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FOURTH EDITION

QUESTIONS YOU WILL BE ASKED

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THEODORE X. O'CONNELL

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USMLE STEP 2

Fourth Edition

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To Nichole, Ryan, Sean, and Claire.
I love you.

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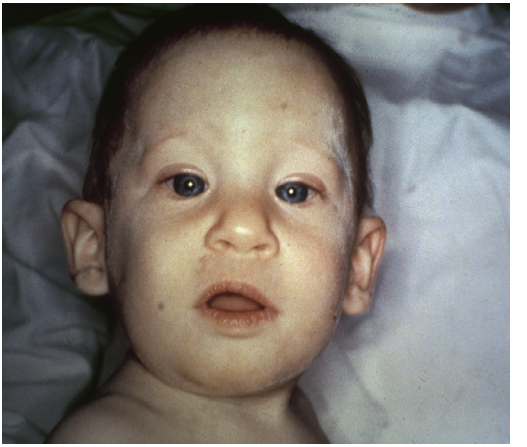


Plate 1. Infant with fetal alcohol syndrome. Note short palpebral fissures, mild ptosis, nostrils, smooth philtrum, and narrow vermillion of the upper lip. See Figure 2-1, p. 26. (From Gilbert-Barness E. Potter's pathology of the fetus, infant, and child, 2nd ed. Philadelphia: Elsevier, 2007, Fig. 4.1.12.)

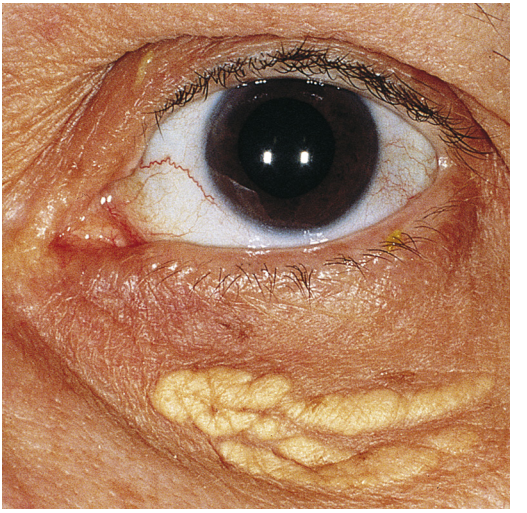


Plate 2. Xanthelasma. Multiple soft, yellow plaques involving the lower eyelid. Xanthelasma is usually a normal finding with no significance but is classically seen on the USMLE because of its association with hypercholesterolemia. Screen affected patients with a fasting lipid profile. See Figure 5-1, p. 52. (From Yanoff M, Duker JS. Ophthalmology, 3rd ed. Philadelphia: Mosby, 2008, Fig. 12-9-18.)

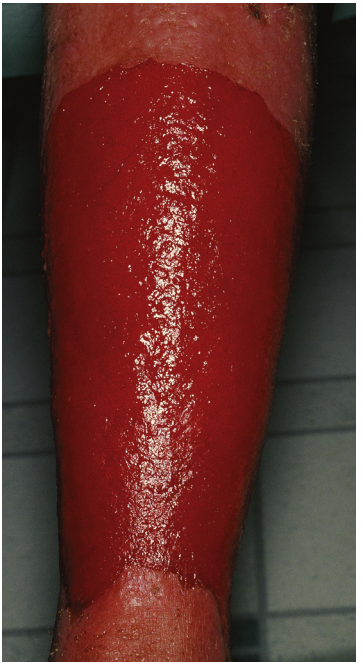


Plate 3. Allergic contact dermatitis of the leg caused by an elastic wrap. Notice the well-marginated distribution that differentiates it from cellulitis. See Figure 6-1, p. 55. (From Auerbach PS. Wilderness medicine, 6th ed. Philadelphia: Mosby, 2011.)

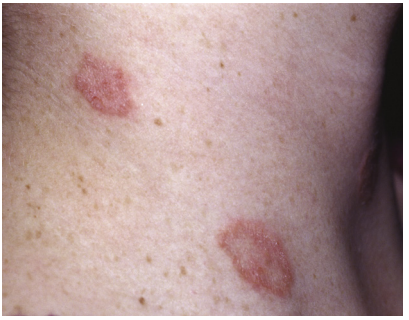


Plate 4. Tinea corporis. Red ring-shaped lesions with scaling and some central clearing. See Figure 6-2, p. 56. (From Kliegman RM. Nelson textbook of pediatrics, 19th ed. Philadelphia: Saunders, 2011.)

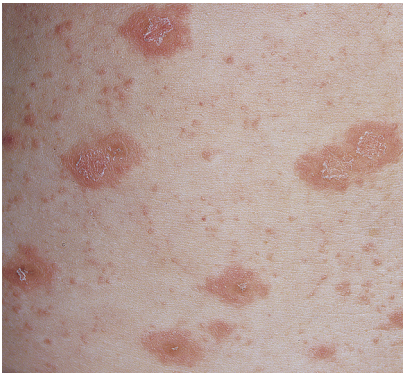


Plate 5. Pityriasis rosea. Small oval plaques as well as multiple small papules are present. See Figure 6-3, p. 59. (From Habif TP. Clinical dermatology, 5th ed. St. Louis: Mosby, 2009.)

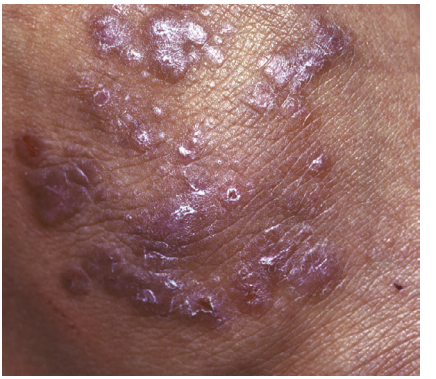
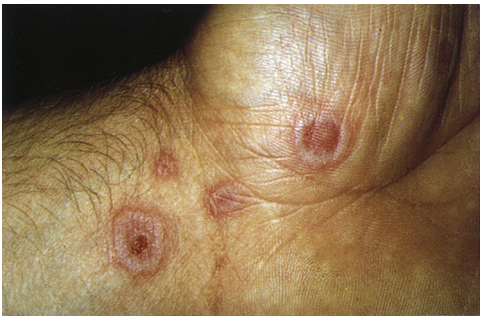


Plate 6. Lichen planus. Flat-topped, purple polygonal papules of lichen planus. See Figure 6-4, p. 60. (From Kliegman RM. Nelson textbook of pediatrics, 19th ed. Philadelphia: Saunders, 2011.)



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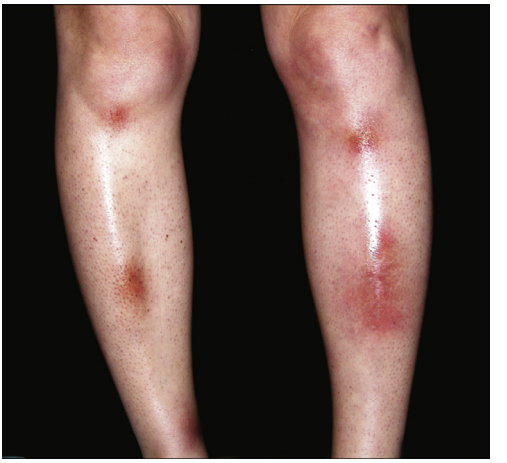

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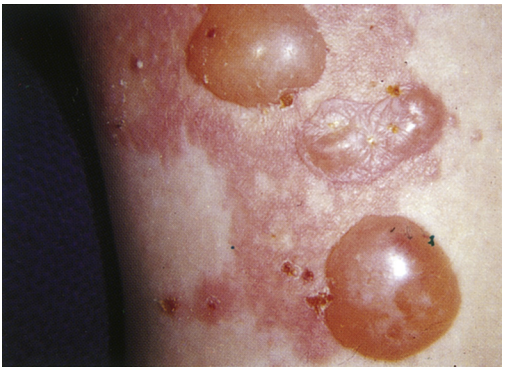

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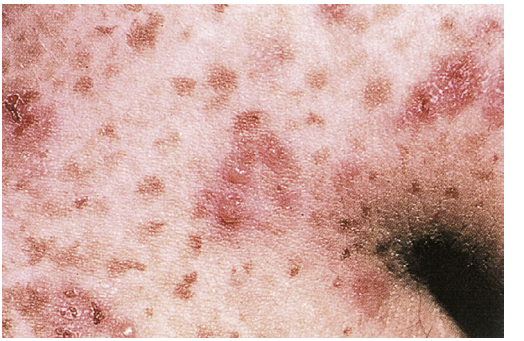

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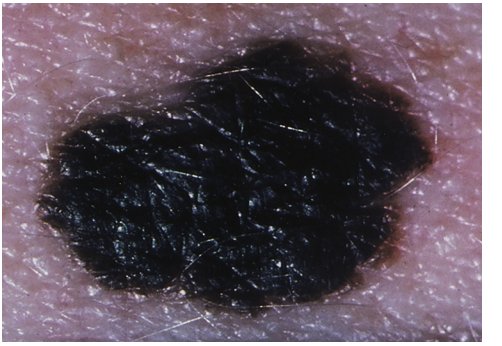

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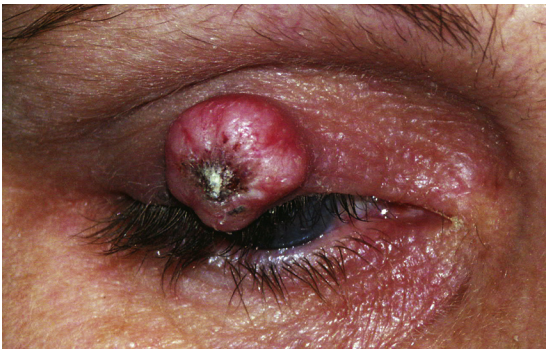

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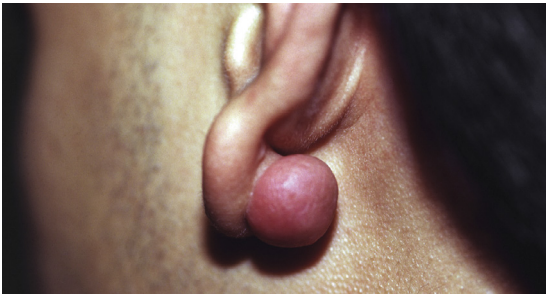

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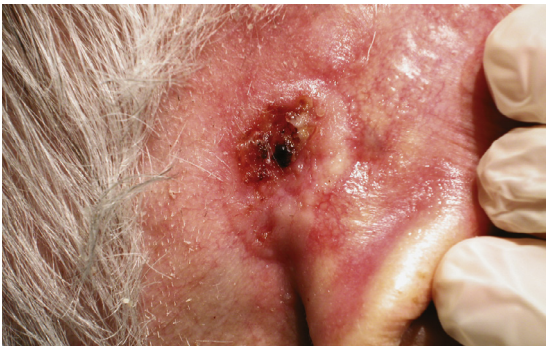

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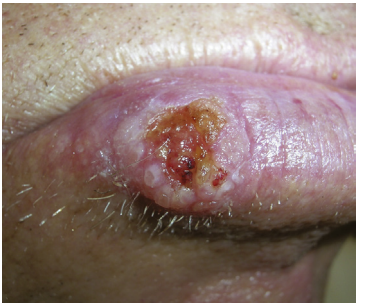

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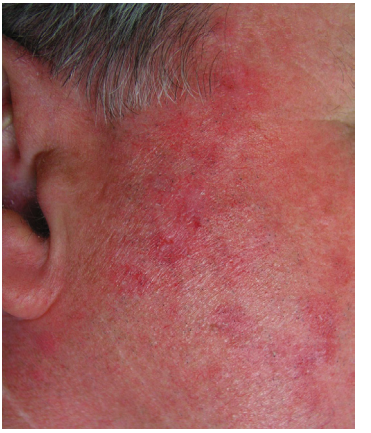

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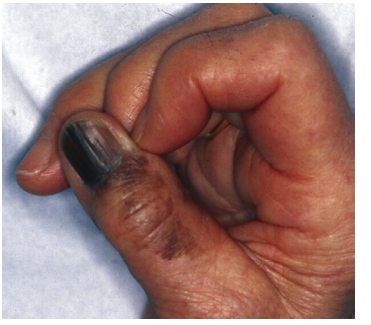

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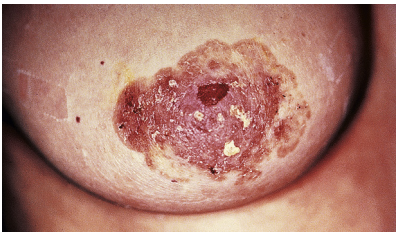

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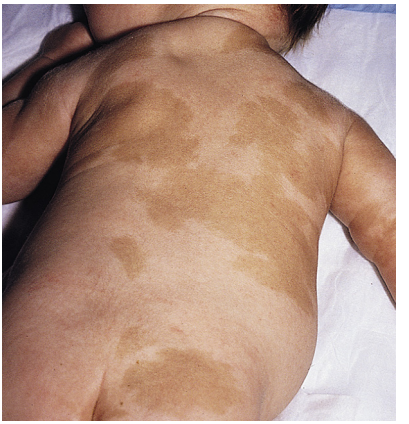

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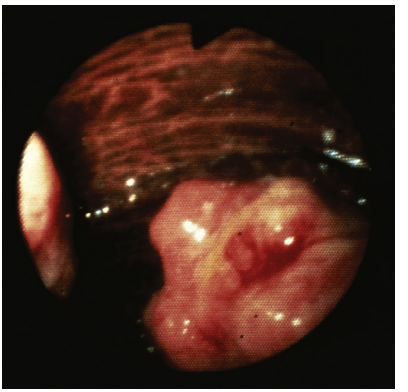

Plate 20. Colonoscopic photograph of a pale colon cancer easily seen against the dark background of pseudomelanosis coli. See Figure 12-3, p. 95. (From Feldman M, Friedman LS, Brandt LJ, eds. Sleisenger and Fordtran's gastrointestinal and liver disease, 9th ed. Philadelphia: Saunders, 2010, Fig. 124-8. Courtesy Juergen Nord, MD, Tampa, Fla.)

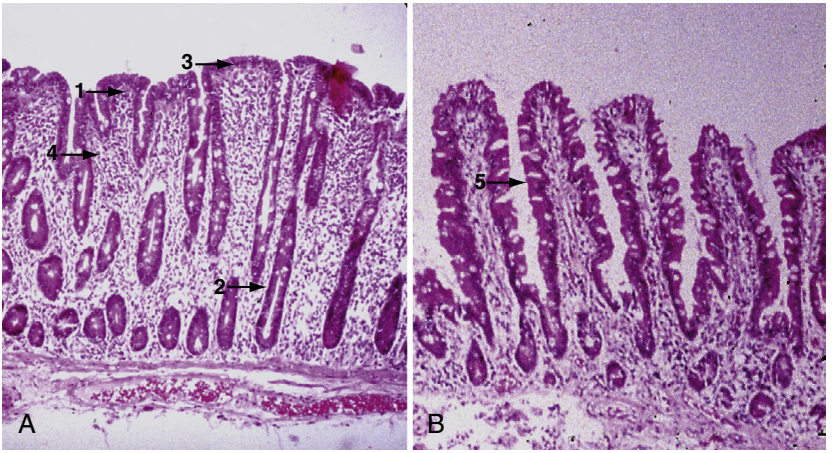

Plate 21. Mucosal pathology in celiac disease. **A,** Duodenal biopsy specimen of a patient with untreated celiac disease. The histologic features of severe villus atrophy *(arrow 1)*, crypt hyperplasia *(arrow 2)*, enterocyte disarray *(arrow 3)*, and intense inflammation of the lamina propria and epithelial cell layer *(arrow 4)* are evident. **B,** Repeat duodenal biopsy after 6 months on a strict gluten-free diet. There is marked improvement, with well formed villi *(arrow 5)* and a return of the mucosal architecture toward normal. See Figure 12-5, p. 97. (From Feldman M, Friedman LS, Brandt LJ. Sleisenger and Fordtran's gastrointestinal and liver disease, 9th ed. Philadelphia: Saunders, 2010, Fig. 104-2.)

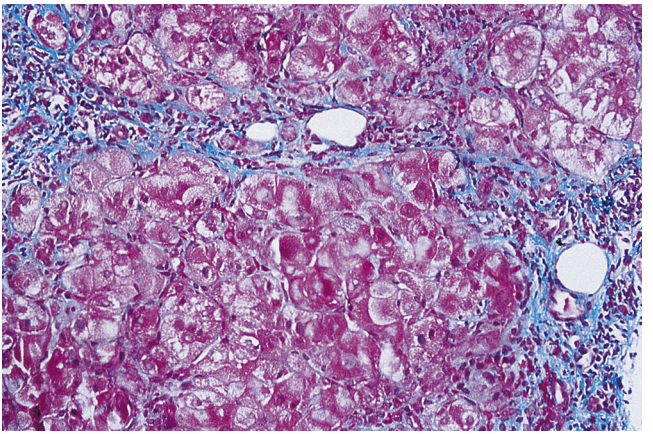

Plate 22. Chronic viral hepatitis. Portal-portal bridging fibrosis is seen in longstanding chronic hepatitis C. See Figure 12-8, p. 102. (From Odze RD, Goldblum JR. Surgical pathology of the GI tract, liver, biliary tract, and pancreas, 2nd ed. Saunders, 2009, Fig. 38-10.)

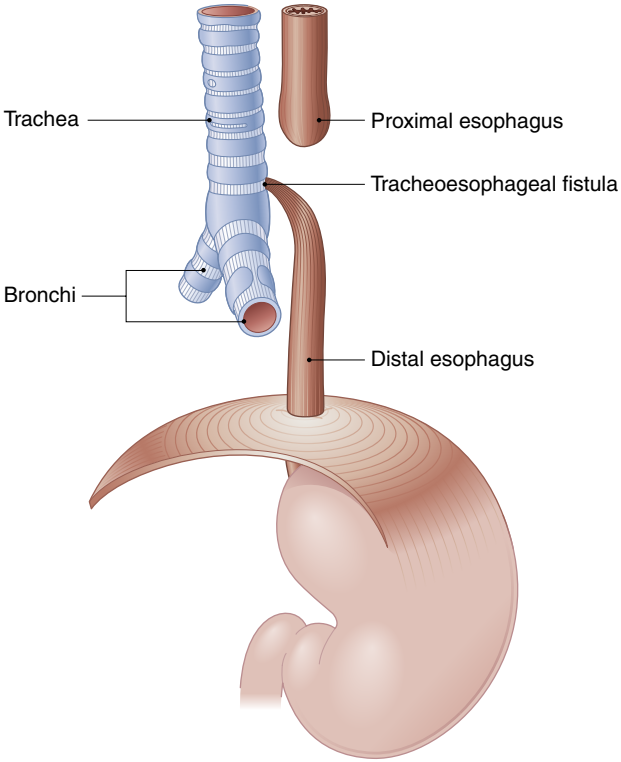

Plate 23. Tracheoesophageal fistula. Diagram of the most common type of esophageal atresia and tracheoesophageal fistula. See Figure 12-11, p. 108. (From Gilbert-Barness E. Potter's pathology of the fetus, infant and child, 2nd ed. Philadelphia: Mosby, 2007, Fig. 25.6.)

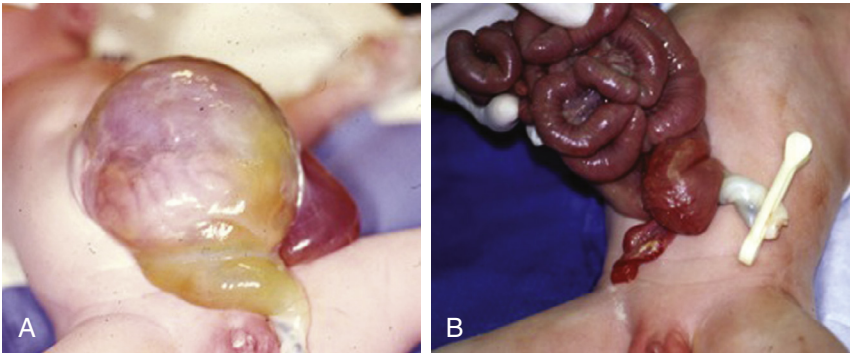

Plate 24. Abdominal wall defects. **A,** Omphalocele with intact sac. **B,** Gastroschisis with eviscerated multiple bowel loops to the right of the umbilical cord. See Figure 12-13, p. 110. (From Sabiston DC, Townsend CM. Sabiston textbook of surgery: the biological basis of modern surgical practice, 19th ed. Philadelphia: Saunders, 2012, Fig. 67-20.)

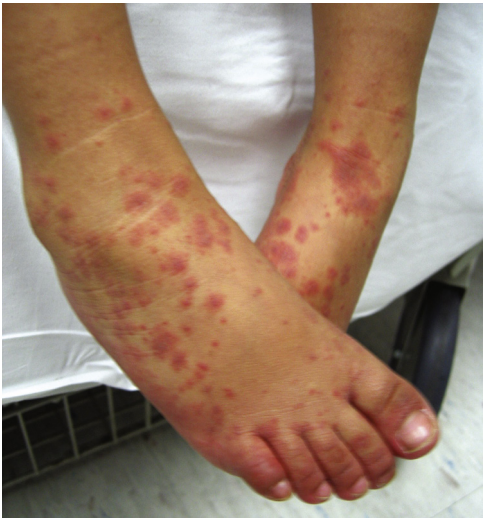

Plate 25. Henoch-Schönlein purpura in a 7-year-old child. Note typical red-purple rash on the lower extremities. See Figure 12-14, p. 111. (From Marx JA, Hockberger RS, Walls RM. Rosen's emergency medicine: concepts and clinical practice, 7th ed. Mosby, 2009, Fig. 170-10. Courtesy Marianne Gausche-Hill, MD.)

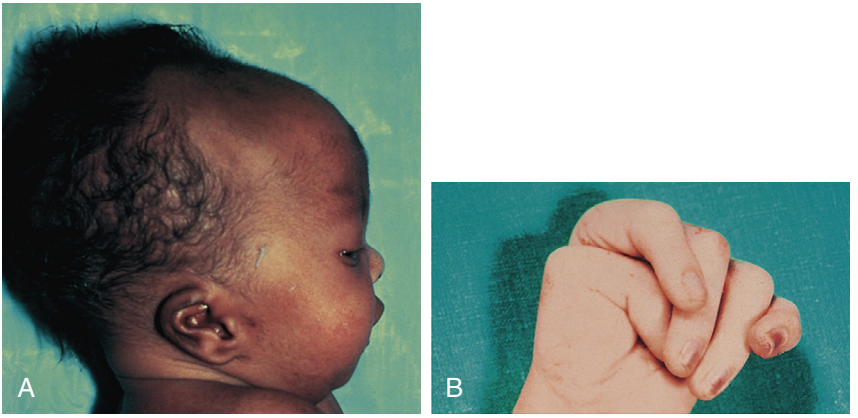

Plate 26. Edward syndrome. **A,** Note the small head, prominent occiput, and low-set, malformed ears. **B,** Clenched hand with overlapping fingers. See Figure 14-2, p. 127. (Kanski JJ. Clinical diagnosis in ophthalmology, 1st ed. Philadelphia: Mosby, 2006, Fig. 15.10. Courtesy BJ Zitelli and HW Davis).

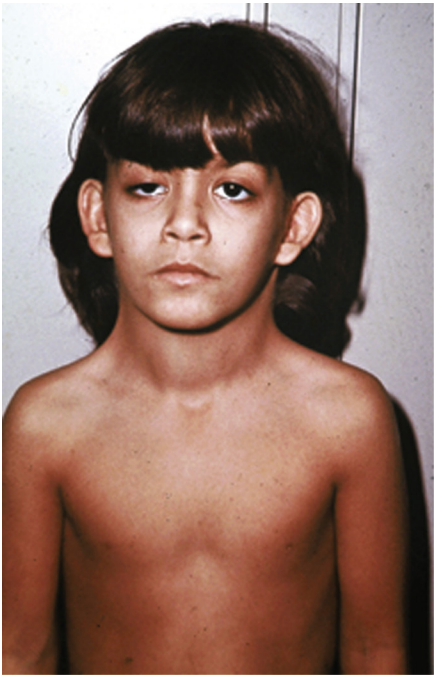

Plate 27. Turner syndrome. This 13-year-old female demonstrates the classic webbed neck and triangular facies of Turner syndrome. She has sexual infantilism and short stature. See Figure 14-3, p. 128. (Moshang T, ed. Pediatric endocrinology: the requisites in pediatrics, 1st ed. St. Louis: Mosby 2005, Plate 8-2.)

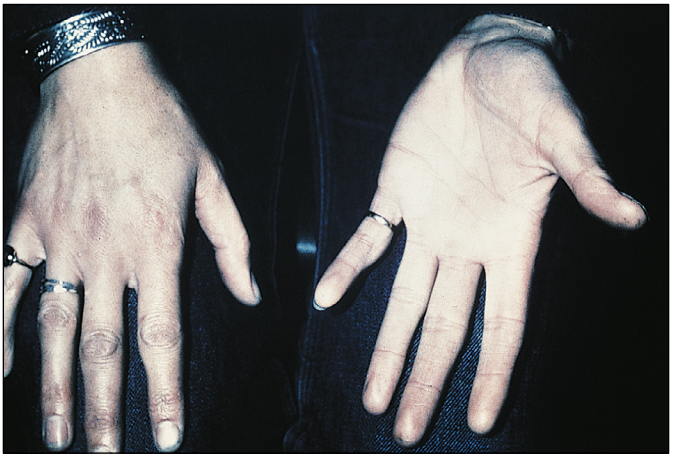

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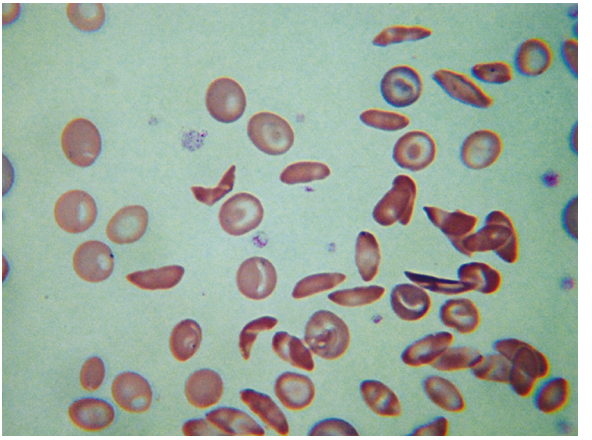
Plate 29. Pigment gallstones within an otherwise unremarkable gallbladder are a marker for hemolytic anemia. See Figure 17-1, p. 145. (From Kumar V, Abbas AK, Fausto N, Aster JC. Robbins and Kotran pathologic basis of disease, professional edition, 8th ed. Philadelphia: Saunders, 2009, Fig. 18-53.)



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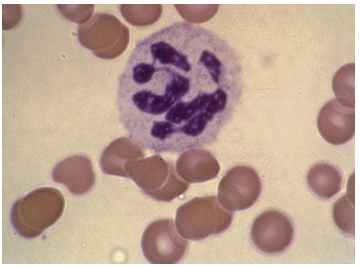

Plate 31. Megaloblastic changes of macrocytosis and a hypersegmented neutrophil. See Figure 17-3, p. 146. (From Rakel RE, Rakel DP. Textbook of family medicine, 8th ed. Philadelphia: Saunders, 2011, Fig. 39-4; The American Society of Hematology Image Bank image #2611. Copyright 1996 American Society of Hematology, used with permission.)

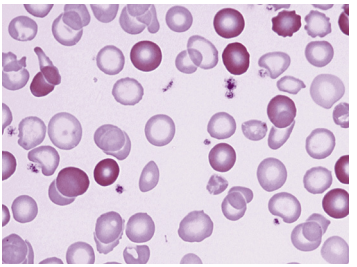

Plate 32. Iron-deficiency anemia. Pale red blood cells with enlarged central pallor. See Figure 17-4, p. 146. (From McPherson R, Pincus M. Henry's clinical diagnosis and management by laboratory methods, 21st ed. Philadelphia: Saunders, 2006, Fig. 31-2.)

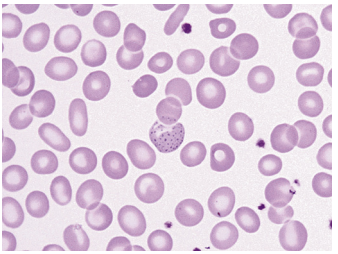

Plate 33. Basophilic stippling. Irregular basophilic granules in red blood cells; often associated with lead poisoning and thalassemia. See Figure 17-5, p. 147. (From McPherson R, Pincus M. Henry's clinical diagnosis and management by laboratory methods, 21st ed. Philadelphia: Saunders, 2006, Fig. 29-23.)

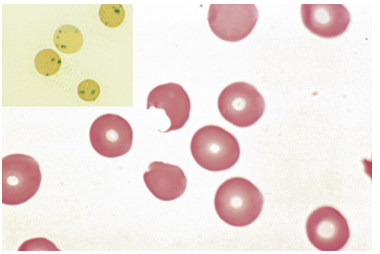

Plate 34. Bite cells with Heinz bodies. See Figure 17-6, p. 147. (Courtesy Dr. Robert W. McKenna, Department of Pathology, University of Texas Southwestern Medical School, Dallas, Texas.)

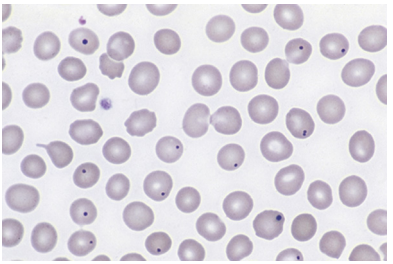

Plate 35. Howell-Jolly bodies in peripheral blood erythrocytes. These nuclear remnants indicate lack of splenic filtrative function. See Figure 17-7, p. 148. (From Orkin SH, et al. Nathan and Oski's hematology of infancy and childhood, 7th ed., Philadelphia: Saunders, 2009, Fig. 14-4.)

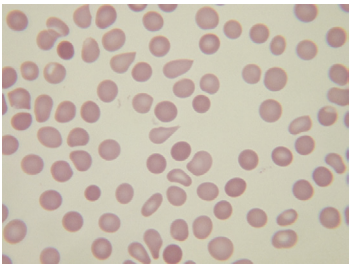

Plate 36. Teardrop red blood cells, usually seen in myelofibrosis. See Figure 17-8, p. 148. (From Goldman L, Ausiello D. Cecil medicine, 23rd ed. Philadelphia: Saunders, 2008, Fig. 161-13.)

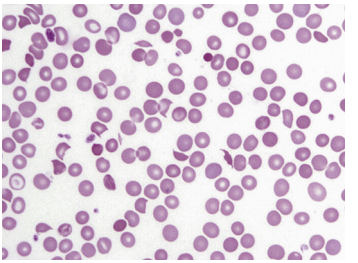

Plate 37. Schistocytes and helmet cells. Red blood cell fragments seen with microangiopathic hemolytic anemia and disseminated intravascular coagulation. See Figure 17-9, p. 148. (From McPherson R, Pincus M. Henry's clinical diagnosis and management by laboratory methods, 21st ed. Philadelphia: Saunders, 2006, Fig. 29-19.)

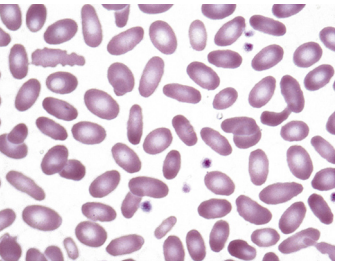

Plate 38. Hereditary elliptocytosis. Blood film reveals characteristic elliptical red blood cells. See Figure 17-10, p. 149. (From McPherson RA, Pincus MR. Henry's clinical diagnosis and management by laboratory methods, 22nd ed. Saunders, 2011, Fig. 30-16.)

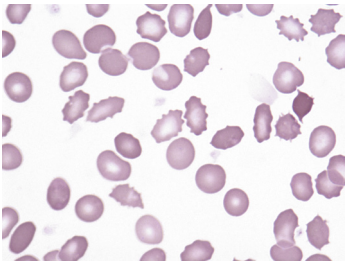

Plate 39. Acanthocytes. Irregularly spiculated red blood cells, frequently seen in abetalipoproteinemia or liver disease. See Figure 17-11, p. 149. (From McPherson R, Pincus M. Henry's clinical diagnosis and management by laboratory methods, 21st ed. Philadelphia: Saunders, 2006, Fig. 29-20.)

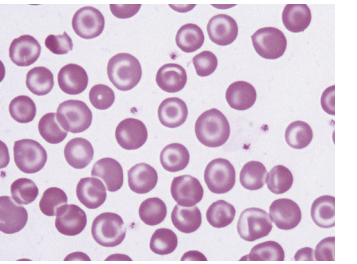

Plate 40. Target cells are frequently seen in hemoglobin C disease and liver disease. See Figure 17-12, p. 149. (From McPherson R, Pincus M. Henry's clinical diagnosis and management by laboratory methods, 21st ed. Philadelphia: Saunders, 2006, Fig. 29-18.)

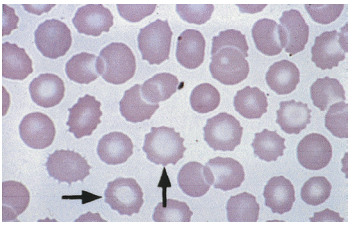

Plate 41. Echinocytes, or burr cells *(arrows),* are the hallmark of uremia. See Figure 17-13, p. 150. (Hoffman R, et al. Hematology: basic principles and practice, 5th ed. Philadelphia: Churchill Livingstone, 2008, Fig. 156-1.)

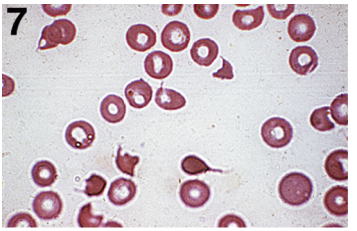

Plate 42. Microangiopathic hemolytic anemia demonstrating red blood cell fragments, anisocytosis, polychromasia, and decreased platelets. See Figure 17-14, p. 150. (From Tschudy MM, Arcara KM, editors. The Harriet Lane handbook, 19th ed. Philadelphia: Mosby, 2011, Plate 7.)

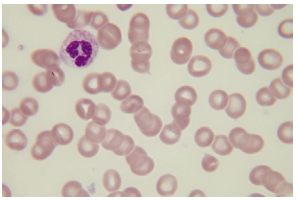

Plate 43. Rouleaux formation of stacked red blood cells seen in multiple myeloma. See Figure 17-15, p. 150. (From Goldman L, Ausiello D. Cecil medicine, 23rd ed. Philadelphia: Saunders, 2008, Fig. 161-19.)

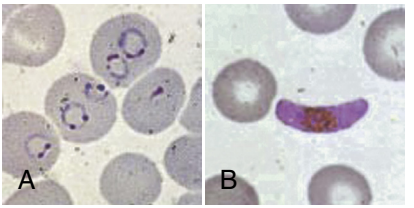

Plate 44. Malaria. Peripheral blood film examples of various stages of *Plasmodium falciparum.* **A,** Small ring forms. **B,** A crescentic gametocyte with centrally placed chromatin. See Figure 17-16, p. 151. (From Hoffman R, et al. Hematology: basic principles and practice, 5th ed. Philadelphia: Churchill Livingstone, 2008, Fig. 159-5.)

