d) Start on oral prednisone

Answer and Discussion
The answer is a.
Objective: Identify drug-induced lupus.
This patient has drug-induced lupus (DIL) secondary to minocycline therapy. Drug-induced lupus is a syndrome of positive ANA associated with symptoms like fever, malaise, arthritis, arthralgia/myalgia, serositis, and rash that follows exposure to certain drugs like procainamide, hydralazine, methyldopa, isoniazid, chlorpromazine, quinidine, and minocycline.

Antibodies to histone are the most specific antibodies in DIL, but patients with active lupus can also have a positive test. However, only 10% to 15% of patients with DIL secondary to minocycline will have antibodies to histone. The main treatment is withdrawal of the offending agent.

Question 46
A 40-year-old woman presents with pain and swelling in the hands, shoulders, and feet for the last 2 months. She also has morning stiffness that lasts for about an hour and malaise with night sweats. She denies any hair loss, oral ulcers, dry eyes, or mouth, rash, fever, or discoloration of hands when exposed to cold. She has no history of psoriasis or inflammatory bowel disease. On physical examination, she has swelling with tenderness in the metacarpophalangeal, proximal phalangeal, and metatarsophalangeal joints. Laboratory tests revealed a hemoglobin of 10.0 g/dL, MCV of 82 fl, and platelet count of 450,000/μL. Which of the following tests is most specific for establishing the diagnosis?

a) Anti-cyclic citrullinated peptide antibodies (anti-CCP)
b) C-reactive protein (CRP)
c) Rheumatoid factor (RF)
d) ANA

Answer and Discussion
The answer is c.
Objective: Understand the use of serologic markers in the diagnosis of rheumatoid arthritis.
This patient has symmetric inflammatory polyarthritis, raising the possibility of rheumatoid arthritis (RA). Erythrocyte sedimentation rate and CRP are nonspecific markers of inflammation that are elevated in active RA and many other conditions. RF is commonly used for the diagnosis of RA but cannot be used alone for making the diagnosis. It can be elevated in 1% to 2% of healthy individuals, other autoimmune diseases, and chronic infections like tuberculosis, hepatitis C, syphilis, and bacterial endocarditis. CCP antibodies are directed against citrulline residues formed by the posttranslational modification of arginine. They are frequently elevated in patients with rheumatoid arthritis. They have a reported sensitivity of 30% to 60% and a specificity of 95% to 98% among patients meeting the clinical criteria for RA. The important clinical utilities of this test include a high disease specificity, the presence in the early-phase RA, and its ability to distinguish RA from the arthritis related to hepatitis C. Hence, CCP antibodies should be checked in patients with the clinical suspicion of RA. Their presence likely also suggests a more aggressive course of the disease.

Question 47
A 55-year-old woman presents with diffuse muscle pain and fatigue for over a year. Her symptoms began after she lost her job. She is unable to exercise because of fatigue. She is currently taking over-the-counter sleep medications. On physical examination, she is anxious and has diffuse muscle tenderness and tender points. Her muscle strength is 5/5 and she has hyperreflexia. Her laboratory tests show a TSH of 3.5 μU/mL, erythrocyte sedimentation rate of 19 mm/hour, CK of 125 U/L, AST of 14 U/L, and ALT of 38 U/L. What is the most likely diagnosis?

a) Polymyalgia rheumatica
b) Fibromyalgia
c) Polymyositis
d) Rheumatoid arthritis
Answer and Discussion

The answer is b.

Objective: Identify the clinical pain syndrome of fibromyalgia.

Diffuse pain present for years and accompanied by subjective complaints like fatigue, memory difficulties, irritable bowel symptoms, and sleep disturbance is likely to be secondary to fibromyalgia. This patient has diffuse pain with fatigue, a sleep disturbance, and physical examination findings of diffuse tender points with hyperreflexia, which are compatible with the diagnosis of fibromyalgia. In patients presenting with diffuse pain, one should focus on the onset and character of the pain and any precipitating events that could have caused the pain. On physical examination, identification of signs of inflammation, like swollen joints or objective muscle weakness, will be against the diagnosis of fibromyalgia. Patients who have diffuse pain should have a complete blood count and tests of liver, kidney, thyroid, hepatitis C infection, muscle enzymes, and sedimentation rate with C-reactive protein performed during the course of the illness. Patients with fibromyalgia have symptoms with normal inflammatory indices, and the symptoms are often minimally responsive to anti-inflammatory regimens.

Question 48

A 49-year-old woman is admitted with a purpuric rash on the legs, pain in the joints, excruciating pain and tingling in her feet, difficulty walking, weight loss, and discoloration of her hands on exposure to cold. These symptoms have been going on for about 6 weeks. PMH includes only a history of several cardiac surgeries for the repair of a congenital cardiac malformation. On physical examination, she has a palpable purpuric rash on her legs and weak dorsiflexion of the right foot. Her laboratory tests show a WBC of 6,600/μL, Hgb of 10 mg/dL, platelets of 50,000/μL, normal C3 but low C4, RF of 30 U/mL (normal: <20 IU/mL), Cr of 1.4 mg/dL, AST of 89 U/L, and ALT of 100 U/L. What is the most likely diagnosis?

a) Systemic lupus erythematosus
b) Rheumatoid vasculitis
c) Cryoglobulinemic vasculitis
d) Sjögren’s syndrome

Answer and Discussion

The answer is c.

Objective: Diagnose cryoglobulinemic vasculitis.

This patient has palpable purpura, arthritis, mononeuritis, and Raynaud’s phenomenon, suggestive of vasculitis. The history of likely blood transfusions in the past with currently elevated liver enzymes and positive risk factors raises the possibility of a chronic hepatitis C infection in this patient. Chronic hepatitis C infection is associated with mixed cryoglobulinemia and sometimes results in cryoglobulinemic vasculitis. Ninety percent of patients with vasculitis secondary to mixed cryoglobulinemia are hypocomplementemic, with C4 levels characteristically more depressed than C3 levels.

Cryoglobulins are cold-precipitable monoclonal or polyclonal antibodies. Mixed cryoglobulinemia is characterized by the presence of monoclonal and polyclonal IgG and IgM antibodies, which often include antibodies with rheumatoid factor activity.
POINTS TO REMEMBER:

- It is estimated that up to 50% of deep vein thromboses (DVTs) are asymptomatic or go undetected.
- In autopsy-based studies, pulmonary embolism (PE) has been identified as the proximate cause or contributor to death in 15% to 30% of all patients.
- Inadequately treated DVT involving the popliteal or more proximal leg veins is associated with a 20% to 50% risk of clinically relevant recurrence and is strongly associated with both symptomatic and fatal PE.
- Upper extremity DVT (UEDVT), usually the result of either mechanical compression from anatomic abnormality or central or peripherally inserted central venous catheters, account for up to 6% of all cases of PE.
- In untreated patients, death from PE occurs most frequently within 24 to 48 hours of initial presentation.
- Predictive scoring rules combine patient history and exam elements with objective testing results and are recommended for the most efficient approach to DVT and PE diagnosis.
- For suspected DVT involving the arms or legs, compression ultrasound is the preferred initial imaging test; screening in asymptomatic patients is less accurate.
- D-dimer levels may be elevated by many acute disease states (including myocardial infarction, pneumonia, sepsis, disseminated intravascular coagulation, liver disease, malignancy, surgery, hemorrhage, and trauma). A positive D-dimer assay is of limited diagnostic use, whereas a negative test essentially excludes venous thromboembolism (VTE) (DVT and PE).
- Consensus is lacking on management of isolated acute, provoked distal (i.e., calf) DVT. At minimum, re-imaging (twice weekly compression ultrasonography for 2 weeks) is advised.
- Anticoagulation is the cornerstone of treatment for documented DVT and PE.
- The placement of an IVC filter at the time of diagnosis of PE should be reserved for those with an absolute contraindication to anticoagulation.
- Idiopathic distal or proximal DVT may be the initial presentation of occult malignancy, and appropriate history, physical examination, and screening tests should be performed to detect cancer at its earliest stage.
- Failure to accurately and promptly diagnose DVT and PE can result in excess morbidity and mortality due to postthrombotic syndrome, pulmonary hypertension, and recurrent venous thromboembolic events.
- A VTE risk assessment and appropriate prophylaxis is essential in all hospitalized patients.
- Novel oral anticoagulants (NOACs) are now available for the prevention and treatment of venous thromboembolism.

SUGGESTED READINGS


Deitcher SR, Gomes MPV. Hypercoagulable state testing and malignancy screening following venous thromboembolic events. Vasc Med. 2003;8:33-46.


POINTS TO REMEMBER:

Epidemiology and Histology
- Lung cancer is the leading cause of cancer-related mortality in both men and women.
- Histopathologically, lung cancer may be categorized as follows:
  - Non-small-cell lung cancer, which includes the following:
    - Adenocarcinoma (40%)  
    - Squamous cell carcinoma (25%)  
    - Large cell carcinoma (10%)  
    - Small cell lung cancer (13%)
- Over the past 30 years, there has been an increased incidence of adenocarcinoma, and this may be attributed to modifications in the histologic classification of lung cancer, increased environmental carcinogens exposure, and increasing incidence of lung cancer detection in women.
- Women have a greater risk of developing lung cancer than men.

Patterns of Metastases
- Adenocarcinoma and large cell carcinoma tend to spread systemically relatively early in their course.
- Squamous cell carcinoma frequently invades locally prior to systemic spread.
- Small cell lung cancer has a very aggressive behavior, with mediastinal and extrathoracic spread at the time of presentation.

Diagnosis and Staging
- Tissue biopsy is required for tumor diagnosis. Flexible bronchoscopy with transbronchial biopsy is a less-invasive means to obtain tissue sample and is particularly useful for biopsy of large central lesions. It is also useful for biopsy/staging of mediastinal disease.
- Brain imaging (MRI, CT) is recommended for all patients with SCLC and for patients with NSCLC who have either signs or symptoms of brain metastases or advanced disease (stage IIIA or higher).
- NSCLC is staged using the TNM system.  
- SCLC is staged using a 2-stage system (VALSG), which characterizes disease as limited stage or extensive stage. Most SCLC is extensive stage at time of diagnosis.

Treatment and Prognosis
- Treatment decisions and prognosis are influenced by histologic subtype, molecular markers, stage of lung cancer, and the patient’s performance status.
- Surgery is the treatment of choice for early stage non-small-cell lung cancer.
- Chemotherapy is the modality of choice for advanced non-small-cell lung cancer.
- Chemotherapy with or without radiation therapy is used to treat small cell lung cancer.
- Palliative services should be utilized early in the course of treatment.

Complications
- Paraneoplastic syndromes occur in 10% to 15% of patients with lung cancer and may be present even before the primary tumor appears. These may include SIADH, ectopic ACTH, and PTH-rp–driven malignant hypercalcemia.
- Small cell lung cancer can be associated with neurologic paraneoplastic syndromes including anti-Hu syndrome and Lambert-Eaton myasthenia gravis.
- Lung cancers may be associated with many syndromes related to regional spread of the cancer including Horner’s, Pancoast, and SVC syndromes.

Screening
- The American College of Chest Physicians/American Society of Clinical Oncology now recommends annual low-dose CT scan screening for the following:
  - Age 55 to 74 years, and  
  - 30 pack-year history of smoking and current smoker, or quit within past 15 years.

Indeterminate Pulmonary Nodule
- Establishing the etiology of an indeterminate pulmonary nodule can be clinically challenging.
- Certain radiographic characteristics of the indeterminate pulmonary nodule can aid in malignant risk assessment.
Ground-glass nodules, defined as nodular ground-glass opacities, are becoming more frequently diagnosed. The risk of malignancy of a GGN depends on the size, the presence of a solid component, and growth.

PET scan can be helpful in evaluating the indeterminate pulmonary nodule, although nodules <1 cm have more false-negative results. They are not useful in the evaluation of GGN.

**SUGGESTED READINGS**


Obstructive Lung Disease: Asthma and Chronic Obstructive Pulmonary Disease

Loutfi S. Aboussouan and Sumita B. Khatri

POINTS TO REMEMBER:

- Asthma affects 3% to 5% of the U.S. population.
- Asthma is a chronic, episodic disease of the airways with protean manifestations and is best viewed as a syndrome. Important features of this syndrome include the following:
  - Episodic symptoms
  - Airflow obstruction with a reversible component
  - Bronchial hyperresponsiveness to a variety of nonspecific and specific stimuli
  - Airway inflammation
  - A tendency toward atopic and allergic inheritable disease
- Asthma treatment has four key components:
  - Measurement of lung function both initially and during periodic evaluation, including home peak expiratory flow monitoring
  - Education of patients in using asthma action plans
  - Avoidance of asthma triggers by controlling the environment
  - Pharmacologic treatment
- The most objective indicator of asthma severity is the measurement of airflow obstruction by spirometry or peak expiratory flow, although spirometry is preferred.
- Spirometry in an asthmatic typically shows obstructive airway disease with reduced expiratory flows [reduced FEV₁/forced vital capacity (FVC) ratio] that improve on administration of bronchodilator therapy; lack of 12% or more bronchodilator response does not rule out asthma.
- An estimated 24 million Americans are afflicted with chronic obstructive pulmonary disease (COPD).
- The Global Initiative for Chronic Obstructive Lung Disease (GOLD) report defines COPD as “a disease state characterized by airflow limitation that is not fully reversible. The airflow limitation is usually both progressive and associated with an abnormal inflammatory response of the lungs to noxious particles or gases.”
- Recent studies identify a composite index combining Body mass index, airflow Obstruction, Dyspnea, and Exercise capacity (the BODE index), as well as the inspiratory capacity-to-total lung capacity ratio, as better than the forced expiratory volume in 1 second in predicting the risk of death in COPD.
- Although smoking is the single most important risk factor for COPD, about 15% to 20% of cases occur in never-smokers.
- Severe deficiency of alpha-1 antitrypsin accounts for emphysema in approximately 2% to 3% of adult COPD patients.
- Pulmonary function testing is essential to establish a diagnosis of COPD and its severity.
- The typical spirometric abnormalities in COPD consist of a reduction in the FEV₁, and in the ratio of the FEV₁ to the FVC.
- The single-breath diffusing capacity for carbon monoxide is usually reduced in emphysema.
- Commonly used therapy for stable COPD includes
  - Preventive measures (smoking cessation, annual flu vaccination, and vaccination for pneumococcus)
  - Supplemental oxygen if indicated
  - Inhaled bronchodilators
  - Theophylline preparations and inhaled or systemic corticosteroids (for a small subset of patients)
- The only interventions that have been shown to prolong survival and affect the natural history of COPD are limited oxygen therapy (continuous or nocturnal) for the chronically hypoxemic patient and smoking cessation.
- In certain patients, noninvasive positive-pressure ventilation (NPPV) is successful for preventing endotracheal intubation, reversing hypercapnia, and reducing mortality and hospitalization in acute exacerbations of COPD (AECOPD).
- In appropriately selected patients with COPD, lung volume reduction surgery (LVRS) has been shown to increase survival, health-related quality of life, and exercise capacity.

SUGGESTED READINGS

**Asthma**


**Chronic Obstructive Pulmonary Disease**


Interstitial Lung Disease
Joseph G. Parambil

POINTS TO REMEMBER:

- Interstitial lung disease (ILD) refers to a broad category of lung diseases rather than a specific disease entity and includes a variety of illnesses with diverse causes, treatments, and prognosis.
- ILD with known causes are further classified based on specific exposure, association with systemic disease, or association with a known genetic disorder.
- There is considerable variability among the specific diseases in presentation, tempo, and distribution of radiographic abnormalities.
- For most ILDs, the plain chest radiographs will reveal reduced lung volumes with bilateral reticular or reticulonodular opacities.
- A more descriptive imaging tool for ILD, high-resolution CT (HRCT), has the ability to better define the specific characteristics of lung parenchyma seen in each disease, increasing the likelihood of establishing a correct diagnosis.
- A restrictive physiological impairment is the most common finding in ILDs. Both forced expiratory volume in 1 second (FEV₁) and forced vital capacity (FVC) are diminished, and the FEV₁/FVC ratio is preserved or even supranormal.
- IPF is the most common ILD worldwide. HRCT typically reveals bilateral, peripheral, and basilar predominant disease with reticulonodular infiltrates, often with honeycomb, cystic change.
- Asbestos-related pulmonary diseases include any diseases caused by asbestos exposure: benign asbestos pleural effusion (BAPE), rounded atelectasis, pleural plaques, mesothelioma, and certain lung cancers. The term asbestosis is not synonymous, and specifically refers to asbestos-related ILD.
- Cigarette smoking is strongly associated with three types of ILD: desquamative interstitial pneumonitis (DIP), respiratory bronchiolitis-associated ILD (RB-ILD), and pulmonary Langerhans’ cell histiocytosis (PLCH).
- Several drugs have been associated with pulmonary complications of various types, including interstitial inflammation and fibrosis, bronchospasm, pulmonary edema, and pleural effusions. Drugs from many different therapeutic classes can cause ILD, including chemotherapeutic agents, antibiotics, antiarrhythmic drugs, and immunosuppressive agents.
- ILD is a well-known complication of several connective tissue diseases. The most commonly implicated disorders are scleroderma, rheumatoid arthritis, Sjögren’s syndrome, polymyositis/dermatomyositis, and systemic lupus erythematosus.

SUGGESTED READINGS


The standard posteroanterior (PA) and lateral chest radiographs remain the most important techniques for the initial detection of pleural effusion.

A major role of ultrasonography in thoracentesis is to guide needles into small or loculated pleural effusions, thereby increasing both the yield and safety of the procedure.

The first diagnostic step in pleural effusion analysis is to classify the effusion as a transudate or an exudate by using the protein and lactate dehydrogenase values of serum and pleural fluid.

Transudative effusions are formed secondary to elevations in hydrostatic pressure or reductions in colloid osmotic pressure within the systemic or pulmonary circulation. Causes include the following:

- Congestive heart failure
- Nephrotic syndrome
- Cirrhosis with ascites
- Peritoneal dialysis
- Atelectasis (early)
- Urinothorax

Once a pleural fluid is established to be transudative in nature, additional pleural fluid studies are usually not indicated.

Once a pleural fluid is established to be exudative, all attempts possible must be made to determine the underlying cause.

Low pleural fluid glucose levels are associated with rheumatoid disease, TB, empyema, and certain tumors.

A high pleural fluid amylase can be seen in pancreatitis, pancreaticpleural fistulas, esophageal rupture, malignancy, and parapneumonic effusions.

A low pleural fluid pH (i.e., <7.30) may be seen with infected parapneumonic effusions, frank empyema, malignancy, collagen vascular disease, TB, esophageal rupture, and urinothorax.

Urinothorax is the only transudative effusion that can present with a low pH.

When ordering pH on pleural fluid, it is essential the fluid be aspirated anaerobically and transported on ice.

In large-volume thoracentesis, if a patient develops chest discomfort or an end-expiratory pleural pressure of less than ~20 cm H₂O by pleural manometry measurements, thoracentesis should be stopped. Continued fluid removal increases the risk of development of pneumothorax, edema in the underlying lung (reexpansion pulmonary edema), or rapid fluid shift from the intravascular space into the pleural space (postthoracentesis shock).

SUGGESTED READINGS


Koegelenberg CF, Diacon AH. Pleural controversy; close needle pleural biopsy or thoracoscopy—which first? Respirology. 2011;16(5):738-746.


General


**Diagnosis**


**Pleural Biopsy**


**Radiographic Evaluation**


**Parapneumonic Effusion and Empyema**


**Malignant Effusion**


**Collagen Vascular Disease**


**Asbestos**


**Esophageal Rupture**


**Urinothorax**


**Chylothorax**


**Postcardiac Injury**


**Indeterminate Effusions**


**AIDS**


**Pneumothorax**

POINTS TO REMEMBER:

Acute Respiratory Distress Syndrome
- The incidence of acute respiratory distress syndrome (ARDS) has been estimated in the range of 5 to 15 cases per 100,000 per year.
- Transfusion-related acute lung injury (TRALI) is becoming an increasingly recognized cause of ARDS. TRALI should be suspected when symptoms of ARDS develop within 6 hours of transfusion of blood or blood products.
- The objectives of mechanical ventilation in ARDS are not to normalize arterial blood gas values, but to provide adequate support for oxygenation and acid–base balance, while avoiding further injury that can be induced by mechanical ventilation.
- The only ventilation strategy that has been demonstrated in randomized controlled trials to improve the mortality in ARDS is the use of low-stretch (6 cc/kg predicted body weight tidal volume) ventilation.
- Current fluid management recommendations for patients in ARDS with adequate urine output and not in shock include use of diuretics as necessary to target CVP <4 mmHg or PAOP <8 mmHg.
- Recent randomized controlled trials of the pulmonary artery catheter utilization in several populations, including ARDS, have failed to demonstrate improved outcomes.
- Patients who survive ARDS tend to recover normal or near-normal lung function, although patients with severe ARDS are sometimes left with some degree of restrictive defect.
- Despite return of lung function, many patients who survive ARDS have persistent functional disability and are not working 1-year post-ICU discharge.

Shock
- Shock is defined as a physiological state characterized by inadequate tissue perfusion leading to decreased tissue oxygen delivery.
- The most common causes of shock in the intensive care unit population may be grouped into several categories.
  - **Hypovolemic shock**—commonly due to hemorrhage, external volume loss (e.g., ketoacidosis), or third spacing (e.g., pancreatitis).
  - **Cardiogenic shock**—predominantly secondary to depressed myocardial function, mostly secondary to acute myocardial infarction, malignant dysrhythmias, acute valvular regurgitation, or nonischemic cardiomyopathies.
  - **Distributive shock**—characterized by loss of vascular tone; septic shock is most frequent; other causes include adrenal insufficiency, neurogenic shock, liver cirrhosis, overdoses, and anaphylaxis.
- Early clinical and laboratory markers of compromised tissue perfusion include decreased urinary output, decreased skin perfusion, changes in mental status, elevated serum lactate levels, and increased heart and respiratory rate.
- Central venous (ScvO₂) or the mixed venous oxygen saturation (SvO₂) can be very useful when assessing a patient in shock.
- Limited echocardiography is increasingly used in the initial diagnosis and evaluation of shock patients.
- Early intubation for airway protection should be considered in all shock patients.
- Crystalloids remain the resuscitative fluids of choice.

Sepsis
- Sepsis is defined as the presence of systemic inflammatory response syndrome (SIRS) secondary to severe infection.
- Severe sepsis is defined as sepsis with at least one organ system failure.
- Septic shock is a more severe clinical picture with persistence of hypotension despite adequate fluid resuscitation.
- Prompt initiation of empiric antimicrobial coverage, addressing source control, and early aggressive fluid resuscitation are associated with improved outcomes.
- Surviving Sepsis Campaign (SSC) guidelines recommend norepinephrine (NE) as the initial vasopressor of choice if needed.
- Use of single-agent, low-dose vasopressin is no longer recommended as initial pressor therapy.
SUGGESTED READINGS


Points to Remember:

- Typical questions on the boards address the following: common features of uncommon diseases, uncommon features of common diseases, disease associations, and knowledge of established treatments.
- Questions on the board examinations are less likely to address straightforward associations, such as common complications of commonly used medications and common medical manifestations of common illnesses.
- Measuring pulmonary function tests can help the astute clinician identify the physiologic signature of the pulmonary illness in order to categorize it as restrictive or obstructive and, in so doing, narrow down a specific etiology.
- In addition to the normal flow-volume loop, three characteristic deviations from the normal flow-volume loop suggest various forms of upper airway obstruction.
- The identifying criterion for restrictive lung disease is decreased total lung capacity.
- Calculation of the alveolar–arterial oxygen gradient is very useful for approaching the differential diagnosis of hypoxemia. Six mechanisms of hypoxemia should be remembered: anatomic shunt, mismatch, diffusion impairment, hypoventilation, inhaling a decreased inspired oxygen fraction (hypoxic hypoxemia) or breathing at altitude (hypobaric hypoxemia), and diffusion–perfusion impairment (e.g., as seen in the hepatopulmonary syndrome).

Typical questions posed in board certification examinations include those addressing the following:

- Common features of uncommon diseases
- Uncommon features of common diseases
- Disease associations, especially those that require integrating knowledge of diagnosis, treatment, and complications of therapy

- Knowledge of established therapies, even if relatively uncommon
- Integration of knowledge (e.g., associating classic disease symptoms with pathologic and radiographic manifestations, associating pathological findings with treatments of choice or complications of therapy)

Suggested Readings

**Question 1**

A 57-year-old man presents to his primary care physician with 3 months of persistent dry cough and unintentional weight loss of 25 lb. He has occasional night sweats. He has a 40 pack-year smoking history and quit 6 months ago. He has worked in a shipyard most of his adult life. His chest X-ray (CXR) shows a right hilar mass. He wishes to know more about the development of his condition. Which one of the following statements is true?

- **a)** The most common histologic type of lung cancer is small cell carcinoma.
- **b)** It is the most common cancer in the United States.
- **c)** Eighty percent of lung cancer deaths among men are attributable to smoking.
- **d)** Screening has proved beneficial in decreasing mortality from lung cancer among the general population.

**Answer and Discussion**

The answer is **c**.

**Objective:** Identify important epidemiology regarding lung cancer.

According to the National Cancer Institute and American Cancer Society, lung cancer was the second most common cancer identified in both men and women, second only to prostate cancer and breast cancer, respectively. Lung cancer, however, remains the most common cause of cancer-related mortality in the United States, claiming over 160,000 deaths in 2012 alone. Less than 20% are small cell in type, whereas over 80% are non-small cell. According to the CDC, 80% of mortality among men and ~50% of mortality among women from lung cancer can be directly attributable to smoking. Despite advances in radiologic imaging with low-dose computed tomography (CT) and positron emission tomography (PET) scanning, screening has not yet proved beneficial in decreasing mortality from lung cancer.

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**Question 2**

A 64-year-old woman presents to clinic with increasing fatigue, cough with scant sputum production, and ~15 lb weight loss over the last 2 months. She has a 45 pack-year smoking history and quit around the time her symptoms started. She also reports increased headache. On examination, she is mildly plethoric. She is comfortable at rest, but dyspneic with any exertion. Her lung examination is unrevealing. Her labwork is remarkable only for Na of 120. Which of the following statements about the management is true for her condition?

- **a)** Surgery is the most important treatment modality.
- **b)** Supraclavicular node involvement ipsilateral to the sentinel lesion qualifies as extensive stage disease.
- **c)** Approximately 80% of patients respond to chemotherapy.
- **d)** Prophylactic cranial irradiation has been shown to prolong survival.

**Answer and Discussion**

The answer is **c**.

**Objective:** Identify the presentation and treatment of small-cell lung cancer (SCLC).

SCLC is considered a systemic disease, and thus surgery plays no part in the management of the disease. Multiple staging systems are used for SCLC, including the American Joint Cancer Commission (AJCC), the Veteran's Administration Lung Study Group (VALG), and the International Association for the Study of Lung Cancer (IASLC). All of these classifications attempt to identify SCLC as either limited stage disease (those lesions that can be encompassed in a single radiation field) or extensive disease. Limited stage disease describes disease confined to one hemithorax that can be included in a reasonable thoracic radiation field. This includes extension to supraclavicular nodes on the same side as the sentinel lesion. Approximately 80% of patients respond to chemotherapy. Prophylactic cranial irradiation reduces the incidence of brain metastases, but has not been shown to prolong survival.

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**Question 3**

A 54-year-old Caucasian man presents to the emergency department (ED) with 6 months of persistent dry cough and unintentional weight loss of 30 lb. He has a 30 pack-year smoking history and quit 6 months ago at the onset of his symptoms. He is found to have a parenchymal mass, which on biopsy shows squamous cell cancer. He wishes to know what his overall treatment and prognosis is. Which one of the following statements is true for non–small-cell lung cancer?

- **a)** Stage IV disease is associated with 5-year survival rates of approximately 10%.
- **b)** About 60% of patients are suitable for resection at diagnosis.
c) Stage IA disease is associated with 5-year survival rates of approximately 40%.
d) Surgery offers the best chance of cure.

**Answer and Discussion**

**Objective: Identify appropriate therapeutic and prognostic information for non–small-cell lung cancers.**

With currently available modalities in thoracic surgery, postoperative mortality rate is <3%. About 20% to 33% of patients are suitable for resection at the time of diagnosis, and lobectomy is the most commonly performed operation. Surgery offers the best chance of cure for non–small-cell lung Ca. Stages IA and IB diseases are associated with 5-year survival rates of 67% and 57%, respectively, whereas stages IIA, IIB, and IIIA have 5-year survival rates of 55%, 39%, and 26%, respectively. Advanced stages such as IIIB and IV have poor 5-year survival rates of 5% and 1%, respectively.

**Question 4**

You are called by the ED to see a 64-year-old male patient with a known history of chronic obstructive pulmonary disease (COPD; FEV₁ of 25% of predicted) secondary to long standing tobacco use. He has been noticing a progressive decline in his functional status due to shortness of breath. He denies any acute change in sputum production, worsening wheezing, or fevers. He reports compliance with his medications, which includes inhaled steroids and long-acting β-agonists (LABAs), along with short-acting β-agonist and anti-cholinergic. He uses his combination inhaled steroids and anti-cholinergic about 4 to 6 times daily. You get an arterial blood gas (ABG), which shows a pH of 7.35, PCO₂ of 88, and PO₂ of 60 with an SaO₂ of 85%. ABG done 2 weeks ago as an outpatient after recovery from an acute COPD exacerbation showed a pH of 7.38, PCO₂ of 86, and PO₂ of 73 and an SaO₂ of 87%.

Which of the following is the most important variable to correct in this patient with very severe COPD?

a) PaCO₂
b) pH
c) Hypoxemia
d) Pulmonary hypertension
e) Cardiac output

**Answer and Discussion**

The answer is c.

**Objective: Identify indications for supplemental oxygen therapy in COPD patients.**

The overriding concern is to improve tissue oxygen delivery. Following are the current guidelines for long-term supplemental O₂ therapy based on the gold criteria: Po₂ of 55 mmHg or less OR an SaO₂ of less than 88% confirmed twice over a 3-week period. Alternatively, supplemental O₂ is also indicated if one has a PaO₂ between 55 and 60 mmHg OR an SaO₂ of 88% if they have one of the following conditions: pulmonary hypertension, peripheral edema suggesting congestive heart failure, or hematocrit >55%. Although supplemental oxygen may contribute to hypercapnia (mostly by affecting ventilation–perfusion mismatching rather than the suppression of hypoxic drive), correcting hypoxemia is critical. The mechanism whereby chronic hypoxemia improves survival is probably by reducing pulmonary hypertension. The best way to reduce pulmonary artery pressures is to correct hypoxemia.

**Question 5**

Which of the following chest radiographic findings is inconsistent with the diagnosis of asbestosis?

a) Presence of pleural plaques
b) Presence of pleural effusion
c) Reticulonodular infiltrates
d) Upper lobe predominance
e) Reduced lung volumes

**Answer and Discussion**

The answer is d.

**Objective: Identify the different pulmonary findings of asbestosis.**

Asbestos exposure represents a spectrum of histopathologic and radiographic findings that are typically broken up into three major categories: pleural disease, interstitial disease, and malignancies.

Pleural disease is often considered the hallmark of asbestos exposure, and upwards of 50% of patients will have some pleural involvement. Pleural disease manifests as either pleural plaques, pleural adhesions causing rounded atelectasis, or benign asbestos pleural effusions (BAPEs). Pleural plaques preferentially involve the parietal pleura adjacent to the ribs. They are considerably less extensive in the visceral pleura and the intercostal space and are almost never seen in the costophrenic angles or the apices. Rounded atelectasis is a non-specific finding and can be seen with just about any type of pleural inflammation. BAPEs are typically very small and unilateral and can be seen before the interstitial disease. Pleural fluid analysis can be varied: up to one-third have increased pleural eosinophils and can be as high as 50% of the total nucleated cell count.

The interstitial process typically involves the lower lung zones and can be seen as non-specific imaging findings of haziness on CXR and ground glass opacities on CT scan early in the disease. This eventually progresses to honeycombing. Lymphadenopathy, either hilar or mediastinal, is not associated with asbestosis.

Asbestos is classically linked to mesothelioma, and along with smoking is a major risk factor for this malignancy. However, asbestos exposure has also been linked to both small- and non–small-cell lung cancers.
**Question 6**

Which one of the following statements is incorrect?

a) Obtaining an occupational history is imperative before diagnosing a patient with sarcoidosis.

b) An elevated serum angiotensin-converting enzyme (ACE) level is not diagnostic.

c) Sarcoidosis can involve any organ system.

d) The presence of sarcoi d granulomas in the pulmonary parenchyma is an indication for treatment.

e) The most common presentation is an asymptomatic chest radiograph abnormality.

**Answer and Discussion**

The answer is d.

Objective: Identify indications for treatment in sarcoidosis.

Sarcoidosis is an inflammatory condition marked by non-caseating granulomas of affected tissue without evidence of another identifiable etiology. Given that infection, particularly mycobacterial and fungal infections are on the differential, a travel and occupational history is important. Occupational history is also important, as there have been association with certain occupational irritants, specifically insecticides and building materials. Clinical presentation can vary substantially and can involve any organ systems. The most common organs involved are the lymphatic system, lungs, skin, and eyes. Up to 90% of patients with sarcoidosis will have some involvement from these systems. The most common presentation is a chest radiograph showing hilar lymphadenopathy or reticulonodular infiltrates in an asymptomatic patient. Angiotensin-converting enzyme (ACE) is produced by granulomas, and elevated levels can be seen in up to 60% of patients. However, genetic polymorphisms can lead to variable levels in individuals, leading to a lack of both sensitivity and specificity in the diagnosis of sarcoidosis. Currently, the role of ACE levels is controversial at best. Making a histologic diagnosis of sarcoidosis is not considered sufficient reason to treat with steroids. Commonly accepted indications for treatment include significant symptoms or progressive loss of lung function. Involvement of critical extrapulmonary organs, such as cardiac or renal sarcoid, also may prompt treatment.

**Question 7**

A 53-year-old man presents to your clinic to establish care. Patient has no significant past history, although has not really followed with a physician. He reports a family history notable for hypertension in his parents, but is otherwise unremarkable. He has a 40 pack-year smoking history and has worked most of his life in demolition of old buildings. He has had multiple former coworkers diagnosed with asbestosis, and he wants to know his risk of developing this condition.

Which one of the following statements to this patient about asbestos-related lung disease is incorrect?

a) Benign asbestos pleural effusion is one of the earliest manifestations of asbestos exposure.

b) Pleural thickening in a patient with asbestos exposure indicates asbestosis.

c) Pleural plaques almost never result in symptoms or physiologic impairment.

d) Mesothelioma may develop in patients with brief, low-level exposure to asbestos.

e) Rounded atelectasis is a benign manifestation of asbestos exposure that can be mistaken for a malignancy.

**Answer and Discussion**

The answer is a.

Objective: Define asbestosis and differentiate from isolated pleural disease.

This question is meant to emphasize the fact that the term asbestosis should be reserved for patients with evidence of pulmonary parenchymal scarring. Pleural disease does not merit the diagnosis of asbestosis. The clinical relevance of this distinction centers around two issues: increased symptoms in patients with asbestosis, as most pleural disease does not cause symptoms or impairment, as well as the increased risk of malignancy in patients with asbestosis versus asbestosis-associated pleural disease. Patients with any asbestos exposure, even low level exposure without evidence of pleural or parenchymal disease are at increased risk for mesothelioma compared with the general population. Those patients with asbestos-associated pleural disease have a comparable risk of mesothelioma as those with asbestos exposure without pleural disease. However, asbestosis is associated with a higher risk of mesothelioma compared with those with pleural disease. This risk is further increased by concurrent smoking, and as such, all patients with asbestosis should be strongly discouraged against smoking. BAPES are typically very small and unilateral and can be seen before the interstitial disease. Patients with evidence of pleural disease can develop rounded atelectasis, which can appear mass like on imaging and is often mistaken for malignancy.

**Question 8**

Which one of the following statements is incorrect?

a) Silicosis shows a predominantly lower zone distribution on the chest radiograph.

b) Progressive massive fibrosis is a complication of silicosis.

c) There is an increased incidence of tuberculosis (TB) in patients with silicosis.

d) There is an increased incidence of rheumatoid arthritis and scleroderma in patients with silicosis.

**Answer and Discussion**

The answer is a.

Objective: Identify clinical features and other conditions associated with silicosis.

Silicosis represents pulmonary manifestations after exposure to silica. Silica exposure is often seen in mining, glass manufacturing, sand blasting, and road and building construction. Silicosis manifests clinically along a spectrum of
simple chronic silicosis (most common), accelerated silicosis and acute silicosis, based on the chronicity of symptom development compared to exposure to silica. They all lead to increased inflammation in the pulmonary parenchyma and intrathoracic lymph nodes, predominantly in the upper lobes. Silicosis is associated with the following complications: progressive massive fibrosis, lung cancer, and respiratory failure. Silicosis is also associated with an increased risk of TB, and therefore, patients should get regular TB testing. Silicosis has also been associated with higher incidence of autoimmune conditions such as rheumatoid arthritis, scleroderma, and systemic lupus erythematosus.

Question 9
Which one of the following statements is correct?

a) Interstitial lung disease (ILD) is more common in women with rheumatoid arthritis than in men with rheumatoid arthritis.

b) Five percent of patients presenting with acute lupus pneumonitis have had no history of lupus.

c) There is poor correlation between the severity of the cutaneous and pulmonary manifestations of scleroderma.

d) Jo-1 antibody is not associated with the presence of ILD in patients with polymyositis.

e) ILD associated with Sjögren syndrome often involves neutrophilic infiltration.

Answer and Discussion
The answer is c.

Objective: Identify features of ILD associated with connective tissue disease.

Pulmonary involvement is a major cause of mortality in connective tissue disease. Pulmonary involvement is most commonly ILD but can also involve pulmonary hypertension, pulmonary thromboembolic disease, and pulmonary nodules. As with many of the connective tissue disease–associated ILDs, there is no real correlation between the severity of the ILD and the extrapulmonary manifestations. It is generally more common in men with rheumatoid arthritis versus women with rheumatoid arthritis. To further underscore the disconnect between pulmonary and extra-pulmonary manifestations of connective tissue disease, lupus pneumonitis can be seen in up to 50% of patients without any previous history of lupus. Jo-1 is associated with dermatomyositis/polymyositis and has a stronger association with ILD. ILD associated with Sjögren syndrome is associated with a lymphocytic infiltrate, not neutrophilic infiltration.

Question 10
A 70-year-old man with a history of insulin-dependent diabetes mellitus, alcohol abuse, severe gastroesophageal reflux disease, emphysema, and benign prostatic hyperplasia requiring an indwelling catheter and frequent courses of intravenous antibiotics presents with high-grade fever; congestion; cough productive of thick, yellow, blood-tinged sputum; and right pleuritic chest pain.

On examination, you are presented with an ill-looking man febrile to 39°C. He has a heart rate (HR) of 110 beats/minute with a blood pressure (BP) of 110/54 mmHg. He has a respiratory rate of 24 breaths/minute. He is able to speak in complete sentences and does not appear to be using accessory muscles. Pulmonary examination reveals a right upper lung consolidation and right base dullness. His chest radiograph shows right upper lobe alveolar infiltrate with cavity and moderate right effusion. Laboratory findings show leukocytosis with left shift. His ABG analysis shows pH, 7.32; PCO₂, 52; and arterial oxygenation, 80 on 3-L forced inspiratory oxygen.

His pleural fluid is thick, yellow, and purulent. Laboratory findings are pH, 7.82; glucose, 30 mg/dL; and lactate dehydrogenase, 1,050 IU/dL.

Along with IV fluids and broad-spectrum antibiotics, what would be the most appropriate immediate action?

a) Urine culture and sensitivity; replace Foley

b) Intubation and mechanical ventilation

c) Thoracic surgery consult for open thoracostomy

d) Tube thoracostomy

e) Stop antacid, order esophagogastroduodenoscopy

Answer and Discussion
The answer is d.

Objective: Identify and manage a gram-negative empyema.

This question identifies a patient with diabetes and alcohol abuse who is at risk for complicated infections, and presenting with sepsis. The management of this patient must be prioritized based on the acuity of the patient. The patient is ill appearing, but is not in acute respiratory distress or in shock. He does not have any indications for urgent intubation and mechanical ventilation. Once emergent issues are addressed, source identification and control is paramount. Patient clearly has a respiratory focus for this infection evidenced by the symptoms of fever, productive cough, and pleuritic chest pain. This is further confirmed by infiltrates on imaging. However, he also has an effusion with pleural fluid analysis suggestive of a urea splitting organism leading to increased ammonia production and increased pH. Some gram-negative bacilli, specifically Proteus is associated with empyema with elevated pH. The mainstay of therapy for an empyema is drainage with tube thoracostomy. If this fails, then open thoracostomy is warranted. Given the overwhelming evidence of a pulmonary infection, management of this should not be delayed looking for other sources. With a chronic indwelling Foley catheter, he is at higher risk for colonization, and a urine culture without urinalysis is of limited utility. Also, EGD would not be warranted in this patient.
cough, or night sweats. On history taking, 15 months ago, this patient had right effusion that resolved spontaneously; 5 years ago, he had occasional bilateral wrist pain, treated with aspirin. An annual purified protein derivative test was negative 3 months ago. On examination, you find bibasilar dullness and a hard nodule on the nose. His chest radiograph shows bilateral moderate pleural effusion.

The pleural fluid analysis reveals a white blood cell (WBC) count of 2,000/mm$^3$; polymorphonuclear leukocytes, 90%; pH, 7.05; lactate dehydrogenase, 1,000 IU/dL; protein, 4 g/dL; and glucose, 5 mg/dL.

Based on the most likely diagnosis, what would be the most appropriate action?

a) Isoniazid, 300 mg; rifampin, 600 mg; ethambutol, 900 mg daily
b) Prednisone, 40 mg daily
c) Bilateral chest tube placement
d) Intravenous ceftazidime and gentamicin
e) Close observation for spontaneous resolution of fluid

**Answer and Discussion**

The answer is b.

**Objective: Identify and manage a rheumatoid effusion.**

Pulmonary complications are a major cause of mortality of rheumatoid arthritis, however, pleural effusions is an uncommon manifestation. Pleural effusions associated with rheumatoid arthritis are more common in men (as are most pulmonary manifestations). Pleural fluid analysis classically shows a low pH, high LDH, low protein, and low glucose. The fluid is predominantly composed of PMNs, and pleural biopsy may show rheumatoid nodules. These last two findings are more specific findings, and the absence of these should not exclude rheumatoid effusion from the differential. This may be difficult to differentiate from empyema and parapneumonic effusion based on fluid analysis alone. However, in this patient, he had a previous pleural effusion and is non-toxic in appearance. He also has a history of articular symptoms, pointing toward underlying RA. He also had a negative PPD 3 months previously, making TB an unlikely possibility of rheumatoid arthritis, however, pleural effusions is an uncommon manifestation. Pleural fluid analysis classically shows a low pH, high LDH, low protein, and low glucose. The fluid is predominantly composed of PMNs, and pleural biopsy may show rheumatoid nodules. These last two findings are more specific findings, and the absence of these should not exclude rheumatoid effusion from the differential. This may be difficult to differentiate from empyema and parapneumonic effusion based on fluid analysis alone. However, in this patient, he had a previous pleural effusion and is non-toxic in appearance. He also has a history of articular symptoms, pointing toward underlying RA. He also had a negative PPD 3 months previously, making TB an unlikely etiology for the pleural effusion.

The mainstay of therapy for rheumatoid arthritis is immunosuppression, especially corticosteroids acutely. Corticosteroids have also been shown to be effective for rheumatoid effusions. There is no role for drainage of a rheumatoid effusion.

**Question 12**

A 30-year-old woman presents with slowly progressing shortness of breath of 6 months’ duration. Her past medical history includes pneumothoraces, one on either side, 4 weeks apart 1 year ago. She denies any previous surgical history.

On examination, she has increased dullness in the left base, right basilar crackles, and small ascites. Her chest radiograph shows hyperinflated lungs, vague interstitial changes, and left effusion. A pleural tap reveals milky white fluid, with triglycerides, 245 mg/dL and a cholesterol level of 14 mg/dL.

The most likely diagnosis is which of the following?

a) Lymphoma
b) Catamenial pneumothorax
c) Gorham syndrome
d) Lymphangioleiomyomatosis (LAM)
e) Histiocytosis X

**Answer and Discussion**

The answer is d.

**Objective: Identify a chylothorax associated with LAM.**

The identification of a young woman with a history of spontaneous pneumothoraces and interstitial markings on CXR as concerning for LAM is the first step in answering this question. This is further confirmed by evidence of a chylothorax with high triglycerides and low cholesterol levels confirms this finding. Chylothoraces is associated with disruption of the thoracic duct or its tributaries and is classified as either a traumatic cause versus non-traumatic causes. The most common non-traumatic causes in younger patients are lymphoma and LAM. Lymphoma is not typically associated with interstitial markings on CXR and would not explain the pneumothoraces 1 year prior.

**Question 13**

A 63-year-old man in a wheelchair presents with crippling rheumatoid arthritis. His annual chest radiograph revealed moderate bilateral effusion. No chest pain, cough, or shortness of breath is present.

You review his old radiographs and observe bilateral subpulmonic effusions for 5 years. His purified protein derivative test is negative. His pleural fluid is milky white and shiny; the analysis reveals a WBC count of 2,000/mm$^3$, 90% L; glucose, 16 mg/dL; lactate dehydrogenase, 1,200 IU/dL; triglycerides, 30 mg/dL; cholesterol, 150 mg/dL; and a large amount of cholesterol crystals.

What would be the most appropriate action?

a) Start medium-chain triglyceride diet
b) Lymphangiography
c) Serology for *Wuchereria bancrofti* infestation
d) Bilateral pleuropertitoneal pump
e) Conservative treatment

**Answer and Discussion**

The answer is e.

**Objective: Identify and manage a cholesterol effusion (a.k.a. pseudochylothorax or chyloform effusion).**

This is a cholesterol, also known as pseudochylothorax or chyloform effusion, as evidence by low triglycerides and elevated cholesterol in the pleural fluid. The presence of cholesterol crystals is also consistent with a cholesterol effusion. The rest of the pleural fluid is consistent with a rheumatoid effusion and high LDH and low glucose. This is also consistent
with the patient’s history of preexisting rheumatoid arthritis. Cholesterol effusion is associated with chronic inflammation or infection of the pleura, most commonly rheumatoid effusions and tuberculosis. The treatment for a cholesterol effusion is treatment of the underlying condition and conservative management. Medium-chain triglyceride diet is the appropriate diet for a chylothorax, not for a pseudochylothorax. Chylothorax is evidenced by fluid analysis high in triglycerides, and low in cholesterol, which is inconsistent with this patient. Chylothorax is caused by obstruction or damage to the lymphatic system. Lymphangiography would potentially be indicated for a chylothorax. *Wuchereria bancrofti* is a parasitic infection associated with lymphatic obstruction. It is responsible for up to 90% of lymphatic filariasis. This would present as a chyloous effusion as well. Bilateral pleuropertitoneal shunt is a treatment for persistent chylothorax.

**Question 14**

A 70-year-old man with a history of congestive heart failure, on optimal medication, underwent thoracentesis in the ED for large right effusion using a 16-gauge spinal needle (3.5 L of serosanguineous fluid was removed uneventfully). Minutes after the procedure, the patient developed progressive shortness of breath and needed 100% fractional inspired oxygen. On examination, you observe tachypnea, right lung wheeze, and basilar rales; BP is 100/70 mmHg, and pulse is 100 beats/minute. What would be the most appropriate statement regarding the event?

a) Place large-bore chest tube for tension pneumothorax  
b) Transfuse 2 U of pack cells for hemothorax  
c) Administer Lasix, 60 mg intravenously  
d) Intrapleural pressure monitoring could have avoided the event  
e) Check creatine phosphokinase and ventilation/perfusion lung scan

**Answer and Discussion**

The answer is d.

**Objective:** Identify and manage a tension pneumothorax.

The patient has signs of a left-sided tension pneumothorax on the left as evidenced by a rapid deterioration of respiratory and hemodynamic status, decreased air entry on the left and tracheal deviation to the right. Tension pneumothorax is a clinical diagnosis and does not require radiographic confirmation prior to intervention. Urgent decompression of the pneumothorax is essential and is achieved by needle thoracostomy in the second intercostal space on the side of the pneumothorax. No other intervention will correct the hemodynamic compromise and may actually worsen it.

**Question 15**

A 35-year-old man who smoked one pack per day for 20 years was diagnosed with AIDS 4 years ago. He is allergic to sulfa and receives aerosolized pentamidine for *Pneumocystis jiroveci* pneumonia prophylaxis. He was doing well until a few days before admission, when he started developing progressive shortness of breath. His respiratory status deteriorated quickly, requiring intubation and mechanical ventilation. The next day, the respiratory therapist called because the patient had developed high airway pressures. This was also associated with a drop in the patient’s BP and arterial oxygen saturation. When you examine the patient, you notice decreased air entry on the left side with a deviation of the trachea to the right.

What should you do next?

a) Order chest radiography  
b) Add 10 cm H$_2$O of positive end-expiratory pressure  
c) Insert a chest tube in the right lung  
d) Insert a large-bore needle in the second intercostal space on the left  
e) Place the patient on his side with the left side down

**Answer and Discussion**

The answer is a.

**Objective:** Identify complications from a thoracentesis.

A thoracentesis is a relatively safe procedure. The major complications are pneumothorax, hemothorax, hemorrhage, and re-expansion pulmonary edema. This patient developed re-expansion pulmonary edema, presumed secondary to rapid change in intrathoracic pressure leading to microvascular injury. The patient develops pulmonary edema following drainage of a large volume of a chronic pleural effusion. Intrapleural pressure monitoring could be used to minimize the risk of this occurring. The physical examination findings are not consistent with hemothorax or pneumothorax.

**Question 16**

A 44-year-old man with type I diabetes, end-stage renal disease, and diabetic retinopathy develops chest pain and low-grade fever (38.5°C) 5 days after a unilateral below-knee amputation done for a poorly healing ulcer. He had been recovering in a nursing facility but has missed two dialysis sessions due to low BP and has refused prophylactic subcutaneous heparin. After a 500-mL bolus of saline in the ED, he is transferred to the intensive care unit for further management. On examination, he is distressed, with a HR 96 beats/minute, respiratory rate 28 breaths/minute, oxygen saturation on room air is 86%, and BP 82/50 mmHg. The examination is difficult due to his obesity, but does not reveal an obvious cause for his hypotension; the surgical site looks clean and intact, and an indwelling tunneled catheter in his right neck also looks unremarkable. A 12-lead ECG shows nonspecific ST- and T-wave abnormalities but no definite signs of ischemia. A central venous catheter is inserted to guide decision-making. Measurement of the a-wave reveals a central venous pressure (CVP) of 19 mmHg; the tracing shows preserved waveforms except for loss of the y descent. Considering the findings of the central venous catheter,
which choice most effectively addresses the likely cause of shock in this patient?

a) Start broad-spectrum antibiotics; remove the tunneled catheter; and start fluids, pressor agents, and other modalities for likely septic shock using a “goal-directed therapy” approach

b) Consult cardiology service for a pericardiocentesis

c) Resuscitate more aggressively with crystalloids and consider thrombolytic therapy versus surgical consult for likely massive pulmonary embolus

d) Urgent coronary angiogram with percutaneous coronary intervention and placement of intra-aortic balloon pump, if needed, in preparation for mitral valve repair

e) Start dobutamine and prostacyclin for right ventricular failure

**Answer and Discussion**

The answer is b.

**Objective:** Identify and manage cardiac tamponade as a cause of shock.

Pericardiocentesis with drainage of effusion leads to cardiac tamponade. Recognition of the right-sided waveforms and their derangements in disease is useful when prioritizing diagnostic tests, when decisions must be made urgently, or when there are conflicting data. It is important to be familiar with expected values for filling pressure (typically 4 to 8 mmHg for CVP). The differential diagnosis for elevated CVP in the setting of shock includes acute right heart failure (massive pulmonary embolism, right ventricular infarction), pericardial disease, and acute left heart disease (large myocardial infarction, acute mitral regurgitation, acute ventricular septal defect). The finding of an attenuated y descent is characteristic of cardiac tamponade because there is equalization of pressures between the atria and ventricles, which impairs atrial emptying. In uremic pericarditis, the expected tachycardia may be absent due to autonomic insufficiency; likewise, the ECG may not reveal diffuse ST segment elevations. In the early stages of septic shock, there is usually hypovolemia, but the CVP should be low. Massive pulmonary embolism and acute mitral valve rupture may cause hypotension but should not preferentially affect the y descent.

**Question 17**

An 18-year-old, 58-kg female asthmatic patient is intubated in the ED for respiratory failure from status asthmaticus. Her initial ventilator settings are assist-control mode with a set rate of 18, tidal volume 500 mL, FiO₂ 1.0, and positive end-expiratory pressure 5 cm H₂O. On arrival to the intensive care unit, she is in shock, with systolic BP of 74 mmHg. Examination reveals an extremely agitated woman with diaphoresis, distended neck veins, and respiratory rate of 36 breaths/minute and SpO₂ of 88%. Her breath sounds are markedly diminished but equal bilaterally. In addition to aggressive volume resuscitation and ensuring adequate sedation, you should institute which of the following to reverse her hypotension prior to cardiac arrest:

a) Reduce her set rate to 10 breaths/minute.

b) Administer 6 mg of pancuronium IV push

c) Insert a 16-gauge angiocatheter needle into the second intercostal space bilaterally.

d) Increase the inspiratory flow rate

e) Administer paralytics, and then remove her from the ventilator for 30 to 60 seconds

**Answer and Discussion**

The answer is e.

**Objective:** Recognize common complications of mechanical ventilation.

It is important to recognize common complications of mechanical ventilation in patients with severe airways obstruction. Development of intrinsic positive end-expiratory pressure (PEEP; auto-PEEP, dynamic hyperinflation) is one of the most significant complications. Intrinsic PEEP can result in patient-ventilator dyssynchrony, agitation, difficulty weaning, ventilation/perfusion mismatch, barotrauma, and impairment of right-sided venous return leading to cardiovascular collapse. An important consideration is tension pneumothorax, but typically the patient will exhibit physical examination signs such as tracheal deviation, unilateral decrease of breath sounds, and hyperresonance on percussion. Prevention of intrinsic PEEP is achieved by maximizing alveolar emptying, either by decreasing airways resistance (bronchodilators) or by increasing expiratory time. Techniques to increase expiratory time include ensuring a low respiratory rate using sedatives and, if necessary, paralytics, decreasing the inspiratory time by adjusting the flow rate or the I:E ratio, and setting the mandatory rate on the ventilator as low as possible. Hypercapnia is acceptable to achieve this goal. However, none of these techniques is generally rapid enough to be helpful when hypotension is already established. Temporarily disconnecting the endotracheal tube from the ventilator circuit, and therefore the effects of positive-pressure ventilation, is the quickest way to effectively restore BP.

**Question 18**

The female patient has been stable for 3 days. She is being treated with clarithromycin, ceftriaxone, Solu-Medrol, bronchodilators, and lorazepam. She became agitated overnight and was given haloperidol. Suddenly, she became hypotensive, and her pulse was not palpable. The ECG tracing is shown (ventricular tachycardia).
The patient is still hypotensive, her WBC count is 15,000/mm³, and her hemoglobin is 10 g/dL. You will do all of the following, except
a) Perform cardioversion-defibrillation
b) Administer magnesium intravenously
c) Temporarily disconnect the patient from the ventilator circuit
d) Correct hypocalcemia, hypokalemia, and alkalosis

**Answer and Discussion**

**Objective:** Identify important drug–drug interactions in critical care medicine.

This question highlights an important topic in critical care medicine–drug interactions. An important effect of drug interaction in the critically ill patient is hypotension caused by partial adrenal insufficiency. This drug interaction occurs in patients receiving drugs that can increase the activity of the P450 system (e.g., phenytoin, phenobarbital). When the P450 system is activated, the metabolism of steroids increases, creating a state of partial adrenal insufficiency. This drug interaction should be suspected in patients receiving medication that can increase the metabolism of the P450 system and who present with persistent hypotension in the absence of other etiologies. An increasingly recognized offender is etomidate, a medication commonly used in rapid-sequence intubation, which blocks adrenal steroid production directly.

Macrolides and haloperidol, drugs commonly used in the intensive care unit, are known to increase the QT interval. Patients with underlying ischemic heart disease and electrolyte and acid–base abnormalities are more likely to develop this complication. Phenothiazines, antiarrhythmic medications, tricyclic antidepressants, and antipsychotic agents and cisapride can prolong the QT interval as well.

**Question 19**

A 34-year-old homeless man is evaluated in the ED, where he was brought after being found obtunded. His medical history is remarkable for HIV and polysubstance abuse. Examination reveals an obtunded man with no focal neurologic signs. He is afebrile, with HR of 104 beats/minute, respiratory rate 22 breaths/minute, and BP 96/68 mmHg. His sodium is 148 mmol/L, potassium 4.0 mmol/L, chloride 115 mmol/L, bicarbonate 10 mmol/L, blood urea nitrogen 47 mg/dL, creatinine 1.3 mg/dL, and glucose 58 mg/dL. Serum albumin is 2.5 g/dL. ABG on room air reveals a pH of 7.12, CO₂ 28 mmHg, and PaO₂ 94 mmHg. His serum lactate is 2.2 mmol/L. Which of the following is true in your evaluation of this patient?

a) He has an anion gap (AG) metabolic acidosis with appropriate respiratory compensation.
b) He has an AG metabolic acidosis and inappropriate respiratory compensation.
c) He has an AG metabolic acidosis, a metabolic alkalosis, and inappropriate respiratory compensation.
d) He has an AG metabolic acidosis, a non-AG metabolic acidosis, and inappropriate respiratory compensation.
e) He has an AG metabolic acidosis, a non-AG metabolic acidosis, and appropriate respiratory compensation.

**Answer and Discussion**

**Objective:** Identify acid–base disorders.

Interpretation of ABG abnormalities is a key skill in critical care medicine. Systematic evaluation of the ABG results often leads to unsuspected findings, such as triple acid–base disorders or respiratory insufficiency. In this case, use of “Winter formula” allows assessment of the adequacy of the respiratory response to the primary acidosis:

\[
\text{Expected, } PCO₂ = (\left[1.5 \times \text{measured HCO}_₃\right] + 8) \pm 2
\]

To evaluate for the presence of two metabolic processes, one must compare the change in AG versus the change in bicarbonate. In the setting of hypoalbuminemia, the expected AG should be reduced by about 2.5 mEq/L for every 1 g/dL decrease in serum albumin, with normal AG in most laboratories ranging from 6 to 12 mEq/L.

Using 12 mEq/L as the AG normal value, in the previous example, the expected AG should be \([12 \text{ mEq/L} - (2.5 \times 1.6 \text{ g/dL decrease of albumin})] = 8 \text{ mEq/L} \). However, the calculated gap is 23 mEq/L. Thus, the AG has increased by 15 mEq/L over the expected value. Has there been an equivalent (equimolar) change in the bicarbonate level? In this case, the bicarbonate has decreased from 24 mEq/L (normal) to 10 mEq/L = 14 mEq/L. Therefore, all the change in bicarbonate level can be explained by the unmeasured anions. If the change in bicarbonate were more severe than that predicted by the change in AG, a superimposed nongapped acidosis would be suspected; if less profound, then a concomitant metabolic alkalosis should be considered.

**Question 20**

The male patient in question 19 is diagnosed with ethylene glycol intoxication, after it is noted that there is an osmolar gap present, and treated with ethanol infusion to competitively prevent metabolism of ethylene glycol to formaldehyde and formic acid. He avoids renal failure; however, on the second day in the intensive care unit, he develops a fever (39.5°C) and hypoxemia. Chest imaging shows bilateral diffuse infiltrates. His hemoglobin is stable at 8.7 g/dL. Over the ensuing 24 hours, he develops refractory hypoxic respiratory failure, requiring intubation. The most appropriate next step now includes

a) Start ceftriaxone and azithromycin
b) Start piperacillin-tazobactam, tobramycin, and vancomycin
c) Start piperacillin-tazobactam, azithromycin, and vancomycin
d) Start piperacillin-tazobactam and ciprofloxacin
e) Perform bronchoalveolar lavage to look for infection with *P. jiroveci*.
Answer and Discussion
The answer is c.

Objective: Identify complication of pneumonia among hospitalized, critically ill patients.

The correct answer depends on recognizing that the likely diagnoses are community-acquired pneumonia or aspiration pneumonitis with acute respiratory distress syndrome (ARDS). The development of pneumonia after 48 hours in the hospital, or within 3 months of a prior hospitalization, classifies as hospital-acquired pneumonia, mandating consideration of antipseudomonal antibiotics as part of the initial therapy. However, in community-acquired pneumonias, there are mitigating factors that may provide indications for more extensive antimicrobial coverage. In patients admitted to the intensive care unit, there is a high likelihood that resistant organisms will be present, including drug-resistant pneumococcus, Legionella species, and community-acquired methicillin-resistant Staphylococcus aureus (MRSA). Therefore, patients with severe community-acquired pneumonia should be treated with a combination of a potent antipseudomonal cephalosporin and either an advanced macrolide or quinolone. In patients with risk factors for Pseudomonas aeruginosa, including immunosuppression, significant structural lung disease [cystic fibrosis (CF), bronchiectasis, or repeated exacerbations of COPD that require frequent glucocorticoid and/or antibiotic use], probable aspiration, or multiple medical comorbidities, an antipseudomonal penicillin should be used. The use of vancomycin in severe community acquired pneumonia is hotly debated, but should generally be reserved for individuals with gram-positive organisms on sputum examination or risk factors for community-acquired MRSA (recent influenza-like illness, prior antibiotic therapy, end-stage renal disease, or injection drug abuse).

Although this individual may have AIDS, the onset of Pneumocystis pneumonia (PCP) is usually subacute. Although the sensitivity of bronchoalveolar lavage for diagnosing PCP is excellent in HIV (97% to 99%), it is less sensitive in the non-HIV population.

Question 21

A 48-year-old man presents with his wife, who complains of her husband’s snoring. Further history reveals snoring for at least 20 years, with restless sleep observed by the wife. The patient denies any problem sleeping, but on direct questioning, he admits to dry mouth and headaches in the morning and sleepiness throughout the day. He confesses that he almost fell asleep at the wheel of the car several times, but he ascribes this to long hours and overwork. Physical examination reveals a stocky man, somewhat overweight, but the examination is otherwise normal. Which would be the most appropriate next step?

a) Sedative medication for the patient to ensure that he gets a better night’s sleep
b) Sedative medication for the wife so that she can sleep through his snoring
c) Sending the patient for sleep studies
d) Advising a weight loss program and following up in 6 months
e) Advising stopping smoking because doing so has been proven to stop snoring in more than 50% of patients

Answer and Discussion
The answer is c.

Objective: Understand the diagnostic evaluation of excessive daytime sleepiness.

This man’s clinical picture suggests obstructive sleep apnea. Patients with unexplained excessive daytime sleepiness deserve further evaluation, and the diagnosis of obstructive sleep apnea requires examining a patient during sleep with a polysomnogram.

Question 22

A 21-year-old male patient comes to the emergency room with itching and jaundice. He has a long history of recurrent pulmonary infections, chronic sinusitis, a recent diagnosis of diabetes, and two prior admissions for pancreatitis. Liver biopsy confirms cirrhosis. In regard to this patient’s diagnosis, which of the following is the most accurate statement?

a) The disease is autosomal dominant in inheritance.
b) Alcohol abuse is a common cause for this disease.
c) The most common cause of death is liver failure.
d) A sweat chloride test result of <70 mEq/L is highly sensitive for diagnosis.
e) Digital clubbing is often seen in patients.

Answer and Discussion
The answer is e.

Objective: Understand the clinical presentation of CF.

CF is a fatal autosomal recessive, multisystem disease that usually presents with persistent pulmonary infection, pancreatic insufficiency, and sinusitis. Additional features include pancreatitis, infertility, diabetes, deep vein thrombosis (DVT), and, rarely, biliary cirrhosis. Although CF is generally diagnosed in infants and children, patients may present later in life with atypical symptoms. One large retrospective cohort study of 1,051 patients with CF found that 7% received a diagnosis at age 18 years or older. Progressive lung disease and eventual respiratory failure continue to be the major causes of morbidity and mortality. The sweat chloride test is the gold standard for CF diagnosis, and a result of >70 mEq/L distinguishes CF from other lung diseases. More than 95% of men with CF are infertile, mostly due to incomplete development of the Wolffian structures, particularly the vas deferens. Digital clubbing is often seen in patients with moderate to severe disease.
having dinner complains of pruritus and appears flushed. He states that he has felt like this previously, is allergic to peanuts, and thinks that there may have been nuts in the cake that he just ate. He states that he does not feel too bad and that this is nothing like the last time, when he had some difficulty with breathing; he says that he will go lie down in the call room for awhile and he should be fine. You assess his airway and breathing, and they are normal. What would be the most appropriate next step?

- a) Let him go and rest; you will go and see a patient who has just arrived and then check on the medical student in an hour or so
- b) Keep him with you so that you can take him to the ED if he starts to feel any worse or has any pulmonary symptoms
- c) Take him to the ED, and administer 1 mL of 1:10,000 epinephrine intravenously with cardiac monitoring
- d) Take him to the ED, recruit assistance from the medical team there, have his airway and cardiopulmonary status assessed and monitored, obtain intravenous access, and administer 0.5 mL of 1:1,000 epinephrine subcutaneously or intramuscularly as soon as possible
- e) Give him an antihistamine that you happen to have in your pocket, and keep him with you so that you can take him to the ED if he starts to feel any worse or has any pulmonary symptoms

**Answer and Discussion**

The answer is d.

**Objective:** Understand the clinical presentation and treatment of anaphylaxis.

Anaphylaxis can occur within 5 to 60 minutes after exposure to an allergen. This medical student is at risk for anaphylaxis and death. He needs a controlled and monitored environment. Epinephrine is the drug of choice; fatality rates are highest in patients in whom epinephrine administration is delayed. Severe airway edema, severe bronchospasm, or hypotension requires intravenous administration of 0.5 to 1.0 mL of epinephrine. Mild or moderate symptoms without laryngeal edema, bronchospasm, or hypotension should be treated with 0.3 to 0.5 mL of 1:1,000 epinephrine subcutaneously or intramuscularly.

**Question 24**

A solitary pulmonary nodule is seen in the right upper lobe on the chest radiograph and CT scan of a 60-year-old woman with a history of stage IB breast cancer. She underwent right lumpectomy 20 years ago without any further treatment. Regularly scheduled follow-up mammograms have been negative to date. She has a 20 pack-year history of tobacco use and quit smoking 7 years ago. The chest CT scan shows a 1.2-cm mass with smooth borders, popcorn calcification, and a density of 214 Hounsfield units. What is the next step in management?

- a) Follow up with serial CTs to evaluate change in size of the nodule
- b) Excise the mass for pathologic diagnosis
- c) Obtain a fluoro-2-deoxyglucose–PET scan
- d) Perform percutaneous needle aspiration and biopsy
- e) Order an MRI of the chest

**Answer and Discussion**

The answer is a.

**Objective:** Understand the diagnostic evaluation of a solitary pulmonary nodule.

A solitary pulmonary nodule is a lesion that is usually <3 cm and surrounded by pulmonary parenchyma. Larger lesions are more likely to be malignant than smaller lesions. Malignant lesions tend to have more irregular and spiculated borders as compared to the smooth and discrete border of benign lesions. Increased density on CT argues against malignancy with the cutoff of >164 Hounsfield units for benign and <164 Hounsfield units for malignant lesions. Certain patterns of calcification such as “popcorn” calcification, laminated (centric) calcification, central calcification, and diffuse homogeneous calcification suggest that a lesion is benign, whereas reticular, punctate, amorphous, or eccentric calcifications raise the concern for malignancy. A nodule with a low probability of being malignant may be followed with serial chest CT scans. A nodule that is ≥1 cm and has an intermediate probability of being malignant should be evaluated by fluoro-2-deoxyglucose–PET. If the nodule is negative by PET, they too can be followed with serial chest CT scans; if the PET is positive, the nodule should be excised. A nodule that is <1 cm and has an intermediate probability of being malignant can be followed by serial chest CT scans. Any nodule that has a high probability of being malignant should be excised. For nodules ≥4 mm, serial CT scans are not required if the patient is at low risk. Patients who are at high risk or have nodules >4 mm should have follow-up chest CT scanning.

**Question 25**

A 30-year-old man, who has been your patient for several years, presents for his regular checkup. He is known to have dextrocardia. He suffers from recurrent sinusitis and, for years, has had mucopurulent sputum and episodic hemoptysis. He has digital clubbing and bilateral crackles on auscultation of the lungs. With which of the following conditions are this patient's symptoms most consistent?

- a) α1-Antitrypsin deficiency
- b) Kartagener syndrome
- c) Young syndrome
- d) Williams-Campbell syndrome
- e) Yellow nail syndrome

**Answer and Discussion**

The answer is b.

**Objective:** Understand the clinical presentation and etiologies of bronchiectasis.

The pulmonary symptoms and signs are suggestive of bronchiectasis. Kartagener syndrome consists of dextrocardia, sinusitis, and bronchiectasis. Young syndrome is defined
as obstructive azoospermia; approximately 20% to 30% of patients have bronchiectasis. Early panacinar emphysema, as well as bronchiectasis, may develop in patients with $\alpha_1$-antitrypsin deficiency. Yellow nail syndrome is characterized by the triad of lymphedema, pleural effusion, and yellow discoloration of the nails; 40% of patients have bronchiectasis. Patients with Williams-Campbell syndrome have a deficiency of the bronchial cartilage of medium-size airways, which dilate and can be complicated by bronchiectasis.

**Question 26**

Which of the following statements regarding complications of mechanical ventilation in patients with ARDS is false?

a) Barotrauma is often a significant direct cause of death in ARDS patients.

b) Tissue breakdown, excessive tidal volumes, and low airway pressures predispose to barotrauma.

c) Although often accompanied by nonspecific findings, nosocomial pneumonia is an important cause of morbidity and mortality in ARDS patients, with a prevalence of approximately 55%.

d) The combination of a corticosteroid and a neuromuscular blocking agent used for paralysis in these patients can lead to a reversible myopathy.

e) Decreased radiolucency at the lung bases and the presence of the deep sulcus sign on a chest radiography are clues to the diagnosis of pneumothorax.

**Answer and Discussion**

The answer is a.

**Objective: Understand the management of ARDS.**

ARDS patients who are mechanically ventilated have an intensive care unit course complicated by barotrauma, nosocomial pneumonia, and multiple organ failure. Additional complications include deep vein thromboses, gastrointestinal bleeding, malnutrition, and side effects from sedatives and paralytics. Barotrauma occurs in a minority of ventilated patients (13% in one study), with barotrauma rarely directly causing death. The tissue breakdown seen in ARDS, high airway pressures, and high tidal volumes predispose to barotrauma. Barotrauma is evidenced by the development of pneumothorax, subcutaneous emphysema, pneumomediastinum, and interstitial emphysema. Increased radiolucency at the lung bases and the presence of the deep sulcus sign on a chest radiograph are clues to barotrauma and pneumothorax. Nosocomial pneumonia is present in 55% of patients with ARDS and is accompanied by nonspecific findings. The combination of a corticosteroid and a neuromuscular blocking agent has been associated with a reversible myopathy that takes several months to resolve.

**Question 27**

A 70-year-old man with a 10-year history of COPD comes to your outpatient office for routine follow-up. He is a current smoker with a 20 pack-year tobacco history. He has had two COPD exacerbations in the past year requiring hospitalization. His last episode was 1 month prior to this visit. He is currently on Advair 500/50 one puff twice a day and Albuterol aerosols as needed. His laboratory values show WBC count of 6.7/mm$^3$, hematocrit 50%, platelets 350,000 µL, a normal basic metabolic profile, and a normal echocardiogram. Vitals signs were normal with an SaO$_2$ of 92% at rest. SaO$_2$ drops to 89% on walking up two flights of stairs. His forced expiratory volume in 1 second (FEV$_1$)/forced vital capacity (FVC) is <70% predicted, and his FEV$_1$ is >50% but <80% predicted. All the following are indicated, except

a) Oxygen

b) Advise patient to quit smoking

c) Tiotropium

d) Pneumococcal vaccination

e) Influenza vaccination

**Answer and Discussion**

The answer is a.

**Objective: Understand the management of COPD.**

Infection is a frequent cause of COPD exacerbation. All patients with stable COPD should be offered pneumococcal vaccine, especially if they are 65 years or older, or with FEV$_1$ <40%. An influenza vaccine should be offered to all patients with COPD annually. All patients should be strongly encouraged to quit smoking because this can minimize exacerbations and retard the rate of FEV$_1$ decline. For all patients with COPD, a short-acting bronchodilator must be used on an as-needed basis and if that is insufficient to control symptoms, a regularly scheduled long-acting inhaled bronchodilator or a long-acting inhaled anticholinergic should be added. Patients who continue to have exacerbations despite being on optimal long-acting inhaled bronchodilators may require inhaled corticosteroids. Indications for continuous long-term oxygen therapy in COPD patients include an arterial partial pressure of oxygen (PaO$_2$) of ≤55 mmHg or arterial oxygen saturation (SaO$_2$) of ≤88%. If patients have cor pulmonale, right heart failure, or hematocrit >55%, oxygen is also warranted. Long-term oxygen therapy improves quality of life and increases survival in these patients.

**Question 28**

A 50-year-old cirrhotic male patient with a past medical history of smoking, substance abuse, and alcohol abuse presents with acute hemoptyis, wheezing, and fever. His examination shows a cachectic individual with diffuse wheezing and thermal burns on his fingers and thumbs. Chest radiograph shows diffuse alveolar infiltrates. Complete blood count shows a WBC count of 14,000/mm$^3$ with eosinophilia. In regard to this patient’s diagnosis, all the following are true, except

a) Expectoration of black sputum is frequently seen

b) He is at an increased risk for pulmonary infections

c) Fresh-frozen plasma is indicated

d) He is at higher risk for acquiring HIV

e) Pneumothorax may be frequently encountered
**Question 29**
A 65-year-old diabetic woman presents to the hospital with fever. On examination, her temperature is 38.5°C, HR 100 beats/minute, BP 120/70 mmHg, and respiratory rate 24 breaths/minute. On physical examination, she does not have a focus for infection. Laboratory studies reveal a WBC count of 12,500 cells/mm³, and urinalysis is positive for leukocyte esterase and nitrites. Urine culture and blood cultures are ordered. Which of the following terms most accurately describes her present condition?

a) Septic shock  
b) Systemic inflammatory response syndrome (SIRS)  
c) Sepsis  
d) Infection  
e) Bacteremia

**Answer and Discussion**

The answer is c.

**Objective: Understand the medical manifestations accompanying substance abuse.**

Crack lung may occur within 48 hours of smoking of cocaine, which presents as diffuse alveolar infiltrates, eosinophilia, and fever. Patients may present with pleuritic chest pain, dyspnea with even mild exertion, dry or productive cough, wheezing, and hemoptysis. Melanoptysis or expectoration of black sputum is seen from inhalation of black carbonaceous residue from inflammable substances that are typically used to set fire to crack. Finger burns are seen from handling crack pipes. Cocaine users are at an increased risk for pulmonary infections, malnutrition, HIV, and TB. Crack smokers often perform Valsalva maneuver after inhalation or exhale vigorously into each other’s mouths to augment the uptake of the drug, which may lead to the development of pneumothorax, pneumomediastinum, and pneumopericardium.

**Question 30**
A 55-year-old woman reports gradually increasing shortness of breath. On examination, respiratory rate is 24 breaths/minute, and she appears in mild distress, with difficulty breathing. BP is 138/89 mmHg. Expansion appears to be normal. Percussion is stony-dull in the right base and halfway up the right lung field, with diminished tactile fremitus, vocal resonance, and breath sounds in the same areas. Chest radiograph is consistent with the clinical suspicion of a pleural effusion. Which of the following statements about pleural effusion is true?

a) An exudative effusion is suggested by pleural fluid lactate dehydrogenase (LDH) more than one-third of the normal upper limit for serum.  
b) A transudative pleural effusion is suggested by a ratio of pleural fluid LDH to serum LDH of >0.6.  
c) Pulmonary emboli may be associated with both transudates and exudates.  
d) The pleural effusion associated with neoplastic disease is usually transudative.  
e) In a patient with a parapneumonic effusion, an indication for thoracostomy tube placement is a pleural fluid glucose level >50 mg/dL.

**Answer and Discussion**

The answer is c.

**Objective: Understand the spectrum of the sepsis syndrome and its associated definitions.**

The American College of Chest Physicians and the Society of Critical Care Medicine have defined this series of terms. This patient meets criteria for having SIRS, as well as clinical evidence of urinary tract infection; thus, the most accurate term for her condition would be sepsis. The terms infection or SIRS would not completely describe her condition. *Infection* is a microbial phenomenon characterized by an inflammatory response to the presence of organisms or to invasion of normally sterile host tissue by these organisms. *Bacteremia* is defined by the presence of viable bacteria in the blood. SIRS is a widespread inflammatory response defined by the presence of two or more of the following:

a) Temperature >38°C or <36°C  
b) HR >90 beats/minute  
c) Respiratory rate >20 breaths/minute or PaCO₂ <32 mmHg  
d) WBC count >12,000/mm³ or <4,000/mm³ or >10% bandemia

Sepsis is the presence of SIRS together with evidence of infection. *Severe sepsis* is the presence of sepsis associated with organ dysfunction, hypotension, or hypoperfusion. *Septic shock* is sepsis with hypotension despite adequate fluid resuscitation and the presence of lactic acidosis, oliguria, or acute mental status changes. Hypotension is defined as a systolic BP of <90 mmHg or a ≥40 mmHg decrease from baseline (in the absence of other causes for the decrease).

**Answer and Discussion**

The answer is c.

**Objective: Understand the diagnostic criteria of pleural effusions and their management.**

An exudative effusion is suggested by at least one of the following three criteria, whereas a transudate has none of these criteria:

a) Pleural fluid LDH more than two-thirds of the normal upper limit for serum  
b) A ratio of pleural fluid LDH to serum LDH of >0.6  
c) A ratio of pleural fluid protein to serum protein of >0.5

The pleural effusion associated with neoplastic disease is usually exudative. Pulmonary emboli are associated with both transudates and exudates. In a patient with a parapneumonic effusion, any of the following is an indication for thoracostomy tube placement:

a) Pleural fluid glucose level <50 mg/dL  
b) Presence of gross pus in the pleural space  
c) Organisms visible on Gram stain of the pleural fluid  
d) Pleural fluid pH <7.0 and 0.15 U lower than arterial blood pH
Question 31
A 56-year-old man asks for advice concerning a nodule seen on a chest radiograph obtained during a physical examination for a new job. Which of the following statements concerning a solitary pulmonary nodule is true?

a) It is a single, radiologically visible lesion that must be surrounded on all sides by pulmonary parenchyma.
b) The upper limit in size is 2 cm.
c) The type of malignancy most commonly presenting as a solitary pulmonary nodule is small cell carcinoma.
d) It may present with associated pleural effusion.
e) It may present with associated mediastinal lymphadenopathy.

Answer and Discussion
The answer is a.

Objective: Understand the diagnostic evaluation of a solitary pulmonary nodule.

The definition of a solitary pulmonary nodule is a single radiologically visible lesion that is within and surrounded on all sides by pulmonary parenchyma. It is not associated with potentially related pathology, such as pleural effusion or mediastinal lymphadenopathy. The upper limit of the size of a nodule may be 3 or 4 cm; larger lesions are considered masses. Adenocarcinoma most commonly presents as a solitary pulmonary nodule; small cell carcinoma usually presents as a central endobronchial lesion.

Question 32
A 76-year-old man admitted to a general medicine ward for pneumonia is found by a nurse to be unresponsive and without a palpable pulse or spontaneous breathing. As the first physician to the scene, you confirm the absence of pulse and respiration. You then ask the respiratory therapist to establish an airway and begin mask-bag ventilation. Meanwhile, leads are placed for cardiac monitoring. A subclavian central access line had already been placed 2 hours before the arrest. The initial rhythm seen is pulseless electrical activity at 70 complexes per minute. A Doppler ultrasound, operated by the nurse, is unable to detect a BP. Cardiopulmonary resuscitation is initiated. According to the American Heart Association guidelines on the advanced cardiac life support (ACLS) protocol, all the following steps are appropriate in the initial management of this patient, except

a) Give epinephrine, 1 mg intravenously
b) Order a draw of arterial blood for blood gas and chemistry
c) Begin synchronized direct-current cardioversion
d) Start intravenous fluid infusion after bolus
e) Order (but do not wait for) a portable chest radiograph and examine the patient for equal breath sounds bilaterally

Answer and Discussion
The answer is c.

Objective: Understand the implementation of ACLS measures.

This man is in cardiopulmonary arrest. Specifically, his electrical cardiac activity is pulseless electrical activity. All the choices are appropriate in the initial management of pulseless electrical activity, except synchronized direct-current cardioversion. In addition to pneumothorax, hypoxia, and hypotension, other causes of pulseless electrical activity that must be investigated in the initial management of these patients include cardiac tamponade, hypothermia, massive pulmonary embolism, drug overdose, hyperkalemia, severe acidosis, and massive myocardial infarction. Atropine may also be given in the event of bradycardia or relative bradycardia.

Question 33
A 78-year-old African American man is brought to the ED by his family. He is known to have a mild baseline dementia but still lives alone and has been able to carry out the basic activities of daily living. The family states that over the past 24 hours, he has become more confused. He has been unable to tolerate anything to eat or drink for the past 2 days and has been incontinent of very loose feces, with nausea, vomiting, and a low-grade fever. On examination, he appears frail and is oriented to person but not to place or time. Skin turgor is decreased. Lying BP and pulse are 128/68 mmHg and 80 beats/minute, and standing readings are 86/50 mmHg and 118 beats/minute, respectively. Examination of the respiratory, cardiovascular, and abdominal systems is normal. Which of the following statements concerning this man’s condition is true?

a) You expect a urinary Na+ level <25 mEq daily
b) You expect a urinary Na+ level >25 mEq daily
c) If the serum Na+ level is >150 mEq/L, vasopressin therapy should be considered
d) Because of the high risk of seizures in this case, prophylactic phenytoin should be started
e) You expect a urinary K+ level >20 mEq daily

Answer and Discussion
The answer is a.

Objective: Understand the pathophysiology of hypovolemia.

This man is hypovolemic from gastrointestinal fluid loss, as evidenced by orthostatic hemodynamic parameters. The serum sodium is likely to be raised and the urinary sodium low (<25 mEq daily) because the kidneys are attempting to retain sodium to compensate for the lost volume. In the same way, potassium is lost in vomiting and diarrhea, and the kidney attempts to compensate for this with a reduced urinary loss of potassium. Vasopressin may be used in the syndrome of central diabetes insipidus, which may also cause elevated
serum sodium, in the setting of lack of access to free water. However, the urine osmolality would be inappropriately low and the urine sodium would not be <25 mEq/day. Phenytoin is not indicated in this patient.

**Question 34**

A 65-year-old man is evaluated in your office for increasing shortness of breath. He states he can no longer walk up a flight of stairs without stopping. He denies fever, cough, chest pain or pressure, palpitations, orthopnea, or paroxysmal nocturnal dyspnea. Cardiovascular examination is unremarkable. There is no jugular venous distention or lower extremity edema. Pulmonary examination is unremarkable. He is a nonsmoker and a retired roofer. All the following statements concerning asbestos-induced lung disease are true, except

a) Most patients are asymptomatic for at least 20 to 30 years.
b) Cough, sputum production, and wheezing are the most common presenting symptoms.
c) Antinuclear antibody and rheumatoid factor may be present.
d) Cigarette exposure increases the risk of lung cancer associated with asbestos exposure.
e) Asbestos exposure increases the risk of lung cancer associated with cigarette smoke exposure.

**Answer and Discussion**

The answer is b.

**Objective: Understand the presentation of asbestosis.**

Dyspnea is the most common presenting symptom of asbestos-induced lung disease. Cough, sputum production, and wheezing are unusual presenting symptoms and, if present, tend to be due to cigarette smoke rather than asbestos exposure. It is true that antinuclear antibody and rheumatoid factor may be present, as may a raised erythrocyte sedimentation rate, but these are not clinically useful, being nonspecific and not related to disease severity. Because the use of asbestos has been ubiquitous, exposure can occur in a variety of occupational and non-occupational settings. As examples, exposure to asbestos results from involvement with mining and milling of the fibers and industrial applications of asbestos (e.g., work with textiles, roofing material, cement, friction materials, insulation, and shipbuilding). Asbestos-induced diseases are probably caused by the direct toxic effects of the fibers on pulmonary parenchymal cells as well as the release of various inflammatory mediators. Although some investigators have questioned the causal relationship between asbestosis and bronchogenic carcinoma, most studies have demonstrated a clear association between the two entities. The risk of lung cancer associated with exposure to both asbestos and cigarette smoke appears to be multiplicative. A 1979 report in the *Annals of the New York Academy of Science* showed that asbestos is associated with a sixfold increase, cigarette smoking with an 11-fold increase, and both cigarette smoke and asbestos exposure with a 59-fold increase in the risk of lung cancer.

**Question 35**

A 35-year-old woman presents with “recurrent chest infections.” She has a long history of asthma, but no other past medical history. She is a nonsmoker. In the past year, she has had several episodes of fever, malaise, and increased sputum production; twice, she had chest radiographs that showed infiltrates consistent with pneumonia. She now has recurrence of her symptoms. Chest radiography shows a parenchymal infiltrate in the left upper lobe and some atelectasis in the right base. Immediate skin test reactivity is positive for *Aspergillus* antigens, and she has serum antibodies to *Aspergillus fumigatus*. All the following statements concerning this woman’s condition are true, except

a) Proximal bronchiectasis is a feature of this disease.
b) Peripheral blood eosinophilia >55/mm³ is a feature of this disease.
c) Treatment should be an antimicrobial effective against *Aspergillus*.
d) Treatment should be a corticosteroid.
e) Serum IgE concentration >1,000 ng/mL is a feature of this disease.

**Answer and Discussion**

The answer is c.

**Objective: Recognize allergic bronchopulmonary aspergillosis (ABPA) as a cause of recurrent respiratory infection.**

ABPA is a hypersensitivity reaction in patients with asthma. Colonization with aspergilli occurs, rather than infection, and an antimicrobial is not indicated. Repeated episodes of bronchial obstruction, inflammation, and mucoid impaction can lead to bronchiectasis, fibrosis, and respiratory compromise. The pathogenesis of ABPA remains incompletely understood. Septated hyphae with acute dichotomous branching may be seen in the mucus-filled bronchial lumen, but fungi do not invade the mucosa. Aspergillus is cultured from the sputum in up to two-thirds of patients with ABPA, but hyphae may not be seen by direct microscopy. The clinical picture of ABPA is dominated by asthma complicated by recurrent episodes of bronchial obstruction, fever, malaise, expectoration of brownish mucus plugs, peripheral blood eosinophilia, and at times hemoptysis. Wheezing is not always evident, and some patients present with asymptomatic pulmonary consolidation. Treatment with a corticosteroid is very effective.

**Question 36**

A 39-year-old man presents with a nonproductive cough for 6 to 8 months. He states that the cough is very irritating because he frequently has to speak in public. Six months ago, he saw your colleague who he reports told him that it was a “postviral cough” and gave him an albuterol inhaler, which he used twice a day for 4 months. He discontinued it 2 months ago because it did not help the cough. Further history reveals nasal discharge, frequent throat clearing, and no wheezing or shortness of breath. The cough is worse in the...
morning but does not wake him from sleep; it is not associated with exercise. On examination, he appears generally well; his respiratory rate is 12 breaths/minute, and his pulse is 72 beats/minute. Nasopharyngeal mucosa has a cobblestone appearance, and the presence of secretions is noted. Auscultation of the lung fields is clear with no wheeze. Cardiovascular and abdominal examinations are normal. You observe his inhaler technique, and it is good. What would be the most appropriate next step in his treatment?

a) Obtain spirometry to investigate for asthma
b) Recommend restarting the albuterol in addition to an inhaled steroid
c) Start a trial of an H₂ blocker
d) Reassure him that the cough is probably postviral and have him return in 3 months if the cough has not resolved
e) Start a trial of a nasal steroid spray

**Answer and Discussion**

**The answer is c.**

**Objective: Identify common etiologies and treatment approach of chronic cough.**

Chronic cough is defined as a cough persisting for 3 weeks or longer. Postnasal drip, asthma, and gastroesophageal reflux represent approximately 90% of the causes found for chronic cough (and an even higher percentage in nonsmokers with a normal chest radiograph). The approach to such patients should include a detailed history, including a drug history to evaluate for the use of an ACE inhibitor (associated with cough in 3% to 20% of patients taking one), and an appropriate physical examination. This man has a history of nasal discharge and frequent throat clearing, and examination revealed nasopharyngeal mucosa with a cobblestone appearance and the presence of secretions, all of which suggest postnasal drip. Hence, a trial of a nasal steroid spray is the most appropriate next step. No clues are suggestive of gastroesophageal reflux, but if there were such clues, a trial of an H₂ blocker would have been a possible option. Postviral cough can persist for up to 8 weeks after the acute syndrome but should resolve after 6 months in this case. The diagnosis of asthma is not suggested as the most likely diagnosis here because no nighttime or exercise-related symptoms are present, and 4 months of twice daily albuterol with a good technique had no effect on the symptoms. Therefore, persisting with albuterol and adding an inhaled steroid are not indicated, and at this point, spirometry would not be the best choice.

**Question 37**

A 39-year-old woman presents to the ED with shortness of breath and chest pain. She reluctantly confesses to smoking two packs of cigarettes per day, although she had told her primary care doctor that she had stopped smoking. The only medication she is taking is an oral contraceptive. The chest pain is sharp and “catches” when she takes a deep breath. She has no fever, cough, or sputum production. She had a history of DVT approximately 6 months ago, for which she was treated with warfarin for 3 months. Her left calf has remained a little swollen since the incident of DVT. On physical examination, she is breathing uncomfortably and rapidly at a rate of 28 breaths/minute; pulse is regular at 110 beats/minute. The trachea is central, percussion is resonant, and breath sounds are normal in all areas. The chest pain is not produced on palpation, although it occurs on deep inspiration. You highly suspect that she may have a pulmonary embolus. All the following statements concerning the diagnosis of pulmonary embolus are true, except

a) In this case, a high-probability perfusion scan would indicate a high likelihood of pulmonary embolus.
b) In this case, a low-probability lung scan does not exclude the diagnosis of pulmonary embolus.
c) A raised D-dimer (>500 ng/mL) is highly specific for the diagnosis of pulmonary embolus.
d) Pulmonary angiography is the gold standard.
e) Echocardiography has a low sensitivity.

**Answer and Discussion**

**The answer is c.**

**Objective: Recognize the utility and limitations of diagnostic tests for pulmonary embolism.**

An elevated D-dimer level (>500 ng/mL) is present in the majority of patients with pulmonary embolus, but raised levels are also found in malignancy and postsurgery. Therefore, a raised D-dimer level is not specific for pulmonary embolus. A D-dimer value <200 ng/mL contributes to excluding the diagnosis of pulmonary embolus, with a negative predictive value of 97% when combined with a nondiagnostic lung scan. This patient has a high pretest probability of pulmonary embolism based on her risk factors [age >35, oral contraceptives, tobacco use, prior history of venous thromboembolism (VTE)], therefore a high probability perfusion scan would confer an even higher post-test probability of pulmonary embolism. However, a low probability perfusion scan would not exclude pulmonary embolism in this high-risk individual. Pulmonary angiography is still considered the gold standard; however, the noninvasive, chest CT with contrast is very sensitive and specific. According to McConnell et al. in a 1996 paper in the *American Journal of Cardiology*, transthoracic echocardiography with McConnell sign (right ventricular akinesia of the mid-free wall but normal motion of the apex) is stated to have a specificity of 97%, however, it is not a very sensitive test at 77%.

**Question 38**

A 63-year-old man with severe COPD presents to the ED with severe respiratory distress. ABG measurement is obtained as follows:

<table>
<thead>
<tr>
<th>Current</th>
<th>1 Mo Ago (Office Visit)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PaO₂</td>
<td>51 mmHg</td>
</tr>
<tr>
<td>PCO₂</td>
<td>73 mmHg</td>
</tr>
<tr>
<td>pH</td>
<td>7.25</td>
</tr>
</tbody>
</table>

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He continues to deteriorate despite maximal therapy, and mechanical ventilation is instituted.

Which of the following ABG values would be most desirable for this patient?

<table>
<thead>
<tr>
<th>PAO₂</th>
<th>PACO₂</th>
<th>PH</th>
<th>FIO₂</th>
<th>SAO₂</th>
</tr>
</thead>
<tbody>
<tr>
<td>a)</td>
<td>91</td>
<td>62</td>
<td>7.31</td>
<td>40%</td>
</tr>
<tr>
<td>b)</td>
<td>55</td>
<td>42</td>
<td>7.43</td>
<td>50%</td>
</tr>
<tr>
<td>c)</td>
<td>65</td>
<td>50</td>
<td>7.37</td>
<td>40%</td>
</tr>
<tr>
<td>d)</td>
<td>65</td>
<td>40</td>
<td>7.47</td>
<td>40%</td>
</tr>
</tbody>
</table>

**Answer and Discussion**

The answer is c.

**Objective: Understand gas exchange parameters in advanced COPD.**

The goal of mechanical ventilation in patients with COPD exacerbation is to achieve an arterial oxygen tension (PaO₂) of 60 mmHg. Although higher levels increase the risk of oxygen toxicity, they do not increase tissue oxygenation. Relative, regional intrapulmonary hypoxia due to damaged alveolar gas exchange causes compensatory pulmonary vasculature vasoconstriction to minimize perfused dead space. Increasing oxygen tension with increased inspired oxygen fraction will relieve this compensation and cause increased dead space, potentiating hypercapnia. PaCO₂ should be brought as close to the baseline value (i.e., the value recorded when the patient was compensated) but not necessarily normalized. Prolonged mechanical ventilation to achieve lower PaCO₂ will reverse the renal compensation for his chronic hypercapnic state and cause an acute metabolic alkalosis on cessation of mechanical ventilation. As demonstrated by his normal pH at elevated PaCO₂ level of 50, renal compensation will remain intact.

**Question 39**

A 21-year-old male college student who was found confused and disruptive by the dorm security staff is brought to the ED. He states that he has no complaints, is not tired, and is “getting ready to party for 8 more hours.” On examination, he is agitated, HR is 113 beats/minute, BP is 155/96 mmHg, respiratory rate is 19 breaths/minute, and temperature is 37.1°C. His pupils are dilated. Heart examination reveals regular tachycardia, and an ECG confirms sinus tachycardia. A urine drug screen is most likely to be positive for which of the following?

a) Nicotine  
b) Cocaine  
c) Opiates  
d) Amphetamines  
e) Hallucinogens

**Answer and Discussion**

The answer is d.

**Objective: Recognize the symptoms of common drugs of abuse.**

The use of amphetamines as drugs of abuse has increased markedly since 1975. This use affects myriad systems, resulting in a wide range of symptoms that may make it a difficult addiction to recognize. The drug is known to cause a massive release of dopamine in the brain, resulting in agitation, anxiety, delirium, hallucinations, and death. In addition, it causes a decrease in N-acetylaspartate in the frontal lobes and basal ganglia that may explain the chronic central nervous system side effects, such as lasting psychosis after its use is stopped and choreoathetoid movements. A high index of suspicion is necessary to make an early diagnosis. Nicotine does cause mild stimulant effects through its hepatic glucose release and epinephrine release, however, is unlikely to cause hyperadrenergic states to the degree demonstrated in this vignette. Hallucinogens can be divided into three broad categories: psychedelics (i.e., LSD), dissociatives (i.e., ketamine, phencyclidine), and deliriants (i.e., belladonna). These classes of psychoactive drugs have in common that they can cause subjective changes in perception, thought, emotion, and consciousness. Unlike other psychoactive drugs, such as stimulants and opioids, these drugs do not merely amplify familiar states of mind, but rather induce experiences that are qualitatively different from those of ordinary consciousness.

**Question 40**

A 67-year-old man presents to your office concerned about his health. Two of his friends have developed lung disease from dusts they inhaled in their workplace. He wonders if his lungs are alright since he had worked in several dusty places, including the shipyards for 20 years followed by foundry work for another 20 years. He is a prior smoker who is currently asymptomatic. He takes amlodipine 5 mg daily for mild hypertension. His vital signs are normal. Physical examination is normal except for decreased breath sounds on lung auscultation. Chest radiography reveals mild hilar adenopathy with eggshell calcification and multiple small upper lobe nodules. Which of the following is the most appropriate next step?

a) Tuberculin skin test  
b) CT scan of the chest  
c) Begin inhaled corticosteroids  
d) Begin systemic corticosteroids  
e) Reassurance

**Answer and Discussion**

The answer is a.

**Objective: Recognize the increased risk for pulmonary infections in chronic silicosis.**

Exposure to crystalline silica occurs when silica-containing rock and sand are encountered. This most commonly occurs in occupations associated with construction, mining, quarrying, drilling, and foundry work. Inhalation of crystalline silica can lead to a fibronodular parenchymal lung disease known as silicosis. This most commonly occurs in a form known as chronic or simple silicosis. Individuals with chronic silicosis typically have had more than 20 years...
of silica exposure. They are frequently without symptoms, although shortness of breath and cough can develop. Their disease is thus recognized radiographically as multiple small nodules with an upper lobe predominance. Hilar adenopathy with “eggshell” calcification can be seen. Individuals with silicosis are known to have a higher incidence of mycobacterial infections. All patients with silicosis should receive a standardized intradermal tuberculin skin test. If positive (>10 mm induration) and there is no sign of active infection, then treatment for latent TB should be administered. If there is evidence of active TB, then a standard treatment regimen including rifampin should be administered. Treatment for nontuberculous mycobacterium is no different in those with silicosis.

**Question 41**

A 36-year-old woman presents to your office with complaints of intermittent shortness of breath, cough, and wheeze of 6 months in duration. She notes that her symptoms are worse during the week than on the weekend and were relieved during a recent vacation. She is a nonsmoker with no prior illnesses who works as a spray-painter in an auto body shop. She does not take any regular medications. She does report occasional use of marijuana. She drinks alcohol socially. Her vital signs and examination, including her lung examination, are normal. Chest radiography is normal. Spirometry with methacholine challenge test reveals obstruction with bronchodilator response. Which of the following is most appropriate next step in this patient’s management?

- a) Skin testing
- b) Inhaled corticosteroids
- c) CT of the chest
- d) Peak flow recordings at home and at work
- e) Serum ACE level

**Answer and Discussion**

The answer is d.

**Objective:** Identify and diagnose occupational asthma.

There are over 250 exposures known to cause occupational asthma. The diagnosis requires the presence of asthma (symptoms and pulmonary function testing), the recognition of an exposure (history, skin testing, RAST testing), and a work-related pattern to the symptoms. The cornerstone of therapy is avoidance of the exposure. Preexisting asthma may be made worse by the exposure, or asthma can be of new onset related to exposure of concern. In this case, the history alone provides recognition of exposure, so skin testing is not necessary. A work-related pattern should be established by peak flow recordings at home and at work. If removal from the offending agent is not possible, treatment should be directed similar to conventional asthma with step-up therapy based on symptoms. Therefore, intermittent short-acting inhaled bronchodilators would be first-line, prior to initiation with inhaled corticosteroids. There is no indication for a CT chest to establish the diagnosis.

Sarcoidal granulomas produce ACE, and ACE levels are elevated in 60% of patients with sarcoidosis. However, the value of serum ACE levels in diagnosing or managing sarcoidosis remains controversial.

**Question 42**

A 37-year-old man comes into your office complaining of chest tightness, cough, and wheezing for the past 2 days. His asthma has been well controlled with low-dose fluticasone inhaled twice a day and albuterol metered dose inhaler as needed, which he requires only about twice a month. He recently strained his calf during a basketball game and began using ibuprofen for the pain. Past medical history is significant for sinus surgery 3 years prior to remove nasal polyps.

Physical examination is significant for a healthy appearance and normal vital signs. Nasal polyps are appreciated bilaterally. Chest auscultation reveals diffuse wheezing. His musculoskeletal examination reveals diffuse rhinitis. His musculoskeletal examination is normal. Which of the following should you recommend next?

- a) Start moderate-dose inhaled fluticasone
- b) Limited CT scan of the sinuses
- c) Discontinue use of nonsteroidal anti-inflammatory drugs (NSAIDs)
- d) Allergy testing for seasonal allergens

**Answer and Discussion**

The answer is c.

**Objective:** Recognize aspirin exacerbated respiratory disease (AERD).

The patient’s presentation is highly suggestive of aspirin (ASA) exacerbated respiratory disease (AERD). His history of recurrent nasal polyps requiring surgery, asthma, and loss of asthma control after exposure to ASA or other NSAIDs is known as Samter triad. Ingestion of any NSAID that inhibits COX-1 temporarily increases formation or release of mediators resulting in exacerbation of disease in the respiratory tract.

The clinical setting in which the physician should be most suspicious of AERD is in an asthmatic patient with formation (often relentless) of nasal polyps and pansinusitis confirmed by imaging procedures. Ingestion of ASA or NSAIDs can induce combinations of intense rhinorrhea, nasal congestion, injection of the conjunctivae, laryngospasm, and bronchospasm.

Avoidance of ASA/NSAIDs is the foundation of therapy. The asthma should otherwise be managed according to current guidelines, which were recently updated in the National Asthma Education Program Export Panel Report 3.

While allergy testing and increasing the patient’s inhaled corticosteroid dose may both be considerations, neither would replace avoidance of NSAIDs. Sinusitis can result in loss of asthma control, and a CT scan of his sinuses would be an appropriate consideration but not until strict avoidance of ASA/NSAIDs has been recommended.
REFERENCES


Question 43

A 19-year-old female college student comes into the office during her winter break after her first semester at college for routine follow-up. She tells you that she has been using albuterol metered-dose inhaler 3 to 4 times a week during the last 3 months for intermittent chest tightness and wheezing. Her symptoms are promptly relieved after each use. She denies daily symptoms and nocturnal symptoms and has not had to limit her activities. Physical examination is normal. Which of the following is the next best step in the management of her asthma?

a) Recommend daily use of albuterol 4 times a day
b) Begin inhaled budesonide twice a day
c) Begin inhaled salmeterol twice a day
d) Perform a methacholine challenge

Answer and Discussion

The answer is b.

Objective: Understand “step-up” therapy for treatment of asthma.

Inhaled short-acting β-agonists (SABAs) taken as needed to treat symptoms are usually sufficient therapy for intermittent asthma when they are effective in relieving the infrequent symptoms and normalizing pulmonary function. Increasing use of SABA or the use of inhaled SABA >2 days a week for symptom relief (not including prevention of exercise-induced bronchospasm or using SABA for exacerbations caused by viral infections) generally indicates inadequate asthma control, and the patient should be considered to have persistent asthma. Daily long-term control medication is recommended for patients who have persistent asthma. The long-term control medication should be one with anti-inflammatory effects. Of the available medications, inhaled corticosteroids are the most effective single agents. This has recently been emphasized in the 2007 National Asthma Education and Prevention Program Export Panel Report 3, which suggests that inhaled corticosteroids be the first-line treatment.

Use of inhaled long-acting β-agonists like salmeterol without concomitant inhaled corticosteroids is not recommended. Scheduled use of SABA is also not recommended for management of chronic asthma.

The patient’s symptoms and appropriate relief with SABA are highly suggestive of a diagnosis of asthma. Were this diagnosis in question, a methacholine challenge could help rule out reactive airways disease as the cause of her symptoms because the negative predictive value of the tests is quite high.

SUGGESTED READING


Question 44

A 73-year-old man with smoking-associated emphysema has been treated with albuterol and ipratropium bromide metered-dose inhaler, periodic pneumonia vaccination, and annual influenza vaccination for the past 10 years. He comes into the office complaining of slowly progressive dyspnea on exertion that prevents him from walking 100 feet and that has worsened over the past year. He denies fevers, cough, or sputum production. He quit smoking 11 years earlier.

He is a thin man who appears comfortable at rest. His breath sounds are markedly diminished bilaterally without wheezing. There is no murmur or gallop, but the second heart sound is accentuated; no parasternal heave is appreciated. He has no digital clubbing or cyanosis, but there is trace pedal edema. Oxygen saturation by pulse oximeter is 89%.

ABG on room air reveals a pH of 7.38, PCO₂ 43 mmHg, and PO₂ 58 mmHg. Complete metabolic panel is normal. WBC count is 8.3, hemoglobin is 17.4, hematocrit is 58%, and platelet count is 290,000.

PA and lateral CXR reveals hyperexpanded lungs bilaterally, a narrow cardiac silhouette, and no infiltrates, nodules, or masses. The ECG is normal.

Spirometry confirms an FEV₁/FVC ratio of 60%, FEV₁ is 45% of predicted, and FVC is 88% of predicted.

Which of the following has been shown to impact this patient’s survival?

a) Supplemental oxygen
b) Combined inhaled corticosteroid and LABA
c) Combined inhaled corticosteroid, inhaled LABA, inhaled tiotropium, and enrollment in a pulmonary rehabilitation program
d) Combined inhaled corticosteroid, inhaled LABA, inhaled tiotropium, and PRN albuterol

Answer and Discussion

The answer is a.

Objective: Recognize obstructive pulmonary disease therapy and their effects on mortality.

In 1980, a study by the Nocturnal Oxygen Therapy Trial Group reported that patients who were provided supplemental oxygen after meeting basic criteria for initiating long-term oxygen therapy experienced a mortality benefit. This was supported by a second study from Medical Research Council Working Party the following year. These criteria include

(A) Room air arterial PO₂ (PaO₂) ≤55 mmHg or an arterial oxygen saturation (SaO₂) ≤88% OR
(B) PaO₂ ≤59 mmHg or an SaO₂ ≤89%, when there is evidence of cor pulmonale, right heart failure, or erythrocytosis defined as a hematocrit >55%
While this man’s resting room air PaO₂ does not qualify him for supplemental oxygen therapy, the erythrocytosis does.

The Global Initiative on Obstructive Lung Disease (GOLD) criteria classify this patient as GOLD class 3 based on his degree of airflow obstruction. Current treatment guidelines recommend combined inhaled corticosteroids, LABA, either short-acting inhaled anticholinergic bronchodilators such as ipratropium bromide or long-acting tiotropium, and SABAs as needed.³

In addition to medications, vaccination against influenza and *Streptococcus pneumoniae* should be kept up to date, and this patient should be enrolled in a formal pulmonary rehabilitation program, which has been shown to improve exercise capacity. Even with appropriate pharmacologic therapy, preventive measures, and rehabilitation, however, supplemental oxygen is the only option provided that would impact his survival.

**REFERENCES**


**Question 45**

A 62-year-old man is hospitalized for cough, wheezing, and dyspnea of 4 days in duration. He denies fever but admits to increased sputum production that has become thick and yellow. He is known to have moderate COPD treated with a LABA and albuterol as needed. He has been using albuterol metered-dose inhaler four to five times daily for the past 3 days with incomplete improvement in symptoms.

He is afebrile, HR is 99 beats/minute, respiratory rate is 24 breaths/minute, and BP is 134/88 mmHg. Physical examination is significant for mild conversational dyspnea, distant breath sounds, rhonchi, and diffuse wheezing. Room air oxygen saturation is 89% but increases to 94% with the addition of 2 L of supplemental oxygen. A chest radiograph shows only hyperinflation and flattened diaphragms but no infiltrate. The ECG is normal.

Which treatment regimen would be most the appropriate initial therapy?

a) Inhaled high-dose fluticasone for 14 days and inhaled albuterol and ipratropium bromide scheduled 4 times a day

b) Oral prednisone and inhaled albuterol and ipratropium bromide as needed

c) Azithromycin and inhaled albuterol and ipratropium bromide as needed

d) Azithromycin, oral prednisone, and inhaled albuterol and ipratropium bromide as needed

**Answer and Discussion**

The answer is d.

**Objective:** Demonstrate appropriate therapeutic intervention in COPD exacerbation.

This patient appears to have suffered an acute exacerbation of his COPD. While the addition of inhaled corticosteroids to a LABA is recommended for stable severe COPD, inhaled corticosteroids have no proven role in the management of an exacerbation.

A study of patients with COPD exacerbations published in 1999 demonstrated that systemic corticosteroids reduced the 30-day treatment failure rate, reduced the 90-day treatment failure rate, and shortened the length of hospital stay by 2 days when compared to placebo.⁴ Therefore, systemic corticosteroids should be given to this patient.

Infection should always be considered a potential cause of a COPD exacerbation. One should consider antibiotic therapy when a patient has increased sputum purulence with either increased dyspnea or increased sputum volume or when experiencing a severe exacerbation requiring mechanical ventilatory support either invasively through an endotracheal tube or noninvasively.²,³

**REFERENCES**


**Question 46**

A 47-year-old man with relapsing polychondritis comes in for the evaluation of shortness of breath. He notes that it has been worsening over the past year. He denies sinus symptoms, cough, hemoptysis, or rash. His joints have not been painful or swollen, and he has had no nasal or ear involvement since starting on oral prednisone and methotrexate 3.5 years ago. Spirometry done in the office shows a severe obstructive ventilatory defect. The flow-volume loop is shown in next page.
Which of the following should be done next?

a) Increase the oral prednisone dose
b) Begin high-dose inhaled fluticasone
c) Obtain a CT of the neck
d) Request bronchoscopy

**Answer and Discussion**

The answer is d.

**Objective:** Recognize variable intrathoracic obstruction of flow-volume loop.

This flow-volume loop suggests a variable intrathoracic obstruction indicated by the flattened expiratory portion above the x-axis. This is seen when an obstructing lesion involving the large airways (trachea and/or main bronchi) limits airflow during expiration but not during inspiration; hence, it is variable.

Relapsing polychondritis is characterized by inflammation of cartilaginous structures including the cartilaginous components of the airways. Airway involvement can result in scarring, stricture formation, and tracheomalacia due to loss of functional tracheal rings. This can result from earlier episodes of inflammation and not necessarily active chondritis; therefore, increasing his anti-inflammatory therapy should be deferred until visualization of the airway has been performed.

Laryngeal or subglottic involvement might be seen on CT imaging, but the flow-volume loop abnormality would be that of a variable extrathoracic obstruction that manifests as flattening of the inspiratory portion under the x-axis. Although a CT scan may be helpful, it would not replace the need for bronchoscopy.

**SUGGESTED READINGS**


**Question 47**

A 28-year-old woman comes in with complaints of 6 months of mild dyspnea on exertion and fatigue. She denies cough or wheezing but admits to intermittent palpitations and heavy menstrual flow. She has no significant past medical history, takes no medications except ibuprofen for menstrual cramping, and does not smoke. Examination is significant for clear lung sounds and a soft systolic murmur.

Spirometry is normal, as are lung volumes. Diffusion capacity of carbon monoxide (DLCO) is moderately reduced and does not correct for alveolar volume.

In this patient, the reduced diffusing capacity of carbon monoxide should prompt you to order which test next?

a) Serum hemoglobin
b) Methacholine challenge
c) Transthoracic echocardiogram
d) V/Q scan

**Answer and Discussion**

The answer is a.

**Objective:** Identify causes of reduced DLCO in the setting of otherwise normal spirometry.

While asthma is a common cause of dyspnea, air trapping associated with bronchospasm has been reported to have either no effect on DLCO or to actually slightly increase the DLCO.

The reduction in DLCO in the setting of otherwise normal pulmonary function tests should always raise the concern for chronic pulmonary vascular disease, such as chronic thromboembolic pulmonary hypertension or idiopathic pulmonary arterial hypertension (PAH), and echocardiography would be the initial test to investigate this. If evidence of pulmonary hypertension had been found, a V/Q scan would certainly be an important tool to assess for evidence of thromboembolic disease as the etiology of her pulmonary hypertension. A far more common cause of reduced DLCO, however, is anemia in which the lung parenchyma, interstitium, and pulmonary vasculature are normal, but there is simply not enough hemoglobin flowing through the lungs to accept carbon monoxide normally. This will be measured as a reduced DLCO. Obtaining a hemoglobin level, which can then be used to as a correction factor to calculate the actual DLCO, would be the best answer to this question.

**SUGGESTED READING**


**Question 48**

A 43-year-old white woman with diagnosis of liver cirrhosis is admitted to the ICU in preparation for possible liver
transplant. A pulmonary artery catheter is placed to assess hemodynamic status and optimize medical therapy prior to surgery. A CXR obtained while in the ICU showed evidence of cardiomegaly but no pulmonary edema. An echocardiogram obtained a couple of months ago showed normal valvular function, stage I diastolic dysfunction, and a normal left ventricular ejection fraction. The physician in the ICU is instructed to try to optimally diurese the patient to keep a pulmonary artery wedge pressure (PCWP) of <18 mmHg. The following measurements were initially obtained:

PA = 24/18 mmHg  
PCWP = 18 mmHg  
CVP = 12 mmHg

After 24 hours, the patient deteriorates and requires placement on mechanical ventilation. The pulmonary artery catheter also has to be repositioned. The patient received diuretics and had a negative balance of 3 L. New hemodynamic measurements were done:

PA = 23/15 mmHg  
PCWP = 20 mmHg  
CVP = 8 mmHg

What should be done next?

a) Continue to diurese the patient with furosemide challenges  
b) Reposition the Swan-Ganz catheter since it may be in a non-zone III position  
c) Replace the pulmonary artery catheter with a new one  
d) Withdraw the tip of the catheter since it may be overwedged

Answer and Discussion
The answer is b.

Objective: Recognize common pulmonary artery catheter hemodynamic patterns to identify non-physiologic results from erroneous data collection.

Considering the diagnostic and therapeutic importance of the PCWP, it is mandatory to confirm the validity of its measurement. The patient had evidence of cardiomegaly on the chest radiograph, but no information is provided to suggest the presence of congestive heart failure. The initial hemodynamic measurements suggested an elevated capillary wedge pressure, and the patient received diuretics with successful negative fluid balance. The new hemodynamic assessment showed an appropriate decrease in the CVP but an inappropriately elevated capillary wedge pressure. The pulmonary artery wedge pressure is typically lower than the pulmonary artery diastolic pressure. The presence of an elevated pulmonary capillary pressure higher than a pulmonary diastolic pressure would be inappropriately elevated capillary wedge pressure. The tip of the catheter is too peripheral and needs to be withdrawn.

REFERENCES

Question 49
A 68-year-old man with history of chronic myelogenous leukemia presents to the ED complaining of fever, dysuria, and dizziness. At his arrival to the hospital, vital signs showed a temperature of 37.9°C, BP of 90/60 mmHg, HR of 115 beats/minute, respirations of 26 breaths/minute, and SpO2 of 95% on room air. Urinalysis confirms the presence of a urinary tract infection, and the patient is admitted to the regular nursing floor. Approximately 2 hours later, the patient collapses in his room and is transferred to the ICU. A central venous catheter is placed and reveals a CVP of 6 mmHg. Vital signs show BP of 80/50 mmHg, HR of 90 beats/minute, SpO2 of 95% on room air, and respirations of 28 breaths/minute. Laboratory workup showed a hematocrit of 25% and elevated WBC of 25,000. A venous blood gas obtained from the distal tip of the central line showed an SvO2 of 60%. What is the most appropriate combination of therapeutic interventions?

a) Start infusion with norepinephrine, recheck SvO2, and add dobutamine if SvO2 <80%  
b) Administer antibiotics and intravenous boluses of fluids to keep CVP 8 to 12 mmHg, transfuse to keep hematocrit >30% if SvO2 <70%  
c) Aggressive fluid resuscitation with fluid boluses, antibiotics, and start norepinephrine and dobutamine  
d) Administer antibiotics, intravenous fluids at 250 mL/hr, and quickly titrate norepinephrine dose to keep MAP >60 mmHg

Answer and Discussion
The answer is b.

Objective: Manage septic shock with early goal-directed therapy.

The patient presents with a clinical picture compatible with septic shock secondary to a urinary tract infection. In this patient, a systemic inflammatory response causes significant
vasodilatation and consequently profound hypotension. The key to the treatment is to restore tissue perfusion to prevent the development of multiorgan failure. Based on results of a randomized controlled trial for management of shock within 6 hours of onset, treatment of patients with septic shock must include prompt recognition of the source of the infection, administration of antibiotics, aggressive fluid resuscitation with intravenous boluses of fluids (preferentially to keep a CVP of 8 to 12 mmHg), and administration of blood products in patients with evidence of low hematocrit (< 30%) to keep a target SvO₂ of at least 70%.¹

This patient presents with evidence of hypovolemia (CVP = 6 mmHg), and appropriate fluid status must be restored before administration of vasopressors. Maintaining a MAP >60 mmHg does not guarantee that the patient will maintain appropriate tissue perfusion, and the physician must ensure fluid resuscitation to keep a CVP of 8 to 12 mmHg before titrating vasopressor agents. The administration of additional agents such as dobutamine is reserved for patients who maintain a low SvO₂ or have evidence of significant left ventricular dysfunction, only after additional strategies have failed to keep a SvO₂ > 70%.

REFERENCE


Question 50

A 35-year-old woman presents to the ED after an episode of syncope. Family members state that she developed acute-onset right-sided chest pain accompanied by shortness of breath earlier that day. She underwent appendectomy approximately 1 month ago. Physical examination shows a HR of 120 beats/minute, respiratory rate of 26 breaths/minute, and BP of 80/50 mmHg. A helical CT of the chest confirms the presence of large bilateral pulmonary emboli. Lower extremity ultrasound is negative for deep venous thrombosis. The patient is started on unfractionated heparin and transferred to an ICU. Four hours later, vital signs show BP of 70/50 mmHg and HR of 125 beats/minute. After appropriate fluid resuscitation, the patient is started on infusion with norepinephrine. Which of the following diagnostic or therapeutic considerations is most appropriate at this time?

a) Administer t-PA; discontinue anticoagulation with heparin during thrombolysis
b) Continue anticoagulation with heparin; do not administer t-PA since it is contraindicated
c) Change anticoagulation to low molecular weight heparin, and then administer t-PA
d) Continue anticoagulation; administer t-PA only if echocardiogram confirms RV strain

Answer and Discussion

The answer is a.

Objective: Manage massive pulmonary embolism.

This patient presents with syncope and clinical evidence of hemodynamic instability associated with massive pulmonary emboli. Although the use of fibrinolytic agents in patients with massive pulmonary embolism has not shown to improve mortality, its use is recommended in patients with persistent hemodynamic compromise because it accelerates clot lysis and improves physiologic variables.¹ Administration of t-PA is indicated in this patient given persistent hypotension and documentation of the pulmonary embolism by the CT scan. Importantly, anticoagulation with heparin products should be discontinued during administration of lytic agent since concomitant administration of both agents may increase bleeding risk.

Given the potential to produce significant bleeding complications, the physician must ensure that no contraindications exist prior to administration of thrombolytic agents. There are no contraindications for thrombolysis in this patient. The list of absolute contraindications includes a history of intracranial neoplasm, recent intracranial surgery or trauma (<2 months), and active or recent internal bleeding (<6 months); the list of relative contraindications includes nonhemorrhagic stroke, bleeding diathesis, thrombocytopenia, uncontrolled hypertension, and recent surgery (<10 days earlier). There is no advantage to switch from unfractionated heparin to low molecular weight heparin. Administration of thrombolytics does not require an echocardiogram confirming evidence of right ventricular strain.¹

REFERENCE


Question 51

A 65-year-old man presents to the outpatient department complaining of 1 week of left lower extremity edema. He was diagnosed with colon cancer 3 months ago and currently receives chemotherapy and radiation therapy. Ultrasound of the left leg confirms the presence of thrombus involving the left common femoral vein. Helical CT of the chest is negative for pulmonary emboli. Which of the following statements is correct regarding length of anticoagulation therapy?

a) The patient should continue anticoagulation with LMWH or Coumadin until clinically cured of malignancy.
b) The patient must be treated with warfarin for at least 3 months.
c) The patient can be transitioned from low molecular weight heparin (LMWH) to Coumadin and continue treatment for 6 months.
d) The patient should continue anticoagulation indefinitely.


**Answer and Discussion**

**The answer is a.**

**Objective: Management of VTE in malignancy.**

This patient presents with a first episode of DVT associated with active malignancy. A recent multicenter randomized controlled trial found that treatment with LMWH is associated with a reduction in rate of recurrent VTE compared with warfarin. Given the underlying active malignancy, the patient should continue treatment for at least 6 months or until the underlying malignancy is not active. If risk of bleeding is low, then extended therapy may be beneficial. Continuing anticoagulation indefinitely is appropriate in patients with a history of recurrent thromboembolic events or when there is active metastatic disease. There is no history of prior or recurrent VTE in this patient, and although there is an underlying malignancy, if the patient is clinically cured of malignancy, there is no need for lifelong anticoagulation therapy.

**REFERENCE**


**Question 52**

A 65-year-old African American man comes to your office for advice regarding smoking cessation. His past medical history is significant for diabetes, hypertension, hyperlipidemia, coronary artery disease, and a recent non-ST elevation myocardial infarction. He has a history of seizure disorder for which he uses phenytoin and carbamazepine, and his last seizure episode was more than 2 years ago. Currently, he smokes about half a pack of cigarettes daily, although he was smoking 3 packs a day prior to his myocardial infarction. Which of the following strategies regarding smoking cessation programs is correct?

a) Treatment with nicotine replacement therapy is contraindicated given the history of coronary artery disease.

b) Bupropion therapy combined with nicotine replacement is the most effective therapy.

c) Bupropion has been associated with seizures in patients with a history of seizure disorder.

d) Varenicline has lower efficacy compared to bupropion but can be used in patients with a history of seizures.

**Answer and Discussion**

**The answer is c.**

**Objective: Nicotine replacement indications and contraindications.**

Bupropion is an antidepressant agent that has been shown to be effective in aiding smoking cessation programs. Studies have shown higher efficacy compared to nicotine replacement and placebo. Side effects include dry mouth, insomnia, and seizures (0.1%). The risk of seizures appears to be higher in patients with a preexisting history of seizure disorder. Studies have shown that treatment with nicotine replacement is safe even in patients with history of cardiovascular disease. The use of nicotine replacement therapy combined with bupropion did not prove to be more effective than nicotine replacement alone. Varenicline is a new pharmacologic agent that can be used in patients with seizure disorder. Varenicline has been shown to have higher rather than lower efficacy when compared with bupropion. There have been recent warnings regarding potentiating neuropsychiatric symptoms with varenicline, as well as small increase in cardiovascular adverse effects.

**REFERENCES**


**Question 53**

A 35-year-old African American man presents to his primary care physician complaining of mild dyspnea, low-grade fevers, night sweats, and muscle and joint pain. He remembers having a chronic cough for at least 1 year, although he attributes this to his smoking habit. He thinks that the symptoms started about a month ago, and he recalls having a rash in his lower extremities, although he assures you that it was related to “bumping into some furniture.” He denies any recent travel or sick contacts. Physical examination shows T = 37°C, HR = 80 beats/minute, BP = 120/85 mmHg, and SpO2 = 96% on room air. Lungs are clear to auscultation. Skin examination reveals pink nodular lesions on the extensor surface of both arms. The chest radiograph shows bilateral hilar adenopathy and mild reticular opacities in the upper lobes. Which of the following statements is correct regarding this patient’s diagnosis?

a) This syndrome is most likely associated with good prognosis and spontaneous remission.

b) The presence of a normal ACE level practically excludes the diagnosis.

c) A negative gallium-67 lung scan excludes the diagnosis of alveolitis.

d) CT of the chest most likely would show evidence of fibrosis and traction bronchiectasis.
Question 54

A 65-year-old white man develops progressive dyspnea on exertion accompanied by a dry chronic cough and a 15-pound weight loss over the last 12 months. Dyspnea has significantly progressed over the last couple of months, and currently he is unable to walk around his house without assistance. His past medical history is significant for hypertension and coronary artery disease. He smoked half a pack of cigarettes for 30 years but quit 5 years ago. He used to work as a truck driver and thinks that he could have been exposed to asbestos. Physical examination shows the following: T = 36.5°C, HR = 90 beats/minute, and SpO₂ = 90% on room air. Lung examination reveals bilateral, dry, end inspiratory crackles. Cardiac examination shows an accentuated second heart sound. A CT of the chest reveals honeycombing and patchy, predominantly peripheral, subpleural, bibasilar reticular infiltrates. There are no ground-glass opacities. What is the most likely diagnosis?

a) Desquamative interstitial pneumonitis
b) Idiopathic pulmonary fibrosis (IPF)
c) Sarcoidosis
d) Lung asbestosis

Answer and Discussion

The answer is b.

Objective: Identify classic signs and symptoms of IPF.

The patient presents with classic signs and symptoms of IPF, including insidious onset, dry nonproductive cough, weight loss, and progressive dyspnea. Physical examination often reveals bilateral bibasilar crackles and can also show cyanosis, cor pulmonale, and clubbing. A high-resolution CT of the chest typically helps to establish the diagnosis; the most common findings are the presence of honeycombing and subpleural and bibasilar reticular infiltrates. The presence of ground-glass opacities or upper lobe predominance of the infiltrates should suggest an alternative diagnosis to IPF such as respiratory bronchiolitis–ILD or desquamative interstitial pneumonitis. Sarcoidosis typically presents with evidence of hilar adenopathy and a mid to upper zone predominance of infiltrates. Finally, there is no evidence of pleural thickening or pleural plaques to suggest asbestos exposure or consequent asbestosis in this patient.

REFERENCE

ARDS as the presence of acute bilateral infiltrates on CXR, hypoxemia quantified as PaO2/FiO2, ratio of <200, and a normal left ventricular function or pulmonary artery occlusion pressure (wedge pressure) of \( \leq 18 \) mmHg. This definition allows the differentiation of cardiogenic from noncardiogenic pulmonary edema. Advanced techniques on transthoracic echocardiogram can help to distinguish LV ejection fraction and LV volume status as well.

The venous blood gases do not provide any added information in this case. The determination of alveolar-blood protein ratio has been described in an attempt to differentiate cardiogenic from noncardiogenic (ARDS) pulmonary edema. The ratio of the pulmonary edema fluid protein concentration to the serum protein concentration may help differentiate cardiogenic from noncardiogenic pulmonary edema. A ratio >75% is associated with increased capillary permeability (noncardiogenic); a ratio <65% is highly suggestive of hydrostatic (cardiogenic) pulmonary edema. This technique is only useful very early in the course of edema formation and is not routinely used due to lack of reproducibility.\(^1\)

The isolation of a microorganism in the presence of the SIRS determines sepsis as being present but does not help confirm or rule out ARDS. CT of the chest in ARDS is characterized by alveolar filling, consolidation, and atelectasis, occurring predominantly in the dependant areas of the lung. However, inflammation occurs throughout the lung, even in areas of relatively normal lung parenchyma. Unfortunately, the radiologic findings of ARDS are not distinguishable from those of cardiogenic pulmonary edema.\(^2\)

**REFERENCES**


**Question 56**

A 35-year-old man is admitted to the hospital with fever, cough, and pleuritic chest pain. On physical examination, he is found to be tachy cardiac and tachypneic and has a BP of 110/74 mmHg. He has diminished breath sounds at the bases. The rest of his examination is normal. The laboratory examination shows an elevated WBC count (20,000/μL). Blood cultures and sputum cultures are pending. The CXR shows a left pleural effusion. The pleural fluid analysis shows the following: cloudy yellow fluid with RBC of 650/μL, WBC count of 42,000/μL, neutrophils of 90%, LDH of 825 U/L (upper limit of normal = 85 U/L), total protein of 5.2 g/dL, glucose of 102 mg/dL, pH of 6.0, and amylase of 18 U/L (upper limit of normal = 180 U/L). Cytology is negative for malignant cells. What is the most appropriate course of action at this time?

a) Wait for blood cultures
b) Request isoenzyme analysis to determine the source of the amylase
c) Await for pleural fluid cultures
d) Place a chest tube
e) Obtain a CT scan of the abdomen to determine pancreatic anatomy

**Answer and Discussion**

The answer is d.

**Objective: Appropriate management of pleural effusion.**

To determine which patients require pleural fluid drainage, certain clinical, radiologic, and laboratory markers can help the clinician to estimate the likelihood that the effusion will not resolve with antibiotics alone. The American College of Chest Physicians has developed a staging system that suggests that large free-flowing effusions, loculated effusions, or effusions with thickened parietal pleura, as well as effusions showing positive bacterial cultures or Gram stain or with pH <7.20, have a moderate risk of poor outcome and should be drained. Furthermore, presence of a purulent exudate suggests high risk of poor outcome and should be drained.

Free-flowing exudates can be drained with small chest tubes (7 to 12 French). If the fluid viscosity is higher, the tube size may have to increase in order to prevent occlusion. Patients with loculated effusions may require medical pleuroscopy or video-assisted thoracoscopy (VATS) in order to break down adhesions and loculations. Thickly organized empyemas require decortication.

It is important to remember that etiologic diagnosis of the cause of pneumonia does not necessarily influence survival, as long as broad-spectrum antibiotics that cover the responsible organism are started early. Overall, causative agents of community-acquired pneumonia are identified in 30% to 60% of cases, even after using extensive diagnostic testing.

Amylase in pleural fluid should be measured whenever pancreatic disease, malignancy, or esophageal rupture is considered in the differential diagnosis. An elevation of amylase over 100,000/μL should be separated into pancreatic or salivary isoenzyme. Salivary isoenzyme is associated with esophageal rupture and with adenocarcinoma of the lung or ovary.\(^3,2\)

Available studies suggest that delayed thora centesis and drainage in cases of complicated parapneumonic effusions is associated with prolonged hospitalization and increased mortality. In the early or exudative phase of an effusion, the fluid is free flowing and easily removable, but in later stages, the fluid becomes viscous, with loculation. This fibrinous stage may cause trapped lung, interfering with lung re-expansion.\(^3,5\)

As discussed earlier, the possibility of a pancreato-pleural fistula should be considered with very elevated levels of amylase in pleural fluid. This fistulous tract between the pseudocyst and the pleural space is a rare complication of chronic pancreatitis.\(^2\)
REFERENCES


Question 57

A 25-year-old man is seen in your clinic for fatigue, pleuritic chest pain, fever for 2 weeks, and nonproductive cough. After a detailed but unremarkable physical examination, a CXR shows an effusion on the left base.

The pleural fluid shows the following: serosanguineous fluid, pH = 7.30, protein = 4.2 g/dL, LDH = 612 IU/L (upper limit of normal = 85 IU/L), glucose = 60, and cell count = 4,000 cells with 92% lymphocytes, 6% neutrophils, and 2% eosinophils. Gram stain and AFB smears are negative. Cytology is positive for malignant cells. CT of the chest shows an infiltrate in >80% of the cases of tuberculosis pleurisy. However, this infiltrate is clinically indistinguishable from other causes of pneumonia. Bronchoscopy is able to diagnose TB in 35% to 50% of cases of smear-negative TB. False-negative PPD results have been described in 7% to 31% of patients with tuberculous pleurisy. PET relies on the increased cellular uptake of glucose by malignant cells. The PET scanner detects radiolabeled 5-fluorodeoxyglucose (FDG) trapped in malignant cells. However, false positives can occur and are usually due to infection or significant inflammation. Furthermore, the patient in the vignette is 25 years old, and the absence of mesothelial cells or readily identifiable risk factors for malignancy makes this a less probable reason for the exudative effusion.

Answer and Discussion

The answer is c.

Objective: Diagnose pulmonary TB.

Whenever the pleural fluid has a lymphocyte predominance (>80%), the differential diagnosis can be narrowed to tuberculous pleurisy, chylothorax, lymphoma, chronic rheumatoid pleurisy, sarcoidosis, or trapped lung. In this particular case, the age of the patient and clinical characteristics of the case point toward tuberculous pleurisy. TB-associated effusions are the result of delayed hypersensitivity reaction in the pleural space. The pleural fluid is usually a serosanguineous exudate, with LDH > 500 IU/L and protein >4 g/dL. Total WBC count is usually <5,000 cells/mL with lymphocytic predominance and with less than 5% eosinophils. Pleural pH is usually between 7.0 and 7.4.

The pleural fluid rarely contains enough bacilli to make the diagnosis by acid-fast stains. The culture of pleural fluid is positive for Mycobacterium tuberculosis in 42% of cases, whereas pleural biopsy culture is positive in 64%. The presence of pleural granulomas is usually diagnostic. The combination of histologic examination and culture pleural biopsy has a sensitivity of >90% for pleural TB.

CT of the chest shows an infiltrate in >80% of the cases of tuberculous pleurisy. However, this infiltrate is clinically indistinguishable from other causes of pneumonia. Bronchoscopy is able to diagnose TB in 35% to 50% of cases of smear-negative TB. False-negative PPD results have been described in 7% to 31% of patients with tuberculous pleurisy. PET relies on the increased cellular uptake of glucose by malignant cells. The PET scanner detects radiolabeled 5-fluorodeoxyglucose (FDG) trapped in malignant cells. However, false positives can occur and are usually due to infection or significant inflammation. Furthermore, the patient in the vignette is 25 years old, and the absence of mesothelial cells or readily identifiable risk factors for malignancy makes this a less probable reason for the exudative effusion.

Question 58

A 52-year-old man comes to the hospital for generalized fatigue, particularly when climbing stairs. He reports waking up tired but slowly improving throughout the day. However, he is unable to perform activities of daily living due to weakness in arms and legs. He denies alcohol use but reports a 50 pack-year history of smoking. He quit 1 year ago. He is currently taking no medications.

His physical examination is remarkable for proximal muscle weakness and normal cardiopulmonary examination. His CXR shows a mediastinal mass suggestive of malignancy. Which of the following conditions is most commonly associated with the patient’s symptoms?

a) Squamous cell carcinoma of the lung
b) Adenocarcinoma of the lung
c) Large-cell carcinoma of the lung
d) Small-cell carcinoma of the lung
e) Bronchoalveolar cell carcinoma
**Answer and Discussion**

The answer is **d**.

**Objective: Identify features of paraneoplastic syndromes associated with malignancy.**

The clinical vignette suggests that the patient has a malignant mediastinal mass, and in the presence of a significant smoking history, his symptoms are compatible with a paraneoplastic syndrome. Paraneoplastic syndromes are signs and symptoms caused by a malignancy but not directly attributable to the tumor or its metastasis but, instead, to secreted peptides that generate a physiologic or immunologic response. The two types of paraneoplastic syndromes due to lung cancer are endocrine [syndrome of inappropriate antidiuretic hormone (SIADH), humoral hypercalcemia, Cushing syndrome, etc.] and neurologic (autonomic dysfunction, Lambert-Eaton myasthenia, encephalomyelitis, and neuropathies).

Lambert-Eaton myasthenia presents with proximal muscle weakness and fatigue. Symptoms usually improve with repeated motion, thus differentiating it from classic myasthenia. Lambert-Eaton myasthenia is present in 3% of patients with SCLC. Fortunately, it usually responds to treatment of the tumor.\(^2\) SCLC is the malignancy most commonly associated with SIADH, Cushing syndrome, VIP-associated diarrhea, and hyperparathyroidism.

Squamous cell carcinoma is associated with hypertrophic osteoarthropathy, hypercalcemia, hCG-associated uterine bleeding, and the sign of Leser-Trelat (multiple seborrheic keratoses of acute onset).\(^3\) Adenocarcinoma is associated with hypertrophic pulmonary osteoarthropathy, rarely with Lambert-Eaton, and subacute cortical cerebellar degeneration.\(^3\) Large-cell carcinoma is not commonly associated with paraneoplastic syndromes.\(^3\) Bronchoalveolar cell carcinoma is not associated with paraneoplastic syndromes.\(^3\)

**REFERENCES**


**Question 59**

A 47-year-old African American man is admitted to the hospital with significant shortness of breath. He reports gradual onset of symptoms that became unbearable and prompted his visit to the emergency room. He admits to a 45 pack-year history of smoking. His physical examination is remarkable for tachycardia, tachypnea, and decreased breath sounds on the left side. A CT of the chest follows.

What is the most likely process responsible for this patient's condition?

a) Adenocarcinoma of the lung  
b) Squamous cell carcinoma of the lung  
c) Mesothelioma  
d) Large-cell carcinoma of the lung  
e) Foreign body aspiration

**Answer and Discussion**

The answer is **b**.