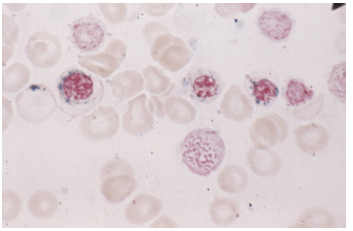

Plate 45. Ringed sideroblasts seen in sideroblastic anemia. See Figure 17-17, p. 151. (From Goldman L, Ausiello D. Cecil medicine, 23rd ed. Philadelphia: Saunders, 2008, Fig. 163-5.)

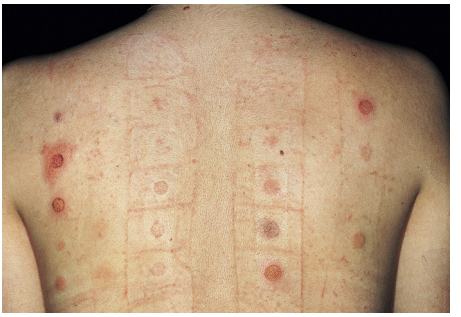

Plate 46. Patch testing. A battery of common and suspected allergens is applied to the back with a patch for 48 hours and then removed. The skin is then examined at 96 hours. Irritant reactions disappear, allergic ones do not.This patient has many positive reactions of varying intensity. See Figure 19-1, p. 166. (From Habif TP. Clinical dermatology, 5th ed. St. Louis: Mosby, 2009, Fig. 4-30.)

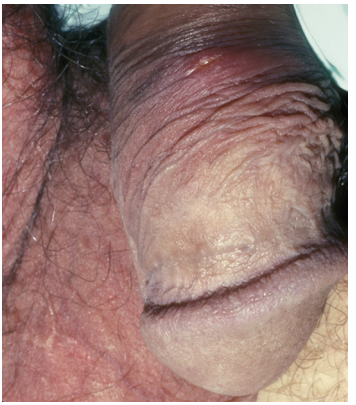

Plate 47. Penile chancre in a patient with primary syphilis. See Figure 20-3, p. 179. (From Wein WS, et al, editors. Campbell-Walsh urology, 10th ed. Philadelphia: Saunders, 2011, Fig. 13-7.)

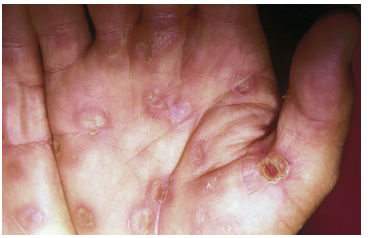

Plate 48. Palmar lesions of secondary syphilis. See Figure 20-4, p. 179. (From Mandell GL, Bennett JE, Dolin R. Mandell, Douglas, and Bennett's principles and practice of infectious diseases, 7th ed. Philadelphia: Churchill and Livingstone, 2009, Fig. 238-5.)

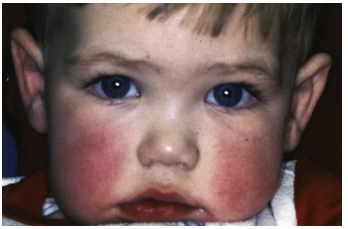

Plate 49. "Slapped cheek" appearance of erythema infectiosum. See Figure 20-5, p. 180. (From Baren JM, Rothrock SG, Brennan JA, Brown, L: Pediatric emergency medicine, 1st ed. Philadelphia: Saunders, 2007, Fig. 123-5.)

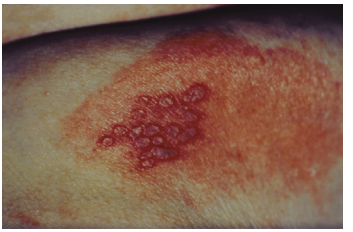

Plate 50. Herpes zoster. Grouped vesicopustules on an erythematous base. See Figure 20-6, p. 181. (From Marx JA. Rosen's emergency medicine, 7th ed. Philadelphia: Mosby, 2009, Fig. 118-28. Courtesy David Effron, MD.)

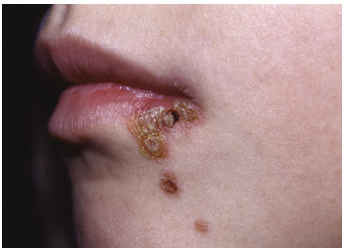

Plate 51. Impetigo. Multiple crusted and oozing lesions. See Figure 20-7, p. 183. (From Kliegman RM, Stanton BF, St. Geme JW III, Schor NF. Nelson textbook of pediatrics, 19th ed. Philadelphia: Saunders, 2011, Fig. 657-1.)

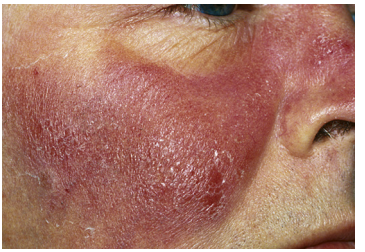

Plate 52. Sharply defined erythema and edema, characteristic of erysipelas. See Figure 20-10, p. 188. (From Zaoutis LB, Chiang VW. Comprehensive pediatric hospital medicine, 1st ed. Philadelphia: Mosby, 2007, Fig. 156-2.)

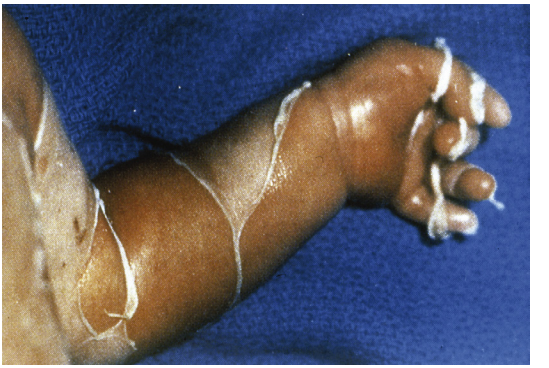

Plate 53. Scalded appearance from widespread desquamation seen in staphylococcal scalded skin syndrome. See Figure 20-11, p. 189. (From Baren JM, Rothrock SG, Brennan JA, Brown L. Pediatric emergency medicine, 1st ed. Philadelphia: Saunders, 2007, Fig. 126-4.)

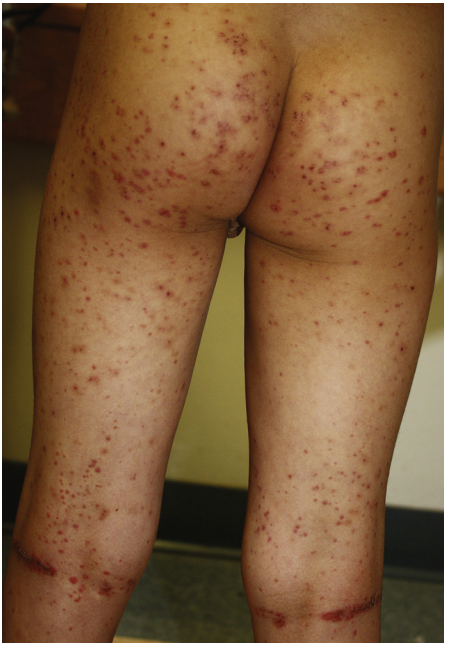

Plate 54. Henoch-Schönlein purpura. Nonblanchable macules and papules on the buttocks and lower extremities. See Figure 22-2, p. 197. (From Taal MW. Brenner and Rector's the kidney, 9th ed. Philadelphia: Saunders: 2011, Fig. 59-20.)

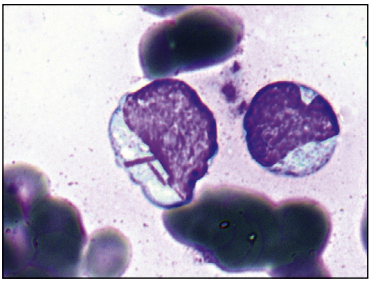

Plate 55. Auer rods vary from prominent, as in this cell, to thin and delicate. See Figure 26-1, p. 241. (From McPherson RA, Pincus MR. Henry's clinical diagnosis and management by laboratory methods, 22nd ed. Philadelphia: Saunders, 2011, Fig. 33-25.)

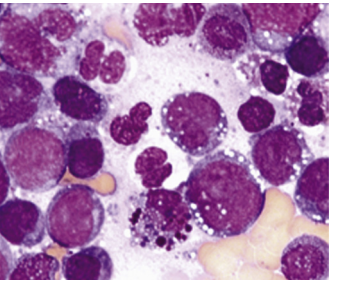

Plate 56. Chronic myelogenous leukemia showing myeloid blast phase. See Figure 26-2, p. 241. (From Hoffman R, Benz EJ Jr, Shattil SJ, et al. Hematology: basic principles and practice, 5th ed. Philadelphia: Churchill Livingstone, 2008, Figure 69-5A.)

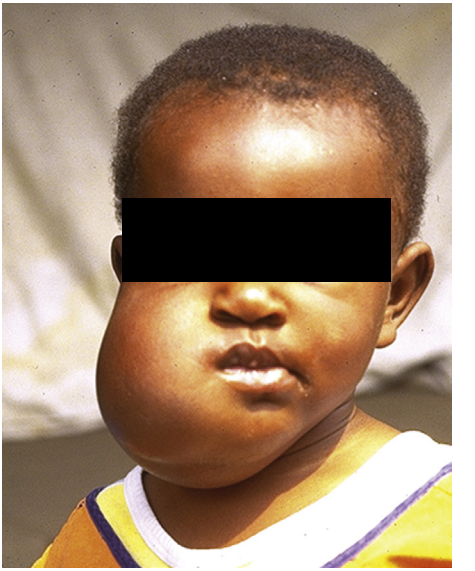

Plate 57. A young boy from South America with typical endemic Burkitt lymphoma presenting in the mandible. See Figure 26-3, p. 242. (From Jaffe ES, Harris NL, Vardiman JW, et al. Hematopathology, 1st ed. St. Louis: Saunders, 2010, Fig. 24-1. Courtesy Prof. Georges Delsol, Toulouse, France.)

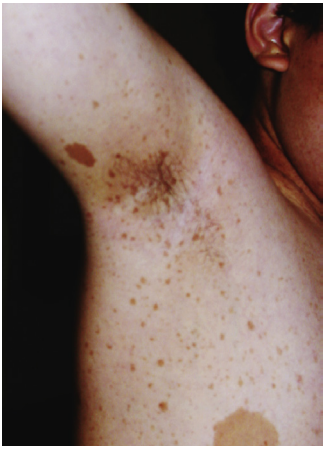

Plate 58. Café-au-lait patches as well as multiple axillary freckles in a 14-year-old boy. See Figure 26-5, p. 244. (From Hoyt CS, Taylor D. Pediatric ophthalmology and strabismus, 4th ed. Edinburgh: Saunders, 2012, Figure 65.4.)

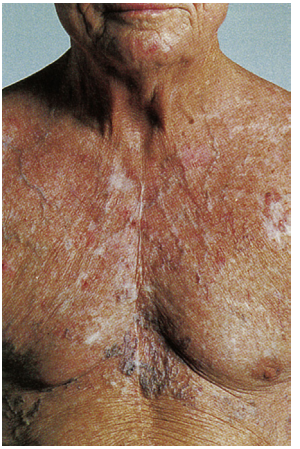

Plate 59. A patient with superior vena cava syndrome and the characteristic venous dilation and facial edema. See Figure 26-7, p. 247. (From Abeloff MD, Armitage JO, Niederhuber JE, et al. Abeloff's clinical oncology, 4th ed. Philadelphia: Churchill Livingstone, 2008, Fig. 54-3.)

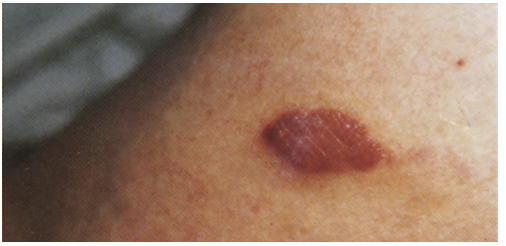

Plate 60. Kaposi sarcoma. See Figure 26-14, p. 259. (From Hoffman R, Benz EJ Jr, Shattil SJ, et al. Hematology: basic principles and practice, 5th ed. Philadelphia: Churchill Livingstone, 2008, Fig. 121-35.)

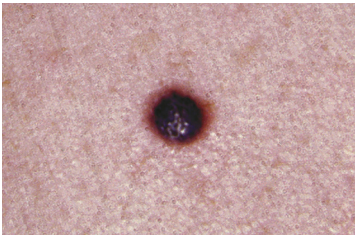

Plate 61. Primary nodular malignant melanoma found on back of patient. See Figure 26-15, p. 259. (From Yanoff M, Sassani JW. Ocular pathology, 6th ed. Philadelphia: Mosby, 2008, Fig. 17.8A.)

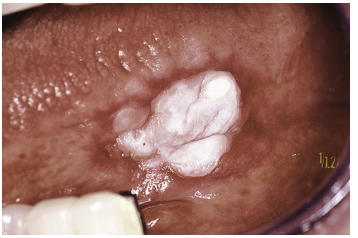

Plate 62. A thick, sharply marginated focal leukoplakia of the ventral/lateral tongue with a uniform erythematous periphery. See Figure 26-16, p. 260. (From Flint PW, Haughey BH, Niparko JK, et al. Cummings otolaryngology: head & neck surgery, 5th ed. Philadelphia: Mosby, 2010, Fig. 91-5C.)

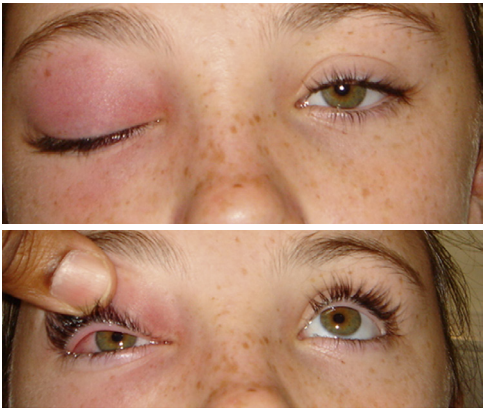

Plate 63. A 12-year-old boy with orbital cellulitis. Note the poor elevation of the affected eye. See Figure 27-1, p. 265. (From Hoyt CS, Taylor D. Pediatric ophthalmology and strabismus, 4th ed., Edinburgh: Saunders, 2012, Fig. 13.10 Ai, Aii.)

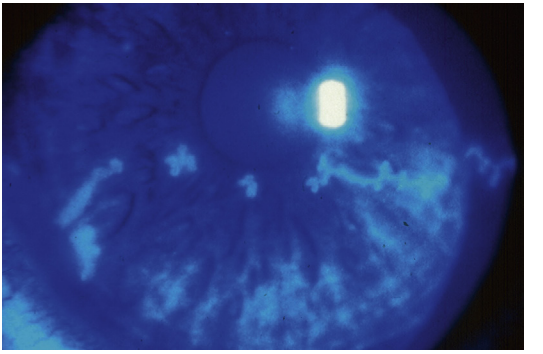

Plate 64. Varicella dendritic keratitis. Numerous dendrites are seen in this slit lamp photograph with fluorescein staining of the dendritic lesions from active viral growth in the corneal epithelium. See Figure 27-2, p. 265. (From Krachmer JH, Mannis MJ. Cornea, 3rd ed., Philadelphia: Mosby, 2010, Fig. 80.2.)

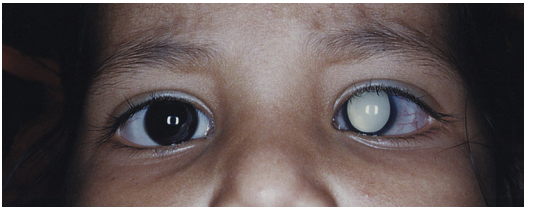

Plate 65. Leukocoria (white pupillary reflex) is the most common presenting feature of retinoblastoma and may be first noticed in family photographs. See Figure 29-1, p. 279. (From Kanski JJ. Clinical diagnosis in ophthalmology, 1st ed. St. Louis: Mosby, 2006, Fig. 9.94. Courtesy U. Raina.)

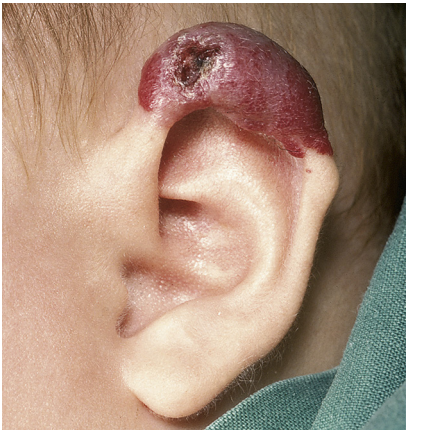

Plate 66. Infantile hemangioma. These lesions grow rapidly during the first few months of life once they appear (20% at birth), but they are asymptomatic unless they bleed, become infected, or obstruct a vital structure. Complete resolution is typical before the age of 7 years, and no treatment is usually required. See Figure 29-2, p. 282. (From du Vivier A. Atlas of clinical dermatology, 3rd ed. New York: Churchill Livingstone, 2002, p. 117, with permission.)

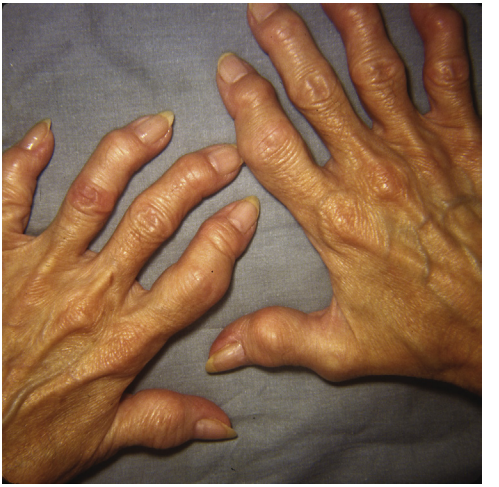

Plate 67. Osteoarthritic hands with Heberden (distal interphalangeal) and Bouchard (proximal interphalangeal) nodes on both index fingers and thumbs. See Figure 35-2, p. 316. (From Canale ST, Beaty JH. Campbell's operative orthopaedics, 11th ed. Philadelphia: Mosby, 2007, Fig. 70-4.)

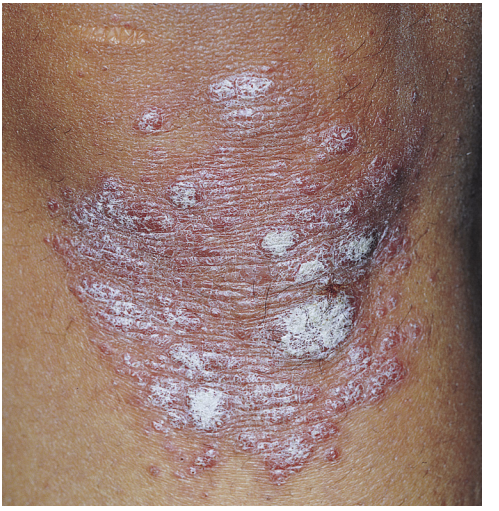

Plate 68. Psoriasis. Typical oval plaque with well-defined borders and silvery scale. See Figure 35-3, p. 318. (From Habi TP. Clinical dermatology, 5th ed. St. Louis: Mosby, 2009, Fig. 8-1.)

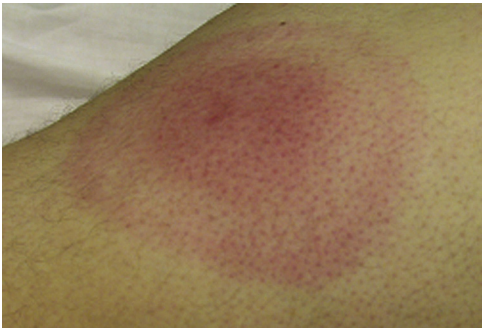

Plate 69. Erythema migrans rash of Lyme disease. Bull's eye lesion on lateral thigh. See Figure 35-5, p. 319. (From Firestein GS, Budd RC, Gabriel SE, et al. Kelley's textbook of rheumatology, 9th ed. Philadelphia: Saunders, 2012, Fig. 110-1.Courtesy Juan Salazar, MD, University of Connecticut Health Center.)

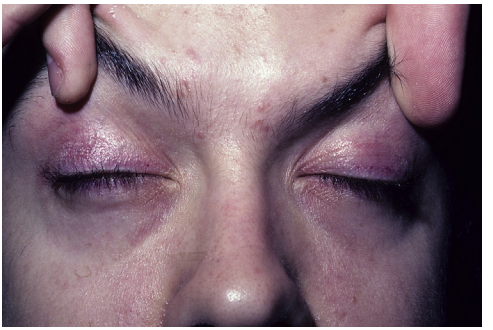

Plate 70. Dermatomyositis. Heliotrope (violaceous) discoloration around the eyes and periorbital edema. See Figure 35-6, p. 321. (From Habif TP. Clinical dermatology, 5th ed. Philadelphia: Mosby, 2009, Fig. 17-19.)

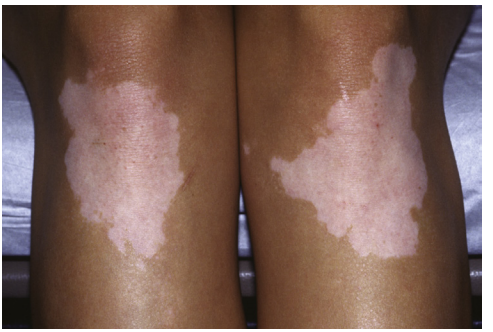

Plate 71. Sharply demarcated, symmetric, depigmented areas of vitiligo. See Figure 40-1, p. 337. (From Kliegman RM, Stanton BF, St. Geme III JW, et al. Nelson textbook of pediatrics, 19th ed. Philadelphia: Saunders, 2011, Fig. 645-4.)

100 TOP SECRETS

These secrets are 100 of the top board alerts. They summarize the concepts, principles, and most salient details that you should review before you take the Step 2 examination. Understanding of these Top Secrets will serve you well in your final review.

1. **Smoking** is the number one cause of preventable morbidity and mortality (e.g., atherosclerosis, cancer, chronic obstructive pulmonary disease) in the United States.

2. **Alcohol** is the number two cause of preventable morbidity and mortality in the United States. More than half of accidental and intentional (e.g., murder, suicide) deaths involve alcohol. Alcohol is the number one cause of preventable mental retardation (fetal alcohol syndrome); it also causes cancer and cirrhosis and is potentially fatal in withdrawal.

3. In **alcoholic hepatitis** the classic ratio of aspartate aminotransferase (AST) to alanine aminotransferase (ALT) is greater than or equal to 2:1, although both may be elevated.

4. **Vitamins:** Give folate to reproductive-age women before pregnancy occurs to prevent neural tube defects. Watch for pernicious anemia, and treat with vitamin B_{12} to prevent permanent neurologic deficits. Isoniazid causes pyridoxine (vitamin B_6) deficiency. Watch for Wernicke encephalopathy in alcoholic patients and treat with thiamine to prevent Korsakoff dementia.

5. **Minerals:** Iron-deficiency anemia is the most common cause of anemia. Think of menstrual loss in reproductive-age women and of cancer in men and menopausal women if no other cause is obvious.

6. **Vitamin A** is a known teratogen. Counsel and treat reproductive-age women appropriately (e.g., take care in treating acne with the vitamin A analog isotretinoin).

7. Complications of **atherosclerosis** (e.g., myocardial infarction, heart failure, stroke, gangrene) are involved in roughly one half of deaths in the United States. The primary risk factors for atherosclerosis are age/sex, family history, cigarette smoking, hypertension, diabetes mellitus, high low-density lipoprotein (LDL) cholesterol, and low high-density lipoprotein (HDL) cholesterol.

8. **Diabetes** leads to atherosclerosis and its complications, retinopathy (a leading cause of blindness), nephropathy (a leading cause of end-stage renal failure), peripheral vascular disease (a leading cause of limb amputation), peripheral neuropathy (sensory and autonomic), and an increased incidence of infections.

9. Although hypertension is most often mild or moderate and clinically silent, **severe hypertension** can lead to acute problems (known as a hypertensive emergency): headaches, dizziness, blurry vision, papilledema, cerebral edema, altered mental status, seizures, intracerebral hemorrhage (classically in the basal ganglia), renal failure/azotemia, angina, myocardial infarction, and/or heart failure.

10. In **milder cases,** lifestyle modifications (e.g., diet, exercise, weight loss, cessation of alcohol/tobacco use) may be able to treat the following disorders without the use of medications: hypertension, hyperlipidemia, diabetes, gastroesophageal reflux disease (GERD), insomnia, obesity, and sleep apnea.

11. **Arterial blood gas analysis:** In general, pH tells you the primary event (acidosis vs. alkalosis), whereas carbon dioxide and bicarbonate values give you the cause (same direction as pH) and suggest any compensation present (opposite of pH).

12. **Exogenous causes of hyponatremia:** Keep in mind oxytocin, surgery, narcotics, inappropriate intravenous (IV) fluid administration, diuretics, and antiepileptic medications.

13. **Electrocardiogram (ECG) findings in electrolyte disturbances:** Tall, tented T waves in hyperkalemia; loss of T waves/T-wave flattening and U waves in hypokalemia; QT prolongation in hypocalcemia; QT shortening in hypercalcemia.

14. **Shock:** First give the patient oxygen, start an IV line, and set up monitoring (pulse oximetry, ECG, frequent vital signs). Then give a fluid bolus (1 L normal saline or lactated Ringer solution) if no signs of congestive heart failure (e.g., bibasilar rales) are present while you investigate the cause.

15. **Virchow triad** of deep venous thrombosis (DVT): Endothelial damage (e.g., surgery, trauma), venous stasis (e.g., immobilization, surgery, severe heart failure), and hypercoagulable state (e.g., malignancy, birth control pills, pregnancy, lupus anticoagulant, inherited deficiencies).

16. **Therapy for congestive heart failure:** Diuretics (e.g., furosemide), angiotensin-converting enzyme (ACE) inhibitors, and beta blockers (for stable patients) are the mainstays of pharmacologic treatment. Be sure to screen for and address underlying atherosclerosis risk factors (e.g., smoking, hyperlipidemia).

17. **Cor pulmonale:** Right-sided heart enlargement, hypertrophy, or failure caused by primary lung disease (usually chronic obstructive pulmonary disease). The most common cause of right-sided heart failure, however, is left-sided heart failure (not cor pulmonale).

18. In patients with **atrial fibrillation,** assess for an underlying cause with thyroid-stimulating hormone (TSH), electrolytes, and echocardiogram. The main management issues are ventricular rate (if needed, slow the rate with medications) and atrial clot formation/embolic disease (consider anticoagulation with warfarin).

19. **Ventricular fibrillation** and pulseless ventricular tachycardia are treated with immediate defibrillation followed by epinephrine, vasopressin, amiodarone, and lidocaine. If ventricular tachycardia with a pulse is present, treat with amiodarone and synchronized cardioversion.

20. **Obstructive vs. restrictive lung disease:** The FEV_1/FEV ratio is the most important parameter on pulmonary function testing to distinguish the two (FEV_1 may be the same). In obstructive lung disease, the FEV_1/FEV ratio is less than normal. In restrictive disease, the FEV_1/FEV ratio is often normal.

21. The **most common type of esophageal cancer** is adenocarcinoma occurring as a result of long-standing reflux disease and the development of Barrett esophagus. Smoking and alcohol abuse contribute to the development of squamous cell carcinoma, the second most common histologic type of esophageal cancer.

22. A biopsy must be performed on all **gastric ulcers,** or they must be followed to resolution to exclude malignancy.

23. Testing a nasogastric tube aspirate for blood is the best initial test **to distinguish upper from lower gastrointestinal (GI) bleeding,** although bright red blood via mouth or anus is a fairly reliable sign of a nearby bleeding source.

24. **Irritable bowel syndrome** is one of the most common causes of GI complaints. Physical examination and diagnostic studies are by definition negative; this is a diagnosis of exclusion. The classic case is a young woman with a history of chronic alternating constipation and diarrhea.

25. **Crohn disease vs. ulcerative colitis**

	CROHN DISEASE	ULCERATIVE COLITIS
Place of origin	Distal ileum, proximal colon	Rectum
Thickness of pathology	Transmural	Mucosa/submucosa only
Progression	Irregular (skip lesions)	Proximal, continuous from rectum; no skipped areas
Location	From mouth to anus	Involves only colon, rarely extends to ileum
Bowel habit changes	Obstruction, abdominal pain	Bloody diarrhea
Classic lesions	Fistulas/abscesses, cobblestoning, string sign on barium x-ray	Pseudopolyps, lead pipe colon on barium x-ray, toxic megacolon
Colon cancer risk	Slightly increased	Markedly increased
Surgery	No (may make worse)	Yes (proctocolectomy with ileoanal anastomosis)

26. All forms of **viral hepatitis** can present similarly in the acute stage; serology testing and history are needed to distinguish them. Hepatitis B, C, and D are transmitted parenterally and can lead to chronic infection, cirrhosis, and hepatocellular carcinoma.

27. **Hereditary hemochromatosis** is currently the most common known genetic disease in white people. The initial symptoms (fatigue, impotence) are nonspecific, but patients often have hepatomegaly. Screen with transferrin saturation test (serum iron/total iron binding capacity) and ferritin level. Treat with phlebotomy after confirming the diagnosis with genetic testing and liver biopsy.

28. **Sequelae of liver failure:** Coagulopathy that cannot be fixed with vitamin K, jaundice/hyperbilirubinemia, hypoalbuminemia, ascites, portal hypertension, hyperammonemia/encephalopathy, hypoglycemia, and disseminated intravascular coagulation.

29. **Pancreatitis** is usually caused by alcohol or gallstones. Patients seek treatment because of abdominal pain, nausea/vomiting, and elevated amylase and lipase. Treat supportively and provide pain control. Complications include pseudocyst formation, infection/abscess, and adult respiratory distress syndrome.

30. **Jaundice/hyperbilirubinemia in neonates** is usually physiologic (only monitoring and follow-up laboratory tests are needed), but jaundice present at birth is always pathologic.

31. **Primary vs. secondary endocrine disturbances.** In primary disorders (e.g., Graves, Hashimoto, or Addison disease), the gland malfunctions but the pituitary or another gland and the central nervous system respond appropriately (e.g., TSH, thyrotropin-releasing hormone [TRH] or adrenocorticotropin hormone [ACTH] elevate or depress as expected in the setting of a malfunctioning gland). In secondary disorders (e.g., ACTH-secreting lung carcinoma, heart failure–induced hyperreninemia, renal failure–induced hyperparathyroidism), the gland itself is doing what it is told to do by other controlling forces (e.g., pituitary gland, hypothalamus, tumor, disease); they are the problem, not the gland.

32. **Corticosteroid side effects:** Weight gain, easy bruising, acne, hirsutism, emotional lability, depression, psychosis, menstrual changes, sexual dysfunction, insomnia, memory loss, buffalo hump,

truncal and central obesity with wasting of extremities, round plethoric facies, purplish skin striae, weakness (especially of the proximal muscles), hypertension, peripheral edema, poor wound healing, glucose intolerance or diabetes, osteoporosis, and hypokalemic metabolic alkalosis (resulting from mineralocorticoid effects of certain corticosteroids). Growth can also be stunted in children.

33. **Osteoarthritis** is by far the most common cause of arthritis (≥75% of cases) and usually does not have hot, swollen joints or significant findings if arthrocentesis is performed.

34. **Cancer incidence and mortality in the United States**

OVERALL HIGHEST INCIDENCE		OVERALL HIGHEST MORTALITY RATE	
MALE	**FEMALE**	**MALE**	**FEMALE**
1. Prostate	1. Breast	1. Lung	1. Lung
2. Lung	2. Lung	2. Prostate	2. Breast
3. Colon	3. Colon	3. Colon	3. Colon

35. **Sequelae of lung cancer:** Hemoptysis, Horner syndrome, superior vena cava syndrome, phrenic nerve involvement/diaphragmatic paralysis, hoarseness from recurrent laryngeal nerve involvement, and paraneoplastic syndromes (Cushing syndrome, syndrome of inappropriate secretion of antidiuretic hormone [SIADH], hypercalcemia, Eaton-Lambert syndrome).

36. **Bitemporal hemianopsia** (loss of peripheral vision in both eyes) is caused by a space-occupying lesion pushing on the optic chiasm (classically a pituitary tumor) until proved otherwise. Order a computed tomography (CT) or magnetic resonance imaging (MRI) scan of the brain.

37. **Potential risks and side effects of estrogen therapy** (e.g., contraception, postmenopausal hormone replacement): Endometrial cancer, hepatic adenomas, glucose intolerance/diabetes, DVT, stroke, cholelithiasis, hypertension, endometrial bleeding, depression, weight gain, nausea/vomiting, headache, weight gain, drug-drug interactions, teratogenesis, and aggravation of preexisting uterine leiomyomas (fibroids), breast fibroadenomas, migraines, and epilepsy. The risks of coronary artery disease and breast cancer are increased with combined estrogen and progesterone therapy.

38. **ABCDE characteristics of a mole** that should make you suspicious of malignant transformation: **A**symmetry, **b**orders (irregular), **c**olor (change in color or multiple colors), **d**iameter (the bigger the lesion, the more likely it is malignant), and **e**volving over time. Do an excisional biopsy of such moles and/or if a mole starts to itch or bleed.

39. **Bronchiolitis vs. croup vs. epiglottitis**

	BRONCHIOLITIS	CROUP (ACUTE LARYNGOTRACHEITIS)	EPIGLOTTITIS
Child's age	0-18 months	1-2 yr	2-5 yr
Common	Yes	Yes	No
Common cause(s)	Respiratory syncytial virus (RSV; ≥75%), parainfluenza, influenza	Parainfluenza virus (50%-75% of cases), influenza	*Haemophilus influenzae,* *Staphylococcus* spp., *Streptococcus* spp.

	BRONCHIOLITIS	CROUP (ACUTE LARYNGOTRACHEITIS)	EPIGLOTTITIS
Symptoms/ signs	Initial viral upper respiratory infection (URI) symptoms followed by tachypnea and expiratory wheezing	Initial viral URI symptoms followed by "barking" cough, hoarseness, and inspiratory stridor	Rapid progression to high fever, toxicity, drooling, and respiratory distress
X-ray findings	Hyperinflation	Subglottic tracheal narrowing on frontal x-ray (steeple sign)	Swollen epiglottis on lateral neck x-ray (thumb sign)
Treatment	Humidified oxygen, bronchodilators (efficacy uncertain); ribavirin used for severe RSV infection or high risk for RSV infection	Dexamethasone, nebulized epinephrine, humidified oxygen	Prepare to establish an airway, antibiotics (e.g., third-generation cephalosporin and antistaphylococcal agent active against methicillin-resistant *Staphylococcus aureus*, such as vancomycin or clindamycin)

40. **Sequelae of streptococcal infection:** Rheumatic fever, scarlet fever, and poststreptococcal glomerulonephritis. Only the first two can be prevented by treatment with antibiotics.

41. **Multiple sclerosis** should be suspected in any young adult with recurrent, varied neurologic symptoms/signs when no other causes are evident. Best diagnostic tests: MRI (most sensitive), lumbar puncture (elevated immunoglobulin G [IgG] oligoclonal bands and myelin basic protein levels, mild elevation in lymphocytes and protein), and evoked potentials (slowed conduction through areas with damaged myelin).

42. For the **unconscious or delirious patient** in the emergency department with no history or signs of trauma, consider empirical treatment for hypoglycemia (glucose), opioid overdose (naloxone), and thiamine deficiency (thiamine should be given before glucose in a suspected alcoholic). Other commonly tested causes are alcohol, illicit or prescription drugs, diabetic ketoacidosis, stroke, epilepsy or postictal state, and subarachnoid hemorrhage (e.g., aneurysm rupture).