**Objective: Identify common characteristics of lung cancer.**

In general, squamous cell and small-cell carcinomas are centrally located.\(^1\) The CXR or CT scan can give some clues to the clinician regarding the type of tumor. Squamous cell carcinomas are centrally located in 64% of the cases and present with atelectasis in 23%, as well as with cavitation in 5%. As part of the pretreatment evaluation, the clinician is obliged to have confirmatory histologic diagnosis by using sputum cytology, bronchoscopic biopsy, transthoracic needle aspiration, mediastinoscopy, or surgical resection.

In this particular patient, as is the case in 85% to 90% of cases of lung cancer, smoking is the most significant risk factor. There is a clear dose–response association between the number of cigarettes smoked and the incidence of lung cancer. Furthermore, secondhand smoking confers a twofold to threefold risk of developing lung cancer.

After histologic diagnosis, the treatment and prognosis are determined by the staging of the tumor and the patient’s tolerance to the therapeutic alternatives.

Non–small-cell lung cancers are staged by the TNM (tumor-node-metastasis) system from 0 to IV. Stage 0 is carcinoma in situ. Stage IA involves tumors <3 cm with no visceral, pleural, or main bronchus involvement and no lymph node involvement or metastases. Stages II and III are different degrees of thoracic involvement. Stage IV is determined by extrathoracic metastasis.

SCLC is staged in a simpler fashion: limited disease (confined to hemithorax with or without ipsilateral mediastinal, hilar, or supraclavicular lymph nodes), and extensive disease.\(^2\)

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Mesothelioma is a rare tumor caused by all forms of asbestos. It usually occurs in the parietal pleura and the peritoneum. Adenocarcinoma usually presents as a defined nodule in 72% of the cases, with peripheral location in 65% and hilar (40%) or mediastinal (27%) involvement. Large-cell carcinoma is peripheral location in 61% and hilar adenopathy in 32% of the cases. Foreign body aspiration with obstruction of the left main bronchus may appear similarly by imaging, with subsequent lobar collapse. However, foreign body aspiration is less probable in the setting of gradual symptoms described by the patient. Inadvertent foreign body aspiration is more common in children.3,4

REFERENCES


Question 60

A 46-year-old man with a history of moderate persistent asthma, allergic rhinitis, and recurrent abdominal pain with emesis is undergoing an exploratory laparotomy. During a recent abdominal CT scan with contrast, he experienced generalized urticaria that resolved after treatment with parenteral antihistamines and corticosteroids. Twenty minutes after the initial incision during his current surgical procedure, the patient became hypotensive, diaphoretic, and flushed and had wheezing noted on examination. Symptoms resolved rapidly after treatment with administration of intravenous epinephrine, H1 and H2 antihistamines, two separate fluid boluses, and corticosteroids. The procedure was stopped and the patient was taken to the Post-Anesthesia Care Unit, where he had an uneventful recovery. Which of the following statements regarding anaphylaxis is true for this patient?

a) Asthma is a significant risk factor in fatal anaphylaxis.
b) He should avoid all shellfish, obtain a Medi-Alert bracelet stating that he has a shellfish allergy, and carry self-injectable epinephrine at all times.
c) A serum tryptase level should be sent at the time of his reaction to help confirm the diagnosis of anaphylaxis.
d) Antibiotics are the most common cause of intraoperative anaphylaxis.

Answer and Discussion

The answer is a.

Objective: Recognize the features of anaphylaxis.

This patient had signs and symptoms of anaphylaxis during his operative procedure. Anaphylaxis is generally defined as a systemic, immediate hypersensitivity reaction caused by immunoglobulin E (IgE)-mediated immunologic release of mediators from mast cells and basophils. The incidence of anaphylaxis cannot be established based on current data, but more studies indicate significant underreporting of episodes. The majority (up to 50% in some reports) of anaphylactic episodes are due to unknown, or idiopathic, causes. Of the known causes, foods are the most frequent offenders, with peanuts, tree nuts (i.e., walnuts, almonds, cashews), fish, and shellfish being the most common foods. Medications are also a common cause of anaphylaxis, with nonsteroidal anti-inflammatory agents and antibiotics being the most frequent cause in the outpatient or inpatient setting and muscle relaxants being the most common cause in the perioperative period.

Anaphylactoid reactions are systemic reactions that resemble IgE-mediated anaphylaxis but are not immunologically mediated. These reactions can occur through several different mechanisms, including direct release of mediators from mast cells and basophils, disturbances in arachidonic acid metabolism, and immune complex formation. Opioid medications and radiocontrast material are two common causes of anaphylactoid reactions and are very rarely due to IgE-mediated hypersensitivity. It is a misconception that patients allergic to fish or shellfish are at increased risk for adverse reactions to radiocontrast media. The epidemiologic association between seafood allergy and radiocontrast media reactions has been attributed to a common iodine allergy since there is a high iodine content in seafood. However, iodine and iodide are small molecules that do not cause anaphylactic or anaphylactoid reactions and are structurally unrelated to shellfish allergens (which are tropomyosin proteins).

Histamine is the most important mediator released from mast cells and basophils in both anaphylactic and anaphylactoid reactions. Histamine is present in a preformed state inside these cells and is available for rapid release upon degranulation. This results in multiple different effects on organs and cells that contain H1 and H2 receptors, including vasodilation, tachycardia, smooth muscle contraction (bronchospasm), and increased glandular secretion. Other mediators such as leukotrienes, prostaglandins, tryptase, chymase, and various chemokines are also released and act to promote inflammation and similar end-organ effects as histamine. The most common clinical signs and symptoms of anaphylaxis involve the skin, with some combination of urticaria, angioedema, flushing, and pruritus occurring in up to 90% of patients. Respiratory symptoms of wheezing, dyspnea, upper airway angioedema, and rhinitis also frequently occur. Additional signs and symptoms include dizziness, syncope, hypotension, abdominal pain, nausea, emesis, or diarrhea.

Diagnosis relies on prompt and accurate recognition of the signs and symptoms of anaphylaxis. A thorough review of any possible causes is indicated. Serum histamine levels begin to rise rapidly, after about 5 to 10 minutes, and may remain elevated for up to 60 minutes after the onset of
symptoms. Serum tryptase levels also rise, but not until 60 minutes or so after the onset of symptoms, and may remain elevated for several hours. Other conditions, such as mastocytosis, can be associated with constitutively elevated levels of both serum histamine and tryptase. Thus, these findings are helpful in establishing a diagnosis of anaphylaxis but are neither diagnostic nor present in all cases. One marker that may be helpful is the ratio of total tryptase (α + β) to β-tryptase. α-Tryptase is secreted constitutively, whereas β-tryptase is released only during degranulation episodes, and a ratio of less than or equal to 10 is indicative of anaphylaxis, whereas a ratio greater than 20 is more consistent with systemic mastocytosis.

Management of acute anaphylaxis consists of rapid assessment of airway, breathing, and circulation. Patients should be placed in a supine position with legs elevated to increase cardiac preload. Peripheral intravenous access with large-bore needles should be obtained as soon as possible, if not already available. Epinephrine should be administered immediately and may be repeated every 10 to 15 minutes as necessary. Delayed administration of epinephrine has been associated with an increased risk of fatality during anaphylaxis. Supplemental oxygen and fluid resuscitation should also be given if necessary. Additional medications include H1 and H2 antihistamines, which may be given intravenously; corticosteroids; and supportive medications for hypotension and bronchospasm, as necessary.

After the patient is stabilized, he/she should be admitted to either the hospital or a short stay unit for further observation. Many patients with anaphylaxis will experience a biphasic reaction, during which symptoms recur 4 to 6 hours after the initial onset; this is most likely due to late-phase inflammatory effects of various leukotrienes and cytokines.

Risk factors affecting the incidence and/or severity of anaphylaxis and anaphylactoid reactions include age (more common in adults), gender (reportedly more common in females except for hymenoptera), route of administration (oral less likely to produce reaction and less severe compared with parenteral), constancy of administration (gaps in administration may predispose), and atopy (higher risk for IgE-mediated hypersensitivity reactions). Factors associated with fatal anaphylaxis include asthma, delay in administration of epinephrine, and concomitant use of β-blocker medications.

**Question 61**

A 37-year-old woman with adult-onset asthma presents to the emergency room with a 3-month history of worsening cough, purulent sputum, dyspnea, wheezing, and chest pain. Her asthma had been previously well controlled on daily inhaled medications (Advair 250/50 1 puff twice daily) with minimal albuterol use but has required three separate courses of oral prednisone since these symptoms began and is currently using her albuterol 7 to 8 times a day. Chest radiograph reveals a left upper lobe consolidation, and chest CT scan reveals central bronchiectasis in the posterior segments of the upper lobes. A CBC with differential reveals a WBC count of 12,000/mm³ and 10% eosinophils. The patient was admitted for further evaluation and treatment.

Additional testing reveals the following information: FEV₁ = 65% predicted, FEV₁/FVC ratio = 105% predicted, immediate hypersensitivity skin prick testing to *A. fumigatus* = 3+, and serum IgE level = 1,560 IU/L. You conclude that the patient most likely has ABPA. Which of the following is the most appropriate next step in treatment?

a) Begin allergen immunotherapy with *A. fumigatus*
b) Increase her dose of Advair to 500/50 1 puff twice daily and add montelukast 10 mg each evening
c) Begin prednisone 60 mg daily
d) Begin itraconazole 200 mg twice daily

**Answer and Discussion**

The answer is a.

**Objective:** Understand the pathophysiology, staging and treatment of ABPA.

ABPA is a hypersensitivity reaction that occurs in patients with asthma or CF when their bronchi become colonized by *Aspergillus* species. The pathophysiology of ABPA remains incompletely understood but is likely secondary to intense IgE- and IgG-mediated immune response to *Aspergillus* in the setting of asthmatic bronchoconstriction, mucus plugging, inflammation, fibrosis, and respiratory compromise.

Clinical presentation can vary but typically involves recurrent episodes of bronchial obstruction, fever, cough, purulent sputum production, dyspnea, chest pain, wheezing, malaise, and hemoptysis. Some patients may be entirely asymptomatic but have findings on examination or radiographic/laboratory evaluation.

Radiographic findings may be completely normal depending upon course of disease and time of presentation but typically include changes on CXR such as infiltrates (typically upper lobe), atelectasis due to mucoid impaction, and findings suggestive of bronchiectasis. Chest CT scan findings can include proximal or central bronchiectasis with bronchial wall thickening as well as changes consistent with mucous plugging, atelectasis, and consolidation. Pulmonary function can be compromised, most often with a reduction in FEV₁. However, more progressive disease can be associated with a mixed obstructive-restrictive pattern.

There is no gold standard or diagnostic test that can firmly establish the diagnosis of ABPA. Diagnosis is made through clinical, laboratory, and radiographic evaluation.

Major diagnostic features of classic ABPA include: (1) history of asthma; (2) immediate skin test reactivity to *Aspergillus* antigens; (3) precipitating serum antibodies to *A. fumigatus*; (4) serum total IgE concentrations > 1,000 ng/mL; (5) peripheral blood eosinophilia > 500/mm³; (6) lung infiltrates on CXR or CT scan; (7) central bronchiectasis on chest CT scan; and (8) elevated serum specific IgE or IgG to *A. fumigatus*.
Because central bronchiectasis may not be seen in all cases, a diagnosis of ABPA-seropositive (ABPA-S) can be made if the first four criteria from above are met. If central bronchiectasis is present, then a diagnosis of ABPA-central bronchiectasis (ABPA-CB) can be made. Several of the above findings can be altered by use of systemic corticosteroids, especially total serum IgE levels, specific IgE levels, and peripheral eosinophilia. However, IgE levels in patients with ABPA would not be expected to be normal, and skin test results are not affected by corticosteroids. Negative percutaneous skin prick tests followed by negative intradermal tests to Aspergillus essentially excludes ABPA as a diagnosis.

ABPA-CB is characterized by five different stages, but this should not be confused with phases because patients do not necessarily progress from one stage to the next. Stages are as follows: I, Acute; II, Remission; III, Exacerbation; IV, Corticosteroid-dependent asthma; and V, Fibrotic.

Treatment is aimed at reducing inflammation, reducing exacerbations, and limiting progression to end-stage lung disease. There is no known cure for ABPA. Systemic corticosteroids are the hallmark of treatment and are very effective in controlling ABPA (stages I, III, and IV; patients in remission or with fibrosis do not require steroids). Treatment typically starts with 0.5 to 1 mg/kg prednisone daily for 14 days followed by every other day dosing and a slow taper over 3 to 6 months, depending on response. Patients should be followed closely for exacerbations, which typically coincide with new chest radiograph findings or dramatic rise in total serum IgE. Inhaled corticosteroids have not been shown to be effective in preventing acute episodes of ABPA but may help control symptoms of asthma. Anti-fungal treatments, such as itraconazole, have been shown to be effective as adjunctive therapy for patients who do not respond initially to corticosteroids but should not be used in place of, or before, systemic corticosteroids in the initial treatment of ABPA. Allergen immunotherapy with Aspergillus is not recommended for patients with ABPA and may be harmful because it could hypothetically promote immune complex formation.

**Question 62**

You are seeing a 65-year-old woman who presents for the first time to your office with a 7-month history of urticaria. The skin findings are described as dime-to nickel-sized, erythematous, raised, extremely pruritic lesions that occur anywhere on her body, typically in clusters of 8 to 10. These appear during various times of the day on an almost daily basis, and individual lesions last for approximately 4 to 6 hours before resolving completely with no residual bruising or hyperpigmentation. Diphenhydramine 50 mg orally every 6 to 12 hours provides moderate relief of her symptoms, but she does not tolerate the sedative side effects. She has missed, on average, 7 days of work a month due to these symptoms. Otherwise, she has been in good health with no constitutional or focal signs or symptoms of underlying disease process. She denies recent travel, HIV risk factors, or any new exposures. Which of the following should be done at this visit?

a) Prescribe daily combination antihistamines and follow-up in 2 to 4 weeks
b) Immediate referral to an allergist for skin testing to various foods
c) Skin biopsy
d) Prescribe daily combination antihistamines and recommend a trial elimination diet

**Answer and Discussion**

**Objective:** Understand the pathophysiology and treatment of chronic urticaria.

Urticaria is a very common skin finding and is frequently described as a typical wheal/flare lesion with an erythematous, raised center that blanches with pressure surrounded by macular erythema. Lesions are typically pruritic but may also burn at times. The pathophysiology of urticaria is local mast cell degranulation and the release of histamine. This can occur from local disturbance, as in patients with dermatographism, or can be systemic in nature. Mast cell degranulation can occur for many different reasons, such as viral or bacterial infections, underlying autoimmune or malignant conditions, or IgE-mediated allergic reactions.

Urticaria is separated into both acute (symptoms lasting <6 weeks) and chronic (symptoms lasting 6 weeks or longer). For patients with acute urticaria, the history is extremely important in attempting to identify any possible etiologic factors. The timing of urticaria in relation to any particular exposures may help identify a systemic or local cause of possible allergic reactions. In addition, associated findings such as signs/symptoms of constitutional or focal disease process may be important as well. The majority of cases of acute urticaria resolve spontaneously with no causal factor identified.

Similarly, for the vast majority of patients who experience chronic urticaria, an underlying etiology will not be identified. IgE-mediated allergic reactions to various exposures such as foods, food additives, cosmetics, and skin care products are frequently blamed but rarely confirmed. IgE-mediated reactions are reproducible with every exposure and only occur within minutes to hours of exposure to an offending agent. Symptoms resolve when the offending agent is avoided. Most patients with chronic urticaria experience a course of waxing and waning symptoms that occur at various times throughout the day and are not associated with one particular exposure. Skin testing to various foods is not indicated for patients with chronic urticaria for several reasons, including a high false-positive rate associated with food skin tests in general and especially in patients who have chronic urticaria, who may have many false-positive skin tests to any allergen due to their underlying condition. Rarely, chronic urticaria may be the harbinger of underlying autoimmune, rheumatologic, or malignant disease processes. A careful review of
systems and screening laboratory tests such as serum electrolytes, liver function studies, complete blood count with differential, T4, TSH, and sedimentation rate are indicated for all new patients who present with chronic urticaria.

Treatment consists of daily use of combination H1 and H2 antihistamines and realistic expectations from both the patient and treating physician. High doses of antihistamines (much higher than typically required for patients with allergic rhinitis) are typically necessary to gain control. Newer generation nonsedating antihistamines, such as fexofenadine, are typically used in the morning, while older generation, sedating antihistamines may be used at night as a sleep aid. Most patients will experience a relapsing/remitting course of symptoms that lasts weeks to months. There are many factors that may exacerbate the underlying condition, such as use of nonsteroidal anti-inflammatory medications (this is not due to an IgE-mediated hypersensitivity), viral or bacterial infections, and physical and emotional stress. An important part of treatment involves a careful explanation of the underlying disease process as well as an understanding that foods or other environmental exposures (assuming the history does not reveal such) are not likely causing their symptoms. Trial elimination diets are not recommended and may lead to exclusion of essential nutrients from the diet.

In addition, systemic corticosteroids are frequently prescribed, sometimes for weeks to months on a daily basis, but should be avoided, if possible, due to a high risk of side effects and relapse of symptoms once the steroids are discontinued. A short prednisone burst may be helpful for an acute flare but should also be avoided unless greater than 60% of the body surface area is covered in urticarial lesions.

Skin biopsy is generally not indicated for most cases of chronic urticaria that respond to treatment with combination antihistamines. Indications for obtaining a skin biopsy include: individual lesions that last longer than 24 to 36 hours, lesions that resolve with residual bruising or hypopigmentation, lesions that are more painful than pruritic, and symptoms that are resistant to regular use of multiple different high-dose antihistamines.
Thyroid Disorders

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Christian Nasr and Charles Faiman

POINTS TO REMEMBER:

Thyroid Function Tests and Screening
- Serum thyroid-stimulating hormone (TSH) is the most useful thyroid function screening for primary disorders of the thyroid (i.e., primary hyper- and hypothyroidism).
- TSH is of no value in the diagnosis and management of secondary (hypothalamic–pituitary) hypothyroidism; free thyroxine index (FTI) or free T4 (FT4) are more useful tests.
- Primary disorders of the thyroid gland are far more common than are secondary.
- The majority of thyroid hormone (both T3 and T4) is protein bound. Factors that affect protein levels will affect total hormone levels.
- Thyroid function tests are readily interpretable in ambulatory patients, but are often not helpful or may be confusing in the hospitalized sick patient.
- Population screening for thyroid dysfunction is not recommended except in the neonate (universal screening) and possibly in pregnancy.

Hypothyroidism
- Hypothyroidism is the single most common cause of abnormal thyroid function.
- TSH >10 to 20 μU/mL is generally diagnostic of primary hypothyroidism.
- Levothyroxine (LT4) is the treatment of choice for hypothyroidism.
- Maintaining the same brand-name levothyroxine preparation is recommended by specialty groups when treating hypothyroidism since significant differences in bioavailability are known to be present in FDA-approved generic interchanges.
- In secondary hypothyroidism, it is important to treat adrenal insufficiency, if present, before thyroid replacement.

Hyperthyroidism
- The clinical diagnosis of hyperthyroidism may prove difficult in the elderly.
- If not contraindicated, a biochemical diagnosis of suppressed TSH and elevated circulating T4 or T3 requires a radioactive iodine uptake (RAIU) test or thyroid scan to confirm the diagnosis of hyperthyroidism and aid in the treatment plan.
- Graves’ disease is the most common cause of non-iatrogenic hyperthyroidism and is associated with many other autoimmune illnesses.
- Patients with toxic multinodular goiter typically present at an older age (>6th decade) than those with Graves’ disease.
- Jod-Basedow is the only form of thyrotoxicosis in which ongoing overproduction of thyroid hormone by the thyroid gland occurs associated with a low RAIU.
- Half of patients with De Quervain’s thyroiditis present with symptoms of hyperthyroidism. Typical findings include an extremely elevated ESR, suppressed TSH, and low RAIU.
- Methimazole is the preferred antithyroid drug except during the first trimester of pregnancy when propylthiouracil is recommended.
- Agranulocytosis is a rare but potentially fatal side effect of antithyroid medications. All patients taking these medications must be counseled to seek medical attention and obtain a white blood cell count in the face of fevers or sore throat.
- 131I therapy can be used to treat hyperthyroid conditions caused by thyroid hormone overproduction, including Graves’ disease, toxic multinodular goiter, and toxic adenoma.

Thyroid Nodules and Thyroid Cancer
- Thyroid nodules are common, and most often benign.
- Fine needle aspiration (FNA) or biopsy is the diagnostic test of choice in evaluating a thyroid nodule.
Thyroid scans are generally not indicated for the evaluation of nonfunctional thyroid nodules.

Risk factors for thyroid cancer include male gender, prior history of head/neck radiation, presence of a dominant nodule, and positive family history.

Papillary and follicular variants are the most common causes of thyroid cancer.

Papillary cancer tends to metastasize to lymph nodes, whereas follicular cancer tends to have earlier hematogenous spread, primarily to lung and bone.

Treatment of thyroid cancer includes surgery, ablative $^{131}$I therapy, and LT$_{3}$ suppression of TSH.

Miscellaneous

Many medications and dietary and/or nutritional supplements can affect the bioavailability of levothyroxine replacement therapy.

Both lithium and amiodarone can cause hyperthyroidism and hypothyroidism.

**SUGGESTED READINGS**


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Surks MI, Ortiz E, Daniels GH, et al. Subclinical thyroid disease: scientific review and guidelines for diagnosis and management. *JAMA.* 2004;291:228-238.


Surks MI, Smith PJ. Multiple effects of 5,5’-diphenylhydantoin on the thyroid hormone system. *Endocrinol Rev.* 1984;5:514-524.


POUNTS TO REMEMBER:

Androgen Excess
- Androgen excess is one of the most common endocrine disorders in women and is the most common cause of anovulatory infertility.
- The most common presentation of androgenic disorders in women is with a complaint of hirsutism, possibly acne, and irregular and infrequent menses.

Polycystic Ovary Syndrome
- Polycystic ovary syndrome (PCOS) is the most common cause of androgen excess in women.
- A working diagnosis of PCOS includes (1) clinical or biochemical evidence of hyperandrogenism; (2) functional or ultrasonographic abnormalities in ovarian function; and (3) the exclusion of other androgen excess or ovulatory disorders.
- 80% of women with PCOS are obese.
- Insulin resistance leading to diabetes may be present in 30% to 40% of women with PCOS.
- While a common finding, diagnosis of PCOS does not require abnormal gonadotropin levels (i.e., elevated luteinizing hormone [LH]:follicle-stimulating hormone ratio).
- Diagnosis of PCOS does not require ultrasonographic evidence of the classic polycystic ovary (i.e., the “pearl necklace” ovary).
- Late complications of PCOS include hypertension, hyperlipidemia, type 2 diabetes mellitus, all components of the metabolic syndrome.

Amenorrhea
- In primary amenorrhea or amenorrhea occurring after only a few irregular cycles in young persons, a karyotype is also indicated.
- The presence of Y chromosome in a phenotypic female subject requires the operative removal of the gonads because they are considered precancerous.

Autoimmune Oophoritis
- Twenty-five percent of patients with Addison disease will also develop autoimmune premature ovarian failure.

Impotence
- Approximately 35% of male patients with impotence have an underlying endocrine cause, with diabetes being most common.
- Up to 60% of males with impotence have clinically significant but silent cardiovascular disease.

Gynecomastia
- In males presenting for evaluation of gynecomastia, the presence of pain, rapid growth, a mass, or tethering require further evaluation including laboratory studies (testosterone, LH, human chorionic gonadotropin, dehydroepiandrosterone sulfate, urinary 17-ketosteroids, E2, prolactin, thyroid, renal, and liver function) and possibly breast imaging.

SUGGESTED READINGS

Brodie BL, Wentz AC. Late onset congenital adrenal hyperplasia: a gynecologist’s perspective. Fertil Steril. 1987;48:175-188.
**Menstrual Disorders**


**Premature Ovarian Failure**


**Male**


POINTS TO REMEMBER:

Screening
- Fasting blood glucose (FBG) remains the screening test of choice for diabetes mellitus (DM)
- FBG ≥ 126 mg/dL is consistent with a diagnosis of DM
- Additional screening tests accepted by the American Diabetes Association (ADA) include:
  - Two-hour postprandial blood glucose (≥200 mg/dL)
  - Oral glucose tolerance test
  - Glycosylated hemoglobin A1c (HbA1c) ≥ 6.5% (the newest accepted criterion)

Risk Factors and General Principles
- Risk factors for DM type 2 include family history, obesity, hypertension, certain ethnicities, history of cardiovascular disease (CVD), history of gestational diabetes, and the presence of hypokalemia (regardless of diuretic use)
- Having a first-degree family member with DM type 1 increases the risk of developing DM type 1 by 10-fold
- DM type 1 results from autoimmune destruction of the pancreas, and patients with DM type 1 are at increased risk for developing other autoimmune diseases

Treatment
- Treatment targets for ambulatory diabetic patients include the following:
  - HbA1c <7.0%
  - Fasting and/or preprandial FBG between 70 and 130 mg/dL
- Based on data from the NICE-SUGAR trial, intensive insulin therapy (maintaining glucose between 80 and 110 mg/dL) in hospitalized patients in the ICU setting is no longer advised. Glycemic target range for hospitalized ICU patients is 140 to 180 mg/dL.
- Type 1 DM results from absolute insulin deficiency and patients must be treated with insulin
- The main role of long-acting insulin administered as part of a multi-dosing insulin regimen is to serve as basal insulin
- For patients with hypoglycemic unawareness, intensive ambulatory insulin therapy is contraindicated
- Because of possible lactic acidosis, metformin should be avoided in patients with cirrhosis, alcoholism, heart failure, or renal failure (serum creatinine >1.5 mg/dL)
- The sulfonylurea medications work best if prescribed to DM type 2 patients who are age >40, with diabetes of <5 years duration who have a fasting blood glucose of <180 mg/dL, are overweight, and are prescribed little or no insulin therapy

Complications
- Diabetic complications can be classified as microvascular (nephropathy, retinopathy, and neuropathy) or macrovascular (CVD and stroke)
- DM is the leading cause of blindness in adults 25 to 74 years old in Europe and North America and one of the leading causes of kidney dialysis
- If a diabetic patient presents with neuropathy, it is crucial to always consider causes other than DM
- In type 2 DM, intensive ambulatory diabetes control has been shown to decrease microvascular complications. Data are inconclusive on macrovascular complication prevention
- Reducing blood pressure with either a β-blocker or an angiotensin-converting enzyme (ACE) inhibitor reduces the risk of both microvascular and macrovascular complications and overall mortality

SUGGESTED READINGS


**POINTS TO REMEMBER:**

**Adrenal Insufficiency**
- Autoimmune adrenal disease and exogenous glucocorticoids are the most common cause of primary and secondary adrenal insufficiency (AI), respectively.
- The initial manifestations of autoimmune polyglandular syndrome type 1 (APS-1) include hypoparathyroidism and mucocutaneous candidiasis followed by AI and primary hypogonadism.
- The manifestations of autoimmune polyglandular syndrome type 2 (APS-2) include AI, autoimmune thyroid disease, type 1 diabetes mellitus (DM-1), primary hypogonadism and hypopituitarism. Hyperparathyroidism does not occur in APS-2.
- Hyperkalemia is commonly seen in patients with primary AI, but it is absent in patients with secondary AI since adrenocorticotropic hormone (ACTH) plays a minor role in regulation of aldosterone secretion.
- Early morning cortisol or ACTH stimulation test is the initial test of choice for evaluation of AI.
  - Hydrocortisone is the commonly used replacement therapy for AI given in two to three divided doses. Mineralocorticoid replacement is necessary in patients with primary AI.
  - Patients with AI should carry medical alert information and double their dose of glucocorticoids for 2 to 3 days during acute illness.

**Cushing Syndrome**
- The 24-hour urine-free cortisol, midnight salivary cortisol, and 1-mg dexamethasone suppression test are reasonable initial screening tests for Cushing syndrome (CS). Two abnormal initial tests are required to diagnose CS.
- Once the diagnosis of CS is established, ACTH level should be measured to differentiate between ACTH-dependent and ACTH-independent CS.
- The inferior petrosal sinus sampling is the gold standard test to differentiate between pituitary and ectopic source of ACTH secretion when pituitary MRI and dynamic studies do not point toward a pituitary source.
- The therapy of choice for patients with CS is surgery depending on the primary etiology (pituitary adenectomy/adrenalectomy/ectopic tumor removal).

**Primary Hyperaldosteronism**
- Most patients with aldosterone-producing adenomas are normokalemic and, therefore, a normal serum potassium should not preclude further evaluation.
- The measurement of plasma aldosterone to renin ratio (ARR) is the best initial test for evaluation of primary aldosteronism.
- The initial screening test (ARR) may be done while patients are on all antihypertensive agents except aldosterone receptor blockers (spironolactone and eplerenone); these need to be discontinued for at least 4 weeks.
- Patients with primary hyperaldosteronism (PA) should undergo CT of the adrenals for adrenal imaging. Bilateral adrenal vein sampling may be necessary to confirm the presence of a unilateral source of hyperaldosteronism.
- Patients with bilateral hyperplasia are treated with aldosterone receptor blockers such as spironolactone or eplerenone.
- Glucocorticoid-suppressible aldosteronism should be suspected in young hypertensive patients with an ARR >20 and family history of early cerebrovascular events.

**Pheochromocytoma**
- Patients with pheochromocytoma (PCC) may present with classic paroxysmal spells (headache, perspiration, and palpitation), hypertensive crises, or come to medical attention secondary to an incidental adrenal mass. Up to 15% of patients with PCC are normotensive at presentation.
- Plasma fractionated metanephrines or 24-hour urine metanephrines are the investigative tests of choice if PCC is suspected. Levels greater than fourfold upper limit of normal range are usually diagnostic.
- Tricyclic antidepressants are among the most common medications that can interfere with the biochemical evaluation for PCCs.
- β-Blockers should only be initiated after adequate α-blockade to prevent unopposed α-adrenergic action which may trigger a hypertensive crisis.
Adrenal Incidentaloma

- The diagnostic approach in patients with adrenal incidentalomas should focus on two main questions: whether the lesion is malignant and if it is hormonally active.
- All patients with an adrenal incidentaloma should be evaluated for autonomous cortisol secretion referred as subclinical Cushing syndrome, PCC and, if hypertensive, for primary aldosteronism.
- Homogenous adrenal tumors with a noncontrast CT attenuation value \(<10 \text{ Hounsfield units (HU)}\) are indicative of benign, lipid-rich adenomas.
- All adrenal incidentalomas \(>4 \text{ cm in size that lack characteristic benign radiologic features}\) should be surgically removed regardless of whether or not they are functional.

SUGGESTED READINGS


**POINTS TO REMEMBER:**

**Pituitary Adenomas**
- Pituitary tumors may present with symptoms of pituitary hypofunction, excess hormone secretion, or symptoms directly related to the mass effect of the tumor.
- Magnetic resonance imaging is the best method for visualizing hypothalamic–pituitary anatomy.
- Up to 20% of normal individuals harbor incidental pituitary tumors, which are almost all microadenomas.
- A limited biochemical workup for asymptomatic patients with microincidentalomas, to include measurement of prolactin (PRL) and insulin-like growth factor-1 (IGF-1) is reasonable, with further studies to be tailored based on the clinical picture.
- While pituitary adenomas are the most common cause of hypopituitarism, other causes, including parasellar diseases, inflammatory disorders, those following pituitary surgery or radiation therapy, and head injury, also must be considered.
- Prolactinomas are the most common secretory pituitary tumors. They account for approximately 30% of all clinically recognized pituitary adenomas.
- A serum PRL level >100 μg/L is usually indicative of a PRL-producing pituitary tumor.
- A serum PRL level <100 μg/L in the presence of a large pituitary adenoma is suggestive of stalk compression. Some medications including metoclopramide and antipsychotics may be associated with hyperprolactinemia up to 250 μg/L.
- Although patients with microprolactinomas can sometimes be followed without therapy, patients with macroprolactinomas must be treated.
- A random growth hormone (GH) level is inadequate to establish the diagnosis of acromegaly.
- IGF-1 has a longer plasma half-life than GH and is an excellent initial screening test for those suspected of acromegaly.
- Current medical therapies for acromegaly include dopamine agonist, somatostatin analogs, and GH receptor antagonist.

In acromegaly, the primary aims of treatment include relieving symptoms, reducing tumor bulk, normalizing IGF-1 and GH levels, and preventing tumor regrowth.

- Adrenocorticotropic hormone–secreting pituitary adenomas account for 65% of endogenous Cushing syndrome (CS).
- The diagnosis of CS involves confirmation of persistent hypercortisolism associated with a lack of cortisol suppressibility with dexamethasone.
- Pituitary apoplexy, resulting from a hemorrhagic infarction of the pituitary, usually associated with a preexisting pituitary tumor, is an endocrine emergency.

**Pituitary Apoplexy**
- If pituitary apoplexy is suspected, anterior pituitary insufficiency should be presumed, and the patient must be treated accordingly. Glucocorticoids, in a dose adequate to the degree of stress and presumptive edema related to hemorrhagic infarction, are the treatment of choice.

**Sheehan Syndrome**
- Sheehan syndrome is the result of an ischemic infarction of the normal pituitary gland, which leads to hypopituitarism secondary to postpartum hemorrhage and hypotension. Patients have a history of failure to lactate postpartum and failure to resume menses.

**Diabetes Insipidus**
- Diabetes insipidus (DI) is diagnosed in those with abnormally high urinary output (>50 mL/kg per day), low urinary osmolality (<300 mOsm/kg), and appropriate creatinine level (14 to 18 mg/kg body weight) indicative of an adequate 24-hour urine collection.

**Multiple Endocrine Neoplasia Syndromes**
- Multiple endocrine neoplasia (MEN) syndromes are inherited as an autosomal dominant trait.
- MEN I consists of parathyroid, pancreatic, and pituitary tumors.
- MEN IIA consists of medullary thyroid carcinoma, pheochromocytoma, and hyperparathyroidism.
MEN IIB consists of medullary thyroid carcinoma, pheochromocytoma, marfanoid body habitus, and mucosal neuromas.

Early diagnosis through screening of at-risk family members is essential because total thyroidectomy can cure or prevent medullary thyroid cancer.

DI is diagnosed in those with abnormally high urinary output (>50 mL/kg per day), low urinary osmolality (<300 mOsm/kg), and appropriate creatinine level (14 to 18 mg/kg body weight) indicative of an adequate 24-hour urine collection.

**SUGGESTED READINGS**


POINTS TO REMEMBER:

Hypercalcemia
- There is an extensive list of possible diagnoses for hypercalcemia, but a workable approach is to consider parathyroid versus nonparathyroid disease.
- Intact parathyroid hormone laboratory assay is used to differentiate hyperparathyroidism from other disorders.
- Most patients with hyperparathyroidism have chronic asymptomatic hypercalcemia.
- Surgery is the treatment of choice for primary hyperparathyroidism.

Hypocalcemia and Osteomalacia
- Osteomalacia is the hallmark of poor skeletal mineralization due to hypocalcemia, hypophosphatemia, or both.
- Primary findings in osteomalacia include hypocalcemia, hypophosphatemia, and hyperphosphatasia.
- The phosphorus level helps to differentiate the cause of hypocalcemia.
- Vitamin D deficiency is commonplace and can be due to sunlight deprivation, inadequate dietary sources, malabsorption, and/or increased catabolism.
- Primary hypoparathyroidism is a very rare phenomenon, and primary disease generally arises early in life.
- Patients who have undergone bariatric surgery are at risk for vitamin D deficiency, secondary hyperparathyroidism, and osteomalacia.

Osteoporosis
- Over 2 million fractures occur in the United States every year with approximately 300,000 hip fractures. Mortality with hip fracture is higher than 20%.
- Osteoporosis remains a clinical diagnosis, with reliance on the medical history, assessment of risk factors, and bone densitometry (DXA).
- FRAX® is a computer-based tool that uses common risk factors to calculate the 10-year probability of fracture, and was developed to assist the clinician identify patients who are most likely to benefit from medical therapy.
- DXA and FRAX have limited utility in the obese and bariatric surgery patient in that neither can quantify bone quality.
- Treatment for primary osteoporosis includes calcium and vitamin D, exercise, and medications.
- Osteonecrosis of the jaw is a very rare occurrence related to the use of bisphosphonates and is typically treated conservatively with antibiotics and oral rinses.
- When considering medical interventions in men with osteoporosis, a thorough investigation for possible secondary causes is essential, and any underlying secondary cause should be the first priority in the treatment plan.
- The decision regarding a drug holiday from osteoporosis agents needs to carefully balance risks versus benefits of continued treatment.

Paget Disease of Bone
- Paget disease of the bone is most often an incidental finding discovered during radiographs taken for other purposes.
- Cranial nerves may become involved when skeletal changes involve the cranial vault; most commonly cranial nerve VIII is affected.
- Pain may present as disease progresses.
- Biochemical evaluation of Paget’s will typically reveal elevated alkaline phosphatase with normal calcium and phosphorus.
- Three- to 6-month course of low-dose bisphosphonates is first-line therapy that may be continued if the alkaline phosphatase or other bone markers fail to return to normal.

SUGGESTED READINGS


Question 1

A patient being screened for intermittent diarrhea has a T₄ (total) value of 19.6 μg/dL (normal, 5.0 to 10.5). No other features of hyperthyroidism are present; no goiter is present. A T₄U test is elevated at 2.01 (normal, 0.8 to 1.20), whereas the T₄RU test is subnormal at 15% (normal, 25% to 35%). The free thyroxine index is calculated to be 9.8 (normal, 5.0 to 10.5). What single test would be most helpful in delineating the patient’s thyroid status?

a) Thyroid-stimulating hormone (TSH)
b) Thyroid receptor antibodies
c) Serum T₃
d) Serum FT₄ equilibrium dialysis
e) None of the above

Answer and Discussion

The answer is a.

Objective: Identify role of laboratory testing in diagnosing hypothyroidism.

The objective is to help gain understanding of the role of free (nonprotein bound) thyroid hormone in regulating TSH secretion. The hypothalamo-pituitary unit “reads” the free hormone level, not the total hormone level, which is subject to changes owing to alterations in protein binding (thyroxine-binding globulin, thyroid-binding prealbumin, albumin, or conditions that may interfere with binding).

In practice, the free thyroxine index can be calculated from total T₄ and an estimate of protein binding (T₄U or T₄RU; T₄U measures binding directly, whereas T₄RU provides an index of unbound hormone). Automated FT₄ assays are replacing these more indirect indices; the gold standard, FT₄ by equilibrium dialysis, is available in some reference laboratories but is rarely needed. Thus, serum TSH in this patient should provide the best indicator of thyroid function status and is independent from thyroid hormone protein-binding abnormalities.

Question 2

A female patient with primary hypothyroidism has been stable (normal TSH) on replacement LT₄ (dose, 1.6 μg/kg of body weight) for several years. On annual follow-up, the following laboratory tests are obtained: T₄, 14.1 μg/dL (normal, 5.0 to 10.5) and TSH, 23.4 μU/mL (normal, 0.4 to 5.5). She saw a gastroenterologist 6 months previously for nonsteroidal anti-inflammatory drug–related gastritis and takes an iron preparation and occasional antacids. Which is the most likely diagnosis?

a) Malabsorption of LT₄ owing to concomitant use of antacids and iron
b) Progressive loss of endogenous thyroid function
c) Development of thyroid hormone resistance
d) Poor compliance this past year, with attempt to “catch up” with excessive LT₄ intake recently
e) None of the above

Answer and Discussion

The answer is d.

Objective: Identify time lag in the hypothalamic–pituitary–adrenal axis.

Although TSH secretion may be acutely altered by stress, illness, or drugs, the major regulation is based on the integrated thyroid hormone exposure over the preceding 2 to 5 weeks. Although iron preparations and aluminum-containing compounds can interfere with T₄ absorption, the elevated serum T₄ level argues against this notion. Similarly, a progressive loss of thyroid function would be expected to lead to low or low-normal T₄ values. Although acquired thyroid hormone resistance may occur hypothetically, no clinical descriptions of such disorders exist. The correct answer is not a rare occurrence: Patients often want to please their health care provider, even if it means not being perfectly honest on occasion.

Question 3

You are asked to see a 75-year-old white man who was admitted to the psychiatric ward with a diagnosis of delirium. The history obtained from the wife revealed that he was well until 6 months before admission. He has had a 30-lb weight loss with a poor appetite since then. No history is present of any medication, with recent investigations involving radiocontrast media, goiter, or neck discomfort. No family history of thyroid disease is present. On physical examination, he is afebrile; he looks cachectic but is not pigmented; no features of infiltrative eye changes are present; and the thyroid gland is prolapsed, but may be just palpable on swallowing. The pulse rate is irregular at 120 beats/minute. The serum T₃ is 19.7 μg/dL (normal, 5.0 to 10.5) with a serum TSH <0.02 μU/mL (normal, 0.4 to 5.5).
The next step in diagnosis is to order

a) Serum T<sub>3</sub>
b) 24-Hour radioactive iodine uptake (RAIU)
c) 24-Hour RAIU and scan
d) Thyroid-stimulating antibodies
e) Thyroid microsomal (TPO) antibodies

**Answer and Discussion**

The answer is c.

**Objective: Identify appropriate workup for patient with thyrotoxicosis.**

This question reinforces the clinical presentation of elderly patients with thyrotoxicosis and their management. Although weight loss despite a generous appetite is characteristic in the younger adult, anorexia is not an uncommon finding in the elderly. Cachexia in an “apathetic” patient should be considered. (Concomitant Addison disease in a patient with known thyroid autoimmunity is a “distractor” in the current case presentation; the lack of pigmentation was intended to get the reader back on focus.) A cardiac dysrhythmia or congestive heart failure may be the major feature(s). The most common cause of hyperthyroidism in this age group is toxic multinodular goiter (sometimes iodide induced), but the absence of a goiter may be seen in up to 25% of elderly patients (5% in young adults).

Serum T<sub>3</sub> may be of academic interest (and occasionally a higher T<sub>3</sub>:T<sub>4</sub> ratio may help discriminate thyroiditis or toxic multinodular goiter from Graves hyperthyroidism), but it is generally reserved for cases in which total T<sub>4</sub> and FT<sub>4</sub> values are normal. Thyroid-stimulating antibodies are of minor value in ruling out Graves disease (usually a positive family history is obtained), but this diagnosis can be inferred from an elevated RAIU and diffuse scan order. Thyroid microsomal antibodies are a less expensive but less specific surrogate for Graves disease. The RAIU is necessary to discriminate thyroid hyperfunction (autonomous nodule[s], receptor antibody, TSH, or human chorionic gonadotropin driven) from subacute or silent thyroiditis, iatrogenic, or factitious causes. (Recent exposure to radiocontrast media or iodine-containing drugs or pregnancy may preclude its use, however.) A scan is of particular value when the clinician is unsure of the size and nature of the thyroid gland.

**Question 4**

The above 75-year-old man is diagnosed with thyrotoxicosis. He has a known history of diabetes and hypertension. He is still tachycardic. Management of the patient in the preceding question should include all of the following, except

a) β-Blockers
b) Digoxin
c) Coumadin
d) Propylthiouracil
e) Stress doses of glucocorticoids

**Answer and Discussion**

The answer is e.

**Objective: Identify appropriate management of patient with thyrotoxicosis.**

β-Blockers and propylthiouracil are helpful as primary therapy for hyperthyroidism in the elderly. Propylthiouracil is initiated only after the diagnosis is confirmed by a radioactive iodine uptake (and scan, if necessary). Radioactive iodine therapy may cause a transient worsening (radiation thyroiditis) of the hyperthyroidism and is often postponed in elderly patients until euthyroidism is attained (and antithyroid medication transiently withdrawn for 2 to 3 days before 131I treatment). β-Blockers and digoxin are helpful in controlling the heart rate in atrial fibrillation. Patient has a CHADS2 score of 3, and Coumadin is indicated in preventing embolic consequences of atrial fibrillation. The only drug not indicated without more data (the patient was not in “thyroid storm”) is the glucocorticoid.

**Question 5**

A 55-year-old businessman comes to your office complaining of fatigue. He denies any weight change but has nocturia one or two times a night. His 75-year-old mother is a diabetic; his father died of premature heart disease at 60 years of age. He has a history of hypertension treated with hydrochlorothiazide, 50 mg per day. Physical examination reveals that he is 50% above his ideal body weight; his blood pressure (BP) is 135/90 mmHg but is otherwise unremarkable. Fasting plasma glucose is 120 mg/dL; sodium, 143 mEq/L; potassium, 3.1 mEq/mL; chloride, 100 mEq/L; bicarbonate, 26 mEq/L; blood urea nitrogen (BUN), 12 mg/dL; and creatinine, 1.1 mg/dL. HgbA<sub>1c</sub> is 6.0% (normal range, 4% to 6%).

Which of the following is true?

a) The normal HgbA<sub>1c</sub> rules out diabetes.
b) An OGTT is not indicated.
c) Risk factors for diabetes mellitus (DM) include his family history, obesity, hypertension, and hypokalemia.
d) His hypokalemia need not be corrected before retesting his plasma glucose level.
e) Exercise should be avoided due to his family history of heart disease.

**Answer and Discussion**

The answer is c.

**Objective: Understand the diagnostic criteria for DM.**

Risk factors for DM include family history, obesity, hypertension, and hypokalemia. The diagnostic criteria for the diagnosis of DM include

1. Hemoglobin A<sub>1c</sub> ≥ 6.5%
2. Fasting plasma glucose ≥ 126 mg/dL
3. 2-Hour plasma glucose ≥ 200 mg/dL during an 75-g oral glucose tolerance test
4. Symptoms of hyperglycemia, hyperglycemic crisis AND random plasma glucose ≥ 200 mg/dL.
Review Questions

Question 6

The patient’s sister, who is visiting from out of town, is also known to have type 2 DM and hypertension. She is treated with glyburide, 10 mg twice daily, and her fasting blood glucose averages 160 mg/dL, with her HgbA1c at 8.8%. She seeks your counsel. Physical examination is unremarkable except for moderate obesity. Fasting glucose is 200 mg/dL; BUN, 25 mg/dL; and creatinine, 1.9 mg/dL. Electrolytes and liver enzymes are normal.

Which of the following would be reasonable recommendations in addition to improving her dietary habits and exercise regimen?

a) Discontinue glyburide
b) Add metformin, 500 mg twice daily after meals
c) Add acarbose, 25 mg three times daily
d) Add rosiglitazone, 4 mg daily

Answer and Discussion

The answer is d.

Glyburide should not be discontinued but could be reduced. With an elevated creatinine, metformin should not be prescribed. One should start a patient on acarbose (Precose), slowly and gradually increasing dosage. Rosiglitazone could be used, starting at 4 mg daily.

Question 7

A 40-year-old white woman with a history of severe asthma and Hashimoto thyroiditis reports 2 months of fatigue, anorexia, nausea, weight loss, and myalgia. Her examination is remarkable only for a BP of 98/60 mmHg and a pulse of 98 beats/minute without orthostasis. She shows no hyperpigmentation. Sodium is 130 mEq/L; potassium, 4.5 mEq/L; chloride, 105 mEq/L; and bicarbonate, 24 mEq/L. ACTH stimulation test shows cortisol at 5.8 μg/dL at T 0 minute and 13.2 μg/dL at T 60 minutes.

Which of the following is correct?

a) The most likely cause of her adrenal insufficiency is Addison disease.
b) The most likely cause of her adrenal insufficiency is prior exogenous corticosteroid use.
c) She does not have adrenal insufficiency because her ACTH stimulation test is normal.
d) She will require treatment with prednisone, 7.5 mg daily, and fludrocortisone, 0.1 mg daily.

Answer and Discussion

The answer is b.

Objective: Understand the diagnostic features of adrenal insufficiency.

This case illustrates the differences between primary and secondary adrenal insufficiency in clinical presentation and treatment. In secondary adrenal insufficiency, the renin–aldosterone axis is intact; therefore, hyperkalemia and metabolic acidosis are not seen, and fludrocortisone is not required for treatment.

Question 8

You are treating a 58-year-old man with hypopituitarism following radiation therapy for craniopharyngioma. He is taking hydrocortisone sodium succinate, 15 mg daily; levothyroxine, 0.15 mg daily; and testosterone injections, 200 mg every 2 weeks. He feels weak and tired. His examination is remarkable only for a BP of 95/58 mmHg. Sodium is 131 mEq/L; potassium, 4.8 mEq/L; TSH, 0.23 μIU/mL; and FTI, 9.0 μg/dL.

Which of the following would you do next?

a) Decrease levothyroxine
b) Increase testosterone
c) Add fludrocortisone
d) Increase hydrocortisone
e) Begin desmopressin acetate

Answer and Discussion

The answer is d.

Objective: Understand the treatment of iatrogenic adrenal insufficiency.

This case illustrates secondary adrenal insufficiency and inadequate glucocorticoid replacement. Physiologic hydrocortisone replacement is 20 to 30 mg daily. No data suggest the need for desmopressin or increased testosterone. Levothyroxine doses should not be adjusted by the TSH in secondary disease.

Question 9

A 37-year-old woman presents to you for evaluation of weight gain and hirsutism of several years duration. Her gynecologist has prescribed an oral contraceptive for oligomenorrhea. She has noted easy bruising but no muscle weakness. On examination, she weighs 240 pounds, with central obesity. BP is 144/92 mmHg. She has significant facial hair, mild acne, and multiple thin whitish striae on her abdomen, and a small buffalo hump. Her proximal muscle strength is normal. A random glucose level is 183 mg/dL, and potassium is 3.9 mEq/L. Her gynecologist sends you the results of an overnight dexamethasone suppression test (ODST) (morning cortisol of 6.2 μg/dL) and a random ACTH level (25 pg/mL).

Which of the following would you do next?

a) Order MRI of the pituitary
b) Order CT of the adrenals
c) Obtain a 24-hour urine free cortisol
d) Perform a high-dose (8 mg) dexamethasone suppression test

Answer and Discussion

Diagnostic criteria 1 to 3 above should be confirmed with repeat testing on a separate occasion.
Answer and Discussion
The answer is c.
Objective: Understand the diagnostic evaluation of Cushing Syndrome.
Generally, the 24-hour urine free cortisol is the best screening test; the 1-mg ODST is easier to perform but has more false-positive results, including increased cortisol-binding globulin owing to the estrogen in oral contraceptives. Radiographic imaging is not indicated until the diagnosis is established biochemically.

Question 10
A 50-year-old woman on chronic warfarin therapy for a previous pulmonary embolus was recently started on an acetylsalicylic acid (ASA)-containing analgesic for joint pain. She suddenly developed severe abdominal pain, and by the time she was taken to the emergency department, she was partially obtunded, hypotensive, and pale. Hemoglobin was found to be 8 mg/dL. What would you do next?

a) Check international normalized ratio
b) Do a 1-hour ACTH stimulation test
c) Administer intravenous saline and dexamethasone
d) Do a blood type and match
e) Obtain an abdominal CT

Answer and Discussion
The answer is c.
Objective: Understand the clinical presentation of acute adrenal hemorrhage.
This patient likely has adrenal insufficiency from an adrenal hemorrhage through the potentiation of warfarin by ASA. Intravenous fluids and dexamethasone can be lifesaving; then other options can be considered. Dexamethasone does not cross react with cortisol in the radioimmune assay. All choices are reasonable, but answer c should be performed first.

Question 11
A 52-year-old woman is referred to you by her urologist for a 3-cm right adrenal mass detected on abdominal CT. Her weight has been stable, and she has generally felt well. She has not noted hirsutism, acne, proximal myopathy, or easy bruising, but she has felt depressed lately. She also has had diaphoresis and occasional headaches but no palpitations. Her last menstrual period was 6 months earlier. She has a 2-year history of DM that is well controlled by diet. Her last mammogram 8 months earlier was negative, and no breast masses are present. She smokes one pack of cigarettes daily. BP is 135/85 mmHg; pulse, 95 beats/minute; and weight, 174 pounds. She has no buffalo hump, supraclavicular fat, or abdominal striae. Proximal muscle strength is normal. Stool is negative for occult blood. Complete blood cell count and chemistry profile are normal.

Which of the following would you do next?

a) Obtain a 24-hour urinary calcium excretion
b) Determine the aldosterone-to-PRA ratio
c) Obtain serum DHEAS and androstenedione levels
d) Obtain a 24-hour urine collection for catecholamines and metanephrines
e) All of the above

Answer and Discussion
The answer is d.
Objective: Understand the evaluation of an incidentally found adrenal mass.
Biochemical testing should be influenced by clinical findings. Even if no evidence of hormone production is apparent through history and physical examination, a biochemical screening for pheochromocytoma should nonetheless be done. A 1-mg overnight dexamethasone suppression test should also be done on all patients to exclude subclinical Cushing syndrome.

Question 12
A 68-year-old man presents for evaluation of a 2.5-cm adrenal mass. History and physical examination are negative for malignancy and overproduction of any adrenal hormones. A biochemical evaluation for pheochromocytoma is negative. No data are present regarding CT attenuation value, and MRI opposed-phase imaging is not available.

Which of the following would you recommend?

a) Surgery
b) Fine-needle aspiration (FNA) biopsy of the mass
c) Conventional MRI
d) Follow-up CT in 3 to 6 months

e) All of the above

Answer and Discussion
The answer is d.
Objective: Understand the evaluation of an incidentally found adrenal mass.
Surgery is not recommended for incidental adrenal masses unless they are large (>4 to 6 cm). A FNA biopsy can be diagnostic but should be used only when an immediate answer is needed and an experienced radiologist is available. FNA biopsy can diagnose metastatic disease but cannot always distinguish adrenal carcinoma from adenoma. Conventional MRI cannot distinguish metastasis from adenoma; only opposed-phase imaging (chemical-shift imaging) can do this. When CT or MRI cannot provide a definite diagnosis (metastasis versus adenoma), follow-up CT is indicated.

Question 13
A 25-year-old shoe salesman reports frontal headaches for 6 months. His free thyroxine (FT4) level is 0.4 ng/dL μg/dL (normal, 0.7 to 2.0 ng/dL), and his TSH level is 1.41 mIU/mL (normal, 0.4 to 5.5 mIU/mL). He also reports some loss of energy, leg cramps, and dry skin.
Which of the following is the most appropriate next step?

a) Start levothyroxine 50 μg every day on empty stomach
b) Check antimicrosomal antibody
c) Repeat thyroid function study in 3 months to see if there is any change
d) Obtain early morning cortisol, testosterone, LH, FSH, PRL, and IGF-1 levels
e) Utilize thyroid ultrasonography

**Answer and Discussion**

The answer is d.

**Objective: Understand the diagnostic evaluation of hypothyroidism.**

The low T₄ along with an inappropriately normal TSH level in an individual who is clinically hypothyroid should prompt a search for hypothalamic-pituitary dysfunction most commonly secondary to a pituitary tumor. Treatment of hypothyroidism in a patient with adrenal insufficiency may result in worsening of adrenal insufficiency symptoms due to an increase in metabolism of an already low cortisol level and should be approached with caution.

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**Question 14**

An MRI of the sella turcica reveals a 2-cm mass. Visual fields appear normal to confrontation, but under Goldmann perimetry, they show bilateral superior temporal defects. Laboratory findings include normal blood urea nitrogen (BUN), creatinine, and electrolyte levels; a testosterone level of 30 ng/dL (normal, 200 to 1,000 ng/dL); LH, 2 mIU/mL (normal, 1 to 7 mIU/mL); FSH, 1.5 IU/mL (normal, 2 to 10 mIU/mL); morning cortisol, 3.5 μg/dL (normal, 5.0 to 26.9 μg/dL); and PRL, 400 ng/mL (normal, <15 ng/mL).

Which of the following is false?

a) The patient has secondary hypogonadism
b) The patient is likely to have cortisol deficiency
c) The patient’s GH reserve is probably normal
d) The patient has a prolactinoma.

d) The patient has a prolactinoma.

**Answer and Discussion**

The answer is c.

**Objective: Understand the clinical presentation of pituitary tumors.**

In the presence of pituitary tumors, the pituitary gland sequentially loses the ability to secrete GH, LH, FSH, TSH, and ACTH. This patient has secondary hypogonadism, hypothyroidism, and likely hypoadrenalism. It is almost certain that GH secretion is low. GH deficiency often goes undetected in adults. Because irregular menses often leads to medical investigation, women often present earlier with small prolactinomas than men.

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**Question 15**

A 45-year-old white woman with clinical findings suggestive of Cushing syndrome has been found to have two elevated urinary free cortisol tests of 220 and 300 (normal, 2 to 50 mg/24 hour); her ACTH level is 55 (normal, 5 to 50 pg/mL), and her pituitary MRI shows a 3-mm adenoma.

Which of the followings is the best next course of action?

a) Repeat 24-hour urinary free cortisol
b) Transphenoidal surgery
c) Low-dose dexamethasone suppression test (LDDST)
d) High-dose dexamethasone suppression test (HDDST) and/or corticotropin-releasing hormone (CRH) stimulation test
e) Midnight serum cortisol level

**Answer and Discussion**

The answer is d.

**Objective: Understand the diagnostic evaluation of Cushing syndrome.**

The diagnosis of Cushing syndrome has been established in this patient with two significantly elevated 24-hour urinary free cortisol tests (>4 times the upper normal limit). A slightly elevated ACTH level excludes adrenal origin but may be seen in both Cushing disease and ectopic ACTH-producing tumors. The next step to differentiate between the two is to use the HDDST and/or CRH stimulation test. If the result is not conclusive, inferior petrosal sinus sampling should be done in an experienced center. The presence of a 3-mm pituitary adenoma is suggestive of a pituitary source for ACTH, but it may be a pituitary incidentaloma.

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**Question 16**

A 65-year-old man with a history of a nonfunctional macroadenoma develops severe retro-orbital headache, nausea, and vomiting with change in mental status. On examination, right third nerve palsy with stiff neck is present. An emergency MRI of the brain shows hemorrhage in the pituitary adenoma, which is enlarged in size.

What is the best next course of action?

a) Emergency transphenoidal surgery
b) Dexamethasone 2 mg intravenously every 6 hours
c) Nitroprusside drip to keep systolic BP between 140 and 160 mmHg systolic
d) Broad-spectrum antibiotic
e) Dopamine agonist

**Answer and Discussion**

The answer is b.

**Objective: Understand the treatment of pituitary apoplexy.**

High-dose steroid therapy is the initial step in treating patients with pituitary apoplexy. The glucocorticoids are used for presumptive ACTH deficiency and cerebral edema due to acute mass effect. Patients with altered mental status and neurologic deficits are candidates for definitive surgery once high-dose steroid use has been initiated.
Question 17

A 35-year-old man reports a 10-year history of renal stone disease and diffuse arthralgia. He is otherwise healthy and uses no vitamins, minerals, or drugs. Review of systems is normal, but a tibial radiograph shows a lesion at the mid-shaft. Serum data include a calcium level of 11.8 mg/dL (normal, 8.5 to 10.5 mg/dL); phosphorus, 2.9 mg/dL (normal, 2.5 to 4.5 mg/dL); creatinine, 1.0 mg/dL (normal, 0.5 to 1.3 mg/dL); intact PTH, 87 pg/mL (normal, 10 to 65 pg/mL); and calcitriol, 52 pg/mL (normal, 13 to 60 pg/mL).

All of the following are true except

a) Treatment with pamidronate is not necessary.
b) Adenomectomy is curative in most cases.
c) Recurrence is unlikely.
d) The chronicity of the problem argues for the presence of a neoplastic disorder.
e) Steroids will not control the problem.

Answer and Discussion

The answer is d.

Objective: Understand the clinical features of hyperparathyroidism.

The chronicity of renal stone disease combined with the increased serum calcium, decreased phosphorus, increased PTH, and high-normal calcitriol is typical of hyperparathyroidism. The radiographic finding of a brown tumor or cyst typifies the bone disease (osteitis fibrosa cystica) of hyperparathyroidism. The best treatment is parathyroidectomy. Hyperplasia is an unusual finding.

Question 18

A 50-year-old woman presents for a routine annual examination. She feels well. Past medical history is notable for peptic ulcer disease. Examination reveals a healthy-appearing, middle-age woman. Results of a chemistry panel are as follows:

<table>
<thead>
<tr>
<th>Test</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Na⁺ 136 mEq/L</td>
<td>136 mEq/L</td>
</tr>
<tr>
<td>K⁺ 3.9 mEq/L</td>
<td>3.9 mEq/L</td>
</tr>
<tr>
<td>Cl 102 mEq/L</td>
<td>102 mEq/L</td>
</tr>
<tr>
<td>HCO₃ 26 mEq/L</td>
<td>26 mEq/L</td>
</tr>
<tr>
<td>Blood urea nitrogen 18 mg/dL</td>
<td>18 mg/dL</td>
</tr>
<tr>
<td>Creatinine 1.0 mg/dL</td>
<td>1.0 mg/dL</td>
</tr>
<tr>
<td>Mg²⁺ 2.1 mg/dL</td>
<td>2.1 mg/dL</td>
</tr>
<tr>
<td>Ca²⁺ 11 mg/dL</td>
<td>11 mg/dL</td>
</tr>
<tr>
<td>P 2.0 mg/dL</td>
<td>2.0 mg/dL</td>
</tr>
<tr>
<td>Albumin 4.0 g/dL</td>
<td>4.0 g/dL</td>
</tr>
</tbody>
</table>

Her parathyroid hormone level is 90 pg/mL. All the following statements about the diagnosis are true, except

a) An increased level of urinary excretion of cyclic adenosine monophosphate is present.
b) The majority of patients are symptomatic at presentation.
c) This condition occurs in multiple endocrine neoplasia types 1 and 2a.
d) Peptic ulceration and pancreatitis may be associated.
e) A single abnormal gland is the cause in approximately 80% of patients.

Answer and Discussion

The answer is b.

Objective: Understand the clinical presentation and treatment of hyperthyroidism.

Methimazole is started. Which of the following statements about this patient’s condition is false?

a) Once a euthyroid state is achieved, the dose of methimazole can be reduced.
b) Once a euthyroid state is achieved, methimazole can be continued at the original dose and levothyroxine supplementation started.
c) Leukopenia is a potential complication.
d) Hypertrophic pulmonary osteoarthropathy may be seen.
e) Thyroglobulin levels will be low at the time of diagnosis.

Answer and Discussion

The answer is e.

Objective: Understand the clinical presentation and treatment of hyperthyroidism.

This case is typical of a patient with Graves disease. The symptoms described are those of hyperthyroidism in general. Older patients may have apathy. Ophthalmopathy with exophthalmos and dermatopathy, also termed pretibial

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myxedema, are often seen and are characteristic of Graves disease. Clubbing may be seen. Treatment is an oral antithyroid agent, and the dose can be lowered when euthyroidism is achieved, or levothyroxine can be added. After 12 to 24 months of treatment, the drug can be discontinued, and up to 50% of patients remain well for an extended time. Thyroglobulin levels are typically low in patients with thyrotoxicosis factitia; levels are usually elevated in Graves disease.

**Question 20**

A 38-year-old female nurse is seen for symptoms consistent with recurrent hypoglycemia. On occasion, she has collapsed at work. Her plasma glucose has been noted as 48 mg/dL on one occasion when she felt faint at work. Her past medical history is notable for irritable bowel syndrome, and her mother is known to be an insulin-requiring diabetic. Fasting laboratory values are as follows:

<table>
<thead>
<tr>
<th>Plasma insulin</th>
<th>468 μU/mL (normal, 626 μU/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>C-peptide</td>
<td>8.0 ng/mL (normal, 1.02.0 ng/mL)</td>
</tr>
<tr>
<td>Proinsulin-to-insulin ratio</td>
<td>15%</td>
</tr>
</tbody>
</table>

What would be the most appropriate next step in management?

a) Angiography with selective venous sampling for insulin levels
b) Two-phase contrast CT
c) Trial of octreotide and two-phase contrast CT
d) Search for needlestick marks
e) Urinary drug testing

**Answer and Discussion**
The answer is e.

**Objective:** Understand the diagnostic evaluation of hypoglycemia.

This woman has a laboratory picture consistent with factitious hypoglycemia. The most likely cause is sulfonylurea abuse. Patients with access to drugs are at higher potential for abuse. An elevated C-peptide level makes surreptitious insulin use an unlikely cause. Angiography and CT may be used to search for an insulinoma. An insulin-producing tumor can cause hypoglycemia; however, the proinsulin-to-insulin ratio is usually >20%. Urinary testing is the most effective way to search for evidence of sulfonylurea intake.

**Question 22 to 24**

Match the laboratory findings of a 72-hour fast with the most likely underlying cause of fasting hypoglycemia in questions

<table>
<thead>
<tr>
<th>INSULIN</th>
<th>C-PEPTIDE</th>
<th>URINE DRUG SCREEN</th>
</tr>
</thead>
<tbody>
<tr>
<td>a) +</td>
<td>+</td>
<td>Negative</td>
</tr>
<tr>
<td>b) +</td>
<td>–</td>
<td>Negative</td>
</tr>
<tr>
<td>c) +</td>
<td>+</td>
<td>Positive</td>
</tr>
<tr>
<td>d) –</td>
<td>+</td>
<td>Negative</td>
</tr>
</tbody>
</table>

**Question 22**

Exogenous insulin use

**Question 23**

Sulfonylurea use

**Question 24**

Insulinoma

**Answers and Discussion**

22. The answer is b.
23. The answer is c.
24. The answer is a.

Plasma C-peptide distinguishes endogenous from exogenous hyperinsulinemia. In the insulin synthesis pathway, first preproinsulin is secreted from the β cells of the pancreas with an A-chain, a C-peptide, a B-chain, and a signal sequence. The signal sequence is cleaved from the N-terminus of the peptide leaving proinsulin. Then the C-peptide is removed,
leaving the A-chain and B-chain that constitute the insulin molecule. Since the C-peptide only occurs with endogenous insulin production, it is high in patients with insulinomas and sulfonylurea-induced hypoglycemia. Plasma insulin values are high in patients with exogenous insulin administration, whereas plasma C-peptide values are appropriately low. There is a unique sulfonylurea drug screen testing that can detect the use of this medication. This often helps in surreptitious use of this medication.

Question 25

A 45-year-old man was seen in your office with complaints of generalized fatigue and unintentional weight loss of 8 lb over 6 months. He denied any palpitations or sleep disturbances. On physical examination, his skin was warm and moist. When his hand was outstretched, there was a fine tremor. His eye examination was unremarkable. His thyroid was asymmetrically enlarged (right > left) and firm, with a palpable nodule in the right lower lobe that measured 3 cm in greatest dimension. His trachea was in the midline. His TSH was <0.01 mU/mL (normal, 0.5 to 5 mU/mL), and free thyroxine T₄ was 2.6 ng/dL (normal, 0.9 to 2.4 ng/dL). What will be your next step in the management of this patient?

a) Start methimazole
b) Refer for FNA biopsy
c) Refer for radionuclide thyroid uptake and scan
d) Refer for subtotal thyroidectomy

Answer and Discussion

The answer is c.

Objective: Approach to the diagnosis of hyperthyroidism.

This young gentleman has presented with a solitary nodule in the background of mild hyperthyroidism. His differential diagnosis includes Graves disease, toxic uninodular goiter, and subacute thyroiditis. The next step would be to determine the etiology of the hyperthyroidism, so a radionuclide uptake and scan would be most helpful to determine the diagnosis and guide further management. In the setting of Graves disease, there will be an increased uptake by both lobes reflecting de novo synthesis of the thyroid hormone by the entire thyroid gland, whereas in a toxic nodule, there is a focus of increased uptake in one part of the thyroid with no uptake in the rest of the gland, which is suppressed. In case of thyroiditis, there will be a low radionuclide uptake secondary to inflammation of the gland.

Because a functioning or a “hot” nodule rarely harbors malignancy, a needle aspiration biopsy would be unnecessary. Methimazole is an option to treat hyperthyroidism from Graves disease and toxic nodule but has no role in treatment of thyroiditis. Hence, the first step is to determine the etiology. Subtotal thyroidectomy is usually reserved for patients who have local symptoms from an enlarged thyroid.

Question 26

A 74-year-old woman is seen in your office for follow-up of left leg cellulitis. Her past medical history is significant for hypertension, asthma, osteoporosis, and Hashimoto thyroiditis. She has been on levothyroxine for the past 40 years. Her home medications include lisinopril 10 mg daily, calcium supplement 1,000 mg daily, daily multivitamin, and levothyroxine 80 mcg daily. Both her sisters are on thyroid hormone replacement as well. On physical examination, she weighs 50 kg. Her BP is 140/90 mmHg, and pulse is 68 beats/minute and regular. Her thyroid is just barely palpable, and she is clinically euthyroid. Her cellulitis appears to be resolving. You note her laboratories as follows: TSH = 20 mU/mL (normal, 0.5 to 5 mU/mL) and free T₄ = 2 ng/dL (normal, 0.9 to 2.4 ng/dL). You see that her TSH was 2 mU/mL, 3 months ago, and she was on the same dose of levothyroxine. She acknowledges that she is supposed to take levothyroxine on an empty stomach, so she takes it right before going to bed and takes the rest of the medications in the morning. Which of the following best explains these results in the setting of this clinical scenario?

a) Her hypothyroidism has worsened, and she requires an increase in her dose of levothyroxine.
b) Decreased absorption
c) Prednisone caused the TSH elevation
d) Noncompliance

Answer and Discussion

The answer is d.

Objective: Recognize medication noncompliance as a cause of hypothyroidism.

In patients who appear to be on a correct dose of levothyroxine per day, an elevated TSH is often a sign of poor compliance. Such patients often have normal or even high unbound free T₄ levels and elevated TSH because they remember to take the medication for a few days before testing and this is sufficient to normalize their T₄. However, the TSH responses are gradual and take about 6 to 8 weeks to reflect the correct value.

Her family history suggests that she does not have Hashimoto thyroiditis. Since she has had longstanding disease, one can assume that there is no residual thyroid function. In this case, the replacement dose of levothyroxine is 1.6 mcg/kg body weight. She appears to be on an adequate replacement dose; thus, she does not need an increase in dose. Corticosteroids cause suppression of TSH and not elevation. She appears knowledgeable of the fact that thyroid medication absorption is highly dependent on food and other medications. Besides, if absorption was poor, her free T₄ would be expected to be subnormal.

Question 27

A 35-year-old woman with a history of type 1 DM for the last 20 years transfers to your practice for further care. During
the initial review of systems, she complains of chronic constipation, cold intolerance, and weight gain. She states that she has had a very poor appetite secondary to nausea for a few months and also feels unusually tired. Her previous physician had suggested a trial of antidepressants, which she had declined. Her only other medical problem is celiac disease.

Based on this information, you order TSH and free T₄ levels and subsequently other tests. The results are as follows: TSH = 22 mIU/mL (normal, 0.5 to 5 mIU/mL); free T₄ = 0.7 ng/dL (normal, 0.9 to 2.4 ng/dL); microsomal antibodies = 295 IU/mL (normal, < 5 IU/mL); ACTH stimulation test (250 mcg): baseline cortisol = 1.2 mcg/dL; cortisol after 30 min = 6.4 mcg/dL; and cortisol after 60 min = 7.1 mcg/dL. Based on the situation and the patient’s results, which of the following statements is true about this patient’s management?

a) Initiate glucocorticoids first, then levothyroxine
b) Initiate levothyroxine first, then glucocorticoids
c) Adrenal function is normal; initiate levothyroxine treatment.
d) This patient will need to be screened for hyperparathyroidism.

**Answer and Discussion**

**Objectives:** Diagnose and treat polyglandular autoimmune (PGA) syndrome.

This patient has clinical features suggestive of PGA syndrome type II. This diagnosis should be suspected when two or more endocrinopathies coexist. Immune dysfunction of nonendocrine glands can also be observed, and patients may have vitiligo, celiac sprue, alopecia, pernicious anemia, or myasthenia gravis.

This patient with a new diagnosis of autoimmune hypothyroidism with a history of type 1 DM and celiac disease fits the picture. All patients in whom PGA syndrome is suspected should be screened for adrenal insufficiency prior to treatment. This is because untreated hypothyroidism decreases the clearance of cortisol and may mask the symptoms of adrenal insufficiency. If levothyroxine treatment is initiated in such a patient, the resultant increased cortisol clearance can precipitate adrenal crises. If adrenal disease is present in the patient, glucocorticoid treatment should begin prior to or concurrent with that of hypothyroidism.

A normal response to the high-dose (250 mcg as an IV bolus) ACTH stimulation test is a rise in serum cortisol concentration after 30 or 60 minutes to a peak of 18 to 20 mcg/dL or more. Hypoparathyroidism and not hyperparathyroidism is a feature of this syndrome.

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**Question 28**

A 45-year-old homeless man is seen in the emergency room with complaints of severe headaches after drinking 12 cans of beer the night before. He also complains of blurry vision. On review of symptoms, he complains of fatigue and decreased libido. Your careful physical examination reveals no visual field deficit. You notice bilateral gynecomastia, but no galactorrhea. Prolactin level is 860 ng/mL. MRI of the pituitary reveals a 2 x 1.5 x 1.5 cm sellar mass that is just abutting but not displacing the optic chiasm. Formal visual field testing is normal. The rest of the pituitary function tests are normal, except for low testosterone and low FSH and LH levels. What is the next step in the management of this patient?

a) Repeat MRI in 3 months
b) Start bromocriptine
c) Refer to radiotherapy
d) Refer for surgery

**Answer and Discussion**

**The answer is b.**

**Objectives:** Diagnose and treat prolactinoma.

This patient has a lactotroph-producing adenoma that is greater than 1 cm in size (macroadenoma). The hyperprolactinemia is causing decreased libido, reduced testosterone, and gynecomastia due to gonadotropin suppression.

This patient needs prompt treatment for the following two reasons: (1) impending visual loss from compression of optic chiasm if the adenoma grows further, and (2) hypogonadism. Hence, waiting for 3 months to repeat imaging is not recommended.

A dopamine agonist is the drug of choice for any cause of hyperprolactinemia. It can decrease the size of the macroadenoma as well as improve symptoms. Surgery is usually reserved if the dopamine agonist therapy fails to decrease the prolactin level or decrease the size of the lactotroph adenoma. It may be considered also in a woman with a giant adenoma (>3 cm) who desires pregnancy. Radiation therapy is usually reserved for patients who have undergone surgery for a large macroadenoma with the aim of preventing regrowth of residual tumor.

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**Question 29**

A 75-year-old man from Alaska noticed sudden-onset back pain while lifting some furniture. X-ray of the back revealed a compression fracture at the level of L1. Routine biochemical evaluation was as follows: serum calcium = 8.4 mg/dL (normal, 8.5 to 10.5 mg/dL); serum phosphorus = 4.2 mg/dL (normal, 2.5 to 4.5 mg/dL); ALP = 210 U/L (normal, 40 to 150 U/L); and PTH = 87 pg/mL (normal, 10 to 60 pg/mL). DEXA bone mineral density measurements were as follows: L-spine: L1–L4: T-score = −2.9. What is the next step in the management of this patient?

a) Start a bisphosphonate
b) Check 1,25-dihydroxy vitamin D
c) Check 25-hydroxy vitamin D
d) Check 24-hour urine for calcium

**Answer and Discussion**

**The answer is c.**

**Objectives:** Diagnose and treat common causes of compression fracture.

In a patient with bone fracture and reduced bone mineral density, the two main differential diagnoses are osteoporosis and...
and osteomalacia. Osteomalacia is characterized by low calcium and phosphorus stores, elevated alkaline phosphatase (ALP) levels (indicating high bone turnover), and elevated parathyroid hormone (PTH), whereas osteoporosis, by definition, implies reduced bone mass in the absence of abnormal calcium, phosphorus, vitamin D, and PTH levels.

Vitamin D deficiency is a very common cause of osteomalacia in the elderly due to lack of sufficient dietary intake and limited sun exposure. It is a common cause of secondary hyperparathyroidism. Vitamin D deficiency is confirmed by measurement of serum 25-hydroxy vitamin D, which is the major storage form of vitamin D in the body. Measurement of 1,25-dihydroxy vitamin D is not helpful because the elevated PTH levels maintain a normal concentration of this active metabolite, even in the face of severe vitamin D deficiency.

Bisphosphonates are used for management of osteoporosis, not osteomalacia. In addition, 24-hour urine for calcium is expected to be low and will not help in further elucidating the diagnosis.

**Question 30**

A 37-year-old French Canadian man was seen in a preventive cardiology clinic after routine cholesterol levels were abnormal. His father died of a myocardial infarction at 45 years of age. You notice arcus cornea on his physical examination. His fasting lipid profile is as follows: LDL = 285 mg/dL; TG = 110 mg/dL; and HDL = 45 mg/dL. What is the most likely diagnosis?

a) Familial hypercholesterolemia  
b) Familial dysbetalipoproteinemia  
c) Lipoprotein lipase deficiency  
d) Familial combined hyperlipidemia

**Answer and Discussion**

The answer is a.

Objective: Recognize the different types of familial hypercholesterolemia.

This patient has heterozygous familial hypercholesterolemia, which is characterized by high LDL levels (>200 mg/dL), tendon xanthomas, and arcus cornea, as well as a family history of premature cardiovascular disease. The triglyceride and HDL levels are usually normal. Heterozygous familial hypercholesterolemia is one of the most common single-gene defects and affects approximately 1 in 500 people worldwide. There is a delayed clearance of LDL apolipoprotein B. Untreated men have a 50% chance of having myocardial infarction before 60 years of age.

Familial combined hyperlipidemia includes hypercholesterolemia (total cholesterol = 200 to 400 mg/dL), hypertriglyceridemia (TG > 200 mg/dL), and low HDL (<40 mg/dL) in the setting of a family history of hyperlipidemia and premature coronary heart disease. Tendon xanthomas are usually not seen. Patients with lipoprotein lipase deficiency often present in childhood with recurrent bouts of acute pancreatitis and have fasting triglyceride levels invariably >1,000 mg/dL. The primary defect is an inability to hydrolyze triglycerides in the chylomicrons. Eruptive xanthomas are a characteristic cutaneous finding.

Dysbetalipoproteinemia is characterized by an apolipoprotein E2/E2 phenotype and is rarely due to apolipoprotein E2 deficiency. Some of the most common precipitating factors are diabetes, obesity, hypothyroidism, renal disease, and alcohol use. Tuberoeruptive and palmar xanthomas are characteristic cutaneous findings. The plasma cholesterol and triglyceride levels are usually elevated to a similar extent until the plasma TG levels are approximately 500 mg/dL, after which TG levels tend to be greater than cholesterol.

**Question 31**

A 32-year-old woman is seen for primary infertility and irregular menses. Menarche was at age 14 years. Her periods have always been irregular, and she has about eight or nine periods a year. She has used birth control pills in the past to induce regular cycles. She also has some facial hirsutism. Her mother and maternal aunt have type 2 DM. On physical examination, she is overweight (BMI = 25.1 kg/m²) and has facial hirsutism. Workup for infertility included a pelvic ultrasound, which was unremarkable. Her laboratories are as follows: fasting glucose = 125 mg/dL; prolactin = 12 ng/mL (normal, <20 ng/mL); FSH = 4 mU/mL; LH = 13 mU/mL; dehydroepiandrosterenedione sulfate (DHEA-S) = 259 mcg/dL (normal, 1 to 47 mcg/dL); and free testosterone = 80 ng/dL (normal, 20 to 75 ng/dL). What is the most likely diagnosis in this patient?

a) Type 2 DM  
b) Late-onset congenital adrenal hyperplasia  
c) Androgen-producing ovarian tumor  
d) Polycystic ovarian syndrome

**Answer and Discussion**

The answer is d.

Objective: Recognize common features of polycystic ovarian syndrome.

This patient has polycystic ovarian syndrome clinically characterized by oligomenorrhea, infertility, hirsutism, and obesity. Biochemical tests that support her diagnosis are a high testosterone and DHEA-S level, an elevated LH-to-FSH ratio, and impaired fasting glucose, which reflects abnormal glucose metabolism. The underlying pathophysiology is thought to be insulin resistance. However, neither an elevated LH-to-FSH ratio nor insulin resistance is required to make the diagnosis.

Irregular menstrual cycle and hirsutism can also be seen in late-onset congenital adrenal hyperplasia; however, this disorder is not characterized by an elevated LH-to-FSH ratio. Testosterone-producing tumors produce symptoms of virilization with a relatively rapid onset and have significantly higher testosterone levels that are not just over the upper limit of normal, as in this case. The definition of diabetes is a fasting glucose of ≥126 mg/dL.
Question 32
A 23-year-old Caucasian woman is seen in your office for polyuria and increased thirst. She craves icy cold water. She denies headaches or visual changes. She has no significant past medical history. She denies using any medications. Family history is unremarkable. On physical examination, her BP is 110/70 mmHg, and pulse is 78 beats/minute. She weighs 50 kg.

Her laboratories are as follows: plasma glucose = 100 mg/dL; serum sodium = 147 mEq/L; serum potassium = 3.7 mEq/L; serum calcium = 9.1 mg/dL; serum creatinine = 0.6 mg/dL; serum osmolality = 297 mOsm/kg H2O; 24-hour urine volume = 5,500 mL; and HbA1c = 5.7. MRI of the pituitary is essentially unremarkable.

Her urine osmolality is 90 mOsm/kg H2O at baseline and 95 mOsm/kg H2O after 12 hours of water deprivation. After administration of vasopressin, her urine osmolality is 266 mOsm/kg H2O. What is this patient’s most likely diagnosis?

a) Primary polydipsia
b) Central diabetes insipidus (DI)
c) Nephrogenic DI
d) SIADH

Answer and Discussion

The answer is b.

Objective: Recognize common features of DI.

This patient had polyuria (defined as urine volume >50 mL/kg over 24 hours) with maximally dilute urine. Her differential diagnosis should include primary polydipsia, central DI, and nephrogenic DI. Other causes of polyuria should also be kept in mind, such as diuretic use, renal failure, hypercalcemia, hyperglycemia, and sickle cell disease. Her urine osmolality did not change with the water deprivation test; thus, primary polydipsia is unlikely. Her urine osmolality increased by >50% with use of vasopressin, making central DI the most likely diagnosis. In nephrogenic DI, there is a small (<45%) change or an absent response to administration of vasopressin. Polyuria and polydipsia are not characteristic symptoms of SIADH, and the sodium levels are low, not high.

Question 33

A 29-year-old Hispanic woman is seen at 10 weeks of pregnancy. She has a history of gestational diabetes during a prior pregnancy 3 years ago and a strong family history of type 2 DI. Her BMI is 31 kg/m2, but she is otherwise in good health. She has had no medical care since her last pregnancy.

A random blood glucose level today is 121 mg/dL. What is the most appropriate advice to give this patient now?

a) Begin metformin
b) Begin sulfonylurea
c) Begin insulin glargine at bedtime and lispro prior to meals
d) Arrange for standardized glucose testing as soon as possible

e) All of the above

Answer and Discussion

The answer is a.

Objective: Diagnose and treat gestational diabetes.

This patient has many risk factors for developing gestational diabetes (prior history of gestational diabetes, family history of diabetes, obesity, and ethnicity). The usual recommended screening test is a 50-g oral glucose challenge test. However, in a patient with high risk for gestational diabetes, obtaining a standardized glucose tolerance test may be more cost effective and therefore the best answer in this clinical situation.

Until the diagnosis of diabetes is established, it would be inappropriate to start any sort of therapy. Once the diagnosis is established, treatment includes medical nutritional therapy, self-monitoring of blood glucose levels, and insulin therapy, when needed.

NPH and regular insulin are United States Food and Drug Administration (FDA) approved for use in pregnancy. Insulin glargine has not been extensively studied in pregnancy and does not have an approval for its use. The American Diabetes Association and the American College of Obstetricians and Gynecologists do not endorse the use of oral hypoglycemic agents such as metformin or sulfonylurea during pregnancy, and such therapy has not been approved by the FDA.

Question 34

A 23-year-old woman with newly diagnosed DM is referred to you. She presents with an 8-lb weight loss over the last 2 to 3 months, random blood glucose values over 200 mg/dL on several occasions, and a hemoglobin A1c of 9%. Her medical history is significant for cystic fibrosis and numerous hospitalizations for lung infections. Her current medications include several inhalers, pancreatic enzyme pills, multivitamins, and ciprofloxacin. Her BMI is 19 kg/m2. She has digital clubbing. Her lungs have course vesicular sounds. She tries medical nutrition therapy, and after 6 weeks, her home glucose monitoring results show that her blood glucose remains elevated. Which of the following is the best therapeutic option at this time?

a) Insulin
b) Metformin
c) Thiazolidinediones
d) Acarbose

e) All of the above

Answer and Discussion

The answer is a.

Cystic fibrosis–related diabetes is a common finding of cystic fibrosis. It is important to understand that the abnormality in glucose metabolism is likely from pathology of endocrine pancreas, causing insulin and possibly glycogen deficiency. Hence, the most physiologic way to manage diabetes would be to replace insulin.

Metformin and thiazolidinediones are insulin sensitizers and will likely be ineffective in this case. α-Glucosidase inhibitors, which act in the gastrointestinal (GI) tract to slow
the absorption of glucose and also cause GI side effects like flatulence and diarrhea, are a poor choice in this patient.

1. 12. A 42-year-old Asian Indian man with type 1 DM for the last 35 years and no evidence of any microvascular complications complains of high early morning fasting blood glucose (>200 mg/dL). Upon questioning, he states that he has been experiencing nightmares recently. What is the best next step in the management of this patient?

a) Ask him to check blood glucose at 2:00 to 3:00 AM
b) Decrease his bedtime dose of glargine
c) Increase his bedtime dose of glargine
d) Ask him to cover his bedtime snack with short-acting insulin

**Answer and Discussion**

The answer is **a**.

This patient is likely experiencing Somogyi phenomenon— nocturnal hypoglycemia (nightmares) that causes rebound hyperglycemia in the early morning. This has to be differentiated from the dawn phenomenon characterized by early morning hyperglycemia secondary to a physiologic surge in counterregulatory hormones like cortisol and growth hormone as well as increased hepatic glucose output. It is essential to differentiate between these two phenomena because the former requires a decrease in the bedtime dose of insulin, whereas the dose needs to be increased in the latter. Hence blood glucose should be checked at 2 or 3 AM before making changes in the regimen. Adding short-acting insulin at bedtime will further worsen the nocturnal hypoglycemia.

**Question 35**

A 45-year-old male smoker has a CAT scan of his chest for evaluation of chronic cough. The scan is unremarkable except for a 2.8-cm right adrenal mass. The rest of his history and physical examination are unremarkable. His comprehensive metabolic panel is normal. What is the next step in the management of this patient?

a) Repeat CT scan of the adrenal mass in 3 to 6 months
b) Check 24-hour urine metanephrines, catecholamines, and cortisol
c) Refer for FNA of the adrenal mass
d) Refer for laparoscopic left adrenalectomy

**Answer and Discussion**

The answer is **b**.

**Objective:** Understand the work-up of an adrenal mass.

The first step in evaluating an incidental adrenal mass is to determine whether the mass is functioning by using appropriate screening tests. All masses should be evaluated for overproduction of catecholamines and cortisol. If the patient has a history of hypertension or hypokalemia, then a screen for hyperaldosteronism is warranted as well.

If malignancy is suspected, one can consider FNA of the mass. But this is contraindicated in a pheochromocytoma, which has to be ruled out first. Features suggestive of malignancy include a mass >4 cm (or >6 cm suggested by some experts), irregular margins, inhomogeneity, and soft tissue calcification as observed on CT scan.

If the mass is nonsecretory and malignancy is not suspected, then a repeat CT should be obtained in 3 to 6 months, but this is not the next best step. Similarly, laparoscopic left adrenalectomy is not the next best step. Some of the indications for laparoscopic adrenalectomy are a mass that is secretory, is >4 to 6 cm in size, or has radiologic characteristics that suggest malignancy.

**Question 36**

A 32-year-old man is seen for evaluation of low testosterone levels and primary infertility. He denies a history of tuberculosis, mumps, or prior radiation therapy. On physical examination, he is about 75” tall and weighs 200 lb. His arms and legs are disproportionately long for his height. He has an intact sense of smell, nontender gynecomastia, and small, firm testes. Visual field testing is normal. Laboratory test results are as follows: serum testosterone = 210 mg/dL; serum LH = 56 mU/mL; and serum FSH = 48 mU/mL. Which of the following is the most helpful next step in the diagnosis of this patient?

a) Serum iron studies
b) Serum prolactin and TSH
c) Pituitary MRI
d) Karyotype

**Answer and Discussion**

The answer is **d**.

**Objective:** Recognize the common features of Klinefelter syndrome.

This patient has clinical characteristics most consistent with Klinefelter syndrome (eunuchoid appearance, gynecomastia, and small testes) and biochemical evidence of hypergonadotropic hypogonadism. A karyotype can provide a definitive diagnosis. The classic form is 47,XXY genotype, whereas 46,XY/46,XXY occurs in mosaicism.

Hemochromatosis usually causes secondary testicular failure, so this phenotype would not be expected. Also, excessive skin pigmentation is usually present in over 90% of symtomatic adults. Hence, iron studies would not be helpful in this case. Pituitary MRI is expected to be essentially unremarkable and will not help in making a definitive diagnosis. Similarly, an abnormality in other pituitary axes is not expected.
Acute kidney injury (AKI) is defined as a rapid decline in renal function characterized by progressive azotemia (clinically measured by serum creatinine and blood urea nitrogen), which may or may not be accompanied by oliguria.

It is important to distinguish the three major causes of AKI: prerenal azotemia, postrenal azotemia or obstruction of the urinary tract, and intrinsic renal disease.

The presence of marked/sudden oliguria or anuria is a powerful diagnostic clue that suggests urinary tract obstruction, severe acute tubular necrosis (ATN) with cortical necrosis, or bilateral vascular occlusion.

If urinary tract obstruction is a diagnostic consideration, renal ultrasonography is sensitive and specific (90% to 95%) in confirming the diagnosis of hydronephrosis.

Diagnostic approach to AKI (see Table 46-6).

The therapy for prerenal azotemia is directed at optimizing volume status with isotonic fluids with the expectant improvement in renal function within 48 hours.

The specific diagnosis of acute interstitial nephritis (AIN) as a cause of acute kidney failure (AKI) should lead to the discontinuation of possibly offending medications. If the renal insufficiency does not resolve in days to weeks, renal biopsy results may confirm the diagnosis of AIN.

The prognosis of ATN is dependent on the underlying primary disease that resulted in AKI as well as any complications that arise during the bout of AKI. The mortality rate for patients with ATN may approach 40% to 50% in certain subgroups.

Data suggest that in azotemic patients who require cardiac angiography, a protocol of intravenous hydration and use of a nonionic contrast material appear warranted. Earlier randomized controlled trials have suggested that pretreatment with acetylcysteine might attenuate contrast injury in at-risk patients; however, more recent reviews have called this putative benefit into question.

SUGGESTED READINGS


POINTS TO REMEMBER:

- Findings on urinalysis that point to a glomerular origin include erythrocyte casts and dysmorphic erythrocytes.
- The nephrotic syndrome (NS) is defined by more than 3.0 to 3.5 g of proteinuria daily accompanied by hypoalbuminemia, edema, and hyperlipidemia. Nephrotic proteinuria is predominantly due to albuminuria and always denotes a glomerular origin of the disease process.
- The initial evaluation of the patient with NS includes laboratory tests to define whether the patient has a primary, idiopathic, or a secondary form of NS [e.g., measurement of fasting blood sugar, antinuclear antibodies, serum complement, hepatitis B virus, hepatitis C virus (HCV), and HIV serology]. Once secondary causes have been excluded, the treatment of the adult nephrotic patient usually requires a renal biopsy to define the pattern of glomerular involvement.
- Minimal-change disease (MCD) is the most common pattern of idiopathic NS in children and comprises approximately 5% of idiopathic NS in adults. Patients typically present with sudden onset of weight gain and both periorbital and peripheral edema.
- Membranous nephropathy (MN) is the most common pattern of idiopathic nephrotic syndrome in white Americans, while focal segmental glomerulosclerosis (FSGS) is the most common in African Americans.
- The presence of sudden flank pain, deterioration of renal function, or symptoms of pulmonary emboli in a patient with MN should prompt an investigation for renal vein thrombosis.
- In certain elderly patients with MN, an underlying carcinoma may be the occult cause of the renal lesion.
- Complement levels and the results of other serologic tests are normal in FSGS. Serum levels of suPAR, the soluble urokinase receptor, have been found to be elevated in FSGS patients as opposed to proteinuric patients with other forms of NS.
- Most patients with idiopathic NS, whether due to MN, FSGS, or MCD, will respond to immunosuppressive regimens with a remission of the nephrotic syndrome. Blockade of the renin–angiotensin–aldosterone system (RAAS) will reduce proteinuria in all nephritic patients.
- IgA nephropathy is the most common pattern of idiopathic glomerulonephritis worldwide.
- The diagnosis of IgA nephropathy is established by finding glomerular IgA deposits either as the dominant or as the codominant immunoglobulin on immunofluorescence (IF) staining. In addition to IgA, deposits of C3 and immunoglobulin G (IgG) are common.
- IgA nephropathy often presents with one of two syndromes: asymptomatic microscopic hematuria and/or proteinuria (most common in adults), or episodic gross hematuria after upper respiratory tract infections or exercise (most common in children).
- Evidence supports using RAAS blockade in all proteinuric IgA nephropathy patients and corticosteroids in those with larger amounts of proteinuria.
- Rapidly progressive glomerulonephritis (RPGN):
  - RPGN includes glomerulonephritides with progression to renal failure in a matter of days to weeks and the presence of extensive extracapillary proliferation (i.e., crescent formation) in a large percentage of the glomeruli.
  - RPGN has been divided into three patterns, defined by immunologic pathogenesis: Those characterized by anti-GBM disease, those characterized by immune complex deposition (e.g., SLE and poststreptococcal GN), and those characterized by the absence of immune deposits or anti-GBM antibodies (i.e., pauciimmune).
  - Most cases of pauciimmune RPGN have circulating antineutrophil cytoplasmic antibodies (ANCA-positive RPGN).
  - Pauicimmune RPGN has the most favorable treatment response rate of all patterns of RPGN.
  - Many patients with parenchymal disease due to acute (AIN) and chronic interstitial nephritis (CIN) will have medication-related disease.
  - When eosinophils comprise more than 5% of the total urinary leukocytes it is strongly suggestive of AIN. Eosinophiluria may also occur in RPGN, cystitis, and prostatitis.
  - The chronic use of analgesics (e.g., nonsteroidal anti-inflammatory drugs) have been associated with CIN.
In cryoglobulinemia, immune complexes deposit in the glomeruli, binding complement and inciting a proliferative response. The MPGN pattern is most common with HCV infection.

Glomerular involvement in HCV infection:
- HCV infection has been associated with arthritis, sicca symptoms, corneal ulcerations, porphyria, autoimmune thyroiditis, and polyarteritis as well as mixed cryoglobulinemia associated with immune complex GN.
- In cryoglobulinemia, immune complexes deposit in the glomeruli, binding complement and inciting a proliferative response. The MPGN pattern is most common with HCV infection.
- Total hemolytic complement, especially C4, is depressed.

**SUGGESTED READINGS**

**Glomerular Disease and Nephrotic Syndrome—General**

**Minimal-Change and Focal Segmental Glomerulosclerosis**

**Membranous Nephropathy**

**Immunoglobulin A Nephropathy**

**Membranoproliferative Glomerulonephritis**

**Rapidly Progressive Glomerulonephritis**

**Hepatitis C Virus**

**Severe Systemic Lupus Nephritis**

**HIV Nephropathy**

**Amyloidosis and Light Chain Deposition Disease**

**Tubulointerstitial Diseases**
Hallmarks of Primary and Secondary Hypertension

George Thomas and Martin J. Schreiber

POINTS TO REMEMBER:

- A complete history, physical examination, basic serum chemistries analysis, urinalysis, and ECG are recommended for the initial evaluation of a hypertensive patient.
- Specific aspects of the patient’s history should include family history, sleep history, nonprescription medication use (nonsteroidal anti-inflammatory drugs, diet pills, decongestants, appetite suppressants, and herbal therapy), oral contraceptive pills, and use of alcohol and recreational drugs.
- In most cases, the presence of significant arteriovenous nicking on fundoscopic examination indicates that the BP has been elevated for more than 6 months.
- Physical exam findings suggesting a secondary cause of hypertension include an abdominal or flank bruit (renal artery stenosis), central obesity with abdominal striae and buffalo hump (Cushing syndrome), enlarged kidneys (polycystic kidney disease), or diminished pedal pulses and a discrepancy between arm and leg pressures (coarctation of the aorta).
- Ambulatory blood pressure monitoring (ABPM) should be considered in the evaluation of patients with elevated office blood pressure readings but normal home readings and no evidence of end organ damage.
- A shift in emphasis from diastolic to systolic blood pressure (BP) has occurred over the years as evidence has mounted that reflects the very strong, positive, and causal relationship between increasing levels of systolic BP and cardiovascular risk.
- Patients presenting with BP > 180/110 mmHg should be classified as severe hypertension, hypertensive urgency, or hypertensive emergency based on clinical features.
- Severe hypertension: BP > 180/110 mmHg in the absence of symptoms beyond mild-to-moderate headache and without evidence of acute target organ damage. Management: Brief office observation, oral antihypertension medication, and short-term follow-up.
- Hypertensive urgency: BP >180/110 mmHg in the presence of significant symptoms such as severe headache or dyspnea but no or only minimal acute target organ damage. Management: Longer observation and treatment with oral agent with rapid onset of action with goal of lowering BP in 24 to 72 hours.
- Hypertensive emergency: BP very high (often >220/140 mmHg) with evidence of life-threatening organ dysfunction. Management: Admission to ICU and treatment with parenteral agent and goal to reduce BP by 15% to 25% within 4 hours.
- Resistant hypertension is defined as the persistence of out-of-office BP levels >140/90 mmHg despite a three-drug regimen that includes a diuretic and should prompt investigation for a secondary cause.
- Primary aldosteronism is the most common endocrine cause of secondary hypertension.
- The best clues to the presence of primary aldosteronism include hypertension with spontaneous hypokalemia (<3.5 mEq/L), hypertension with provoked hypokalemia (<3.0 mEq/L during diuretic therapy), and hypertension with difficulty maintaining normokalemia despite potassium supplementation. However, not all patients with primary aldosteronism have hypokalemia.
- The plasma aldosterone and plasma renin activity together can be used to screen for primary aldosteronism and a 24-hour urine aldosterone level can be used for confirmation.
- Among patients with pheochromocytoma, 80% present with headache, 57% with sweating, 48% with paroxysmal hypertension, 39% with persistent hypertension, and 64% with palpitations.
- The measurement of fractionated plasma-free metanephrines is the best test for familial pheochromocytoma, whereas 24-hour urine metanephrines and catecholamines provide adequate sensitivity and specificity for sporadic pheochromocytoma.
- Phenoxybenzamine, a relatively nonspecific, complete, and prolonged α-1 blocker that has traditionally been used perioperatively in the setting of pheochromocytoma, is now often replaced by calcium channel blockers, angiotensin receptor blockers, and selective α-1 blockers.
SUGGESTED READINGS


POINTS TO REMEMBER:

- Loss of water from the body should be referred to as dehydration. Loss of salt and water from the body should be termed extracellular fluid volume contraction or volume contraction.
- It is important to recognize the difference between dehydration and volume contraction: Normal saline, not dextrose 5% concentration in water (D5W), is the treatment for extracellular fluid (ECF) volume contraction. Fluid resuscitation for patients who are truly dehydrated should consist primarily of hypotonic fluids (e.g., D5W or D5W with normal saline).
- The serum sodium concentration is regulated primarily by water balance, not by the total amount of sodium in the body.
- Patients with congestive heart failure, nephrotic syndrome, and decompensated liver disease with ascites are examples of sodium excess states with increased ECF volume, but these patients may have normal, expanded, or contracted plasma volumes.
- A useful approach to the patient with hyponatremia attempts to place the hyponatremic patient into one of three broad categories based on the history, physical examination, and basic laboratory tests:
  - Hyponatremia with hypovolemia (inadequate circulation):
    - With renal salt retention (urinary sodium concentration <10 to 15 mEq/L):
      - Gastrointestinal losses, profuse sweating.
    - With urinary sodium wasting (urinary sodium >20 mEq/L):
      - Adrenal insufficiency, diuretics, renal salt wasting, as in chronic renal failure or distal renal tubular acidosis.
  - Hyponatremia with edema (urinary sodium concentration usually <10 mEq/L):
    - Congestive heart failure, hepatic cirrhosis with ascites, nephrotic syndrome.
  - Hyponatremia without evidence of hypovolemia or edema:
    - Syndrome of inappropriate secretion of antidiuretic hormone (SIADH), reset osmostat, drugs.
- SIADH is a relatively rare condition characterized by:
  - Hyponatremia with corresponding hypoosmolality of the serum and ECFs.
  - Continued renal excretion of sodium.
  - Absence of clinical evidence of fluid volume depletion or edema.
  - Normal renal function.
  - Normal adrenal and thyroid function.
  - Osmolality of the urine greater than that appropriate for the concomitant osmolality of the plasma or urine that is less than maximally dilute.
  - Most patients with SIADH have a low or low-normal serum uric acid level.
- As a general principle, the treatment for hyponatremia depends on the underlying cause:
  - If there is contracted ECF volume, the depleted volume should be replenished with sodium and water, usually in the form of normal saline.
  - If an edematous state exists, water should be restricted; in most circumstances, both salt and water should be restricted. If congestive heart failure is the reason for the hyponatremia, water restriction, loop diuretics, and cardiotoxic measures, such as the use of an angiotensin-converting enzyme (ACE) inhibitor, should alleviate the hyponatremia, especially if cardiac function improves.
  - If SIADH is diagnosed, water restriction is the mainstay of therapy. In certain patients, additional treatment could include administration of sodium chloride, a loop diuretic, demeclocycline or a vasopressin receptor antagonist.
- Severe acute hyponatremia (i.e., hyponatremia developing over 24 to 48 hours) may be associated with considerable morbidity, including seizures, coma, irreversible neurologic abnormalities, and death. This is most likely to occur with water administration to postoperative patients or in patients with thiazide-induced hyponatremia. Rapid initial treatment is both safe (because the cerebral adaptation is not complete) and may be lifesaving.
- For patients with hyponatremia of unknown duration, overly rapid correction may lead to central pontine myelinolysis, particularly if plasma sodium is increased by more than 25 mEq/L per day to above 140 mEq/L.
The electrocardiography (ECG) is frequently, but not always, useful in assessing the magnitude of hyperkalemia: For patients with elevated serum potassium levels in the range of 6.5 to 7.5 mEq/L, ECG typically demonstrates tall, peaked, or tented T waves. Serum potassium levels in the range of 7.5 to 8.0 mEq/L may be associated with loss of T waves or widening of electrocardiographic wave complexes.

Pinpointing the reason for hypokalemia may be simplified by measuring the 24-hour urinary potassium excretion in conjunction with a simultaneous serum potassium value. Classifying the cause of hypokalemia as either renal or extra-renal guides the differential diagnosis of hypokalemia.

SUGGESTED READINGS


Forrest JN Jr, Cox M, Hong C, et al. Superiority of demeclocycline over lithium in the treatment of chronic syndrome of inap-


RAPID BOARD REVIEW—KEY POINTS TO REMEMBER:

Steps in analyzing acid–base disorders:

1. Verify the internal consistency of the data:
   Calculated \([H^+] = 24 \times \frac{PCO_2}{[HCO_3^-]}\) should equal the estimated \([H^+] = 40 + (7.4 - \text{pH}_{\text{measured}}) \times 100\).

2. Determine the arterial blood pH:
   a. In the presence of a normal pH:
      - Normal \([HCO_3^-]\) indicates normal arterial blood gases.
      - Decreased \([HCO_3^-]\) indicates a mixed metabolic acidosis and respiratory alkalosis.
      - Elevated \([HCO_3^-]\) indicates a mixed metabolic alkalosis and respiratory acidosis.
   b. If pH < 7.35 patient has acidemia.
   c. If pH > 7.45 patient has alkalemia.

3. Determine if the primary disorder is:
   a. metabolic, when pH and \([HCO_3^-]\) are moving in the same direction;
   b. respiratory when pH and \([HCO_3^-]\) are moving in opposite directions.

4. In metabolic acidosis:
   a. The expected decrease in \(\Delta PCO_2 = 1.2 \times \Delta [HCO_3^-]\):
      - if \(CO_2\) is higher, a respiratory acidosis is also present;
      - if \(CO_2\) is lower, a respiratory alkalosis is also present.
   b. Calculate the anion gap (AG) = \(Na^+ - Cl^- - HCO_3^-\) (normal 10 to 12 mEq/L).
   c. When the patient has normal AG (hyperchloremic) metabolic acidosis, calculate the urine anion gap (UAG) = urine \(Na^+ + \text{urine K}^+ - \text{urine Cl}^-\):
      - if negative, it suggests gastrointestinal loss of \(HCO_3^-\);
      - if positive, it suggests renal loss of \(HCO_3^-\) as in renal tubular acidosis.
   d. When the patient has high AG metabolic acidosis, calculate the osmolal gap = osmolality_{\text{measured}} - (2\cdot[Na^+] + \text{glucose}/18 + \text{BUN}/2.8) and measure toxins if poisoning suspected, or osmolal gap is high (\(N < 10 \text{ mOsm/L}\)).

5. In metabolic alkalosis:
   a. The expected increase in \(\Delta PCO_2 = 0.6 \cdot \Delta [HCO_3^-]\).

6. In respiratory acidosis:
   a. When acute, the expected increase in \([HCO_3^-] = 1 \times \Delta PCO_2/10\).
   b. When chronic, the expected increase in \([HCO_3^-] = 3 \times \Delta PCO_2/10\):
      - if \(HCO_3^-\) is higher, a metabolic alkalosis is also present;
      - if \(HCO_3^-\) is lower, a metabolic acidosis is also present.

7. In respiratory alkalosis:
   a. When acute, the expected decrease in \([HCO_3^-] = 2 \times \Delta PCO_2/10\).
   b. When chronic, the expected decrease in \([HCO_3^-] = 5 \times \Delta PCO_2/10\).

8. Corroborate the results with the information obtained from history and physical examination.

DEFINITIONS

- **Acid** is a substance that can donate protons or hydrogen ions (H+).
- **Base** is a substance that can accept protons or hydrogen ions (H+).
Acidemia and alkalemia are descriptions of the patient’s actual blood pH.

- **Acidemia** is an increase in $[\text{H}^+]$ and a decrease in arterial pH below 7.35.
- **Alkalemia** is a decrease in $[\text{H}^+]$ and an increase in arterial pH above 7.45.

Acidosis and alkalosis are descriptions of pathophysiologic processes.

- **Acidosis** is a process that acidifies body fluids and, if unopposed, leads to a fall in pH and acidemia.
- **Alkalosis** is a process that alkalinizes body fluids and, if unopposed, leads to an increase in pH and alkalemia.
- **Buffer** is a substance that consumes or releases $\text{H}^+$, minimizing the pH changes.
- **Buffering capacity** is the ability of the buffer to resist changes in pH.

**SUGGESTED READINGS**


Question 1

A 44-year-old man reports intermittent gross hematuria. He is very concerned about his health following the recent death of his younger brother from a subarachnoid hemorrhage. Family history is remarkable for kidney disease. On examination, he is hypertensive with a mitral regurgitation murmur. No rash or skin lesions are found. Urinalysis shows more than 25 red blood cells but no white blood cells, casts, protein, or stones. Blood urea nitrogen (BUN) is 31 mg/dL and creatinine is 2 mg/dL. Of the following tests, which is most likely to be helpful in diagnosis?

a) 24-Hour urine collection for protein
b) Plasma immunoglobulin A levels
c) Renal ultrasound
d) Total and C3 complement levels
e) Renal biopsy

Answer and Discussion

The answer is c.

Objective: Diagnose polycystic kidney disease (PKD).

This patient has adult PKD. In PKD, thin-walled spherical cysts develop in the cortex and medulla of both kidneys from birth. The cysts range from millimeters to centimeters in diameter and are usually visible on ultrasonography or computed tomography (CT) by 25 years of age. Renal ultrasound is the diagnostic method of choice for screening individuals at risk. Sensitivity is >85% in those from 20 to 30 years of age. Although proteinuria is common in PKD, it rarely exceeds 2 g/day. Immunoglobulin A nephropathy may present with hematuria but is usually associated with erythrocyte casts and glomerulonephritis. Complement levels are normal in PKD and have no role in the diagnosis of this disorder. Renal biopsy is not necessary for the diagnosis.

Question 2

A 50-year-old woman presents with chronic elevation in blood pressure (BP). Which of the following clinical findings is/are suggestive of renovascular hypertension?

a) Systolic/diastolic epigastric bruit
b) Refractory hypertension
c) Gradual onset of hypertension at age 45
d) Choices a and b
e) Choices a, b, and c

Answer and Discussion

The answer is d.

Objective: Recognize features suggestive of renovascular hypertension.

An epigastric bruit with both systolic and diastolic components is suggestive of renal artery stenosis, which if hemodynamically significant may manifest as renovascular hypertension. This disorder may present as refractory (resistant) hypertension. Abrupt onset of hypertension as well as onset prior to age 30 years or after age 55 years is suggestive of renovascular hypertension. Conversely, gradual onset of hypertension during middle age is typical of essential or primary hypertension.

Question 3

A 60-year-old man is referred by his primary care physician to the emergency department for a severe elevation in BP. He denies any symptoms. The office BP was 206/110 mmHg, and on presentation to the emergency department, it has now increased to 212/116 mmHg with a heart rate of 84 beats/minute. He has been prescribed amlodipine, lisinopril, and hydrochlorothiazide in the past but ran out of all medications 1 week prior. Physical examination is unremarkable. Serum creatinine is 1.1 mg/dL, potassium is 4.1 mEq/L, and urinalysis is normal. What is the most appropriate management?

a) Measure 24-hour urine catecholamines and metanephrines
b) Resume the same antihypertensive medications, counsel on the importance of adherence, and schedule a follow-up office appointment with the primary physician
c) Clonidine 0.1 mg orally every 30 to 60 minutes until BP is <180/110 mmHg, then proceed as described in choice b
d) Prescribe new regimen of minoxidil 5 mg twice daily and arrange follow-up with the primary physician
e) Labetalol intravenously to achieve a 25% reduction in BP within 3 hours, then proceed as in choice b

Answer and Discussion

The answer is b.

Objective: Identify severe hypertension without crisis and manage appropriately.

Acute lowering of BP in this instance has not been shown to be of benefit, and there may be risks attributable to
You are evaluating a 74-year-old man for secondary causes of hypertension due to a BP of 164/74 mmHg despite a regimen consisting of chlorthalidone 25 mg daily, amlodipine 10 mg daily, doxazosin 4 mg daily, and metoprolol 100 mg twice daily as well as strict adherence to a low-salt diet. Laboratory testing while on this regimen are as follows:

- Serum potassium: 3.5 mEq/L
- Serum creatinine: 1.2 mg/dL
- Supine plasma renin activity: 0.8 μg/L per hour (0.5 to 1.8)
- Supine plasma aldosterone: 37.1 ng/L (4.5 to 35.4)
- Urinalysis: Normal

Which is the best next step to evaluate for primary aldosteronism?

a) Hold diuretic, advise the patient to add one teaspoon of salt to the daily diet for 5 days, and then collect a 24-hour urine sample for creatinine, sodium, and aldosterone
b) Adrenal CT
c) Adrenal magnetic resonance imaging (MRI)
d) Adrenal vein sampling
e) Iodine-131 metaiodobenzylguanidine iothalamate scan

**Answer and Discussion**

**The answer is a.**

**Objective:** Recognize factors that may lead to elevated catecholamine levels in the absence of pheochromocytoma.

In this case, the mildly elevated catecholamines may be due to a rebound effect from stopping clonidine; given her history, poor adherence to medications should be strongly suspected. Another possible reason for the elevated catecholamines is a false-positive test due to analytical interference from labetalol. Regardless, pheochromocytoma is not strongly suggested from the above information, and imaging is not warranted prior to biochemical confirmation. Repeat testing for catecholamines as well as metanephrines is in order; consider a clonidine suppression test only if these results are equivocal.

**Question 6**

A 52-year-old man with a 20-year history of cigarette smoking is admitted to the hospital because of cough and weakness. On admission, his serum electrolytes reveal a serum sodium concentration of 112 mEq/L; potassium, 4.5 mEq/L; chloride, 80 mEq/L; and HCO₃⁻, 26 mEq/L. The BUN was 8 mg/dL; serum creatinine, 0.8 mg/dL; and serum uric acid, 3.0 mg/dL.

These data are most consistent with which of the following?

a) Addison disease
b) Congestive heart failure
c) Cirrhosis with ascites
d) Syndrome of inappropriate antidiuretic hormone (SIADH)
Review Question 7

A 47-year-old man presents to the emergency room with a serum sodium concentration of 115 mEq/L. Physical examination reveals a supine BP of 120/80 mmHg and a standing BP of 90/60 mmHg. The skin turgor is diminished.

Which one of the following is the best treatment for this man’s hyponatremia?

a) Restriction of free water
b) Restriction of salt and water
c) Administration of normal saline
d) Treatment of the hyponatremia with demeclocycline

Answer and Discussion

The answer is c.

Objective: Recognize the clinical and laboratory features of SIADH.

The hyponatremia and normal renal function (normal BUN and serum creatinine) in conjunction with a low serum uric acid level all suggest SIADH. SIADH is also associated with low uric acid levels. The long history of cigarette smoking and cough suggest the possibility of a lung cancer, well known to be associated with SIADH. No evidence of congestive heart failure or cirrhosis with ascites is described on the physical examination. Although the values for sodium, chloride, and potassium concentration are consistent with adrenal insufficiency, one would expect hyponatremia of this magnitude due to adrenal insufficiency to have clinical and biochemical evidence of extracellular fluid (ECF) volume contraction—that is, a higher BUN, possibly a higher serum creatinine level (depending on the patient’s muscle mass), and a higher serum uric acid level.

Question 8

A 55-year-old white man with type 2 diabetes mellitus and diabetic nephropathy presents to the emergency department for evaluation of malaise and fatigue. He had previously been healthy and recently started on metformin to control his diabetes. His laboratory work reveals the following:

Na+: 140 mEq/L
K+: 5.5 mEq/L
Cl−: 104 mEq/L
HCO3−: 14 mEq/L
Glucose: 180 mg/dL
BUN: 56 mg/dL
Creatinine: 3.0 mg/dL
Arterial pH: 7.31
PCO2: 28 mmHg
Urine ketones: Trace+
Lactate: 10 mEq/L
Serum osmolality: 315 mOsm/L
Urinalysis: No crystals

Which of the following is the most likely scenario?

a) Diabetic ketoacidosis
b) Proximal renal tubular acidosis (RTA)
c) Metformin-induced lactic acidosis
d) Ethylene glycol intoxication
e) Isopropanol ingestion

Answer and Discussion

The answer is d.

Objective: Understand a systemic approach to acid–base disturbances.

The approach to all acid–base questions should involve the following steps:

1. Are the data internally consistent?

   Predicted [H+] (nEq/L) = 24 × P CO2/[HCO3−]
   = 24 × 28/14 = 48 nEq/L.

   The pH corresponding to this is ∼7.32, which is very close to the measured pH. Thus, the data are internally consistent.

2. Is the primary disturbance acidosis or alkalosis?

   The pH is <7.35; therefore, the patient is acidic, and the primary disturbance is an acidosis.

3. Is the primary disturbance metabolic or respiratory?

   HCO3− is 14 mEq/L, which is consistent with a metabolic acidosis.

   P CO2 is 28, which is consistent with a respiratory alkalosis. We therefore conclude that respiratory response is likely compensatory and that the primary disturbance is a metabolic acidosis.

4. Is the compensation adequate?

   For metabolic acidosis, use the Winter formula to estimate the appropriate P CO2:

   Predicted P CO2=1.5 × [HCO3−] + 8 (±2)=1.5×14 + 8 = 29.

   This is within 2 of the measured P CO2, so the respiratory compensation is adequate.

5. What is the anion gap (AG)?

   The AG is calculated as Na+ − (Cl− + HCO3−) = 140 − 118 = 22. The “normal” AG may vary based on the clinical laboratory, but a typical AG is ~12. Therefore, there is a wide AG metabolic acidosis, which prompts the clinician to consider a different set of diagnoses. Further testing reveals that lactic acidosis is present. Although trace ketones...
are present, the glucose is only mildly elevated, and diabetic ketoacidosis is less likely given the more impressive elevation of serum lactate. The patient also has renal insufficiency, which would be a risk factor for the development of lactic acidosis during treatment with metformin. Isopropanol ingestion often produces a ketosis but would not cause an elevated AG. Ethylene glycol ingestion could produce a similar scenario (including the presence of lactic acidosis). However, it is also associated with an elevated osmolar gap and the presence of urinary calcium oxalate monohydrate crystals. Detection of lactic acidosis should prompt the clinician to determine the cause such as tissue hypoperfusion, medications (e.g., metformin, linezolid, stavudine, and didanosine), or toxins (methanol, ethylene glycol, or salicylate). This case is not consistent with an RTA because of the presence of a wide AG.

6. If there is an AG, calculate the ΔAG.

The AG in this case was 22 (normal AG = 12 but may vary by the clinical laboratory), or a ΔAG of 10. If we assume that the ΔAG provides an estimate of the acid load and that 1 mEq/L of acid reduces [HCO₃⁻] by 1 mEq/L, then this can be added back to the actual [HCO₃⁻] (14 mEq/L) to estimate the starting concentration of [HCO₃⁻]. In this case, the [HCO₃⁻] is estimated to be 24 mEq/L before the acidosis occurred.

**Question 9**

A 47-year-old woman with advanced amyotrophic lateral sclerosis is evaluated in the clinic. She has recently been stable with no major changes in medical conditions. She is receiving magnesium, potassium, and HCO₃⁻ supplementation. She has advanced muscle weakness and requires a home mechanical ventilator:

- Na⁺: 142 mEq/L
- K⁺: 3.2 mEq/L
- Cl⁻: 118 mEq/L
- HCO₃⁻: 12 mEq/L
- Glucose: 96 mg/dL
- BUN: 6 mg/dL
- Creatinine: 0.2 mg/dL
- Arterial pH: 7.49
- PCO₂: 16 mmHg
- Urine Na⁺: 50 mEq/L
- Urine K⁺: 20 mEq/L
- Urine Cl⁻: 10 mEq/L

The single most appropriate treatment for this patient is

a) Increase oral HCO₃⁻ supplementation
b) Increase oral potassium supplementation
c) Increase magnesium supplementation
d) Increase the respiratory rate (minute ventilation) setting on the ventilator
e) Decrease the respiratory rate (minute ventilation) setting on the ventilator

**Answer and Discussion**

**Objective: Understand a systemic approach to acid–base disturbances.**

The approach to all acid–base questions should involve the following steps:

1. Are the data internally consistent?
2. Is the primary disturbance acidosis or alkalosis?
3. Is the primary disturbance metabolic or respiratory?
4. Is the compensation adequate?
5. What is AG?
6. If there is an AG, calculate the ΔAG.

A breakdown of this case is as follows:

1. The data are internally consistent (calculated H⁺ = 32, corresponding to pH ~7.48).
2. Alkalosis.
3. Respiratory alkalosis. There is a metabolic acidosis, which could be compensatory.
4. Compensation is adequate, assuming the process is chronic.

Using the formula for chronic respiratory alkalosis: \( \downarrow \Delta [HCO₃⁻] = 5 \times \Delta PCO₂ / 10 \), we expect [HCO₃⁻] to decrease by 12, which matches the observed change exactly.

5. AG is normal (10).
6. Because the AG is normal, ΔAG cannot be calculated.

**Further discussion:** If assessment of the [HCO₃⁻] were performed without an AG, it might be concluded that treatment with oral HCO₃⁻ supplementation would be appropriate. This would lead to further renal HCO₃⁻ wasting, which would obligate an equal loss of cations (e.g., K⁺, Mg²⁺, Ca²⁺) to maintain electroneutrality, further exacerbating the hypokalemia and hypomagnesemia. Although supplementation with oral potassium or magnesium may be warranted, it does not address the underlying problem. In this case, the respiratory set rate was decreased (gradually over a period of weeks), and HCO₃⁻, potassium, and magnesium supplementation were gradually tapered. The urinary AG is positive in this case due to renal HCO₃⁻ loss to compensate for the respiratory alkalosis, but this does not diagnose an RTA, as the primary process is not an acidosis. The very low creatinine provides a clue to the low muscle mass of this patient and may suggest that her metabolic demand and thus the need for respiratory excretion of CO₂ may not be as high as a normal patient.

**Question 10**

A 24-year-old woman is brought to the emergency department after a family member found her comatose at home. She had recently told her boyfriend that she would commit suicide if he broke up with her. The following laboratory values were obtained:

- Na⁺: 137 mEq/L
- K⁺: 3.6 mEq/L
Cl⁻: 100 mEq/L
HCO₃⁻: 16 mEq/L
Glucose: 96 mg/dL
BUN: 15 mg/dL
Creatinine: 0.9 mg/dL
Arterial pH: 7.39
PCO₂: 27 mmHg

Urine drug screen: Pending
Serum drug screen: Pending

Which of the following substances would produce this clinical scenario?

a) Oxazepam
b) Aspirin
c) Acetaminophen
d) Methanol
e) Ethylene glycol

Answer and Discussion

The answer is b.

Objective: Understand a systemic approach to acid-base disturbances.

The approach to all acid–base questions should involve the following steps:

1. Are the data internally consistent?
2. Is the primary disturbance acidosis or alkalosis?
3. Is the primary disturbance metabolic or respiratory?
4. Is the compensation adequate?
5. What is AG?
6. If there is an AG, calculate the ΔAG.

A breakdown of this case is as follows:

1. The data are internally consistent.
2. Acidosis. The pH is near normal, although both HCO₃⁻ and PCO₂ are clearly abnormal. The approach to evaluating acidosis is chosen because it is generally simpler and more commonly encountered than for an alkalosis.
4. To calculate compensation for metabolic acidosis:
   
   Predicted PCO₂ = 40 + 0.6 (Δ[HCO₃⁻]) = 40 + 0.6 (16) = 47.

   Further discussion: The finding of an elevated AG acidosis with a respiratory alkalosis should prompt a clinician to consider salicylate overdose. Salicylates stimulate central respiratory drive, and respiratory alkalosis is frequently observed in the initial stage of overdose. Salicylates also cause mitochondrial dysfunction and thus accumulation of excess CO₂ and lactic acid. In later stages, the excess CO₂ production overwhelms the ability to compensate, so absence of respiratory alkalosis may reflect a tenuous respiratory status. It is important to recognize that lactic acidosis is also found in the setting of salicylate overdose and should not dissuade the clinician from evaluating further for salicylate ingestion in the appropriate setting. Sepsis is another important cause of concurrent metabolic acidosis and respiratory alkalosis. Benzodiazepines commonly cause respiratory acidosis in overdose. Acetaminophen may cause high AG acidosis due to accumulation of 5-oxoproline (pyroglutamic acid). Methanol and ethylene glycol may also cause high AG acidosis but do not classically cause a respiratory alkalosis.

Question 11

A 24-year-old man presents to your office with complaints of leg cramps. He denies any other complaints or medical problems and is not taking any medications. The following laboratory values were obtained:

Na⁺: 142 mEq/L
K⁺: 3.2 mEq/L
Cl⁻: 100 mEq/L
HCO₃⁻: 34 mEq/L
Glucose: 85 mg/dL
BUN: 25 mg/dL
Creatinine: 0.9 mg/dL
Arterial pH: 7.48
PCO₂: 47 mmHg

What is the appropriate characterization of this acid–base disorder?

a) Metabolic alkalosis
b) Metabolic alkalosis and respiratory acidosis
c) Metabolic acidosis and respiratory alkalosis
d) Metabolic alkalosis and respiratory alkalosis
e) Metabolic acidosis

Answer and Discussion

The answer is a.

Objective: Understand a systemic approach to acid-base disturbances.

The approach to all acid–base questions should involve the following steps:

1. Are the data internally consistent?
2. Is the primary disturbance acidosis or alkalosis?
3. Is the primary disturbance metabolic or respiratory?
4. Is the compensation adequate?
5. What is AG?
6. If there is an AG, calculate the ΔAG.

A breakdown of this case is as follows:

1. The data are internally consistent.
2. Alkalosis.
3. Metabolic.
4. To calculate compensation for metabolic alkalosis:
   
   Predicted PCO₂ = 40 + 0.6 (Δ[HCO₃⁻]) = 47.

   Further discussion: The finding of an elevated AG acidosis with a respiratory alkalosis should prompt a clinician to consider salicylate overdose. Salicylates stimulate central respiratory drive, and respiratory alkalosis is frequently observed in the initial stage of overdose. Salicylates also cause mitochondrial dysfunction and thus accumulation of excess CO₂ and lactic acid. In later stages, the excess CO₂ production overwhelms the ability to compensate, so absence of respiratory alkalosis may reflect a tenuous respiratory status. It is important to recognize that lactic acidosis is also found in the setting of salicylate overdose and should not dissuade the clinician from evaluating further for salicylate ingestion in the appropriate setting. Sepsis is another important cause of concurrent metabolic acidosis and respiratory alkalosis. Benzodiazepines commonly cause respiratory acidosis in overdose. Acetaminophen may cause high AG acidosis due to accumulation of 5-oxoproline (pyroglutamic acid). Methanol and ethylene glycol may also cause high AG acidosis but do not classically cause a respiratory alkalosis.
Measured $P_{CO_2}$ is equal to the predicted $P_{CO_2}$, so this is a simple metabolic alkalosis. Because the compensation is a component of the metabolic alkalosis, it is not necessary to state that the patient has a respiratory acidosis.

5. The AG is normal.

Further discussion: In the absence of an obvious cause of gastrointestinal (GI) chloride loss, renal chloride or acid loss is likely. Measuring a urinary chloride would assist in this determination. Additional history is needed in this case, including BP and family history of similar disturbances.

**Question 12**

A 70-year-old man with recently diagnosed anemia is referred to you for evaluation of acidosis that was detected on routine blood work. He complains of weakness and fatigue but has had no recent illnesses or other chronic medical conditions. The following laboratory values were obtained:

- $Na^+: 142$ mEq/L
- $K^+: 3.2$ mEq/L
- $Cl^-: 111$ mEq/L
- $HCO_3^-: 18$ mEq/L
- Phosphorus: 1.9 mg/dL
- Glucose: 85 mg/dL
- BUN: 25 mg/dL
- Creatinine: 1.2 mg/dL
- Arterial pH: 7.33
- $PCO_2: 35$ mmHg
- Urine $Na^+: 50$ mEq/L
- Urine $K^+: 30$ mEq/L
- Urine $Cl^-: 50$ mEq/L

Urinalysis: pH 5.5, specific gravity 1.015, 2+ glucose, negative albumin

The metabolic disturbance is most likely due to

a) Diarrhea  
b) Type IV RTA  
c) Proximal (type II) RTA  
d) Distal (type I) RTA  
e) Vomiting

**Answer and Discussion**

The answer is c.

**Objective:** Understand a systemic approach to acid–base disturbances.

The approach to all acid–base questions should involve the following steps:

1. Are the data internally consistent?
2. Is the primary disturbance acidosis or alkalosis?
3. Is the primary disturbance metabolic or respiratory?
4. Is the compensation adequate?
5. What is AG?
6. If there is an AG, calculate the $\Delta$AG.

A breakdown of this case is as follows:

1. The data are internally consistent.
2. Acidosis.
3. Metabolic.
4. For metabolic acidosis, use the Winter formula to estimate the appropriate $PCO_2$:

   $$\text{Predicted } PCO_2 = 1.5 \cdot [HCO_3^-] + 8 (\pm 2) = 1.5 \times 18 + 8 = 35.$$  
   This is equal to the measured $PCO_2$, so compensation is adequate.

5. The AG is normal.

6. An additional step to take in the setting of a normal AG acidosis is measurement of the urinary AG. This will help to distinguish between GI $HCO_3^-$ loss and renal defects.

   $\text{Urine } AG = (\text{urine } Na^+ + \text{urine } K^+) - (\text{urine } Cl^-) = 50 + 30 - 50 = +30$. The positive urinary AG is indicative of an RTA.

Further discussion: The constellation of an RTA with renal glucosuria (glucose loss in the setting of normoglycemia), hypokalemia, and hypophosphatemia suggests global proximal tubular dysfunction (proximal, or type II, RTA). The patient’s advanced age and recently diagnosed anemia in this setting further suggests the diagnosis of multiple myeloma as a cause of the RTA.

**Question 13**

A 72-year-old man with a history of cirrhosis complicated by recurrent ascites is awaiting liver transplantation. He presents to the emergency department with a recent episode of upper GI bleed 5 days ago and decreased urine output for the past 3 days. His white blood cell count is 10,000/mm$^3$, hemoglobin is 9.7 g/dL, serum creatinine is 3.0 mg/dL, and baseline serum creatinine is 0.6 mg/dL. Which of the following factors would not support the diagnosis of hepatorenal syndrome (HRS)?

a) Acute onset of the renal failure  
b) Oliguria  
c) Benign urinary sediment  
d) Fractional excretion of sodium <1%  
e) History of primary biliary cirrhosis

**Answer and Discussion**

The answer is e.

**Objective:** Recognize the features of HRS.

The development of acute renal failure in advanced cirrhotic liver disease, severe alcoholic hepatitis, metastatic tumor, or fulminant hepatic failure from any cause is called the HRS. In patients with cirrhosis and ascites, the HRS has been shown to occur in about 19% of patients at 1 year and in 39% of patients at 5 years. It is characterized by oliguria, benign urine sediment, a very low fractional excretion of sodium, and a progressive rise in the plasma creatinine concentration. Onset is typically insidious, but it can be acute following an insult, such as GI bleeding, infection, or rapid diuresis.
Patients with hyponatremia or those with hyperreninemia or preexisting renal failure are at high risk for the HRS. Strangely enough, patients with primary biliary cirrhosis are comparatively protected against the development of the HRS. The best treatment is an improvement in hepatic function due to improvement of the primary disease or due to successful liver transplantation. Growing data suggest that combination therapy with midodrine and octreotide may be effective.

**Question 14**

A 55-year-old man undergoing hemodialysis three times a week missed his previous dialysis 2 days ago and presents to the emergency department, concerned about his missed dialysis. He is without specific complaints, except stating that he is several pounds over his dry weight. His vital signs reveal that he is afebrile at 36.5°C, heart rate is 80 beats/minute, respiratory rate is 14 breaths/minute, and BP is 130/80 mmHg. He has no jugular venous distention. His lungs are clear, and his heart sounds are regular with no S3 gallop or murmur. He has 1+ peripheral edema. His chemistry profile shows Na⁺ 138 mEq/L, K⁺ 5.8 mEq/L, Cl⁻ 104 mEq/L, HCO₃⁻ 22 mEq/L, BUN 120 mg/dL, creatinine 7.0 mg/dL, and glucose 125 mg/dL. An electrocardiogram (ECG) performed because of hyperkalemia is normal. Which of the following is an indication for emergent hemodialysis in this patient?

a) Hyperkalemia  
b) Elevated BUN  
c) Elevated creatinine  
d) Metabolic acidosis  
e) None of the above

**Answer and Discussion**

The answer is e.

**Objective:** Understand the indications for emergent hemodialysis.

Indications for emergent hemodialysis should not be based on the value of BUN or creatinine levels. Indications for emergent hemodialysis include symptomatic uremia (including pericarditis, neuropathy, or unexplained alterations in mental status), significant fluid overload, refractory hyperkalemia, or refractory metabolic acidosis. This man is neither symptomatic from uremia nor significantly fluid overloaded. Furthermore, his ECG does not demonstrate changes typically seen with significant hyperkalemia (he may have a baseline K⁺ of 5.5 mEq/L). His metabolic acidosis is probably also near his baseline. He may need hemodialysis in the very near future, but not emergently.

**Question 15**

A previously healthy 25-year-old man presents to his internist after referral from the emergency department for microhematuria. His vital signs and physical examination are normal. His urine dipstick is positive for both 1+ protein and 3+ hemoglobin, and the urine sediment, examined under the microscope, reveals red and white blood cells with granular and red cell casts. On further questioning, he denies a history of cough, hemoptysis, chest pain, sinus infections, or dyspnea. The chemistry profile reveals a BUN level of 40 mg/dL and a creatinine level of 4.0 mg/dL. He is sent for further testing, including a chest radiograph, which is reportedly normal. Anti-glomerular basement membrane (GBM) antibody testing is positive, as is testing for perinuclear pattern antineutrophil cytoplasmic antibodies (P-ANCA). A complete blood count is normal. Which of the following statements is false?

a) He has Goodpasture syndrome.  
b) He has anti-GBM antibody disease.  
c) He has antibodies directed against myeloperoxidase.  
d) He has antibodies directed against a chain of the type IV collagen found in basement membranes.  
e) He has a more treatable disease than he would if P-ANCA tests were negative.

**Answer and Discussion**

The answer is a.

**Objective:** Recognize the features of acute glomerulonephritis.

With his positive anti-GBM antibody status, this man has evidence of glomerulonephritis. These antibodies are directed to a target on the NC1 domain of the α₃ chain of type IV collagen found in the basement membrane. Goodpasture syndrome requires the presence of glomerulonephritis, pulmonary hemorrhage, and anti-GBM antibodies. This man does not have evidence of pulmonary hemorrhage. He is also positive for P-ANCAs, which can be seen in 10% to 38% of patients with anti-GBM antibody disease. P-ANCAs are directed against myeloperoxidase. Thus, overlap with Granulomatosis with polyangiitis or a related disease may exist, with occasional evidence of a systemic vasculitis. Treatment for these patients has a more favorable outcome than for P-ANCA–negative individuals.

**Question 16**

The following statements regarding uremic pericarditis are true, except

a) Pericarditis in patients with advanced renal failure is an indication for dialysis.  
b) The ECG shows diffuse ST-segment–T-wave elevations.  
c) Symptoms include pleuritic chest pain, which is worse in the recumbent position.  
d) If dialysis is performed, it should be heparin free due to risks of pericardial hemorrhage.  
e) It occurs in approximately 13% of patients on maintenance hemodialysis.

**Answer and Discussion**

The answer is b.

**Objective:** Recognize the complications of chronic kidney disease.

Renal failure is a common cause of pericardial disease. Uremic pericarditis is observed in approximately 10% of patients with
advanced renal failure and approximately 13% of patients on hemodialysis. Presenting signs and symptoms include fever and pleuritic chest pain. The pain increases with the recumbent position. Uremic pericarditis may be associated with worsening anemia. A strange feature of uremic pericarditis is that the typical diffuse ST- and T-wave elevations seen with other causes of acute pericarditis are absent on an ECG. This is secondary to the lack of penetration of the inflammatory cells into the myocardium. Systemic corticosteroids and indomethacin have had limited success in the treatment of uremic pericarditis. Unexplained pericarditis in a patient with advanced renal failure is an indication to institute dialysis provided the patient is hemodynamically stable. The response to dialysis is usually dramatic. Because heparin increases the risk of hemorrhage into the pericardial space, heparin-free hemodialysis should be performed. Pericardial effusion drainage may be required if intensive dialysis is ineffective.

Question 17

A 55-year-old man with a history of hypertension and renal artery stenosis is brought to the emergency department by his wife because of confusion. His BP is 220/120 mmHg. Head CT is negative for ischemia or hemorrhage. Which of the following additional findings would be least consistent with malignant hypertension?

a) Retinal hemorrhages and exudates
b) Hematuria
c) Proteinuria
d) Abrupt onset of confusion
e) Bilateral papilledema

Answer and Discussion

The answer is d.

Objective: Recognize the features of hypertensive emergency.

Malignant hypertension is characterized by elevated BP. Retinal involvement may include hemorrhages, exudates, and bilateral papilledema. Malignant nephrosclerosis leads to hematuria, proteinuria, and acute renal failure. Renal injury is due to fibrinoid necrosis in arterioles and capillaries, the same pathology as in hemolytic-uremic syndrome and scleroderma. Neurologic symptoms may be due to intracerebral or subarachnoid bleeding, lacunar infarction, or hypertensive encephalopathy. The encephalopathy seen in malignant hypertension is insidious in onset, unlike the abrupt onset of encephalopathy seen in strokes or hemorrhage.

Question 18

Which of the following statements regarding renovascular hypertension is false?

a) Renovascular hypertension is less common in African Americans.
b) Renovascular hypertension should be suspected when an abrupt rise in plasma creatinine levels occur after the institution of an angiotensin-converting enzyme (ACE) inhibitor.
c) Patients with moderate-to-severe hypertension who have recurrent episodes of acute “flash” pulmonary edema should be screened for renovascular hypertension.
d) The gold standard for diagnosing renal artery stenosis is the renal arteriogram.
e) The baseline plasma renin level is elevated in virtually all patients with renovascular hypertension.