43. **Delirium vs. dementia**

	DELIRIUM	DEMENTIA
Onset	Acute and dramatic	Chronic and insidious
Common causes	Illness, toxin, withdrawal	Alzheimer disease, multiinfarct dementia, HIV/AIDS
Reversible	Usually	Usually not
Attention	Poor	Usually unaffected
Arousal level	Fluctuates	Normal

44. **Always consider the possibility of pregnancy** (and order a pregnancy test to rule it out, unless pregnancy is an impossibility) in reproductive-age women before advising potentially teratogenic therapies or tests (e.g., antiepileptic drugs, x-ray, CT scan). Pregnancy is in the differential diagnosis of both primary and secondary amenorrhea.

45. **Anaphylaxis** is commonly caused by bee stings, food allergy (especially peanuts and shellfish), medications (especially penicillins and sulfa drugs), or latex allergy. Patients become agitated and flushed, and shortly after exposure develop itching (urticaria), facial swelling (angioedema), and difficulty breathing. Symptoms develop rapidly and dramatically in true anaphylaxis. Treat immediately by securing the airway (laryngeal edema may prevent intubation, in which case do a cricothyroidotomy if needed), and give subcutaneous or IV epinephrine. Antihistamines and corticosteroids are not useful for immediate severe reactions that involve the airway.

46. **Cancer screening in asymptomatic adults**

CANCER	PROCEDURE	AGE	FREQUENCY
Colorectal	Colonoscopy	>50 yr for all studies	Every 10 yr
	Flexible sigmoidoscopy		Every 5 yr
	Double-contrast barium enema		Every 5 yr
	CT colonography		Every 5 yr
	Fecal occult blood test		Annually
	Fecal immunochemical test		Annually
	Stool DNA test		Interval uncertain
Colon, prostate	Digital rectal examination	>40 yr	Annually
Prostate	Prostate-specific antigen test	>50 yr*	Controversial, but offer annually
Cervical	Pap smear	Beginning at age 21 yr regardless of sexual activity	If conventional Pap test is used, test annually, then every 2-3 yr for women ≥30 yr old who have had 3 negative cytology test results If Pap and human papillomavirus (HPV) testing are used, test every 3 yr if both HPV and cytology results are negative
Gynecologic	Pelvic examination	21-64 yr	Annually After 3 normal examinations, every 2-3 yr
		≥65 yr	Annually; when to stop is not clearly established

CANCER	PROCEDURE	AGE	FREQUENCY
Endometrial	Endometrial biopsy	Menopause	No recommendation for routine screening in the absence of symptoms
Breast	Breast self-examination	>20 yr	Benefits and limitations should be discussed, but breast self-examination is no longer recommended by the American Cancer Society
Breast	Physical examination by doctor	20-40 yr	Every 3 yr
		>40 yr	Annually
Breast	Mammography	>40 yr	Annually
Lung	Sputum, chest x-ray		Testing is not recommended for asymptomatic individuals, even if they are at high risk
	CT scan		Annual CT scan is controversial but may be indicated for smokers and former smokers aged 55-74 yr who have smoked at least 1 pack of cigarettes per day for at least 30 yr

This table is for the screening of asymptomatic, healthy patients. Other guidelines exist, but follow this table for the USMLE. Controversial areas usually are not tested on the USMLE.
*Start at age 45 years in African Americans and at age 40 years for patients with a first-degree relative diagnosed at an early age.

47. **Biostatistics calculations using a 2 × 2 table**

	DISEASE			TEST NAME	FORMULA
Test or exposure		(+)	(–)		
	(+)	A	B	Sensitivity	A/(A + C)
				Specificity	D/(B + D)
				PPV	A/(A + B)
				NPV	D/(C + D)
	(–)	C	D	Odds ratio	(A × D)/(B × C)
				Relative risk	[A/(A + B)]/[C/(C + D)]
				Attributable risk	[A/(A + B)] – [C/(C + D)]

48. The ***P*-value** reflects the likelihood of making a type I error, or claiming an effect or difference where none existed (i.e., results were obtained by chance). When we reject the null hypothesis (i.e., the hypothesis of no difference) in a trial testing a new treatment, we are saying that the new treatment works. We use the *P*-value to express our confidence in the data.

49. **Side effects of antipsychotics:** Acute dystonia (treat with antihistamines or anticholinergics), akathisia (beta blocker may help), tardive dyskinesia (switching to a newer agent may be beneficial), parkinsonism (treat with antihistamines or anticholinergics), neuroleptic malignant syndrome, hyperprolactinemia (may cause breast discharge, menstrual dysfunction, and/or sexual dysfunction), and autonomic nervous system–related effects (e.g., anticholinergic, antihistamine, and alpha$_1$ receptor blockade).

50. Asking about **depression and suicidal thoughts/intent** is important in the right setting and does not cause people to commit suicide. Hospitalize psychiatric patients against their will if they are a danger to self or others.

51. **Drugs of abuse:** Those that are potentially fatal in withdrawal include alcohol, barbiturates, and benzodiazepines. Alcohol, cocaine, opiates, barbiturates, benzodiazepines, phencyclidine (PCP), and inhalants are potentially fatal in overdose.

52. **Pelvic inflammatory disease (PID)** is the most common preventable cause of infertility in the United States and the most likely cause of infertility in younger, normally menstruating women.

53. **Polycystic ovarian syndrome** is classically associated with women who are "heavy, hirsute, and [h]amenorrheic." It is the most common cause of dysfunctional uterine bleeding. Remember the increased risk of endometrial cancer as a result of unopposed estrogen.

54. **Fetal/neonatal macrosomia** is caused by maternal diabetes until proved otherwise. Use diet and insulin (not oral agents) to treat maternal diabetes.

55. **Causes of low maternal serum alpha-fetoprotein:** Down syndrome, inaccurate dates (most common), and fetal demise. **Causes of high maternal serum alpha-fetoprotein:** Neural tube defects, ventral wall defects (e.g., omphalocele, gastroschisis), inaccurate dates (most common), and multiple gestation. Measurement generally is obtained between 16 and 20 weeks' gestation.

56. Hypertension plus proteinuria in pregnancy equals **preeclampsia** until proved otherwise.

57. Positive pregnancy test (i.e., not a clinically apparent pregnancy) plus vaginal bleeding and abdominal pain equals **ectopic pregnancy** until proved otherwise. Order a pelvic ultrasound if the patient is stable.

58. **Decelerations during maternofetal monitoring:** *Early* decelerations are normal and caused by head compression. *Variable* decelerations are common and usually are caused by cord compression (turn the mother on her side, give oxygen and fluids, and stop oxytocin). *Late* decelerations are caused by uteroplacental insufficiency and are the most worrisome pattern (turn the mother on her side, give oxygen and IV fluids, stop oxytocin, and measure fetal oxygen saturation or scalp pH). Prepare for prompt delivery.

59. Always perform an ultrasound before a pelvic examination in the setting of **third trimester bleeding** (in case placenta previa is present).

60. **Uterine atony** is the most common cause of postpartum bleeding and is typically caused by uterine overdistention (e.g., twins, polyhydramnios), prolonged labor, and/or oxytocin usage.

61. **Acute abdomen pathology localization by physical examination**

AREA	ORGAN (CONDITIONS)
Right upper quadrant	Gallbladder/biliary (cholecystitis, cholangitis) or liver (abscess)
Left upper quadrant	Spleen (rupture with blunt trauma)
Right lower quadrant	Appendix (appendicitis), PID
Left lower quadrant	Sigmoid colon (diverticulitis), PID
Epigastric area	Stomach (peptic ulcer) or pancreas (pancreatitis)

62. The **"6 Ws" of postoperative fever:** Water, wind, walk, wound, "wawa," and weird drugs. *Water* stands for urinary tract infection; *wind,* for atelectasis or pneumonia; *walk,* for DVT; *wound,* for surgical wound infection; *wawa,* for breast (usually relevant only in the postpartum state), and *weird drugs,* for drug fever. In patients with daily fever spikes that do not respond to antibiotics, think about a postsurgical abscess. Order a CT scan to locate, then drain the abscess if one is present.

63. **ABCDEs of trauma** (follow in order if you are asked to choose): **A**irway, **b**reathing, **c**irculation, **d**isability, and **e**xposure.

64. **Six rapidly fatal thoracic injuries** that must be recognized and treated immediately:

    1. Airway obstruction (establish airway).
    2. Open pneumothorax (intubate and close defect on three sides).
    3. Tension pneumothorax (perform needle thoracentesis followed by chest tube).
    4. Cardiac tamponade (perform pericardiocentesis).
    5. Massive hemothorax (place chest tube to drain; thoracotomy if bleeding does not stop).
    6. Flail chest (consider intubation and positive pressure ventilation if oxygenation is inadequate).

65. **Neonatal conjunctivitis** may be caused by chemical reaction (in the first 12-24 hours of giving drops for prophylaxis), gonorrhea (2-5 days after birth; usually prevented by prophylactic drops), and chlamydial infection (5-14 days after birth; often not prevented by prophylactic drops).

66. **Glaucoma** is usually (90%) the open-angle form, which is painless (no "attacks") and asymptomatic until irreversible vision loss (that starts in the periphery) occurs. Screening is thus important. Open-angle glaucoma is the most common cause of blindness in African Americans.

67. **Uveitis** is often a marker for systemic conditions: Juvenile rheumatoid arthritis, sarcoidosis, inflammatory bowel disease, ankylosing spondylitis, reactive arthritis, multiple sclerosis, psoriasis, or lupus. Photophobia, blurry vision, and eye pain are common complaints.

68. **Bilateral (although often asymmetric) painless gradual loss of vision** in older adults usually results from cataracts, macular degeneration, or glaucoma, which can be distinguished on physical examination. Presbyopia is a normal part of aging and affects only near vision (i.e., accommodation).

69. **Compartment syndrome,** usually in the lower extremity after trauma or surgery, causes the "6 Ps":

    1. Pain (present on passive movement and often out of proportion to the injury).
    2. Paresthesias (numbness, tingling, decreased sensation).
    3. Pallor (or cyanosis).
    4. Pressure (firm feeling muscle compartment, elevated pressure reading).
    5. Paralysis (late, ominous sign).
    6. Pulselessness (very late, ominous sign; treat with fasciotomy to relieve compartment pressure and prevent permanent neurologic damage).

70. **Peripheral nerve evaluation**

NERVE	MOTOR FUNCTION	SENSORY FUNCTION	CLINICAL SCENARIO
Radial	Wrist extension (watch for wrist drop)	Back of forearm, back of hand (first 3 digits)	Humeral fracture
Ulnar	Finger abduction (watch for "claw hand")	Front and back of last 2 digits	Elbow dislocation
Median	Pronation, thumb opposition	Palmar surface of hand (first 3 digits)	Carpal tunnel syndrome, humeral fracture
Axillary	Abduction, lateral rotation	Lateral shoulder	Upper humeral dislocation or fracture
Peroneal	Dorsiflexion, eversion (watch for foot drop)	Dorsal foot and lateral leg	Knee dislocation

71. **Pediatric hip disorders**

NAME	AGE	EPIDEMIOLOGY	SYMPTOMS/SIGNS	TREATMENT
CHD	At birth	Female, firstborn, breech delivery	Barlow and Ortolani signs	Harness
LCPD	4-10 yr	Short male with delayed bone age	Knee, thigh, groin pain, limp	Orthoses
SCFE	9-13 yr	Overweight male adolescent	Knee, thigh, groin pain, limp	Surgical pinning

CHD, Congenital hip dysplasia; *LCPD*, Legg-Calvé-Perthes disease; *SCFE*, slipped capital femoral epiphysis
Note: All of these conditions may present in an adult as arthritis of the hip.

72. **Avoid lumbar puncture** in a patient with head trauma or signs of increased intracranial pressure because of the risk of herniation. Perform CT scan without contrast instead.

73. In children, 75% of **neck masses** are benign (e.g., lymphadenitis, thyroglossal duct cyst), but 75% of neck masses in adults are malignant (e.g., squamous cell carcinoma and/or metastases, lymphoma).

74. Manage symptomatic **carotid artery stenosis** of 70% to 99% with carotid endarterectomy; less than 50% with medical management (e.g., antihypertensive agents, statins, and antiplatelet therapy) and treatment of atherosclerosis risk factors. For stenosis between 50% and 69%, the data on management is less clear, and patient-specific factors affect the decision.

75. Pulsatile abdominal mass plus hypotension equals ruptured **abdominal aortic aneurysm** until proved otherwise. Perform an immediate laparotomy (90% mortality rate).

76. Conditions best viewed as **anginal equivalents:** Transient ischemic attacks, claudication, and chronic mesenteric ischemia. Arterial workup and imaging are indicated.

77. **Cryptorchidism** is the main identifiable risk factor for testicular cancer and can also cause infertility. Treat with surgical retrieval and orchiopexy or orchiectomy.

78. **Benign prostatic hypertrophy/hyperplasia** can present as acute renal failure. Patients have a distended bladder and bilateral hydronephrosis on ultrasound (neither is present with "medical" renal

disease). Drain the bladder first (catheterize), then perform transurethral resection of the prostate (TURP).

79. **Impotence** may be physical (e.g., vascular, nervous system, drugs) or, less commonly, psychogenic (patients have normal nocturnal erections and a history of dysfunction only in certain settings).

80. The **overall pattern of growth** in a child is more important than any one measurement. Consider close follow-up and remeasurement of growth parameters if you do not have enough data. A stable pattern is less worrisome and less likely to be correctable than a sudden change in previously stable growth. For example, the most common cause of delayed puberty is constitutional delay, a normal variant.

81. **Findings suspicious for child abuse,** assuming that other explanations are not provided: Failure to thrive, multiple injuries in different stages of healing, retinal hemorrhages plus subdural hematomas (shaken baby syndrome), sexually transmitted diseases, a caretaker story that does not fit the child's injury or complaint, childhood behavioral or emotional problems, and multiple personality disorder as an adult.

82. The **APGAR score** (commonly performed at 1 and 5 minutes after birth; the maximum score is 10):

	NUMBER OF POINTS GIVEN		
CATEGORY	**0**	**1**	**2**
Color	Pale, blue	Body pink, extremities blue	Completely pink
Heart rate	Absent	<100 beats/min	>100 beats/min
Reflex irritability*	None	Grimace	Grimace and strong cry, cough, and sneeze
Muscle tone	Limp	Some flexion of extremities	Active motion
Respiratory effort	None	Slow, weak cry	Good, strong cry

*Reflex irritability usually is measured by the infant's response to stimulation of the sole of the foot or catheter put into the nose.

83. **Diuretics** are a common cause of metabolic derangement. *Thiazide diuretics* cause calcium retention, hyperglycemia, hyperuricemia, hyperlipidemia, hyponatremia, hypokalemic metabolic alkalosis, and hypovolemia; because they are sulfa drugs, watch out for sulfa allergy. *Loop diuretics* cause hypokalemic metabolic alkalosis, hypovolemia (more potent than thiazides), ototoxicity, and calcium excretion; with the exception of ethacrynic acid, they also are sulfa drugs. *Carbonic anhydrase inhibitors* cause metabolic acidosis, and *potassium-sparing diuretics* (e.g., spironolactone) may cause hyperkalemia.

84. **Overdoses and antidotes**

POISON OR MEDICATION	ANTIDOTE
Acetaminophen	Acetylcysteine
Benzodiazepines	Flumazenil
Beta blockers	Glucagon
Carbon monoxide	Oxygen (hyperbaric in cases of severe poisoning)
Cholinesterase inhibitors	Atropine, pralidoxime
Copper or gold	Penicillamine
Digoxin	Normalize potassium and other electrolytes; digoxin antibodies

Continued

POISON OR MEDICATION	ANTIDOTE
Iron	Deferoxamine
Lead	Edetate (EDTA); use succimer in children
Methanol or ethylene glycol	Fomepizole, ethanol
Muscarinic blockers	Physostigmine
Opioids	Naloxone
Quinidine or tricyclic antidepressants	Sodium bicarbonate (cardioprotective)

85. **Aspirin/nonsteroidal antiiinflammatory drugs (NSAID) side effects:** GI bleeding, gastric ulcers, renal damage (e.g., interstitial nephritis, papillary necrosis), allergic reactions, platelet dysfunction (life of platelet for aspirin, reversible dysfunction with NSAIDs), and Reye syndrome (encephalopathy and/or liver failure in a child taking aspirin in the setting of a viral infection). Aspirin overdose can be fatal and classically leads to both metabolic acidosis and respiratory alkalosis.

86. **Central pontine myelinolysis** (brainstem damage and possibly death) may result from overly rapid correction of hyponatremia.

87. Because of cellular shifts, **alkalosis and acidosis** can cause symptoms of potassium and/or calcium derangement (e.g., alkalosis can lead to symptoms of hypokalemia or hypocalcemia). In this setting, pH correction is needed (rather than direct treatment of the calcium or potassium levels). Magnesium depletion can also make hypocalcemia and hypokalemia unresponsive to replacement therapy (until magnesium is corrected).

88. Adult patients of sound mind are allowed to **refuse any form of treatment.** Watch for depression as a cause of "incompetence." Treat depression before wishes for death are respected.

89. **If a patient is incompetent** (including younger minors who lack adequate decision-making capacity) and an emergency treatment is needed, seek a family member or court-appointed guardian to make healthcare decisions. If no one is available, treat as you see fit in an emergency or contact the courts in a nonemergency setting.

90. **Respect patient wishes and living wills** (assuming that they are appropriate) even in the face of dissenting family members, but take time to listen to family members' concerns.

91. **Always be a patient advocate** and treat patients with respect and dignity, even if they refuse your proposed treatment or are noncompliant. If patients' actions puzzle you, do not be afraid to ask them why they are doing or saying what they are.

92. **Break doctor-patient confidentiality only in the following situations:**

    1. The patient asks you to do so.
    2. Child abuse is suspected.
    3. The courts mandate you to do so.
    4. You must fulfill the duty to warn or protect (if a patient says that he is going to kill someone or himself, you have to tell the person who is threatened, the authorities, or both).
    5. The patient has a reportable disease.
    6. The patient is a danger to others (e.g., if a patient is blind or has seizures, let the proper authorities know so that they can revoke the patient's license to drive; if the patient is an airplane pilot and is a paranoid, hallucinating schizophrenic, then authorities need to know).

93. **Causes of "false" laboratory disturbances:** Hemolysis (hyperkalemia), pregnancy (elevated sedimentation rate and alkaline phosphatase), hypoalbuminemia (hypocalcemia), and hyperglycemia (hyponatremia).

94. **ECG findings of myocardial infarction:** Flipped or flattened T waves, ST-segment elevation (depression means ischemia; elevation means injury), and/or Q waves in a segmental distribution (e.g., leads II, III, and AVF for an inferior infarct). ST depression may also be seen in "reciprocal"/opposite leads.

95. Drugs that may be useful in the setting of **acute coronary syndrome:** Aspirin, morphine, nitroglycerin, beta blocker, ACE inhibitor, clopidogrel, HMG-CoA reductase inhibitor, glycoprotein IIb/IIIa receptor inhibitors, heparin (unfractionated or low-molecular-weight heparin), and tissue-plasminogen activator (t-PA; strict criteria for use).

96. **Cholesterol management guidelines** (numbers in the chart represent mg/dL)

NO CHD RISK FACTORS	≥2 CHD RISK FACTORS*	KNOWN CHD/ EQUIVALENT†	VERY HIGH RISK‡	INTERVENTION
LDL <160	LDL <100	LDL <100	LDL <70	None (meets goal)
LDL 160-189	LDL 100-129		LDL 70-99	Diet ± medications§
LDL ≥190	LDL ≥130	LDL ≥100	LDL ≥100	Medications (+ diet)

*_CHD,_ Coronary heart disease. Risk factors for CHD are listed in Chapter 4.
†CHD equivalents include diabetes mellitus, peripheral arterial atherosclerotic disease, symptomatic carotid artery disease, and abdominal aortic aneurysm.
‡"Very" high-risk patients are those with CHD who have a heart attack, diabetes, or other severe and poorly controlled risk factors (e.g., metabolic syndrome, heavy smoking).
§"Diet" includes general lifestyle modifications, such as eating less and healthier, decreasing alcohol intake, and exercising. The trend is toward more aggressive intervention, so you will not be faulted for initiating medications at these "gray area" LDL levels, particularly in higher-risk people.

97. **Type 1 vs. Type 2 diabetes**

	TYPE 1 (10% OF CASES)	TYPE 2 (90% OF CASES)
Age at onset	Most commonly <30 yr	Most commonly >30 yr
Associated body habitus	Thin	Obese
Development of ketoacidosis	Yes	No
Development of hyperosmolar state	No	Yes
Level of endogenous insulin	Low to none	Normal to high (insulin resistance)
Twin concurrence	<50%	>50%
Human leukocyte antigen association	Yes	No
Response to oral hypoglycemics	No	Yes
Antibodies to insulin	Yes (at diagnosis)	No
Risk for diabetic complications	Yes	Yes
Islet-cell pathology	Insulitis (loss of most B cells)	Normal number, but with amyloid deposits

Findings may overlap.

98. Hypertension classification

SYSTOLIC BP* (mm Hg)	DIASTOLIC BP* (mm Hg)	CLASSIFICATION
<120	<80	Normal
120-139	80-89	Prehypertension
140-159	90-99	Stage I hypertension
≥160	≥100	Stage II hypertension

*Classification is based on the worst number (e.g., 168/60 mm Hg is considered stage II hypertension even though diastolic pressure is normal).

99. Word associations (not 100%, but they can help when you have to guess)

BUZZ PHRASE OR SCENARIO	CONDITION
Friction rub	Pericarditis
Kussmaul breathing (deep, rapid breathing)	Diabetic ketoacidosis
Kayser-Fleischer ring in the eye	Wilson disease
Bitot spots	Vitamin A deficiency
Dendritic corneal ulcers on fluorescein stain of the eye	Herpes keratitis
Cherry-red spot on the macula without hepatosplenomegaly	Tay-Sachs disease
Cherry-red spot on the macula with hepatosplenomegaly	Niemann-Pick disease
Bronze skin plus diabetes	Hemochromatosis
Malar rash on the face	Systemic lupus erythematosus
Heliotrope rash (purplish rash on the eyelids)	Dermatomyositis
Clue cells	*Gardnerella vaginalis* infection
Meconium ileus	Cystic fibrosis
Rectal prolapse	Cystic fibrosis
Salty-tasting infant	Cystic fibrosis
Café-au-lait spots with normal IQ	Neurofibromatosis
Café-au-lait spots with mental retardation	McCune-Albright syndrome or tuberous sclerosis
Worst headache of the patient's life	Subarachnoid hemorrhage
Abdominal striae	Cushing syndrome or pregnancy
Honey ingestion	Infant botulism
Left lower quadrant tenderness/rebound	Diverticulitis
Children who torture animals	Conduct disorder
Currant jelly stools in children	Intussusception
Ambiguous genitalia and hypotension	21-Hydroxylase deficiency in girls
Catlike cry in an infant	Cri-du-chat syndrome
Infant weighing more than 10 lb	Maternal diabetes
Anaphylaxis from immunoglobulin therapy	IgA deficiency
Postpartum fever unresponsive to broad-spectrum antibiotics	Septic pelvic thrombophlebitis

BUZZ PHRASE OR SCENARIO	CONDITION
Increased hemoglobin A2 and anemia	Thalassemia
Heavy young woman with papilledema and negative CT/MR scan of head	Pseudotumor cerebri
Low-grade fever in the first 24 hr after surgery	Atelectasis
Vietnam veteran	Posttraumatic stress disorder
Bilateral hilar adenopathy in an African American patient	Sarcoidosis
Sudden death in a young athlete	Hypertrophic obstructive cardiomyopathy
Fractures or bruises in different stages of healing in a child	Child abuse
Absent breath sounds in a trauma patient	Pneumothorax
Shopping sprees	Mania
Constant clearing of throat in a child or teenager	Tourette syndrome
Intermittent bursts of swearing	Tourette syndrome
Koilocytosis	HPV or cytomegalovirus
Rash develops after administration of ampicillin or amoxicillin for sore throat	Epstein-Barr virus infection
Daytime sleepiness and occasional falling down (cataplexy)	Narcolepsy
Facial port wine stain and seizures	Sturge-Weber syndrome

100. **Signs and syndromes**

SIGN/SYNDROME	EXPLANATION
Babinski sign	Stroking the bottom of the foot yields extension of the big toe and fanning of other toes (upper motor neuron lesion)
Beck triad	Jugular venous distention, muffled heart sounds, and hypotension (cardiac tamponade)
Brudzinski sign	Pain on neck flexion with meningeal irritation (meningitis)
Charcot triad	Fever/chills, jaundice, and right upper quadrant pain (cholangitis)
Chvostek sign	Tapping on the facial nerve elicits tetany (hypocalcemia)
Courvoisier sign	Painless, palpable gallbladder plus jaundice (pancreatic cancer)
Cullen sign	Bluish discoloration of periumbilical area (pancreatitis with retroperitoneal hemorrhage)
Cushing reflex	Hypertension, bradycardia, and irregular respirations (high intracranial pressure)
Grey Turner sign	Bluish discoloration of flank (pancreatitis with retroperitoneal hemorrhage)
Homans sign	Calf pain on forced dorsiflexion of the foot (DVT)
Kehr sign	Pain in the left shoulder (ruptured spleen)
Leriche syndrome	Claudication and atrophy of the buttocks with impotence (aortoiliac occlusive disease)
McBurney sign	Tenderness at McBurney point (appendicitis)

Continued

SIGN/SYNDROME	EXPLANATION
Murphy sign	Arrest of inspiration during palpation under the rib cage on the right (cholecystitis)
Ortolani sign/test	Abducting an infant's flexed hips causes a palpable/audible click (congenital hip dysplasia)
Prehn sign	Elevation of a painful testicle relieves pain (epididymitis vs. testicular torsion)
Rovsing sign	Pushing on left lower quadrant then releasing your hand produces pain at McBurney point (appendicitis)
Tinel sign	Tapping on the volar surface of the wrist elicits paresthesias (carpal tunnel syndrome)
Trousseau sign	Pumping up a blood pressure cuff causes carpopedal spasm (tetany from hypocalcemia)
Virchow triad	Stasis, endothelial damage, and hypercoagulability (risk factors for DVT)

ACID–BASE AND ELECTROLYTES

1. How do you analyze arterial blood gas values?

Remember three basic points:

1. pH tells you whether you are dealing with acidosis or alkalosis as the primary event. The body will compensate as much as it can (secondary event).
2. Look at the carbon dioxide (CO_2) value. If it is high, the patient either has respiratory acidosis (pH < 7.4) or is compensating for metabolic alkalosis (pH > 7.4). If CO_2 is low, the patient either has respiratory alkalosis (pH > 7.4) or is compensating for metabolic acidosis (pH < 7.4).
3. Look at the bicarbonate value. If it is high, the patient either has metabolic alkalosis (pH > 7.4) or is compensating for respiratory acidosis (pH < 7.4). If bicarbonate is low, the patient either has metabolic acidosis (pH < 7.4) or is compensating for respiratory alkalosis (pH > 7.4).

2. True or false: The body does not compensate beyond a normal pH.

True. For example, a patient with metabolic acidosis will eliminate CO_2 to help restore a normal pH. However, if respiratory alkalosis is a compensatory mechanism (and not a rare, separate primary disturbance), then the pH will not correct to greater than 7.4. Overcorrection does not occur.

3. List the common causes of acidosis.

Respiratory acidosis: Chronic obstructive pulmonary disease, asthma, drugs (e.g., opioids, benzodiazepines, barbiturates, alcohol, other respiratory depressants), chest wall problems (paralysis, pain), and sleep apnea.

Metabolic acidosis: Ethanol, diabetic ketoacidosis, uremia, lactic acidosis (e.g., sepsis, shock, bowel ischemia), methanol/ethylene glycol, aspirin/salicylate overdose, diarrhea, and carbonic anhydrase inhibitors.

4. List the common causes of alkalosis.

Respiratory alkalosis: Anxiety/hyperventilation and aspirin/salicylate overdose.

Metabolic alkalosis: Diuretics (except carbonic anhydrase inhibitors), vomiting, volume contraction, antacid abuse/milk-alkali syndrome, and hyperaldosteronism.

5. What type of acid-base disturbance does aspirin overdose cause?

Respiratory alkalosis and metabolic acidosis (two different primary disturbances). Look for coexisting tinnitus, hypoglycemia, vomiting, and a history of "swallowing several pills." Alkalinization of the urine with bicarbonate speeds excretion.

6. What happens to the blood gas of patients with chronic lung conditions?

In certain people with chronic lung conditions (especially those with sleep apnea), pH may be alkaline during the day because they breathe better when awake. In addition, just after an episode of bronchitis or other respiratory disorder, the metabolic alkalosis that usually compensates for respiratory acidosis is no longer a compensatory mechanism and becomes the primary disturbance (elevated pH and bicarbonate). As a side note, remember that sleep apnea, like other chronic lung diseases, can cause right-sided heart failure (cor pulmonale).

7. Should you give bicarbonate to a patient with acidosis?

For purposes of the Step 2 boards, almost never. First try intravenous (IV) fluids and correction of the underlying disorder. If all other measures fail and the pH remains less than 7.0, bicarbonate may be given.

8. The blood gas of a patient with asthma has changed from alkalotic to normal, and the patient seems to be sleeping. Is the patient ready to go home?

For Step 2 purposes, this scenario means that the patient is probably crashing. Remember that pH is initially high in patients with asthma because they are eliminating CO_2. If the patient becomes tired and does not breathe appropriately, CO_2 will begin to rise and pH will begin to normalize. Eventually the patient becomes acidotic and requires emergency intubation if appropriate measures are not taken. If this scenario is mentioned on boards, the appropriate response is to prepare for possible elective intubation and to continue aggressive medical treatment with beta$_2$ agonists, steroids, and oxygen. Fatigue secondary to work of breathing is an indication for intubation. Asthmatic patients are supposed to be slightly alkalotic during an asthma attack. If they are not, you should wonder why.

9. List the signs and symptoms of hyponatremia.

- Lethargy
- Seizures
- Mental status changes or confusion
- Cramps
- Anorexia
- Coma

10. How do you determine the cause of hyponatremia?

The first step in determining the cause is to look at the volume status:

	HYPOVOLEMIC	EUVOLEMIC	HYPERVOLEMIC
Think of	Dehydration, diuretics, diabetes, Addison disease/ hypoaldosteronism (high potassium)	SIADH, psychogenic polydipsia, oxytocin use	Heart failure, nephrotic syndrome, cirrhosis, toxemia, renal failure

SIADH, Syndrome of inappropriate antidiuretic hormone secretion

11. How is hyponatremia treated?

For hypovolemic hyponatremia, the treatment is normal saline. Euvolemic and hypervolemic hyponatremia are treated with water/fluid restriction; diuretics may be needed for hypervolemic hyponatremia.

12. What medication is used to treat the syndrome of inappropriate antidiuretic hormone secretion (SIADH) if water restriction fails?

Demeclocycline, which induces nephrogenic diabetes insipidus.

13. What happens if hyponatremia is corrected too quickly?

Overly quick correction may cause brainstem damage (**central pontine myelinolysis**). Hypertonic saline is used only when a patient has seizures from severe hyponatremia—and even then, only briefly and cautiously. Normal saline is a better choice 99% of the time for board purposes. In chronic severe symptomatic hyponatremia, the rate of correction should not exceed 0.5 to 1 mEq/L/hr.

14. What causes spurious (false) hyponatremia?

- Hyperglycemia (Once glucose is greater than 200 mg/dL, sodium decreases by 1.6 mEq/L for each rise of 100 mg/dL in glucose. Make sure you know how to make this correction.)
- Hyperproteinemia
- Hyperlipidemia

In these instances, the laboratory value is low, but the total body sodium is normal. Do not give the patient extra salt or saline.

15. What causes hyponatremia in postoperative patients?

The most common cause is the combination of pain and narcotics (causing SIADH) with overaggressive administration of IV fluids. A rare cause that you may see on the USMLE is adrenal insufficiency; in this instance, potassium is high and the blood pressure is low.

16. What is the classic cause of hyponatremia in pregnant patients about to deliver?

Oxytocin, which has an antidiuretic hormone–like effect.

17. What are the signs and symptoms of hypernatremia?

Basically the same as the signs and symptoms of hyponatremia:

- Mental status changes or confusion
- Seizures
- Hyperreflexia
- Coma

18. What causes hypernatremia?

The most common cause is dehydration (free water loss) caused by inadequate fluid intake relative to bodily needs. Watch for diuretics, diabetes insipidus, diarrhea, and renal disease, as well as iatrogenic causes (administration of too much hypertonic IV fluid). Sickle cell disease, which may lead to renal damage and isosthenuria (inability to concentrate urine), is a rare cause of hypernatremia, as are hypokalemia and hypercalcemia, which also impair the kidney's concentrating ability.

19. How is hypernatremia treated?

Treatment involves water replacement, but the patient is often severely dehydrated; therefore normal saline is used most frequently. Once the patient is hemodynamically stable, he or she is often switched to ½ normal saline. Five percent dextrose in water (D_5W) should not be used for hypernatremia.

20. What are the signs and symptoms of hypokalemia?

Hypokalemia causes muscular weakness, which can lead to paralysis and ventilatory failure. When smooth muscles also are affected, patients may develop ileus and/or hypotension. However, the best known and most tested effect of hypokalemia is on the heart. Electrocardiogram (ECG) findings include loss of the T wave or T-wave flattening, the presence of U waves, premature ventricular and atrial complexes, and ventricular and atrial tachyarrhythmias.

21. What is the effect of pH on serum potassium?

Changes in pH cause changes in serum potassium as a result of cellular shift. Alkalosis causes hypokalemia, whereas acidosis causes hyperkalemia. For this reason, bicarbonate is given to severely hyperkalemic patients. If the pH is deranged, normalization most likely will correct the potassium derangement automatically without the need to give or restrict potassium.

22. Describe the interaction between digoxin and potassium.

The heart is particularly sensitive to hypokalemia in patients taking digoxin. Potassium levels should be monitored carefully in all patients taking digoxin, especially if they are also taking diuretics (a common occurrence).

23. How should potassium be replaced?

Like all electrolyte abnormalities, hypokalemia should be corrected slowly. Oral replacement is preferred, but if the potassium must be given intravenously for severe derangement, do not give more than 20 mEq/hr. Put the patient on an ECG monitor when giving IV potassium because potentially fatal arrhythmias may develop.

24. When hypokalemia persists even after administration of significant amounts of potassium, what should you do?

Check the magnesium level. When magnesium is low, the body cannot retain potassium effectively. Correction of a low magnesium level allows the potassium level to return to normal.

25. What are the signs and symptoms of hyperkalemia?

Weakness and paralysis may occur, but the cardiac effects are the most tested. ECG changes (in order of increasing potassium value) include **tall peaked T waves,** widening of QRS, prolongation of the PR interval, loss of P waves, and a sine wave pattern (Figure 1-1). Arrhythmias include asystole and ventricular fibrillation.