Answer and Discussion

The answer is e.

Objective: Recognize the features of renovascular hypertension.

Renovascular hypertension is less common in African Americans. Moderately or severely hypertensive individuals with atherosclerosis, recurrent “flash” pulmonary edema, or asymmetric kidney sizes should be screened. In addition, patients who have a rise in serum creatinine levels after the initiation of an ACE inhibitor should also be screened. The gold standard for diagnosing renal artery stenosis is renal arteriography; however, intravenous pyelography can demonstrate delayed calyceal appearance of contrast and diminished kidney size in the presence of unilateral stenosis. In bilateral stenosis, the differences between the two kidneys may be difficult to see. Other methods for noninvasive screening are available; these include renogram, duplex Doppler ultrasound, magnetic resonance angiography, and spiral CT with angiography. The baseline plasma renin level is elevated in only 50% to 80% of patients with renovascular hypertension, but the administration of an ACE inhibitor can increase the predictive value of obtaining an elevated plasma renin level.

Question 19

All the following statements regarding RTA are true, except a) All forms of RTA are characterized by a normal AG (hyperchloremic) metabolic acidosis.
b) Proximal (type 2) RTA originates from the inability to reabsorb bicarbonate normally in the proximal tubule and is marked by a urine pH >7.5 and the appearance of filtered bicarbonate during bicarbonate infusion. This is often associated with Fanconi syndrome.
c) The most common causes of distal (type 1) RTA in adults are autoimmune disorders, such as Sjögren syndrome and other hyperglobulinemic states.
d) Distal RTA is associated with hyperkalemia, unless decreased tubular sodium reabsorption occurs, in which case hypokalemia is present.
e) Type 4 RTA is due to aldosterone deficiency or resistance of the tubular cells to aldosterone; typically, urinary pH is acidic, and serum bicarbonate is >17 mEq/L.

Answer and Discussion

The answer is d.

Objective: Understand the features and associations of the various RTAs.

All forms of RTA lead to a normal AG metabolic acidosis. Fanconi syndrome is a generalized proximal tubular...
dysfunction and is most often associated with proximal or type 2 RTA. In Fanconi syndrome, glucose, phosphate, uric acid, and amino acids are also spilled inappropriately, in addition to bicarbonate. The most common causes of Fanconi syndrome in adults include the excretion of light chains in multiple myeloma and the use of a carbonic anhydrase inhibitor. Multiple myeloma should be excluded in all patients with a proximal RTA unless another cause is identified. Urinary pH is variable in proximal RTA.

Distal RTA results from defects in hydrogen ion secretion: decreased proton pump (H⁺-adenosine triphosphatase) activity, hydrogen back-leak due to increased luminal membrane permeability, and reduction of the electrical gradient necessary for proton secretion due to decreased distal tubular sodium reabsorption. Distal RTA is often associated with hyperglobulinemic states. The urinary pH is inappropriately high (>5.5) and is often associated with hypercalciiuria due to bone loss from the chronic metabolic acidosis. In addition, hypokalemia is often seen, unless it is caused by decreased tubular sodium reabsorption. In this case, hyperkalemia is seen.

Type 4 RTA is due to either aldosterone deficiency or resistance by the tubular cells. The most common cause of aldosterone deficiency in adults is hyporeninemic hypoaldosteronism, seen in mild-to-moderate renal insufficiency (especially diabetic nephropathy). Finally, aldosterone resistance is commonly seen with potassium-sparing diuretics and chronic tubulointerstitial disease. It is associated with a mild metabolic acidosis due to the suppression of ammonia excretion due to hyperkalemia and an appropriately low urinary pH (<5.3) and serum bicarbonate >17 mEq/L.

**Question 20**

A 65-year-old man with a history of chronic renal insufficiency is now progressing to end-stage renal disease. In preparation for hemodialysis, you counsel him about the possible complications of chronic hemodialysis. Which of the following do you not discuss as a possible complication?

- a) GI bleeding
- b) Hepatitis
- c) Dementia
- d) Osteoporosis
- e) Cerebrovascular accidents

**Answer and Discussion**

The answer is d.

**Objective: Recognize the complications of chronic kidney disease.**

Osteomalacia, not osteoporosis, is a complication of dialysis. In addition to osteomalacia, aluminum toxicity is also associated with dialysis dementia. Hepatitis is a potential complication arising from the increased need for blood product transfusions. Liver failure arising from hepatitis can lead to portal hypertension that can lead to GI bleeding. In addition, heparin used during dialysis can also increase the risk of GI bleeding. Cerebrovascular accidents and cardiovascular disease are seen with increased frequency in uremic patients, accounting for 50% of deaths of hemodialysis patients.

**Question 21**

Which of the following statements regarding the diagnosis of minimal change disease (MCD) is incorrect?

- a) It accounts for 90% of nephrotic syndrome cases in children younger than 10 years, 50% in older children, and approximately 15% to 25% in adults.
- b) On electron microscopy, diffuse fusion of the epithelial cell foot processes is seen.
- c) A renal biopsy is necessary in both children and adults to confirm the diagnosis before the start of treatment.
- d) Corticosteroids are the mainstay of therapy in MCD.
- e) Nonsteroidal anti-inflammatory drugs (NSAIDs) are the most common cause of secondary MCD, and most affected patients concurrently have an acute interstitial nephritis.

**Answer and Discussion**

The answer is c.

**Objective: Understand key features of MCD.**

MCD is the most common cause of nephrotic syndrome in children (age younger than 10 years, 90%; older than 10 years, 50%), but accounts for only 15% to 25% in adults. Immunofluorescence and light microscopy do not show immune complex disease, but electron microscopy reveals diffuse fusion of the epithelial cell foot processes. Corticosteroid therapy is the mainstay of empiric treatment in children without biopsy because of the high frequency of MCD in this nephrotic population. Even in young adults (20 to 30 years), corticosteroids treat both MCD and focal glomerulosclerosis, the second most common cause of nephrotic syndrome. In older adults, other causes (e.g., primary amyloid and membranous nephropathy) of nephrotic syndrome must be ruled out with a renal biopsy before treatment. NSAIDs, ampicillin, rifampin, and interferon are not commonly used in MCD. MCD may be associated with an underlying hematologic malignancy (Hodgkin disease and, less commonly, other lymphomas or leukemias), whereas solid tumors usually produce an immune complex–mediated disease such as membranous nephropathy.

**Question 22**

A 52-year-old man comes to the clinic because he has had a cough and been feeling weak for the past several weeks. His past medical history is significant for some mild chronic low back pain for which he occasionally takes acetaminophen or ibuprofen up to four times daily. He smokes cigarettes (1 pack per day for 30 years). His temperature is 37.0°C (98.6°F), BP is 112/70 mmHg, pulse is 78 beats/minute, and respirations...
are 18/minute. Physical examination shows basilar crackles in the lungs. Laboratory studies are as follows:

Glucose: 115 mg/dL
Sodium: 126 mEq/L
Potassium: 3.8 mEq/L
Bicarbonate: 24 mEq/L
BUN: 9 mg/dL
Creatinine: 0.6 mg/dL
Serum osmolality: 258 mOsm/kg
Urine sodium: 30 mEq/L
Urine osmolality: 252 mOsm/L

What is the most appropriate next step in the management of this patient?

a) Admit the patient to the hospital and start an infusion of normal saline and obtain a chest x-ray
b) Restrict the patient to 1,500 mL of water per day and obtain a chest x-ray
c) Prescribe demeclocycline 150 mg orally 4 times per day, then follow up in 2 weeks
d) Discontinue the NSAIDs and acetaminophen

**Answer and Discussion**

**Objective:** Diagnose and treat SIADH.

This patient is presenting with a classic SIADH secretion. He has hyponatremia with elevated urine osmolality in the presence of decreased serum osmolality. Without evidence for kidney dysfunction, a urine sodium of >20 mEq/L essentially rules out volume depletion as a cause for the hyponatremia; therefore, therapy with normal saline is not indicated. The clinical symptoms are often vague like his; more severe cases present with seizures. One of the most common causes of SIADH is small-cell cancer of the lung, and as a smoker, he is at risk. The mainstay of treatment is with fluid restriction. A chest x-ray is a reasonable diagnostic test.

Demeclocycline is a medication that actually has nephrogenic diabetes insipidus (the opposite of SIADH) as one of its side effects by blocking the action of antidiuretic hormone. This medication is often adjunctive in the treatment of SIADH. However, you would not simply want to follow up with the patient in 2 weeks. These patients need much more vigilant care because further hyponatremia can result in severe neurologic sequelae. Acetaminophen and NSAIDs are not likely causes for SIADH.

### Question 23

A 37-year-old man with advanced cirrhosis secondary to hepatitis C is admitted with lower extremity edema and ascites. His home medications include spironolactone 25 mg daily. He undergoes a 4-L paracentesis and is begun on furosemide 40 mg PO three times daily. Over the next 4 days, he has a net diuresis of 3.3 kg during which his creatinine has steadily increased from 0.5 to 1.5 mg/dL and his urine output has dropped off to just over 400 cc/day. Physical examination is notable for a BP of 89/42 mmHg. He has modest ascites and minimal edema. Pulmonary examination reveals reduced breath sounds at lung bases. Laboratory studies are as follows:

BUN: 20 mg/dL
Creatinine: 1.5 mg/dL
Sodium: 119 mEq/L
Potassium: 3.7 mEq/L
Chloride: 82 mEq/L
Bicarbonate: 28 mEq/L
Urinalysis: Several granular and hyaline casts/high power field

Urine sodium: 11 mEq/L
Total bilirubin: 19 mg/dL
International normalized ratio: 2.4

In addition to discontinuing all diuretics, what is the most appropriate next step in management of this patient?

a) Repeat large-volume paracentesis
b) Initiate midodrine and octreotide
c) Infuse 1.5 L of normal saline over 24 hours
d) Place a transjugular intrahepatic portosystemic shunt

**Answer and Discussion**

**Objective:** Differentiate between prerenal azotemia from the HRS in a cirrhotic patient with acute kidney injury.

The differential diagnosis of renal failure in this patient includes prerenal azotemia, HRS, ischemic tubular injury, and sepsis. The first two are likely to cause low urinary sodium. Therefore, the first step is expansion of plasma volume with colloid or crystalloid to exclude a prerenal cause.

Two forms of HRS have been defined: Type 1 HRS entails a rapidly progressive decline in kidney function, while type 2 HRS is associated with ascites that does not improve with standard diuretic medications. A diagnosis of HRS is suspected in patients with liver disease with portal hypertension; renal failure; the absence of shock, infection, recent treatment with medications that affect the function of the kidney (nephrotoxins), and fluid losses; the absence of sustained improvement in renal function despite treatment with 1.5 L of intravenous normal saline; the absence of proteinuria; and the absence of renal disease or obstruction of renal outflow as seen on ultrasound. Therefore, a withdrawal of diuretics, exclusion of infections, and a trial of intravenous volume replacement is required in this patient to diagnose HRS.

Placement of a transjugular intrahepatic portosystemic shunt or the use of octreotide and midodrine is premature because the diagnosis of HRS has not been established. Repeat large-volume paracentesis in a patient like this may increase the risk of further ischemic renal injury.

### Question 24

A 29-year-old woman, who has been undergoing treatment for hypertension for the past 2 years, comes to the office...
because of chills and right-sided flank pain. She has had chronic “low back pain” that you have been treating unsuccessfully with NSAIDs. She has never had any diagnostic studies performed to evaluate her hypertension or back pain. She is estranged from her family, but she knows that her mother and brother have been treated for hypertension starting at age 27. Her temperature is 38.1°C (100.6°F), BP is 130/90 mmHg, and pulse is 85 beats/minute. On physical examination today, there is marked right-sided flank tenderness. Cardiac examination reveals a mid-systolic click. Urinalysis shows pyuria. You prescribe a 14-day course of trimethoprim–sulfamethoxazole and schedule a renal ultrasound and a follow-up visit. You tell her to call your office immediately if the symptoms worsen. On the return visit, she says that she feels much better but still has dull flank pain. Her temperature is 37.0°C (98.6°F). The ultrasound report is in the chart and states that there are seven cysts in her right kidney and five cysts in her left kidney. At this time, the most correct statement about her condition would be which of the following?

a) She is at an increased risk for developing colonic diverticular disease with perforation.

b) Her hypertension is unrelated to the kidney disease.

c) She has a 15% chance of developing end-stage renal disease by age 70.

d) There is a 70% chance that she has an intracranial aneurysm and will suffer from a subarachnoid hemorrhage.

**Answer and Discussion**

**Objective: Identify extrarenal manifestations of adult PKD.**

This patient most likely has PKD, and one of the most common extrarenal manifestations is colonic diverticular disease with an increased risk of perforation. The exact cause of this increased risk of perforation is not known. The hypertension, chronic flank pain, and the ultrasound findings are diagnostic for PKD. These patients tend to develop urinary tract infections, including acute pyelonephritis.

Her hypertension is related to PKD. It is most likely caused by the activation of the renin–angiotensin system secondary to ischemia caused by the distortion of the renal architecture by the cysts.

This patient has approximately a 50% chance of developing end-stage renal disease by age 70, not a 15% chance. PKD is associated with slowly progressive renal failure. The factors that are associated with an earlier onset of renal failure are male sex, hypertension, early age at diagnosis, and multiple infections. Only about 10% to 15% of patients with PKD have an intracranial aneurysm and will suffer from a subarachnoid hemorrhage, not 70%.

**Question 25**

A 44-year-old man is evaluated in your clinic for hypertension. He has a family history of essential hypertension, and both of his parents have type 2 diabetes mellitus. On physical examination, BP is 161/96 mmHg, and body mass index is 34. The remainder of the examination is normal. Laboratory studies are as follows:

- Electrolytes: Normal
- BUN: 25 mg/dL
- Creatinine: 0.9 mg/dL
- Fasting glucose: 92 mg/dL
- Total cholesterol: 218 mg/dL
- Low-density lipoprotein cholesterol: 138 mg/dL
- High-density lipoprotein cholesterol: 33 mg/dL
- Triglycerides: 240 mg/dL

You arrange for repeat BP testing and confirm the diagnosis of hypertension. You provide counseling regarding lifestyle modification. Therapy with which of the following treatments is the most appropriate at this time?

a) Hydrochlorothiazide
b) Benazepril and amlodipine
c) Salt restriction
d) Atenolol

**Answer and Discussion**

The answer is b.

**Objective: Identify and treat stage 2 hypertension.**

Since the patient has stage 2 hypertension, which is defined as a systolic BP of >160 mmHg and/or a diastolic BP of >100 mmHg, treatment initiation with a pharmacologic therapy in addition to lifestyle modification is warranted because lifestyle modification alone is unlikely to bring BP to goal. The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 7) recommends starting two antihypertensive agents initially for stage 2 hypertension.

Comorbidities or risk of comorbidities should be considered when selecting antihypertensive medications. The Antihypertensive and Lipid Lowering Treatment to Prevent Heart Attack Trial (ALLHAT) demonstrated that thiazide diuretics, ACE inhibitors, and calcium channel blockers were equally effective in preventing coronary artery disease in patients >55 years of age. However, patients randomized to the diuretic arm had a significantly higher incidence of type 2 diabetes within a 5-year follow-up period in this large trial. This patient has several risk factors (family history, obesity, and dyslipidemia) for the development of diabetes in the future. Both ACE inhibitors and angiotensin receptor antagonists have been associated with a lower incidence of new-onset diabetes compared with diuretics and β-blockers. Furthermore, the Avoiding Cardiovascular Events Through Combination Therapy in Patients Living With Systolic Hypertension (ACCOMPLISH) showed that a benazepril–amlodipine combination was superior to the benazepril–hydrochlorothiazide combination in reducing cardiovascular events in patients with hypertension who were at high risk for such events. Salt restriction should have been the first lifestyle modification technique employed but by itself will not be enough.
Question 26

A 62-year-old man has recently moved to your area and sees you as a new patient in the office. He brings his medical records with him. He has type 2 diabetes mellitus and hypertension, and recently had an abnormal stress test. Cardiac catheterization was done 1 month ago, which shows moderate triple vessel that is not amenable to revascularization. His medications are metformin, aspirin, a statin, a β-blocker, and an ACE inhibitor.

On physical examination, BP is 158/90 mmHg. There is evidence of early diabetic nephropathy on funduscopic examination. Laboratory studies are as follows:

- Sodium: 139 mEq/L
- Potassium: 5.1 mEq/L
- BUN: 18 mg/dL
- Creatinine: 1.2 mg/dL
- Spot urine albumin/creatinine: 135 mg/g
- Bicarbonate: 14 mEq/L
- Chloride: 115 mEq/L
- Potassium: 3.8 mEq/L
- Sodium: 139 mEq/L
- Glucose: 120 mg/dL
- Albumin: 3.9 g/dL
- BUN: 25 mg/dL
- Creatinine: 0.9 mg/dL
- Urine sodium: 42 mEq/L
- Urine pH: 5

Which of the following agents would you add to treat this patient’s hypertension?

a) A thiazide diuretic
b) A loop diuretic
c) An α-blocker
d) An angiotensin receptor blocker

**Answer and Discussion**

The answer is a.

**Objective:** Identify appropriate antihypertensive therapies based on comorbidities and compelling indications.

Therapy with a thiazide diuretic is indicated in this patient. He has evidence of diabetic nephropathy and coronary artery disease; therefore, his current regimen of a β-blocker and ACE inhibitor is appropriate for target organ prevention. Lowering his BP will likely reduce his level of proteinuria. Addition of a thiazide diuretic is most appropriate to lower BP without further exacerbating his hyperkalemia. Loop diuretics are weak antihypertensives, angiotensin receptor blockers will further worsen his hyperkalemia, and α-blocker therapy has been associated with increased incidence of cardiovascular endpoints in the ALLHAT trial and is not indicated at this time.

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**Question 27**

A 58-year-old woman with a history of coronary artery disease, peripheral vascular disease, difficult to control hypertension, and chronic kidney disease with a serum creatinine of 1.3 mg/dL is seeing you in the office for a follow-up after being discharged from the hospital for treatment of shortness of breath.

Her medications are aspirin 81 mg/day, metoprolol 50 mg twice daily, furosemide 40 mg twice daily, amlodipine 5 mg/day, clonidine 0.2 mg twice daily, and lisinopril 40 mg/day.

On physical examination, her BP is 177/74 mmHg and pulse rate is 62 beats/minute. Cardiac examination is significant for an S4 gallop. Her lungs are clear. An abdominal bruit is heard. She has 1+ bilateral lower extremity edema. She had a renal ultrasound in the hospital that showed a left kidney of 8.9 cm and a right kidney of 11.2 cm. There was increased echogenicity of both kidneys. Her urinalysis is negative for any protein or blood.

What is the next step to manage this patient’s hypertension?

a) Add irbesartan
b) Increase amlodipine to 10 mg/day
c) Perform a CT abdomen with intravenous contrast
d) Perform magnetic resonance angiography of the abdomen

**Answer and Discussion**

The answer is d.

**Objective:** Identify the correct diagnostic study for suspected renovascular hypertension.

Renovascular hypertension should be suspected in this elderly patient with diffuse atherosclerosis and chronic kidney disease and bland urine sediment. Hyperreninemia secondary to renal ischemia can lead to recurrent episodes of pulmonary edema. Magnetic resonance angiography is most appropriate for this patient with her level of renal function because she is at risk for contrast-induced renal failure with a CT scan. Gadolinium would be safe in this patient; it has been associated with nephrogenic systemic fibrosis only in those with advanced renal failure. This test could result in a false-positive result and therefore should be used in accordance with clinical features suggestive of renovascular hypertension. Adding irbesartan in this setting of possible renovascular disease may result in hyperkalemia or acute renal failure. Increasing amlodipine to 10 mg/day will likely only provide marginal benefit in reducing her uncontrolled hypertension.

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**Question 28**

A 44-year-old man is admitted with low-grade fevers, abdominal pain, poor intake of solid foods, and diarrhea for a week. He states that he has been trying to drink liquids to stay hydrated. He has a history of type 2 diabetes mellitus, coronary artery disease, and hypertension. His medications are aspirin 81 mg/day, metformin 500 mg twice daily, atenolol 50 mg/day, hydrochlorothiazide 12.5 mg/day, and lisinopril 20 mg/day. On physical examination, he is afebrile, BP is 122/70 mmHg, pulse rate is 74 beats/minute, and respiratory rate is 24/minute. Laboratory studies are as follows:

- Glucose: 120 mg/dL
- Sodium: 139 mEq/L
- Potassium: 3.8 mEq/L
- Chloride: 115 mEq/L
- Bicarbonate: 14 mEq/L
- Albumin: 3.9 g/dL
- BUN: 25 mg/dL
- Creatinine: 0.9 mg/dL
- Urine pH: 5

**Answer and Discussion**

The answer is c.

**Objective:** Identify appropriate diuretic therapy for diabetes.

On physical examination, BP is 158/90 mmHg. There is evidence of early diabetic nephropathy on funduscopic examination. Laboratory studies are as follows:

- Creatinine: 0.9 mg/dL
- BUN: 25 mg/dL
- Albumin: 3.9 g/dL
- Potassium: 3.8 mEq/L
- Sodium: 139 mEq/L
- Chloride: 115 mEq/L
- Glucose: 120 mg/dL

**Answer and Discussion**

The answer is c.

**Objective:** Identify appropriate diuretic therapy for diabetes.

The answer is c.

**Answer and Discussion**

The answer is c.

**Objective:** Identify appropriate diuretic therapy for diabetes.

The answer is c.

**Answer and Discussion**

The answer is c.

**Objective:** Identify appropriate diuretic therapy for diabetes.

The answer is c.

**Answer and Discussion**

The answer is c.

**Objective:** Identify appropriate diuretic therapy for diabetes.

The answer is c.

**Answer and Discussion**

The answer is c.

**Objective:** Identify appropriate diuretic therapy for diabetes.

The answer is c.
Urine potassium: 18 mEq/L
Urine chloride: 85 mEq/L
Arterial blood gas on room air:
\[ \text{pH}: 7.28 \]
\[ \text{PCO}_2: 29 \text{ mmHg} \]
\[ \text{PO}_2: 93 \text{ mmHg} \]

Which of the following is most likely responsible for this patient’s acid–base disorder?

a) Metformin  
b) Diarrhea  
c) Type 4 RTA  
d) Type 1 RTA

**Answer and Discussion**

**The answer is b.**

**Objective: Identify primary causes of normal AG metabolic acidosis.**

This patient has a normal AG metabolic acidosis. He has adequate respiratory compensation, which can be calculated by Winter’s formula: \[ \text{PCO}_2 = 1.5 \times \text{HCO}_3 \] (14 in this case) + 8 ± 2, which in this case is 29 ± 2.

This excludes a complex acid–base disorder. A major renal response to systemic acidosis is to increase urinary ammonium excretion. The amount of ammonium in the urine can be calculated using the urinary AG and the following formula: \[ [\text{Na}^+] + [\text{K}^-] - [\text{Cl}^-] \], which in this case is [42] + [18] − [85] = −25.

A negative urinary AG implies that there is an unmeasured cation such as ammonium present in the urine. This implies a normal renal response to acidosis, rules out an RTA, and suggests an extrarenal cause of acidosis such as diarrhea. Also in most RTAs, the renal pH will be >5. Metformin is associated with a lactic acidosis, which is not consistent with this patient’s lack of an elevated AG.

**Question 29**

An 84-year-old woman is admitted to the hospital from a nursing home with increasing lethargy. She has history of hypertension, dementia, constipation, and congestive heart failure. Her family is with her and reports that she is new to the nursing home because they could not take care of her. Her medications are docusate 100 mg PO twice daily, enalapril 10 mg/day, and donepezil 10 mg/day.

On examination, she is afebrile, BP is 129/74 mmHg, and pulse is 70 beats/minute. She is lethargic but responds to pain. Her mucous membranes and skin are mildly dry. She moves all her extremities spontaneously and has no focal neurologic deficits. A CT brain scan without contrast was obtained and was negative. Laboratory studies are as follows:

- Glucose: 122 mg/dL
- Sodium: 158 mEq/dL
- Potassium: 4.6 mEq/L
- Chloride: 124 mEq/L
- Bicarbonate: 24 mEq/L
- BUN: 35 mg/dL
- Creatinine: 1.1 mg/dL

What is the most appropriate therapy for this patient?

a) Oral free water repletion  
b) Intravenous normal saline  
c) Intravenous 1/2 normal saline  
d) Intravenous D5W

**Answer and Discussion**

The answer is d.

**Objective: Recognize common features and appropriately treat hypernatremia.**

Clinical manifestations of hypernatremia can be subtle, consisting of lethargy, weakness, irritability, neuromuscular excitability, and edema. With more severe elevations of the sodium level, seizures and coma may occur. The only situation in which you give normal saline in hypernatremia is when the patient is hypotensive and hemodynamically unstable. She has a normal BP and heart rate. Absence of tachycardia makes intravascular volume depletion unlikely. Reduced skin turgor and dry mucous membranes do not necessarily correlate well with intravascular volume status. Otherwise, the water deficit is always replaced with hypotonic fluid: D5W or 1/2 normal saline. D5W is the preferred fluid because you need to give less volume to replace the free water. With 1/2 normal saline, the required infusion rate to correct her total-body free water deficit to achieve a fall in serum sodium of 0.5 mEq/L per hour is high. Because this patient is elderly with a history of congestive heart failure, giving her large amounts of intravenous fluids could lead to pulmonary edema. With her lethargy, it would be unwise to initiate oral free water repletion until she is more awake.

**Question 30**

A 50-year-old man is seeing you as a follow-up for kidney stones. He has not had a kidney stone for 1.5 years but has previously had two episodes where he passed the stones spontaneously. He does not recall the exact type of stone that he formed previously. He does not recall the exact type of stone that he formed but remembers it being a calcium stone. He is otherwise healthy except for mild diet-controlled hyperlipidemia. He is on no medications. He had a plain radiograph of the abdomen 6 months ago, which was negative for any genitourinary calcifications. He asks your advice on how to reduce his chances of developing another kidney stone. He states that he is already consuming >2.5 L of fluids per day and drinks two glasses of lemonade every day. Laboratory values are as follows:

- Sodium: 140 mEq/L
- Bicarbonate: 28 mEq/L
- BUN: 22 mg/dL
- Creatinine: 1 mg/dL
- Calcium: 8.8 mg/dL
- Albumin: 3.9 mg/dL
- Phosphorus: 3.9 mg/dL
- Uric acid: 3 mg/dL

Which of the following is the best therapy for this patient?

a) Increase dietary citrate intake  
b) Increase dietary sodium intake
c) Increase dietary calcium intake
d) Increase dietary animal protein intake

Answer and Discussion
The answer is c.

Objective: Identify dietary changes to decrease calcium-based nephrolithiasis.

Nephrolithiasis is a chronic recurrent condition. Almost 50% of patients have a recurrence by 10 years. Calcium oxalate stones are the most common type of kidney stone.

Increasing urine volume like this patient is doing reduces the concentration of stone promoters in the urinary tract. High calcium intake has a positive effect on calcium-containing stone disease as higher amounts of calcium bind to oxalate in the GI tract and therefore prevents its absorption and reduces both hyperoxaluria and calcium oxalate stone formation. Increasing dietary citrate consumption as this patient is already doing by consuming lemon-containing beverages increases urinary citrate concentration and reduces urinary calcium levels. High animal protein reduces urinary pH and increases calcium crystallization. Finally high sodium diet is not recommended because it increases urinary calcium excretion as well.

Question 31

A 38-year-old man with type 1 diabetes mellitus and HIV presents to your clinic complaining of worsening lower extremity edema. You have not seen him for 3 years, and he has missed several appointments. He was recently admitted to the hospital for treatment of edema. The following results were obtained:

- BUN: 28 mg/dL
- Creatinine: 1.6 mg/dL
- Albumin: 2.5 g/dL
- HbA1c: 11.5
- CD4 count: 220 cells/μL
- HIV RNA viral load: 4,000 copies/mL
- UA: 4+ protein, 1+ blood, many oval fat bodies, no casts

A kidney biopsy was obtained and is shown here.

The man was discharged on furosemide 80 mg twice daily and his usual insulin therapy and was instructed to follow up with you for results of biopsy and further therapy. In addition to BP control to a target of <130/80 mmHg, quantifying the amount of proteinuria, and initiation of an ACE inhibitor to reduce proteinuria, which of the following is the next best step in the management of this patient?

a) Initiation of highly active antiretroviral therapy
b) Aggressive glycemic control
c) Initiation of steroids alone
d) Broad-spectrum antibiotics

Answer and Discussion
The answer is a.

Objective: Identify appropriate therapy for HIV-associated nephropathy.

The patient has nephrotic syndrome from HIV nephropathy. He has heavy proteinuria on a urinalysis, and his kidney biopsy reveals the collapsing form of focal segmental glomerulosclerosis. Although he has severe uncontrolled diabetes mellitus, which should be addressed, his biopsy is consistent with HIV nephropathy, and the priority is to initiate HAART therapy, which could reduce the progression to end-stage renal disease. Steroids alone without HAART therapy have not been shown to be effective. Broad-spectrum antibiotics are not indicated without a severe systemic bacterial infection. Other causes of renal disease in patients with HIV infection include tubular injury from drugs such as pentamidine, sepsis-induced tubular injury, indinavir-associated renal calculi, concomitant hepatitis-associated membranous or membranoproliferative glomerulonephritis, and other glomerulonephritides.

Question 32

A 55-year-old man is brought to the emergency department after a confessed toxic ingestion. He is lethargic and weak and is disoriented. His medical history is significant for hypertension, smoking, and hyperlipidemia.

On physical examination, he is afebrile, BP is 148/80 mmHg, pulse rate is 84 beats/minute, and respiratory rate is 30/minute. Cardiovascular and pulmonary examinations are normal. Laboratory studies are as follows:

- Glucose: 126 mg/dL
- Sodium: 140 mEq/L
- Potassium: 4.4 mEq/L
- Chloride: 105 mEq/L
- Bicarbonate: 10 mEq/L
- BUN: 20 mg/dL
- Creatinine: 1.1 mg/dL

Arterial blood gas on room air:
- pH: 7.47
- PCO₂: 16 mmHg
- PO₂: 70 mmHg

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Which of the following will most likely establish the diagnosis?

a) Serum osmolality  
b) Salicylate level  
c) Methanol level  
d) Chest x-ray

**Answer and Discussion**

**The answer is b.**

**Objective: Diagnosis the mixed acid–base disorder associated with salicylate toxicity.**

Salicylate toxicity is present in this patient and is associated with his AG acidosis and respiratory alkalosis. This presentation is not consistent with a simple metabolic acidosis with respiratory compensation because the compensation to acidosis would not raise pH above normal. The AG is 25 (AG = Na – [Cl + HCO3]; 140 – [105 + 10] =25); giving an elevated AG metabolic acidosis. Therefore, Winter’s formula should be used to estimate the respiratory compensation, with expected \( P_{CO_2} \): \( P_{CO_2} = 1.5 \times HCO_3 \) (10 in this case) + 8 ± 2, which in this case is 23 ± 2.

However, the patient has a \( P_{CO_2} \) of 16, which confirms the presence of a primary respiratory alkalosis as well and not from compensation alone. Measurement of serum osmolality and calculation of the osmolar gap will detect the presence of an unmeasured osmole (like methanol or ethylene glycol); however, none of these disorders gives you a respiratory alkalosis, and therefore, this is not consistent with the patient's presentation. Although salicylate intoxication can be associated with noncardiogenic pulmonary edema, chest x-ray will not be able to establish the diagnosis.

**Question 33**

A 74-year-old woman with end-stage renal disease from type 2 diabetes mellitus is admitted for incision and drainage of an infected below-knee amputation stump. She undergoes her hemodialysis treatments three times a week via a left upper extremity fistula. She had her dialysis treatment yesterday, and her next dialysis session is scheduled for tomorrow. She also has hypertension and hyperlipidemia. You have been asked to see her to assist with medical management of her chronic diseases.

She currently complains of pain around the operative site. On physical examination, she is afebrile, BP is 127/74 mmHg, pulse rate is 70 beats/minute, and respiratory rate is 14/minute. Cardiac exam is normal. Her lungs are clear, and abdomen is benign. She has mild lower extremity edema. Below are the results of the blood tests she obtained 1 week prior, per your request:

- Glucose: 125 mg/dL
- Sodium: 140 mEq/L
- Potassium: 4.9 mEq/L
- Chloride: 107 mEq/L
- Bicarbonate: 18 mEq/L
- Creatinine: 2.6 mg/dL
- Calcium: 9.2 mg/dL
- Albumin: 3.7 g/dL
- Phosphorus: 6.8 mg/dL

Which of the following is likely the cause of her hyperphosphatemia?

a) Low glomerular filtration rate  
b) High phosphorus intake  
c) Secondary hyperparathyroidism  
d) Vitamin D deficiency

**Answer and Discussion**

The answer is a.

**Objective: Identify the cause of hyperphosphatemia in a patient with chronic kidney disease.**

Low glomerular filtration rates (<60 mL/minute) lead to reduced phosphate excretion and phosphate retention. Increased phosphorus levels cause a decrease in ionized...
calcium, and together with hyperphosphatemia, this stimulates parathyroid hormone secretion. The increase in parathyroid hormone secretion will tend to normalize phosphorus levels. High phosphorus intake can worsen hyperphosphatemia in chronic kidney disease patients but is not the main cause of hyperphosphatemia. Vitamin D deficiency causes hypocalcemia but not hyperphosphatemia.
POINTS TO REMEMBER:

Serum-Based Liver Tests
- Basic approach to the interpretation of serum-based liver tests: The first pattern distinction is to determine whether the abnormalities are more suggestive of cholestatic or liver cell injury.
- Cholestatic liver disease refers to impairment of hepatic excretion into the biliary system. This type of “blockage” of excretion may occur at any level (intrahepatic or extrahepatic). The alkaline phosphatase and γ-glutamyl transpeptidase (GGTP) are elevated to a much greater degree than that of the transaminases. The bilirubin level may or may not be elevated.
- When liver disease primarily affects hepatocytes, as in viral hepatitis, alcoholic hepatitis, and many drug-induced problems, a pattern of liver cell injury is seen. The transaminases are elevated predominantly.

Fatty Liver
- Fatty liver or steatohepatitis (termed nonalcoholic steatohepatitis) in patients who do not drink alcohol should be suspected in patients with mild-to-moderate transaminase elevations and whose serologic studies for viral hepatitis, iron overload, and autoimmune disorders are negative.
- Neither blood tests nor scans are able to distinguish benign fatty liver from steatohepatitis before cirrhotic changes become apparent and therefore a liver biopsy is often necessary.
- Weight loss in obese patients with steatohepatitis has shown to be associated with normalization of liver enzymes and improved hepatic histology.

Alcoholic Liver Disease
- In the United States, alcohol is the most common cause of liver cirrhosis.

- The so-called Maddrey discriminant function (MDF) identifies a group of patients at substantial risk for dying from alcoholic hepatitis.
  \[
  MDF = 4.6 \times (\text{pro time} - \text{control (in seconds)}) + \text{serum bilirubin (mg/dL)}
  \]
- When severely ill patients (severe alcoholic hepatitis) with a discriminant function score of ≥32 (with or without encephalopathy) are given 40 mg of prednisone daily for 28 days, survival is nearly twice as likely and should always be considered in the absence of a contraindication for the use of corticosteroids.

Viral Hepatitis A, B, C
- Hepatitis A vaccination is recommended for all susceptible persons with chronic liver disease.
- Hepatitis B antigen and antibodies: examples of select clinical situations.
  - Acute hepatitis B: Serologically identified by the presence of hepatitis B surface antigen (HBsAg) and the presence of IgM class anti-hepatitis B core (IgM anti-HBc).
  - Remote resolved infection: These patients have a serological profile consistent of anti-hepatitis B surface (anti-HBs) and IgG anti-hepatitis B core (anti-HBc) in the serum. In some cases and over time, patients may lose anti-HBs and maintain an isolated anti-HBc as the only serological evidence of old exposure to HBV.
  - Chronic hepatitis B: The key serological feature is the presence of hepatitis B5 antigen (HBsAg). In cases of chronic inactive infection (previously termed healthy carrier), patients will have normal liver enzymes, low hepatitis B DNA (HBV DNA) titer and minimal histological changes on liver biopsy. In contrast, those with chronic active infection may have elevated liver
enzymes, high HBV DNA and necroinflammation on liver biopsy.

- Successful immunization status: The patient has anti-HBs as the only serological finding.
- Hepatitis C is much more likely than hepatitis B to become chronic (70% to 85%) with more than three-fourths of patients developing chronic liver disease. Daily alcohol consumption increases the risk of developing symptomatic cirrhosis.
- Hepatitis C increasingly is recognized as a risk factor for liver cancer and currently is believed to be the most common cause of hepatocellular carcinoma in the United States.
- Several extrahepatic manifestations of hepatitis C may overshadow hepatic involvement.
- Cryoglobulinemia with its associated vasculitis and skin rash is perhaps the most established extrahepatic feature of hepatitis C and responds well to viral eradication with therapy.
- Renal injury particularly membranoproliferative glomerulonephritis has been well established and may also improve if the hepatitis C is treated successfully using interferon.
- Porphyria cutanea tarda (PCT), as a result of reduced activity of the enzyme uroporphyrinogen decarboxylase, may be either inherited as an autosomal dominant trait or acquired. Hepatic dysfunction is nearly always seen in PCT, and anti-HCV antibodies are present in 80% patients with acquired PCT but not in patients with familial PCT.
- The introduction of protease inhibitors (boceprevir and telaprevir) in combination with pegylated interferon and ribavirin have significantly improved the rate of sustained virologic responses (SVRs) and are currently the standard of care for the treatment of chronic hepatitis C virus (HCV).

Autoimmune Chronic Hepatitis

- Autoimmune-type hepatitis predominates in women.
- Transaminases are markedly elevated; progression to cirrhosis and death within just a few months or years may occur unless treatment is given.
- Fatigue, malaise, change in menstruation patterns (often amenorrhea), and prominent extrahepatic effects such as arthritis and arthralgias may be present, in which case confusion with rheumatoid arthritis or systemic lupus erythematosus may occur.
- A number of autoantibodies are present, including antinuclear antibody (ANA), smooth muscle antibody (SMA), and antibody to liver/kidney microsome type 1 (anti-LKM1). In North American adults, 96% have ANA, SMA, or both.
- In all types of autoimmune hepatitis, the globulin fraction of protein is elevated markedly.
- Prednisone and Azathioprine and standard treatments and many patients require lifelong treatment to maintain disease remission.

Primary Biliary Cirrhosis and Primary Sclerosing Cholangitis

- Autoantibodies are a nearly universal feature of primary biliary cirrhosis (PBC)–antimitochondrial antibodies (AMA).
- PBC has a tendency to be associated with other autoimmune diseases including thyroid disease, Sjögren syndrome, Raynaud syndrome, and occasionally CREST syndrome.
- Malabsorption of fat-soluble vitamins can be seen in PBC.
- Besides Ursodiol, no therapy is known to reverse PBC in the native liver or to slow progression.
- Once a patient with PBC falls into the Child B range, liver transplantation should be given serious consideration.
- Primary sclerosing cholangitis (PSC) is a chronic progressive hepatobiliary disease of unknown cause that is characterized by diffuse or multifocal fibrosing inflammatory changes in the bile ducts. It is seen most often in association with inflammatory bowel disease.
- Diagnosis requires cholangiography, although a strong inferential case can be made clinically, especially in those patients with inflammatory bowel disease and a markedly elevated alkaline phosphatase level. The cholangiogram reveals a ratty, irregular biliary tree produced by the fibrosing process.
- There is no proven therapy for PSC and, as in PBC, once a PSC patient is classified as Child B, liver transplantation evaluation should be considered.

Inherited Liver Diseases

- Wilson disease (known also as hepatolenticular degeneration) may present with either neurological symptoms or liver disease or both. It is a disease of abnormal copper metabolism, inherited in an autosomal recessive pattern, and it should be suspected in any young person with chronic or severe acute liver disease.
- It is rare for Wilson disease to manifest for the first time after the age of 50 years.
- Serum ceruloplasmin is depressed in 95% of persons.
- Hereditary hemochromatosis (genetic hemochromatosis, idiopathic hemochromatosis), a heterogeneous group of disorders, is characterized by excessive iron deposition in many organs, including, importantly, the liver. Other targets for excess iron include the pancreas (diabetes may result), heart (conduction disturbances, heart failure), joints (arthritis), gonads (impotence), and skin (darkening).
- The diagnosis should be suspected in the following situations:
  - Any adult with liver disease, especially men
  - Ferritin elevations (>200 μg/L in premenopausal women; >300 μg/L in men and postmenopausal women)
Cirrhosis

- Model for End Stage Liver Disease (MELD) score has replaced Child–Turcotte–Pugh (CTP) scoring at least for assessment of priority for liver transplantation in patients with liver cirrhosis.
- The MELD system is a mathematical score driven from three simple laboratory values [serum bilirubin, serum creatinine, and the international normalized ratio (INR)].
- It has been demonstrated that the MELD score is a good predictor of 3-month and 1-year survival and is applicable to most liver diseases.
- The SAAG (serum albumin–ascitic fluid albumin gradient) has been established as a clinical valuable test with high specificity to differentiate ascites due to portal hypertension (cirrhosis, Budd-Chiari syndrome, or right heart failure) from other causes of ascites. Low gradients (<1.1) suggest a noncirrhotic (and a noncardiac) cause for ascites, such as malignancy or infection.
- The mainstay of treatment for ascites is dietary sodium restriction with spironolactone as the diuretic of first choice.
- In SBP, the ascitic fluid cell count almost always reveals a polymorphonuclear (PMN) count >250/mm³.
- When should antibiotic prophylaxis be given to cirrhotic patients with ascites? Based on available evidence for those particularly at risk, it seems prudent to consider prophylaxis for those with one or more of the following risk factors:
  - Previous history of SBP (lifelong prophylaxis or until liver transplantation).
  - Ascitic fluid protein concentration <1 g/dL (lifelong prophylaxis or until liver transplantation).
  - Acute upper gastrointestinal bleeding (short course for 10 days at the time of bleeding).

- Primary Prevention of Portal Hypertensive Bleeding: Currently, noncardioselective β-blockers (e.g., propranolol, nadolol, and timolol) are the mainstay therapy for the prophylaxis of variceal bleeding in patients with varices from portal hypertension.
- Secondary Prevention of Portal Hypertensive Bleeding: The optimal strategy to prevent hemorrhage recurrence appears to be with combined pharmacotherapy (β-blockers) plus repetitive band ligation sessions.
- The endoscopic treatment of esophageal varices with band ligation appears superior to injection sclerotherapy.

Liver Disease in Pregnancy

- Acute fatty liver of pregnancy most often presents dramatically with signs and symptoms of acute liver failure between weeks 30 and 38 of gestation.
- Vomiting, jaundice, and encephalopathy are frequent.
- Laboratory tests reveal hyperbilirubinemia (usually <15 mg/dL) and moderately elevated ALT and AST values (usually <1,000).
- Because of the rarity of the condition and the frequency with which it may be mimicked by other liver disorders such as viral hepatitis, a liver biopsy is recommended.
- Prompt delivery of the infant is the treatment.
- Hemolysis, elevated liver enzymes, and low platelets (HELLP syndrome) is part of the spectrum of preeclampsia–eclampsia.
- Most patients, therefore, have arterial hypertension and frequently other features, such as edema, excessive weight gain, and sometimes renal abnormalities.
- Nausea, vomiting, and upper abdominal pain are frequent in HELLP.
- Laboratory values in HELLP include features of microangiopathic hemolytic anemia, elevated bilirubin and lactic dehydrogenase levels, and platelet counts <100,000. Transaminases usually are only slightly elevated.
- For mature fetuses over 35 weeks of gestation, immediate delivery is recommended.

SUGGESTED READINGS


POINTS TO REMEMBER:

Acute Pancreatitis
- Pancreas has close proximity to the stomach, duodenum, and the common bile duct, predisposing these structures to external compression by different pancreatic disorders.
- The most common causes of acute pancreatitis are alcohol and gallstones (80%).
- Idiopathic pancreatitis is seen in 10% of cases.
- The diagnosis of pancreatitis requires two out of the three features: abdominal pain characteristic of acute pancreatitis, serum amylase and/or lipase ≥ 3 times upper limit of normal, characteristic findings on CT scan.
- Prognosis in acute pancreatitis depends on the severity of the disease.
- Predicting severity of acute pancreatitis is important because early recognition of severe disease will enable the clinician to consider more aggressive interventions.
- BISAP is a relatively new index of severity that can be of use in stratifying patients with acute pancreatitis (BUN, Impaired mental status, SIRS, Age, Pleural effusion).
- Cornerstones of treatment for acute pancreatitis are fluid resuscitation and pain control.
- Hematocrit level can be helpful in gauging adequacy of fluid resuscitation in patients with acute pancreatitis.
- Gallstone Pancreatitis may require ERCP intervention to remove impacted gallstones.

Chronic Pancreatitis
- Chronic pancreatitis generally presents with abdominal pain and weight loss.
- Alcohol abuse accounts for more than two-thirds of all cases of chronic pancreatitis.
- Chronic pancreatitis can cause splenic vein thrombosis and gastric varices.
- The treatment of chronic pancreatitis is mainly symptomatic.
- In chronic pancreatitis, exocrine pancreatic insufficiency usually occurs a few years before the development of endocrine insufficiency.

Pancreatic Adenocarcinoma
- Pancreatic carcinoma has the lowest survival rate of any of the solid organ cancers.
- Painless jaundice is a common presentation of pancreatic carcinoma (60% of cancers occur in the head of the gland).
- The risk factors for developing pancreatic carcinoma include advancing age, cigarette smoking, chronic pancreatitis, and hereditary pancreatitis.

SUGGESTED READINGS

KEY POINTS:

- In most patients with classic symptoms of heartburn or regurgitation, the history alone is sufficient to diagnose gastroesophageal reflux disease (GERD) to permit a trial of therapy without diagnostic tests.
- Diagnostic procedures
  - Barium esophagram: Single-most important test for the diagnosis of structural and motor abnormalities of the esophagus
  - Upper endoscopy with biopsy and brush cytology is the best method for identifying mucosal abnormalities
  - High-resolution esophageal manometry: Definitive test for diagnosis esophageal motility disorders
  - Ambulatory esophageal pH monitoring: For the diagnosis of gastroesophageal reflux
    - A pH evaluation is the single-best test for diagnosing GERD, with a sensitivity of 85% and a specificity > 95%.
- GERD is classified into esophageal and extraesophageal syndromes
  - Extraesophageal symptoms are cough, laryngitis, asthma, and dental erosions. These symptoms are usually multifactorial with GERD being one of the contributing factors. In the absence of heartburn or regurgitation, unexplained cough, asthma, or laryngitis are unlikely to be related to GERD.
- Early endoscopy is indicated in GERD patients with "alarm symptoms" such as dysphagia, vomiting, weight loss, anemia, or epigastric mass.
- Protein pump inhibitors (PPIs) are the mainstay of therapy for GERD
  - Potential risks of long-term use of PPI therapy include increased risk of osteoporosis, clostridium difficile colitis, aspiration pneumonia, and Vitamin B₁₂ deficiency.
- Odynophagia
  - If there are symptoms of GERD, an empiric trial of PPI is warranted, followed by endoscopy if there is no improvement in the symptoms.
  - If the patient is taking any medications known to cause esophagitis, this puts them at risk for pill-induced esophagitis.
  - The presence of odynophagia in immunocompromised patients should trigger an evaluation for infectious esophagitis.
  - Candidal esophagitis is most commonly seen in patients who are infected with HIV or have granulocytic cancer.
  - Viral esophagitis predominates in patients who have received bone marrow transplants.
  - Both candidal and viral esophagitis are encountered after solid organ transplantation.
- Esophagogastroduodenoscopy (EGD) is the preferred method for identifying reflux esophagitis, infectious esophagitis, and neoplasms.
- Eosinophilic esophagitis (EoE) should be considered in the differential diagnosis of dysphagia in young adults with allergies.
  - In adults, the most common clinical manifestations of EoE are dysphagia, food bolus impaction, chest pain, and upper abdominal pain.
  - Topical steroids are a mainstay of treatment.
- Achalasia
  - Characterized by aperistalsis of the esophagus with impaired lower esophageal sphincter relaxation
  - Present with gradual onset of dysphagia to solids and liquids. Weight loss is common.
  - Diagnostic testing: Barium esophagram, esophageal manometry, and endoscopy (to rule out pseudoachalasia secondary to carcinoma)
  - Treatment: Pharmacologic, pneumatic dilation and surgical myotomy
- Adenocarcinoma is the most common malignant tumor of the esophagus in the United States and other Western countries. Squamous cell carcinoma remains the most common malignant tumor in other parts of the world.

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SUGGESTED READINGS


Peptic Ulcer Disease

Sunguk Jang

POINTS TO REMEMBER:

- Despite its decrease in incidence in recent decades, the peptic ulcer disease remains as the most common cause of acute upper GI bleed.
- *Helicobacter pylori* infections remain as the most common cause of peptic ulcer disease despite its declining prevalence in the Western world due to improved hygiene.
- *Helicobacter pylori* serology testing has been replaced by breath testing and fecal antigen testing.
- Fecal antigen testing 7 or more days after the completion of eradication therapy has identified patients with persistent infection in about 95% of cases.
- *Helicobacter pylori* test and treat strategies are still appropriate in younger dyspeptic patients without alarm symptoms.
- Infection with *H. pylori* is an important risk factor for the development of distal gastric cancer and also is associated with gastric MALT lymphoma, which is a low-grade, B-cell subtype of non-Hodgkin lymphoma of the stomach.
- Nonsteroidal anti-inflammatory drugs (NSAIDs) are the second most common cause of ulcer disease.
- NSAIDs, via alteration of prostaglandin synthesis pathway, diminish the potency of the protective mechanism of the gastric lining, resulting in increased susceptibility of gastric lining to acid-induced injury.
- The development of PUD from NSAIDs is dose and duration dependent. The frequent use of NSAIDs is associated with reported 1% to 4% risk of developing PUD per annum.
- Zollinger-Ellison (ZE) syndrome, which results in multiple gastric and duodenal ulcers from acid hypersecretion state, accounts for 0.1% of PUD patients.
- ZE syndrome should be suspected in patients with recurrent peptic ulcer disease in the absence of *H. pylori* infection or NSAID consumption and up to 50% of patients may have diarrhea.
- Dyspepsia (epigastric discomfort) is the most common symptom reported by patients with PUD. However, less than 20% of patients with chronic dyspepsia are found to have evidence of active or previous PUD.
- Patients with PUD from NSAIDs use are often asymptomatic.
- It is recommended that patients with a prior history of PUD or its complications should be tested for *H. pylori* and treated, if necessary, before long-term NSAID therapy is commenced.
- Empiric trial of antacid medication such as H2 receptor antagonist or Proton pump inhibitors (PPIs) in patients with suspected uncomplicated PUD is justified and should be implemented prior to invasive testing in the absence of worrisome clinical features/signs in younger patients.
- Upper endoscopy (EGD) is indicated in patients with worrisome signs/symptoms such as melena, hematemesis, weight loss, older population with chronic dyspepsia, or those who fail to achieve clinical response with PPI trial.
- Peptic ulcer disease accounts up to 40% of the etiology for the acute overt upper GI bleed.
- Because most rebleeding from PUD occurs within 3 days of initial presentation, patients with active bleeding or stigmata of hemorrhage, such as pigmented spots in an ulcer crater or clot, can typically be discharged within 3 days if they are stable. In patients with clean-based ulcers, discharge within 24 hours of presentation is reasonable.
- Proton pump inhibitors (PPIs) are the most effective agents for healing ulcers by reducing acid secretion in three discrete pathways.
- The standard of care for patients with bleeding peptic ulcers now consists of high-dose PPI therapy (the equivalent of omeprazole 40 mg two times a day) as soon as oral medications are permitted or with parenteral PPI therapy for 3 days, followed by conventional-dose PPI therapy for ulcer healing.
- Malignancy accounts for approximately 50% of cases of gastric outlet obstruction and should be excluded with adequate biopsy and cytology samples.

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SUGGESTED READINGS


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RAPID BOARD REVIEW—KEY POINTS

TO REMEMBER:

- ETIOLOGY AND RISK FACTORS
  1. A total of 80% of colorectal cancers are believed to arise from adenomatous polyps. As much as 20% to 30% of colorectal cancer are believed to arise from sessile serrated polyps.
  2. Sessile serrated polyps are neoplastic colorectal lesions and must be removed in their entirety.
  3. Approximately 70% of newly diagnosed colorectal cancers arise in patients without known risk factors.
  4. Risk Factors: personal history of polyps/cancer, first-degree relative < 60 or two first-degree relatives of any age, inflammatory bowel disease, inherited colorectal cancer syndromes
  5. Inherited colorectal cancer syndromes: familial adenomatous polyposis (FAP), Gardner syndrome, hereditary nonpolyposis colon cancer (HNPCC), Lynch syndrome

- COLORECTAL CANCER SCREENING
  1. Colorectal cancer screening decreases colorectal cancer incidence and mortality
  2. Screening Modalities: Fecal occult blood test, sigmoidoscopy, Stool DNA, CT Colonography, Colonoscopy
  3. USPSTF Guidelines (2008): In average-risk individuals, start screening with annual high sensitivity guaiac testing, Colonoscopy every 10 years or flexible sigmoidoscopy every 5 years
    - New colorectal cancer screening guidelines recommend high sensitivity guaiac–based FOBT or FIT instead of low sensitivity guaiac–based options for testing.
  4. Family history of colon cancer: Colonoscopy every 5 years starting at age 40 or 10 years younger that the age at which the relative developed cancer.
  5. Ulcerative or Crohn colitis: Colonoscopy every 1 to 2 years after 8 years of pancolitic disease.
  7. Hereditary nonpolyposis colon cancer: Colonoscopy every 1 to 2 years from age 25 to 40 years and then yearly screening

- TREATMENT
  1. For most early-stage tumors (e.g., stages I and II) surgery alone is curative
  2. Adjuvant therapy for patients with stage III colon cancer improve overall and disease-free survival

- SURVEILLANCE
  1. Colon cancer: surveillance examination should occur within 1 year and, if results are negative at that time, 3 years, and, if normal, every 5 years thereafter.
  2. Colon polyps in average-risk patients
    - 1 to 2, < 1 cm, tubular adenomas: 5 to 10 years recheck
    - ≥ 3, or ≥ 1 cm, or advanced adenoma: 3 year recheck

SUGGESTED READINGS


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Inflammatory Bowel Disease

Aaron Brzezinski

POINTS TO REMEMBER

- It is estimated that approximately 1.5 million Americans have inflammatory bowel disease (IBD).
- The presentation of ulcerative colitis (UC) in children is usually with severe and extensive disease, whereas adults usually have milder disease that is limited to the left colon. In adults at presentation, the disease is limited to the rectum in 30% of patients, and in 60% it is distal to the splenic flexure.
- Patients with UC usually present with nonbloody diarrhea that progresses to bloody diarrhea.
- Stool studies to exclude bacterial and parasitic infections are indicated at the time of initial presentation.
- Histology is the most sensitive way of establishing the extent of the disease, and unless there is a contraindication, a colonoscopy with biopsies is indicated in all patients in whom UC is suspected.
- The main role of radiologic tests in patients with UC is to exclude complications associated with severe or fulminant disease and to exclude Crohn’s disease.
- Most patients with UC have intermittent attacks, with remissions lasting from a few weeks to many years. At presentation, 5% to 10% have a severe attack that requires urgent colectomy, and 10% to 15% of patients have chronic active disease. The course and prognosis are largely determined by the extent of the disease.
- Patients with UC and Crohn’s disease of the colon have an increased risk of colorectal cancer.
- Patients who have had UC pancolitis for more than 7 to 10 years are advised to undergo surveillance colonoscopies with biopsies.
- Crohn’s disease is a heterogeneous disease that has different clinical presentations, which are determined by the site of involvement and disease behavior (inflammatory, stricturing, or fistulizing).
- In Crohn’s disease, any segment of the gastrointestinal tract can be involved, but the most common distribution is ileocolic disease that is seen in 50% of patients, small bowel involvement alone occurs in 30%, and colonic involvement alone in 20% of the patients.
- Perianal disease occurs in 30% of patients with Crohn’s disease, and approximately 10% of female patients with Crohn’s colitis develop rectovaginal fistulas.
- A larger-than-expected number of patients with Crohn’s disease are cigarette smokers.
- Contrast studies play a major role in the diagnosis of small bowel and gastroduodenal Crohn’s disease.
- In the past decade the new imaging modalities such as computed tomography enterography (CTE) and magnetic resonance enterography (MRE) have become the preferred imaging modalities in the diagnosis of Crohn’s disease.
- Distinguishing between UC and Crohn’s disease can be difficult.
- About 50% to 60% of patients with IBD have extraintestinal manifestations (EIMs).
- The EIMs that parallel disease activity include
  - Peripheral arthritis
  - Erythema nodosum
  - Pyoderma gangrenosum
  - Keratoconjunctivitis
  - Episcleritis
  - Hypercoagulability (if related to thrombocytosis and acute-phase reactants, not if it is related to primary abnormalities in the coagulation system such as protein S, C deficiency, or factor V Leiden mutations)
- The EIMs that run a course independent of disease activity include
  - Ankylosing spondylitis, which more commonly occurs in patients with UC who are HLA-B27 positive
  - Sacroiliitis
  - Primary sclerosing cholangitis
  - Uveitis
- Treatment can be divided into two phases: therapy for the acute attack (induction of remission) and maintenance of remission.
- Medications used to treat patients with IBD include
  - 5-Aminosalicylic acid (5-ASA)
  - Antibiotics
  - Crohn’s disease only
Corticosteroids

Corticosteroids are indicated for induction of remission in patients with moderate or severely active UC or Crohn’s disease, but are not indicated for maintenance of remission.

Immunosuppressive medications

The most commonly used medications in this group are the thiopurines (6-mercaptopurine and azathioprine), and the antimitobolite methotrexate.

Biologic medications

Biologic agents that block tumor necrosis factor-α are indicated for induction and maintenance of remission in IBD patients.

Infections are one of the most common and significant complications of these agents

Between one-third and one-half of patients with IBD require surgery. Patients with UC and extensive Crohn’s colitis require surgery because of failure to respond to medical treatment, hemorrhage, toxic dilatation, perforation, strictures causing obstruction, and dysplasia or cancer.

Depending on the indication, patients with Crohn’s disease may undergo a segmental resection, strictureplasty, or both.

Patients with UC should undergo total colectomy, regardless of the extent of the disease.

SUGGESTED READINGS


RAPID BOARD REVIEW—KEY POINTS TO REMEMBER

Diarrhea
- Clinical clues
  - Acute diarrhea (<4 weeks) is generally infectious in etiology.
  - Presence of blood is a useful clue suggesting invasive infections, inflammation, ischemia, or neoplasm.
  - Large-volume diarrhea suggests small bowel or proximal colonic disease.
  - Small-volume, frequent stools suggest left colon or rectal disease.
  - In the history, do not forget to ask about the intake of “sugar-free” foods (nonabsorbed carbohydrates).
  - Oral ulcers and pyoderma gangrenosum suggests inflammatory bowel disease.
  - Dermatitis herpetiformis is associated with celiac disease.
- Categorize diarrhea as watery diarrhea (secretory and osmotic), inflammatory diarrhea, and fatty diarrhea
  - Osmotic diarrhea tends to stop during fasting and is associated with an osmotic gap >50 mOsm.
  - Secretory diarrhea persists with fasting and has osmotic gap <50 mOsm. It can be caused by underlying mucosal disease, bacterial toxins, stimulant use, and neuroendocrine tumors.
  - Inflammatory diarrhea is usually associated with bleeding, fecal leukocytes, fever, and abdominal pain.
  - Functional diarrhea is a diagnosis of exclusion.
- Foodborne illness with Escherichia coli is the most common cause of traveler’s diarrhea.

Malabsorption
- Diarrhea is almost universally present in malabsorption.
- Steatorrhea can be due to pancreatic insufficiency, decreased luminal bile salt concentration, mucosal diseases (celiac disease, Whipple’s disease, inflammatory bowel disease), small bowel bacterial overgrowth (commonly due to diabetes and previous bowel surgeries), short bowel syndrome.
- Workup for malabsorption can include fecal fat analysis, tests of pancreatic exocrine function, radiographic studies, breath tests, and endoscopic and histologic testing.

Specific Disorders
- Bacterial overgrowth—Conditions that impair gastrointestinal motility can result in bacterial overgrowth. Diagnosis is generally made by breath tests or empiric treatment.
- Celiac sprue is a common disease at a rate of 1:150 among general population. Serology with total immunoglobulin A and tissue transglutaminase can be a good screening test. It is associated with some other autoimmune conditions and has 30 times increase in the risk of lymphoma.
- Microscopic colitis includes lymphocytic or collagenous colitis, and both have normal endoscopic and radiologic appearance. Diagnosis is made on the histology.

SUGGESTED READINGS


A 56-year-old white man with a history of pseudogout and type 2 diabetes mellitus complains of fatigue and weight loss. His family history is significant for diabetes, liver cancer, and arthritis. On examination, a mildly enlarged liver is noted, together with palmar erythema and bilateral knee effusions. Blood chemistry reveals mildly elevated alanine transaminase (ALT) and aspartate transaminase (AST) values, total bilirubin is 2.0 mg/dL, international normalized ratio (INR) is 1.95, and ferritin is 2,500 ng/mL (normal, 10 to 200 ng/mL). The treatment most likely to decrease this patient's risk of hepatocellular carcinoma (HCC) is which of the following?

a) Ursodeoxycholic acid (ursodiol)
b) Repeated phlebotomy
c) Penicillamine
d) Deferoxamine
e) None of the above

**Answer and Discussion**

The answer is e.

**Objective:** Identify modifiable risk factors for HCC in patients with cirrhosis.

This case illustrates the clinical presentation of symptomatic hereditary hemochromatosis (HHC), one of the most common autosomal recessive disorders. HHC is a disorder of iron storage, whereby an inappropriate increase in intestinal iron absorption results in deposition of excessive quantities of iron in parenchymal cells, with eventual tissue damage and functional impairment. The liver is usually the first affected organ. Hepatomegaly develops and, when hepatic iron concentration reaches a threshold of 400 μmol/g dry weight, cirrhosis is common. The iron threshold is lower in patients with other risk factors for liver diseases, such as heavy alcohol consumption or chronic hepatitis. Splenomegaly develops in 50% of symptomatic patients. Manifestations of portal hypertension and esophageal varices occur less commonly than in alcoholic cirrhosis. HCC develops in 30% of those with cirrhosis and is the most common cause of death among treated patients. Clinical HHC is only present in the setting of iron overload. The serum ferritin level defines the point at which hemochromatosis is expressing iron overload and treatment should be initiated. Treatment involves removal of mobilizable iron stores. Weekly phlebotomy is usually required for 2 to 3 years. When the transferrin saturation and ferritin level become normal, phlebotomy is performed at the time intervals required to maintain levels in the normal range. Chelating agents, such as deferoxamine, are more expensive and less effective than phlebotomy, but may play a role in HHC when anemia or hypoproteinemia are severe enough to preclude further blood removal. When treatment is initiated before the development of hepatic cirrhosis or diabetes, patients with HHC appear to have a normal life expectancy. In the case example, elevations in INR, bilirubin, and transaminases suggest that liver damage and cirrhosis have already occurred. Once hepatic cirrhosis develops, no treatment is available to alter the risk of HCC.

**Question 2**

Which of the following approaches has shown to improve liver enzymes and liver histology for nonalcoholic steatohepatitis?

a) Weight loss
b) Control of elevated triglycerides
c) Avoidance of alcohol
d) Control of elevated blood sugar
e) The use of insulin-sensitizing agents

**Answer and Discussion**

The answer is a.

**Objective:** Understand the treatment of nonalcoholic steatohepatitis.

Weight loss in obese patients, the control of elevated triglycerides and diabetes, and the avoidance of alcohol are recommended. Of several treatment strategies tested in clinical trials, weight loss (at least 5% to 10% of total body weight) seems to be the most effective. Weight loss in obese patients with steatohepatitis has shown to be associated with normalization of liver enzymes and improved hepatic histology. Newer studies are targeting insulin resistance as a potential underlying mechanism of fatty liver. Clinical trials assessing the use of insulin-sensitizing agents developed for patients with type 2 diabetes mellitus are currently under way.
Question 3
Which of the following identifies a group of patients at substantial risk of dying from alcoholic hepatitis?

a) Child-Pugh score
b) Discriminant function
c) Model for End-Stage Liver Disease score
d) Milan criteria
e) Ranson criteria

Answer and Discussion
The answer is b.

Objective: Understand the prognosis and treatment of alcoholic hepatitis.

Several studies suggest that steroids improve survival for patients with severe alcoholic hepatitis without gastrointestinal (GI) bleeding. The definition of severity requires an evaluation of the bilirubin level and the pro time. The so-called discriminant function value identifies a group of patients at substantial risk for dying from alcoholic hepatitis.

Discriminant function:
4.6 (pro time – control [in seconds]) + (serum bilirubin [mg/dL]) = 32

When severely ill patients with a discriminant function score of ≥32 (without GI hemorrhage) are given 40 mg of prednisone daily for 28 days, survival is nearly twice as likely.

Question 4
According to the CDC, in the absence of an outbreak (single case exposure), which of the following contacts should receive hepatitis A postexposure prophylaxis with immune globulin?

a) Household contacts under 12 months of age
b) Office coworkers
c) Sexual contacts 18 to 40 years of age
d) Elementary school contacts
e) All of the above

Answer and Discussion
The answer is a.

Objective: Identify and treat those at risk for infection with hepatitis A virus.

Immune globulin provides protection against hepatitis A. Formerly, preexposure prophylaxis was recommended for those who travel internationally to endemic regions, but currently such persons are advised to receive active immunization. Postexposure prophylaxis with immune globulin is recommended for (a) household and sexual contacts under the age of 12 months or over the age of 40 years (for those between 12 months and 40 years, hepatitis A vaccine is preferred); (b) in day care centers (if children in diapers attend) but not to elementary or secondary school contacts unless an outbreak (more than a single case) has been identified; (c) within institutions to contacts only; and (d) in hospitals only if an outbreak occurs. Immune globulin is not recommended for coworkers in offices or factories.

Restaurant-exposed persons also may get immune globulin unless the contact was more than 2 weeks previous, in which case no vaccine is recommended. Postexposure prophylaxis is not needed for persons who have been immunized.

Question 5
Which of the following is not an extrahepatic manifestation of hepatitis C virus infection?

a) Glomerulonephritis
b) Porphyria cutanea tarda
c) Cryoglobulinemia
d) Type 2 diabetes
e) Cardiomyopathy

Answer and Discussion
The answer is e.

Objective: Understand the extrahepatic manifestations of hepatitis C virus infection.

Cardiomyopathy is not an extrahepatic manifestation of hepatitis C. All other choices can be seen along with the addition of lymphoproliferative disorders and leukocytoclastic vasculitis.

Question 6
Which of the following is associated with a low (<1.1) serum-ascites albumin gradient (SAAG)?

a) Wilson disease
b) Autoimmune hepatitis
c) Ovarian cancer
d) Budd-Chiari syndrome
e) Nonischemic cardiomyopathy

Answer and Discussion
The answer is c.

Objective: Understand the differential diagnosis of ascites based on the SAAG calculation.

Cirrhotic ascites is similar to serum, except it contains less protein. The SAAG is usually >1.1. This ratio is calculated by subtracting the albumin concentration of ascites from that of serum (albumin serum minus albumin ascites). Cardiac ascites will have a similarly high gradient. The SAAG has been established as a clinical valuable test with high specificity to differentiate ascites due to portal hypertension (cirrhosis, Budd-Chiari syndrome, or right heart failure) from other causes of ascites. Low gradients (<1.1) suggest a noncirrhotic (and a noncardiac) cause for ascites, such as malignancy and infection.

Question 7
A 75-year-old man who had open cholecystectomy due to choledocholithiasis more than 20 years ago underwent endoscopic retrograde cholangiopancreatography (ERCP) for the treatment of choledocholithiasis. Unfortunately, he has developed post-ERCP pancreatitis and has been admitted to your hospital for

A 75-year-old man who had open cholecystectomy due to choledocholithiasis more than 20 years ago underwent endoscopic retrograde cholangiopancreatography (ERCP) for the treatment of choledocholithiasis. Unfortunately, he has developed post-ERCP pancreatitis and has been admitted to your hospital for
pain control, intravenous fluid therapy, and observation. On the fourth hospital day, he develops fever (39°C) with a rising white blood cell (WBC) count. Blood and urine cultures have been obtained. What is the most appropriate imaging study?

a) Ultrasound of the right upper quadrant and the pancreas  
b) Contrast-enhanced computed tomography (CT) of the abdomen  
c) HIDA scan to assess for bile leak  
d) Chest CT with intravenous contrast  

**Answer and Discussion**  
The answer is b.  

**Objective: Understand the complications of acute pancreatitis.**  
This man has symptoms suggesting complicated acute pancreatitis. A contrast-enhanced CT is indicated to determine the presence of pancreatic necrosis. The presence of necrosis on CT requires prompt evaluation for infection. Fine needle aspiration (FNA) with Gram stain has been shown to be most effective at determining the presence or absence of microorganisms.

**Question 8**  
A 35-year-old obese woman who has been hospitalized for acute pancreatitis for a week starts spiking temperatures and becomes hypotensive. Two days before this acute episode, she underwent a contrast-enhanced CT due to continued severe abdominal pain. The CT revealed an area of nonenhancement in the pancreatic body. After adequate resuscitation in the intensive care unit and stabilization of the patient, what is the appropriate next step in the management of this patient?

a) FNA of the pancreatic necrosis  
b) Angiography  
c) Magnetic resonance imaging  
d) Total parenteral nutrition  

**Answer and Discussion**  
The answer is a.  

**Objective: Understand the complications of acute pancreatitis.**  
The CT scan done 2 days prior to the acute episode had already shown the presence of pancreatic necrosis. The development of fever and hypotension should raise suspicion for infected pancreatic necrosis. FNA of the necrotic material is the best way to detect infection. Intravenous antibiotic therapy would be indicated for infected necrosis.

**Question 9**  
A 21-year-old woman has had recurrent abdominal pain since 3 years of age. She gives a history of similar symptoms in an uncle who died of pancreatic cancer at age 45 years. Plain x-ray films of the abdomen show extensive calcification in the upper abdomen. What is the most likely diagnosis for this patient?

a) Celiac sprue  
b) Zollinger-Ellison syndrome  
c) Hereditary pancreatitis  
d) Gastric carcinoma  

**Answer and Discussion**  
The answer is c.  

**Objective: Understand the presentation and natural history of hereditary pancreatitis.**  
This woman has the classic presentation of hereditary pancreatitis: acute bouts of abdominal pain starting in childhood with the eventual development of chronic pancreatitis. Her family history is positive for pancreatitis. Patients with hereditary pancreatitis have a fivefold greater risk of pancreatic cancer than the risk in the average population.

**Question 10**  
A 65-year-old man seeks your advice due to pressure from his wife who thought his color has changed to “yellow” for the past 3 weeks. He does not have any history of liver or bile duct disease. He denies abdominal pain, fever, or chills and says that other than mild fatigue, he feels fine. He does not take any medication on a regular basis. On physical examination, he has scleral icterus, appears jaundiced, and has a palpable but nontender gallbladder. Laboratory evaluation shows the following: total bilirubin, 8.9 mg/dL (reference range, 0 to 1.5); alkaline phosphatase, 382 U/L (reference range, 40 to 150), AST, 66 U/L (reference range, 7 to 40); ALT, 92 U/L (reference range, 5 to 50); amylase 23 U/L (reference range, 0 to 137); normal electrolytes; kidney function; and complete blood count. A right upper quadrant ultrasound shows a dilated intrahepatic biliary tree and distended gallbladder. What is the most likely diagnosis?

a) Acute cholecystitis  
b) Chronic pancreatitis  
c) Choledocholithiasis  
d) Pancreatic cancer  

**Answer and Discussion**  
The answer is d.  

**Objective: Understand the differential diagnosis of painless jaundice.**  
This man has painless jaundice, which along with a palpable, nontender gallbladder (Courvoisier sign) and his age (over 50 years old) is strongly suggestive of pancreatic cancer. Acute cholecystitis, chronic pancreatitis, and choledocholithiasis are usually associated with abdominal pain. Although chronic pancreatitis and choledocholithiasis can very rarely present this way, pancreatic cancer is more likely.

**Question 11**  
Achalasia is usually not characterized by which of the following symptoms?

a) Dysphagia for solids and liquids  
b) Dysphagia for solids only  
c) Bland regurgitation  
d) Heartburn
**Answer and Discussion**

The answer is b.

**Objective: Understand the differential diagnosis of dysphagia.**

Dysphagia for solids suggests an anatomic (i.e., structural) rather than a functional (i.e., motility) disorder. Dysphagia resulting from a motor source is usually manifested by difficulty with both solids and liquids.

**Question 12**

Which pill is most commonly associated with esophagitis?

a) A nonsteroidal anti-inflammatory drug (NSAID)
b) Quinidine
c) Doxycycline
d) Slow-release potassium

**Answer and Discussion**

The answer is c.

**Objective: Understand the differential diagnosis of esophagitis.**

All these medications are associated with pill-induced esophagitis. However, the most frequent culprit is doxycycline, as it is a widely used antibiotic. Classically, young adults taking doxycycline for acne present with dysphagia and odynophagia because they take their medication either with a minimal amount of water or immediately before bedtime.

**Question 13**

Which of the following has been associated with gastroesophageal reflux disease (GERD)?

a) Noncardiac chest pain
b) Asthma
c) Dental erosion
d) Laryngeal cancer
e) All of the above

**Answer and Discussion**

The answer is e.

**Objective: Understand the common findings associated with GERD.**

More than 50% of patients with noncardiac chest pain have GERD. Extraesophageal presentations of GERD include damage to the lungs (i.e., asthma) and oropharynx (e.g., hoarseness, vocal cord granulomas, dental erosions, and laryngeal cancer) secondary to high acid reflux.

**Question 14**

A 65-year-old woman presents to the office with a complaint of a gnawing epigastric pain. She denies bleeding but has a hemoglobin of 10.9. Her most significant risk factor for ulcer disease is

a) Use of a nonselective NSAID
b) Age
c) Presence of *Helicobacter pylori* infection
d) Use of a cyclooxygenase (COX)-2 inhibitor
e) Cardiac prophylactic-dose aspirin

**Answer and Discussion**

The answer is c.

**Objective: Understand the etiologies of peptic ulcer disease.**

*Helicobacter pylori* is the most common cause for ulcer disease—especially duodenal ulcer (70% to 75%). NSAIDs are causative in approximately 25% of ulcer disease. Ulcers increase with age because these two risk factors increase with age. Cardiac prophylactic doses of aspirin are a risk factor but have a low incidence of ulcer disease (1%). COX-2–selective inhibitors (0.5%) have the same ulcer risk as placebo.

**Question 15**

A 39-year-old man presents with epigastric fullness and discomfort, which worsens following meals. A review of systems is otherwise negative. He is a smoker. There is no prior ulcer disease. The single best diagnostic approach would be:

a) An initial 8-week trial of a proton pump inhibitor (PPI)
b) Immediate upper endoscopy
c) Breath testing for *H. pylori* and providing treatment if results are positive
d) Empiric antimicrobial treatment of *H. pylori*
e) Performing a gastric-emptying study

**Answer and Discussion**

The answer is c.

**Objective: Understand the treatment approach for uncomplicated dyspepsia.**

The most appropriate approach in uncomplicated dyspepsia in this young patient would be *H. pylori* breath testing. This test-and-treat method is warranted as a cost-effective approach for a young patient with new-onset dyspepsia, as breath testing is noninvasive. A short course of a PPI is a reasonable strategy, but a full 8-week course would not be warranted. No justification ever exists for treating anyone for *H. pylori* without proof of infection.

Patients younger than 45 to 50 years of age with new-onset dyspepsia without alarm symptoms such as hematemesis, melena, anemia, nausea, vomiting, and weight loss do not warrant immediate upper endoscopy, and the incidence of gastric cancer is low. This patient’s symptoms could be related to gastroparesis. However, a gastric-emptying study would not be the best initial diagnostic study.

**Question 16**

A 34-year-old woman was found to have a duodenal ulcer and *H. pylori* on upper endoscopy with biopsies and was treated with combination lansoprazole, amoxicillin, and clarithromycin (PrevPac) for 10 days. She completed
therapy a few days ago but has persistent epigastric discomfort. She is concerned that her ulcer is still there. Select the most appropriate statement that applies to her case.

a) Her *H. pylori* has not been fully eradicated.
b) Her dyspeptic symptoms might persist despite eradication.
c) An immediate *H. pylori* breath test could be repeated to facilitate rescue therapy, if positive.
d) Quadruple therapy with a bismuth and tetracycline combination should be initiated to increase the likelihood of clearance.
e) Performing fecal antigen testing for *H. pylori* after 2 months is an excellent way of promptly evaluating treatment failures.

**Answer and Discussion**

The answer is b.

**Objective: Understand the treatment of peptic ulcer disease.**

Dyspeptic symptoms frequently may persist long after the course of *H. pylori* eradication therapy. Symptoms, therefore, cannot help to determine if eradication has been achieved. Breath testing would not be accurate this soon after eradication therapy due to the decreased sensitivity from the use of antibiotics and a PPI. Although confirmation of eradication by all testing is most reliable 4 weeks after treatment, fecal antigen testing has the advantage of being a more prompt test to determine treatment failure and can be used as soon as 7 days after the completion of therapy. Quadruple therapy is appropriate as a first-, second-, or even a third-line option. However, in this recently treated patient, it should be initiated only when it has been determined that eradication was unsuccessful.

**Question 17**

A 41-year-old male patient is seen in the emergency room with hematemesis. He smokes, uses NSAIDs on occasion, and has a history of a prior bleeding ulcer. He is otherwise healthy on no medications. The patient is tachycardic and orthostatic on examination. His systolic blood pressure is 90 and hemoglobin is 8.9 g. Gastroenterology consultation has been requested.

Which is the most accurate statement?

a) He should be medically stabilized and then undergo immediate endoscopy.
b) He should be started on an intravenous PPI and monitored for signs of persistent bleeding. Endoscopy should be performed if symptoms persist or worsen.
c) If initial endoscopy fails to stop his bleeding, surgical intervention is needed.
d) Intravenous PPI therapy and eradication of *H. pylori* may be more helpful in this patient than endoscopic management.

e) A 41-year-old male patient is seen in the emergency room with hematemesis. He smokes, uses NSAIDs on occasion, and has a history of a prior bleeding ulcer. He is otherwise healthy on no medications. The patient is tachycardic and orthostatic on examination. His systolic blood pressure is 90 and hemoglobin is 8.9 g. Gastroenterology consultation has been requested.

**Answer and Discussion**

The answer is a.

**Objective: Understand the treatment of peptic ulcer disease.**

This is an unstable patient with risk factors for adverse outcomes with ulcer disease. Medical stabilization is most appropriate, then endoscopy. Intravenous PPI therapy and *H. pylori* eradication are beneficial but not as helpful in this acute bleed as is prompt endoscopic intervention. Rebleeding after initial endoscopic management occurs in 20% to 25% of cases. Repeat endoscopy is very successful, and combined with the use of intravenous PPIs, surgery is needed significantly less often. In addition, interventional radiology procedures in many centers have essentially replaced surgery for intractable GI bleeding.

**Question 18**

A 57-year-old woman with a history of morbid obesity, hyperlipidemia, and osteoarthritis presents for a physical examination. She takes a lipid-lowering agent as her only medication. Her COX-2–selective inhibitor was taken off the market a few months ago, and she wonders what can be done for her joint pain. She has been unable to work due to her arthritic pain and states that money is limited right now. She has no GI complaints at this time and has no history of ulcer.

What further management is the most appropriate?

a) Start back on an available COX-2–selective inhibitor
b) Test and treat for *H. pylori*
c) Start on an NSAID and prescribe a PPI
d) Start on an NSAID and caution her to alert you to any dyspeptic symptoms or bleeding
e) Start back on an available COX-2–selective inhibitor and begin a PPI

**Answer and Discussion**

The answer is d.

**Objective: Understand the GI side effects of anti-inflammatory medications.**

This is a low-risk patient who should do well with simply starting an NSAID. Starting on a COX-2–selective inhibitor is reasonable, but cost is a concern. Test and treat for *H. pylori* in this asymptomatic patient is not the appropriate management. Prophylaxis with a PPI and NSAID has an equivalent ulcer risk to that of a COX-2–selective inhibitor but may be more costly. Neither of these regimens is warranted in this low-risk patient. Because NSAID use is so widespread, the economic consequences of universal prophylaxis are prohibitive. Therefore, prophylaxis is warranted only in high-risk patients, such as those who are older than 60 years, have had prior peptic ulcer disease, or are taking a high dosage of or more than one NSAID, use corticosteroids or anticoagulants concurrently with an NSAID, or have a serious systemic disorder. A COX-2–selective inhibitor and PPI is the least appropriate therapy in this low-risk patient.
For the cases in questions 19 through 22, choose the appropriate recommendation from the lettered list:

**Question 19**
A single 3-mm rectal adenoma is found on flexible sigmoidoscopy in a 32-year-old woman.

a) Colonoscopy and polypectomy
b) Yearly fecal occult blood test and flexible sigmoidoscopy every 5 years
c) Colonoscopy at age 40 years
d) Colonoscopy in 5 years
e) Colonoscopy in 3 years
f) Colonoscopy in 1 year

**Answer and Discussion**
The answer is a.

Objective: Understand screening guidelines for the prevention of colorectal cancer.

Until further studies are performed, all patients with an adenoma detected by flexible sigmoidoscopy should undergo a full colonoscopy to detect synchronous, more proximal neoplasms, as well as polypectomy of all detected polyps.

**Question 20**
A 62-year-old man with an 18-year history of pancolitis just underwent colonoscopy without any changes of dysplasia seen.

a) Colonoscopy and polypectomy
b) Yearly fecal occult blood test and flexible sigmoidoscopy every 5 years
c) Colonoscopy in 10 years
d) Colonoscopy in 5 years
e) Colonoscopy in 3 years
f) Colonoscopy in 1 year

**Answer and Discussion**
The answer is f.

Objective: Understand screening guidelines for the prevention of colorectal cancer.

All patients with ulcerative pancolitis who have had the diagnosis for more than 8 years are at increased risk for colorectal dysplasia and cancer. Yearly colonoscopy with four-quadrant biopsy every 10 cm to detect dysplasia is indicated.

**Question 21**
A 55-year-old woman has a lifelong history of irritable bowel syndrome (IBS) and had a colonoscopy at the age of 50.

a) Colonoscopy now
b) Yearly fecal occult blood test and flexible sigmoidoscopy every 5 years
c) Colonoscopy in 5 years
d) Colonoscopy in 3 years
e) Colonoscopy in 1 year

**Answer and Discussion**
The answer is b or c.

Objective: Understand screening guidelines for the prevention of colorectal cancer.

Patients with IBS and no risk factors are at average risk for colorectal cancer. Colonoscopy every 10 years (or a flexible sigmoidoscopy every 5 years or annual fecal occult blood testing) is an appropriate screening method for patients at average risk.

**Question 22**
A 68-year-old African American man recently underwent removal of an 8-mm tubular adenoma.

a) Colonoscopy and polypectomy
b) Yearly fecal occult blood test and flexible sigmoidoscopy every 5 years
c) Colonoscopy in 10 years
d) Colonoscopy in 5 years
e) Colonoscopy in 3 years
f) Colonoscopy in 1 year

**Answer and Discussion**
The answer is d.

Objective: Understand screening guidelines for the prevention of colorectal cancer.

The postpolypectomy surveillance interval is 5 years in patients with less than three tubular adenomas <1 cm detected on colonoscopy. New data have shown that those individuals are not at high risk for having numerous, large, or advanced adenomas on their subsequent colonoscopy.

**Question 23**
A 62-year-old woman arrives in your office with recent-onset abdominal pain and a change in bowel habit. She has no family history of cancer and is otherwise in good health. Physical examination reveals some tenderness in the supra-pubic area but is otherwise normal. Fecal occult blood test reveals one of three smears to be positive. Which of the following options is most appropriate?

a) Repeat the fecal occult blood test
b) Schedule a colonoscopy
c) Order a flexible sigmoidoscopy and, if results are negative, do no further evaluation
d) Reassure the patient that she has symptoms of IBS and treat with fiber

**Answer and Discussion**
The answer is b.

Objective: Understand the clinical presentation and evaluation of colorectal cancer.

Any patient with symptoms of colorectal cancer should have a complete colonic evaluation. A positive fecal occult blood test result includes a positive finding in any of three sample
windows; retesting should not be performed. A complete colonoscopy is the diagnostic test of choice when evaluating for colorectal cancer.

Question 24

A 42-year-old father with familial adenomatous polyposis (FAP) has two children, ages 12 and 14 years. He is interested in knowing if his children have FAP. No APC mutation was found on his genetic testing, however. What would be the appropriate management of this family?

a) Recommend flexible sigmoidoscopy when the children begin to show symptoms of colonic disease
b) Offer MYH testing to the father
c) Advise the father that he cannot pass FAP on to his children because he has no detectable APC mutation

Answer and Discussion

The answer is b.

Objective: Identify those at risk for a hereditary colorectal cancer syndrome.

It is not appropriate to wait for colonic symptoms in individuals “at risk” for FAP. Surveillance should begin at the time of puberty, and colectomy should be performed before bleeding, pain, or cancer develops. About 10% of individuals with FAP are APC negative but still have a 50% chance of passing an FAP disease-causing mutation on to their children. It has recently been discovered that biallelic germline mutations in MYH account for up to 7.5% of APC-negative FAP patients. MYH testing should be offered to any patient with multiple adenomas or those with classic FAP who are APC negative.

Question 25

A 30-year-old white woman presents to your office because of diarrhea and tender nodules on her legs. Three years before this episode, she was on vacation in Mexico and developed bloody diarrhea on returning home. She was treated with ciprofloxacin, 750 mg two times a day for 7 days, and the diarrhea resolved. A year later, she had a similar episode of diarrhea that was diagnosed as IBS. She discontinued cigarette smoking after an episode of shortness of breath and sharp chest pain that lasted 1 week 2 months earlier. Four weeks before consultation, she developed four red “lumps” on her legs that were extremely painful to touch. She was started on ibuprofen and 2 weeks later developed bloody diarrhea. Her symptoms are predefecational cramps that are followed by small, loose bowel movements and, at times, bloody mucus. On two occasions, she has had nocturnal bowel movements.

She has no systemic symptoms. Her past medical history is unremarkable. She takes ibuprofen for menstrual cramps and is on birth control pills.

On examination, she is in no distress. She has a heart rate of 84 beats/ minute, respiratory rate of 16 breaths/minute, and a temperature of 37.6°C.

Examination of the abdomen reveals normal bowel sounds; the abdomen is soft but tender to palpation in the left lower quadrant. Rectal examination reveals soft stool with bloody mucus. On the shins, she has four quarter-size brown nodules.

Which is the most likely diagnosis?

a) IBS
b) Infectious diarrhea
c) Ulcerative colitis (UC)
d) Crohn disease (CD)
e) Collagenous colitis

Answer and Discussion

The answer is c.

Objective: Understand the clinical presentation and diagnosis of UC.

UC is an inflammatory bowel disease with a clinical presentation that ranges in severity depending on the age of presentation and extent of initial disease. Signs and symptoms include progressive non-bloody to bloody diarrhea, fecal urgency, tenesmus, mucous per rectum. Most young adults present with mild disease involving the left side of the colon and rectum. They are rarely toxic and systemic symptoms in mild disease are rare.

Question 26

Which is the best diagnostic test in the evaluation of a patient suspected to have UC?

a) Complete blood cell count/differential
b) Stool test for Clostridium difficile
c) Flexible sigmoidoscopy with biopsies
d) Air-contrast barium enema
e) Small bowel series

Answer and Discussion

The answer is c.

Objective: Understand the diagnosis of UC.

The diagnosis of UC is made by histologic assessment of tissue by a trained pathologist. Unless contraindicated, endoscopy with biopsies is indicated in all patients in whom UC is suspected. The underlying clinical picture, stool testing, and occasional serologic testing are all adjuvant studies and are less sensitive in diagnosing and determining the extent of disease than the histologic analysis.

Question 27

What is the initial step in the management of mild UC once the diagnosis has been confirmed?

a) Admission to hospital for IV steroid therapy
b) Metronidazole (Flagyl) 500 mg orally three times a day for 1 week
c) Fiber and an anticholinergic agent
d) Prednisone 40 mg orally once a day
e) 5-Aminosalicylic acid (ASA) enemas at bedtime
**Answer and Discussion**

**The answer is e.**

**Objective: Understand the treatment of mild UC.**

The initial treatment of choice for mild UC is a 5-ASA agent. These medications are effective in inducing and maintaining remission in patients with mild to moderately active UC. Importantly, the therapeutic effect of the 5-ASA is topical and for these medications to work, the drug must be delivered to the site of disease.

**Question 28**

What is the treatment of UC that worsens or does not respond to initial 5-ASA medications?

- a) Ciprofloxacin 750 mg BID
- b) Prednisone 60 mg/day
- c) Infliximab infusions 5 mg/kg at 0, 2, and 6 weeks
- d) 6-Mercaptopurine daily
- e) Surgery

**Answer and Discussion**

The answer is b.

**Objective: Understand the treatment of moderate-to-severe UC.**

Corticosteroids play a significant role in the medical treatment of inflammatory bowel disease. Corticosteroids are indicated in patients with moderate or severely active UC and in patients who fail to respond to 5-ASA. Immunosuppressive and biologic agents are indicated in steroid refractory or steroid-dependent patients. Patients with UC require surgery because of failure to respond to medical treatment, hemorrhage, toxic dilatation, perforation, strictures causing obstruction, and dysplasia or cancer.

**Question 29**

A 34-year-old female patient with a 12-year history of UC comes with her husband for advice regarding the use of medications in pregnancy. She developed bloody diarrhea when she was 22 years old. The initial presentation was severe and was treated with prednisone. She was able to wean off prednisone and has remained on sulfasalazine since then. She has mild flare-ups every year during spring. These are controlled by increasing the dose of sulfasalazine from 2 g/day that she takes for maintenance of remission to 4 g/day. She is otherwise healthy and takes a multivitamin "when I remember." What is your recommendation to the patient regarding the use of sulfasalazine in pregnancy?

- a) Sulfasalazine should not be used during pregnancy because of the risk of kernicterus; therefore, discontinue and start another 5-ASA
- b) Discontinue sulfasalazine and do not institute treatment unless there is an exacerbation
- c) Continue sulfasalazine at the present dose
- d) Add folic acid 1 mg orally once a day
- e) Discontinue sulfasalazine postpartum to decrease the risk of kernicterus and start another 5-ASA medication

**Answer and Discussion**

The answer is d.

**Objective: Understand the treatment of inflammatory bowel disease during pregnancy.**

All 5-ASA compounds are safe during pregnancy and lactation. The treatment with 5-ASA should be continued during pregnancy to decrease the risk of a flare-up with potentially disastrous consequences. Sulfasalazine contains sulfapyridine, and all sulfas have the potential for inducing kernicterus. However, this is only a theoretical concern; sulfasalazine has been available since the early 1940s, and there are no reports of kernicterus in association with sulfasalazine. The patient should take folic acid at a minimum dose of 1 mg/day. Sulfasalazine interferes with folic acid absorption, and folic acid decreases the risk of spina bifida.

**Question 30**

A 68-year-old woman reports diarrhea and occasional fecal incontinence. She is otherwise healthy, her appetite is good, and her weight is stable. Which of the following helps you decide whether her diarrhea is significant?

- a) Passage of liquid stools
- b) Frequent passage of stools
- c) Presence of large bowel movements
- d) 24-Hour stool weight >250 g
- e) History of fecal incontinence

**Answer and Discussion**

The answer is e.

**Objective: Understand the evaluation of fecal incontinence and the definition of diarrhea.**

The history of fecal incontinence should always be considered significant and evaluated. In a patient with fecal incontinence who is otherwise healthy, the involuntary loss of stool can be perceived as diarrhea. Although liquid stools are usually associated with increased weight, stool weight remains the only objective way of assessing the degree of diarrhea (thus, answer d is also considered an acceptable answer, but not the best answer).

**Question 31**

Which of the following features can help distinguish osmotic from secretory diarrhea?

- a) Secretory diarrhea decreases or disappears with fasting.
- b) There is usually no osmotic gap in secretory diarrhea.
- c) Osmotic diarrhea is often accompanied by bleeding.
- d) Stool weight is higher in osmotic diarrhea due to the nonabsorbable solutes.
Answer and Discussion
The answer is b.
Objective: Understand the diagnostic evaluation of diarrhea.
Because secretory diarrhea is associated either with the active secretion of electrolytes and water or impaired absorption, no increase in osmotic gap occurs in this condition. Secretory diarrhea is usually not affected by food intake. Osmotic diarrhea is not accompanied by bleeding. Stool volumes may be high in either osmotic or secretory diarrhea. The nonabsorbable solutes in osmotic diarrhea do not cause the stool weight to rise.

Question 32
A 55-year-old woman with diarrhea is found to have lymphocytic colitis. She has iron-deficiency anemia, and the diarrhea is difficult to control. With which would you proceed?

a) Iron supplementation  
b) Antigliadin antibody  
c) Small bowel radiograph  
d) 72-Hour stool collection for fat  
e) Upper endoscopy and small bowel biopsy

Answer and Discussion
The answer is e.
Objective: Understand the diagnostic evaluation of diarrhea.
Lymphocytic colitis is usually not associated with anemia. Because the diarrhea is difficult to control and the patient also has iron-deficiency anemia, the possibility of celiac disease should be kept in mind. An upper GI endoscopy and small bowel biopsy to exclude celiac, as well as other upper GI sources for anemia, would be the most appropriate way to proceed.

Question 33
A 38-year-old man with a history of hepatitis B virus infection and significant alcohol abuse, who has not seen a physician in 7 years, presents to the emergency department with fever and altered sensorium. On examination, he is febrile, tachycardic, hypotensive, and somnolent. He is markedly jaundiced, with a distended abdomen. Initial blood work reveals a Na+ level of 130 mg/dL, creatinine level of 1.6 mg/dL, hemoglobin of 10 mg/dL, and platelet count of 90,000/mm^3. Which of the following diagnoses is most consistent with these findings?

a) Splenic sequestration  
b) Idiopathic thrombocytopenic purpura  
c) Thrombotic thrombocytopenic purpura  
d) Heparin-induced thrombocytopenia  
e) Systemic lupus erythematosus

Answer and Discussion
The answer is a.
Objective: Understand the complications of cirrhosis.
This man most likely has portal hypertension and ascites. Splenic sequestration of platelets secondary to portal hypertension often leads to a decrease in the platelet count. Alcohol also has a direct cytotoxic effect on megakaryocytes. Furthermore, inadequate thrombopoietin production may be present in the failing liver, also leading to the decreased production of platelets. Nevertheless, the platelet count rarely falls to <10,000/mm^3.

Question 34
A 26-year-old man has had recurrent episodes of mild, crampy abdominal pain accompanied by bloody diarrhea over the past year. He has no other significant past medical history and does not smoke or drink alcohol. He has undergone colonoscopy as part of his evaluation. The colon appears to be continuously inflamed from the anal verge to the more proximal colon. Shallow ulcers were noted, and there were no hemorrhoids. Biopsy is consistent with UC. He now presents with a 5-day history of bloody diarrhea and mild abdominal pain with a rather abrupt onset. Stool studies are negative for C. difficile or a microbiologic cause of colitis. All the following are true about this patient’s condition, except

a) Total parenteral nutrition is not effective as primary therapy.  
b) Sulfasalazine can be effective in maintaining remission, as well as in acute disease.  
c) If he responds to a corticosteroid, he should be maintained on it indefinitely once in remission.  
d) Sclerosing cholangitis may be an associated condition.  
e) Oral anticholinergics for control of symptoms are contraindicated.

Answer and Discussion
The answer is c.
Objective: Understand the treatment of UC.
This man most likely has UC. Corticosteroids are used in the treatment of UC and CD, but controlled trials have shown no benefit in maintaining remission. In patients with a severe exacerbation of colitis, oral intake can promote colonic activity and intravenous alimentation serves as a component of therapy, although no evidence suggests that it alone is effective as primary therapy. Sulfasalazine is a well-established agent for use in remission, but can also be used in therapy of an acute flare. Drugs such as codeine, diphenoxylate, and anticholinergics are contraindicated because they can promote colonic dilatation and toxic megacolon.

Question 35
A 69-year-old businessman is assessed for halitosis and a sensation of fullness in his throat. On being questioned, he
Explains that he is embarrassed by this and has started to avoid social situations. He has also found that he has some difficulty in swallowing that seems to be relieved by bringing up foul-smelling food particles. He has tried over-the-counter famotidine without relief. Which of the following is the single, most likely diagnosis?

a) Dental abscess  
b) GERD  
c) Zenker diverticulum  
d) Globus pharyngeus  
e) Progressive systemic sclerosis

Answer and Discussion

The answer is c.

Objective: Identify the differential diagnosis of oropharyngeal dysphagia.

The symptoms are most likely to be explained by the presence of a Zenker diverticulum, which is an outpouching of the esophageal wall. This condition usually presents in older individuals complaining of cervical dysphagia, gurgling in the throat, halitosis, and regurgitation of foul food. Regurgitation of old food is unlikely with a dental abscess or GERD. Symptoms of globus pharyngeus do not include dysphagia. Scleroderma of the esophagus can cause GERD, but if dysphagia occurs, it is progressive.

Question 36

A 42-year-old man is found to be anemic on workup for fatigue. He has been taking multivitamins and oral iron supplements for the past 20 years. He is a nonsmoker and seldom drinks alcohol. On direct questioning, he explains that he has frequent bowel movements with stools that are difficult to flush away. Physical examination is notable for a blistering rash at the elbows and knees. On testing, he is found to be anemic, with a mean corpuscular volume of 65. Review of his peripheral blood smear demonstrates Howell-Jolly bodies. Endomysial antibody test result is positive, and antinuclear antibody test is negative. He is instructed to eat a gluten-free diet, and his symptoms improve. All the following statements about this patient’s condition are true, except

a) A positive endomysial antibody test is consistent with the clinical picture.  
b) Small bowel biopsy shows periodic acid–Schiff-positive granules in macrophages.  
c) Lymphoma is a late complication.  
d) Osteomalacia is an association.  
e) Response to the gluten-free diet is diagnostic.

Answer and Discussion

The answer is b.

Objective: Understand the clinical findings and presentation of celiac sprue.

This man has a history suggestive of celiac sprue, a gluten-sensitive enteropathy. Iron-deficiency anemia unresponsive to oral supplements is often seen. Dermatitis herpetiformis and Howell-Jolly bodies are clues to the diagnosis. Although a positive endomysial antibody test is not specific, it is sensitive, and the response to the gluten-free diet is virtually diagnostic. If a patient becomes unresponsive to dietary therapy after many years, lymphoma should be a consideration. Periodic acid–Schiff-positive granules on small bowel biopsy are seen in Whipple disease, not in celiac sprue.

Question 37

A 25-year-old woman reports rectal bleeding. She is admitted for further investigation. Physical examination reveals pigmented lesions of the mouth, hands, and feet. Radiologic investigation shows multiple polypoid tumors of the small bowel, which are also found on endoscopic evaluation of the ascending colon. Biopsy demonstrates findings consistent with hamartomas. Which of the following statements about this woman’s condition is correct?

a) An increased incidence of ovarian sex cord tumors is present in patients with this condition.  
b) A high risk of colonic malignancy is present.  
c) Total colectomy is absolutely indicated.  
d) First-line treatment is a corticosteroid.  
e) The inheritance pattern of this condition is autosomal recessive.

Answer and Discussion

The answer is c.

Objective: Understand the natural history of the Peutz-Jeghers syndrome.

This woman most likely has Peutz-Jeghers syndrome of hamartomas and pigmented lesions. This condition is associated with an increased risk of ovarian sex cord tumors. The risk of colonic malignancy is close to that of the general population, and the inheritance pattern is autosomal dominant. Corticosteroids do not play a role in management. Total colectomy is not mandatory for this syndrome.

Question 38

A 30-year-old man is evaluated for dyspepsia. His history is remarkable for an 11-lb weight loss in the past month, and he also complains of diarrhea. He denies any nonsteroidal anti-inflammatory drug use. On endoscopic examination, duodenal bulb ulceration is noted. Biopsy of the involved area is negative for *H. pylori*. What would be the most appropriate next step in managing this patient?

a) Culture of the biopsy specimen for *H. pylori*  
b) A 4-week trial of oral famotidine with follow-up endoscopy  
c) Breath test for *H. pylori*  
d) CT of the abdomen  
e) Serum gastrin level
**Answer and Discussion**

The answer is e.

**Objective: Understand the clinical features of Zollinger-Ellison syndrome.**

The coexistence of duodenal bulb ulceration with diarrhea is suspicious for Zollinger-Ellison syndrome. This patient also lacks risk factors for *H. pylori* or nonsteroidal anti-inflammatory drug use. Histologic evaluation for *H. pylori* is 98% sensitive, and workup with culture and breath test is redundant here. CT can be used to localize a gastrinoma, but the first step would be to evaluate the serum gastrin level.

### Questions 39 to 44

For each patient listed, select the most likely set of liver function test findings.

<table>
<thead>
<tr>
<th>ALT (U/L)</th>
<th>AST (U/L)</th>
<th>ALKALINE PHOSPHATASE (U/L)</th>
<th>TOTAL BILIRUBIN (MG/DL)</th>
<th>ALBUMIN (G/DL)</th>
<th>PT/CONTROL (SECONDS)</th>
</tr>
</thead>
<tbody>
<tr>
<td>a) 994</td>
<td>518</td>
<td>110</td>
<td>2.2</td>
<td>4.1</td>
<td>11.8/11</td>
</tr>
<tr>
<td>b) 87</td>
<td>81</td>
<td>902</td>
<td>6.1</td>
<td>3.1</td>
<td>14.8/11</td>
</tr>
<tr>
<td>c) 18,900</td>
<td>17,230</td>
<td>269</td>
<td>7.1</td>
<td>3.1</td>
<td>20/11</td>
</tr>
<tr>
<td>d) 63</td>
<td>273</td>
<td>121</td>
<td>3.7</td>
<td>2.2</td>
<td>16/11</td>
</tr>
<tr>
<td>e) 21</td>
<td>23</td>
<td>70</td>
<td>2.6</td>
<td>4.1</td>
<td>11.2/11</td>
</tr>
<tr>
<td>f) 44</td>
<td>46</td>
<td>444</td>
<td>0.9</td>
<td>4.5</td>
<td>12.2/11</td>
</tr>
</tbody>
</table>

### Answers and Discussion

**Objective: Identify causes of liver function test abnormalities.**

**Question 39: The answer is e; Gilbert syndrome.**

Gilbert syndrome is the most common inherited disorder of bilirubin glucuronidation. Routine laboratory tests are usually normal, except for hyperbilirubinemia. Baseline bilirubin levels are usually <3 mg/dL. Certain stressors such as fasting (or receiving a lipid-free diet), febrile illnesses, and physical exertion cause further elevation in serum bilirubin levels, but the level usually stays <6 mg/dL. The bilirubin level returns to normal 12 to 24 hours after resuming normal diet, removal of the stressor, or both.

**Question 40: The answer is a; Hepatitis A infection.**

Hepatitis A infection is common in areas in which food and water hygiene and sanitation are suboptimal. The incubation period averages 30 days. Patients experience prodromal symptoms, including malaise, nausea, vomiting, anorexia, fever, and right upper quadrant pain. Jaundice and hepatomegaly are the most common physical findings in symptomatic patients. Serum aminotransferases are markedly elevated (usually >1,000 IU/dL); serum bilirubin (total and direct) and alkaline phosphatase are also elevated. ALT is commonly higher than AST.

**Question 41: The answer is b; Primary biliary sclerosis.**

Ninety-five percent of primary biliary cirrhosis patients are women. Although fatigue and pruritus were once the most common presenting symptoms of primary biliary cirrhosis, presently up to half the patients are asymptomatic at diagnosis. Significantly elevated serum alkaline phosphatase is characteristic of primary biliary cirrhosis. The aminotransferases may be normal, and, when elevated, they rarely increase more than fivefold above nor-
The serum bilirubin concentration becomes elevated in most patients as the disease progresses. Antimitochondrial antibodies are the serologic hallmark of primary biliary cirrhosis.

**Question 42: The answer is d; Alcoholic liver disease.**  
A disproportionate elevation of serum AST compared with ALT is the most common biochemical abnormality in alcoholic liver disease. Although the absolute values of serum AST and ALT are almost always <500 IU/L, the AST-to-ALT ratio is usually <2.0.

**Question 43: The answer is f; Hepatic granuloma.**  
Although hepatic granulomas are present in almost all patients who have sarcoidosis with involvement of their GI tract, clinically apparent liver disease is uncommon even in patients who have numerous hepatic granulomas. Mild elevation in alkaline phosphatase and γ-glutamyltransferase is the usual laboratory finding.

**Question 44: The answer is c; Acetaminophen overdose.**  
Liver function abnormalities peak from 72 to 96 hours after ingestion in patients with acetaminophen overdose. The plasma ALT and AST levels often exceed 10,000 IU/L. Total bilirubin concentration generally does not exceed 4.0 mg/dL, which is primarily indirect.

**Question 45**

A 53-year-old man with a history of chronic pancreatitis secondary to alcoholism presents to the emergency department complaining of acute worsening of epigastric pain and dizziness. Recently, his chronic pain has been hard to control despite adequate pain medications. On examination, he is afebrile, orthostatic, and has heme-positive stool. Laboratory evaluation reveals the following:

<table>
<thead>
<tr>
<th>Test</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemoglobin</td>
<td>5.0 g/dL</td>
</tr>
<tr>
<td>Platelets</td>
<td>402,000/μL</td>
</tr>
<tr>
<td>Mean corpuscular volume</td>
<td>86.4</td>
</tr>
<tr>
<td>WBC</td>
<td>9,800/mm³</td>
</tr>
<tr>
<td>Prothrombin time</td>
<td>11.2 s</td>
</tr>
<tr>
<td>International normalized ratio</td>
<td>0.98</td>
</tr>
<tr>
<td>Partial thromboplastin time</td>
<td>31.1 s</td>
</tr>
<tr>
<td>Albumin</td>
<td>3.0 g/dL</td>
</tr>
<tr>
<td>AST</td>
<td>81 U/L</td>
</tr>
<tr>
<td>ALT</td>
<td>56 U/L</td>
</tr>
<tr>
<td>Alkaline phosphatase</td>
<td>377 U/L</td>
</tr>
<tr>
<td>Bilirubin</td>
<td>0.8 mg/dL</td>
</tr>
<tr>
<td>Amylase</td>
<td>55 U/L</td>
</tr>
<tr>
<td>Lipase</td>
<td>12 U/L</td>
</tr>
</tbody>
</table>

Fresh blood is apparent on gastric lavage, and an urgent esophagogastroduodenoscopy confirms the presence of fresh blood clots in the fundus, with multiple gastric varices and one bleeding varix. The bleeding site is successfully injected with epinephrine. Blood transfusion, octreotide, and propranolol therapy are initiated. The bleeding does not recur, and his hospital course is uncomplicated. Before discharge, which of the following diagnostic tests is indicated to further explore the cause of this patient’s gastric varices?

- a) Endoscopic retrograde cholangiopancreatography  
- b) Percutaneous transhepatic cholangiography  
- c) Visceral angiography  
- d) Transjugular hepatic biopsy  
- e) Radionuclide (hepatobiliary iminodiacetic acid) biliary scan

**Answer and Discussion**

The answer is c.

**Objective: Identify causes of acute portal hypertension in chronic pancreatitis.**

Splenic and portal vein thrombosis is a relatively common complication of chronic pancreatitis. In patients with the disorder, studies have estimated a splenic vein thrombosis prevalence rate of between 5% and 24%. In a surgical series, a surprising 10% prevalence of portal or superior mesenteric vein thrombosis has been noted. Besides the fact that many cases are silent, splenic and portal vein thrombosis symptoms in chronic pancreatitis patients may be indistinguishable from the patients’ chronic symptoms. Hence, it is not uncommon that many cases go undetected until patients present with complications of portal hypertension. Worsening of the chronic abdominal pain in chronic pancreatitis patients warrants further evaluation to rule out splenic and portal vein thrombosis. Visceral angiography is the diagnostic test of choice for splenic and portal vein thrombosis.

**Question 46**

A 28-year-old Caucasian woman presents with a 1-year history of diarrhea that started after a bout of *Shigella* colitis following a trip to Mexico. She typically describes having three to four loose stools per day that are precipitated by food intake. These episodes are associated with abdominal discomfort for most of the day. Use of bowel-slowing drugs, such as Imodium, results in constipation with no bowel movement for 1 to 2 days. She is concerned about colon cancer because one of her closest friends was diagnosed with colon cancer at age 30 years. She has no family history of colon polyps or cancer. Physical examination reveals a healthy woman with no abnormal findings. What is the most likely diagnosis in this patient?

- a) IBS—diarrhea predominant  
- b) Celiac disease  
- c) IBS—constipation predominant  
- d) IBS—mixed type  
- e) Persistent *Shigella* infection

**Answer and Discussion**

The answer is a.

**Objective: Identify causes of chronic diarrhea.**

The patient gives a classic story of postinfectious IBS that is diarrhea predominant. The history of constipation is
secondary only to medications without which she only has diarrhea. It is unlikely to be persistent *Shigella* dysentery because there is no blood or mucus in the stools. Celiac disease should always be ruled out in such patients; however, the diarrhea from malabsorption does not usually resolve with bowel-slowing agents.

**Question 47**

A 39-year-old woman with a history of gastric bypass Roux-en-Y procedure complains of nausea, vomiting, and abdominal pain for the last 2 months. Esophagogastroduodenoscopy (EGD) was performed that showed a very tight stricture at the G-J anastomosis. Balloon dilation was performed up to 15 mm. Six hours after the procedure, the patient starts complaining of abdominal pain.

Vital signs: temperature = 99.8°F, heart rate = 110, blood pressure = 100/60, respiratory rate = 20

Examination: anxious, alert
Abdomen: distended, diffusely tender with rebound, bowel sound sluggish

Repeat kidneys, ureters, and bladder (KUB) shows the following.

[Image of radiograph]

What is the most appropriate next step in the management of this patient?

a) Gastrografin swallow to assess leak
b) Observe and reassure
c) Barium swallow to assess leak
d) Emergency laparotomy
e) Repeat EGD

**Answer and Discussion**

The answer is a.

**Objective: Identify appropriate diagnostic work for esophageal tear.**

Gastrografin swallow should be the next step in the evaluation because if there is no active leak, the patient can be managed conservatively with IV fluids, antibiotics, and nothing per oral for 1 to 2 days. Active leak should lead to urgent surgery. This patient had no leak on gastrografin swallow. She was managed conservatively and was discharged home in 4 days. Barium swallow is not recommended when trying to rule out active leak. Chemical mediastinitis can occur if barium extravasates outside of the esophagus. Repeat EGD could cause more harm in a potential esophageal tear from mechanical trauma and insufflation and is insensitive at identifying a small tear.

**Question 48**

A 58-year-old man is seen in the clinic with a history of dyspepsia for 3 months. He also complains of nausea but no acid reflux. Vital signs are normal. Examination is benign. Labs are normal. EGD reveals normal esophagus and inflamed stomach with a 5-mm ulcer on the lesser curvature. Biopsies of the ulcer show no malignant cells but are positive for *H. pylori*. Which of the following is the best treatment for this patient?

a) A course of triple therapy for *H. pylori* followed by PPI for 1 month
b) Repeat EGD in 2 weeks to document ulcer healing
c) A course of triple therapy for *H. pylori* for 14 days
d) Lifelong PPIs
e) Lifelong H₂ receptor antagonists

**Answer and Discussion**

The answer is c.

**Objective: Understand *H. pylori* management.**

The current guidelines suggest that a 14-day course of treatment for *H. pylori* is sufficient to treat ulcers without further PPI therapy for 1 month. The regimen most commonly recommended for first-line treatment of *H. pylori* triple therapy consists of a PPI, amoxicillin (1 g twice daily), and clarithromycin (500 mg twice daily) for 14 days. Metronidazole (500 mg twice daily) can be substituted for amoxicillin, but only in penicillin-allergic individuals since metronidazole resistance is common and can reduce the efficacy of treatment. Some clinicians have opted for quadruple therapy, which consists of a PPI, combined with bismuth (525 mg four times daily) and two antibiotics (e.g., metronidazole 250 mg four times daily and tetracycline 500 mg four times daily) given for 10 to 14 days. Quadruple therapy is appropriate as initial therapy in areas in which the prevalence of resistance to clarithromycin or metronidazole is >20%, or in patients with recent or repeated exposure to clarithromycin or metronidazole. Repeat EGD is controversial for such solitary ulcers on lesser curvature, and it should be done at 6 to 8 weeks, if at all, but not at 2 weeks.

**Question 49**

A 45-year-old man was diagnosed with an *H. pylori*–induced duodenal ulcer 6 weeks ago when he had EGD done for
dyspepsia and nausea. He completed a 14-day triple therapy for the eradication of *H. pylori*. Although his symptoms of nausea and dyspepsia are much improved, he is still not completely asymptomatic. There is no significant family history of cancer. He is a lifelong nonsmoker. Vital signs are normal. Examination is normal. Labs are normal. What is the most appropriate next step in the management of his condition?

a) Perform urea breath test  
b) Repeat EGD  
c) Perform *H. pylori* antibody test  
d) CT scan of the abdomen  
e) Ultrasound scan of the abdomen

**Answer and Discussion**

**Objective:** Understand diagnostic testing after *H. pylori* treatment.

It is important to demonstrate the eradication of *H. pylori* in such patients because the treat–retest–retreat policy has been shown to be cost-effective. Eradication should be confirmed if the patient has persistent symptoms after *H. pylori* treatment for dyspepsia, if the patient had an *H. pylori*–associated ulcer, if the patient had gastric mucosa–associated lymphoid tissue lymphoma, and if the patient had resection for early gastric cancer. Eradication may be confirmed by a urea breath test or fecal antigen test. Therefore, the first step in this patient is to perform a urea breath test. Repeat EGD is not necessary for documenting healing of duodenal ulcers. *H. pylori* antibodies will be positive for 1 to 3 years after successful eradication and therefore not useful at this time as a proof of eradication. Imaging studies should be performed if *H. pylori* test is negative to investigate the possibility that symptoms may be due to a different cause.

**Question 50**

A 38-year-old man (body mass index = 26) who has a history of hypertension, controlled with hydrochlorothiazide, and acid reflux for 2 years. His reflux symptoms had been well controlled for more than a year on lansoprazole 40 mg once daily. However, his symptoms have not been well controlled over the last 3 months. He denies changing to any new brand of medicine or changes in the dose of hydrochlorothiazide. He smokes one to two cigarettes every 2 days, which is improved from his previous habit of smoking half a pack per day. He had an EGD 1 month ago that revealed normal findings. Vital signs, examination, and labs are normal. What is the most likely cause of the recurrent symptoms?

a) Not taking medications at the right time  
b) Continuing to smoke  
c) Taking other medications simultaneously  
d) Need to reduce his weight  
e) PPI tachyphylaxis

**Answer and Discussion**

The answer is a.

**Objective:** Understand mechanism of PPI effect loss.

The PPIs are the most potent inhibitors of gastric acid secretion available. The most common cause of PPI loss of effect is not taking medicines at the right time. They are most effective when the parietal cell is stimulated to secrete acid postprandially, a relationship that has important clinical implications for timing of administration. Because the amount of H-K-ATPase present in the parietal cell is greatest after a prolonged fast, PPIs should be administered before the first meal of the day. In most individuals, once-daily dosing is sufficient to produce the desired level of acid inhibition, and a second dose, which is occasionally necessary, should be administered before the evening meal. PPIs should not be given concomitantly with H₂-antagonists, prostaglandins, or other antisecretory agents because of the marked reduction in their acid inhibitory effects when administered simultaneously.

**Question 51**

A 44-year-old man complains of heartburn for 4 months, particularly after eating pizza. He has tried over-the-counter omeprazole with only partial benefit. One month ago, he started taking pantoprazole 40 mg twice daily. His symptoms improved partially. An EGD reveals no abnormal findings. Vital signs, examination, and labs are normal. What should be the next step in the management of this patient?

a) Reassurance  
b) Ambulatory pH monitoring after stopping PPIs for 2 weeks  
c) Repeat EGD in 6 weeks  
d) Referral to surgeon  
e) Referral for behavioral therapy

**Answer and Discussion**

The answer is b.

**Objective:** Diagnose reflux in the setting of PPI treatment failure.

Even though the patient has partial response to PPIs, recurrent symptoms in the setting of normal EGD mean that other diagnoses should be entertained. The first step is to perform pH monitoring off PPIs to document acid reflux. If there is no documented reflux, other diagnoses should be pursued. Other options are not appropriate at this time.

**Question 52**

A 60-year-old previously healthy man presents with sudden-onset upper abdominal pain radiating to the back that is associated with nausea and vomiting. He denies similar previous symptoms.

Vital signs: pulse = 92 beats/minute, temperature = 99°F, respiratory rate = 20, blood pressure = 110/70

Abdominal examination: not distended, tenderness in the upper abdomen, no rebound, bowel sound normal.
Pertinent labs:

- WBC = 17,000/µL
- Amylase = 2,000 U/L
- Lipase = 2,000 U/L
- Bilirubin = 3.1 mg/dL
- Rest of the labs are normal.
- KUB is normal.

A diagnosis of acute pancreatitis is made, and the patient is scheduled to be transferred to the medical floor. You contemplate performing a CT scan to evaluate his pancreas. At what point should you perform the CT scan?

a) Only if the clinical situation worsens
b) In the emergency room
c) On the same day of admission
d) Within 48 hours of admission
e) No need for a CT scan, an abdominal ultrasound scan is a better test to visualize the pancreas

**Answer and Discussion**

**The answer is a.**

**Objective: Recognize the need and timing for imaging in acute pancreatitis.**

There is no need to get a CT scan for every patient with acute pancreatitis if the diagnosis is straightforward, as in this patient, unless the clinical condition deteriorates.

Most patients with acute pancreatitis do not require a CT scan at admission or at any time during the hospitalization. A reasonable indication for a contrast-enhanced CT scan 72 hours after admission is to distinguish interstitial from necrotizing pancreatitis when there is clinical evidence of increased severity. An ultrasound should be done on admission in patients with acute pancreatitis to look for the evidence of gallbladder disease/gallstones.

### Question 53

A 52-year-old man underwent screening colonoscopy for colorectal cancer. He does not have any family members with colon cancer or polyps. During colonoscopy, an 8-mm polyp was noted in the ascending colon and was excised. The biopsy showed sessile-serrated polyp. Another polyp was seen in the descending colon measuring 6 mm, and the biopsy showed tubular adenoma. What type of surveillance is advised for this person?

a) Repeat colonoscopy in 6 months to document completion polypectomy
b) Repeat colonoscopy in 1 year
c) Repeat colonoscopy in 3 years
d) Repeat colonoscopy in 5 years
e) Repeat colonoscopy in 10 years

**Answer and Discussion**

**The answer is d.**

**Objective: Identify appropriate post-polypectomy colon cancer surveillance.**

Surveillance colonoscopy should be performed in 3 years if there are more than or equal to three polyps with tubular adenoma histology or ≥10 mm in size. Patients with a small sessile-serrated polyp (<10 mm) with no dysplasia should have repeat colonoscopy in 5 years. Patients with a sessile-serrated polyp ≥10 mm, a sessile-serrated polyp with dysplasia, or a traditional serrated adenoma should undergo repeat colonoscopy in 3 years. Serrated polyposis syndrome should be followed at 1 year, though subsequent examinations that identify a decreasing polyp burden can be followed by expanded intervals. Small hyperplastic polyps do not carry increased colon cancer risk and require average-risk screening (every 10 years).

### Question 54

A 22-year-old male university athlete is seen in the clinic for chronic abdominal pain that gets worse postprandially. He also feels that he is losing his stamina and cannot run like he used to about 6 months ago. He complains of occasional diarrhea but no blood in stools. He denies any vomiting.

**Vital signs:** normal

**Examination:** pale, thin built

**Heart/lungs:** normal

**Abdomen:** soft, mild tenderness in the right lower quadrant, no rebound, bowel sound slightly increased

**Labs:**

- Hgb = 6.5 g/dL
- WBC = 6,500/µL
- Platelets = 330,000/µL

**Basic metabolic panel:** normal

**Stool cultures:** negative

The stool was guaiac positive.

A colonoscopy was performed and showed normal colon up to ascending colon but ulcers in the cecum and terminal ileum. What is the most likely diagnosis?

a) CD of the small bowel
b) CD of the small and large bowel
c) UC with backwash ileitis
d) *Yersinia* colitis
e) Ischemic colitis

**Answer and Discussion**

**The answer is b.**

**Objective: Identify the clinical presentation of CD compared with UC.**

The clinical scenario is classical for CD involving the small and large bowel. CD is a disorder of uncertain etiology that is characterized by transmural inflammation of the GI tract. CD may involve the entire GI tract from the mouth to the perianal area. Approximately 80% of patients have small bowel involvement, usually in the distal ileum, with one-third of patients having ileitis exclusively; approximately 50% of patients have ileocolitis; and approximately 20% of patients have colon-limited disease. The clinical manifestations of CD are more variable than those of UC. Patients can have symptoms for many years prior to diagnosis. Fatigue,
prolonged diarrhea with abdominal pain, weight loss, and fever, with or without gross bleeding, are the hallmarks of CD. Although stools frequently reveal the presence of microscopic levels of blood (e.g., positive guaiac or immunochemical test), gross bleeding is less frequent than in UC.

UC is unlikely in the setting of a normal-looking colon all the way up to ascending colon. In the absence of negative workup for infections and a catastrophic event precipitating ischemia, infectious and ischemic causes are less likely.

**Question 55**

A 28-year-old woman presents to your office with increasing jaundice, mild nausea, fatigue, and dark-colored urine. She presented with similar symptoms 2 to 3 months ago when she was discovered to have an ALT of 1,400 U/L, serum bilirubin of 9 mg/dL, and positive IgM anti-hepatitis A virus 4 weeks after returning from a 1-month visit to Jordan and Syria. She fully recovered from this episode without complications. Laboratory studies approximately 1 month ago showed an ALT of 48 U/L and a serum bilirubin of 1.8 mg/dL. The patient is currently 23 weeks pregnant with her first pregnancy. She has no other significant past medical history, and her only medications are prenatal vitamins. She is married and currently studying archeology at the local university. Today she appears jaundiced and tired. Vital signs are as follows: temperature = 38.1°C, pulse = 90 beats/minute, respiration rate = 20/minute, and blood pressure = 100/60 mmHg. Sclerae are icteric. Lungs are clear. Heart tones are normal. Liver is not palpable, and there is no abdominal tenderness. Uterus is gravid and of appropriate size. Hepatitis B and C serologies are negative for acute or chronic infection. Antinuclear antibody is negative. Laboratory studies are performed and shown:

Na: 143 mmol/L  
K: 4.2 mmol/L  
Cl: 98 mmol/L  
HCO3: 27 mmol/L  
BUN: 28 mg/dL  
Cr: 0.9 mg/dL  
WBC: 7.1/µL  
Hgb: 12.8 mg/dL  
Platelets: 183,000/µL  
PT/INR: 0.9  
AST: 296 U/L  
ALT: 420 U/L  
TBili: 7.0 mg/dL  
Alkaline phosphatase: 85 U/L

Which of the following is the most likely diagnosis at this time?

a) Relapsing hepatitis A  
b) Fatty liver of pregnancy  
c) Autoimmune hepatitis  
d) HELLP (microangiopathic hemolysis, elevated liver enzymes, and low platelets) syndrome  
e) Acute cholecystitis

**Answer and Discussion**

The answer is a.

**Objective: Identify the etiology of elevated liver function tests in pregnancy.**

The temporal relationship, along with the clinical and laboratory features, is entirely consistent with relapsing hepatitis A. The antinuclear antibody is negative, making autoimmune hepatitis improbable. The complete blood cell count is normal, which excludes HELLP syndrome. The most common clinical presentation of HELLP is abdominal pain and tenderness in the midepigastrium, or right upper quadrant. Hypertension (blood pressure ≥ 140/90) and proteinuria are present in approximately 85% of cases, but it is important to remember that either or both may be absent in women with otherwise severe HELLP syndrome. In this patient, the abdomen is benign on examination, which makes acute cholecystitis unlikely. Although fatty liver of pregnancy can present like this, the prior history of hepatitis A makes this diagnosis less likely as well. Relapsing hepatitis A is a self-limited entity and has a good overall prognosis. Acute viral hepatitis can complicate pregnancy. The course of hepatitis A, B, and C is similar to that of nonpregnant patients. By contrast, hepatitis E is more severe during pregnancy. Several other viral infections have been reported in pregnancy.

**Question 56**

A 45-year-old man presents to the emergency department with nausea, vomiting, abdominal pain, and jaundice. There is no history of fever. The symptoms began earlier in the week and have become progressive. His past medical history is unremarkable, and he does not see a physician with any regularity. He is not taking any medications currently. He was diagnosed with hypertension over 10 years ago but did not follow up or adhere to prescribed medications at that time. He does not smoke, but he does report consuming a fifth of vodka per day for the past 15 years. His last drink was yesterday afternoon. In general, he appears older than his stated age and uncomfortable. His vital signs are as follows: temperature = 38.0°C, pulse = 104 beats/minute, respiration rate = 23/minute, and blood pressure = 139/89 mmHg. Sclerae are icteric, and dentition is poor. The neck is supple without jugular venous distention (JVD), adenopathy, or bruits. Lungs are clear to auscultation. Heart tones are normal but tachycardic. The abdomen is protuberant. The liver is enlarged and tender to palpation. Spleen tip is not felt, and there are no peritoneal signs. There is 1+ peripheral edema. Skin examination reveals spider angiomas scattered across the chest. On neurologic examination, he is awake and alert. There are no tremors, and asterixis is not present. The rest of the neurologic examination is nonfocal. Laboratory studies are as follows:

Na: 133 mmol/L  
K: 4.5 mmol/L  
Cl: 96 mmol/L
HCO₃: 23 mmol/L
BUN: 45 mg/dL
Cr: 2.1 mg/dL
WBC: 11.2/µL
Hgb: 10.3 g/dL

In addition to vitamin B₁₂, thiamine, and intravenous hydration with dextrose, which of the following is the most appropriate pharmacotherapy at this time?

a) Vitamin K 5 mg daily
b) Prednisone 30 mg daily
c) Metoprolol 25 mg BID
d) Lorazepam 2 mg QID
e) Norfloxacin 500 mg daily

Answer and Discussion

The answer is a.

Objective: Identify the appropriate management of alcoholic hepatitis.

This patient has a Maddrey discriminant function <32 and no hepatic encephalopathy and, therefore, does not meet the criteria for severe alcoholic hepatitis. Therefore, steroid therapy is not indicated for this patient. This patient should be monitored for signs of alcohol withdrawal, but he does not currently need benzodiazepines. There is no documentation of ascites or low ascitic protein to warrant spontaneous bacterial peritonitis prophylaxis with norfloxacin. Similarly, there is no documentation of esophageal or gastric varices to justify β-blockers at this time. The elevated creatinine and nausea suggest that the patient is dehydrated and may be vitamin K deficient. Vitamin K administration would also help determine whether prolongation of the prothrombin time is due to intrinsic liver disease or vitamin K deficiency.

His fractional excretion of sodium is <1%.

Which of the following is the most likely explanation of his worsening renal function?

a) Acute tubular necrosis
b) Contrast nephropathy
c) Hepatorenal syndrome
d) Interstitial nephritis
e) Immune complex–mediated glomerulonephritis

Answer and Discussion

The answer is c.

Objective: Recognize causes of acute renal injury in advanced cirrhosis.

The development of acute renal failure in advanced cirrhotic liver disease, severe alcoholic hepatitis, metastatic tumor, or fulminant hepatic failure from any cause is called hepatorenal syndrome. In patients with cirrhosis and ascites, the hepatorenal syndrome has been shown to occur in around 19% of patients at 1 year and in 39% of patients at 5 years. It is characterized by oliguria, benign urine sediment, a very low fractional excretion of sodium, and a progressive rise in the plasma creatinine concentration. Onset is typically insidious, but it can be acute following an insult, such as GI bleeding, infection, or rapid diuresis. Patients with hyponatremia or those with hyperreninemia or preexisting renal failure are at high risk for hepatorenal syndrome. Strangely enough, patients with primary biliary cirrhosis are comparatively protected against the development of the hepatorenal syndrome. The best treatment is an improvement in hepatic function due to improvement of the primary disease or due to successful liver transplantation. Growing data suggest that combination therapy with midodrine and octreotide may be effective.
Coronary Artery Disease

Michael D. Faulx

POINTS TO REMEMBER

- Coronary artery disease (CAD)–related mortality is decreasing in the United States but it nonetheless remains the principal cause of death in American adults.
- The worldwide prevalence of CAD and its risk factors is increasing.
- Most major CAD risk factors (diabetes, high blood pressure, cigarette smoking, and hyperlipidemia) are reversible, treatable, or preventable.
- Coronary artery atherosclerosis is a diffuse multisystem process that produces the vulnerable and fibrotic subendothelial atheromatous plaques that cause acute coronary syndromes and stable angina, respectively.
- The clinical history provides the foundation for the diagnosis of CAD.
- Angina, or chest pain secondary to myocardial ischemia, is the most commonly reported symptom in CAD. It is frequently described as pressure-like, squeezing, or heavy, although an inability to adequately describe the sensation is also suggestive of angina. Angina tends to localize to the mid-chest over a broad area and it commonly radiates to the neck, jaw, or arms. Associated symptoms such as diaphoresis or dyspnea are common.
- Chest pain that is fleeting (seconds in duration) or unremitting for hours is seldom due to angina.
- It is important for clinicians to try to characterize chest pain as typical for angina, atypical for angina, or nonanginal chest pain.
- Certain groups of patients are more likely to present with atypical angina symptoms, including women, the elderly, and diabetics.
- ECG findings suggestive of the presence of CAD:
  - Pathologic Q waves in two contiguous leads suggest the presence of a prior myocardial infarction.
  - Horizontal or downsloping ST segment depression suggests subendocardial ischemia, although ST depression does not localize the culprit vessel well.
  - Deep, symmetrical T-wave inversion is a more specific indicator of myocardial ischemia in a particular arterial territory.
  - Horizontal or concave ST segment elevation suggests acute myocardial injury and infarction.
  - A left bundle branch block pattern can indicate either myocardial infarction or the presence of underlying structural heart disease and it should not be considered a “normal variant.”
- Functional, noninvasive testing for myocardial ischemia (stress testing) is most appropriate for patients at intermediate risk for CAD.
- Fundamental questions to ask when considering a noninvasive evaluation for myocardial ischemia are “Can my patient exercise?” (Exercise testing should be ordered if patient can exercise), “Does my patient have a normal resting ECG?” (If “yes,” consider treadmill ECG testing), and “Does my patient have any comorbid conditions that would favor the use of one modality over another?” (e.g., heart murmur needed investigation; consider stress echo).
- Coronary angiography remains the gold standard for the diagnosis of obstructive CAD but adjunctive invasive coronary imaging with modalities such as intravascular ultrasound are playing an increasing role in the diagnosis and management of CAD.
- Lumen stenosis of ≥70% is generally considered to be significant and worthy of revascularization in the context of convincing symptoms or noninvasive findings.
- Optimized evidence-based medical therapy (OEBMT) improves both symptoms and outcomes in most patients with CAD.
Antianginal therapy
- First line: nitrates, β-blockers, calcium channel antagonists
- β-Blockers confer survival benefit in patients with a history of myocardial infarction or left ventricular systolic dysfunction
- Secondary prevention therapy
- Aspirin, 3-hydroxy-3-methyl-glutaryl-CoA reductase inhibitors ("statins"), angiotensin-converting enzyme inhibitors
- Coronary revascularization is indicated when angina persists despite appropriate OEBMT or when the patient has high-risk clinical or imaging features that suggest a survival benefit with revascularization.
- The most appropriate mode of revascularization varies from patient to patient; in general percutaneous revascularization offers lower procedural morbidity and stroke risk than surgical revascularization, whereas surgical revascularization offers greater freedom from repeat revascularization.

SUGGESTED READINGS

POINTS TO REMEMBER

- The initial interpretive step for each electrocardiogram (ECG) is to identify atrial activity and determine the cardiac rhythm.
- A varying PR interval supports the possibilities of atrioventricular dissociation of differing types of heart block, both requiring further detailed analysis.
- If >120 msec, a careful assessment of the QRS complex morphology is important, as complete left or right bundle-branch block may exist. Complete left bundle-branch block represents a QRS complex duration >120 msec, the absence of a Q wave (septal depolarization) in leads I and V_{5-6}, an upright QRS complex in leads I and V_{5-6}, and ST segment depression and T-wave inversion in leads I and V_{5-6}.
- To successfully interpret ECGs, a deliberate, consistent, and reproducible approach is essential. Through experience and repetition, the interpreter will demonstrate improved interpretive abilities and confidence, rendering greater diagnostic accuracy.
POINTS TO REMEMBER

- The heart comprises four valves, two atrioventricular valves (mitral on the left and tricuspid on the right) and two semilunar valves (aortic on the left and pulmonary on the right). Valvular heart disease may cause problems when the valve becomes stenotic; when it is regurgitant; or, as frequently occurs, a combined stenotic and regurgitant lesion is present.
- Stenotic lesions produce problems by reducing cardiac output, particularly during stress, and by increasing the pressure in the chambers proximal to the valve.
- Regurgitant lesions cause problems by increasing the volume load on the ventricles.
- While history and physical examination will often identify the lesion in question, an electrocardiogram and chest x-ray provide supportive information.
- Physical exam: a few key points
  - Blood pressure: A narrow pulse pressure (i.e., difference between systolic and diastolic blood pressure) may be related to aortic stenosis while a wide pulse pressure with low diastolic pressure may be secondary to aortic regurgitation.
  - Venous pressure: Venous pressure height and wave pattern should be assessed. Valvular disease is characterized by large A waves in pulmonary hypertension and pulmonary stenosis and large V waves in tricuspid regurgitation.
  - An anacrotic pulse with diminished volume and delayed upstroke (pulsum parvus et tardus). This is the most reliable physical sign of significant aortic stenosis. The pulse is best examined at the carotid artery.
  - Respiration: Right-sided lesions increase in intensity with inspiration (due to increased flow through the right heart). Left-sided lesions are louder with expiration.
  - Valsalva: The Valsalva maneuver decreases intracardiac volume and reduces the intensity of most murmurs. Exceptions are the murmurs of hypertrophic cardiomyopathy, which become louder, and of mitral valve prolapse, which become longer and louder.
  - Position: With standing, intracardiac volume decreases; therefore, most murmurs decrease in intensity (except those of hypertrophic cardiomyopathy and mitral valve prolapse). Squatting accentuates intracardiac volume. Therefore, most murmurs become louder, but those of mitral valve prolapse and hypertrophic cardiomyopathy usually decrease.
  - The severity of the lesion often relates to the loudness of the murmur in systolic murmurs (e.g., aortic stenosis and mitral regurgitation). The severity of diastolic murmurs relates more to the duration of the murmur than to intensity.
  - Echocardiography provides information on the mechanism and severity of the lesion and identifies concomitant pathology and is therefore the most important test currently used for the diagnosis of valvular heart disease. The advent of three-dimensional echocardiography has improved the ability to clearly visualize the lesion in question and is particularly useful when measuring the stenotic mitral orifice area and chamber volumes.
  - Cardiac catheterization is less frequently used but may play a role in clarifying the severity of the pathology if there is a discrepancy in other findings. Cardiac magnetic resonance imaging increasingly plays an adjunctive role.
  - The general principles for treating patients with valvular heart disease are as follows:
    - Assess the severity of symptoms.
    - Determine the nature of the valvular lesion and its severity.
    - Assess the effects of the lesion on ventricular function.
    - Assess for nonvalvular cardiac (or other) pathologies.
  - In general, symptoms of left ventricular systolic dysfunction/dilation are indications for definitive management. Traditionally, surgical valve replacement has been the treatment of choice and remains an effective and safe therapy; however, certain lesions are increasingly amenable to percutaneous therapy. Balloon valvuloplasty is the treatment of choice for select patients with mitral stenosis. For severe aortic stenosis, transcatheter aortic valve replacement is a reasonable alternative in select patients who are ineligible or are at high risk for surgical valvular replacement.
The AHA guidelines recommend that prophylaxis should be used only in patients with underlying cardiac conditions associated with the highest adverse outcome from infective endocarditis. These conditions include prothetic heart valves, previous infective endocarditis, certain classes of congenital heart disease, and in valvulopathy occurring postcardiac transplantation.