26. What causes hyperkalemia?

- Renal failure (acute or chronic)
- Severe tissue destruction (because potassium has a high intracellular concentration)
- Hypoaldosteronism (watch for hyporeninemic hypoaldosteronism in diabetes)
- Medications (stop potassium-sparing diuretics, beta blockers, nonsteroidal antiinflammatory drugs (NSAIDs), angiotensin-converting enzyme (ACE) inhibitors, and angiotensin receptor blockers)
- Adrenal insufficiency (also associated with low sodium and low blood pressure)

27. What should you suspect if an asymptomatic patient has hyperkalemia?

With hyperkalemia, the first consideration (especially if the patient is asymptomatic and the ECG is normal) is whether the laboratory specimen is hemolyzed. Hemolysis causes a false hyperkalemia result because of high intracellular potassium concentrations. Repeat the test.

28. The specimen was not hemolyzed. What is the first treatment?

Obtain an ECG first to look for cardiotoxicity. In general, the best therapy for hyperkalemia is decreased potassium intake and administration of oral sodium polystyrene resin (Kayexalate). But if the potassium level is greater than 6.5 or cardiac toxicity is apparent (more than peaked T waves), immediate IV therapy is needed. First give **calcium gluconate** (which is cardioprotective, although it does not change potassium levels); then give **sodium bicarbonate** (alkalosis causes potassium to shift inside cells) and **glucose with insulin** (insulin also forces potassium inside cells and glucose prevents hypoglycemia). $Beta_2$ agonists also drive potassium into cells and can be given if the other choices are not listed on the test. If the patient has renal failure (high creatinine) or initial treatment is ineffective, prepare to institute emergent dialysis.

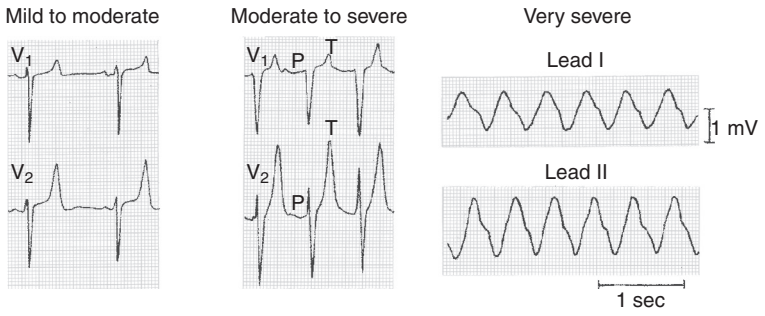

Figure 1-1. The earliest electrocardiogram (ECG) change with hyperkalemia is peaking of the T waves. As the serum potassium concentration increases, the QRS complexes widen, the P waves decrease in amplitude and may disappear, and finally a sine wave pattern leads to asystole unless emergency therapy is given. (From Goldberger A. Clinical electrocardiography: a simplified approach. 7th ed. Philadelphia: Mosby, 2006, Fig. 10-6.)

29. What are the signs and symptoms of hypocalcemia?

Hypocalcemia produces neurologic findings, the most tested of which is tetany. Tapping on the facial nerve at the angle of the jaw elicits contraction of the facial muscles (**Chvostek sign**), and inflation of a tourniquet or blood pressure cuff elicits hand muscle (carpopedal) spasms (**Trousseau sign**). Other signs and symptoms are depression, encephalopathy, dementia, laryngospasm, and convulsions/seizures. The classic ECG finding is QT-interval prolongation.

30. What should you do if the calcium level is low?

First, remember that hypoproteinemia (i.e., low albumin) of any etiology can cause hypocalcemia because the protein-bound fraction of calcium is decreased. In this instance, however, the patient is asymptomatic because the ionized (unbound, physiologically active) fraction of calcium is unchanged. Thus you should first check the albumin level and/or the ionized or free calcium level to make sure "true" hypocalcemia is present. For every 1 g/dL decrease in albumin below 4 g/dL, correct the calcium by adding 0.8 mg/dL to the given calcium value.

31. What causes hypocalcemia?

- DiGeorge syndrome (tetany 24–48 hr after birth, absent thymic shadow on x-ray)
- Renal failure (remember the kidney's role in vitamin D metabolism)
- Hypoparathyroidism (watch for a postthyroidectomy patient; all four parathyroids may have been accidentally removed)
- Vitamin D deficiency
- Pseudohypoparathyroidism (short fingers, short stature, mental retardation, and normal levels of parathyroid hormone with end-organ unresponsiveness to parathyroid hormone)
- Acute pancreatitis
- Renal tubular acidosis

32. Describe the relationship between low calcium and low magnesium.

It is difficult to correct hypocalcemia until hypomagnesemia (of any cause) is also corrected.

33. How does pH affect calcium levels?

Alkalosis can cause symptoms similar to hypocalcemia through effects on the ionized fraction of calcium (alkalosis causes calcium to shift intracellularly). Clinically, this scenario is most common with hyperventilation/anxiety syndromes, in which the patient eliminates too much CO_2, becomes alkalotic, and develops perioral and extremity tingling. Treat by correcting the pH. Reduce anxiety if hyperventilation is the cause.

34. Describe the relationship between calcium and phosphorus.

Phosphorus and calcium levels usually go in opposite directions (when one goes up, the other goes down), and derangements in one can cause problems with the other. This relationship becomes clinically important in patients with chronic renal failure, in whom you must not only try to raise calcium levels (with vitamin D and calcium supplements) but also restrict/reduce phosphorus.

35. What are the signs and symptoms of hypercalcemia?

Hypercalcemia is often asymptomatic and discovered by routine lab tests. When symptoms are present, recall the following rhyme:

Bones (bone changes such as osteopenia and pathologic fractures).
Stones (kidney stones and polyuria).
Groans (abdominal pain, anorexia, constipation, ileus, nausea, and vomiting).
Psychiatric overtones (depression, psychosis, and delirium/confusion).

Abdominal pain may also be caused by peptic ulcer disease and/or pancreatitis, both of which have an increased incidence with hypercalcemia. The ECG classically shows QT-interval shortening when hypercalcemia is present.

36. What causes hypercalcemia?

Hypercalcemia in outpatients is most commonly caused by hyperparathyroidism. In inpatients, the most common cause is malignancy. Check the parathyroid hormone level to differentiate hyperparathyroidism from other causes.

Other causes include vitamin A or D intoxication, sarcoidosis, thiazide diuretics, familial hypocalciuric hypercalcemia (look for low urinary calcium, which is rare with hypercalcemia), and immobilization. Hyperproteinemia (e.g., high albumin) of any etiology can cause hypercalcemia because of an increase in the protein-bound fraction of calcium, but the patient is asymptomatic because the ionized (unbound) fraction is unchanged.

37. Why is asymptomatic hypercalcemia usually treated?

Prolonged hypercalcemia can cause nephrocalcinosis, urolithiasis, and renal failure because of calcium salt deposits in the kidney and may result in bone disease secondary to loss of calcium.

38. How is hypercalcemia treated?

First, give IV fluids. Once the patient is well hydrated, give furosemide (i.e., a loop diuretic) to cause calcium diuresis. Thiazides are contraindicated because they increase serum calcium levels. Other treatments include phosphorus administration (use oral phosphorus; IV administration can be dangerous), calcitonin, bisphosphonates (e.g., etidronate, which is often used in Paget disease), plicamycin, or prednisone (especially for malignancy-induced hypercalcemia). Correction of the underlying cause of hypercalcemia is the ultimate goal. The previous measures are all temporary until definitive treatment can be given. For hyperparathyroidism, surgery is the treatment of choice.

39. In what clinical scenario is hypomagnesemia usually seen?

Alcoholism. Magnesium is wasted through the kidneys.

40. What are the signs and symptoms of hypomagnesemia?

Signs and symptoms are similar to those of hypocalcemia (prolonged QT interval on ECG and possibly tetany).

41. In what clinical scenario is hypermagnesemia seen?

Hypermagnesemia is classically iatrogenic in patients who are pregnant and are treated for preeclampsia with magnesium sulfate. It also commonly occurs in patients with renal failure. Patients who receive magnesium sulfate should be monitored carefully because the physical findings of hypermagnesemia are progressive. The initial sign is a decrease in deep tendon reflexes, then hypotension and respiratory failure occur sequentially.

42. How is hypermagnesemia treated?

First, stop any magnesium infusion. Remember the ABCs (airway, breathing, circulation), and intubate the patient if necessary. If the patient is stable, start IV fluids. Furosemide can be given next, if needed, to cause a magnesium diuresis. The last resort is dialysis.

43. In what clinical scenarios is hypophosphatemia seen? What are the signs and symptoms?

Primarily in patients with uncontrolled diabetes (especially diabetic ketoacidosis) and alcoholic patients. Signs and symptoms of hypophosphatemia include neuromuscular disturbances (encephalopathy, weakness), rhabdomyolysis (especially in alcoholic patients), anemia, and white blood cell and platelet dysfunction.

44. What is the IV fluid of choice in hypovolemic patients?

Normal saline or lactated Ringer solution (regardless of other electrolyte problems). First fill the tank; then correct the imbalances that the kidney cannot sort out on its own.

45. What is the maintenance fluid of choice for patients who are not eating?

One half normal saline with 5% dextrose in adults. Typically one fourth normal saline with 5% dextrose in children weighing less than 10 kg; one third or one half normal saline with 5% dextrose in children weighing more than 10 kg.

46. Should anything be added to the IV fluid for patients who are not eating?

Usually potassium chloride, 10 or 20 mEq, is added to a liter of IV fluid each day to prevent hypokalemia (assuming that the baseline potassium level is normal).

CHAPTER 2

ALCOHOL

1. With which cancers is alcohol intake associated?

Cancers of the oral cavity, larynx, pharynx, esophagus, liver, and lung. It may also be associated with gastric, colon, pancreatic, and breast cancer.

2. What is the most common cause of cirrhosis and esophageal varices?

Alcohol.

3. Describe the relationship between alcohol and accidental or intentional (i.e., suicide, murder) death?

Alcohol is involved in roughly 50% of fatal car accidents, 67% of drownings, 67% of homicides, 35% of suicides, and 70% to 80% of deaths caused by fire.

4. What may happen if you give glucose to an alcoholic without giving thiamine first?

You may precipitate Wernicke encephalopathy. **Always give thiamine before glucose** to avoid this complication.

5. What is the difference between Wernicke and Korsakoff syndromes? What causes each?

Wernicke syndrome is an acute encephalopathy characterized by ophthalmoplegia, nystagmus, ataxia, and/or confusion. It can be fatal, but is often reversible with thiamine.

Korsakoff syndrome is a chronic psychosis characterized by anterograde amnesia (inability to form new memories) and confabulation (lying) to cover up the amnesia. Korsakoff syndrome is generally irreversible and is thought to be due to damage to the mamillary bodies and thalamic nuclei. Both conditions result from thiamine deficiency.

6. True or false: Alcohol withdrawal can be fatal.

True. Alcohol withdrawal needs to be treated on an inpatient basis because it can result in death (mortality rate of 1% to 5% with delirium tremens).

7. How is alcohol withdrawal treated?

With benzodiazepines (or, in rare cases, barbiturates). The dose is tapered gradually over several days until symptoms have resolved.

8. What are the stages of alcohol withdrawal?

Acute withdrawal syndrome (12 to 48 hours after last drink): Tremors, sweating, hyperreflexia, and seizures ("rum fits").

Alcoholic hallucinosis (24 to 72 hours after last drink): Auditory and visual hallucinations and illusions without autonomic signs.

Delirium tremens (2 to 7 days after last drink, possibly longer): Hallucinations and illusions, confusion, poor sleep, and autonomic lability (sweating, increased pulse and temperature). Fatality is usually associated with this stage.

These stages may overlap. Delirium tremens may occur several days after the last drink. The classic example is a patient who develops delirium on postoperative day 2 but was fine before surgery. He or she could be a closet alcoholic, assuming other causes for delirium have been ruled out.

9. What are the classic physical stigmata of liver disease in alcoholics?

- Abdominal wall varices (caput medusae)
- Testicular atrophy
- Esophageal varices
- Encephalopathy
- Hemorrhoids (internal)
- Asterixis
- Jaundice
- Scleral icterus
- Ascites
- Edema
- Palmar erythema
- Spider angiomas
- Gynecomastia
- Terry nails (white nails with a ground glass appearance and no lunula)
- Fetor hepaticus ("breath of the dead" which is a sweet, fecal smell)
- Dupuytren contractures

10. What are the classic laboratory findings of liver disease in alcoholics?

- Anemia (classically macrocytic)
- Prolonged prothrombin time
- Hyperbilirubinemia
- Hypoalbuminemia
- Thrombocytopenia

11. What diseases and conditions may be caused by chronic alcohol intake?

- Gastritis
- Fatty change in the liver
- Mallory-Weiss tears
- Hepatitis
- Pancreatitis (acute or chronic)
- Cirrhosis
- Peripheral neuropathy (via thiamine deficiency and a direct effect)
- Wernicke or Korsakoff syndrome
- Cerebellar degeneration (ataxia, past-pointing)
- Dilated cardiomyopathy
- Rhabdomyolysis (acute or chronic)

12. Describe the classic derangement of aspartate aminotransferase (AST) and alanine aminotransferase (ALT) in alcoholic hepatitis.

The ratio of AST (also known as serum glutamate oxaloacetate transaminase [SGOT]) to ALT (also known as serum glutamate pyruvate transaminase [SGPT]) is at least 2:1, although both may be elevated. Other causes of hepatitis usually are associated with the opposite ratio or equal elevation of both AST and ALT.

13. What is the best treatment for alcoholism?

Alcoholics Anonymous or other peer-based support groups have had the best success rates. Disulfiram (an aldehyde dehydrogenase enzyme inhibitor that makes people sick when they drink) can be used in some patients. Be sure to warn patients that metronidazole and certain cephalosporins have a similar effect on those who drink alcohol.

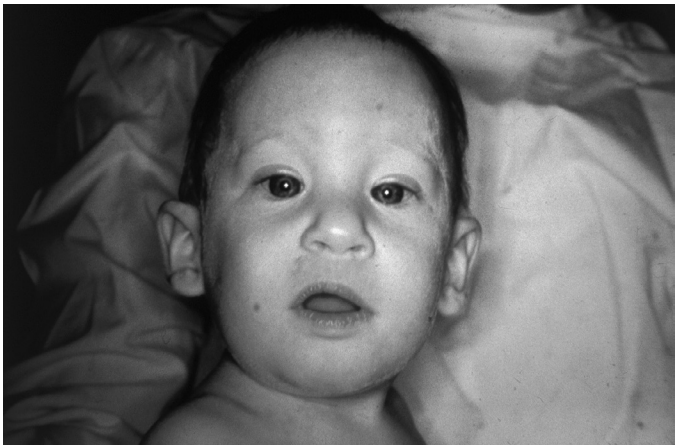

Figure 2-1. Infant with fetal alcohol syndrome. Note short palpebral fissures, mild ptosis, nostrils, smooth philtrum, and narrow vermillion of the upper lip. See Plate 1. (From Gilbert-Barness E. Potter's pathology of the fetus, infant and child. 2nd ed. Philadelphia. Elsevier, 2007, Fig. 4.1.12.)

14. Describe the effects of alcohol on pregnancy

Alcohol is a definite teratogen and the most common cause of preventable mental retardation in the United States. You should be able to recognize the classic presentation of a child affected by fetal alcohol syndrome: mental retardation, microcephaly, microphthalmia, short palpebral fissures, midfacial hypoplasia, and cardiac defects (Fig. 2-1; Plate 1). No amount of alcohol consumption can be considered safe during pregnancy. Fetal alcohol syndrome rates vary, but may affect as many as 1 in 1000 births in the United States.

15. Discuss the epidemiology of alcohol abuse.

Roughly 10% to 15% of the population abuses alcohol. Alcohol abuse is more common in men. The genetic component is passed most easily from father to son.

16. What kind of pneumonia should you suspect in a homeless alcoholic patient?

Aspiration pneumonia. Look for enteric organisms (anaerobes, *Escherichia coli*, streptococci, and staphylococci) as the cause. Think of *Klebsiella* spp. if the sputum resembles currant jelly or if thick, mucoid capsules are mentioned in culture reports.

17. True or false: Alcohol can precipitate hypoglycemia.

True. But give thiamine first, then glucose in an alcoholic.

18. What are the classic electrolyte and vitamin/mineral abnormalities in alcoholics?

Electrolytes: Low magnesium, low potassium, low sodium, and elevated uric acid (resulting in gout)

Vitamins: Deficiencies of folate and thiamine

Remember that alcoholics tend to have poor nutrition and may develop just about any deficiency.

19. How are bleeding esophageal varices treated?

First, think of the ABCs (airways, breathing, and circulation). Stabilize the patient with intravenous (IV) fluids and blood, if needed. If indicated, correct clotting factor deficiencies with fresh frozen plasma, fresh blood, and vitamin K. Next, perform upper endoscopy to determine the cause of the upper

gastrointestinal (GI) bleed (there are many possibilities in an alcoholic). Once varices are identified on endoscopy, sclerotherapy of the veins is attempted with cauterization, banding, or vasopressin. The mortality rate is high, and rebleeding is common. If you must choose, try a transjugular intrahepatic portosystemic shunt (TIPS) over an open surgical portacaval shunt for more definitive management, if needed. The most physiologic shunt type among surgical options is the splenorenal shunt. However, open surgical shunt procedures are now rarely performed.

20. How are varices with no history of bleeding treated?

With nonselective beta blockers (propranolol, nadolol, and timolol) to relieve portal hypertension, provided that there is no contraindication to the use of beta blockers.

CHAPTER 3

BIOSTATISTICS

1. How is the sensitivity of a test defined? What are highly sensitive tests used for clinically?

Sensitivity is defined as the ability of a test to detect disease—mathematically, the number of true positives divided by the number of people with the disease. Tests with high sensitivity are used for disease screening. False-positive results occur, but the test does not miss many people with the disease (low false-negative rate).

2. How is the specificity of a test defined? What are highly specific tests used for clinically?

Specificity is defined as the ability of a test to detect health (or nondisease)—mathematically, the number of true negatives divided by the number of people without the disease. Tests with high specificity are used for disease confirmation. False-negative results occur, but the test does not call anyone sick who is actually healthy (low false-positive rate). The ideal confirmatory test must have high sensitivity and high specificity; otherwise, people with the disease may be called healthy.

3. Explain the concept of a trade-off between sensitivity and specificity.

The trade-off between sensitivity and specificity is a classic statistics question. For example, you should understand how changing the cutoff glucose value in screening for diabetes (or changing the value of any of several screening tests) will change the number of true- and false-negative as well as true- and false-positive results. If the cutoff glucose value is raised, fewer people will be called diabetic (more false-negative results, fewer false-positive results), whereas if the cutoff glucose value is lowered, more people will be called diabetic (fewer false-negative results, more false-positive results) (Fig. 3-1).

4. Define positive predictive value (PPV). On what does it depend?

When a test is positive for disease, the PPV measures how likely it is that the patient has the disease (probability of having a condition, given a positive test). PPV is calculated mathematically by dividing the number of true-positive results by the total number of people with a positive test. PPV depends on the prevalence of a disease (the higher the prevalence, the higher the PPV) and the sensitivity and specificity of the test (e.g., an overly sensitive test that gives more false-positive results has a lower PPV).

5. Define negative predictive value (NPV). On what does it depend?

When a test comes back negative for disease, the NPV measures how likely it is that the patient is healthy and does not have the disease (probability of not having a condition, given a negative test). It is calculated mathematically by dividing the number of true-negative results by the total number of people with a negative test. NPV also depends on the prevalence of the disease and the sensitivity and specificity of the test (the higher the prevalence, the lower the NPV). In addition, an overly sensitive test with lots of false-positive results makes the NPV higher.

6. Define attributable risk. How is it measured?

Attributable risk is the number of cases of a disease attributable to one risk factor (in other words, the amount by which the incidence of a condition is expected to decrease if the risk factor in question is removed). For example, if the incidence rate of lung cancer is 1/100 in the general population and

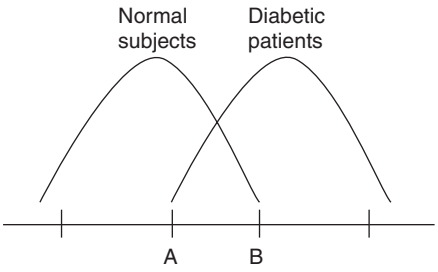

Figure 3-1. If the cutoff serum glucose value for a diagnosis of diabetes mellitus is set at point A, no cases of diabetes will be missed, but many people without diabetes will be mislabeled as diabetics (i.e., higher sensitivity, lower specificity, lower positive predictive value (PPV), higher negative predictive value (NPV)). If the cutoff is set at B, the diagnosis of diabetes will not be made in healthy people, but many cases of true diabetes will go undiagnosed (i.e., lower sensitivity, higher specificity, higher PPV, lower NPV). The optimal diagnostic value lies somewhere between points A and B.

10/100 in smokers, the attributable risk of smoking in causing lung cancer is 9/100 (assuming a properly matched control).

7. Develop the habit of drawing a 2 × 2 table for Step 2 statistics questions. Given the 2 × 2 table below, define the formulas for calculating the following test values:

	DISEASE		TEST NAME	FORMULA
	(+)	(–)		
Test or exposure (+)	A	B	Sensitivity	A/(A + C)
Test or exposure (+)			Specificity	D/(B + D)
Test or exposure (+)			PPV	A/(A + B)
Test or exposure (–)	C	D	NPV	D/(C + D)
			Odds ratio	(A × D)/(B × C)
			Relative risk	[A/(A + B)]/[C/(C + D)]
			Attributable risk	[A/(A + B)] – [C/(C + D)]

8. Define relative risk. From what type of studies can it be calculated?

Relative risk compares the disease risk in people exposed to a certain factor with the disease risk in people who have not been exposed to the factor in question. Relative risk can be calculated only after prospective or experimental studies; it cannot be calculated from retrospective data. If a Step 2 question asks you to calculate the relative risk from retrospective data, the answer is "cannot be calculated" or "none of the above."

9. What is a clinically significant value for relative risk?

Any value for relative risk other than 1 is clinically significant. For example, if the relative risk is 1.5, a person is 1.5 times more likely to develop the condition if exposed to the factor in question. If the relative risk is 0.5, the person is only half as likely to develop the condition when exposed to the factor; in other words, the factor protects the person from developing the disease.

10. Define odds ratio. From what type of studies is it calculated?

Odds ratio attempts to estimate relative risk with retrospective studies (e.g., case-control). An odds ratio compares the incidence of disease in persons exposed to the factor and the incidence of nondisease in persons not exposed to the factor with the incidence of disease in persons unexposed to the factor and the incidence of nondisease in persons exposed to the factor to see whether there is a difference between the two. As with relative risk, values other than 1 are significant. The odds ratio is a less than perfect way to estimate relative risk (which can be calculated only from prospective or experimental studies).

11. What do you need to know about standard deviation (SD) for the USMLE?

You need to know that with a normal or bell-shaped distribution, 1 SD holds 68% of the values, 2 SD hold 95% of the values, and 3 SD hold 99.7% of the values. A classic question gives you the mean and standard deviations and asks you what percentage of values will be above a given value. For example, if the mean score on a test is 80 and the standard deviation is 5, 68% of the scores will be within 5 points of 80 (scores of 75 to 85) and 95% of the scores will be within 10 points of 80 (scores of 70 to 90). The question may ask what percentage of scores are over 90. The answer is 2.5%, because 2.5% of the scores fall below 70 and 2.5% of the scores are over 90. Variations of this question are common.

12. Define mean, median, and mode.

The mean is the average value, the median is the middle value, and the mode is the most common value. A question may give you several numbers and ask you for their mean, median, and mode. For example, if the question gives you the numbers 2, 2, 4, and 8:
The mean is the average of the four numbers: $(2 + 2 + 4 + 8)/4 = 16/4 = 4$.
The median is the middle value. Because there are four numbers, there is no true middle value. Therefore, take the average between the two middle numbers (2 and 4). The median is 3.
The mode is two, because the number two appears twice (more times than any other value).
Remember that in a normal distribution, mean = median = mode.

13. What is a skewed distribution? How does it affect mean, median, and mode?

A skewed distribution implies that the distribution is not normal; in other words, the data do not conform to a perfect bell-shaped curve. **Positive skew** is an asymmetric distribution with an excess of high values, in other words, the tail of the curve is on the right (mean > median > mode) (Fig. 3-2). **Negative skew** is an asymmetric distribution with an excess of low values, in other words, the tail of the curve is on the left (mean < median < mode). Because they are not normal distributions, SD and mean are less meaningful values.

14. Define test reliability. How is it related to precision? What reduces reliability?

Practically speaking, the reliability of a test is synonymous with its precision. Reliability measures the reproducibility and consistency of a test. For example, if the test has good interrater reliability,

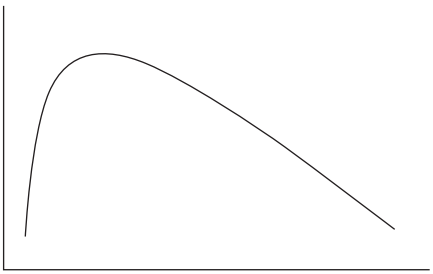

Figure 3-2. Positive skew. An excess of higher values makes this a nonnormal distribution.

the person taking the test will get the same score if two different people administer the same test. Random error reduces reliability and precision (e.g., limitation in significant figures).

15. Define test validity. How is it related to accuracy? What reduces validity?

Practically speaking, the validity of a test is synonymous with its accuracy. Validity measures the trueness of measurement, in other words, whether the test measures what it claims to measure. For example, if you give a valid IQ test to a genius, the test should not indicate that he or she is challenged. Systematic error reduces validity and accuracy (e.g., when the equipment is miscalibrated).

16. Define correlation coefficient. What is the range of its values?

A correlation coefficient measures to what degree two variables are related. The value of the correlation coefficient ranges from –1 to +1.

17. True or false: A correlation coefficient of –0.6 is a stronger correlation coefficient than +0.4

True. The important factor in determining the strength of the relationship between the two variables is the distance of the value from zero. A zero correlation equals no association whatsoever; the two variables are totally unrelated. Positive 1 equals a perfect positive correlation (when one variable increases, so does the other), whereas negative 1 equals a perfect negative correlation (when one variable increases, the other decreases). Therefore, use the absolute value to give you the strength of the correlation (e.g., –0.3 is equal to +0.3).

18. Define confidence interval. Why is it used?

When you take a set of data from a subset of the population and calculate its mean, you want to say that it is equivalent to the mean of the whole population. However, the two means are usually not exactly equal. A confidence interval of 95% (the value used in most medical literature before data are accepted by the medical community) says that you are 95% confident that the mean of the entire population is within a certain range (usually two SD of your experimental or derived mean, calculated from the subset of the population that you examined). For example, if you sample the heart rate of 100 people and calculate a mean of 80 beats per minute and a standard deviation of 2, your confidence interval (also known as confidence limits) is written as $76 < X < 84 = 0.95$. In other words, you are 95% certain that the mean heart rate of the whole population (X) is between 76 and 84 (within 2 SD of the mean).

19. What five types of studies should you know for the Step 2 exam?

From highest to lowest quality and desirability:

1. Experimental studies.
2. Prospective studies.
3. Retrospective studies.
4. Case series.
5. Prevalence surveys.

20. What is an experimental study?

Experimental studies are the gold standard. They compare two equal groups in which one variable is manipulated and its effect is measured. Experimental studies use double-blinding (or at least single-blinding) and well-matched controls to ensure accurate data. It is not always possible to do experimental studies because of ethical concerns.

21. What are prospective studies? Why are they important?

Prospective studies (also known as observational, longitudinal, cohort, incidence, or follow-up studies) involve choosing a sample, dividing it into two groups based on the presence or absence of a risk factor, and then following the groups over time to see what diseases they develop. For example, you can follow people with and without asymptomatic hypercholesterolemia to see if people with

hypercholesterolemia have a higher incidence of myocardial infarction later in life. You can calculate relative risk and incidence from this type of study. Prospective studies are time-consuming and expensive, but are practical for common diseases.

22. What are retrospective studies? Discuss their advantages and disadvantages

Retrospective (case-control) studies choose population samples after the fact, based on the presence (cases) or absence (controls) of disease. Information can be collected about risk factors; for example, you can compare people with lung cancer and people without lung cancer to see if people with lung cancer smoked more before they developed lung cancer. With a retrospective study you can calculate an odds ratio, but you cannot calculate a true relative risk or measure incidence. Compared with prospective studies, retrospective studies are less expensive, less time-consuming, and more practical for rare diseases.

23. What is a case series study? How is it used?

A case series study simply describes the clinical presentation of people with a certain disease. This type of study is good for extremely rare diseases (as are retrospective studies) and may suggest a need for a retrospective or prospective study.

24. What is a prevalence survey? How is it used?

Prevalence (cross-sectional) surveys look at the prevalence of a disease and its risk factors. When used to compare two different cultures or populations, a prevalence survey may suggest a possible cause of a disease. The hypothesis can then be tested with a prospective study. For example, researchers have found a high prevalence of colon cancer and a diet high in fat in the United States versus a low prevalence of colon cancer and a diet low in fat in Japan.

25. What is the difference between incidence and prevalence?

Incidence is the number of new cases of a disease in a unit of time (generally 1 year, but any time frame can be used). The incidence of a disease is equal to the absolute (or total) risk of developing a condition (as distinguished from relative or attributable risk).
Prevalence is the total number of cases of a disease (new or old) at a certain point in time.

26. If a disease can only be treated to the point that people can be kept alive longer without being cured, what happens to the incidence and prevalence of the disease?

This is the classic question about incidence and prevalence on the Step 2 exam. Nothing happens to the incidence (the same number of people contract the disease every year), but the prevalence will increase because people with the disease live longer. In short-term diseases (e.g., influenza), the incidence may be higher than the prevalence, whereas in chronic diseases (e.g., diabetes, hypertension), the prevalence is greater than the incidence.

27. Define epidemic.

In an epidemic, the observed incidence greatly exceeds the expected incidence.

28. When do you use a chi-squared test, *t*-test, and analysis of variance test?

All of these tests are used to compare different sets of data:
Chi-squared test: Compares percentages or proportions (nonnumeric or nominal data).
***t*-test:** Compares two means.
Analysis of variance (ANOVA): Compares three or more means.

29. What is the difference between nominal, ordinal, and continuous types of data?

Nominal data have no numeric value; for example, the day of the week. Ordinal data give a ranking but no quantification; for example, class rank, which does not specify how far number 1 is ahead of number 2. Most numerical measurements are continuous data; for example, weight, blood pressure,

and age. This distinction is important: Chi-squared tests must be used to compare nominal or ordinal data, whereas a *t*-test or ANOVA test is used to compare continuous data (see question 28).

30. Define *P*-value.

The significance of the *P*-value is high yield on the Step 2 exam. If *P* is less than 0.05 for a set of data, there is less than a 5% chance (0.05 = 5%) that the data were obtained by random error or chance. If *P* is less than 0.01, the chance is less than 1%. For example, if the blood pressure in a control group is 180/100 mm Hg, but falls to 120/70 mm Hg after drug X is given, a *P*-value less than 0.10 means that the chance that this difference was caused by random error or chance is less than 10%. It also means, however, that the chance that the result is random and unrelated to the drug may be as high as 9.99%. $P < 0.05$ is generally used as the cutoff for statistical significance in medical literature.

31. What three points about *P*-value should be remembered for the Step 2 exam?

1. A study with a *P*-value less than 0.05 may still have serious flaws.
2. A low *P*-value does not imply causation.
3. A study that has statistical significance does not necessarily have clinical significance. For example, if I tell you that drug X can lower blood pressure from 130/80 to 129/80 mm Hg with $P < 0.0001$, you will not use drug X because the result is not clinically important given the minimal blood pressure reduction, the cost, and probable side effects.

32. Explain the relationship of the *P*-value to the null hypothesis.

The *P*-value is also related to the null hypothesis (the hypothesis of no difference). For example, in a study of hypertension, the null hypothesis says that the drug under investigation does not work; therefore, any difference in blood pressure is because of random error or chance. When the drug works beautifully and lowers blood pressure by 60 points, the null hypothesis must be rejected because clearly the drug works. When $P < 0.05$, I can confidently reject the null hypothesis because the *P*-value tells me that there is less than a 5% chance that the null hypothesis is correct. If the null hypothesis is wrong, the difference in blood pressure is not caused by chance; therefore, it must be because of the drug.

In other words, the *P*-value represents the chance of making a type I error—that is, claiming an effect or difference when none exists, or rejecting the null hypothesis when it is true. If $P < 0.07$, there is less than a 7% chance that you are making a type I error if you claim a true difference (not because of random error) in blood pressure between the control and experimental groups.

33. What is a type II error?

In a type II error, the null hypothesis is accepted when in fact it is false. In the above example, it would mean that the antihypertensive drug works, but the experimenter says that it does not.

34. What is the power of a study? How do you increase the power of a study?

Power measures the probability of rejecting the null hypothesis when it is false (a good thing). The best way to increase power is to **increase the sample size.**

35. What are confounding variables?

Confounding variables are unmeasured variables that affect both the independent (manipulated, experimental) variable and dependent (outcome) variables. For example, an experimenter measures the number of ashtrays owned with the incidence of lung cancer and finds that people who have lung cancer have more ashtrays. He concludes that ashtrays cause lung cancer. Smoking tobacco is the confounding variable because it causes the increase in ashtrays and lung cancer.

36. Discuss nonrandom or nonstratified sampling.

City A and city B can be compared, but they may not be equivalent. For example, if city A is a retirement community and city B is a college town, city A will have higher rates of mortality and heart disease if the groups are not stratified into appropriate age-specific comparisons.

37. What is nonresponse bias?

Nonresponse bias occurs when people do not return printed surveys or answer the phone in a phone survey. If nonresponse accounts for a significant percentage of the results, the experiment will suffer. The first strategy in this situation is to visit or call the nonresponders repeatedly. If this strategy is unsuccessful, list the nonresponders as unknown in the data analysis and see if any results can be salvaged. *Never* make up or assume responses.

38. Explain lead-time bias.

Lead-time bias is caused by time differentials. The classic example is a cancer screening test that claims to prolong survival compared with older survival data, when in fact the difference is only due to earlier detection—*not* improved treatment or prolonged survival.

39. Explain admission rate bias.

The classic admission rate bias occurs when an experimenter compares the mortality rates for myocardial infarction (or some other disease) in hospitals A and B and concludes that hospital A has a higher mortality rate. The higher rate may be caused by tougher admission criteria at hospital A, which admits only the sickest patients with myocardial infarction. Hence, hospital A has higher mortality rates, although its care may be superior. The same bias can apply to a surgeon's mortality and morbidity rates if he or she takes only tough cases.

40. Explain recall bias.

Recall bias is a risk in all retrospective studies. When people cannot remember exactly, they may inadvertently overestimate or underestimate risk factors. For example, John died of lung cancer and his angry widow remembers him as smoking “like a chimney,” whereas Mike died of non–smoking-related causes and his loving wife denies that he smoked “much.” In fact, both men smoked one pack per day.

41. Explain interviewer bias.

Interviewer bias occurs in the absence of blinding. The scientist receives big money to do a study and wants to find a difference between cases and controls. Thus he or she inadvertently calls the same patient comment or outcome “not significant” in the control group and “significant” in the treatment group.

42. What is unacceptability bias?

Unacceptability bias occurs when people do not admit to embarrassing behavior, claim to exercise more than they do to please the interviewer, or claim to take experimental medications when they spit them out.

CARDIOLOGY

1. What is your job when the Step 2 examination describes a patient with chest pain?

Make sure that the chest pain is not because of any life-threatening condition. Usually you must try to make sure that the patient has not had a heart attack.

2. What elements of the history and physical examination steer you away from a diagnosis of myocardial infarction (MI)?

Wrong age: In the absence of known heart disease, strong family history, or multiple risk factors for coronary artery disease, a patient younger than age 40 is extremely unlikely to have an MI.

Lack of risk factors: A 60-year-old marathon runner who eats well and has a high level of high-density lipoprotein (HDL) and no cardiac risk factors (other than age) is unlikely to have a heart attack.

Physical characteristics of pain: If the pain is reproducible by palpation, it is from the chest wall, not the heart. The pain associated with an MI is usually not sharp or well localized. The pain should not be related to certain foods or eating.

Even so, many physicians still want to make sure that a heart attack has not occurred with at least an electrocardiogram (ECG) and possibly one or more sets of cardiac enzyme levels. For the Step 2 examination, however, these clues should steer you toward an alternative diagnosis.

3. What findings on ECG should make you suspect an MI?

After a heart attack, ECG would show flipped or flattened T waves, ST segment elevation (depression means ischemia; elevation means injury), and/or Q waves in a segmental distribution (e.g., leads II, III, and aVF for an inferior infarct) (Fig. 4-1).

4. Describe the classic pattern of chest pain in an MI.

The pain is classically described as a crushing or pressure sensation; it is a poorly localized substernal pain that may radiate to the shoulder, arm, or jaw. The pain is usually not reproducible on palpation, and in patients with a heart attack, often does not resolve with nitroglycerin (as it often does in angina). The pain usually lasts at least half an hour.

5. What tests are used to diagnose an MI?

Other than an ECG, the patient with a possible MI should have serial determinations of troponin (usually drawn every 8 hours three times before a heart attack is ruled out). Troponin levels stay elevated for more than 24 hours. Radiographs may show cardiomegaly and/or pulmonary vascular congestion; echocardiography may show ventricular wall motion abnormalities.

6. Describe the classic physical examination findings in patients with MI.

Patients are often diaphoretic, anxious, tachycardic, tachypneic, and pale; they may have nausea and vomiting. With large heart attacks that cause heart failure, look for bilateral pulmonary rales in the absence of other pneumonia-like symptoms, distended neck veins, S_3 or S_4 heart sound, new murmurs, hypotension, and/or shock.

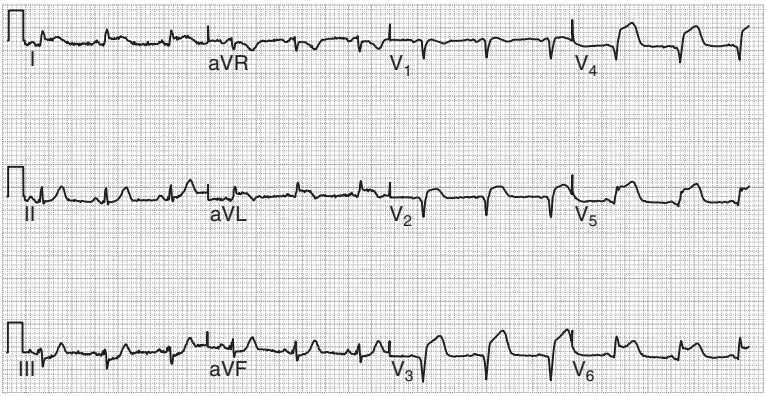

Figure 4-1. This figure shows an anterolateral acute myocardial infarction (MI) caused by a lesion in the proximal left anterior descending artery. ST-segment elevation is seen in leads I, aVL, and V_2 through V_6. (From Marx J, Hockberger R, Walls R. Rosen's emergency medicine: concepts and clinical practice. 6th ed. Philadelphia: Mosby, 2006, Fig. 77-6.)

7. What historical points should steer you toward a diagnosis of MI?

Patients often have a history of angina or previous chest pain, murmurs, arrhythmias, risk factors for coronary artery disease, hypertension, or diabetes. They also may be taking digoxin, furosemide, cholesterol medications, antihypertensives, or other cardiac medications.

8. Describe the treatment for an MI.

Treatment involves admission to the intensive or cardiac care unit. Several basic principles should be kept in mind:

1. Early reperfusion is indicated if the time from onset of symptoms is less than 12 hours; the patient and medical center criteria determine choice of reperfusion therapy. Early reperfusion (fewer than 4 to 6 hours) is preferred to try to salvage myocardium. Reperfusion may be accomplished by fibrinolysis or percutaneous coronary intervention (i.e., balloon angioplasty/stent). Coronary artery bypass grafting may be required.
2. ECG monitoring is essential. If ventricular tachycardia occurs, use amiodarone.
3. Give oxygen by nasal cannula and maintain an oxygen saturation greater than 90%.
4. Control pain with **morphine**, which may improve pulmonary edema, if present.
5. Administer **aspirin.**
6. Administer **nitroglycerin.**
7. **Beta blockers**, which patients without contraindications should take for life, reduce the mortality rate of MI as well as the incidence of a second heart attack.
8. Administer **clopidogrel.**
9. Administer **unfractionated or low-molecular-weight heparin.**
10. An **angiotensin-converting enzyme (ACE) inhibitor** or **angiotensin receptor blocker (ARB)** should be started within 24 hours.
11. Administer an **HMG-CoA reductase inhibitor** (statin).

9. True or false: With good management, patients with an MI will not die in the hospital.

False. Even with the best of medical management, patients may die from an MI. They also may have a second heart attack during hospitalization. Watch for sudden deterioration.

10. When is heparin indicated in the setting of chest pain and MI?

Heparin should be started if unstable angina is diagnosed, if the patient has a cardiac thrombus, or if severe congestive heart failure (CHF) is seen on echocardiogram. The Step 2 examination will not ask about other indications, which are not as clear-cut. Do not give heparin to patients with contraindications to its use (e.g., active bleeding).

11. What clues suggest the common noncardiac causes of chest pain?

Gastroesophageal reflux/peptic ulcer disease: Look for a relation to certain foods (spicy foods, chocolate), smoking, caffeine, or lying down. Pain is relieved by antacids or acid-reducing medications. Patients with peptic ulcer disease often test positive for *Helicobacter pylori.*

Chest wall pain (costochondritis, bruised or broken ribs): Pain is well localized and reproducible on chest wall palpation.

Esophageal problems (achalasia, nutcracker esophagus, or esophageal spasm): Often a difficult differential. The question will probably give a negative workup for MI or mention the lack of atherosclerosis risk factors. Look for abnormalities with barium swallow (achalasia) or esophageal manometry. Treat achalasia with pneumatic dilatation or botulism toxin administration; treat nutcracker esophagus or esophageal spasm with calcium channel blockers. If medical treatments are ineffective, surgical myotomy may be needed.

Pericarditis: Look for viral upper respiratory infection prodrome. The ECG shows diffuse ST segment elevation, the erythrocyte sedimentation rate is elevated, and a low-grade fever is present. Classically, the pain is relieved by sitting forward. The most common cause is infection with coxsackievirus. Other causes include tuberculosis, uremia, malignancy, and lupus erythematosus or other autoimmune diseases (Fig. 4-2).

Pneumonia: Chest pain is caused by pleuritis. Patients also have cough, fever, and/or sputum production. Ask about possible sick contacts.

Aortic dissection: Associated with severe tearing or ripping pain that may radiate to the back. Look for hypertension or evidence of Marfan syndrome (tall, thin patient with hyperextensible joints). Blunt chest trauma can cause aortic laceration and pseudoaneurysm, which are different conditions that are often managed similarly (Fig. 4-3).

12. How can you recognize stable angina?

The chest pain of stable angina begins with exertion or stress and remits with rest or calming down. The pain is described as a pressure or squeezing pain in the substernal area and may radiate to the shoulders, neck, and/or jaw. It is often accompanied by shortness of breath, diaphoresis, and/or nausea. The pain is usually relieved by nitroglycerin. An ECG done during an acute attack often shows ST segment depression, but in the absence of pain, the ECG is often normal. The pain should last less than 20 minutes or be relieved after a sublingual nitroglycerin; otherwise, there may be progression to unstable angina or MI.

13. Define unstable angina. How is it diagnosed and treated?

In strict terms, unstable angina is defined as a change from previously stable angina. If a patient used to experience angina once a week and now experiences it once a day, the patient technically has unstable angina. Unstable angina usually consists of normal or only minimally elevated cardiac enzymes, ECG changes (ST depression), and prolonged chest pain that does not respond to nitroglycerin initially (like a heart attack). The pain often begins at rest. Treatment is similar to that for MI. The patient is admitted to the coronary or intensive care unit. Initial treatment begins with oxygen, aspirin, and nitroglycerin. The patient should be given a beta blocker, clopidogrel, heparin (unfractionated or low-molecular-weight) and a glycoprotein IIb/IIIa receptor inhibitor. An ACE inhibitor or ARB should be given as well. Consider emergent percutaneous transluminal coronary angioplasty (PTCA) if the pain does not resolve. Almost all patients have a history of stable angina and coronary artery disease risk factors.

14. Describe variant (Prinzmetal) angina.

This rare type of angina is characterized by pain at rest (unrelated to exertion) and ST-segment elevation; cardiac enzymes are normal. The cause is coronary artery spasm. Prinzmetal angina usually

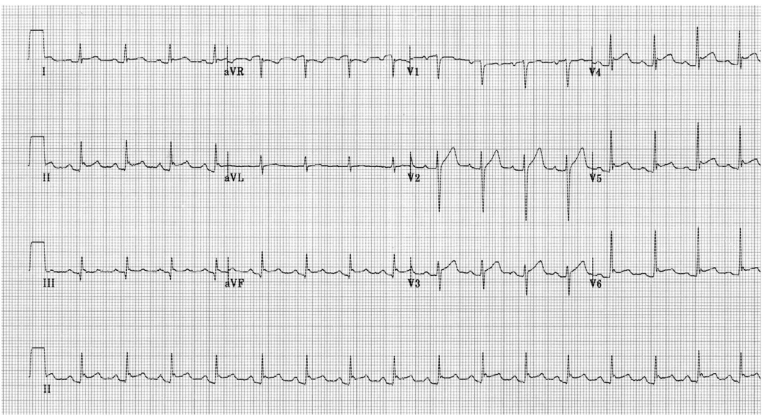

Figure 4-2. Acute pericarditis in a 30-year-old man presenting with pleuritic chest pain. The electrocardiogram demonstrates ST-segment elevation most clearly seen in leads I, II, aVF, and V3–V6; diffuse PR-segment depression; and PR-segment elevation in lead aVR. (From Demangone D. ECG manifestations: noncoronary heart disease. *Emerg Med Clin North Am* 24(1):113-1, 2006.)

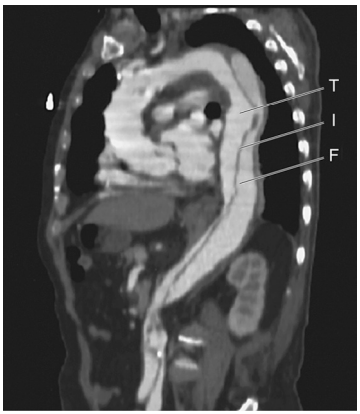

Figure 4-3. Aortic dissection is seen in this contrast-enhanced spiral computed tomography (CT) scan of the chest at the level of the pulmonary artery showing an intimal flap (I) in the descending thoracic aorta separating the two lumina in a type B aortic dissection. F, False lumen; T, true lumen. (From Libby P, et al. Braunwald's heart disease: a textbook of cardiovascular medicine. 8th ed. Philadelphia: Saunders, 2008, Fig. 56-19.)

responds to nitroglycerin and is treated over the long term with calcium channel blockers, which reduce arterial spasm.

15. Define silent MI. How common is it?

Patients with a silent MI do not develop chest pain; their symptoms include CHF, shock, or confusion and delirium (especially elderly patients). MIs are silent in up to 25% of cases (especially in diabetic patients with neuropathy).

16. Describe the etiology and classic history of the various heart valve abnormalities?

VALVE PROBLEM	PHYSICAL CHARACTERISTICS	OTHER FINDINGS
Mitral stenosis	Late diastolic blowing murmur (best heard at apex)	Opening snap, loud S_1, AF, LAE, PH
Mitral regurgitation	Holosystolic murmur (radiates to axilla)	Soft S_1, LAE, PH, LVH
Aortic stenosis	Harsh systolic ejection murmurs (best heard in aortic area; radiates to carotids)	Slow pulse upstroke, S_3/S_4, ejection click, LVH, cardiomegaly, syncope, angina, heart failure
Aortic regurgitation	Early diastolic decrescendo murmur (best heard at apex)	Widened pulse pressure, LVH, LV dilatation, S_3
Mitral prolapse	Midsystolic click, late systolic murmur	Panic disorder

AF, Atrial fibrillation; *LAE*, left atrial enlargement; *LV*, left ventricle; *LVH*, left ventricular hypertrophy; *PH*, pulmonary hypertension

17. What physical examination findings are associated with various heart valve abnormalities?

VALVE PROBLEM	ETIOLOGY	HISTORY
Mitral stenosis	Rheumatic fever is the most common etiology	Dyspnea, orthopnea, and PND
Mitral regurgitation	Typically results from rheumatic fever or chordate tendineae rupture after MI	Fatigue, dyspnea, orthopnea
Aortic stenosis	Typically seen in the older adults Bicuspid or unicuspid valves may appear with symptoms in childhood	Usually asymptomatic for years and begins with dyspnea on exertion Progresses to angina, syncope, and heart failure, with the mortality rate increasing through this progression
Aortic regurgitation	**CREAM** mnemonic: **C**ongenital **r**heumatic damage, **e**ndocarditis, **a**ortic dissection/**a**ortic root dilatation, **M**arfan syndrome	Can present acutely with severe dyspnea, acute pulmonary congestion, and cardiogenic shock Can also present chronically with DOE, orthopnea, and PND

DOE, Dyspnea on exertion; *MI*, myocardial infarction; *PND*, paroxysmal nocturnal dyspnea

18. Describe the treatment of each of the aforementioned valvular disorders.

Mitral stenosis is a mechanical problem and requires balloon valvotomy or surgery if it becomes severe. Medical management (diuretics, digoxin, beta blockers) is only adjunctive to either percutaneous or surgical intervention. **Mitral regurgitation** is treated with corrective surgery if certain indications are present (flail leaflet, severe regurgitation). Vasodilators (nitroprusside, hydralazine) may be used in symptomatic patients. Atrial fibrillation is common because left atrial enlargement is treated (with rate control and anticoagulation, as appropriate) if it is present. Aortic valve replacement should be performed in essentially all patients with symptomatic **aortic stenosis**. Aortic valve replacement or repair is indicated in symptomatic patients with chronic **aortic regurgitation**. Aortic valve replacement or repair may be indicated for asymptomatic patients under certain circumstances, such

as progressive left ventricular enlargement (along with specific echocardiographic findings that are beyond the scope of the USMLE). Vasodilators may be used to reduce the hemodynamic burden and possibly delay the need for surgery in asymptomatic patients.

19. True or false: An understanding of the pathophysiology behind the various changes associated with longstanding valvular heart disease is high-yield for the Step 2 examination.

True. For example, it is advisable to understand why right-side heart failure may occur with longstanding mitral stenosis. This is not memorization, but rather the ability to determine rationally which changes are associated with each type of valvular dysfunction.

20. Who should receive endocarditis prophylaxis?

The 2008 American Heart Association recommendations conclude that only an extremely small number of cases of infective endocarditis might be prevented by antibiotic prophylaxis for dental procedures. Cardiac conditions for which prophylaxis before dental procedures is recommended include prosthetic cardiac valve, previous infectious endocarditis, congenital heart disease, and cardiac transplant recipients who develop valvulopathy. Antibiotic prophylaxis is no longer recommended for genitourinary or gastrointestinal (GI) procedures.

21. Describe the protocols for endocarditis prophylaxis.

An antibiotic for prophylaxis should be administered in a single dose before the procedure. Amoxicillin is the preferred choice for oral therapy. Cephalexin, clindamycin, azithromycin, or clarithromycin may be used in patients with penicillin allergy. Ampicillin, cefazolin, ceftriaxone, or clindamycin may be used for patients unable to take oral medication.

22. What is the Virchow triad?

The Virchow triad consists of three findings associated with deep venous thrombosis (DVT): endothelial damage, venous stasis, and hypercoagulable state. These three broad categories should help you remember when to think about the possibility of DVT.

23. List the common clinical scenarios for development of DVT.

- Surgery (especially orthopedic, pelvic, abdominal, or neurosurgery)
- Malignancy
- Trauma
- Immobilization
- Pregnancy
- Use of birth control pills
- Disseminated intravascular coagulation
- Hypercoagulable states such as factor V (Leiden), antithrombin III deficiency, protein C deficiency, protein S deficiency, prothrombin *G20210A* gene mutation, hyperhomocysteinemia, or antiphospholipid antibodies

24. Describe the physical signs and symptoms of DVT. How is it diagnosed?

Signs and symptoms include unilateral leg swelling, pain or tenderness, and/or **Homan sign** (present in 30% of cases). Superficial palpable cords imply superficial thrombophlebitis rather than DVT (see question 25). DVT is best diagnosed by Doppler compression ultrasonography or impedance plethysmography of the veins of the extremity. The gold standard is venography, but this invasive test is reserved for situations when the diagnosis is not clear.

25. True or false: Superficial thrombophlebitis is a risk factor for pulmonary embolus (PE).

False. Superficial thrombophlebitis (erythema, tenderness, edema, and palpable clot in a superficial vein) affects superficial veins and does not cause PEs. It is considered a benign condition, although

recurrent superficial thrombophlebitis can be a marker for underlying malignancy (e.g., Trousseau syndrome, or migratory thrombophlebitis, is a classic marker for pancreatic cancer). Treat affected patients with nonsteroidal antiinflammatory drugs (NSAIDs) and warm compresses.

26. How is DVT treated and for how long?

Systemic anticoagulation is necessary. Use IV heparin or subcutaneous low-molecular-weight heparin initially, followed by crossover to oral warfarin. Patients should be maintained on warfarin for at least 3 to 6 months, possibly for life if more than one episode of clotting occurs.

27. What is the best way to prevent DVT in patients undergoing surgery?

Prophylactic measures for patients undergoing surgery depend on the risk for developing DVT or PE. Early ambulation is recommended for low-risk patients. Low-molecular-weight heparin, low-dose unfractionated heparin, or fondaparinux is recommended for patients at moderate risk. High-risk patients should be given low-molecular-weight heparin, fondaparinux, or an oral vitamin K antagonist. Alternatively, pneumatic compression stockings should be used if the patient is at moderate risk or higher and is at high risk for bleeding.

28. In what clinical settings does PE occur? Describe the symptoms and signs.

PE commonly follows DVT, delivery (amniotic fluid embolus), or fractures (fat emboli). Classically, the patient recently went on a long car ride, took a long airplane flight, or has been immobilized. Symptoms include tachypnea, dyspnea, chest pain, hemoptysis (if a lung infarct has occurred), hypotension, syncope, or death in severe cases. In rare instances, the chest radiograph shows a wedge-shaped defect because of pulmonary infarct.

29. True or false: DVT can lead to a stroke.

False, with one rare exception. Embolization of left-sided heart clots (because of atrial fibrillation, ventricular wall aneurysm, severe CHF, or endocarditis) causes arterial infarcts (stroke and renal, GI, or extremity infarcts), **not** PEs. DVTs (or right-sided heart clots) that embolize cause PEs, **not** arterial emboli. The exception is the patient with a right-to-left shunt, such as a patent foramen ovale, atrial or ventricular septal defect, or pulmonary arteriovenous fistula. In such a patient, a venous clot may embolize and cross over to the left side of the circulation, causing an arterial infarct. This event is quite rare.

30. How is PE diagnosed?

Use a computed tomography (CT) pulmonary angiogram or ventilation/perfusion (V/Q) scan to evaluate for PE (Fig. 4-4). If the test is positive, PE is diagnosed and treatment is started. If the test is

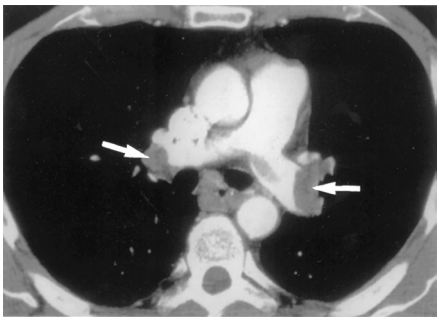

Figure 4-4. Spiral computed tomographic (CT) image of acute pulmonary emboli (PEs) in both main pulmonary arteries in a postoperative patient who suddenly developed dyspnea, hypoxemia, and hypotension. (From Goldman L, Ausiello D. Cecil medicine. 23rd ed. Philadelphia: Saunders, 2008, Fig. 99-1.)

indeterminate, a conventional pulmonary angiogram is used to confirm the diagnosis. Conventional pulmonary angiography is the gold standard, but it is invasive and carries substantial risks. If a CT angiogram or V/Q scan is negative, it is highly unlikely that the patient has a significant PE; thus no treatment is needed. In the setting of a low-probability V/Q scan and high clinical suspicion, a CT angiogram or conventional pulmonary angiogram is needed.

31. How is PE treated?

PE is treated initially with low-molecular-weight heparin or IV unfractionated heparin to prevent further clots and emboli. Then the patient switches gradually to oral warfarin, which must be taken for at least 3 to 6 months. In patients with recurrent clots on anticoagulation or contraindications to anticoagulation, an inferior vena cava filter (e.g., Greenfield filter) should be used. In patients with massive PE, embolectomy (surgical or catheter embolectomy) or pharmacologic thrombolysis (e.g., giving tissue plasminogen activator [t-PA]) may be attempted.

32. What is the most important side effect of heparin?

Heparin can cause two types of thrombocytopenia. The first is a nonimmune form that is of no clinical consequence and is characterized by a slight fall in platelet count during the first 2 days. The platelet count generally returns to normal with continued heparin administration. The second form is less common, but more serious, and is called type II heparin-induced thrombocytopenia (HIT). In this immune-mediated disorder, antibodies are formed against the heparin-platelet factor 4 complex and platelet count falls more than 50%, typically 5 to 10 days after heparin therapy is initiated. Immune-mediated HIT can lead to both arterial and venous thrombosis. The diagnosis of HIT is made on clinical grounds but can be confirmed with a functional assay. If HIT is suspected, heparin (and low-molecular-weight heparin) should be discontinued immediately.

Measure complete blood counts to monitor platelet counts in patients being treated with heparin.

33. How are the effects of aspirin, heparin, and warfarin monitored?

Heparin is monitored with the **partial thromboplastin time (PTT),** a measure of the internal coagulation pathway. Warfarin is monitored with the **prothrombin time (PT),** a measure of the external coagulation pathway. Aspirin prolongs the **bleeding time,** a measure of platelet function. Clinically, the effect of aspirin is not monitored with laboratory testing, but be aware that it prolongs the bleeding time test.

34. How are the effects of low-molecular-weight heparin monitored?

Low-molecular-weight heparin does not affect any of the coagulation parameters mentioned in question 33, and its effect is not clinically monitored. Rarely, a special type of factor X assay (anti-Xa) is used to measure the effect.

35. In an emergency, how can you reverse the effects of heparin, warfarin, and aspirin?

Heparin and low-molecular-weight heparin can be reversed with **protamine**, warfarin with fresh frozen plasma (contains clotting factors; immediate effect) and/or vitamin K (takes a few days to work), and aspirin with platelet transfusions.

36. How do the conditions below affect coagulation tests?

CONDITION	PROLONGS	AIDS TO DIAGNOSIS
Hemophilia A	PTT	Low levels of factor VIII; normal PT and bleeding time; X-linked
Hemophilia B	PTT	Low levels of factor IX; normal PT and bleeding time; X-linked
vWF deficiency	Bleeding time and PTT	Normal or low levels of factor VIII; normal PT; autosomal dominant

CONDITION	PROLONGS	AIDS TO DIAGNOSIS
Disseminated intravascular coagulation	PT, PTT, bleeding time	Positive D-dimer or FDPs; postpartum, infection, malignancy; schistocytes and fragmented cells on peripheral smear
Liver disease	PT	PTT normal or prolonged; all factors but factor VIII are low; stigmata of liver disease; no correction with vitamin K
Vitamin K deficiency	PT, PTT (slight)	Normal bleeding time; low levels of factors II, VII, IX, and X, as well as proteins C and S; look for a neonate who did not receive prophylactic vitamin K; malabsorption, alcoholism, or prolonged antibiotic use (which kills vitamin K–producing bowel flora)

FDPs, Fibrin degradation products; *PT*, prothrombin time; *PTT*, partial thromboplastin time; *vWF*, von Willebrand factor

Remember also that uremia causes a qualitative platelet defect and that vitamin C deficiency and chronic corticosteroid therapy can cause bleeding tendency with normal coagulation tests.

37. What are the general symptoms and signs of CHF?

- Fatigue
- Ventricular hypertrophy on ECG
- Dyspnea
- S_3 or S_4 on cardiac examination
- Cardiomegaly on chest radiograph
- Specific left- and right-sided findings (see question 38)

38. What symptoms and signs help determine whether CHF is because of left or right ventricular failure?

Left ventricular failure: Orthopnea (shortness of breath when lying down, the patient sleeps on more than one pillow or even sitting up), paroxysmal nocturnal dyspnea, pulmonary congestion (rales), Kerley B lines on chest radiograph, pulmonary vascular congestion and edema, bilateral pleural effusions.

Right ventricular failure: Peripheral edema, jugular venous distention, hepatomegaly, ascites, underlying lung disease (cor pulmonale; see question 42).

Note: Both ventricles are commonly affected, so a mixed pattern is commonly seen.

39. How is chronic CHF treated?

Chronic CHF is treated on an outpatient basis with sodium restriction, ACE inhibitors (first line agents that reduce mortality rate), beta blockers (somewhat counterintuitive but proven to work), diuretics (furosemide, spironolactone, metolazone), digoxin (not used in diastolic dysfunction; usually reserved for moderate-to-severe CHF with low ejection fraction or systolic dysfunction), and vasodilators (arterial and venous).

40. How is acute CHF treated?

Acute CHF is treated on an inpatient basis with oxygen, diuretics, and positive inotropes. Digoxin may be used if the patient is stable. IV sympathomimetics (dobutamine, dopamine, amrinone) are used for severe CHF.

41. What factors precipitate exacerbations in previously stable patients with CHF?

The most common is noncompliance with diet or medications, but watch for **MI,** severe hypertension, arrhythmias, infections and fever, PE, anemia, thyrotoxicosis, and myocarditis.

42. Define cor pulmonale. With what clinical scenarios is it associated?

Cor pulmonale is right ventricular enlargement, hypertrophy, and failure because of primary lung disease. Common causes are chronic obstructive pulmonary disease and PE. In a young woman

(20 to 40 years old) with no other medical history or risk factors, think of idiopathic pulmonary arterial hypertension. Treat with prostacyclin (parenteral epoprostenol), antiendothelin (bosentan), phosphodiesterase 5 inhibitors, and calcium channel blockers while awaiting heart-lung transplantation. Sleep apnea also can cause cor pulmonale; look for an obese snorer who is sleepy during the day. Patients with cor pulmonale may have tachypnea, cyanosis, clubbing, parasternal heave, loud P2, and right-sided S_4 in addition to the signs and symptoms of pulmonary disease.

43. What causes restrictive cardiomyopathy? How is it different from constrictive pericarditis?

Restrictive cardiomyopathy involves a problem with the ventricles and usually is because of amyloidosis, sarcoidosis, hemochromatosis, or myocardial fibroelastosis. A ventricular biopsy is abnormal in all of these conditions. **Constrictive pericarditis** can be fixed simply by removing an abnormal pericardium; look for a pericardial knock on examination, calcification of the pericardium, and a normal ventricular biopsy. Watch for an S_4 (which indicates stiff ventricles) and signs of right-sided heart failure (jugular venous distention and peripheral edema) in both conditions. These two disorders are mentioned together because both can cause a "restrictive"-type cardiac physiology, but the treatments are different.

44. What is the most common kind of cardiomyopathy and what causes it?

Dilated cardiomyopathy, which is most commonly caused by chronic coronary artery disease or ischemia, though by strict definition this is not a true cardiomyopathy. For the USMLE, watch for alcohol, myocarditis, or doxorubicin as the cause of dilated cardiomyopathy.

45. Which cardiomyopathy is likely in a young person who passes out or dies while exercising or playing sports and has a family history of sudden death?

Hypertrophic cardiomyopathy, which may be autosomal dominant. This idiopathic condition causes an asymmetric ventricular hypertrophy that reduces cardiac output (an example of diastolic dysfunction). Look for a systolic ejection murmur along the left sternal border (similar to aortic stenosis) that increases with standing or with a Valsalva maneuver (these maneuvers decrease the volume of blood in the left ventricle). Treat with beta blockers or disopyramide (to allow the ventricle more time to fill). Competitive sports should be avoided. Positive inotropes (e.g., digoxin), diuretics, and vasodilators are contraindicated because they worsen the condition.

46. What ECG abnormalities do you need to know about for the Step 2 examination? How are they treated?

Figures 4-5 through 4-17 demonstrate the arrhythmias noted below. Always check for electrolyte disturbances as a cause for any arrhythmia.

ARRHYTHMIA	TREATMENT AND WARNINGS
Atrial fibrillation	In symptomatic patients, first slow the ventricular rate with beta blocker, calcium channel blocker, or digoxin; if acute (onset < 24 hr), cardiovert with amiodarone, procainamide, or DC cardioversion. If chronic, first anticoagulate, then cardiovert; if this approach fails or atrial fibrillation recurs, leave the patient on rate control medications (beta blocker, calcium channel blocker, or digoxin) and warfarin.
Atrial flutter	Treat like atrial fibrillation. You may try to stop the arrhythmia with vagal maneuvers (e.g., carotid massage).
Heart block:	
First degree	No treatment, but avoid beta blockers and calcium channel blockers, both of which slow conduction.
Second degree	For Mobitz type I, use pacemaker or atropine only in symptomatic patients; use pacemaker in all patients with Mobitz type II.

ARRHYTHMIA	TREATMENT AND WARNINGS
Third degree	Use pacemaker.
WPW syndrome	Use procainamide or quinidine; avoid digoxin and verapamil.
Ventricular tachycardia	If pulseless, treat with immediate defibrillation followed by epinephrine, vasopressin, amiodarone, or lidocaine. If a pulse is present, treat with amiodarone and synchronized cardioversion.
Ventricular fibrillation	Immediate defibrillation followed by epinephrine, vasopressin, amiodarone, or lidocaine.
PVCs	Usually not treated; if severe and symptomatic, consider beta blockers or amiodarone.
Sinus bradycardia	Usually not treated; use atropine or pacing if severe and symptomatic (e.g., after heart attack). Avoid beta blockers, calcium channel blockers, and other conduction-slowing medications.
Sinus tachycardia	Usually none; correct the underlying cause. Use beta blocker or calcium channel blocker if symptomatic.

DC, Direct current; *PVC*, premature ventricular complex; *WPW*, Wolff-Parkinson-White

47. What endocrine disease is suggested when a patient has sinus tachycardia or atrial fibrillation?

Hyperthyroidism. Check the level of thyroid-stimulating hormone (TSH) as a screening test.

48. Which patients with atrial fibrillation should receive anticoagulation?

The $CHADS_2$ score is used to estimate the risk of stroke in patients with nonrheumatic atrial fibrillation. The score is used to determine whether the patient should be treated with anticoagulation (with warfarin or dabigatran) or aspirin.

The points in the table below are added to determine the $CHADS_2$ score.

- A score of 0 is low risk for stroke, so aspirin can be used.
- A score of 1 is moderate risk, so aspirin or warfarin can be used.
- A score of 2 or greater is moderate or high risk, so warfarin should be used unless contraindicated (e.g., significant fall risk).

	CONDITION	POINTS
C	CHF	1
H	Hypertension: blood pressure consistently > 140/90 mm Hg (or treated hypertension on medication)	1
A	Age > 75 yr	1
D	Diabetes mellitus	1
S_2	Prior stroke or transient ischemic attack	2

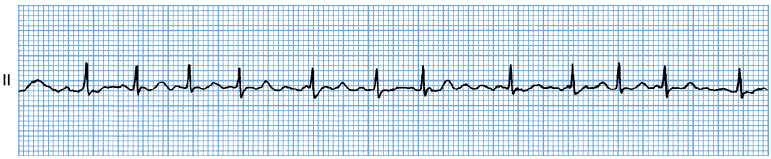

Figure 4-5. Atrial fibrillation. There are no true P waves, and the ventricular rate is irregular. (From Goldberger AL. Clinical electrocardiography: a simplified approach. 7th ed. Philadelphia: Mosby, 2006, Fig. 15-4).

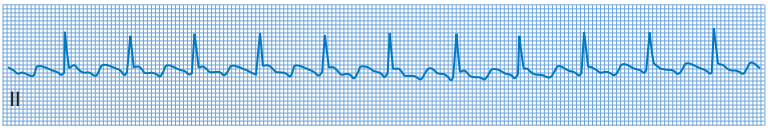

Figure 4-6. An example of atrial flutter. In contrast to atrial fibrillation, atrial flutter is regular. The baseline has a sawtooth shape. (From Walsh D. Palliative medicine. 1st ed.Philadelphia: Saunders, 2008, Fig. 80-2.)

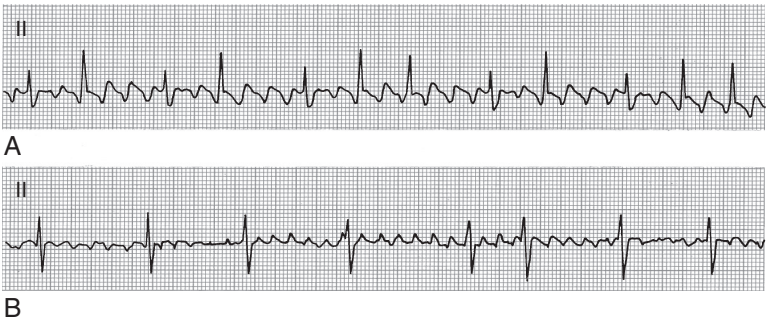

Figure 4-7. Atrial flutter with variable block **(A)** and coarse atrial fibrillation **(B)** may be easily confused. Notice that with atrial fibrillation the ventricular rate is erratic and the atrial waves are not identical from segment to segment, while these atrial waves are identical with atrial flutter. (From Goldberger A. Clinical electrocardiography: a simplified approach. 7th ed. Philadelphia, Mosby, 2006, Fig. 23-3.)

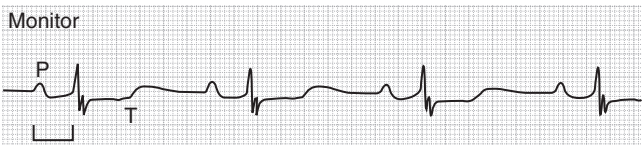

Figure 4-8. First degree atrioventricular block with a PR interval of 0.32 seconds (normal is 0.12-0.20 sec). (From Goldberger E. Treatment of cardiac emergencies. 5th ed. St. Louis, Mosby, 1990.)

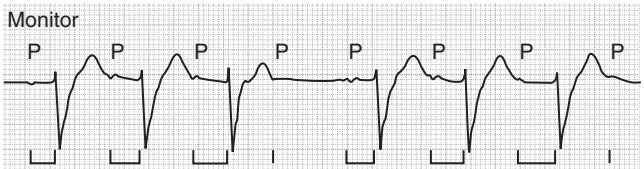

Figure 4-9. Mobitz type I second degree atrioventricular block (Wenckebach; a second degree AV block in which the PR interval becomes progressively longer from cycle to cycle until the AV node no longer conducts a stimulus from above). Notice the progression of the PR interval before the impulse is completely blocked. (From Goldberger E. Treatment of cardiac emergencies. 5th ed. St. Louis, Mosby, 1990.)