SUGGESTED READINGS


POINTS TO REMEMBER

- The most common mechanism of tachyarrhythmias is reentry. Examples include atrial flutter, supraventricular tachycardias (SVTs) due to atrioventricular (AV) nodal reentry or reentrant circuits involving an accessory pathway, and ventricular tachycardia (VT) associated with ischemic cardiomyopathy after myocardial infarction.
- In narrow QRS complex tachycardias, activation of the ventricles occurs via the His-Purkinje system, and the relationship of the QRS complex and P waves can be important in establishing the type of SVT.
- Vagal maneuvers and adenosine can terminate supraventricular arrhythmias resulting from reentry involving the atrioventricular or sinus node, or it can allow the demonstration of atrial flutter waves, atrial tachycardia, or atrial fibrillation (AF).
- The diagnosis of wide complex tachycardia (WCT) often can be established on the basis of clinical presentation, physical examination, electrocardiogram findings, and provocative maneuvers.
- Algorithms using QRS morphology (i.e., the Brugada criteria) and presence of AV dissociation can help differentiate VT from SVT with aberrancy.
- As a general rule, however, treat as a VT when in doubt, particularly in patients with structural heart disease.
- It is important that intravenous verapamil not be used to treat WCT—hemodynamic collapse and death have been reported, regardless of the cause of the WCT.
- AF, the most common sustained arrhythmia, can occur in the absence of structural heart disease, but more commonly occurs with older age, hypertension, diabetes mellitus, and structural heart disease, including coronary and valvular disease, and congestive heart failure.
- AF is associated with higher risk for thromboembolic complications, including stroke.
- Addressing and treating risk for stroke, controlling ventricular rate and atrial rhythm are key components of treatment for AF.
- In general, implantable cardioverter-defibrillator (ICD) implantation is justified for patients with nonischemic or ischemic cardiomyopathy, left ventricular ejection fraction (LVEF) ≤35%, and NYHA FC II or greater heart failure symptoms.
- ICD implantation after a myocardial infarction (MI): ICD implantation for primary prevention of sudden cardiac death usually should be deferred until 40 days after MI, after which time ICDs are indicated for patients with LVEF ≤35%.
- In the presence of acute MI, temporary pacing via a temporary transvenous pacing lead, or with backup transcutaneous pacing patches, is indicated for:
  - Third-degree atrioventricular block
  - Second-degree atrioventricular block
  - Mobitz II with anterior MI
  - Mobitz II with inferior MI and wide QRS complex or recurrent block with narrow QRS complex
  - Mobitz I with marked bradycardia and symptoms
- Atrioventricular block associated with marked bradycardia and symptoms (e.g., hypotension, heart failure, low cardiac output)
- Bundle-branch block (BBB)
  - New bifascicular block
  - Alternating BB
  - New BBB with anterior MI
  - Bilateral BBB of indeterminate age with anterior or indeterminate MI
  - Bilateral BBB with first-degree atrioventricular block

SUGGESTED READING

Atrial Fibrillation Follow-Up Investigation of Rhythm Management (AFFIRM) Investigators. A comparison of rate control and


POINTS TO REMEMBER

- There are two populations of adult congenital patients: those who have been managed and followed throughout their pediatric years, and those who present de novo (previously unrecognized adults who may or may not be symptomatic at the time of diagnosis).
- The congenital diseases commonly encountered in adults are atrial septal defect (ASD), ventricular septal defect (VSD), and patent ductus arteriosus (PDA) (shunt lesions); coarctation of the aorta and pulmonary stenosis (PS) (obstructive lesions); and tetralogy of Fallot (TOF), transposition of the great arteries, and Ebstein anomaly (complex lesions).
- ASD:
  - If congenitally bicuspid aortic valve and mitral valve prolapse are excluded, ASD is the most common form of congenital heart disease in adults, constituting approximately 25% of these patients.
  - Some 65% to 75% of ASDs are ostium secundum type and represent true defects of the atrial septum in the region of the fossa ovalis.
  - A wide, fixed-split S2 is the hallmark auscultatory feature of ASD.
  - Because of the reduced life expectancy of patients with uncorrected ASDs, those who have a significant shunt, classically defined as a pulmonary blood flow to systemic flow (Qp:Qs) shunt fraction $>1.5$ to 1, symptoms, or evidence of right heart enlargement should be offered repair.
- VSD:
  - VSDs are frequently found in conjunction with other cardiac anomalies, including coarctation of the aorta and PDA.
  - The majority (~70%) of VSDs are located in the membranous septum, approximately 20% in the muscular portion of the trabecular septum (muscular VSD), about 5% in the infundibular septum beneath the pulmonary valve (subpulmonary VSD), and about 5% in the inlet septum near the tricuspid valve (atrioventricular canal-type VSD).
- The size of the VSD, ventricular pressure, and pulmonary vascular resistance are determinants of hemodynamic significance. If the pulmonary hypertension is severe enough, this can result in reversal of flow, leading to right-to-left shunt and cyanosis (Eisenmenger’s syndrome).
- The classic auscultatory finding in a VSD is a holosystolic murmur, the intensity of which depends on the velocity of flow.
- Indications for VSD repair include a significant left-to-right shunt (Qp:Qs $>2$) with evidence of left ventricular volume overload, or a history of endocarditis.
- A contraindication for VSD repair is severe irreversible pulmonary arterial hypertension.
- PDA:
  - The ductus arteriosus is a fetal structure connecting the proximal descending aorta just distal to the left subclavian artery to the distal main pulmonary artery.
  - Like ASDs and VSDs, PDA is a shunt lesion that results in left-to-right flow.
  - Some adults with PDA will develop signs of congestive heart failure from chronic left-to-right shunting.
  - The classic auscultatory feature of PDA is the harsh continuous murmur at the left upper sternal border. This murmur involves S2 and is decreased in intensity during diastole.
  - In general, closure of the PDA is recommended for all patients with left atrial and/or left ventricular enlargement, net left-to-right shunting across the PDA, pulmonary vascular disease, or a history of endarteritis.
  - A contraindication to PDA closure is severe pulmonary hypertension that results in right-to-left shunting across the PDA.
  - If the PDA is amenable, transcatheter closure using a coil or an Amplatzer ductal occluder (AGA Medical, Golden Valley, MN) is the treatment of choice for adults, with surgery being reserved for very large PDAs.
- Coarctation of the aorta:
  - Aortic coarctation usually presents as a discrete narrowing in the thoracic aorta in the region of the ligamentum arteriosum.
Associated lesions include bicuspid aortic valve in up to 50% of cases, intracranial aneurysms in 10%, and less commonly VSDs.

Young adults classically present upper extremity hypertension with diminished or delayed femoral pulses. Any young patient with hypertension should be evaluated clinically for coarctation by simultaneous palpation of the brachial and femoral pulses to assess for “brachial-femoral delay,” as well as by comparing blood pressures in the right and left upper extremity and one lower extremity.

The classic finding on chest radiography is the “3,” or “reverse E” sign, representing a dilated left subclavian artery above the coarctation and poststenotic aortic dilatation beyond the coarctation.

Untreated patients with aortic coarctation have poor survival, with an estimated mortality of 75% by 46 years of age and median age of death being only 31 years.

Stent implantation for coarctation became a treatment option in the early 1990s and is preferred in adults and adult-size adolescents.

TOF:

- TOF is characterized by pulmonic stenosis, overriding aorta, interventricular communication, and right ventricular hypertrophy, with considerable variability in morphology.
- Adult TOF patients will likely present after primary repair. The repaired patient will no longer be cyanotic but can present with a host of other problems that require lifelong follow-up, including pulmonic insufficiency, ventricular tachycardia, atrial arrhythmias, right heart failure, and ascending aortic dilatation.

SUGGESTED READINGS


POINTS TO REMEMBER

- Acute coronary syndromes (ACSs) represent a spectrum of ischemic heart events that share a common pathophysiology and encompass the following entities: unstable angina, non–ST elevation myocardial infarction (NSTEMI), and ST elevation myocardial infarction (STEMI).
- ACS usually is caused by an unstable atheromatous plaque that fissures or ruptures in an epicardial coronary artery, which results in the formation of a superimposed platelet and fibrin thrombus.
- Unstable plaques associated with ACS are most often lipid-rich, atheromatous lesions with a thin fibrous cap and increased macrophage infiltration, whereas stable plaques causing chronic stable angina generally possess a thick fibrous cap and less lipid core and inflammatory burden.
- Most coronary artery unstable plaques leading to ACS were not flow-limiting prior to fissuring or rupture (70% of these plaques have <50% angiographic stenosis).
- The differential diagnosis of chest pain encompasses multiple other conditions, some of which can be life-threatening. Aortic dissection and pulmonary embolism are particularly important to consider and diagnose in a timely manner.
- Aortic dissection is abrupt in onset, perceived as “ripping” chest, interscapular, or lower back pain. Patients often have a history of hypertension and manifest pulse deficits and a widened mediastinum on the chest radiograph.
- When seeing patients with chest discomfort it is helpful to assign patients into one of four categories: a noncardiac diagnosis, chronic stable angina, possible ACS, and definite ACS.
- The diagnosis of a STEMI can be made on the basis of electrocardiogram criteria, including ST segment elevation >1 mm in at least two contiguous leads. Reciprocal ST segment depression is an associated and helpful finding that makes the possibility of acute pericarditis mimicking acute STEMI less likely.
- Serial testing of serum cardiac enzyme levels should be performed routinely in patients with a suspected ACS.
- Troponins T and I are components of the cardiac myocyte contractile apparatus and are highly specific for a cardiac origin. They are also highly sensitive for the detection of myocardial necrosis and are available in rapid assay forms. Troponins begin to rise 3 hours after onset of chest pain and last longer in the circulation (7 to 14 days) than creatine kinase (CK).
- Medical therapy for ACS:
  - Oxygen for hypoxic patients.
  - All patients with ACS should receive dual antiplatelet therapy (aspirin and an oral P2Y12 receptor inhibitor).
  - Glycoprotein IIb/IIIa receptor inhibitors can be used as adjunct therapy in patients with STEMI or non–ST segment elevation ACS undergoing percutaneous coronary intervention (PCI) and for all patients undergoing high-risk PCI.
  - Anticoagulants should be used in patients presenting with ACS (duration and type of agent vary with patient characteristics and practice preferences).
  - In general, β-blockers should be administered as early as possible after ACS.
  - Early in the course of an acute myocardial infarction (MI), administration of an ACE inhibitor is associated with reduced mortality.
  - Early use of high-dose hydroxymethylglutaryl–coenzyme A (HMG-CoA) reductase inhibitors (“statins”).
  - The mainstay of treatment for acute STEMI is immediate reperfusion therapy based on the observation that myocardial necrosis occurs as a wave front over 4 to 6 hours after coronary artery occlusion.
  - Indications for fibrinolytic therapy in patients with acute MI include ST segment elevation in two or more contiguous leads or new (or presumably new) left bundle-branch block, with ischemic symptoms <12 hours in duration.
  - Randomized clinical trials have shown that primary PCI for STEMI (PCI as the primary means of reperfusion used instead of fibrinolytic therapy) is associated with lower mortality compared with fibrinolytic therapy.

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mortality and reduced rates of intracranial hemorrhage compared with fibrinolytic therapy.

- Fibrinolytic therapy should be administered to patients with STEMI at non-PCI-capable hospitals when transfer time to a PCI-capable hospital will be >120 minutes.
- Atrial fibrillation is the most common sustained arrhythmia, occurring in approximately 10% of patients with acute MI.
- Early administration of β-blockers (in the absence of contraindications) has a favorable impact on the frequency of ventricular fibrillation and should be implemented routinely in patients with acute infarction devoid of advanced heart block, significant hypotension, or cardiogenic shock.

Acute mitral regurgitation, which usually occurs 2 to 7 days after an acute myocardial infarction (MI), is mostly associated with an inferior MI. It is an indication for prompt surgical repair, with an overall mortality ranging from 40% to 90%.

**SUGGESTED READINGS**


POINTS TO REMEMBER

- There is a strong, independent, continuous, and graded relation between total cholesterol (TC) and low-density lipoprotein cholesterol (LDL-C) level and risk of coronary events.
- Cholesterol screening:
  a. The NCEP Adult Treatment Panel III recommends that adults 20 years of age or older and without a history of coronary artery disease (CAD) or other atherosclerotic disease should have a fasting lipid panel [i.e., TC, LDL-C, high-density lipoprotein cholesterol (HDL-C), and triglycerides (TG)] every 5 years.
  b. The United States Preventive Services Task Force (USPSTF) recommends cholesterol screening starting at age 35 for men and 45 for women. You can screen patients starting at age 20 if they are at increased risk for coronary artery disease.
- The five traditional risk factors for CAD are as follows:
  a. Age (male >45, female >55)
  b. Tobacco use
  c. Hypertension
  d. HDL level <40
  e. Family history of premature CAD (male <55 and female <65)
- The treatment of hyperlipidemia requires two approaches: therapeutic lifestyle changes and medications.
- NCEP Adult Treatment Panel III Treatment goals for LDL
  a. LDL <100:
     i. CAD, atherosclerosis in noncoronary beds, diabetes, a calculated 10-year Framingham risk score >20%
     ii. An LDL goal of <70 is a “reasonable therapeutic option”
  b. LDL <130:
     i. Two or more traditional risk factors for CAD whose 10-year Framingham risk score falls between 10% and 20%
  c. LDL <160:
     i. Zero or one risk factor with a 10-year Framingham risk score <10%
- American College of Cardiology (ACC)/American Heart Association (AHA) Cholesterol Guideline 2013
  1. Focus Lipid Lowering Therapy to these 4 Groups
     a. Group 1: Patients with clinical atherosclerotic cardiovascular disease (ASCVD)
     b. Group 2: Patients age ≥21 years with LDL ≥190
     c. Group 3: Patients with Diabetes, with age 40-75, LDL 70-189
     d. Group 4: Patients aged 40-75, LDL 70-189 who are without ASCVD / DM but with coronary risk score of 10 yr ASCVD risk ≥7.5%
  2. Treatment - Focus has shifted from Target LDL levels to Dose intensity of a Statin Drug
     a. Group 1: ASCVD: HIGH INTENSITY STATIN
     b. Group 2: LDL > 190: HIGH INTENSITY STATIN
     c. Group 3: Diabetic with LDL 70-189, Age 40-75
        i. 10 year ASCVD risk < 7.5 %: MODERATE INTENSITY STATIN
        ii. 10 year ASCVD risk ≥ 7.5 : HIGH INTENSITY STATIN
     d. Group 4: 10 year ASCVD risk ≥ 7.5 % (in absence of DM / ASCVD): Moderate - high intensity statin
  3. Statins
     a. High Intensity Statins – atorvastatin 40mg-80mg, rosuvastatin 20mg-40mg
     b. Moderate Intensity Statins - atorvastatin 10mg-20mg, rosuvastatin 5mg-10mg, simvastatin 20mg-40mg, pravastatin 40mg-80mg
  4. The Risk Calculator can be accessed on-line through AHA and ACC websites
  5. Statins are the lipid-modifying drugs of choice
  6. Lifestyle modifications are still recommended for all patients

- The class of medications that have the strongest evidence of effectiveness are the 3-hydroxy-3-methylglutaryl coenzyme A reductase inhibitors (“statins”).
- Routine monitoring of liver function tests in patients on statins is no longer recommended. (A baseline measurement is recommended before starting therapy.)

SUGGESTED READINGS


Thompson PD, Clarkson FM, Rosenson RS. An assessment of statin safety by muscle experts. *Am J Cardiol.* 2006;97(8A):69C-76C.

Heart Failure

Sangjin Lee and Robert E. Hobbs

POINTS TO REMEMBER

- The most common cause of heart failure in the United States is end-stage coronary artery disease, accounting for more than half of cases.
- **Systolic heart failure** refers to contractile impairment manifested by low left ventricular ejection fraction (LVEF).
- **Diastolic heart failure**, also called heart failure with preserved ejection fraction occurs in the setting of preserved LVEF and is associated with abnormal left ventricular relaxation and filling, left ventricular hypertrophy, and elevated intracardiac pressures.
- Diastolic dysfunction occurs with hypertensive heart disease, ischemic heart disease, hypertrophic cardiomyopathy, restrictive cardiomyopathy (including infiltrative diseases), and aortic valve disease.
- High-output heart failure is rare. The causes of high-output heart failure include thyrotoxicosis, arteriovenous fistula, pregnancy, Paget’s disease, anemia, and beriberi.
- Jugular venous distension is the most important and sensitive physical exam finding in patients with decompensated failure, indicating fluid overload.
- The degree of functional impairment usually is stated in terms of the New York Heart Association classification:
  - **Class I** refers to no limitation of physical activity and no dyspnea or fatigue with ordinary physical activities.
  - **Class II** indicates mild limitation of physical activity and dyspnea or fatigue occurring with ordinary physical activities. The patient has no symptoms at rest.
  - **Class III** implies marked limitation of activity. Less than ordinary physical activities cause symptoms. The patient is asymptomatic at rest.
  - **Class IV** refers to symptoms at rest and with any physical exertion.
- The B-type natriuretic peptide (BNP) assay is a useful test for determining whether dyspnea is due to heart failure. Elevated levels of BNP in general correlate with the severity and prognosis of heart failure. BNP levels are not as reliable in the setting of chronic kidney disease.
- Echocardiography is the single most useful diagnostic test in heart failure.

Many therapies for heart failure attempt to modulate neurohormonal factors. Sympathetic nervous system excess may be modulated through the use of β-blockers and possibly digoxin. The renin–angiotensin system may be inhibited by angiotensin-converting enzyme inhibitors, angiotensin II receptor blockers, and aldosterone receptor antagonists.

Current indications for implantable cardiac defibrillator placement include survivors of a cardiac arrest, sustained ventricular tachycardia, unexplained syncope with inducible ventricular tachycardia, and dilated or ischemic cardiomyopathy with ejection fraction ≤35%.

SUGGESTED READINGS


KEY POINTS TO REMEMBER:

Cardiac Tamponade
- The most common cause of cardiac tamponade in developed countries is malignancy, whereas in developing countries, tuberculosis is still a common culprit.
- Characteristic physical signs of cardiac tamponade are pulsus paradoxus, increased jugular venous pressure (JVP), and low blood pressure.
- Additional findings that support tamponade include: absence of Kussmaul sign, pressure equalization of all heart chambers in diastole and prominent x descent (and absent or attenuated y descent) on venous waveform.
- Transthoracic echocardiogram (TTE) is the diagnostic test of choice in making the diagnosis of tamponade.
- Avoid diuretics and vasodilators when tamponade is suspected. Volume resuscitation and immediate drainage of pericardial effusion is essential treatment.

Papillary Muscle Rupture
- Occurs most commonly 1 to 7 days after an inferior MI
- Papillary muscle rupture is most serious cause of post-MI mitral regurgitation, which can be rapidly fatal.
- Acute pulmonary edema is the most common clinical presentation of papillary muscle rupture.
- A new holosystolic murmur may be an early clue in papillary muscle rupture.
- Echocardiography is the diagnostic imaging modality of choice for papillary muscle rupture.
- Immediate surgical repair can be lifesaving in these patients.

Free Wall Rupture
- Most commonly occurs 1 to 4 days after an anterior wall MI.
- More common in elderly women with hypertension with prior steroid use and nonsteroidal anti-inflammatory drugs.
- More common with first MI, late thrombolytic therapy and large transmural MI involving ≥20% of myocardium
- If suspected, anticoagulation should be stopped immediately and surgery is the only treatment option.

Left Ventricular Pseudoaneurysm
- A contained left ventricular (LV) free wall rupture is known as a pseudoaneurysm.
- Irrespective of size and symptoms, LV pseudoaneurysm harbors the risk of sudden death and rupture.
- Surgical repair is the definitive treatment for LV pseudoaneurysm.

Ventricular Septal Defect
- Most common 3 to 7 days after MI
- Equal incidence after anterior and inferior MI
- The clinical presentation of ventricular septal defect (VSD) can be acute pulmonary edema, biventricular failure, or shock.
- A new holosystolic murmur with thrill is the important physical sign of VSD.
- Color flow Doppler echocardiography and right heart catheterization with oxygen step-up are confirmatory tests.

Aortic Dissection
- Sharp or tearing chest pain radiating to the back in a hypertensive patient should alert the clinician to the possibility of aortic dissection.
- Aggressive blood pressure control is essential in both ascending and descending aortic dissection.
- Preferred diagnostic imaging modality depends on clinical scenario, but TEE and CT are the most important diagnostic tests in emergency situations
- Emergent surgery is needed for the best outcome after ascending aortic dissection, while conservative management with blood pressure control is preferred for descending aortic dissection.
- Stenting of the aortic dissection is emerging as a promising new therapy for some patients with aortic dissection.
SUGGESTED READINGS


Question 1
A 55-year-old woman smoker is seen in the emergency room (ER) complaining of several days of increasing facial fullness, orthopnea, and swelling in her neck and hands. Physical examination is notable for obvious facial swelling, with conjunctival edema, jugular venous distention, and symmetric swelling of both upper extremities. Fullness is present in both supraclavicular fossae, but there is no clear lymph node enlargement, and the lungs are clear. The patient is tachycardic, but no gallop, murmur, or rub is present. No hepatomegaly, ascites, or pedal edema is present. Chest radiography reveals a right hilar mass. The patient is admitted to the hospital at midnight, and you order which of the following?

a) An emergency upper extremity venogram  
b) An emergency computed tomography (CT) scan of the chest  
c) An emergency echocardiogram (ECHO)  
d) Diuretics and elevation of the head of the bed until the morning

Answer and Discussion
The answer is d.

Objective: Understand the urgent management of superior vena cava (SVC) syndrome.

All of these tests are used to identify the etiology of SVC syndrome. Malignancy is the most common cause of SVC syndrome and is suggested by this patient’s chest radiograph. Therefore, a CT scan should be the next test to determine both the etiology and further anatomic definition of the process. A thyroid scan helps identify a thyroid mass causing extrinsic compression, but would not present as a right hilar mass. An upper extremity venogram is helpful for intravascular obstruction, but would not give further definition of a mass.

Question 2
You see the previous patient the next morning. She feels better, although she remains quite edematous and cannot lie flat. You order the following test to determine the etiology of the patient’s SVC syndrome:

a) CT scan of the chest  
b) Thyroid scan  
c) Serologic test for syphilis  
d) Upper extremity venogram  
e) All of the above

Answer and Discussion
The answer is a.

Objective: Understand the appropriate diagnostic workup for SVC syndrome.

All of these tests are used to identify the etiology of SVC syndrome. Malignancy is the most common cause of SVC syndrome and is suggested by this patient’s chest radiograph. Therefore, a CT scan should be the next test to determine both the etiology and further anatomic definition of the process. A thyroid scan helps identify a thyroid mass causing extrinsic compression, but would not present as a right hilar mass. An upper extremity venogram is helpful for intravascular obstruction, but would not give further definition of a mass.

Question 3
You are called by the radiologist that afternoon with the results of the chest CT scan. This study reveals a large right hilar and a mediastinal mass, with evidence of compression of the SVC. Your response is which of the following?

a) Expeditiously proceed to bronchoscopy or mediastinoscopy to establish the tissue diagnosis  
b) Recognize the risk of invasive diagnostic procedures in patients with SVC syndrome and order sputum cytology  
c) Identify this as an incurable malignancy and refer the patient for urgent radiation therapy  
d) Identify this as an incurable malignancy and refer the patient for hospice care

Answer and Discussion
The answer is a.

Objective: Identify the most common etiology of SVC syndrome.

Invasive diagnostic procedures do not pose any increased risk in patients with SVC syndrome. Although the etiology is likely to be malignant, several of the potential malignant diagnoses are curable with appropriate treatment, and this treatment may include chemotherapy. Aggressive and expeditious attempts to establish a histologic diagnosis are indicated so that the most effective treatment can be initiated in an organized fashion.
Question 4

An 18-year-old, 58-kg female asthmatic patient is intubated in the emergency department for respiratory failure from status asthmaticus. You aggressively fluid resuscitate her. She is being treated with clarithromycin, ceftriaxone, Solu-Medrol, bronchodilators, and lorazepam and has been stable for 3 days. On day 3, she became agitated overnight and was given haloperidol. Suddenly, she became hypotensive, and her pulse was not palpable. The electrocardiogram (ECG) tracing is shown below.

The patient is still hypotensive, her white blood cell count is 15,000/mm³, and her hemoglobin is 10 g/dL. You will do all of the following, except

a) Perform cardioversion-defibrillation
b) Administer magnesium intravenously
c) Temporarily disconnect the patient from the ventilator circuit
d) Correct hypocalcemia, hypokalemia, and alkalosis

c) Exercise echocardiography
d) Dipyridamole-thallium imaging
e) echocardiography (ECHO)

Answer and Discussion

The answer is c.

Objective: Identify drug–drug interaction in the intensive care unit (ICU) setting.

This question highlights an important topic in critical care medicine–drug interactions. This scenario demonstrates the ability of drugs to lengthen the QT interval, thereby predisposing to torsades de pointes. Another important effect of drug interaction in the critically ill patient is hypotension caused by partial adrenal insufficiency. This drug interaction occurs in patients receiving drugs that can increase the activity of the P450 system (e.g., phenytoin, phenobarbital). When the P450 system is activated, the metabolism of steroids increases, creating a state of partial adrenal insufficiency. This drug interaction should be suspected in patients receiving medication that can increase the activity of the P450 system and in patients with persistent hypotension in the absence of other etiologies. An increasingly recognized offender is etomidate, a medication commonly used in rapid-sequence intubation, which blocks adrenal steroid production directly.

Macrolides and haloperidol, drugs commonly used in the ICU, are known to increase the QT interval. Patients with underlying ischemic heart disease and electrolyte and acid–base abnormalities are more likely to develop this complication. Phenothiazines, antiarrhythmic medications, tricyclic antidepressants, and antipsychotic agents and cisapride can prolong the QT interval as well.

Question 5

A 56-year-old woman with advanced arthritis of the right knee and a diagnosis of hypertension and hyperlipidemia has atypical chest pain with a normal ECG. The best diagnostic option is

a) Stress (exercise or dobutamine) ECG
b) Coronary angiography
c) Exercise echocardiography
d) Dipyridamole-thallium imaging
e) None of the above

Answer and Discussion

The answer is e.

Objective: Identify the optimal method of stress testing in the diagnosis of coronary artery disease (CAD).

This is a 56-year-old woman who is described as having advanced arthritis. Therefore, exercise stress will likely result in the patient being unable to exercise maximally or even at all. Because the patient is a female with atypical pain, she would be considered to have an intermediate pretest probability and therefore would be a good candidate for a stress-imaging study. Proceeding directly to coronary angiography with such a relatively low pretest probability would potentially subject the patient to an unnecessary invasive test.

Question 6

A 28-year-old woman with hypertension and diabetes presents with left-sided chest pain at rest and exercise. The best diagnostic option is

a) Exercise ECG
b) Coronary angiography
c) Exercise echocardiography
d) Exercise thallium imaging
e) None of the above

Answer and Discussion

The answer is e.

Objective: Identify the pretest probability of CAD and the subsequent level of evaluation required.

This patient has a very low pretest probability for having CAD (~4%) due to her age, gender, and the atypical nature of the pain. Because of this low pretest probability, the accuracy of a given test will not significantly affect the post-test probability of disease. It is only in those patients with an intermediate pretest likelihood of disease that the accuracy of the test will have a significant effect on post-test probability. Therefore, none of the choices provides the best diagnostic option, as that likely includes consideration of another etiology for the pain other than cardiac.
**Question 7**

A 68-year-old man presents with central retrosternal chest pain on exercise. The best diagnostic option is

a) Exercise ECG  
b) Coronary angiography  
c) Exercise echocardiography  
d) Exercise thallium imaging  
e) None of the above

**Answer and Discussion**

The answer is b.

**Objective:** Understand the identification of the pretest probability of CAD and the subsequent level of evaluation required.

This patient would have a high pretest probability of disease; therefore, coronary angiography would provide information on the site, the severity, and extent of the disease. Although an exercise electrocardiography study as well as an imaging study with echocardiography or thallium perfusion imaging would be useful in risk stratifying such a patient, the definitive test to detect disease in this patient with such a high pretest probability would be coronary angiography.

**Question 8**

A 48-year-old man with hypertensive left ventricular (LV) hypertrophy complains of atypical chest pain. The best diagnostic option is

a) Exercise ECG  
b) Coronary angiography  
c) Exercise echocardiography  
d) Dipyridamole-thallium imaging  
e) None of the above

**Answer and Discussion**

The answer is c.

**Objective:** Identifying the optimal method of stress testing in the diagnosis of CAD.

An exercise ECG stress test is likely to be nondiagnostic in patients with LV hypertrophy. As a result of the resting secondary ST-T wave repolarization changes characteristic of LV hypertrophy, a false-positive result is likely and may therefore inappropriately lead to further testing. A coronary angiogram would lead to undue risk from an invasive procedure, particularly in a 48-year-old man with atypical pain. A dipyridamole-thallium study is also limited by the potential of falsely positive perfusion defects that likely are secondary to subendocardial ischemia from abnormal coronary flow reserve. Subendocardial ischemia can occur in hypertrophied hearts despite the presence of normal epicardial vessels. Exercise echocardiography has been demonstrated to be more specific in this patient population, as the basis for this test is an assessment of LV function rather than perfusion, which can be affected by abnormalities in coronary flow reserve.

**Question 9**

A 52-year-old man needs a femoropopliteal bypass. What would you recommend first for risk stratification?

a) Exercise ECG  
b) Coronary angiography  
c) Dobutamine echocardiography  
d) Dipyridamole-thallium imaging  
e) Clinical evaluation

**Answer and Discussion**

The answer is e.

**Objective:** Identify the initial assessment for risk stratification and cardiac optimization prior to a vascular surgical procedure.

The initial risk stratification should include a clinical examination that initially is directed at determining the urgency of surgery, assessing risk, identifying the need for noninvasive testing in selected patients, and initiating measures to reduce operative risk in those at high risk. Those patients identified to have three or more revised cardiac index criteria (high-risk surgery, history of ischemic heart disease, history of cerebrovascular disease, insulin-dependent diabetes mellitus, or preoperative serum creatinine >2.0 mg/dL) and poor functional capacity (<4 METs) should undergo stress testing if it will change management.

**Question 10**

The following probably constitute significant CAD, except

a) Proximal left anterior descending (LAD) stenosis of 80%  
b) LAD stenosis of 60% with angina  
c) Right coronary artery stenosis of 50%  
d) Left circumflex coronary artery stenosis of 50% with a positive exercise ECG  
e) None of the above

**Answer and Discussion**

The answer is c.

**Objective:** Understand the definition of significant CAD.

Significant CAD is typically considered to be present with lesions >50% of the artery diameter. But coronary stenoses in the 50% range may or may not be functionally significant in terms of a reduction in coronary flow, as flow reduction is modulated by collateral vessels, location, and length of stenoses and related to bends and bifurcations as well as other variables. Coronary artery stenoses >90% have been demonstrated to restrict flow at rest without the provocation of stress. Therefore, in this question, a proximal LAD stenosis of 80% almost certainly is considered significant disease, and an LAD stenosis of 60% in the presence of typical angina pectoris also quite likely represents significant flow-limiting coronary disease. Finally, a left circumflex coronary stenosis of 50% with the presence of positive exercise ECG changes is likely to represent significant CAD, yet a right coronary stenosis of 50% in the absence of a functional test that is positive for ischemia or the presence of...
concomitant symptoms may represent the presence of significant stenosis.

**Question 11**
Which of the following patients has the greatest probability of CAD?

- a) A 48-year-old woman with atypical chest pain
- b) A 25-year-old man with typical angina
- c) A 45-year-old man with atypical chest pain
- d) A 70-year-old man with atypical chest pain

**Answer and Discussion**
The answer is d.

**Objective:** Identify the pretest probability of CAD.

Based on the Diamond and Forester estimate of pretest probability of disease, which is based on age, gender, and symptoms of chest pain, a 70-year-old man with atypical chest pain is likely to have a pretest probability of disease approximating 70%. Of note, the 25-year-old man with typical angina also would have a significant but slightly lower pretest probability of disease. A 45-year-old man with atypical chest pain would have a pretest probability of approximately 46%, whereas a woman of similar age with atypical symptoms would have a dramatically lower pretest probability of disease, estimated to be approximately 13% and reflecting the delayed onset of disease among the female population, which likely is related to the protective effect of estrogen prior to menopause.

**Question 12**
All of the following are indications for surgery in severe chronic mitral regurgitation (MR), except

- a) Shortness of breath on exertion
- b) LV ejection fraction (EF) of 45%
- c) Dilated left ventricle (end-systolic dimension of 5 cm)
- d) Frequent ventricular ectopy
- e) Recurrent atrial fibrillation

**Answer and Discussion**
The answer is d.

**Objective:** Identify the indications for surgery in the treatment of severe chronic MR.

In severe MR, repair/replacement is indicated with New York Heart Association (NYHA) class II–IV symptoms or in the absence of symptoms with decreased LV ejection fraction (LVEF) less than 60% or LV end-systolic dimension greater than 4 cm. Frequent ventricular ectopy is common and does not necessarily improve with surgery. It is not considered an indication for valve surgery in MR.

**Question 13**
Consider the following hemodynamic data: left atrial pressure, 25 mmHg; LV pressure, 120/10 mmHg; aortic pressure, 120/80 mmHg; and cardiac index, 1.9 L/minute/m². These are most consistent with which valvular lesion?

- a) Mitral stenosis (MS)
- b) MR
- c) Aortic stenosis
- d) Aortic regurgitation (AR)
- e) None of the above

**Answer and Discussion**
The answer is a.

**Objective:** Understand the relevant hemodynamic parameters associated with valvular heart disease.

High left atrial pressure with a pressure gradient across the mitral valve in diastole and a low cardiac output is consistent with a diagnosis of MS.

**Question 14**
Recognized complications of isolated MS include all of the following, except

- a) Atrial fibrillation
- b) Pulmonary hypertension
- c) Atrial thrombus
- d) Right heart failure
- e) LV enlargement

**Answer and Discussion**
The answer is e.

**Objective:** Understand the natural history and complications associated with MS.

Isolated MS does not cause LV enlargement; left ventricle size is normal or small due to reduced inflow to the left ventricle.

**Question 15**
The following statements concerning surgical correction of MR are correct, except

- a) Repair is most likely to be possible in rheumatic valves.
- b) Repair has a lower complication rate than prosthetic replacement.
- c) LV function declines more after prosthetic replacement than with repair.
- d) Surgery is indicated in severe MR with symptomatic deterioration.
- e) Men are more likely to require surgical correction of regurgitation than women.

**Answer and Discussion**
The answer is a.

**Objective:** Understand indications for surgical correction of MR, as well as the surgical limitations of the treatment of MR.

Mitrval valve repair is considered superior to replacement in most patients meeting criteria for surgical correction.
valve repair is most likely to be successful in mitral valve prolapse (MVP) and least likely in rheumatic disease and endocarditis. Mitral valve repair in ischemic and functional MR is also less beneficial.

Question 16

Common symptoms of aortic stenosis include all of the following, except
a) Dyspnea
b) Syncope
c) Ankle edema
d) Angina
e) Fatigue

Answer and Discussion

The answer is c.

Objective: Identify the common symptoms and manifestations of aortic stenosis.

The cardinal features of symptomatic aortic stenosis are heart failure, syncope, and angina. Other common findings are dyspnea on exertion, decreased exercise tolerance, and dizziness. Ankle edema and other signs of right heart failure are uncommon in aortic stenosis.

Question 17

The most reliable physical finding in predicting severe aortic stenosis is
a) Loudness of the murmur
b) Absent first heart sound
c) Loud second heart sound
d) Delayed carotid upstroke
e) Palpable fourth heart sound

Answer and Discussion

The answer is d.

Objective: Understand the physical examination findings found in aortic stenosis.

All of the choices with the exception of absent first heart sound can be found in aortic stenosis (first heart sound is usually normal). However, delayed carotid upstroke is the most reliable predictor of severe aortic stenosis. Examination findings can be reliably used to confirm the suspicion of aortic stenosis, but echocardiography is still needed to exclude the diagnosis unequivocally.

Question 18

Surgical intervention is indicated in severe aortic stenosis for all of the following, except
a) Recent exercise-induced syncope
b) LV EF of 45% with normal coronary vessels
c) Shortness of breath on walking two blocks
d) Associated significant AR
e) Exertional chest pain usually relieved by rest

Answer and Discussion

The answer is a.

Objective: Identify the indications for surgery in the treatment of severe AR.

Replacement/repair of the aortic valve is indicated when symptoms are present. Asymptomatic patients should have surgical treatment when there is a reduced LV EF less than 50%, or if they have aortic root dilatation, or progressive LV dilatation on serial ECHOs.

Question 19

Consider the following hemodynamic data: left atrial pressure, 15 mmHg; LV pressure, 220/15 mmHg; aortic pressure, 100/60 mmHg; and cardiac index, 1.9 L/minute/m². These are most consistent with which valvular lesion?

a) Tricuspid stenosis
b) MS
c) Aortic stenosis
d) AR
e) Tricuspid regurgitation

Answer and Discussion

The answer is c.

Objective: Understand relevant hemodynamic parameters associated with valvular heart disease.

Low cardiac output and a large pressure gradient between the left ventricle and aorta during systole suggest the diagnosis of aortic stenosis.

Question 20

Indications for surgical treatment in severe AR include the following, except
a) LV EF of 53%
b) Increasing LV size on sequential echo (LV end-systolic dimension of 6 cm)
c) Shortness of breath
d) Aortic root size >6 cm
e) Anginal chest pain

Answer and Discussion

The answer is a.

Objective: Identify the indications for surgery in the treatment of severe AR.

Replacement/repair of the aortic valve is indicated when symptoms are present. Asymptomatic patients should have surgical treatment when there is a reduced LV EF less than 50%, or if they have aortic root dilatation, or progressive LV dilatation on serial ECHOs.
Question 21

A 27-year-old woman has recent onset of shortness of breath going upstairs and a history of palpitations. Physical examination reveals a regular pulse, a loud $S_1$, and an apical diastolic murmur. The most likely diagnosis is

a) Aortic stenosis
b) MS
c) AR
d) Tricuspid stenosis
e) None of the above

Answer and Discussion

The answer is b.

Objective: Understand the physical examination findings seen in MS.

The physical findings associated with MS can be subtle, but in addition to clinical history can help in making a diagnosis that is confirmed by echocardiography. A loud $S_1$ and an apical diastolic murmur that is low-pitched are classic findings. Pink to purple colored patches (termed mitral facies) and signs of right-sided congestive heart failure can also be seen.

Question 22

A 36-year-old man presents to the ER with sudden onset of atrial fibrillation. He is hemodynamically stable but has a systolic murmur at the left upper sternal border radiating to the back, a widely fixed split second heart sound, and a diastolic flow rumble along the right lower sternal border. The most likely diagnosis is

a) Ventricular septal defect (VSD)
b) Atrial septal defect (ASD)
c) Pulmonic stenosis (PS)
d) Aortic stenosis

d) Patent ductus arteriosus (PDA)

Answer and Discussion

The answer is b.

Objective: Understand commonly seen congenital heart disease findings and presentations.

ASD commonly presents in the adult, and the first symptom may be the sudden onset of atrial flutter or atrial fibrillation. At least 12% to 15% of adult patients have atrial fibrillation preoperatively. Physical findings that demonstrate this as an ASD are the murmur of increased pulmonary blood flow at the left upper sternal border radiating to the back, the pathognomonic finding of a fixed split-second heart sound, and the diastolic flow rumble along the right mid-right lower sternal border (functional tricuspid stenosis), which suggests that this patient has a large left-to-right shunt at the atrial level. Adult patients with ASD tend to have large defects that raise the question of whether somewhat smaller defects in childhood actually get stretched and become larger defects in adults with significant left-to-right shunts. ASDs are also more common in women, with a female-to-male ratio of 2 to 3:1.

Question 23

A 22-year-old professional female basketball player was noted to have an unusual murmur on her sports physical before the season began. The doctor thought he heard a continuous murmur at the left upper sternal border associated with a slightly widened pulse pressure and brisk to bounding pulses. The most likely diagnosis is

a) VSD
b) ASD
c) Coarctation of the aorta
d) Patent ductus arteriosus (PDA)

d) Ventricular septal defect (PDA)

Answer and Discussion

The answer is d.

Objective: Understand commonly seen congenital heart disease findings and presentations.

Many adult patients with patent ductus are asymptomatic, depending on the size of the left-to-right shunt and the size of the ductus. Frequently, the condition is discovered by the unusual quality of a continuous murmur at the left upper sternal border that can sound like an innocent venous hum. Because a patent ductus is an aortopulmonary runoff; however, the pulse pressure frequently is widened, and the pulses are brisk to bounding. Today, most lesions of ductus can be closed in the catheterization laboratory without surgery.

Question 24

A 32-year-old woman is noted to have a systolic blood pressure (BP) of 170/100 mmHg. She has a prominent aortic ejection click and murmurs heard over the ribs on both sides anteriorly and over the back posteriorly. In addition, no pulses are palpable in the lower extremities, and she complains of mild claudication with exertion. The most likely diagnosis is

a) ASD
b) Aortic stenosis
c) Coarctation of the aorta
d) VSD

c) Coarctation of the aorta

Answer and Discussion

The answer is c.

Objective: Understand commonly seen congenital heart disease findings and presentations.

Adult patients with coarctation almost always present with systolic hypertension, and diastolic hypertension may occasionally be seen as well. A bicuspid aortic valve is noted in a significant proportion of patients with coarctation; therefore, an aortic ejection click may be heard. These patients frequently have collateral murmurs from intercostal arteries heard over the anterior and posterior chest as well as increased collaterals from the thyrocervical trunk. The pulses in the lower extremity may be weak to absent. If the coarctation is severe enough, the individuals may complain of claudication with exercise. The approach to correction in adult patients is usually percutaneous stent placement.
Question 25
A 42-year-old man presents for his first visit to your clinic. He has always been cyanotic, clubbed, and physically restricted. His hematocrit is 68%, with a hemoglobin level of 24 g. He has never undergone surgery, and his oxygen saturation on room air is 62%. Cardiac catheterization demonstrates a large VSD, overriding aorta, and severe calcification of the entire right ventricular outflow tract with small pulmonary arteries bilaterally. The diagnosis in this patient is
a) Double-outlet right ventricle
b) Truncus arteriosus
c) Tetralogy of Fallot (TOF)
d) Atrioventricular (AV) canal

Answer and Discussion
The answer is c.
Objective: Understand commonly seen congenital heart disease findings and presentations.

TOF is the most common form of cyanotic congenital heart disease in adolescents and adults. The hallmark of tetralogy is severe valvular and subvalvular PS associated with a large VSD. Patients shunt right to left at the ventricular level; therefore, they are cyanotic and clubbed. In addition, cyanotic patients are polycythemic; once their hematocrit is > 65%, they are at increased risk for stroke or spontaneous cerebral hemorrhage. The approach to tetralogy is surgical, with relief of the right ventricular outflow tract obstruction and closure of the VSD.

Question 26
A 30-year-old woman presents to your office with the murmur of MR. She has been known to have a complete heart block since childhood and is now somewhat fatigued and short of breath. You notice that on her chest radiograph she has a completely straight left heart border. The most likely diagnosis in this patient is
a) VSD
b) Rheumatic MR
c) Corrected transposition of the great arteries
d) PDA

Answer and Discussion
The answer is c.
Objective: Understand commonly seen congenital heart disease findings and presentations.

Patients with congenitally corrected transposition frequently present as adults. Although a morphologic right atrium is connected to a morphologic left ventricle via the mitral valve, the blood flows from that ventricle to the pulmonary artery. It returns then to a morphologic left atrium, which crosses a tricuspid valve into a morphologic right ventricle that pumps blood out the aorta, and the aorta is anterior and to the left. Patients with this condition frequently present in adulthood because the blood is flowing from inverted ventricles but out the appropriate arteries. Patients with corrected transposition, however, are either born with complete heart block or develop heart block at a rate of 2% per year. In addition, they often have VSD and PS. The chest radiograph shows a completely straight left heart border because of the anterior and leftward position of the aorta. Patients also frequently have an Ebstein-like malformation of the left-sided AV valve (tricuspid valve), and that valve is frequently regurgitant.

Question 27
A 28-year-old man has been known to have Wolff-Parkinson-White syndrome with episodes of supraventricular tachycardia. You order a chest radiograph and are surprised at the significant cardiomegaly, with what appears to be marked right atrial enlargement. The patient also has a murmur of tricuspid regurgitation. The most likely diagnosis is
a) ASD
b) VSD
c) Tricuspid stenosis
d) Ebstein anomaly

Answer and Discussion
The answer is d.
Objective: Understand commonly seen congenital heart disease findings and presentations.

Ebstein anomaly is the only congenital cardiac defect commonly associated with preexcitation syndromes like Wolff-Parkinson-White. Patients frequently have significant tricuspid regurgitation with a markedly dilated right atrium. Ebstein patients are prone to all rhythm disorders, including both atrial and ventricular arrhythmias, and they have a significant incidence of sudden death.

Question 28
Which of the following statements is incorrect after acute myocardial infarction (MI)?

a) Even during an acute MI, angiography remains safe to perform.
b) More than 85% of infarct-related arteries are totally occluded during the acute phase of ST segment elevation MI (STEMI).
c) The incidence of totally occluded infarct vessels decreases with time after STEMI secondary to spontaneous fibrinolysis.
d) Most patients who die from an acute MI have advanced coronary atherosclerosis involving significant obstruction in at least one coronary artery.
e) None of the above

Answer and Discussion
The answer is e.
Objective: Understand the natural history of acute MI and its evaluation.

During an acute MI, angiography remains safe, with primary percutaneous coronary intervention (PCI) often considered
the appropriate treatment. Of importance, most infarction-related arteries are occluded during the acute STEMI phase. This is reduced after infarction secondary to spontaneous fibrinolysis. Most patients who die of an acute infarction have advanced coronary atherosclerosis involving a significant coronary obstruction in at least one coronary artery.

**Question 29**

Which of the following statements concerning risk stratification after an acute MI is not correct?

a) Women possess an improved postinfarction prognosis compared with that of men.

b) The single most important determinant of both short- and long-term survival is the residual LV systolic function.

c) Silent ischemia, as detected by Holter monitoring, has a similar prognosis to that of symptomatic ischemia after infarction.

d) Diabetes mellitus contributes to an increased postinfarction risk.

**Answer and Discussion**

The answer is a.

**Objective:** Understand the role of risk stratification on prognosticating outcome after acute MI.

Important adverse prognostic predictors after an MI include the extent of LV systolic dysfunction and coexistent morbidity, including diabetes mellitus. Silent ischemia, as detected at Holter monitoring, portends a worse prognosis, as does being of female gender.

**Question 30**

The following items are features of non-ST elevation MI (NSTEMI), except

a) The residual coronary artery stenosis generally is severe.

b) Prominent collaterals serve the infarct-related artery.

c) A greater likelihood of a previous infarction exists.

d) Recurrent infarction is less likely compared with STEMI patients.

**Answer and Discussion**

The answer is d.

**Objective:** Understand the features of NSTEMI.

NSTEMI are characterized by the residual, high-grade coronary stenosis, prominent collaterals, and greater likelihood of previous MI. The EF is lower, but the reinfarction rate is higher compared with that in patients with STEMI.

**Question 31**

The following statements regarding fibrinolytic therapy are true, except

a) An improved mortality has been shown in patients with inferior infarction after fibrinolytic administration.

b) The earlier the fibrinolytic treatment is administered, the greater the impact on survival.

c) Preservation of LV function depends on early fibrinolytic administration.

d) Cardiopulmonary resuscitation is an absolute contraindication for fibrinolytic therapy.

**Answer and Discussion**

The answer is d.

**Objective:** Understand the usage, outcomes, and contraindications of fibrinolitics in the treatment of acute MI.

Fibrinolytic therapy is most beneficial within the early phases of an acute MI. Its use is primarily reserved for situations where access to primary PCI is not available in a timely fashion. Reduced morbidity and mortality is shown for all infarction, including inferior infarction. Enhanced LV systolic function is noted with earlier fibrinolytic administration. Cardiopulmonary resuscitation remains a relative, not an absolute, contraindication to fibrinolytic therapy.

**Question 32**

You are called to see a patient whose cardiac monitor reveals bradycardia. Indications for a temporary pacemaker in patients with acute MI include the following, except

a) New left anterior fascicular and right bundle-branch block

b) New second-degree Mobitz type I AV block responsive to atropine administration

c) New left bundle-branch block with first degree AV block

d) Complete heart block

**Answer and Discussion**

The answer is b.

**Objective:** Understand the complications encountered after acute MI.

It is important to consider that bradycardia can further decrease myocardial perfusion and temporary pacing may be required. Indications for temporary pacing during an acute MI include new-onset bifascicular block, second-degree Mobitz type II AV block, and complete heart block. First-degree AV block and Mobitz type I Wenckebach second-degree AV block require careful observation but not temporary pacing.

**Question 33**

True statements concerning the ECG findings during an acute MI include the following, except

a) Sinus tachycardia is frequently present.

b) An accelerated idioventricular rhythm postfibrinolytic therapy warrants urgent electric cardioversion.

c) Atrial dysrhythmias such as atrial fibrillation are commonly observed.

d) The development of complete heart block portends a worse prognosis.
**Answer and Discussion**

**The answer is b.**

**Objective: Understand the ECG findings associated with an acute MI.**

In the presence of an acute MI, increased sympathetic tone often is reflected in the form of sinus tachycardia. Atrial arrhythmias frequently are demonstrated in part related to atrial ischemia, increased circulating catecholamines, acutely elevated intracardiac pressures, and cardiac chamber dilatation. Advanced forms of heart block are associated with larger infarction, which portend a worse prognosis. Accelerated idioventricular rhythms frequently manifest after successful reperfusion during the acute myocardial injury phase, rarely require treatment other than careful observation, and represent a noninvasive marker of successful coronary blood flow restoration.

**Question 34**

In a patient presenting with an acute coronary syndrome (ACS) and an ECG demonstrating an extensive anterolateral myocardial injury pattern, appropriate treatment measures would include the following, except

a) The prophylactic placement of an intra-aortic balloon pump to attenuate the degree of myocardial injury given the large MI
b) Intravenous fibrinolytic therapy
c) Intravenous β-blocker administration in the absence of advanced heart failure and hemodynamic compromise
d) An urgent coronary angiography with the goal of performing a PCI and possible coronary stent placement

**Answer and Discussion**

**The answer is a.**

**Objective: Understand the treatment of acute MI.**

In the presence of an acute chest discomfort syndrome and an ECG demonstrating acute myocardial injury, the restoration of coronary artery blood flow in the most expedient manner results in reduced morbidity and mortality. This can be achieved by administering intravenous fibrinolytic therapy or proceeding directly with coronary angiography and PCI. β-Blockers reduce myocardial oxygen demand, attenuate myocardial ischemia, and limit the size of an infarction. β-Blockers should be administered to all acute MI patients in the absence of a hemodynamic contraindication. In the presence of cardiogenic shock, drug-refractory congestive heart failure, and recurrent life-threatening cardiac dysrhythmias believed to be ischemia-mediated, the placement of an intra-aortic balloon pump in the peri-infarction period can achieve a positive clinical benefit. The routine use of an intra-aortic balloon pump is not indicated and may subject the patient to excess morbidity secondary to vascular injury, cholesterol and systemic embolization, and infection, all without a tangible benefit. The use of an intra-aortic balloon pump is an individualized decision for each acute MI patient.

**Question 35**

A 60-year-old Asian man is referred to you for evaluation of a heart murmur. He speaks no English and is not accompanied by any family member able to translate. As you wait for the translator to arrive, you are able to communicate sufficiently to obtain permission for a physical examination. His pulse is regular, with a rate of 80 beats/minute, and his BP is 100/85 mmHg. Carotid pulse has a slow upstroke. No jugular venous distension is present. The apex is slightly displaced laterally. A systolic thrill is palpable over the aortic area and carotids. Auscultation reveals a harsh ejection systolic murmur. Valsalva maneuver does not accentuate the murmur. The second aortic sound is soft. With which of the following are these findings most consistent?

a) MR
b) MVP
c) Aortic stenosis
d) Hypertrophic obstructive cardiomyopathy (HOCM)
e) MS

**Answer and Discussion**

**The answer is c.**

**Objective: Understand the clinical findings associated with valvular heart disease.**

All the signs and symptoms in this case point to aortic stenosis. This is a systolic murmur, which eliminates MS. The murmur of HOCM is increased with Valsalva maneuver. Neither MR nor MVP is associated with narrowed pulse pressure or slow upstroke.

**Question 36**

A 42-year-old man presents with intermittent chest pain. Further history reveals that the character of the pain is typical of angina. He also has had episodes of dyspnea, dizziness, and syncope. He is a nonsmoker and denies illicit drug use. His past medical history (PMH) is significant for tonsillectomy in childhood. Family history includes the sudden death of his brother of unknown cause at age 33 years. On examination of the cardiovascular system, the pulse is regular, with a rate of 68 beats/minute, and no jugular venous distension is present. The apical impulse is forceful and displaced laterally. A double apical impulse and a palpable systolic thrill are present. On auscultation of the heart, an S₃ and an ejection systolic murmur are heard. ECG shows LV hypertrophy and Q waves in the inferior and lateral precordial leads. Chest radiograph reveals a mild increase in the cardiac silhouette. Echocardiographic findings include LV hypertrophy with asymmetric septal hypertrophy and a small LV cavity. This murmur may be increased by all of the following, except

a) Dopamine
b) Amyl nitrite
c) Diuretics
d) Valsalva maneuver
e) Handgrip
Answer and Discussion
The answer is e.

Objective: Understand the clinical findings and diagnosis of HOCM.

Features of HOCM include LV hypertrophy with asymmetric septal hypertrophy, causing a dynamic LV outflow tract pressure gradient and diastolic dysfunction from stiffness of the hypertrophied muscle. Interventions that increase the murmur include those that decrease preload (diuretics, nitrates, Valsalva maneuver, standing from squatting), decrease afterload (vasodilators, amyl nitrite, angiotensin-converting enzyme (ACE) inhibitor), or increase contractility (digoxin, dopamine, and premature ventricular contractions). Interventions that decrease the murmur include those that increase preload (intravenous fluids, passive leg raising, squatting), increase afterload (handgrip), or decrease contractility (β-blockers, disopyramide, verapamil).

Question 37

A 29-year-old woman presents to the emergency department with shortness of breath and palpitations. The triage nurse finds that she has a heart rate of 170 beats/minute and establishes an intravenous line, starts oxygen therapy, and attaches a cardiac monitor. You assess her airway, breathing, and circulation. Her respiratory rate is 24 breaths/minute and BP 70/40 mmHg. She starts to complain of chest tightness. What should your next step be?

a) Drawing blood for a metabolic profile and cardiac enzymes
b) Synchronized cardioversion
c) Defibrillation
d) Lidocaine
e) Verapamil

Answer and Discussion

The answer is a.

Objective: Understand immediate lifesaving treatment of an unstable tachycardia.

This woman has unstable tachycardia with serious signs and symptoms, including hypotension, heart rate >150 beats/minute, shortness of breath, and chest tightness. According to the American Heart Association, this should be treated with immediate synchronized cardioversion.

Question 38

Emergency medical services bring a 55-year-old man with a previous history of CAD and prior MI to the emergency department with severe substernal chest pain radiating to the left shoulder and jaw. The pain has been persistent for approximately 20 minutes. On questioning, he has experienced similar pain intermittently throughout the previous 48 hours. In addition to the pain, he has experienced shortness of breath, diaphoresis, and nausea. His pain improves somewhat after he is given two nitroglycerin tablets sublingually. His vital signs are stable, and his ECG reveals changes consistent with an anterior MI. He is admitted to the coronary ICU. While there, severe systemic hypotension (BP 80/30 mmHg) and dyspnea develop. He is given vasopressor and inotrope support. A pulmonary artery catheter is placed. The pulmonary artery wedge pressure is 18 mmHg, and the cardiac index is calculated to be 2.0 L/minute/m². All the following statements regarding this man's diagnosis are true, except

a) It is unusual for cardiogenic shock to develop in this man because in most patients, it develops before presentation to the hospital.
b) The hemodynamic measurements obtained for this patient are consistent with those for classic cardiogenic shock.
c) Severe MR from a ruptured chordae tendineae or papillary muscle, cardiac tamponade, or rupture of the intraventricular septum may also lead to cardiogenic shock in the setting of an acute MI.
d) Urgent echocardiography with Doppler flow is indicated and would be helpful in narrowing the differential for this man's hypotension.
e) All the above statements are true.

Answer and Discussion

The answer is a.

Objective: Understand the complications that can result from an acute MI.

Cardiogenic shock, clinically described as severe systemic hypotension, cool extremities, and respiratory distress, occurs in approximately 6% to 7% of patients with acute MI. These patients are often older and of the female gender and have an anterior or large infarction, previous MI, or diabetes mellitus. In the Global Utilization of Streptokinase and t-PA for Occluded Coronary Arteries I trial, however, only 0.8% of patients had shock on presentation to the hospital, with shock developing either suddenly (as in this patient) or gradually in the remaining 5.3% after admission. Most cases occur within 24 hours to days afterward, with cases occurring 1 week afterward being rare. Severe LV dysfunction is the most common cause of cardiogenic shock, most commonly from an anterior MI. Right ventricular dysfunction does not usually lead to respiratory distress unless the left ventricle is also involved. Acute MR from ruptured chordae tendineae or papillary muscle, ruptured intraventricular septum, or cardiac tamponade may all lead to cardiogenic shock from mechanical means. As with any patient who is in “shock” (hypo-perfusion), other causes and types of shock must be ruled out. Echocardiography (either transthoracic or transesophageal) is essential in the initial evaluation of patients with cardiogenic shock. Not only is left and right ventricular function assessed but also mechanical complications of MI can be ruled in or out. Finally, the insertion of a balloon-tipped pulmonary artery
catheter can confirm the hemodynamic criteria for cardiogenic shock. The American College of Cardiology and the American Heart Association Task Force guidelines define cardiogenic shock as two subsets:

1. Pulmonary capillary wedge pressure >15 mmHg, systolic BP (SBP) <100 mmHg, and CI <2.5 L/minute/m²
2. Pulmonary capillary wedge pressure >15 mmHg, SBP <90 mmHg, and cardiac index (CI) <2.5 L/minute/m²

Subset 2 has a worse prognosis.

**Question 39**

A 32-year-old woman reports increasing shortness of breath. On examination, pulse is regular, and a parasternal heave is noted. On auscultation, a continuous, machinery-type murmur is present, with systolic accentuation that is best heard at the second intercostal space and left sternal border; it is also heard posteriorly. Clubbing and cyanosis of the toes is present, but not of the fingers. All the following are true of this condition, except

a) It is more common in men.
b) Endocarditis prophylaxis should be given before dental procedures.
c) Cyanosis of the lower extremities is associated with the development of Eisenmenger syndrome.
d) Maternal rubella is associated.
e) It is normal anatomy before birth.

**Answer and Discussion**

The answer is a.

**Objective: Understand commonly seen congenital heart disease findings and presentations.**

PDA is more common in women than in men (3:1). It is associated with maternal rubella. Complications include infective endocarditis (IE) and Eisenmenger syndrome. Prophylaxis for endocarditis is indicated, unless treatment by surgical ligation has been performed. Severe pulmonary vascular disease leads to a reversal of flow and shunting of deoxygenated blood to the lower extremities, resulting in differential cyanosis. Once Eisenmenger syndrome has developed, corrective surgical intervention is no longer an option. The ductus is patent in the fetus but normally closes immediately after birth.

**Question 40**

A 51-year-old man consults you because he is concerned about his risk of cardiovascular disease. His father died at 52 years of age from MI. For exercise, he runs for 30 minutes 5 times per week. In discussing his diet, you find that he typically eats eggs for breakfast and usually has some sort of fast food for lunch on working days. He does not smoke or drink alcohol and is normotensive on examination. Results of fasting cholesterol and glucose testing are as follows:

<table>
<thead>
<tr>
<th>Test</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total cholesterol</td>
<td>231 mg/dL</td>
</tr>
<tr>
<td>Low-density lipoprotein cholesterol (LDL-C)</td>
<td>161 mg/dL</td>
</tr>
<tr>
<td>High-density lipoprotein cholesterol (HDL-C)</td>
<td>56 mg/dL</td>
</tr>
<tr>
<td>Triglycerides</td>
<td>72 mg/dL</td>
</tr>
<tr>
<td>Glucose</td>
<td>107 mg/dL</td>
</tr>
</tbody>
</table>

Liver function tests are normal. He is concerned that he may die of a heart attack and urges you to treat him with “some of the pills” that he has seen advertised. What would be the most appropriate response?

a) Explain that he should be treated with active diet therapy, and there is no need to start medication at this time.
b) Repeat his laboratory work in 3 to 6 months and discuss the matter further at that time if the lipid profile has not improved.
c) Evaluate for primary and secondary causes of hypercholesterolemia and institute drug therapy.
d) Reassure him, explaining that he is not at increased risk and that he should continue exercising.

**Answer and Discussion**

The answer is c.

**Objective: Understand risk factor modification in the primary prevention of CAD.**

This man has two risk factors for CAD: being a man older than 45 years and a significant family history. The National Cholesterol Education Program suggests that with an LDL-C level >160 mg/dL, active drug therapy should be instituted. Although epidemiologic studies suggest that a lowered risk of coronary events is present in those consuming certain types of alcohol, the recommendation that someone who does not otherwise drink starts taking red wine is controversial.

**Question 41**

A 34-year-old man with a PMH of hypertension and obstructive pulmonary disease presented to his PCP for 6-month follow-up. His medications include enalapril, hydrochlorothiazide and albuterol inhaler as needed. He quit smoking 5 years ago. All the following statements about cholesterol screening are true, except

a) Measuring blood cholesterol levels is widely accepted as a convenient, safe, and inexpensive screening test.
b) Cholesterol lowering and, therefore, cholesterol screening are more effective in primary prevention than in secondary prevention.
c) Elevated blood cholesterol levels increase the risk for coronary heart disease (CHD).
d) The effects on CHD from lowering cholesterol depend on the magnitude of the cholesterol reduction.
e) In men and women with CHD, cholesterol reduction retards or reverses the progression of atherosclerotic plaques and reduces mortality from CHD.
Answer and Discussion

The answer is b.

Objective: Demonstrate the benefit of primary and secondary prevention of cholesterol screening.

The net benefit of cholesterol lowering depends on the underlying risk for death from CHD. The risks for developing and dying of CHD are much lower in primary prevention settings than in secondary prevention settings. Hence, cholesterol lowering is more effective in secondary prevention (patients who have had a MI) than in primary prevention. The effects of lowering cholesterol on CHD depend on the magnitude of cholesterol reduction. Each 10% reduction in cholesterol levels is associated with roughly a 20% to 30% reduction in the incidence of CHD.

Question 42

According to the 2007 American Heart Association guidelines for the prevention of IE, prophylaxis is indicated in all the following except

a) Prosthetic heart valves, including bioprosthetic and homograft valves
b) A prior history of IE
c) Unrepaired cyanotic congenital heart disease, including palliative shunts and conduits
d) Hypertrophic cardiomyopathy with latent or resting obstruction
e) Cardiac valvulopathy in a transplanted heart

Answer and Discussion

The answer is d.

Objective: Identify appropriate scenarios for IE prophylaxis.

According to the 2007 American Heart Association guidelines for the prevention of IE, prophylaxis is indicated in prosthetic heart valves, patients with a prior history of IE, “valvulopathy” in a transplanted heart, un repaired cyanotic congenital heart disease, completely repaired congenital heart defects within the first 6 months after the procedure, or repaired congenital heart disease with residual defects at the site or adjacent to the site of the prosthetic device. Prophylaxis is no longer indicated in common valvular lesions such as bicuspid aortic valve, acquired aortic or mitral valve disease, MVP with regurgitation, and hypertrophic cardiomyopathy. High-risk procedures that warrant antibiotic prophylaxis include all dental procedures that involve manipulation of gingival tissue or the periapical region, or that involve perforation of the oral mucosa; all respiratory procedures that involve incision of the respiratory mucosa; all procedures in patients with ongoing gastrointestinal (GI) or genitourinary tract infection; all procedures on infected skin or musculoskeletal tissue; and surgery to place prosthetic heart valves or prosthetic intravascular or intracardiac materials.

Question 43

While on call in the hospital, you are walking through a ward when a nurse comes running to you, requesting your help with a patient whose doctor she is unable to locate. The patient is a 62-year-old man who has a heart rate of 38 beats/minute and is feeling lightheaded and short of breath. Which of the following statements concerning this situation is true?

a) Atropine, 1 mg intravenously, is an appropriate treatment if the patient is recovering from heart transplantation.
b) High-dose isoproterenol is an appropriate treatment for this bradycardia.
c) Adenosine is a first-line choice of drug therapy.
d) Transcutaneous pacing can be effective treatment, but it is often painful.
e) If the patient is unstable with a falling BP, then synchronized direct-current cardioversion is the appropriate therapy.

Answer and Discussion

The answer is d.

Objective: Identify the appropriate treatment for symptomatic bradycardia.

Atropine, 1 mg intravenously, is not an appropriate treatment if the patient is recovering from heart transplantation because denervated hearts do not respond to atropine; transcutaneous pacing or catecholamine infusion would be an appropriate therapy in this situation. Low-dose isoproterenol may be used with caution after other therapeutic options have failed, but at high doses, it is a class III drug, has been shown to be harmful, and is thus never an appropriate treatment for bradycardia. Adenosine is an appropriate first-line choice of drug therapy for some tachycardias, but not bradycardia. If a patient is unstable with tachycardia and a falling BP, then synchronized direct-current cardioversion is appropriate therapy; however, if a patient with bradycardia is unstable, then transcutaneous pacing is indicated.

Question 44

A 59-year-old man with a history of hypertension and end-stage renal disease develops refractory hypotension during dialysis. He has missed two dialysis sessions, and his blood urea nitrogen (BUN) level on presentation is 109 mg/dL. He reports constant chest discomfort, dyspnea on exertion, and easy fatigability over the past week. On examination, he is alert and oriented, heart rate is 112 beats/minute and regular, and BP is 88/57 mmHg. On inspiration, his systolic BP falls to 62 mmHg. His jugular veins are distended and elevated to the jaw angle. Chest radiography shows cardiomegaly and mild interstitial edema, and the ECG reveals diffuse low voltage. The most appropriate next step in management is which of the following?

a) Start heparin infusion, aim for a prothrombin time of 55 to 75 seconds, and obtain a lung perfusion scan
b) Start dobutamine and place a pulmonary artery catheter to guide management
c) Infuse 1 L of normal saline followed by dextrose 5% in water and observe
d) Admit to the telemetry unit and obtain a set of cardiac enzymes
e) Admit to the ICU and obtain an urgent ECHO

Answer and Discussion

The answer is e.

Objective: Recognize and stabilize pericardial tamponade.

Pericardial tamponade is a well-recognized complication in patients with chronic renal failure and uremic pericarditis. Pericardial tamponade is a medical emergency. Common clinical presentation for pericardial tamponade is Beck triad: hypotension, muffled heart tones, and Kussmaul sign (elevated JVP on inspiration). Pulsus paradoxus can also be measured as a bedside maneuver. The management of patients suspected of having pericardial tamponade includes aggressive fluid resuscitation and immediate echocardiography by a cardiologist trained to perform pericardiocentesis.

Question 45

A 65-year-old man with a past cardiovascular history of well-controlled hypertension, presented to his PCP for annual physical. On examination, he had normal jugular venous pulsation. Cardiac examination was significant for a normal S1, paradoxically split S2, and 2/6 systolic ejection murmur. Paradoxical splitting of the second heart sound may be heard with which of the following?

a) Right bundle branch block
b) Restrictive cardiomyopathy
c) PS
d) Aortic dissection with new diastolic murmur
e) Aortic stenosis

Answer and Discussion

The answer is e.