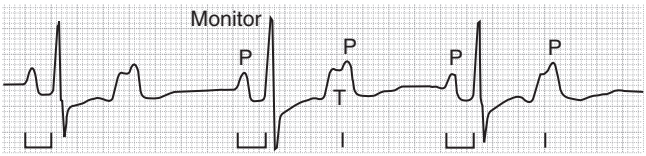

Figure 4-10. Mobitz type II second degree atrioventricular block (an intermittent dropped QRS). Notice that every alternate P wave is blocked (2:1 block in this case). (From Goldberger E. Treatment of cardiac emergencies. 5th ed. St. Louis, Mosby, 1990.)

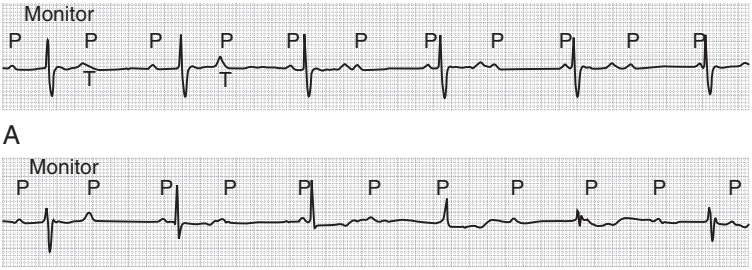

Figure 4-11. Third degree atrioventricular block (none of the atrial depolarizations conduct to the ventricles). Strips A and B were obtained several hours apart. Strip A demonstrates an atrial rate of 75 bpm but the ventricles are beating independently at a slow rate of approximately 40 bpm. Strip B, obtained a few hours later in the same patient demonstrates variations in the shape of QRS complex from beat to beat. (From Goldberger E. Treatment of cardiac emergencies. 5th ed. St. Louis, Mosby, 1990.)

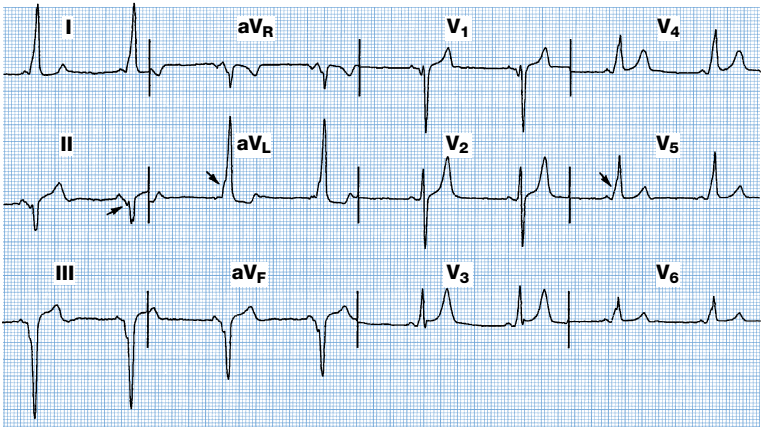

Figure 4-12. Wolff-Parkinson-White syndrome. Triad of a wide QRS complex, a short PR interval, and delta waves *(arrows)*. (From Goldberger AL. Clinical electrocardiography: a simplified Approach. 7th ed. Philadelphia: Mosby, 2006, Fig. 12-3.)

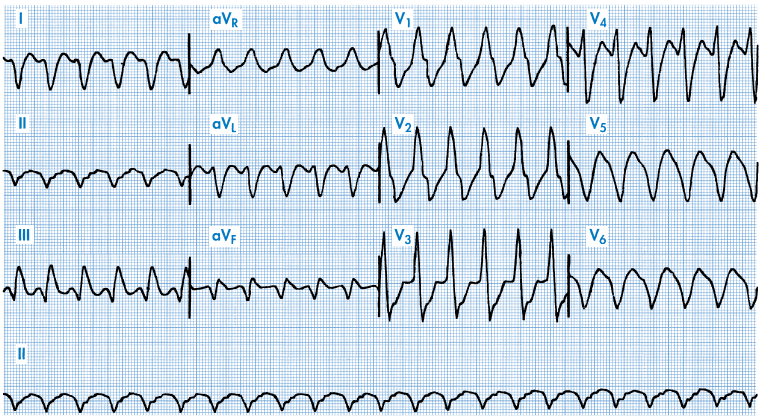

Figure 4-13. Ventricular tachycardia. Wide complex QRS tachycardia. (From Goldberger AL. Clinical electrocardiography: a simplified Approach. 7th ed., Philadelphia: Mosby, 2006, Part 4, Case 3.)

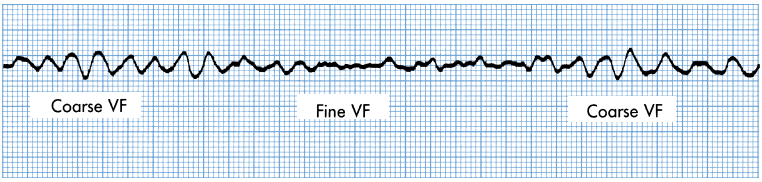

Figure 4-14. Ventricular fibrillation. Fibrillatory waves in an irregular pattern. (From Goldberger AL. Clinical electrocardiography: a simplified Approach. 7th ed., Philadelphia: Mosby, 2006, Fig. 16-13.)

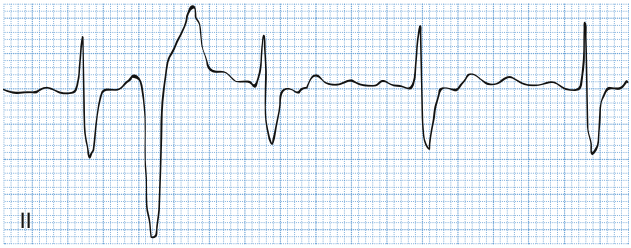

Figure 4-15. A single premature ventricular complex. (From Marx J. Rosen's emergency medicine. 7th ed. Philadelphia: Mosby, 2009, Fig. 77-22.)

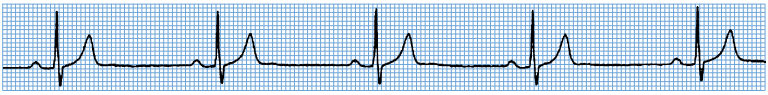

Figure 4-16. Sinus bradycardia at a rate of about 40 beats per minute. (From Goldberger AL. Clinical electrocardiography: a simplified Approach. 7th ed., Philadelphia: Mosby, 2006, Fig. 20-1.)

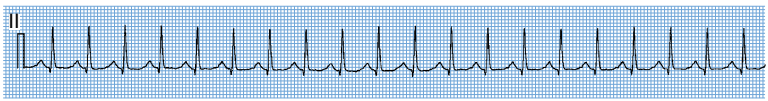

Figure 4-17. Sinus tachycardia at a rate of about 150 beats per minute. (From Goldberger AL. Clinical electrocardiography: a simplified Approach. 7th ed., Philadelphia, Mosby, 2006, Fig. 13-2.)

49. What are the classic symptoms of Wolff-Parkinson-White syndrome?

A child becomes dizzy, dyspneic, or passes out after playing, then recovers and has no other symptoms. The cause is a transient arrhythmia via the accessory pathway. ECG shows the infamous delta wave. The treatment of choice for these patients is radiofrequency catheter ablation of the pathway.

50. What do you need to know about common congenital heart defects?

DEFECT	SYMPTOMS, TREATMENT, AND OTHER INFORMATION
Patent ductus arteriosus	Constant, machine-like murmur in upper left sternal border; dyspnea and possible CHF. Close with indomethacin or surgery (if indomethacin fails). Keep open with prostaglandin E_1. Associated with congenital rubella and high altitudes.
Ventricular septal defect (VSD)	*Most common congenital heart defect.* Characterized by holosystolic murmur next to sternum. Most cases resolve on their own. Watch for fetal alcohol, TORCH, or Down syndrome.
Atrial septal defect	Often asymptomatic until adulthood. Characterized by fixed, split S_2 and palpitations. Most defects do not require correction (unless very large).
Tetralogy of Fallot	*Most common cyanotic congenital heart defect.* Characterized by four-anomalies: VSD, RVH, pulmonary stenosis, and overriding aorta. Look for "tet" spells (squatting after exertion).
Coarctation of aorta	Upper extremity hypertension only; radiofemoral delay; systolic murmur heard over mid-upper back; rib notching on radiograph; associated with Turner syndrome.

CHF, Congestive heart failure; *RVH*, right ventricular hypertrophy; *TORCH*, toxoplasma, other, rubella, cytomegalovirus, and herpes infections
Endocarditis prophylaxis is required for all of these cardiac defects except asymptomatic secundum-type atrial septal defect.

51. Name the noncyanotic congenital heart defects.

Noncyanotic heart diseases result in left-to-right shunts in which oxygenated blood from the lungs is shunted back into the pulmonary circulation, resulting in a “pink baby.” These noncyanotic heart conditions can be remembered by the three Ds: VS**D**, AS**D**, and P**D**A.

52. Name the cyanotic congenital heart defects.

Cyanotic heart disease results in a right-to-left shunt in which deoxygenated blood is shunted into the systemic circulation, resulting in a "blue baby." These cyanotic heart conditions can be remembered by the mnemonic 12345:

1. Truncus arteriosus; there is just **one** common vessel leaving the ventricles.
2. Transposition of the great vessels; the **two** great vessels (aorta and pulmonary artery) are transposed.
3. Tricuspid atresia; **three** for **tri**cuspid.
4. Tetralogy of Fallot; **four** for **tetra**logy.
5. Total anomalous pulmonary venous return (TAPVR); there are **five** words in TAPVR.

53. What is important to remember about tachycardia in children?

Heart rates over 100 beats per minute may be normal in a child, as may respiratory rates greater than 20 respirations per minute.

54. In the fetal circulation, where is the highest and lowest oxygen content?

The highest oxygen content in fetal circulation is in the umbilical vein (the blood coming from the mother) and the lowest is in the umbilical arteries. Remember that oxygen content is higher in blood going to the upper extremities than in blood going to the lower extremities.

55. What changes occur in circulation as an infant goes from intrauterine to extrauterine life?

The first breaths inflate the lungs and cause decreased pulmonary vascular resistance, which increases blood flow to the pulmonary arteries. This and the clamping of the cord increase left-sided heart pressures, causing functional closure of the foramen ovale. Increased oxygen concentration shuts off prostaglandin production in the ductus arteriosus, causing gradual closure.

CHOLESTEROL

1. When is cholesterol screening done?

Although no protocol is universally accepted, measurement of total cholesterol and high-density lipoprotein (HDL) cholesterol every 5 years once a person turns 20 years old is considered reasonable by most authorities. Start sooner and screen more frequently for obese patients and patients with a family history of hypercholesterolemia.

2. Why is cholesterol so important?

Cholesterol is one of the main known modifiable risk factors for atherosclerosis. Atherosclerosis is involved in about one half of all deaths in the United States and one third of deaths between the ages of 35 and 65 years. Atherosclerosis is the most important cause of permanent disability and accounts for more hospital days than any other illness. *(Translation: Atherosclerosis and high cholesterol are high-yield USMLE topics.)*

3. What physical findings will the Step 2 test use as clues to hypercholesterolemia?

Xanthelasma (Fig. 5-1; Plate 2), tendon xanthomas (cholesterol deposits in the skin, classically over tendons in the lower extremities), corneal arcus in younger patients, "milky"-appearing serum, and obesity are possible markers for familial hypercholesterolemia. Family members should be tested if a case of familial hypercholesterolemia is found. Pancreatitis in the absence of obvious risk factors may be a marker for familial hypertriglyceridemia.

4. What are the current recommendations for management of cholesterol levels?

The following information is from the Third Report of the National Cholesterol Education Program, Adult Treatment Panel III (ATP III). Total cholesterol goal is less than 200 mg/dL, with more than 240 mg/dL considered high, and normal triglyceride levels are less than 150 mg/dL, with more than 200 mg/dL considered high. Low-density lipoprotein (LDL) is usually the main player for treatment decisions. The numbers in the chart below represent mg/dL:

NO CHD RISK FACTORS	≥2 CHD RISK FACTORS*	KNOWN CHD/ EQUIVALENT†	VERY HIGH RISK‡	INTERVENTION
LDL <160	LDL <100	LDL <100	LDL <70	None (meets goal)
LDL 160-189	LDL 100-129		LDL 70-99	Diet ± medications§
LDL ≥190	LDL ≥130	LDL ≥100	LDL ≥100	Medications (+ diet)

**CHD* = coronary heart disease. Risk factors for CHD are listed in question 5.

†CHD equivalents include diabetes mellitus, peripheral arterial atherosclerotic disease, symptomatic CHD, and abdominal aortic aneurysm.

‡Very high-risk patients are those with CHD who have a heart attack, diabetes, or other severe and poorly controlled risk factors (e.g., metabolic syndrome, heavy smoking).

§"Diet" includes general lifestyle modifications, such as eating less and more healthfully, decreasing alcohol intake, and exercising. The trend is toward more aggressive intervention, so you will not be faulted for initiating medications at these "gray area" LDL levels, particularly in higher risk people.

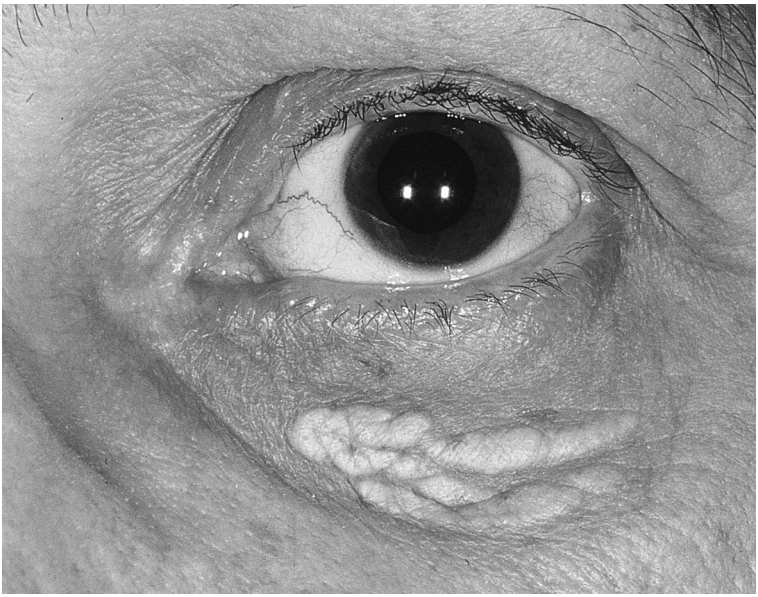

Figure 5-1. Xanthelasma. Multiple soft, yellow plaques involving the lower eyelid. Xanthelasma is usually a normal finding with no significance but is classically seen on the USMLE because of its association with hypercholesterolemia. Screen affected patients with a fasting lipid profile. See Plate 2. (From Yanoff M, Duker JS. Ophthalmology, 3rd ed. Philadelphia: Mosby, 2008, Fig. 12-9-18.)

5. List the major risk factors for coronary heart disease (CHD).

Although elevated levels of LDL and total cholesterol are risk factors for CHD, do not count them as risk factors when deciding to treat or not to treat high cholesterol. The following factors should be counted:

- **Age** (men aged 45 years and older; women aged 55 years and older, or with premature menopause and no estrogen replacement therapy).
- **Family history of premature heart attacks** (defined as definite myocardial infarction [MI] or sudden death in father or first degree male relative younger than 55 years old or mother or first degree female relative younger than 65 years old).
- **Cigarette smoking.**
- **Hypertension** (≥140/90 mm Hg or prescription for antihypertensive medications).
- **Diabetes mellitus.**
- **Low HDL** (<40 mg/dL).

Note: An HDL level greater than or equal to 60 mg/dL is considered protective and negates one risk factor.

6. Discuss other possible risk factors for heart disease.

C-reactive protein (CRP) and homocysteine are hot topics, but ATP III does not list elevated CRP or homocysteine as major risk factors for coronary artery disease. Obesity and type A personality (the hard-driving attorney) are weaker risk factors, as are stress and physical inactivity. Hypertriglyceridemia alone is not a significant risk factor, but in association with high cholesterol causes more CHD than high cholesterol alone. For Step 2 boards, use only the definite risk factors mentioned in the previous question (especially when deciding how to treat a patient with high cholesterol), but keep these other factors in mind.

7. How is LDL calculated?

Lipoprotein analysis involves measuring total cholesterol, HDL, and triglycerides. LDL then can be calculated from the following formula:

$$\text{LDL} = \text{total cholesterol} - \text{HDL} - (\text{triglycerides}/5)$$

8. Describe the treatment for hypercholesterolemia.

As with hypertension, give patients a few months to try lifestyle modifications (decreased calories, cholesterol, and saturated fat in diet; decreased alcohol and smoking; exercise and weight loss) before initiating drug therapy. If the patient has coronary artery disease or a coronary artery disease equivalent (e.g., diabetes, peripheral vascular disease) and the LDL is greater than or equal to 100, medication therapy is indicated. Once the decision to start medications is made, first line agents are HMG CoA reductase inhibitors (statins); watch for rare, but potentially serious, side effects (liver and muscle damage). Second line agents include niacin (poorly tolerated, but effective and raises HDL), ezetimibe (selectively inhibits the intestinal absorption of cholesterol), and bile acid-binding resins (e.g., cholestyramine).

9. How is HDL affected by alcohol? Estrogens? Exercise? Smoking? Progesterone?

High HDL is protective against atherosclerosis and is increased by moderate alcohol consumption (1 to 2 drinks/day; but not by high alcohol intake), exercise, and estrogens. HDL is decreased by smoking, androgens, progesterone, and hypertriglyceridemia.

10. What causes hypercholesterolemia?

Genetics play a role (e.g., familial hyperlipidemia), but most cases are thought to be multifactorial. Western diet and inactive lifestyle contribute. Secondary causes of increased cholesterol include uncontrolled diabetes, hypothyroidism, uremia, nephrotic syndrome, obstructive liver disease, excessive alcohol intake (which increases triglycerides), and medications (e.g., birth control pills, glucocorticoids, thiazides, beta blockers).

CHAPTER 6

DERMATOLOGY

1. Cover the two right-hand columns in the following table and define the common terms used in dermatology to describe skin findings:

TERM	DEFINITION	EXAMPLES
Macule	<1 cm; flat spot (nonpalpable, just visible)	Freckles, tattoos
Patch	>1 cm; otherwise, same as macule	Port-wine birthmarks
Papule	<1 cm; solid, elevated (palpable)	Wart, acne, lichen planus
Plaque	>1 cm; otherwise, same as papule and flat-topped	Psoriasis
Nodule	>1 cm; palpable, solid lesion; not flat-topped	Small lipoma, erythema nodosum
Vesicle	<5 mm; elevated, circumscribed lesion containing clear fluid (small blister)	Chickenpox, genital herpes
Bulla	>5 mm; otherwise, same as vesicle (large blister)	Contact dermatitis, pemphigus
Wheal	Itchy, transiently edematous area	Allergic reaction

2. Define vitiligo. With what diseases is it associated?

Vitiligo is characterized **by skin depigmentation of unknown etiology. It is associated with autoimmune conditions such as pernicious anemia, hypothyroidism, Addison disease, and type 1 diabetes.** Patients often have antibodies to melanin, parietal cells, and thyroid peroxidase.

3. Name several conditions to think about on the Step 2 examination in patients with pruritus.

Think of serious conditions first, such as obstructive biliary disease, uremia, and polycythemia rubra vera (classically seen after a warm shower or bath). Pruritus may also be caused by contact or atopic dermatitis, scabies, and lichen planus.

4. Define contact dermatitis. How do you recognize it? What are the classic causes?

Contact dermatitis is usually caused by a type IV hypersensitivity reaction, although it may be result from an irritating or toxic substance. Look for a new exposure to a classic offending agent, such as poison ivy, nickel earrings, or deodorant. The rash is well circumscribed and occurs only in the area of exposure. The skin is red and itchy and often has vesicles or bullae (Fig. 6-1; Plate 3). The causal agent should be avoided. Patch testing may determine the antigen.

5. Define atopic dermatitis. What history points to this diagnosis?

Atopic dermatitis is a chronic allergic type of condition that begins in the first year of life with red, itchy, weeping skin on the head, upper extremities, and sometimes around the area a diaper covers. The clue to diagnosis is a family and/or personal history of allergies (e.g., hay fever) and asthma. The biggest problem is scratching of affected skin, which leads to skin breaks and possible bacterial

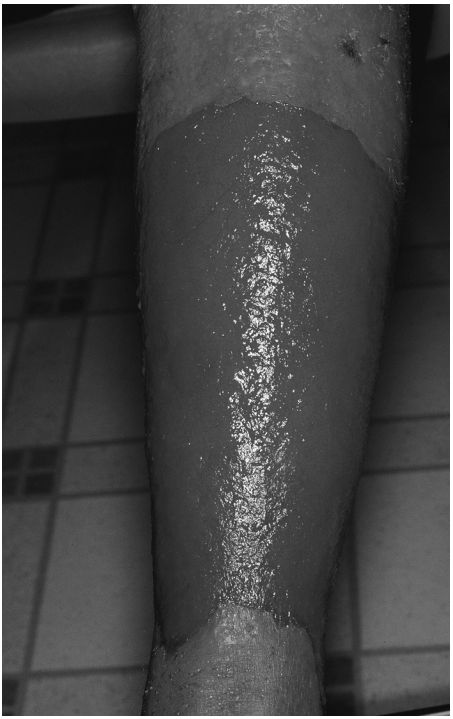

Figure 6-1. Allergic contact dermatitis of the leg caused by an elastic wrap. Notice the well-marginated distribution that differentiates it from cellulitis. See Plate 3. (From Auerbach PS. Wilderness medicine. 6th ed. Philadelphia: Mosby, 2011.)

infection. Treatment involves avoiding the use of antihistamines and drying soaps and applying moisturizing creams, topical steroids, and immune modulating agents (topical pimecrolimus or tacrolimus).

6. Define seborrheic dermatitis. What part of the body does it involve and how is it treated?

Seborrheic dermatitis causes the common conditions known as cradle cap and dandruff, as well as blepharitis (eyelid inflammation). Look for scaling skin with or without erythema on the hairy areas of the head (scalp, eyebrows, eyelashes, mustache, beard), as well as on the forehead, nasolabial folds, external ear canals, and postauricular creases. Treat with dandruff shampoo (e.g., selenium or tar shampoo), topical corticosteroids, and/or ketoconazole cream.

7. Name the various dermatologic fungal infections.

Known as dermatophytosis, tinea, and ringworm, fungal infections include the following:

Tinea corporis (body/trunk): Look for red ring-shaped lesions with raised borders that tend to clear centrally while expanding peripherally (Fig. 6-2; Plate 4).

Tinea pedis (athlete's foot): Look for macerated, scaling web spaces between the toes that often itch and may be associated with thickened, distorted toenails (onychomycosis). Good foot hygiene is part of treatment.

Tinea unguium (onychomycosis): thickened, distorted nails with debris under the nail edges.

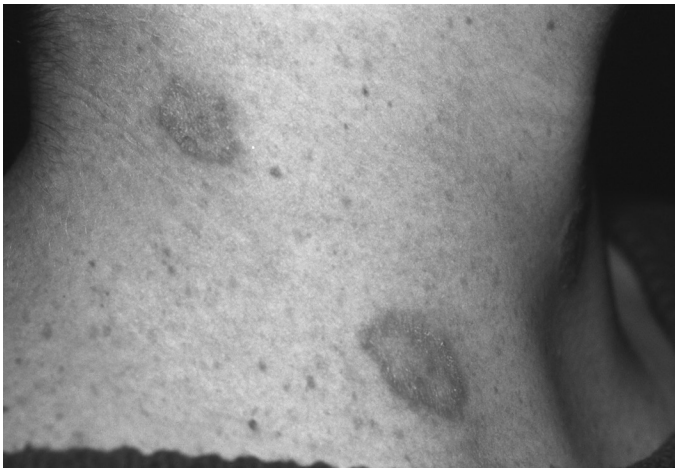

Figure 6-2. Tinea corporis. Red ring-shaped lesions with scaling and some central clearing. See Plate 4. (From Kliegman RM. Nelson textbook of pediatrics. 19th ed. Philadelphia: Saunders, 2011.)

Tinea capitis (scalp): Mainly affects children (highly contagious), who have scaly patches of hair loss and may have an inflamed, boggy granuloma of the scalp (known as a kerion) that usually resolves on its own.

Tinea cruris (jock itch): More common in obese males; usually is found in the crural folds of the upper, inner thighs.

8. What organisms cause fungal infections?

Most fungal infections are caused by *Trichophyton* species. In tinea capitis, if the hair fluoresces under the Wood lamp, *Microsporum* species is the cause; if not, *Trichophyton* species is more likely.

9. How are fungal infections diagnosed and treated?

To make a formal diagnosis, visualize the fungus via a microscope after scraping the lesion and performing a potassium hydroxide (KOH) preparation, or culture the specimen. Because these infections are clinically common, empirical treatment is often done without a formal diagnosis; for USMLE testing, however, a formal diagnosis should be sought before treating. Oral antifungals must be used to treat tinea capitis and onychomycosis; the other infections can be treated with topical antifungals (imidazoles such as miconazole, clotrimazole, or ketoconazole) or griseofulvin, which is better for severe or persistent infections.

10. True or false: Candidiasis is often a normal finding in women and children.

True. Oral thrush (creamy white patches on the tongue or buccal mucosa that can be scraped off) is seen in normal children, and *Candida* vulvovaginitis is seen in normal women, especially during pregnancy or after taking antibiotics. However, during other periods and in different patients, candidal infections may be a sign of diabetes or immunodeficiency; for example, thrush in a man should make you think about the possibility of AIDS, and recurrent vulvovaginal candidiasis should prompt screening for diabetes.

11. How is candidiasis treated?

Treat with local/topical nystatin or imidazoles (e.g., miconazole, clotrimazole). Oral therapy (nystatin or ketoconazole) is used for extensive or resistant disease.

12. What causes scabies? How do you recognize it?

Scabies is caused by the mite *Sarcoptes scabei,* which tunnels into the skin and leaves visible burrows, classically in the finger web spaces and flexor surface of the wrists. You should know what these burrows look like. Facial involvement sometimes is seen in infants. Patients may also have severe pruritus, and scratching can lead to secondary bacterial infection.

13. How do you diagnose and treat scabies?

Diagnose by scraping a mite out of a burrow and viewing it under a microscope. Treat scabies with permethrin cream applied to the whole body. Treat all contacts (e.g., the whole family). Do *not* use lindane unless permethrin is not an option. Lindane used to be the treatment of choice but can cause neurotoxicity, especially in young children.

14. How do you recognize and treat tinea versicolor?

Tinea versicolor (also known as pityriasis versicolor) is a *Pityrosporum* fungal infection that presents most commonly with multiple patches of various size and color (brown, tan, and white) on the torso of young adults. It often becomes noticeable in the summer because the affected areas fail to tan and look white. Diagnose from lesion scrapings (KOH preparation). Treat with selenium sulfide shampoo or topical imidazoles.

15. What causes lice? How are lice treated?

Lice (pediculosis) can involve the head (caused by *Pediculus capitis;* common in school-aged children), body (caused by *Pediculus corporis;* unusual in people with good hygiene), or pubic area (known as crabs; caused by *Phthirus pubis* and transmitted sexually). Infected areas tend to itch. Diagnosis is made by seeing the lice on hair shafts. Treat with permethrin cream (preferred over lindane because of lindane's neurotoxicity), and decontaminate sources of reinfection (wash or sterilize combs, hats, bed sheets, clothing).

16. What causes warts? How are they treated?

Warts are caused by the human papillomavirus (HPV). They are infectious and are most commonly seen in older children, classically on the hands. The most common serotypes are 6 and 11. Multiple treatments are available, including salicylic acid, liquid nitrogen, and curettage. Genital warts also are caused by HPV. Approximately 15 of the HPV serotypes are considered high-risk types for the development of cervical cancer; serotypes 16 and 18 are associated with the majority of cases of cervical cancer.

17. Define molluscum contagiosum. How do you recognize it? How is it treated?

Molluscum contagiosum is a poxvirus infection that is common in children but may also be transmitted sexually. Diagnosis is made based on the characteristic appearance of the lesions (skin-colored, smooth, waxy papules with a central depression [umbilicated] that are roughly 0.5 cm) or the contents of the lesion, which include cells with characteristic inclusion bodies. The usual treatment is freezing or curettage.

18. True or false: A child with genital molluscum is probably a victim of sexual abuse.

False. A child who has genital molluscum may or may not have contracted the disease from sexual contact. The more common mechanism is autoinoculation, in which the child has a lesion on the hand that spreads to the genital area from scratching. Do *not* automatically assume child abuse, although it must be ruled out.

19. How is acne described in medical terms? What bacteria may be partially involved in its pathogenesis?

The description of acne includes comedones (whiteheads and blackheads), papules, pustules, inflamed nodules, superficial pus-filled cysts, and/or possible inflammatory skin changes, including

scar formation. *Propionibacterium acnes* is thought to be partially involved in pathogenesis, as is blockage of pilosebaceous glands.

20. True or false: Acne is not related to food, exercise, or sex.

True. Acne has *not* been proved to be related to food, exercise, or sex (including masturbation). However, if the patient relates acne to a food, you can encourage discontinuing the consumption of that food. Cosmetics may aggravate acne.

21. What are the treatment options for acne?

Multiple treatment options are available. Start with topical benzoyl peroxide; then try topical clindamycin or a topic tretinoin, either with or without an oral antibiotic (typically a tetracycline or erythromycin for *Propionibacterium acnes* eradication). Oral isotretinoin is the *last resort.* Although highly effective, isotretinoin is teratogenic; pregnancy testing in women before and during therapy as well as contraceptive use is mandatory. In addition, it may cause dry skin and mucosae, muscle and joint pain, and liver function test abnormalities.

22. Define rosacea. In what age group is it seen? How do you treat it?

Rosacea often looks like acne but begins in middle age. There are numerous triggers for rosacea, including sun exposure, emotional stress, alcohol consumption, spicy foods, and hot weather. Look for **rhinophyma** (bulbous red nose) and coexisting blepharitis. Treat with topical metronidazole or oral tetracycline.

23. What should you think about if hirsutism is described on the Step 2 examination?

Hirsutism is most commonly idiopathic, but other signs of virilization (e.g., deepening voice, clitoromegaly, frontal balding) suggest an androgen-secreting ovarian tumor. In the absence of virilization, consider Cushing syndrome, polycystic ovary syndrome (Stein-Leventhal syndrome), and drugs (minoxidil, corticosteroids, and phenytoin).

24. What are the common pathologic causes of baldness?

Watch out for trichotillomania (a psychiatric disorder in which patients pull out their hair; baldness is patchy and irregular) and alopecia areata (idiopathic but associated with antimicrosomal and other autoantibodies). Baldness also may be seen in patients with lupus erythematosus or syphilis and after chemotherapy.

25. What causes ordinary male pattern baldness?

Although the exact pathophysiology is still unclear, male pattern baldness is considered a genetic disorder that requires androgens for expression.

26. Describe the classic psoriatic lesion.

Psoriatic lesions are classically described as dry, well-circumscribed, silvery, scaling papules and plaques that are *not* pruritic. Classic lesions are found on the scalp and extensor surfaces of the elbows and knees.

27. What other historical points and physical findings may be seen with psoriasis? How is it diagnosed and treated?

A family history of psoriasis is often present, and the disease occurs mostly in Caucasians with onset in early adulthood. Affected patients may have pitting of the nails and an arthritis that resembles rheumatoid arthritis but is rheumatoid–factor-negative. Diagnosis of psoriasis can often be made by appearance alone, but a biopsy can be used in doubtful cases. Treatment is complex but involves exposure to ultraviolet light, lubricants, topical corticosteroids, and keratolytics (e.g., coal tar, salicylic acid, anthralin). Oral therapies may include immunosuppressive and immunomodulating drugs such as methotrexate, cyclosporine, and biologic agents.

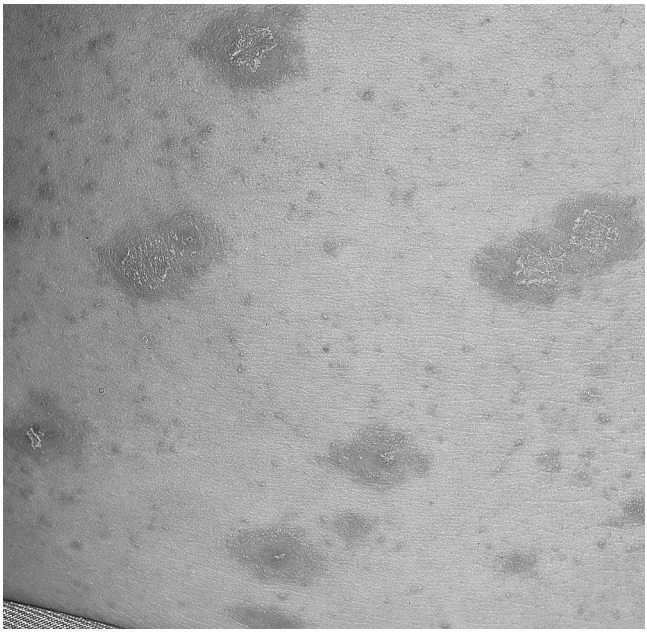

Figure 6-3. Pityriasis rosea. Small oval plaques as well as multiple small papules are present. See Plate 5. (From Habif TP. Clinical dermatology. 5th ed. St. Louis: Mosby, 2009.)

28. Give the classic description and natural course of pityriasis rosea.

Pityriasis rosea is typically seen in young adults. Look for a herald patch (slightly erythematous, scaly, ring-shaped or oval patch classically seen on the trunk), followed 1 week later by many similar lesions that tend to itch (Fig. 6-3; Plate 5). Look for lesions on the back with a long axis that parallels the Langerhans skin cleavage lines, typically in a "Christmas tree" pattern. The condition usually remits spontaneously in 1 month. Think about syphilis in the differential diagnosis. Treat with reassurance.

29. What are the four Ps that confirm a diagnosis of lichen planus?

Pruritic, **p**urple, **p**olygonal **p**apules classically on the wrists or lower legs, usually of adults (Fig. 6-4; Plate 6). Oral mucosal lesions (whitish, with a lacelike pattern) may also be present. These oral lesions must be monitored because they may increase the risk for oral cancer.

30. List the classic drugs that cause photosensitivity of the skin.

Tetracyclines, phenothiazines, and birth control pills.

31. Describe the classic lesion of erythema multiforme. What drugs classically cause it?

Look for the classic target (iris) lesions (Fig. 6-5; Plate 7). The classic cause is sulfa drugs or penicillins, but herpes infections may also cause erythema multiforme and some cases are idiopathic. In its severe form, erythema multiforme is known as **Stevens-Johnson syndrome,** which is often fatal because of severe, widespread skin involvement. Patients with Stevens-Johnson syndrome are treated supportively with therapy similar to what a burn victim would receive (wound care, fluid and electrolyte management, pain control, nutritional support, and monitoring for and treatment of superinfections).

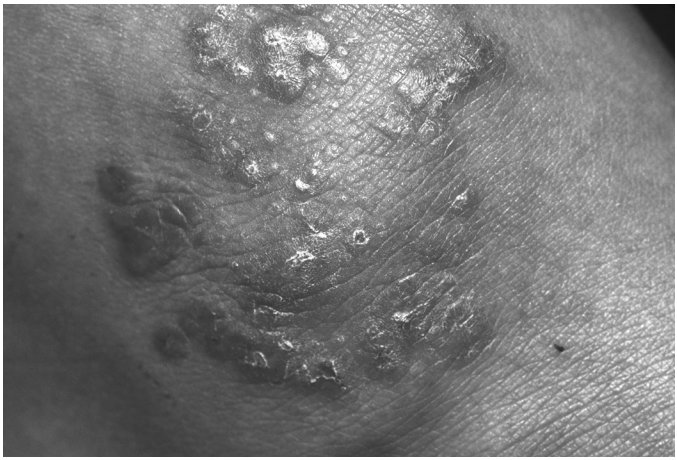

Figure 6-4. Lichen planus. Flat-topped, purple polygonal papules of lichen planus. See Plate 6. (From Kliegman RM. Nelson textbook of pediatrics. 19th ed. Philadelphia: Saunders, 2011.)

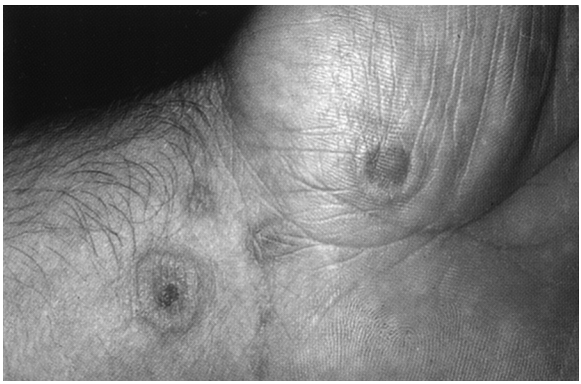

Figure 6-5. Erythema multiforme. "Bull's-eye" annular lesions with central vesicles and bullae. See Plate 7. (From Goldman L. Goldman's Cecil medicine. 24th ed. Philadelphia: Saunders, 2011.)

32. Describe the classic lesion of erythema nodosum. With what diseases is it commonly associated?

Erythema nodosum (Fig. 6-6; Plate 8) is an inflammation of the subcutaneous tissue and skin, classically over the shins (pretibial). Look for tender, red nodules. Sarcoidosis, coccidioidomycosis, or ulcerative colitis classically accompany this condition on the USMLE, although multiple other infections (e.g., streptococcal, tuberculosis) and drugs (e.g., sulfonamides) can also result in this finding.

33. Define and describe pemphigus vulgaris. How is it different from bullous pemphigoid?

Pemphigus vulgaris is a potentially life-threatening autoimmune disease of middle-aged and older patients. It presents with multiple bullae, starting in the oral mucosa and spreading to the skin of

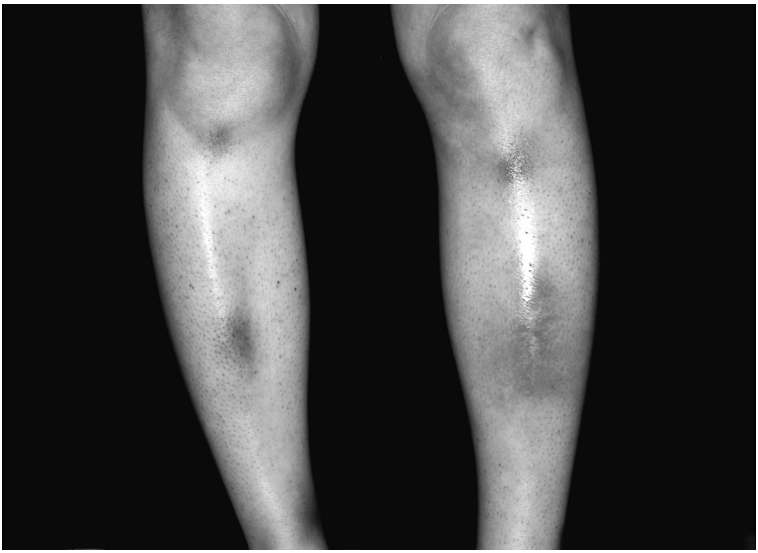

Figure 6-6. Erythema nodosum on the legs of a young woman. See Plate 8. (From Hochberg MC. Rheumatology. 5th ed. Philadelphia: Mosby, 2010.)

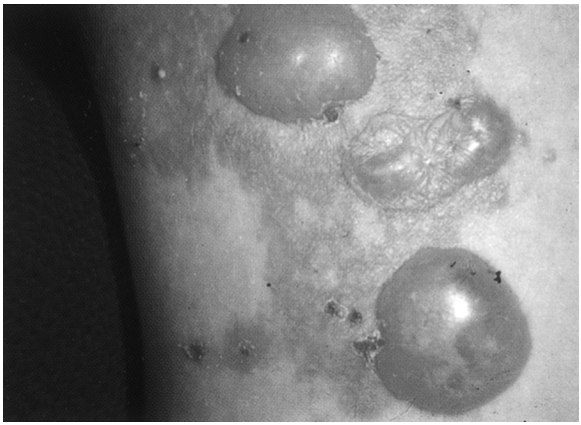

Figure 6-7. Bullous pemphigoid. Tense subepidermal bullae on an erythematous base. See Plate 9. (From Goldman L. Goldman's Cecil medicine. 24th ed. Philadelphia: Saunders, 2011.)

the rest of the body. Biopsy can be stained for antibody (an IgG antibody to desmoglein III, which is associated with desmosomes) and shows a lacelike or fishnet immunofluorescence pattern. Treat with oral corticosteroids.

Bullous pemphigoid is a similar but milder condition that results in a linear immunofluorescence pattern (different antibody) and is treated similarly (Fig. 6-7; Plate 9).

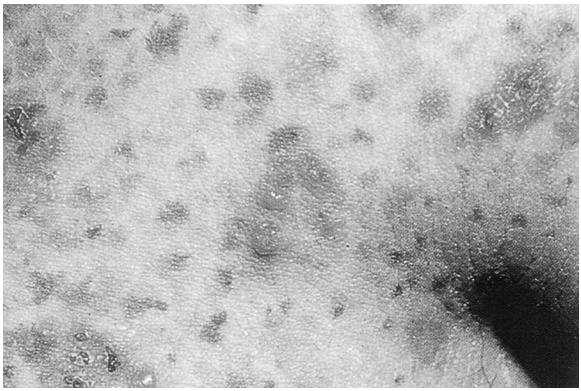

Figure 6-8. Dermatitis herpetiformis is characterized by pruritus, urticarial papules, and small vesicles. See Plate 10. (From Feldman M. Sleisenger and Fordtran's gastrointestinal and liver disease. 9th ed. Philadelphia: Saunders, 2010; Courtesy Dr. Timothy Berger, San Francisco, Calif.)

34. What skin disease is associated with celiac disease (gluten intolerance or sensitivity)? How is it treated?

Dermatitis herpetiformis is associated with celiac disease. Patients have intensely pruritic vesicles, papules, and wheals on the extensor aspects of the elbows and knees and possibly on the face or neck (Fig. 6-8; Plate 10). Look for diarrhea and weight loss (caused by gluten sensitivity). On biopsy, the skin has IgA deposits even in unaffected areas. Test for celiac disease and treat both conditions with a gluten-free diet.

35. What are decubitus ulcers? What is the best method of prevention?

Decubitus ulcers (bedsores or pressure sores) are skin ulcers caused by prolonged pressure against the skin. The best treatment is prophylaxis. Periodic turning of paralyzed, bedridden, or debilitated patients (the populations in which they are most common) and use of special air mattresses prevents bedsores. Cleanliness and dryness also help prevent decubitus ulcers. Periodic skin inspection ensures that the problem is recognized early. When missed, the lesions can ulcerate down to the bone and become infected, possibly leading to sepsis and death. Treat major skin breaks with aggressive surgical debridement; if signs of infection are present, administer antibiotics.

36. How are decubitus ulcers staged?

Stage 1 is intact skin with nonblanchable redness of a localized area. Stage 2 is partial thickness loss of the dermis presenting as a shallow open ulcer. These also may present as an intact or ruptured blister. Stage 3 is full thickness tissue loss. Subcutaneous fat may be visible, but bone, tendon, and muscle are not exposed. Stage 4 is full thickness skin loss with exposed bone, tendon, or muscle. An unstageable ulcer has full thickness loss in which the base of the ulcer is covered with slough or eschar. The true depth of the ulcer cannot be determined until the slough or eschar is removed.

37. What conditions should excessive perspiration suggest on the USMLE?

We all know people who sweat too much for no apparent reason. On the Step 2 examination, however, look for a serious cause, such as a myocardial infarction, tuberculosis or other infection, hyperthyroidism, or pheochromocytoma.

38. True or false: Most melanomas start out as simple moles.

True. Moles are common and benign, but malignant transformation is possible (Fig. 6-9; Plate 11). **ABCDE characteristics of a mole** that should make you suspicious of malignant transformation: **a**symmetry,

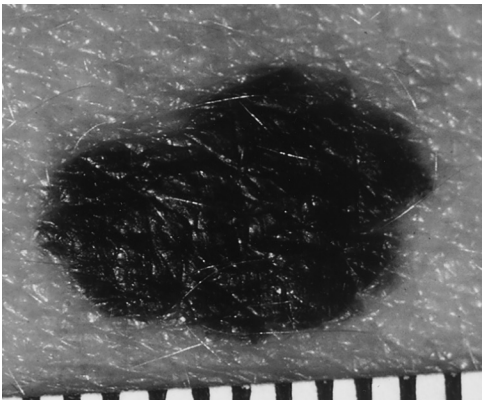

Figure 6-9. Melanoma (superficial spreading type). See Plate 11. (From Goldman L. Goldman's Cecil medicine. 24th ed. Philadelphia: Saunders, 2011.)

borders (irregular), **c**olor (change in color or multiple colors), **d**iameter (the bigger the lesion, the more likely that it is malignant), and **e**volving over time. Excise any mole (or do a biopsy if the lesion is very large) if it enlarges suddenly, develops irregular borders, darkens or becomes inflamed, changes color (even if only one small area of the mole changes color), begins to bleed, begins to itch, or becomes painful.

39. Define dysplastic nevus syndrome. How is it managed?

Dysplastic nevus syndrome is a genetic condition with multiple dysplastic-appearing nevi (usually more than 100 moles). Also look for a family history of melanoma. Treat with careful follow-up, excision or biopsy of any suspicious lesions, avoidance of sun exposure, and sunscreen use.

40. Why is keratoacanthoma of note?

Keratoacanthoma can mimic skin cancer (especially squamous cell cancer). Look for a flesh-colored lesion with a central crater that contains keratinous material, classically on the face (Fig. 6-10; Plate 12). Keratoacanthoma has a very rapid onset and grows to its full size in 1 to 2 months (which almost never happens with squamous cell cancer). The lesion involutes spontaneously in a few months and requires no treatment. If unsure, the best step is a biopsy, but choose observation as the answer in patients with a classic history of keratoacanthoma.

41. When and where are keloids seen?

Keloids are overgrowths of scar tissue after an injury; they are seen most frequently in black patients. They are usually slightly pink and classically appear on the upper back, chest, and deltoid area. Also look for keloids to develop after ear piercing (Fig. 6-11; Plate 12). Do not excise these lesions because it may worsen scarring.

42. Describe the classic lesion of basal cell cancer. What should you do if you suspect it?

Basal cell cancer classically begins as a shiny papule on a skin-exposed area (the head is classic) and slowly enlarges and develops an umbilicated center (which later may ulcerate) with peripheral telangiectasias (Fig. 6-12; Plate 14). Like all skin cancers, sunlight exposure increases the risk. It is more common in older, light-skinned people. Treat with excision. Biopsy any suspicious skin lesions in older adults.

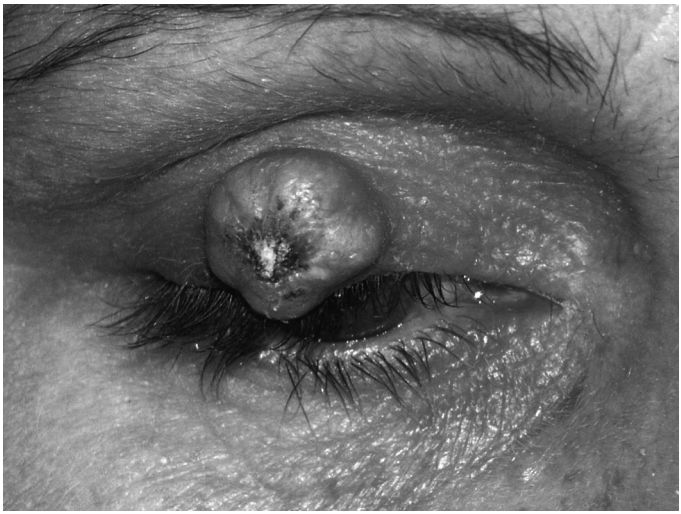

Figure 6-10. Keratoacanthoma on the right upper lid. Lesions are solitary, smooth, dome-shaped red papules or nodules with a central keratin plug. See Plate 12. (From Albert DM. Albert & Jakobiec's principles and practice of ophthalmology. 3rd ed. Philadelphia: Saunders, 2008.)

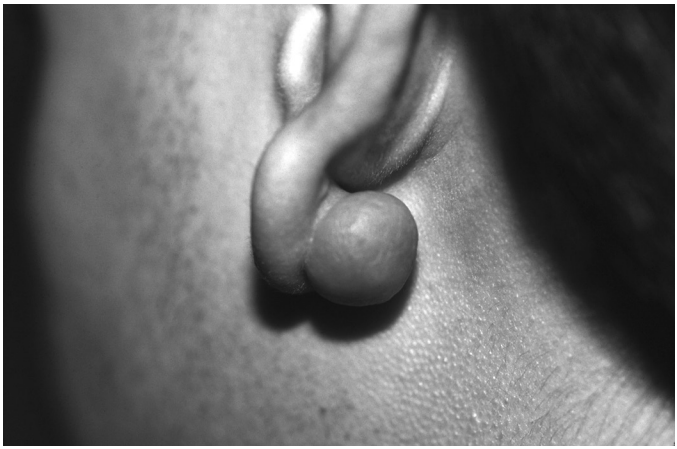

Figure 6-11. Keloid of the earlobe after piercing. See Plate 13. (From Kliegman RM, Stanton BF, St. Geme JW, et al. Nelson textbook of pediatrics. 19th ed. Philadelphia: Saunders, 2011.)

43. True or false: Basal cell skin cancer almost never develops metastases.

True. However, it may be locally invasive and destructive.

44. From what lesion does squamous cell cancer classically develop? What is Bowen disease?

Squamous cell cancer (Fig. 6-13; Plate 15) often develops in areas with preexisting actinic keratoses (hard, sharp, red, often scaly lesions in sun-exposed areas; Fig. 6-14; Plate 16) or burn scars. The lesions

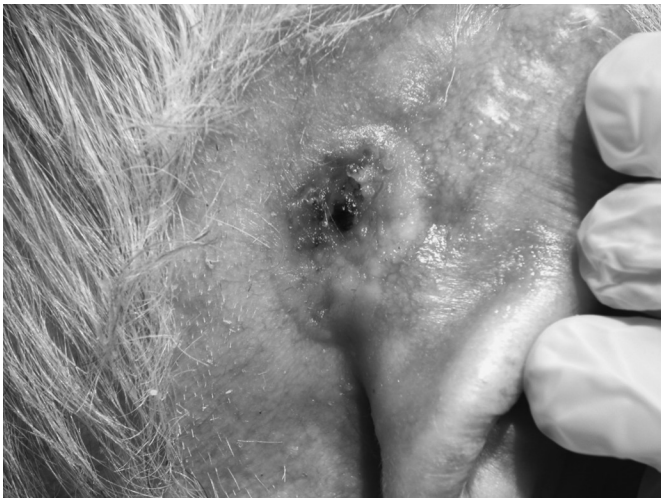

Figure 6-12. An ulcerated basal cell carcinoma with rolled borders on the posterior ear. See Plate 14 . (From Abeloff DA, Armitage JO, Niederhuber JE. Abeloff's clinical oncology. 4th ed. Philadelphia: Churchill Livingstone, 2008.)

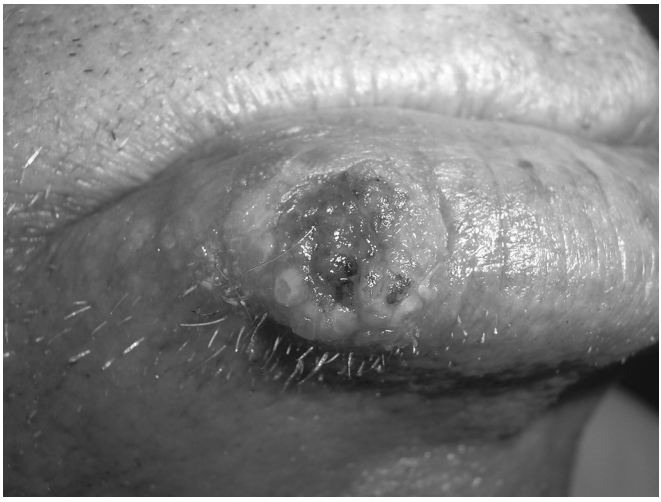

Figure 6-13. Squamous cell carcinoma on the lower lip. See Plate 15. (From Rakel RE, Rakel DP. Textbook of family medicine. 8th ed. Philadelphia: Saunders, 2011. © Richard P. Usatine.)

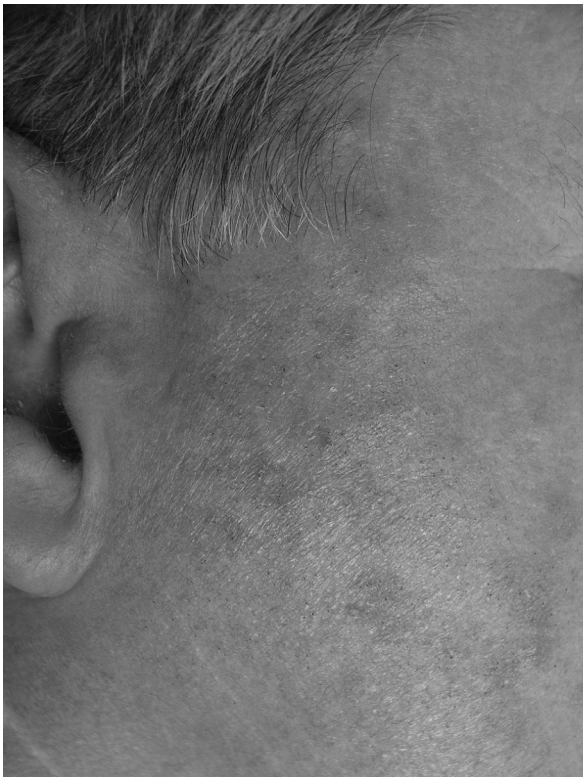

Figure 6-14. Multiple actinic keratoses visible as thin, red, scaly lesions. See Plate 16. (From Goldberg DJ. Procedures in cosmetic dermatology: lasers and lights. Vol 1, 2nd ed. Philadelphia: Saunders, 2008.)

become nodular, warty, or ulcerated; do a biopsy if such transformation occurs. Squamous cell cancer in situ is known as Bowen disease. Although metastases are rare in squamous cell cancer, they occur more frequently than in basal cell cancer.

45. To what parameter is the prognosis of malignant melanoma most closely related?

The thickness of the tumor. The 10-year survival rate decreases as the thickness of the tumor increases. Tumors less than 1 mm thick have the best prognosis.

46. What type of melanoma do black patients tend to develop? How do you recognize it?

Although uncommon in black patients, melanoma tends to be of the acrolentiginous type. Look for black dots on the palms, soles or under the fingernails (Fig. 6-15; Plate 17) that start to change in appearance or cause symptoms.

47. Describe Paget disease of the nipple. What is its significance?

Paget disease of the nipple presents as a unilateral, red, oozing or crusting nipple in an adult woman that fails to respond to typical dermatology treatments (Fig. 6-16; Plate 18). Although rare (roughly 1% to 2% of breast cancers), it signifies an underlying breast cancer (usually invasive ductal carcinoma or ductal carcinoma in situ) with extension to the skin.

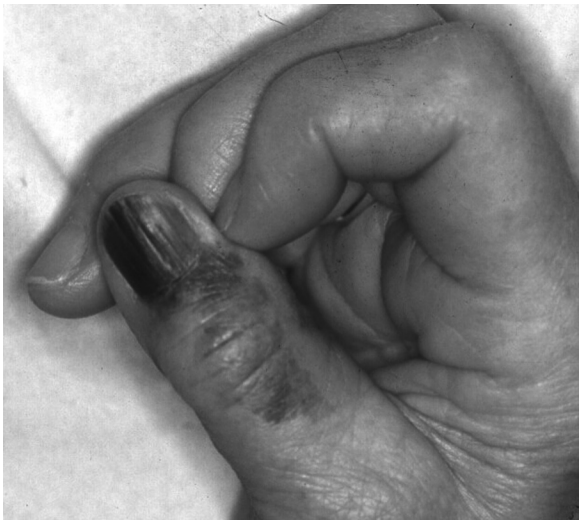

Figure 6-15. Nailbed melanoma. See Plate 17. (From Goldman L, Schafer, AI. Goldman's Cecil medicine. 24th ed. Philadelphia: Saunders, 2011.)

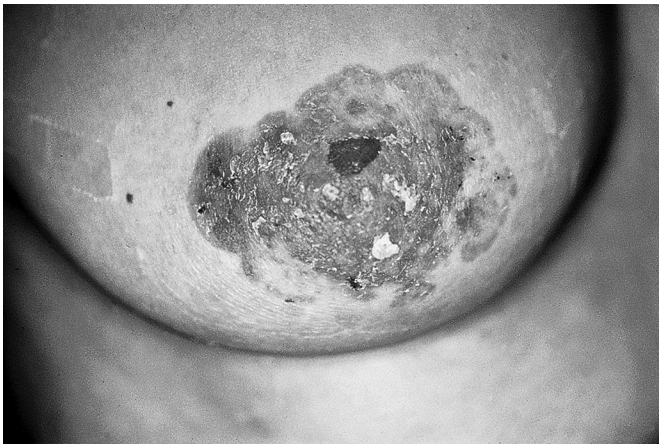

Figure 6-16. Paget disease of the nipple. Note the erythematous plaques around the nipple. See Plate 18. (From Lentz GM, Lobo RA, Gershenson DM, Katz VL. Comprehensive gynecology. 6th ed. Philadelphia: Mosby, 2011. Originally from Callen JP. Dermatologic signs of systemic disease. In Bolognia JL, Jorizzo JL, Rapini RP [eds]. Dermatology. Edinburgh: Mosby, 2003, p 714.)

48. Define stomatitis. What does it suggest?

Stomatitis is an inflammation of the mucous membranes of the mouth. The classic finding is fissuring of the corners of the mouth (angular stomatitis). Watch for deficiencies of B-complex vitamins (riboflavin, niacin, pyridoxine) or vitamin C.

CHAPTER 7

DIABETES MELLITUS

1. Outline the current recommendations for diabetes mellitus screening.

Universal screening is not generally recommended. Screening is more accepted, but not universal, in patients who are obese, people older than 45 years of age, people with a family history of diabetes, and members of certain minority groups (black, Hispanic, Pima Indian). Screening in pregnancy is mandatory!

2. Define diabetes.

Diabetes is defined when one of the following criteria is met: (1) a glucose level greater than or equal to 126 mg/dL after an overnight (or 8-hour) fast on two separate occasions, (2) a random glucose level greater than 200 mg/dL, or (3) a hemoglobin A1c (Hb A_{1c}) level of greater than or equal to 6.5% on two separate occasions. If the patient has classic symptoms of diabetes (see question 10), one test is sufficient to make the diagnosis. In an asymptomatic patient, it is best to repeat the test. An oral glucose tolerance test is commonly used in pregnant women; otherwise, it is rarely used because of poor reproducibility and patient compliance. With a glucose tolerance test, diabetes is diagnosed when serum glucose levels in the blood reach or exceed 200 mg/dL within 2 hours of receiving a 75-g oral dose of glucose.

3. What are the classic differences between type 1 and type 2 diabetes?

	TYPE 1 (10% OF CASES)	TYPE 2 (90% OF CASES)
Age at onset	Most commonly < 30 yr	Most commonly > 30 yr
Associated body habitus	Thin	Obese
Development of ketoacidosis	Yes	No
Development of hyperosmolar state	No	Yes
Level of endogenous insulin	Low to none	Normal to high (insulin resistance)
Twin concurrence	<50%	>50%
HLA association	Yes	No
Response to oral hypoglycemics	No	Yes
Antibodies to insulin	Yes (at diagnosis)	No
Risk for diabetic complications	Yes	Yes
Islet-cell pathology	Insulitis (loss of most B cells)	Normal number, but with amyloid deposits

These findings may overlap.

4. What are the goals of treatment in terms of glucose levels?

The goals are to keep postprandial glucose levels less than 180 mg/dL and fasting glucose levels between 70 and 130 mg/dL. Attempts at stricter control may result in hypoglycemia; watch for symptoms of sympathetic nervous system activation and mental status changes.

5. What is a good measure of long-term diabetes control?

A1c measures the "average" control of blood glucose level over the prior 2 to 3 months. The current recommendation is to keep the hemoglobin A_{1c} level below 7% in most patients. Less stringent A1c goals (e.g., <8%) may be appropriate for patients with a history of severe hypoglycemia, limited life expectancy, advanced microvascular or macrovascular complications, and extensive comorbid conditions.

The Hb A_{1c} is a good way to catch patients with nocturnal hyperglycemia or less-than-honest patients who falsely record low glucose test readings. A rough rule of thumb is that Hb A1c times 20 equals the average blood glucose level.

6. When a nondiabetic patient presents with hypoglycemia, how can you distinguish between factitious disorder (exogenous insulin) and an insulinoma (endogenous insulin)?

Measure the **C-peptide level.** C-peptide is produced whenever the body makes insulin, but it is absent in prescription insulin preparations. Therefore C-peptide is high with an insulinoma and low with factitious disorder. This is a classic USMLE question.

7. What should you remember before giving intravenous iodinated contrast material to a patient with diabetes or a patient with renal insufficiency?

Diabetic patients and patients with renal insufficiency are prone to acute renal failure from the intravenously administered iodinated contrast agents used for intravenous pyelography, conventional angiography, and computed tomography (CT). Weigh carefully the risk-benefit ratio of using intravenous contrast agents. If you give contrast, first hydrate the patient well with intravenous fluids to avoid renal shutdown. Acetylcysteine and bicarbonate may decrease the risk of contrast nephropathy in patients at high risk. The concerns about intravenous iodinated contrast do not apply to oral contrast agents (e.g., barium).

8. What is diabetic ketoacidosis (DKA)? How is it treated?

Patients with type 1 diabetes will die without insulin. DKA is a medical emergency that occurs in those patients when their insulin levels become depleted. Clinically, look for Kussmaul breathing (deep, rapid respirations), dehydration, hyperglycemia, acidosis (caused by excessive ketone formation), and increased ketones in the serum (often associated with a fruity odor of the breath) and urine.

Treatment involves intravenous fluids, insulin, and replacement of electrolytes (especially potassium and phosphate). For the USMLE, do not choose to use bicarbonate to correct acidosis. Rather, search for the cause of DKA, which most commonly is noncompliance with insulin therapy. The second most common cause is an infection. The mortality rate of DKA with current treatment efforts is less than 10%.

9. What is nonketotic hyperglycemic hyperosmolar state? How is it treated?

Hyperglycemic hyperosmolar state is a medical emergency that occurs predominantly in patients with type 2 diabetes. Hyperglycemia and increased serum osmolarity are present in the absence of ketones and acidosis. Most patients are severely dehydrated; the first three treatments are thus "fluids, fluids, and fluids" (i.e., intravenous hydration with normal saline). Insulin and electrolyte replacement also is required. The mortality rate can approach 50% if mental status changes are present at the time of diagnosis.

10. What are the classic presenting symptoms of new-onset diabetes?

Polyuria, polydipsia, and polyphagia (pee a lot, drink a lot, and eat a lot). Presenting symptoms may also include candidal infections (e.g., thrush or vaginal yeast infection), weight loss (as a result of excessive urination), or blurry vision. Prolonged hyperglycemia causes the lenses in the eyes to swell, and the patient may become myopic. Older patients may even claim that they no longer need their reading glasses (i.e., presbyopia is temporarily corrected by lens swelling).

11. What are the common long-term complications of diabetes mellitus?

- **Atherosclerosis, coronary artery disease, myocardial infarction [MI].** Patients with diabetes often have "silent" heart attacks (no chest pain because of autonomic neuropathy).
- **Retinopathy.** Diabetes is the leading cause of blindness in the United States for persons younger than age 50 years.
- **Nephropathy.** Diabetes is the number one cause of end-stage renal disease requiring hemodialysis (roughly 30% of cases; hypertension is a close second).
- **Peripheral vascular disease.** Diabetes is a leading cause of limb amputation and may lead to claudication, strokes, and impotence.
- **Peripheral neuropathy.** This complication causes "silent" heart attacks, numbness in the feet, and other findings (see question 12).
- **Increased risk for infection.** White blood cells do not function as well in a hyperglycemic environment; moreover, clogged arteries cannot deliver white cells to the site of an early infection and patients with diabetes have decreased ability to sense pain, leading to increased risk for infection.

All of these complications can be delayed or even prevented by good glucose control.

12. What problems may result from diabetic peripheral neuropathy?

- **Gastroparesis.** Because the stomach does not empty well, patients experience early satiety and vomiting. Treat with motility enhancers, such as metoclopramide**.**
- **Charcot joints.** Joints are deformed secondary to lack of sensation. Patients may break a bone and not feel it.
- **Impotence.** The causes are neuropathy and atherosclerosis.
- **Cranial nerve palsies** (especially of cranial nerves III, IV, and VI). Patients present with diplopia and extraocular muscle paralysis, which should resolve within 8 weeks without treatment.
- **Orthostatic hypotension.** This problem occurs even when the patient is well hydrated because the arteries do not "clamp down" when the patient stands up, and the heart rate fails to increase appropriately.
- **Pressure ulcers in the feet.** As with Charcot joints, lack of sensation leads to overuse or failure to rest an injured or tired foot because it is numb and the patient is unaware. Diabetic patients with foot numbness should wear socks and comfortable shoes and inspect their feet regularly. Most cases of foot gangrene in patients with diabetes begin as a simple callous or blister.

13. Describe the treatment for diabetic retinopathy.

If the retinopathy is proliferative (neovascularization or new, irregular vessel formation), the treatment is **panretinal laser photocoagulation.** A laser beam is used to burn tiny spots around the periphery of the retina, sparing the central retina, to prevent progression to blindness. Focal (limited) laser photocoagulation generally is done for nonproliferative retinopathy only when symptoms are present (from macular edema). All diabetic patients should be seen annually by an ophthalmologist to monitor retinal changes.

14. Describe the onset, peak, and duration of action of each of the insulin preparations.

INSULIN PREPARATION	ONSET (HR)	PEAK (HR)	DURATION (HR)
Ultra rapid acting			
Insulin aspart	<0.25	1-3	3-5
Insulin lispro	0.25-0.5	0.5-2.5	3-5
Insulin glulisine	0.2-0.5	1.5-2.5	3-4
Rapid acting			
Regular insulin	0.5-1	2-4	5-8
Intermediate to long acting			
NPH insulin	2-3	4-12	12-20
Long acting			
Insulin glargine	1.5-4	None	24+
Insulin detemir	3-4	3-9	Dose dependent; 6-23 hr

NPH, Neutral protamine Hagedorn

15. How do you adjust the dosage of neutral protamine Hagedorn (NPH) or regular insulin for high glucose levels?

Regular insulin starts to work in 45 minutes; its action peaks around 2 to 4 hours after injection, and the duration of action is 5 to 8 hours. NPH insulin takes 1 to 1.5 hours until onset of action; its action peaks at 4 to 12 hours, and the total duration of action is about 12 to 20 hours. For insulin adjustments, therefore, the following guidelines apply:

- If the patient has high (low) glucose at 7 AM, increase (decrease) NPH insulin at dinner the night before.
- If the patient has high (low) noon glucose, increase (decrease) the morning dose of regular insulin.
- If the patient has high (low) glucose at 5 PM, increase (decrease) the morning dose of NPH insulin.
- If the patient has high (low) glucose at 9 PM, increase (decrease) the dinnertime dose of regular insulin.

16. Define the Somogyi effect and the dawn phenomenon.

The **Somogyi effect** is the body's reaction to hypoglycemia. If too much NPH insulin is given at dinnertime, the glucose level at 3 AM the next morning will be low (hypoglycemia). The body reacts to hypoglycemia by releasing stress hormones, which cause a high glucose level at 7 AM. The treatment is to decrease evening (NPH) insulin. The **dawn phenomenon** is hyperglycemia caused by normal secretion of growth hormone early in the morning. The glucose level is high at 7 AM and normal or high at 3 AM (no hypoglycemia). The treatment is to increase evening (NPH) insulin.

17. How do you manage diabetic patients who are not allowed to eat because they are scheduled for surgery?

Generally, one third to one half of the normal dose of insulin is given. Glucose is monitored closely intraoperatively and postoperatively by the anesthesiologist. Regular intravenous insulin can be given to control glucose levels based on blood glucose measurements.

18. How do beta blockers interact in a hypoglycemic diabetic patient?

If you give a beta blocker to a diabetic patient, you may mask the classic symptoms of hypoglycemia (tachycardia, diaphoresis), which are caused by catecholamine release. As for all patients, you must weigh the risk-benefit ratio of using beta blockers in patients with diabetes. If a diabetic patient is having or has had a previous myocardial infarction, the benefits outweigh the risks of treatment.

19. What are the best oral agents to use in type 1 diabetes?

None. Patients with type 1 diabetes require insulin. Currently available oral agents do not work for type 1 diabetic patients.

20. What is the first treatment for type 2 diabetes?

Weight loss, which may reduce glucose levels by reducing insulin resistance. However, medications are usually needed, and oral agents are tried first, typically beginning with metformin. Other agents include insulin secretagogues (glipizide, glimepiride, nateglinide, glyburide, repaglinide), thiazolidinediones (rosiglitazone, pioglitazone), alpha-glucosidase inhibitors (acarbose, miglitol), GLP-1 agonists (exenatide, liraglutide), DPP-IV inhibitors (saxagliptin, sitagliptin, linagliptin), and amylin analogues (pramlintide). The thiazolidinediones are falling out of favor because of the risk of fluid retention and exacerbation of congestive heart failure (CHF; rosiglitazone and pioglitazone), the risk of myocardial infarction (rosiglitazone), and the risk of bladder cancer (pioglitazone).

Many patients with type 2 diabetes eventually require insulin, which may be required early if the blood glucose or Hb A_{1c} levels are significantly elevated. In fact, current guidelines suggest using a basal insulin early in therapy (generally after one or two oral agents have been started) in order to get the blood glucose and Hb A_{1c} under control as early as possible.

EAR, NOSE, AND THROAT SURGERY

1. What is the most common cause of lower motor neuron facial nerve paralysis? What are the classic symptoms?

The most common cause is Bell palsy. Look for sudden unilateral onset, usually after an upper respiratory infection (URI). The cause is thought to be a reactivation of latent herpes simplex 1 infection in most cases. Patients may have *hyperacusis,* in which everything sounds loud because the stapedius muscle in the ear is paralyzed. In severe cases, patients may be unable to close the affected eye; if so, use drops to keep the eye moist. Most cases resolve spontaneously in about 1 month, although some have permanent sequelae. Oral prednisone and antiviral treatment for herpes (e.g., valacyclovir, acyclovir) may improve outcomes and lessen duration of symptoms.