Objective: Identify possible etiologies for a paradoxical split second heart sound.

Because the LV systole may become prolonged in severe aortic stenosis, the aortic valve closure may no longer precede the pulmonic valve closure. This phenomenon causes paradoxical splitting in the second heart sound. Left bundle branch block is another common cause of paradoxical splitting in S2. In right bundle branch block, however, the delayed activation of the right ventricle causes the S2 splitting, which normally occurs during inspiration, to persist during expiration (fixed splitting).

Question 46

A 70-year-old man seeks a second opinion regarding frequent episodes of paroxysmal atrial fibrillation that were detected on 48-hour Holter monitor. He is markedly symptomatic, with frequent palpitations and presyncope. Each episode can last from 30 minutes to 2 hours. His PMH is significant for old anterior wall MI, and his LVEF is 20%. His medications include enalapril, carvedilol, digoxin, and warfarin. On physical examination, his BP is 120/80 mmHg, and his heart rate is 78 beats/minute. He appears well compensated and is free of signs of congestive heart failure (CHF). Which of the following is the most appropriate antiarrhythmic agent?

a) Amiodarone
b) Sotalol
c) Flecainide
d) Disopyramide
e) Quinidine

Answer and Discussion

The answer is a.

Objective: Identify contraindications to antiarrhythmic medications.

This patient had a previous MI and has depressed LV systolic function. He is symptomatic with his atrial fibrillation and must be treated aggressively. Amiodarone, a class III antiarrhythmic medication, is a potent agent that exerts its effect broadly on all phases of the action potential. It is ideal in this situation because it has a negligible negative inotropic effect. Patients are orally loaded in the hospital and are observed for the development of symptomatic bradycardia and torsade de pointe due to QT prolongation (an uncommon complication). Sotalol, a class III antiarrhythmic drug, is classified as a nonselective β-blocker and blocks the potassium channel and prolongs the repolarization phase. It has negative inotropic properties and can induce or exacerbate heart failure. Sotalol should not be prescribed if the EF is <35%. Flecainide is a class IC antiarrhythmic agent, and its use is contraindicated in patients with structural heart disease (CAD, MI, CHF, or undifferentiated cardiomyopathy). Disopyramide is a class IA antiarrhythmic agent that has profound negative inotropic properties, and its use is contraindicated in patients with depressed LV systolic function. Quinidine is a class IA agent that has negative inotropic properties. A meta-analysis of several small trials demonstrated excess mortality in patients taking quinidine, and its use has become quite limited. The only other viable option in this patient is dofetilide, a new class III antiarrhythmic therapy that is given to patients with a low EF who have a contraindication to amiodarone.

Question 47

A 45-year-old man developed an acute anterior wall MI that was treated with primary PCI. His cardiac catheterization study showed 100% occlusion of the mid-left anterior descending artery; this was successfully opened, with residual narrowing of 10%. His other coronary arteries demonstrated mild atherosclerotic changes. His LVEF is 40%. On admission, his total serum cholesterol level was 230 mg/dL,
and his LDL-C level was 140 mg/dL. He had an uneventful hospital course. His discharge medications should include all the following, except

a) Carvedilol
b) Atorvastatin
c) Isosorbide dinitrate
d) Captopril
e) Aspirin

**Answer and Discussion**

The answer is c.

**Objective: Understand post-acute MI interventions.**

After successful revascularization with establishment of coronary patency, nitroglycerin is not usually needed, and hence, patients do not need to be discharged on isosorbide dinitrate. Because he has mild LV dysfunction, captopril and carvedilol are appropriate, as is atorvastatin for hyperlipidemia. Aspirin should be continued for life after MI, and clopidogrel (dual antiplatelet therapy) should be continued at least for a year if a drug-eluting stent (DES) is placed or for 6 months with a bare metal stent.

**Question 48**

An active 32-year-old woman presents with a chief complaint of fatigue and exercise intolerance. She had an uncomplicated pregnancy and delivered her second child 2 months ago. On examination, her BP is 110/80 mmHg, and her heart rate is 86 beats/minute. Her neck veins are flat, without elevation of jugular venous pressure, and her point of maximal intensity is enlarged and laterally displaced. A 2/6 holosystolic murmur is present at the apex, without an S3 gallop. The rest of the examination is unremarkable. Her chest radiograph shows cardiomegaly. An EKG reveals normal sinus rhythm (NSR) with complete left bundle branch block. Her two-dimensional echo shows biventricular enlargement with an LVEF of 30% and 2+ MRs. Which of the following agents is first-line therapy in this patient?

a) Spironolactone
b) Prazosin
c) Digoxin
d) Enalapril
e) Carvedilol

**Answer and Discussion**

The answer is d.

**Objective: Identify and treat postpartum cardiomyopathy.**

The patient’s diagnosis is postpartum cardiomyopathy, and she has moderate LV systolic dysfunction and moderate MR. She is clinically well-compensated and has mild limitation in her activities of daily living. The first-line therapy for her is the ACE inhibitor enalapril. The Studies of Left Ventricular Dysfunction (SOLVD) trial demonstrated a significant reduction in both mortality and rate of hospitalization in both symptomatic and asymptomatic patients with reduced LV systolic function regardless of etiology. Spironolactone has shown a mortality benefit in patients with severe forms of heart failure [New York Heart Association (NYHA) functional classification III/IV]. Digoxin has a neutral effect on mortality and has been shown to reduce the rate of hospitalization for CHF in patients with depressed systolic function. It is not considered first-line therapy, however. Carvedilol, a nonselective β-blocker with α-blocker and antioxidant properties, has been shown in clinical trials to have a mortality benefit in patients with moderate and severe forms of heart failure when compared with placebo. However, carvedilol was added to a background regimen of ACE inhibitor and, therefore, is not the correct answer.

**Question 49**

A 27-year-old white woman has had recurrent palpitations for the past 5 years. Her most recent episode was 2 days ago; that episode lasted 45 minutes and resulted in near syncope. Her PMH is unremarkable, and she takes no medications. Her thyroid-stimulating hormone level is normal. Her EKG today is shown in the figure.
What is the most appropriate recommendation at this time?

a) No treatment; provide reassurance
b) Radiofrequency ablation of accessory pathway
c) Procainamide
d) Digoxin
e) Verapamil

Answer and Discussion

The answer is b.

Objective: Recognize and treat Wolf-Parkinson-White (WPW) syndrome.

One must recognize that the patient’s EKG demonstrates Δ-waves and a pseudo-inferior wall MI pattern suggestive of accessory AV conduction or WPW syndrome. The main symptom of this congenital abnormality is palpitations. The most feared complication is atrial tachyarrhythmias, with 1:1 AV conduction via the accessory pathway resulting in ventricular fibrillation and sudden death. Thus, nodal blocking agents (digoxin, β-blockers, and calcium channel blockers) must not be used in patients with WPW syndrome and tachycardia. Our patient with presyncope and recurrent palpitations is a very good candidate for ablation of the accessory pathway as a definitive treatment option.

Question 50

A 55-year-old man with multiple cardiac risk factors presents to the emergency department with acute onset of intermittent chest pressure that occurred while he was sitting and watching TV, lasted 6 hours, and was associated with dyspnea and diaphoresis. Each episode lasted 30 minutes, and there was no relief with Maalox. On physical examination, his BP is 150/90 mmHg, and his heart rate is 130 beats/minute. His examination is remarkable for tachycardia and no murmurs. He has bibasilar rales. His creatine phosphokinase level is 140 mg/dL, with a creatine kinase-muscle brain (CK-MB) level of 3 (normal, 0 to 4), and his troponin T level is 5.6 (normal, 0 to 0.1). His EKG is shown in the below figure.

What is the most appropriate combination therapy in this patient?

a) Aspirin, clopidogrel, fibrinolysis with tissue plasminogen activator (tPA), heparin, metoprolol, nitroglycerin
b) Aspirin, clopidogrel, fibrinolysis with streptokinase, metoprolol, nitroglycerin
c) Aspirin, clopidogrel, IV heparin, tirofiban, metoprolol, nitroglycerin
d) Aspirin, clopidogrel, enoxaparin, nitroglycerin, magnesium
e) Aspirin, clopidogrel, enoxaparin, metoprolol, magnesium

Answer and Discussion

The answer is c.

Objective: Demonstrate appropriate treatment of ACS.

This patient is experiencing a non-ST elevation MI. He has chest pains, marked dynamic ST depressions, and an elevation in troponin T. Fibrinolytic agents are only indicated in the treatment of STEMI. The only exception is isolated 2-mm ST depressions in V_1–V_3 that correspond to ST elevations in posterior leads V_7–V_9; this indicates acute posterior infarction. Evidence suggests that fibrinolytic agents cause harm to patients with non-ST elevation MI by inducing a heightened thrombotic state; therefore, these agents are contraindicated. Low molecular weight heparins, such as enoxaparin, have a role in the management of this patient, but β-blocking agents and nitrates also must be included. The current guidelines call for a combination of aspirin, clopidogrel, standard heparin (or low molecular weight heparin), and potent antiplatelet glycoprotein IIb/IIIa receptor antagonists (tirofiban or eptifibatide) in addition to β-blockers and nitrates. When these glycoprotein IIb/IIIa receptor blockers were added to aspirin, clopidogrel, and heparin in the Platelet Receptor Inhibition for Ischemic Syndrome
A 60-year-old woman presents for preoperative consultation prior to her abdominal aortic aneurysm (AAA; 6 cm) surgery. She is a chronic smoker and has an extensive history of hypertension. She is inactive and has exercise intolerance secondary to her obstructive pulmonary disease. She has no prior cardiac history and reports no angina pectoris. Her medications include theophylline, albuterol inhaler, and hydrochlorothiazide.

On physical examination, her BP is 150/90 mmHg, and her heart rate is 86 beats/minute. Her cardiovascular examination is normal, with no evidence of fluid overload or congestion. She has decreased breath sounds with diffuse expiratory wheezes throughout both lung fields and has a palpable pulsatile abdominal mass. Her chest radiograph reveals hyperinflation of both lungs, with flattening of both diaphragms and normal cardiac silhouette. Her EKG shows NSR, with Q waves in inferior leads suggesting remote inferior wall MI. What is the most appropriate initial recommendation for this patient?

a) Dobutamine stress echocardiography
b) Schedule cardiac catheterization
c) Dipyridamole nuclear study
d) Cancel her operation
e) Proceed with surgery without further workup

**Answer and Discussion**

The answer is a.

**Objective: Determine the need for appropriate preoperative cardiac functional test.**

One of the most common consults for an internist is to provide a preoperative assessment for patients who are scheduled for noncardiac surgery. Our patient is scheduled for AAA repair, which carries a high surgery-specific risk. She has active asthma and an abnormal EKG. Cardiac catheterization is an invasive and aggressive approach and is reserved for symptomatic patients (unstable coronary symptoms or evidence of CHF). A dipyridamole nuclear study is contraindicated due to her active bronchospastic state. Dipyridamole can cause severe bronchospasm and has the potential to induce respiratory failure in asthmatic patients. She needs the operation because the risk of rupture is high and increases with time. She deserves a functional test because a large proportion of patients with AAA harbor atherosclerotic CAD that requires further risk stratification.

Dobutamine stress echocardiography provides valuable information on the status of her LV systolic function and valvular function, and it can determine presence or absence of myocardial ischemia. Patients with normal dobutamine stress echoes have a very low risk of perioperative MI, and dobutamine echo can be performed safely in patients with AAA.

**Question 52**

A 35-year-old man is hit in the chest by a baseball and visits the emergency department with pleuritic chest wall pain. He states that when he was a child, his pediatrician heard a heart murmur, but he never followed up and has not seen a physician since age 8. He has felt well and takes no medications.

On examination, his BP is 130/40 mmHg, and his heart rate is 90 beats/minute. He has a left lateral ribcage contusion without deformity. On auscultation, he is found to have a 3/6 diastolic murmur that is heard best at the left upper sternal border in a sitting position. His chest radiograph shows incidental cardiomegaly with clear lungs, no infiltrates, and no rib fractures. A 2D-echo reveals a dilated left ventricle with mild global systolic dysfunction and an EF of 45%. He has a bicuspid aortic valve with severe 4+ aortic insufficiency.

What is the most appropriate long-term therapeutic strategy in this asymptomatic patient with severe aortic insufficiency?

a) Watchful waiting and repeat 2D-echo in 6 months
b) Afterload reduction with enalapril
c) Oral furosemide
d) Cardiothoracic surgical consultation for corrective aortic valve surgery
e) Aortic valve valvuloplasty

**Answer and Discussion**

The answer is d.

**Objective: Identify the appropriate surgical treatment for bicuspid aortic valve with severe aortic insufficiency.**

The diagnosis of aortic insufficiency was made incidentally in this patient due to the injury to his chest. Bicuspid aortic valve is the most common underlying etiology for aortic insufficiency in young individuals. In this patient, echo demonstrates severe AI with decreased LV function. Despite the absence of symptoms, surgical aortic valve replacement is the correct answer to prevent further reduction in LV dysfunction. Watchful waiting would lead to further reduction in LV function and hence is not correct. Vasodilators have been studied, including enalapril, nifedipine, and even digoxin and have not shown any benefit in preventing either worsening of AI or need for surgery. Furosemide may be used in a patient with congestive symptoms, but our patient is asymptomatic and hence would not use furosemide. Aortic valvuloplasty is used in severe aortic stenosis and not in aortic insufficiency.
Question 53

A 32-year-old Vietnamese female nurse requested a routine physical examination and an EKG because of a strong family history of CAD. She is asymptomatic. On examination, she appears healthy, with a BP reading of 122/76 mmHg and a heart rate of 76 beats/minute. Her cardiac examination is notable for a regular rate and rhythm, with normal S1 and widely fixed split S2. She has a 2/6 systolic ejection murmur that is heard best at the left upper sternal border, third interspace, and no gallops or diastolic murmurs are present. Her lungs are clear, and she has no evidence of ascites or peripheral edema. No cyanosis or clubbing is present. Her chest radiograph demonstrates enlarged pulmonary arteries with increased vascularity in both lung fields. Her EKG is shown in the below figure.

What is this patient’s most likely diagnosis?

a) Ventricular septal defect
b) Aortic stenosis
c) Atrial septal defect
d) PDA
e) MR

Answer and Discussion

The answer is c.

Objective: Recognize the signs and symptoms of an atrial septal defect.

This patient has evidence of right-sided volume overload with EKG changes consistent with right ventricular hypertrophy. The fixed split S2 is the key distinguishing feature that is pathognomonic for atrial septal defect. Ventricular septal defect produces a loud, harsh murmur that is best heard in the mid to lower left sternal border. The murmur of aortic stenosis is a crescendo/decrescendo systolic ejection murmur that radiates to the left carotid. Aortic stenosis does not cause an increase in pulmonary vascularity. PDA is characterized by a continuous systolic/diastolic murmur. MR produces a rumbling systolic murmur at the apex of the heart.

Question 54

A 54-year-old white man with a history of uncontrolled hypertension and end-stage renal disease on hemodialysis develops shortness of breath and hypotension 2 days after missing a dialysis session. His BP is 92/60 mmHg, his heart rate is 116 beats/minute, his respiratory rate is 32, and his temperature is 37°C. His cardiac examination demonstrates elevated jugular venous pulsation with muffled heart sounds and clear lungs. No ascites or peripheral edema is present. What would you do next?

a) ECHO
b) Ventilation–perfusion (VQ) scan
c) Obtain blood cultures
d) Perform pericardiocentesis
e) Measure pulsus paradoxus

Answer and Discussion

The answer is e.

Objective: Rapidly identify cardiac tamponade.

The patient’s clinical presentation should elevate the existence of symptomatic pericardial effusion and cardiac tamponade to the top of the differential diagnosis list. In a previously hypertensive patient with end-stage renal disease who acutely becomes hypotensive without obvious blood loss, uremic pericarditis should be considered strongly. The triad of Kussmaul sign (increased JVP on inspiration), muffled heart sounds, and hypotension—or Beck triad—can help identify the signs of cardiac tamponade. The next step is to check for pulsus paradoxus, which is an exaggeration of inspiratory drop in systolic BP (a drop of >10 mmHg). A 2D-echo is then ordered to confirm the diagnosis. (Note: The board members who make up board examination questions place heavy emphasis on physical examination findings and cost-effective strategies in diagnostic workups.)

Question 55

A 55-year-old man presents with severe chest pressure and is promptly diagnosed with acute inferior wall MI and receives reteplase. His chest pressure and ST segment elevations completely resolve after 40 minutes of thrombolytic
administration. He is then placed on a regimen of aspirin, clopidogrel, heparin, and metoprolol. On the fourth hospital day, he develops sudden-onset dyspnea, diaphoresis, palpitations, and dizziness.

On examination, his respiratory rate is 38 breaths/minute, his BP is 86/60 mmHg, and his heart rate is 130 beats/minute. He has an irregularly irregular rhythm with a loud 4/6 holosystolic murmur that is heard best at the apex. Pulmonary rales are present two-thirds of the way up both lung fields. The rest of the examination is unremarkable. His EKG demonstrates atrial fibrillation with rapid ventricular response, Q waves inferiorly, and no acute ST segment changes. His chest radiograph is consistent with acute pulmonary edema. Pulmonary artery catheter hemodynamics reveal the following:

<table>
<thead>
<tr>
<th>Pressure (mm Hg)</th>
<th>Oxygen Saturation (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Right atrium</td>
<td>5</td>
</tr>
<tr>
<td>Right ventricle</td>
<td>50/8</td>
</tr>
<tr>
<td>Pulmonary artery</td>
<td>50/28 (mean 36)</td>
</tr>
<tr>
<td>Mean pulmonary artery wedge</td>
<td>26 (v wave = 42)</td>
</tr>
</tbody>
</table>

What is the most appropriate treatment strategy in this patient?

a) Surgical repair of the ventricular septum  
b) Surgical repair or replacement of the mitral valve  
c) Pericardiocentesis  
d) Thrombolytic therapy  
e) Direct current cardioversion (DCCV)

**Answer and Discussion**

The answer is b.

**Objective:** Diagnose and treat mechanical complications of acute MIs.

The board examination will likely ask you to diagnose and treat all of the mechanical complications of acute MI. The mechanical complications associated with acute MI include ventricular septal defect, rupture of free wall of the left ventricle, right ventricular infarction, and papillary muscle rupture with acute MR. The characteristic holosystolic murmur and presence of atrial fibrillation (acute left atrial dilatation) point toward papillary muscle rupture, which is a true cardiac surgical emergency. The triad of right ventricular infarction includes hypotension, elevated jugular venous pressure, and clear lung fields on auscultation.

Dressler syndrome is an autoimmune reaction with resultant pericarditis weeks after MI. The hemodynamics do not demonstrate diastolic equalization, and therefore, cardiac tamponade is excluded, and pericardiocentesis is the wrong choice. The EKG failed to show recurrent ST elevation; therefore, reinfarction or infarct extension is less likely, and a trip to the catheterization laboratory or thrombolysis is not warranted. Atrial fibrillation is likely related to the acute LA stretch from acute MR and should correct with surgical repair. DCCV will likely not revert the rhythm long-term and will not change the hemodynamics.

**Question 56**

A 32-year-old previously healthy woman has experienced four recurrent episodes of transient ischemic attacks (TIAs) with right hemiparesis and dysarthria. She is on no medications. Her physical examination, laboratory evaluation (including coagulation studies), and carotid ultrasound are all within normal limits. Her transesophageal echo (TEE) reveals a patent foramen ovale (PFO) and no aortic arch atheroma. Which of the following is most likely responsible for her symptoms?

a) Endocarditis  
b) Atrial myxoma  
c) Atrial dysrhythmias  
d) Munchausen syndrome by proxy  
e) Paradoxical emboli

**Answer and Discussion**

The answer is e.

**Objective:** Identify a PFO as a possible cause of cryptogenetic transient ischemic attack / cerebrovascular accident.

This young woman has had recurrent neurologic events with an essentially negative workup and cryptogenic TIAs. The most common indication for ordering a TEE is to rule out a cardiac source of emboli. PFO is present in about 25% to 30% of the general population. It is not entirely clear if the presence of PFO is a definite cause, a major contributing factor, or an innocent bystander in this case. Because of the seriousness of recurrent neurologic event(s), most experts will refer the patient for PFO closure, using either a percutaneous or surgical approach. The clinical findings and absence of vegetations on TEE rule out endocarditis and atrial myxoma. Atrial fibrillation should be in the differential diagnosis. No history of palpitations is present, and objective evidence of arrhythmias, such as from an abnormal EKG or Holter findings, is also not present; therefore, atrial dysrhythmias would not be the best answer.

**Question 57**

A 46-year-old woman presents with acute inferior wall MI 3 hours within onset of chest pain, sinus bradycardia of 36 beats/minute, and BP of 92/70 mmHg. She received aspirin, clopidogrel, immediate reteplase (r-PA), and heparin. She complains of lightheadedness. Which of the following therapeutic strategies should be implemented next at the bedside?

a) Tirofiban  
b) Atropine and transcutaneous pacing  
c) Nitroglycerine  
d) Metoprolol  
e) Magnesium

**Answer and Discussion**

The answer is b.

**Objective:** Understand the treatment of symptomatic bradycardia.

Nitroglycerin is wrong because of borderline systolic pressure and lack of active chest pain. Metoprolol will
exacerbate the patient’s bradycardia further, which is her primary problem at this time. There is no role for tirofiban in ST elevation MI patients who receive a fibrinolytic. If needed, atropine and transcutaneous pacing are highly effective in raising the heart rate and improving marginal hemodynamics.

**Question 58**

A 76-year-old previously healthy, active man accidentally falls and fractures his right hip at the femoral neck. On review of systems, he denies any cardiovascular symptoms, and he has been able to swim 45 minutes 3 times a week for the past 10 years. His BP is 130/70 mmHg, and his heart rate is regular at 70 beats/minute. Further examination is unremarkable except for right hip swelling and tenderness and immobile right lower extremity. His EKG is normal. Which of the following would you recommend?

a) Proceed with urgent right hip surgery  
b) Cardiac catheterization  
c) Cardiac catheterization  
d) Proceed with urgent right hip surgery with pulmonary artery catheter hemodynamic monitoring  
e) Right lower extremity duplex ultrasound

**Answer and Discussion**

The answer is **a**.

**Objective: Assess preoperative cardiac risk prior to non-cardiac surgery.**

Patients with acute hip fractures are at an increased risk for major morbidity and mortality if their surgical treatment is delayed. This elderly patient is quite active and is free of any cardiovascular symptoms. His EKG is normal; therefore, he is at low risk for perioperative complications. Delaying his surgery by performing various noninvasive tests can potentially harm him. Cardiac catheterization is not indicated and should not be done.

Concomitant hemodynamic monitoring using a pulmonary artery catheter is currently performed very infrequently and is reserved for selected patients with tenuous volume or hemodynamic states; pulmonary artery catheterization would not be indicated in this relatively healthy, active individual. There is no indication for lower extremity duplex to rule out venous thromboembolism, since his unilateral lower extremity swelling is likely related to his hip fracture.

**Question 59**

A 54-year-old white man with a prior medical history of mild hypercholesterolemia, erectile dysfunction treated with sildenafil, hypertension, left lower extremity deep venous thrombosis (DVT) last year, and ongoing tobacco abuse presents to the local emergency department at 8:50 AM complaining of sudden-onset retrosternal chest pressure associated with dyspnea, diaphoresis, and nausea that woke him from sleep 30 minutes prior to arrival. The patient states that he awoke with a sensation of “a belt around my chest,” and his wife called 911 immediately. After the patient is placed into a room, a 12-lead EKG is obtained that reveals sinus tachycardia at 110 beats/minute with an S wave in lead I, a Q wave with T wave inversion in lead III, and 2-mm ST-segment elevation in leads V 2–V 5 with ST depression inferiorly. Vital sign measurement reveals the BP to be 170/100 mmHg, heart rate 110 beats/minute, and pulse oximetry 95% on 2 L of supplemental oxygen by nasal cannula. Physical examination reveals a white man in obvious distress complaining of chest pressure and pain. There is no JVD or carotid bruits noted. The cardiac examination is notable for normal first and second heart sounds with a prominent fourth heart sound noted at the apex. The lungs are clear bilaterally. The abdominal examination is benign. The lower extremities are unremarkable with intact dorsalis pedis pulses noted bilaterally.

**Laboratories:**

- Na: 139 mmol/L  
- K: 3.4 mmol/L  
- Creatinine: 113 mg/dl  
- Glucose: 113 mg/dL  
- Hemoglobin: 12.1 g/dL  
- Hematocrit: 36.2%  
- Platelets: 354,000/µL  
- Total cholesterol: 205 (160 to 200 mg/dL)  
- LDL-C: 157 (100 to 160 mg/dL)  
- HDL-C: 28 (40 to 55 mg/dL)  
- Triglycerides: 135 (100 to 150 mg/dL)  
- CXR: Normal cardiac silhouette, no pulmonary infiltrates or edema

Given that your hospital is 110 minutes away from the nearest tertiary referral center capable of performing emergency procedures, which of the following courses of action is most appropriate at this immediate point in time?

a) Stat spiral CT to assess for pulmonary embolism (PE) and aortic dissection  
b) Administration of full-dose, fibrin-specific IV fibrinolytics  
c) Administer IV nitroglycerin to control chest pain and manage BP  
d) Draw blood for immediate cardiac biomarker assay  
e) Transfer the patient to the tertiary referral center for immediate catheterization

**Answer and Discussion**

The answer is **b**.

**Objective: Identify and treat ACS.**

This patient is presenting with symptoms and clinical findings consistent with an ACS in general and STEMI specifically. Immediate recognition and initiation of a reperfusion strategy is critical for reducing mortality in this patient population. Based on a wealth of data, the cur-
rent ACC/AHA guidelines for the management of STEMI recommend that patients presenting to a facility without the capability of performing expert PCI within 90 minutes of first medical contact should undergo rapid fibrinolysis unless otherwise contraindicated. Specifically, fibrinolysis should be considered in patients who present with symptom onset in the prior 12 hours with ST segment elevation of 0.1 mV in two or more contiguous precordial leads or adjacent limb leads if the option of percutaneous intervention is not immediately available or if the anticipated delay of transferring the patient to the closest facility capable of performing PCI would result in a “door to balloon time” of greater than 90 minutes. Important contraindications to lysis include patients with any known history of intracranial hemorrhage, cerebral abnormalities such as arteriovenous malformation or tumor, ischemic stroke within 3 months, active bleeding diathesis, or aortic dissection.

It has become increasingly commonplace for smaller institutions without PCI capability to transfer patients presenting with STEMI to a nearby tertiary referral center for catheter-based revascularization. This is a reasonable endeavor as long as the goal door to balloon time of less than 90 minutes can be achieved; in many instances, the logistics of patient transfer result in prolonged door to balloon times, which may adversely affect patient outcome.

While it is important to consider an appropriate differential diagnosis for any patient presenting to the ED, in this case, there is no clear evidence of PE (hypotension, hypoxia) or symptoms of aortic dissection; therefore, obtaining a CT to evaluate for PE would only serve to increase the time to reperfusion. In patients presenting with ACS and ongoing chest pain with elevated BP, it is very reasonable to initiate sublingual or IV nitrate therapy. However, it is imperative to ensure that the patient has not recently used an erectile dysfunction agent as is the case with this patient.

Although cardiac biomarker assays are important tools to assess the presence and even the extent of MI, there is no need to wait for positive serum biomarkers to make the diagnosis of STEMI. In fact, awaiting the return of serum biomarkers wastes valuable time that should be used to achieve reperfusion by the appropriate means.

**Question 60**

Following a minor motor vehicle accident, an obese 36-year old woman is seen in the clinic by her primary care physician and given prescription-strength ibuprofen on an as-needed basis to treat musculoskeletal pain. She returns to the clinic 5 days later with complaints of weakness and dizziness. Point-of-care glucose testing reveals a level of 212 mg/dL. An ECG obtained follows.

Which of the following is the next best step in managing the patient’s care?

a) The patient should be placed on a cardiac monitor and transported for emergent inpatient evaluation.

b) She should be referred for emergent hemodialysis to correct her underlying condition.

c) Administer 325 mg of aspirin and arrange for monitored transport to the coronary ICU for treatment of an ACS.

d) Obtain intravenous access and administer one ampule of calcium gluconate because this will help correct the cause of the patient's EKG abnormality.

e) Sodium polystyrene is helpful in managing this condition because it provides safe and rapid correction of this patient's condition.

**Answer and Discussion**

The answer is a.

**Objective:** Identify cardiac sequelae of acute renal injury.

The woman has unrecognized diabetes, and her use of a powerful nonsteroidal anti-inflammatory drug has precipitated acute renal failure. The EKG demonstrates peaking of the T waves throughout the precordium associated with hyperkalemia. She requires urgent measurement and correction of her electrolytes in a hospital setting. Arrhythmias associated with hyperkalemia require prompt and aggressive management, and thus, the patient should be monitored at all times while awaiting definitive therapy. Hyperacute T waves associated with ACSs are typically limited to a single anatomic distribution (i.e., anterior) and are more diffuse on this recording. The administration of intravenous calcium is one of the first recommended steps in the management of hyperkalemia. However, it does nothing to correct hyperkalemia but, instead, serves to stabilize myocardial membrane and reduce the incidence of arrhythmia. Sodium polystyrene (Kayexalate) works by binding potassium in the stool, and although it is an effective measure to reduce total-
body potassium, its actions take several hours to become significant. Either intervention should be done as an inpatient with cardiac monitoring.

**Question 61**

A 58-year-old female elementary school teacher presents to the ER for evaluation following a 30-minute period of dysarthria and tingling in her left arm and thigh. Neurologic examination demonstrates complete resolution of symptoms, and CT of the head without contrast is normal. Electrocardiography reveals rate-controlled atrial fibrillation with a rate of 95. Review of systems reveals a 3-week history of fever and unintentional 10-lb weight loss. A transthoracic ECHO (TTE) demonstrates a 1.5 x 2.0 cm pedunculated intracardiac mass consistent with a myxoma. All of the following statements about this patient’s condition are true, except:

a) Embolic stroke is an uncommon presentation of myxoma due to its right-sided predominance.

b) Constitutional symptoms are common likely due to increased production of cytokines.

c) Myxomas are the most common primary cardiac tumor and are found predominantly in the atria.

d) Symptoms of heart failure due to flow obstruction are frequently associated with larger masses.

e) Rare genetic disorders have been associated with familial cases of myxoma.

**Answer and Discussion**

The answer is a.

**Objective:** Identify the presentation of cardiac myxoma as a cause for TIA/stroke.

Stroke due to tissue or thrombus embolization to the cerebral circulation is unfortunately one of the most common presenting symptoms of cardiac myxoma. The most common site of tumor insertion is the left atrium, and 85% of myxomas occur on the left side of the heart. Constitutional symptoms, such as fever, weight loss, rash, arthralgia, or altered mental status, have been attributed to increased levels of IL-6. Heart failure does occur when tumors achieve sufficient mass to cause outflow obstruction, usually at the level of the mitral valve. Familial myxomas represent a minority of cases and are typically associated with spotty pigmentation of the skin and endocrine disorders.

**Question 62**

A 43-year-old woman is transferred from oncology to the ICU for hypotension and chest pain. The chest pain is sharp, nonradiating, and associated with dyspnea. She has a history of recently diagnosed advanced breast cancer, already underwent radiation therapy, and is scheduled to initiate chemotherapy. She denies any headaches, fevers, chills, or rigors. There are no GI or genitourinary symptoms. She also reports some lightheadedness and palpitations.

**Physical examination:**

- Heart rate = 120 beats/minute, BP = 98/60 mmHg, respiratory rate = 20 breaths/minute, hemoglobin saturation is 98% on 2 L of oxygen
- Neck vein examination reveals elevated jugular venous pressure, preserved “x” descent, and absent “y” descent
- Carotid pulse is palpable
- Heart examination reveals tachycardia with decreased cardiac sounds
- Lung examination reveals decreased breath sounds at the bases
- Abdominal examination is unremarkable
- Lower extremities show no evidence of swelling

On further examination, it is noticed that the systolic BP decreases by about 19 mmHg during inspiration. ECG shows sinus tachycardia, nonspecific ST segment and T wave changes, and electrical alternans in the rhythm lead. The CXR reveals increased cardiac size and small bilateral pleural effusions.

**What is the most likely diagnosis?**

- a) Constrictive pericarditis
- b) Congestive heart failure due to LV systolic dysfunction
- c) Restricted cardiomyopathy
- d) Cardiac tamponade

**Answer and Discussion**

The answer is d.

**Objective:** Review the usefulness of neck veins in distinguishing among the various cardiac etiologies of hypotension.

When visible, the normal jugular venous pulse is composed of an initial “a” wave (positive deflection) that represents the atrial systole, followed by an “x” descent (negative deflection) that represents atrial relaxation (a positive deflection on the “x” descent, designated the “c” wave), represents upward annular motion during ventricular contraction). The “x” descent is followed by a “v” wave (positive deflection) that represents right atrial filling. The final component of the jugular venous pulse is a “y” descent (negative deflection) that represents right ventricular diastolic filling after opening of the tricuspid valve. Constrictive pericarditis and restrictive cardiomyopathy are associated with elevated jugular venous pressure and a rapid “y” descent due to rapid right ventricular filling in diastole. Congestive heart failure, especially if associated with severe tricuspid valve regurgitation, may be associated with both elevated jugular venous pressure and a rapid “y” descent. Cardiac tamponade is associated with a blunted or absent “y” descent due to abnormal right ventricular filling caused by elevated pericardial pressure. The history of breast cancer and presence of paradoxical pulse (decrease in systolic BP of >15 mmHg with inspiration), electrical alternans on the ECG, and increased cardiac silhouette on the CXR also point toward cardiac tamponade.
Question 63

A 32-year-old woman with a history of congenital heart disease presents to clinic with exertional dyspnea. A murmur that increases with handgrips and decreases with inspiration is heard. Based on the history and examination, a ventricular septal defect is suspected. Which of the following statements about dynamic auscultatory maneuvers is incorrect?

a) In general, right-sided heart murmurs and sounds increase with inspiration, and left-sided murmurs and sounds decrease with inspiration.
b) Prompt squatting increases the murmur of AR.
c) Leg raise increases the murmur of HOCM.
d) Amyl nitrite increases the murmur of MS and decreases the Austin Flint murmur.

Answer and Discussion

The answer is c.

Objective: Identify dynamic maneuvers used to distinguish among various systolic and diastolic cardiac sounds and murmurs.

The maneuvers are intended to alter the preload or the afterload of the heart and observe for any changes that may occur with the specific cardiac sounds or murmurs. In general, right-sided heart murmurs and sounds increase with inspiration; this occurs because, in inspiration, there is increased blood return to the right side of the heart. Left-sided murmurs and sounds decrease with inspiration for two reasons: the increased filling of the right ventricle pushes the septum toward the left ventricle compromising its filling, and with inspiration, more blood stays behind in the lungs, leading to decreased venous return to the left ventricle. Prompt squatting causes an increase in afterload, leading to an increase in the diastolic murmur of AR. Amyl nitrite decreases preload and afterload and results in tachycardia. In true MS, tachycardia increases blood flow velocity across the right mitral valve, leading to an increase in the murmur. An Austin Flint murmur is a diastolic murmur caused by the aortic regurgitant column to prematurely close the anterior mitral leaflet (functional MS). Since this murmur is dependent on the amount of AR, decreasing the regurgitant volume by decreasing afterload will cause a decrease in the Austin Flint murmur. Listening to the first heart sound ($S_1$) will also help distinguish between MS and Austin Flint murmurs. In MS, the first heart sound is usually more pronounced. The Austin Flint murmur has a soft first heart sound. Leg raise increases preload, which decreases contractility, leading to a decrease (not an increase) in the murmur of HOCM. Handgrip will increase afterload, thereby decreasing the murmur of HOCM. Finally, the Valsalva maneuver decreases preload, leading to accentuation of the murmur of HOCM.

Question 64

A 45-year-old man presents to establish routine medical care. Other than occasional palpitations and mild anxiety, he has no symptoms. He has no PMH. He is on no medications. Review of systems is unremarkable.

Physical examination:

Vital signs: Heart rate = 70 beats/minute, BP = 125/80 mmHg, respiratory rate = 14 breaths/minute
Neck: No JVD, carotid upstroke is normal
Chest: Clear to auscultation, mild anterior chest deformity
Cardiac: Regular rate, regular rhythm, $S_1$ is normal, $S_2$ is normal, there is no $S_3$. There is a mid-systolic click followed by a 2/6 late systolic murmur that radiates to the base of the heart. The click and murmur become earlier and louder with standing and with the Valsalva maneuver and become softer and later with squatting.

The abdominal and lower extremity examinations are unremarkable.

An ECHO is ordered. What is the most likely diagnosis?

a) MR due to MVP.
b) Aortic stenosis due to bicuspid aortic valve.
c) MS due to rheumatic heart disease.
d) MR due to rheumatic heart disease.

Answer and Discussion

The answer is a.

Objective: Recognize the signs and symptoms of MVP.

This patient’s presentation is most consistent with MVP. Other than the findings on the cardiac examination, he also has evidence of a hyperadrenergic state based on his palpitations and anxiety and has evidence of connective tissue disorder with mild anterior chest deformity. The constellation of cardiac findings of MVP, hyperadrenergic state, and connective tissue disorder is described as floppy valve syndrome. The remaining cardiac valves may also be affected. MVP is diagnosed by careful physical examination. Presence of a mid-systolic click is usually associated with MVP. The click is due to ballooning of part of the valve into the atrium and varies with loading conditions. Aortic stenosis is usually associated with an early systolic click or ejection sound. That click is due to sudden opening of a poorly compliant valve and does not vary with loading conditions. MS has an early diastolic opening snap that may be associated with a click. MR due to rheumatic heart disease may be associated with a mid-to-late systolic murmur and even a click; however, only MR associated with MVP varies with changes in preload such as the Valsalva maneuver (decrease in preload moves the click closer to $S_1$ and the murmur becomes louder) or squatting (increase in preload moves the click to later in systole and makes the murmur more soft). The only other left-sided murmur that increases with the Valsalva maneuver is the systolic ejection murmur of HOCM.

Question 65

A 45-year-old woman presents to your clinic for a routine visit. She denies any symptoms. You perform a thorough physical examination and discover that she has 3/6 holosystolic...
murmur most consistent with MR. Which of the following statements regarding MRs is incorrect?

a) Although vasodilators may decrease the severity of MR, the treatment of severe symptomatic MR is generally surgical.

b) MVP is the most common cause of MR in the United States.

c) The natural history of MVP is frequently benign.

d) The timing of surgical intervention for severe MR is determined solely by the development of symptoms.

**Answer and Discussion**

The answer is d.

**Objective: Describe common features of MR.**

Most MRs in the United States result from MVP, which affects 3% to 5% of the population. Most patients with MVP do quite well without developing heart failure, atrial fibrillation, stroke, or syncope. Only a small proportion of patients develop more severe MR that ultimately may lead to congestive heart failure and arrhythmias. Vasodilator therapy may decrease the severity of MR and delay the need for surgery; however, treatment of severe symptomatic MR is generally surgical. Severe symptomatic MR is an indication for valve surgery; however, because progressive and irreversible deterioration of left ventricle may occur before the onset of symptoms, echocardiography may guide the timing of surgery in asymptomatic patients with a declining EF (<60%) or marked LV dilation (end-systolic LV dimension >45 mm).

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**Question 66**

A 53-year-old white woman with a prior history of hypertension, hyperlipidemia, and diet-controlled type 2 diabetes presents to your office for her annual physical examination. Since her last visit, the patient states that she has developed a "pressure sensation" in the center of her chest that initially was noted only with higher levels of activity (e.g., brisk walking) but is now noted to occur with less activity (e.g., climbing a flight of steps). The patient notes that the sensation is associated with mild dyspnea, diaphoresis, and nausea. The symptoms resolve several minutes after cessation of activity but have been increasing in duration over the past 2 months. She is concerned given her family history of premature cardiac disease in both of her parents and her brother, who underwent triple-vessel bypass last year.

Vital sign measurement reveals her BP to be 150/90 mmHg, heart rate is 85 beats/minute and regular, and the patient's body mass index (BMI) is 42. Physical examination reveals an obese white woman with no xanthelasma or acanthosis noted on skin examination. There is no JVD noted and no carotid bruits. The cardiac examination is notable for normal first and second heart sounds with no gallops or murmurs. The lungs are clear to auscultation bilaterally. The abdominal examination is limited due to her body habitus. The lower extremities are unremarkable except for trace edema bilaterally.

Laboratories:

- Na: 138 mmol/L
- K: 3.6 mmol/L
- BUN: 18 mg/dL
- Creatinine: 0.9 mg/dL
- Glucose: 273 mg/dL
- Hemoglobin: 12.1 g/dL
- Hematocrit: 36.2%
- Platelets: 245,000/µL
- Total cholesterol: 225 (normal: 160 to 200 mg/dL)
- LDL-C: 140 mg/dL
- HDL-C: 40 mg/dL
- TG: 335 mg/dL

Cardiac panel:

- CK: 112 (normal: 30 to 220 U/L)
- CK-MB fraction: 2.4 (normal: 0.0 to 8.8 ng/mL)
- Troponin T: <0.01
- CXR: Normal cardiac silhouette, no pulmonary infiltrates or edema
- EKG: 85 beats/minute, NSR, left axis deviation, evidence of LV hypertrophy, nonspecific ST-T wave changes in the anterior leads

Which of the following strategies is the most appropriate method of evaluating this patient for symptomatic CAD?

a) A TTE
b) An exercise (treadmill) stress test with continuous EKG monitoring
c) A cardiac catheterization
d) An adenosine stress test with nuclear (single-photon emission computed tomography [SPECT]) imaging

**Answer and Discussion**

The answer is c.

**Objective: Identify the appropriate diagnostic work-up for suspected CAD.**

This patient presents with classic symptoms of new-onset exertional angina. Given her large number of risk factors for CAD (hypertension, hyperlipidemia, type 2 diabetes, family history, and obesity) and her clinical presentation, a cardiac catheterization is the most appropriate diagnostic modality to establish the presence of epicardial CAD. While a TTE may demonstrate a focal wall motion abnormality (i.e., hypokinesis) or a reduction in EF due to ischemia or scarring (prior MI), a regular TTE without a stress modality, such as exercise or dobutamine, would not be sensitive or specific enough to be useful for the detection of CAD. Exercise stress testing is a very useful and inexpensive tool for the detection of CAD. However, stress tests using strictly continuous EKG are limited by sensitivity of only 50% in patients with single-vessel disease and about 80% when all three arteries are diseased. Furthermore, approximately 20% of middle-aged women may have a false-positive test. In addition, prognosis can be accurately determined based on the patient’s exertional...
capacity [measured in metabolic equivalents (METs)] during exercise, but not chemical, stress testing. Indications for treadmill stress testing include evaluation of chest pain, prognosis and severity of cardiovascular disease, screening for latent coronary disease, and evaluation of arrhythmias. Contraindications to stress testing include ACS, rapid atrial or ventricular arrhythmias, and severe aortic stenosis. Thus, an exercise (treadmill) stress test would not be the best diagnostic modality. In many circumstances, the vasodilating agent, adenosine, is used to pharmacologically “stress” patients in whom exercise is difficult or unsafe. Infusion of adenosine results in dilatation of normal coronary arteries and allows homogeneous uptake of radiotracer in the myocardium. In diseased vessels with flow-limiting stenoses, there is an inability to further dilate, resulting in “drop out” or decreased delivery of radiotracer to the affected area of myocardium on nuclear (SPECT) imaging. Adding nuclear perfusion imaging technology improves the sensitivity of stress testing to 85% with a specificity of 81%, which is comparable to stress echocardiography. However, given this patient’s history of increasing and progressive anginal symptoms at lower levels of activity in the setting of her medical and family history, there is a very high pretest probability of symptomatic coronary stenosis, and proceeding directly to cardiac catheterization would be the most appropriate next step.

Question 67
A 74-year-old white man with a past history of hypertension, hyperlipidemia, severe osteoarthritis of the knees, and a 40-pack-year habit of cigarette smoking complicated by severe COPD presents to your office complaining of a sharp, stabbing chest pain that he states has been increasingly worse over the past 3 weeks since the resolution of an upper respiratory infection. The patient states that the pain is aggravated by deep inspiration and elevation of his left arm. However, the patient also notes that the symptoms seem to be provoked by walking up the flight of steps in his home. The last time he noted the sensation, his neighbor gave him a sublingual nitroglycerin tablet that aborted the attack.

Vital sign measurement reveals BP to be 130/83, heart rate is 95 beats/minute and regular, and the patient’s body mass index (BMI) is 22. Physical examination reveals a thin and undernourished white man in no acute distress. There is no JVD noted; there is a carotid bruit over the left carotid artery. The cardiac examination is notable for normal first and second heart sounds with no gallops or murmurs noted. There are inspiratory and expiratory wheezes noted in the bilateral lungs. The abdominal examination is benign. The lower extremities are unremarkable except for a bruit noted over the left femoral artery.

Which of the following diagnostic modalities would be the most appropriate in order to evaluate this patient for flow-limiting CAD?

a) An exercise (treadmill) stress test with continuous EKG monitoring
b) An adenosine stress test with nuclear (SPECT) imaging
c) A dobutamine stress ECHO
d) A cardiac catheterization

Answer and Discussion
The answer is c.

Objective: Review the indications and contraindications for cardiac functional testing.

This patient presents with a challenging clinical history that has features of both typical and atypical chest pain. While he certainly has risk factors for CAD (hypertension, hyperlipidemia, cigarette smoking, prior stroke, and increased age), his history has several characteristics atypical for cardiac chest pain (pleuritic, reproduced with upper extremity movement). However, given his history and risk for CAD, further risk stratification is required. Exercise stress testing is a very useful and inexpensive tool for the detection of CAD. However, stress tests using strictly continuous EKG are limited by an accuracy of only 50% in patients with single-vessel disease and about 80% when all three arteries are diseased. Chest pain induced by exercise stress testing is strongly predictive of CAD, especially when associated with horizontal or downsloping ST segment depression on the ECG. Exercise-induced hypotension or arrhythmias is also often associated with significant CAD. In addition, prognosis can be accurately determined based on the patient’s exertional capacity [measured in metabolic equivalents (METs)] during exercise, but not chemical, stress testing. Indications for treadmill stress testing include: evaluation of chest pain, prognosis and severity of cardiovascular disease, screening for latent coronary disease, and evaluation of arrhythmias. Contraindications to stress testing include ACS, rapid atrial or ventricular arrhythmias, and severe aortic stenosis. However, given the fact that this patient has severe COPD and arthritis, it is doubtful that he would be able to achieve the needed 85% of maximal predicted heart rate necessary to perform a satisfactory stress test; thus, an exercise (treadmill) stress test would not be the best diagnostic modality.

In many circumstances, the vasodilating agent, adenosine, is used to pharmacologically “stress” patients in whom exercise is difficult or unsafe. Infusion of adenosine results in dilatation of normal coronary arteries and allows homogeneous uptake of radiotracer in the myocardium. In diseased vessels with flow-limiting stenoses, there is an inability to further dilate, resulting in “drop out” or decreased delivery of radiotracer to the affected area of myocardium on nuclear (SPECT) imaging. However, a notable side effect of adenosine infusion is bronchospasm, which is a contraindication in patients with known COPD and wheezing. Therefore, an adenosine stress test would not be appropriate. Adding nuclear perfusion imaging technology improves the sensitivity of stress testing to 85% with a specificity of 81%. Using stress echocardiography, the diagnosis of ischemia is related to the development of a detectable wall motion abnormality during either exercise or infusion of dobutamine for those patients unable to exercise. Findings suggestive of ischemia include LV dilatation, a decrease in EF, and most specifically,
a lack of endomyocardial wall thickening. When performed in experienced centers, stress echocardiography has a sensitivity of 85% with a specificity of 81%, which is similar to nuclear perfusion imaging. Therefore, a dobutamine stress ECHO would be most appropriate in this patient.

**Question 68**

A 72-year-old African American woman with a history of peptic ulcer disease complicated by recent upper GI bleed and CAD with placement of two DES in the LAD coronary artery 3 months ago presents to your clinic noting a heavy sensation in her chest that began 2 hours prior to arrival. A brief interview reveals that the patient was told to discontinue her clopidogrel therapy that was prescribed to her after her revascularization due to the development of the above noted GI bleed. The patient states that she complied with the instructions and was doing well for the past several weeks, until this morning when the chest pain began. After the patient is placed in a room, a 12-lead EKG is obtained that reveals NSR at 80 beats/minute with 4-mm ST segment elevation in leads V5–V6 with reciprocal ST depression noted in the inferior leads. Vital sign measurement reveals BP to be 110/64 mmHg, heart rate is 80 beats/minute, and pulse oximetry is 95% on 2 L of supplemental oxygen by nasal cannula. Physical examination reveals a well-nourished African American woman in moderate distress complaining of chest pressure and pain. There is no JVD, and no carotid bruits are noted. The cardiac examination is notable for normal first and second heart sounds with a prominent fourth heart sound noted at the apex. The lungs are clear bilaterally. The abdominal examination is benign. The lower extremities are unremarkable with intact dorsalis pedis pulses noted bilaterally.

**Labs:**

- Na: 141 mmol/L
- K: 4.1 mmol/L
- BUN: 12 mg/dL
- Creatinine: 0.8 mg/dL
- Glucose: 126 mg/dL
- Hemoglobin: 11.1 g/dL
- Hematocrit: 33.3%
- Platelets: 185,000/µL
- Total cholesterol: 245 (normal: 160 to 200 mg/dL)
- LDL-C: 170 (normal: 100 to 160 mg/dL)
- HDL-C: 54 (normal: 40 to 55 mg/dL)
- Triglycerides: 125 (normal: 100 to 150 mg/dL)

Which of the following courses of action is most appropriate at this immediate point in time?

**Answer and Discussion**

**Objective:** Recognize and manage acute stent thrombosis in setting of cessation of dual antiplatelet therapy.

This patient is presenting with symptoms and clinical findings consistent with an ACS in general and STEMI specifically. In this case, it is important to recognize that the patient is at high risk of stent thrombosis due to the fact that she was recently treated for CAD with two DES in the LAD (the arterial distribution represented on the previously noted EKG) and was advised to discontinue taking her clopidogrel therapy due to recent GI bleed. An important consideration when dealing with patients who have recently undergone DES implantation is that maintenance of dual antiplatelet therapy is essential for at least the first and premature cessation of antiplatelet therapy places such patients at an increased risk for stent thrombosis due to incomplete endothelialization of the stent in the short term. Just as with non-stent-related ACS, immediate recognition and initiation of a reperfusion strategy is critical for reducing mortality in this patient population.

While fibrinolytic therapy has been shown to be a safe and effective method of reperfusion, it is critical to carefully evaluate the patient for contraindications, which in this case exist in the form of recent GI bleed.

While cardiac biomarker assays are important tools to assess the presence and extent of MI, there is no need to wait for positive serum biomarkers to make the diagnosis of STEMI. In fact, awaiting the return of serum biomarkers wastes valuable time that should be used to achieve reperfusion by the appropriate means.

**Question 69**

A 62-year-old man presents to your office for routine medical evaluation. He reports having been in excellent health, and his PMH is significant only for hypertension and a heart murmur. He denies any symptoms at this time, including dyspnea, chest discomfort, palpitations, and orthopnea.

**Physical examination:**

He is in no acute distress.

BP is 160/50 mmHg, and heart rate is 70 beats/minute. A bisferiens pulse is noted at the femoral arteries, and the extremity pulses are brisk.

Neck examination reveals normal jugular venous pulsations. The apical cardiac impulse is displaced laterally and is hyperdynamic. Cardiac auscultation reveals a regular rhythm with a holodiastolic murmur heard best at the left sternal border in the third and fourth intercostal spaces. There is also a late diastolic rumble at the apex.

The lungs are clear to auscultation. The extremities show no edema.

You refer the patient for TTE. The ECHO shows mildly reduced LV systolic function with an EF of 45%, severe AR,
and a severely dilated LV cavity (end-systolic diameter of 60 mm). Which of the following is the best approach to manage this patient?

a) Begin vasodilator therapy with an ACE inhibitor and repeat an ECHO in 6 months
b) Refer the patient for surgical evaluation for aortic valve replacement
c) Start β-blocker therapy and reassess the patient in 6 months
d) Reassure the patient that the natural history of AR is usually benign and reassess in 6 months

**Answer and Discussion**

The answer is b.

**Objective: Understand the management of chronic AR.**

This patient’s case illustrates many of the difficulties of evaluating patients with chronic AR. Based on the physical examination and ECHO, it is clear that the patient has severe AR. The apical murmur represents an Austin Flint murmur, which is common in severe AR. However, the patient reports none of the typical symptoms of dyspnea, fatigue, or orthopnea. Unlike acute AR, chronic AR imposes a gradually increasing volume load on the left ventricle, resulting in progressive LV dilatation followed by interstitial fibrosis and eventually heart failure. Patients often remain asymptomatic for decades and may only present after the fourth or fifth decades, when signs of cardiomegaly and myocardial dysfunction have already occurred, as in this case. The ECHO in this case indicates a reduced EF of 45% with severe LV dilatation. Both of these findings are suggestive of fairly advanced AR, and studies have suggested that patients with subnormal EF (EF ≤ 50%) or a dilated LV cavity [end-systolic diameter (ESD) > 55 mm or end-diastolic diameter (EDD) > 75 mm] are at high risk for progression to cardiac symptoms and mortality. Accordingly, the relatively low EF and dilated LV give this patient a class I indication for aortic valve replacement according to the most recent ACC/AHA practice guidelines (2006).

Therapy with vasodilating agents is designed to improve forward stroke volume and reduce regurgitant volume. In asymptomatic patients with normal EF, vasodilator therapy with hydralazine or ACE inhibitors can be considered, although results from trials of these agents in patients with AR have been mixed. However, vasodilator therapy is not appropriate for long-term therapy in a patient who already demonstrates impairment in EF and severe LV dilatation.

β-Blockers are contraindicated in patients with severe AR because they can depress LV function and prolong the LV diastolic filling period, thereby increasing regurgitant volume.

While the natural history of AR is indeed relatively benign in its early stages, the onset of LV dysfunction and cavity dilatation are markers for worse outcome, and observation is not appropriate once these features are present.

**Question 70**

A 40-year-old woman presents to you for evaluation of a cardiac murmur first noted several years ago. She denies any symptoms but has not been very active. She was born in Mexico and reports having had a febrile illness in childhood. She has otherwise been healthy and reports no additional PMH.

**Physical examination:**

She is in no acute distress
BP is 120/60 mmHg, and heart rate is 75 beats/minute
Neck examination reveals normal carotid pulsations and jugular venous pulsations
Her cardiac examination reveals a regular rhythm and a nondisplaced point of maximal impulse. There is a pronounced S1, a prominent P2, and an early diastolic sound followed by a low-pitched rumbling holodiastolic murmur at the apex.

**Her lungs are clear to auscultation**

The extremities show no edema and normal peripheral pulses

A TTE is performed and reveals moderate MS with a valve area of 1.4 cm² and pulmonary artery pressure of 35 mmHg. The mitral valve leaflet tips are calcified, but the remainder of the valve is fairly pliable (splitability score = 5). Which of the following would be the appropriate next step in management?

a) Refer the patient for percutaneous balloon mitral valvotomy (PBMV)
b) Order a stress ECHO to assess mitral valve gradients and PA pressure with exercise
c) Refer the patient for mitral valve replacement
d) Begin treatment with a β-blocker and reassess with TTE in 1 year

**Answer and Discussion**

The answer is b.

**Objective: Understand the management of MS.**

As in this patient’s case, rheumatic heart disease is the most common etiology of MS. Pathologically, rheumatic disease is manifested as thickening of the mitral valve leaflets with fusion of the commissures and progressive fibrosis. As the mitral valve area drops from its normal value of 4 to 5 cm² to below 2 cm², a gradient begins to form between the left atrium and left ventricle. With time and further narrowing of the valve, the elevated left atrial pressure will be transmitted to the pulmonary circulation and right heart, producing pulmonary congestion and hypertension, as well as right-sided pressure overload. This patient’s examination and ECHO indicate that she has moderate MS, but she remains ostensibly asymptomatic. Her pulmonary pressure is only mildly elevated at rest, but it is important to pursue exercise testing to ascertain whether she develops severe pulmonary hypertension (pulmonary artery systolic pressure > 60 mmHg) or limitation to exercise. Given her
favorable MV anatomy, these findings would constitute class I indications for PBMV.

Given her degree of MS and lack of physical activity, it would be inappropriate to pursue medical therapy without further testing. If the stress ECHO findings were reassuring (i.e., no significant pulmonary hypertension or elevation in MV gradients), medical therapy with β-blockade and reassessment in 1 year would be reasonable. PBMV would be appropriate only if stress testing showed pulmonary hypertension or poor exercise tolerance. Mitral valve replacement is generally reserved for patients with heavily calcified valves and subvalvular calcification or significant concurrent MR, where PBMV is not feasible and may carry excess risk.

**Question 71**

A 70-year-old man comes to visit you for a routine medical examination. Five years earlier, he underwent aortic valve replacement with a bioprosthetic valve for severe calcific aortic stenosis. His most recent ECHO performed 1 year previously showed normal LV function with a well-seated aortic valve prosthesis, peak transaortic gradient of 20 mmHg, and mean gradient of 12 mmHg. He reports feeling well and denies any symptoms. His PMH is notable for an adenomatous colon polyp removed 3 years previously.

His gastroenterologist recommends a repeat colonoscopy given his history of adenomatous polyps. What is your recommendation regarding IE prophylaxis for this patient’s upcoming colonoscopy?

a) Single dose of amoxicillin (2.0 g) should be taken orally 30 to 60 minutes before procedure.

b) A repeat ECHO should be done and prophylaxis given only if the prosthetic valve shows evidence of degeneration (e.g., stenosis, regurgitation).

c) Routine antibiotic prophylaxis to prevent IE is not necessary for GI tract procedures.

d) Ampicillin (2.0 g IV) and gentamicin (1.5 mg/kg IV) should be administered 30 minutes prior to procedure.

**Answer and Discussion**

The answer is c.

**Objective:** Review the indications for IE prophylaxis.

The revised 2007 guidelines from the American Heart Association represented a dramatic shift in position on IE prophylaxis when compared with prior consensus statements. On careful review of the literature, the AHA committee concluded that bacteremia is far more common from daily activities such as brushing than from dental or other procedures. Given the dearth of data showing that antibiotic prophylaxis significantly reduced the risk of IE, the committee recommended prophylaxis in only a very limited number of situations. Specifically, only patients with prosthetic cardiac valves, prior endocarditis, certain types of congenital heart disease, or cardiac transplantation with valvulopathy now warrant prophylaxis.

The patient in this case does have a prosthetic aortic valve, which places him in a higher risk group for IE. However, the recent guidelines state that IE prophylaxis is not needed for any routine diagnostic genitourinary or GI procedures. Accordingly, antibiotics would not be recommended in this case. While the patient likely does warrant a repeat ECHO to assess his prosthetic valve, the status of the valve has no bearing on the decision to give IE prophylaxis.

**Question 72**

A 40-year-old obese, nulliparous woman is seen for the evaluation of the acute onset of abdominal pain that began shortly after she finished dinner. Her vital signs include a temperature of 38.8°C, BP of 96/58 mmHg, respiratory rate of 26 breaths/minute, and heart rate of 115 beats/minute. She reports moderate to severe abdominal pain in the mid-epigastrium radiating to her back on physical examination. The lungs are clear, and there are no murmurs elicited on auscultation of the precordium. After volume resuscitation with isotonic saline is initiated, the below ECG is obtained.

![ECG Image]

Shortly after this EKG is obtained, she collapses and is returned to sinus rhythm after successful defibrillation of polymorphic ventricular tachycardia. What is the next best step in managing this patient?

a) Conduct a detailed review of her medications to determine whether any could be responsible

b) Obtain intravenous access and administer 4 of g magnesium sulfate

c) Obtain intravenous access and administer 2 amps (180 mg) of calcium gluconate

d) Obtain intravenous access and administer 2 amps (180 mg) of calcium gluconate and 4 g of magnesium sulfate

**Answer and Discussion**

The answer is d.

**Objective:** Identify appropriate management of polymorphic ventricular tachycardia in the setting of electrolyte disturbances.

This woman is presenting with pancreatitis likely due to an entrapped gallstone. The ECG demonstrates a prolonged QT interval likely due to the presence of hypocalcemia. Hypocalcemia accompanies pancreatitis largely due to free fatty acid precipitation of calcium. Given the critical nature of her situation, urgent correction of this problem is required, and a review of her medications is not warranted.

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at this time but certainly should be done after she is stabilized. Hypomagnesemia may also occur in pancreatitis and, unless addressed, may hinder the ability to correct the serum calcium. The preferred agent to correct hypocalcemia is calcium gluconate and, in addition to correcting possible hypomagnesemia in this situation, represents the best course of action.

**Question 73**

A 75-year-old man reports the acute onset of shortness of breath to a 911 operator and is transported to the ER with tachycardia. Upon arrival to the ER, his BP is 112/78 mmHg, and his respiratory rate is 28 breaths/minute. An ECG is obtained, and the results are shown below.

Which of the following statements is most true about the EKG findings?

a) The administration of intravenous adenosine may help with identification of the rhythm.

b) This arrhythmia requires no specific treatment and is associated with situations causing increased sympathetic tone, like pain and fever.

c) The administration of intravenous adenosine will likely terminate the reentrant pathway responsible for the rhythm.

d) This rhythm would respond best to intravenous procainamide loading followed by maintenance therapy.

**Answer and Discussion**

The answer is a.

**Objective:** Understand an approach to supraventricular arrhythmias.

The EKG demonstrates 2:1 atrial flutter with rapid ventricular response. P waves are clearly seen in leads V2–V3 following the QRS complex, confirming the diagnosis. The administration of intravenous adenosine briefly blocks transmission of atrial activity at the level of the AV node, allowing for visualization of the flutter waves that may be buried in the QRS complex. Adenosine may terminate supraventricular reentrant tachycardias but not atrial flutter. Procainamide is useful in the management of both atrial and ventricular tachyarrhythmias, but other medications like β-blockers or non-dihydropyridine calcium channel blockers would likely be the first choice in this situation. Sinus tachycardia is commonly associated with fever and pain but is not shown in this EKG.

**Question 74**

An 82-year-old woman with a history of hypertension, atrial fibrillation, and prior MI with resultant LV dysfunction is admitted to your service through the ER for a 3-day history of shortness of breath and a 15-lb weight gain. Chest radiography demonstrates bilateral pulmonary congestion in the lower lung fields. The patient’s medications include metoprolol 25 mg bid, digoxin 0.125 mg daily, aspirin 81 mg daily, Coumadin as directed, and atorvastatin 40 mg daily. Electrocardiography in the ER demonstrates rate-controlled atrial fibrillation. Laboratories at the time of admission include a sodium of 130, potassium of 4.2, BUN of 38, and a creatinine of 1.3. She is given a dose of intravenous furosemide to treat the presumptive diagnosis of an exacerbation of congestive heart failure. She has diuresis of 4 L over the next 48 hours with a mild rise in her creatinine to 1.6 mg/dL. An ECG is obtained the morning of discharge, and the results follow.
What is the next best step in managing this patient?

a) Schedule an outpatient stress test to assess for myocardial ischemia
b) Cancel her discharge and order cardiac enzymes to assess for myocardial necrosis
c) Cancel her discharge and obtain laboratory analysis of her electrolytes, renal function, and digitalis levels
d) Discharge the patient home with potassium supplementation because hypokalemia can worsen the condition shown on her EKG

**Answer and Discussion**

The answer is c.

**Objective:** Identify cardiac effects of delayed renal clearance of cardiac medications.

The EKG demonstrates prominent digitalis effect with slowing of the ventricular response. This patient's creatinine clearance is significantly reduced, and her baseline digitalis dose was inappropriately high. The acute worsening of her renal function due to diuretic therapy has likely caused an increase in the serum levels of digitalis. The ST changes seen do not represent myocardial ischemia. While hypokalemia can potentiate the effects of digitalis toxicity, she needs to have inpatient monitoring of her renal function and an assessment of her digitalis level prior to discharge.

**Question 75**

You are caring for a 68-year-old woman who was transferred emergently from an outside hospital 3 days ago with an inferior ST elevation MI. Although she presented with a several-day history of chest discomfort, she was taken immediately to the cardiac catheterization laboratory and found to have a completely occluded right coronary artery that was successfully stented with good result. This morning on rounds, she reports the acute onset of dyspnea 20 minutes earlier as she was returning to her bed from the bathroom. On examination, she is tachycardic, with a 3/6 systolic murmur at the apex, and has labored breathing. Urgent chest radiography demonstrates pulmonary congestion of the left lung. Which of the following statements is most correct about the cause of the change in this patient's condition?

a) Ventricular septal rupture frequently occurs between 2 to 5 days following a MI and is most common with right coronary infarcts.
b) Pseudoaneurysm of the lateral wall usually does not require surgical intervention.
c) PE following MI is common with right ventricular involvement and should initially be managed with intravenous fluids.
d) Acute MR from a papillary muscle rupture is a surgical emergency and requires prompt attention to maximize the chances of successful repair.

**Answer and Discussion**

The answer is d.

**Objective:** Understand mechanical complications of acute MIs.

The posteromedial papillary muscle typically receives single blood supply via the right coronary artery and is thus exquisitely susceptible to necrosis. Papillary muscle rupture caused by acute MR complicates approximately 1% of acute MIs. Asymmetry of the regurgitant flow can be a source of differential or unilateral pulmonary congestion as was seen on this patient's CXR. Urgent surgical management is the treatment of choice. Ventricular septal rupture may be accompanied by shortness of breath, but the loud apical murmur and chest radiograph findings would support an alternate diagnosis. Pseudoaneurysm formation does occur following MI, but flow is typically not sufficient to cause a murmur. PE can be a complication of massive right ventricular infarction but would not be associated with the physical findings in this case.
A 52-year-old man is transported to the ER by ambulance after experiencing the acute onset of severe chest pain and shortness of breath while he was watching TV. He is a chronic 1-pack per day smoker with a history of treated hypertension and hyperlipidemia. Physical examination reveals a heart rate of 112 beats/minute and frequent cough. Electrocardiography is performed and reveals a sinus rhythm with nonspecific ST-T wave changes predominantly in the lateral leads. Laboratory analysis in the ER demonstrates a creatine kinase of 154 U/L (normal: 38 to 174 U/L), CK-MB of 4.5 U/L (normal: 0.0 to 8.0 U/L), and troponin T of 0.42 ng/mL (normal: <0.01 ng/mL). CXR is normal. What is next best step in the management of this patient?

a) Administer 325 mg of aspirin, initiate weight-based intravenous heparin bolus and drip and obtain a venous phase contrast-enhanced chest CT to evaluate for PE.

b) Initiate evidence-based treatment of non-ST segment elevation MI including a glycoprotein IIb/IIIa inhibitor and clopidogrel and arrange for admission to the coronary ICU.

c) Administer 325 mg of aspirin, initiate weight-based intravenous heparin bolus and drip, and obtain an arterial phase contrast-enhanced chest CT to evaluate for aortic dissection.

d) Obtain urgent TTE to evaluate for the presence of ventricular dysfunction to appropriately risk stratify the patient before admission for an ACS.

**Answer and Discussion**

The answer is a.

**Objective: Identify noncardiac pathology that can cause chest pain and elevated cardiac biomarkers.**

The patient’s presentation could be consistent with several causes of chest pain and shortness of breath. Admitting the patient to the coronary care unit with evidence-based therapy for an NSTEMI would be appropriate if the diagnosis is confirmed. The history of cough and shortness of breath in addition to the finding of an isolated elevated troponin T should raise the suspicion of PE. Elevations in troponin T frequently accompany PE and are thought to occur due to right ventricular stretching resulting from increased pulmonary vascular resistance. Pursuing the diagnosis of PE would be the next best step because the addition of aggressive antiplatelet therapy is not without risk of serious bleeding. Myocardial necrosis caused by aortic dissection is typically not a subtle finding and represents complete occlusion of a coronary artery by direct extension of the dissection across its ostium and is unlikely in this case. TTE has poor sensitivity for diagnosing PE or aortic dissection and would be unnecessary prior to admission for an ACS.
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