2. What are the other causes of lower motor neuron facial nerve paralysis?

- Herpes infection (Ramsay Hunt syndrome), which commonly involves the eighth nerve. Look for vesicles on the pinna and inside the ear; encephalitis or meningitis may be present.
- Lyme disease (one of the most common causes of bilateral facial nerve palsy)
- Stroke
- Middle ear or mastoid infection
- Meningitis
- Temporal bone fracture (look for Battle sign and/or bleeding from the ear)
- Tumor, classically an acoustic schwannoma (i.e., neuroma) of the cerebellopontine angle (Fig. 8-1)

Order a computed tomography (CT) or magnetic resonance imaging (MRI) scan of the head if the cause is not apparent or if the history or physical exam raises suspicion—especially in the presence of additional neurologic signs.

3. What are the common causes of hearing loss?

The most common cause is **aging** (presbyacusis); prescribe a hearing aid, if needed. The history may suggest other causes:

- Prolonged or intense exposure to loud noise (e.g., work-related).
- Congenital TORCH infection (**t**oxoplasmosis, **o**thers, **r**ubella, **c**ytomegalovirus, **h**erpes virus).
- Ménière disease (accompanied by severe vertigo, tinnitus, nausea and vomiting; treat acute episodes with benzodiazepines, anticholinergics [scopolamine], and antihistamines [meclizine or dimenhydrinate]; diuretics are often used for ongoing treatment; surgery may be used for refractory cases).
- Drugs (e.g., aminoglycosides, aspirin, quinine, loop diuretics, cisplatin).
- Tumor (classically acoustic neuroma).
- Labyrinthitis (may be viral or follow or extend from meningitis or otitis media).
- Miscellaneous causes (diabetes, hypothyroidism, multiple sclerosis, sarcoidosis, pseudotumor cerebri).

4. What is the usual cause of sudden deafness?

Sudden sensorineural hearing loss (SSNHL) involves acute unexplained hearing loss that is usually unilateral and occurs over hours (usually less than 72 hours). More than 90% of patients with SSNHL report tinnitus. Most cases are idiopathic but have been postulated to be caused by viral causes, microvascular

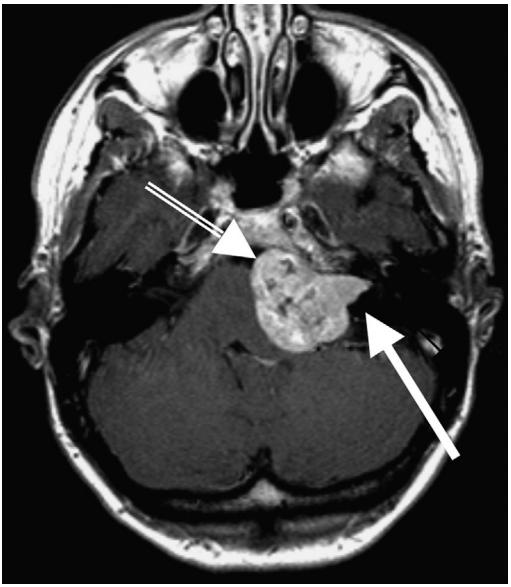

Figure 8-1. Acoustic neuroma. On this T1-weighted magnetic resonance image (MRI), a large acoustic neuroma widens the left internal auditory canal *(solid arrow)* and compresses the brain stem *(hollow arrow).* (From Goldman L, Ausiello D. Cecil medicine. 23rd ed. Philadelphia: Saunders, 2008, Fig. 419-9.)

events, or autoimmune causes. Physical examination is unremarkable. MRI is indicated to rule out etiologies such as acoustic neuroma, multiple sclerosis, or vascular insufficiency. Glucocorticoids (administered orally or by intratympanic injection) are considered first line therapy; antiviral agents are sometimes used, although there is not much evidence to support their use. Two thirds of patients recover, although the resolution is often not complete. Among those who recover, hearing usually returns within 2 weeks.

5. What is the most common cause of acquired hearing loss in children?

Bacterial meningitis. All children should receive formal hearing testing after a bout of meningitis.

6. What are the common causes of vertigo?

Vertigo can result from the same eighth cranial nerve lesions that cause hearing loss (Ménière disease, tumor, infection, multiple sclerosis). Another common cause is benign positional (paroxysmal) vertigo, which is induced by certain head positions, may be accompanied by nystagmus, and is not associated with hearing loss. This condition often resolves spontaneously; no treatment is required. Epley maneuver, or modified Epley maneuvers, may help with resolution of symptoms.

7. How is a deviated nasal septum treated in patients with recurrent sinusitis?

Surgical correction.

8. What are the three common causes of rhinitis?

Viral, allergic, and bacterial.

9. How do you recognize and treat viral rhinitis?

Viral rhinitis (the common cold) may be because of rhinovirus (the most common cause), influenza, parainfluenza, coxsackie virus, adenovirus, respiratory syncytial virus, coronavirus, or echovirus.

Treatment is symptomatic. Vasoconstrictors such as phenylephrine can be used for short-term symptomatic relief, but they may cause rebound congestion when discontinued.

10. How do you recognize and treat allergic rhinitis?

Allergic rhinitis (hay fever) is associated with seasonal flare-ups, boggy and bluish turbinates, onset before 20 years of age, nasal polyps, sneezing, pruritus, conjunctivitis, wheezing or asthma, eczema, positive family history, eosinophils in nasal mucous, and elevated serum Immunoglobulin E (IgE). Skin tests may identify an allergen. Treat with avoidance of known antigens (e.g., pollen). Antihistamines, nasal steroids, and/or cromolyn may be used for more severe symptoms. Desensitization is also an option.

11. What causes bacterial rhinitis? How is it treated?

Group A streptococci, pneumococci, or staphylococci are the most common culprits. Look for coexisting sore throat, fever, and tonsillar exudate. Obtain streptococcal throat cultures and treat with antibiotics, if appropriate.

12. What causes nosebleeds?

The most common cause of nosebleed is trauma; for example, nose-picking is a common cause in children. Also watch for the following causes:

- Local tumor (nasopharyngeal angiofibroma; seen in adolescent boys with no history of trauma or blood dyscrasia; signs include recurrent nosebleeds and/or obstruction).
- Leukemia (from pancytopenia; typically in children with associated fever and anemia).
- Other causes of thrombocytopenia (e.g., idiopathic thrombocytopenic purpura, hemolytic uremic syndrome).

13. True or false: A neck mass is more likely to be benign in a child than in an adult.

True. Roughly 75% of neck masses are benign in children, whereas 75% are malignant in patients older than 40 years of age.

14. What are the common causes of a neck mass?

In **children**, watch for thyroglossal duct cysts, which have a *midline* location and elevate with tongue protrusion; branchial cleft cysts, which are *lateral* in location and often become infected; cystic hygroma, a benign tumor also known as lymphangioma that is associated with Turner syndrome and treated with surgical resection; and cervical lymphadenitis. Cervical lymphadenitis is usually because of streptococcal pharyngitis, Epstein-Barr virus (common in the second and third decades), cat-scratch disease, or mycobacterial infection (scrofula). In terms of malignancy in children, leukemia or lymphoma may present with cervical lymphadenopathy.

In **adults,** suspect malignancy, either lymphadenopathy from a primary tumor (lymphoma) or metastatic neoplasm (usually squamous cell carcinoma). The mass may also represent the tumor itself (especially with thyroid cancer).

15. Describe the workup for an unknown cancer in the neck.

The workup includes random biopsy of the nasopharynx, palatine tonsils, and base of the tongue as well as laryngoscopy, bronchoscopy, and esophagoscopy (with biopsies of any suspicious lesions). This approach is known as “triple endoscopy with triple biopsy.”

16. What is the scientific name for “swimmer's ear?” What causes it?

Otitis externa (inflammation of the outer ear), which most often is because of infection with *Pseudomonas aeruginosa.* Patients have pain with manipulation of the auricle and erythematous, swollen skin in the auditory canal. Foul-smelling discharge and conductive hearing loss also may be present. Treat with topical antibiotics (e.g., ofloxacin, neomycin, polymyxin B) and possibly topical steroids to reduce swelling.

17. What causes otitis media? How do you recognize it?

Otitis media (inflammation of the middle ear) is an extremely common pediatric infection, most often because of infection with *Streptococcus pneumoniae, Haemophilus influenzae,* or *Moraxella catarrhalis.* Patients have no pain with manipulation of the auricle; positive symptoms include earache, fever, erythematous and bulging tympanic membranes (the light reflex and landmarks are difficult to see with otoscopy), and nausea and vomiting.

18. What are the complications of otitis media? How are they avoided?

Complications include tympanic membrane perforation (bloody or purulent discharge), mastoiditis (fluctuance and inflammation over the mastoid process roughly two weeks after the onset of otitis media), labyrinthitis, palsies of cranial nerves VII and VIII, meningitis, cerebral abscess, dural sinus thrombosis, and chronic otitis media (because of permanent perforation of the tympanic membrane). Patients with chronic otitis media may develop cholesteatomas with marginal perforations that require surgical excision.

Otitis media generally is treated with antibiotics to avoid these complications (e.g., amoxicillin, second generation cephalosporin such as cefuroxime, macrolide).

19. What is the problem with recurrent otitis media? How is it treated?

Recurrent otitis media is a common pediatric problem (along with prolonged secretory otitis, a result of incompletely resolved otitis media) and can cause hearing loss with resultant developmental problems (speech, cognitive functions). Treat with prophylactic antibiotics or tympanostomy tubes. Adenoidectomy is controversial, but may help in some cases; it is thought to help prevent blockage of the eustachian tubes.

20. What causes infectious myringitis? How do you recognize and treat it?

Infectious myringitis, also known as bullous myringitis, is an inflammation of the tympanic membranes that can be diagnosed when otoscopy reveals vesicles on the tympanic membrane. Infectious myringitis is classically caused by *Mycoplasma* species, but *Streptococcus pneumoniae* or viruses may also be the culprit. Treat with erythromycin or clarithromycin to cover *Mycoplasma* species and *S. pneumoniae.*

21. What are the common bacterial causes of sinusitis? How is this condition recognized clinically?

Sinusitis is often caused by *S. pneumoniae, H. influenzae,* or other streptococcal or staphylococcal species. Look for tenderness over the affected sinuses, headache, and purulent nasal discharge (yellow or green). Associated symptoms are headache and/or toothache (maxillary sinusitis). Radiographs or CT are used to confirm the diagnosis and show opacification of the sinus, classically with an air-fluid level in acute sinusitis; CT scans are preferred to evaluate chronic sinusitis or suspected extension of infection outside the sinus (watch for high fever and chills). Treat with antibiotics (amoxicillin, trimethoprim-sulfamethoxazole, a second or third generation cephalosporin, a macrolide, or amoxicillin clavulanate for 10 to 14 days or for up to 6 weeks in chronic cases). Culture usually is not necessary unless the patient fails to respond to antibiotics. Operative intervention (drainage procedure, sinus obliteration) may be required for resistant cases.

22. By what age are the frontal sinuses well developed in children?

The frontal sinuses may not be well developed until the age of 10 years.

23. Define otosclerosis. How is it treated?

In otosclerosis, the otic bones become fixed together and impede hearing. It is the most common cause of progressive conductive hearing loss in adults, whereas presbyacusis is the most common cause of sensorineural hearing loss in adults. Treat with a hearing aid or surgery.

24. What causes parotid gland swelling?

The classic cause is mumps. The best treatment for mumps and the complication of infertility is prevention through immunization. Parotid gland swelling also may be caused by neoplasms, of

which pleomorphic adenoma is the most common type; Sjögren syndrome; sialolithiasis (a stone in the parotid duct); sarcoidosis; and bulimia. Alcoholism can cause parotid gland hypertrophy as well. Remember that the parotid gland contains lymph nodes within its parenchyma (unique in this regard), which can become enlarged in a number of conditions, as with lymph nodes elsewhere.

25. How do you recognize a nasal fracture? What complication may result?

A nasal fracture can be seen on radiographs or CT scan. Watch for a septal hematoma, which must be removed surgically to prevent pressure-induced septal necrosis.

26. What is the Weber test used to evaluate? How is it performed and interpreted?

The Weber test compares bone conduction in the two ears. A vibrating tuning fork is placed on the forehead, and the patient is asked where the vibrating sound is heard best. The normal response is to hear the vibration in the middle (or equally in both ears). In patients with conductive hearing loss, the sound is heard best in the affected ear, whereas in patients with sensorineural hearing loss, the sound is heard best in the unaffected ear.

27. What is the Rinne test used to evaluate? How is it performed and interpreted?

The Rinne test compares air conduction with bone conduction. A vibrating tuning fork is placed on the tip of the mastoid process. When the patient can no longer hear the sound, the tuning fork is removed from the mastoid and placed next to the auditory meatus of the external ear and the patient is asked if the sound can be heard.

Because air conduction is normally greater than bone conduction, patients can hear the tuning fork when it is placed next to the auditory meatus (air conduction) even after they can no longer hear it vibrating on the mastoid (bone conduction). In patients with conductive hearing loss, bone conduction is greater than air conduction; thus they cannot hear the tuning fork when it is placed next to the external auditory meatus. In patients with sensorineural hearing loss, both air and bone conduction are impaired, but the normal ratio (air conduction > bone conduction) is maintained. Thus, they still hear the tuning fork next to the ear after they can no longer hear it on the mastoid.

CHAPTER 9

EMERGENCY MEDICINE

1. What are the three causes of burns? How should all burns be managed initially?

Burns may be thermal, chemical, or electrical. Initial management of all burns includes lots of intravenous fluids (first choice: lactated Ringer solution; backup choice: normal saline), removal of all clothes and other smoldering items on the body, copious irrigation of chemical burns, and, of course, the ABCs (airway, breathing, circulation). You should have a low threshold for intubation. In the setting of burns related to a fire, give 100% oxygen until significant carboxyhemoglobin in the blood from carbon monoxide inhalation is ruled out.

2. What are the important sequelae of electrical burns?

Because most of the tissue destruction caused by electrical burns is internal, sequelae include muscle necrosis, myoglobinuria, acidosis, and renal failure. Use large amounts of intravenous hydration to prevent renal shutdown. The immediate life-threatening risk associated with electrical shock and burn (e.g., from lightning or household outlets) is cardiac arrhythmia; obtain an electrocardiogram (ECG).

3. How are chemical burns managed? Which is worse, acid or alkali burns?

All chemical burns should be treated with copious irrigation from the nearest source (e.g., tap water) because the sooner you dilute the chemical, the less damage will be done. Alkali burns are worse than acidic burns because alkaline substances penetrate more deeply.

4. What is burned skin prone to develop?

Burned skin is much more prone to infection, usually by *Staphylococcus aureus* or *Pseudomonas aeruginosa.* With pseudomonal infection, look for a fruity smell and/or blue-green appearance. Prophylactic antibiotics are given topically only. Give a tetanus booster to all burn patients unless they have recently received one (within the past 5 years).

5. How is burn severity classified? Describe the management of each class.

Burn depth terminology no longer includes the use of first-, second-, and third-degree burns. Burn severity is now classified as superficial, superficial partial thickness, deep partial thickness, and full thickness burns.

Superficial burns are erythematous without blister formation, involve only the epidermis, and pain is localized.

Superficial partial thickness burns are painful, warm, and moist with blister formation and involve the epidermis and superficial papillary dermis.

Deep partial thickness burns reveal skin that is mottled, waxy, and white in appearance with ruptured blisters. Pain sensation is absent, but pressure sensation is intact.

Full thickness burns involve both the epidermis and dermis, have a white to gray leathery appearance, and do not blanch with pressure.

6. Define hypothermia. How is it managed? What are the complications?

Hypothermia is defined as a body temperature <95°F (35°C), usually accompanied by mental status changes and generalized neurologic deficits. If the patient is conscious, you can rewarm the patient

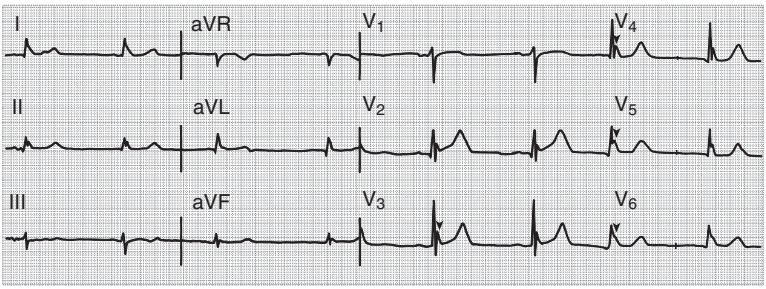

Figure 9-1. Systemic hypothermia resulting in prominent sinus bradycardia. The arrowheads (V3 through V6) point to the characteristic convex J waves, termed Osborn waves. (From Libby P, et al. Braunwald's heart disease: a textbook of cardiovascular medicine. 8th ed. Philadelphia: Saunders, 2008, Fig. 12-53.)

slowly with blankets. If the patient is unconscious, consider gastric and bladder lavage with warm water as well as warm intravenous fluids.

Monitor the ECG for arrhythmias, which are common in hypothermic patients. You may see the classic **J wave—**a small, positive deflection following the QRS complex (Fig. 9-1). Also monitor electrolytes, renal function, and acid-base status.

7. Distinguish between frostnip and frostbite. How are they managed?

In **frostnip,** a mild form of cold injury, the affected skin is cold and painful. In **frostbite,** a more severe form of cold injury, the skin is cold and numb. Treat both with warming of the affected areas, using warm water (not scalding hot), and generalized warming (e.g., blankets).

8. True or false: You should not give up resuscitation efforts until the patient is fully warmed in the setting of hypothermic cardiac arrest.

True. An old saying in medicine claims that the patient is not considered dead "until warm and dead." Hypothermia can slow body function to a remarkable degree, and there are case reports of resuscitation hours after initial attempts in the field once the body was warmed.

9. Define hyperthermia. What causes it? How is it managed?

Hyperthermia is defined as a body temperature greater than 104°F. The three primary causes are infections, medications, and heat stroke. If heat stroke is the cause, look for a history of prolonged heat exposure and a high temperature (>104°F), without clues to other culprits. Treat with immediate cooling (e.g., wet blankets, ice, cold water). The immediate threats to life are convulsions (treat with diazepam) and cardiovascular collapse. Always rule out infection and medications (especially those with anticholinergic activity such as antihistamines, antipsychotics, and antidepressants) as the cause.

10. What are the two classic examples of hyperthermia caused by medication?

Malignant hyperthermia is an idiosyncratic, genetically related reaction to general anesthesia, usually caused by succinylcholine or halothane exposure. Treat with dantrolene.

Neuroleptic malignant syndrome is thought to be related to malignant hyperthermia and is an idiosyncratic, genetically related reaction to an antipsychotic. Look for extremely high levels of creatine phosphokinase and mental status changes in a patient taking antipsychotics. The first step in management is to stop the medication. The second step is supportive treatment, especially with lots of intravenous fluids to prevent renal shutdown because of rhabdomyolysis. The third step, if necessary, is to treat with dantrolene.

Drug fevers are idiosyncratic reactions to a medication that was typically started within the past week. They rarely cause fever above 104°F.

11. How are patients managed after a near-drowning episode?

Some experts believe that fresh water is worse than salt water because fresh water if aspirated, can cause hypervolemia, electrolyte disturbances, and hemolysis. Intubate patients after a near-drowning episode if they are unconscious, and monitor arterial blood gases if they are conscious. Patients who experience near-drowning in cold water often do better than those who experience near-drowning in warm water because of decreased metabolic needs. Death is usually because of hypoxia and/or cardiac arrest.

12. What are toxidromes? Describe the toxidromes associated with cholinergic crisis, anticholinergic crisis, sympathomimetics, and opiates.

Toxidromes are syndromes caused by dangerously high levels of toxic substances in the body.

- Cholinergic crisis classically develops with SLUDG (excessive **S**alivation, **L**acrimation, **U**rination, **D**efecation, and **G**astrointestinal activity). Also look for pinpoint pupils and decreased heart rate.
- Anticholinergic crisis develops with a patient who is blind as a bat (eye muscles unable to focus), hot as a hare (temperature dysregulation), mad as a hatter (CNS disturbances), dry as a bone (decreased secretion of bodily fluids), and red as a beet (flushing). Also look for dilated pupils and increased heart rate.
- Sympathomimetics can cause hypertension, tachycardia, increased activity, anxiety, dilated pupils, diaphoresis, and possibly altered mental status.
- Opiates cause coma, pinpoint pupils, and respiratory depression. Also look for bradycardia and hypotension.

13. Name the antidote for each of the poisonings or overdoses listed on the left side of the table.

POISONING OR OVERDOSE	ANTIDOTE
Acetaminophen	Acetylcysteine
Benzodiazepines	Flumazenil
Beta blockers	Glucagon
Carbon monoxide	Oxygen (hyperbaric if severe)
Cholinesterase inhibitors	Atropine, pralidoxime
Copper or gold	Penicillamine
Digoxin	Normalize potassium and other electrolytes, digoxin antibodies
Iron	Deferoxamine
Lead	Edetate
Methanol or ethylene glycol	Fomepizole, ethanol
Muscarinic receptor blockers	Physostigmine
Opioids	Naloxone
Quinidine or tricyclic antidepressants	Sodium bicarbonate (cardioprotective)

ENDOCRINOLOGY

1. What are the common symptoms and signs of hyperthyroidism?

Symptoms: Nervousness, anxiety, irritability, insomnia, heat intolerance, sweating, palpitations, tremors, weight loss with increased appetite, fatigue, weakness, emotional lability, and diarrhea.

Signs: Enlarged thyroid gland, warm skin, thyroid "stare"—lid lag, exophthalmos, proptosis, ophthalmoplegia (Graves disease), pretibial myxedema (Graves disease), tremor, tachycardia, and atrial fibrillation. Check thyroid-stimulating hormone (TSH) when patients come to the hospital with new-onset atrial fibrillation.

2. What are the most common causes of hyperthyroidism?

The most common cause is **Graves disease,** which is characterized by a diffusely enlarged thyroid gland, positive thyroid-stimulating immunoglobulins and antibodies, exophthalmos, proptosis, ophthalmoplegia, and pretibial myxedema. In older patients, look for toxic multinodular goiter (individual lumps instead of diffuse enlargement of the gland and "hot" nodules on thyroid nuclear scan). Other causes include adenoma (single lump that is "hot" on nuclear scan), subacute thyroiditis (viral infection with **tender, painful** thyroid gland), and factitious hyperthyroidism (in which the patient takes thyroid hormone). Rare, exotic causes include amiodarone (which can cause hypothyroidism or hyperthyroidism), TSH-producing pituitary tumor, thyroid carcinoma, and struma ovarii (an ovarian teratoma that secretes thyroid hormone).

3. Describe the classic laboratory pattern of hyperthyroidism.

The TSH level is low (unless the patient has a TSH-secreting tumor), whereas triiodothyronine (T_3) and thyroxine (T_4) are increased.

4. How is hyperthyroidism treated?

Short-term (stabilizing) treatment: Propylthiouracil (PTU) and methimazole/carbimazole can be used as suppressive agents. Beta blockers are used in the setting of thyroid storm (severe hyperthyroid state—an emergency). Iodine can also suppress the thyroid gland but is rarely used for this purpose clinically.

Definitive (curative) treatment: Radioactive iodine ablation of the thyroid gland is typically used. Surgery is preferred in pregnant patients. Hypothyroidism may result from either treatment; if so, it is treated with thyroid hormone replacement (for life).

5. What are the symptoms and signs of hypothyroidism?

Symptoms: Weakness, lethargy, fatigue, cold intolerance, weight gain with anorexia, constipation, loss of hair, hoarseness, menstrual irregularity (menorrhagia is classic), myalgias and arthralgias, memory impairment, and dementia. Always rule out hypothyroidism as a cause of dementia.

Signs: Bradycardia; dry, coarse, cold, and pale skin; periorbital and peripheral edema; coarse, thin hair; thick tongue; slow speech; decreased reflexes; hypertension; carpal tunnel syndrome and paresthesias; vitiligo, pernicious anemia, and diabetes (remember the autoimmune association between these three conditions and Hashimoto disease); and coma (severe disease).

In children, congenital hypothyroidism may occur (mental, motor, and growth retardation).

6. What are the common causes of hypothyroidism?

The most common known cause is Hashimoto thyroiditis. Women of reproductive age are affected 8 times more often than men. Histology reveals lymphocytes in the thyroid gland as well as antithyroid and antimicrosomal antibodies. Other autoimmune diseases may coexist. The associated goiter is nontender. The second most common cause is iatrogenic after treatment of hyperthyroidism. Other less common causes include iodine deficiency, amiodarone, lithium, and secondary hypothyroidism because of pituitary or hypothalamic failure (look for decreased TSH), such as with Sheehan syndrome (hypopituitarism caused by pituitary necrosis from blood loss and hypovolemic shock during and after childbirth).

7. Describe the laboratory findings in hypothyroidism.

Elevated TSH (unless caused by secondary causes), decreased T_3 and T_4, antithyroid and antimicrosomal antibodies (if caused by Hashimoto thyroiditis), hypercholesterolemia, and anemia (which may be because of chronic disease or coexisting pernicious anemia).

8. Why is free T_4 (or free T_4 index) better than total T_4 for measuring thyroid hormone activity?

Free T_4 (free T_4 index) measures the active form of thyroid hormone. Many conditions cause a change in the amount of thyroid-binding globulin (TBG), thus changing total T_4 levels in the absence of hypothyroidism or hyperthyroidism. Common examples include pregnancy, estrogen therapy, and oral contraceptive pills, all of which increase TBG. Nephrotic syndrome, cirrhosis, and corticosteroid treatment all decrease TBG. T_3 resin uptake is an older test that is not likely to appear on Step 2, but if you are asked, it should rise or fall in the same way as free T_4. Although an oversimplification, this principle should serve you well on the examination.

9. How is hypothyroidism treated?

With T_4 or thyroxine. T_3 should not be used. In older patients, it is important to "start low and go slow" because overtreatment can be dangerous.

10. What is sick euthyroid syndrome?

Any patient with any illness may have temporary derangements in thyroid function tests that resemble hypothyroidism. TSH ranges from normal to mildly elevated, and serum T_4 ranges from normal to mildly decreased. Clinical circumstances and physical findings are the best guides to whether the patient has true hypothyroidism. In patients with sick euthyroid syndrome, simply treat the underlying illness. If the diagnosis is in doubt, repeat the thyroid tests after the patient recovers (preferred) or give an empirical dose of levothyroxine (if the patient does not respond to treatment of the underlying illness).

11. What are the symptoms and signs of Cushing syndrome (increased corticosteroids)?

Symptoms: Weight gain, changes in appearance, easy bruising, acne, hirsutism, emotional lability, depression, psychosis, weakness, menstrual changes, sexual dysfunction, insomnia, and memory loss.

Signs: Buffalo hump, truncal and central obesity with wasting of extremities, round plethoric facies, purplish skin striae, acne, hirsutism, weakness (especially of the proximal muscles), hypertension, depression, psychosis, peripheral edema, poor wound healing, glucose intolerance or diabetes, osteoporosis, and hypokalemic metabolic alkalosis (because of mineralocorticoid effects of certain corticosteroids). Growth may be stunted in children.

12. What causes Cushing syndrome?

The most common cause is iatrogenic because steroids are prescribed for many different disorders. The second most common cause is Cushing disease (a pituitary adenoma that secretes adrenocorticotropic hormone [ACTH]), which causes roughly 60% of noniatrogenic cases. Women of reproductive age are affected 5 times more often than men. Other causes include ectopic ACTH production (classically by small cell lung cancer, which is more common in men) and adrenal adenomas or carcinomas (more common in children).

13. How is Cushing syndrome diagnosed?

The first test is either a 24-hour measurement of free cortisol in urine (free cortisol levels are abnormally elevated) or a dexamethasone suppression test (cortisol levels are not appropriately suppressed several hours after administration of dexamethasone). Random cortisol level is an inappropriate test because of wide interpatient and intrapatient variations. **ACTH is elevated in Cushing disease but decreased with an adrenal adenoma**. If ACTH is increased, a magnetic resonance imaging (MRI) scan of the brain should be obtained to look for a pituitary adenoma. If ACTH is decreased and the patient has no history of taking steroids, an abdominal computed tomography (CT) or MRI scan should be obtained to look for an adrenal tumor. Primary cancer is usually obvious when ectopic ACTH is the cause (e.g., weight loss, hemoptysis with lung mass on chest radiograph in patients with small cell lung cancer). Treatment is based on the cause and usually involves surgery.

14. What are the symptoms and signs of hypoadrenalism (Addison disease)?

Symptoms: Anorexia, weight loss, weakness, apathy.

Signs: Hypotension, hyperkalemia, hyponatremia, hyperpigmentation (only if the pituitary is functioning because of melanocyte stimulating hormone), nausea and vomiting, diarrhea, abdominal pain, mild fever, hypoglycemia, acidosis, eosinophilia, and shock.

15. What is the most common type of hypoadrenalism?

Secondary (iatrogenic) hypoadrenalism because of steroid treatment. People who are removed from long-term steroid therapy may be unable to secrete an appropriate amount of corticosteroids in response to stress for up to 1 year. Watch for the classic postoperative patient who crashes (with hypotension, shock, and hyperkalemia) shortly after surgery and has a history of a disease requiring steroid therapy within the past year. You may assess ACTH (usually high) and cortisol levels (inappropriately low) to help make the diagnosis, but do not wait for the results to give steroids. The patient may die. Give prophylactic stress doses of corticosteroids in the setting of an illness, operation, or other stressor to prevent an adrenal crisis.

16. What are the other causes of hypoadrenalism?

The most common primary (noniatrogenic) cause is autoimmune (idiopathic) disease. Patients may have other autoimmune diseases, such as hypothyroidism, pernicious anemia, vitiligo, diabetes, or hypoparathyroidism. Other causes include metastatic cancer (especially lung cancer), infection (tuberculosis, fungal infections, and opportunistic infections in AIDS and other immunosuppressed states), ketoconazole, and pituitary/hypothalamic failure.

17. How is hypoadrenalism diagnosed?

An ACTH stimulation test can be done. Plasma cortisol is measured, ACTH is administered, and cortisol is measured again in 1 hour. The cortisol level should rise appropriately, usually to 18 μg/dL or doubling of the baseline, depending on the baseline value. An inappropriate response to ACTH indicates hypoadrenalism. Do not withhold treatment to make a diagnosis if the patient is crashing.

18. Define hirsutism. What causes it?

Hirsutism is a male hair growth pattern in women or prepubescent children. The most common cause is familial, genetic, or idiopathic hirsutism, but on the USMLE watch for **polycystic ovary syndrome** (Stein-Leventhal syndrome), Cushing syndrome, and drugs (minoxidil, phenytoin, cyclosporine). These disorders do not produce virilization. If virilization (clitoral enlargement, deepening of the voice, temporal balding) accompanies the hirsutism, an androgen-secreting ovarian tumor (e.g., Sertoli-Leydig cell tumor, arrhenoblastoma) or adrenal source (congenital adrenal hyperplasia, Cushing syndrome, or adrenal tumor) is likely.

19. What causes virilization in children?

In female neonates, congenital adrenal hyperplasia is a likely cause of virilization. The classic example is a female infant born with ambiguous genitalia. However, the patient may also be a male child

with precocious puberty. At least 90% of cases are because of **21-hydroxylase deficiency.** Because 21-hydroxylase is involved in the production of both aldosterone and cortisol, children develop signs of hypoadrenalism, with salt-wasting, hypotension, hyperkalemia, hyponatremia, hypoglycemia, acidosis, and nausea and vomiting. Abnormally high levels of serum 17-hydroxyprogesterone or urinary 17-ketosteroids (dehydroepiandrosterone [DHEA], DHEA sulfate, and androsterone), along with decreased free cortisol in the serum, clinch the diagnosis. Give corticosteroids to prevent death. In older children, worry about a testosterone-secreting gonadal neoplasm.

20. What are the symptoms and signs of hyperparathyroidism?

The same as those for hypercalcemia ("bones, stones, groans, and psychiatric overtones"; see question 24). In primary cases, serum calcium is high, phosphorus is normal to low, and parathyroid hormone (PTH) is increased. In secondary cases, calcium is low.

21. What causes hyperparathyroidism?

Ninety percent of primary cases are caused by a parathyroid adenoma, which can usually be confirmed with a nuclear medicine scan (Fig. 10-1). Other causes include parathyroid hyperplasia and parathyroid carcinoma. Secondary cases include low calcium levels (e.g., from renal failure), to which an increase in PTH is a normal physiologic response. Tertiary hyperparathyroidism occurs when PTH has been elevated for too long (secondary to long-standing hypocalcemia) and continues to be oversecreted even when calcium is normalized with treatment. Translation: Put all patients with renal failure on calcium supplements to prevent this complication.

22. What are the signs and symptoms of hypoparathyroidism?

The same as those for hypocalcemia (tetany, prolonged QT interval on electrocardiogram [ECG]; see question 26). Calcium is low, phosphorus is high, and PTH is low.

23. What causes hypoparathyroidism?

The most common cause is accidental removal or damage during thyroid surgery. Watch for tetany after thyroid surgery. Rare causes are genetic. Watch for **DiGeorge syndrome** in children with congenital absence of parathyroid glands, tetany in the first 48 hours of life, absent thymus gland, immunodeficiency, cardiac anomalies, and midline facial defects.

24. What are the symptoms and signs of hypercalcemia?

Symptoms: "Bones, stones, groans, and psychiatric overtones." In other words: bone resorption with osteomalacia and osteitis fibrosa cystica; kidney stones; abdominal pain secondary to nausea and vomiting, ileus, nephrolithiasis, peptic ulcer disease, constipation, or pancreatitis

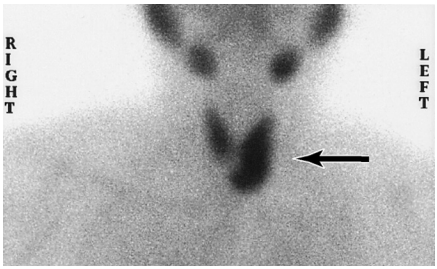

Figure 10-1. Parathyroid adenomas are almost always solitary lesions. This technetium-99m-sestamibi radionuclide scan demonstrates an area of increased uptake corresponding to the left inferior parathyroid gland *(arrow)*. This patient had a parathyroid adenoma. (From Kumar V, Abbas A, Fausto N. Robbins and Cotran: pathologic basis of disease. 7th ed. Philadelphia: Saunders, 2005, Fig. 24-24.)

(all increased with hypercalcemia); and emotional lability, delirium, depression, and/or psychosis.

Signs: Shortened QT interval on ECG, weakness, polyuria, bone changes and kidney stones on radiograph, and renal failure.

25. What causes hypercalcemia?

In outpatients, the most common cause is hyperparathyroidism. In hospitalized patients, the most common cause is malignancy. The first test to order is the PTH, which helps differentiate hyperparathyroidism (high PTH) from other causes of hypercalcemia such as malignancy, vitamin D intoxication, or thiazide diuretic use (low PTH). Multiple types of cancer can cause hypercalcemia, but the classic USMLE question involves either multiple myeloma or secretion of PTH-like hormone by a squamous cell carcinoma, especially in the lung. Familial hypocalciuric hypercalcemia is characterized by hypercalcemia with low calcium levels in the urine (in contrast to other hypercalcemias). Other causes include vitamin A or D intoxication, sarcoidosis or other granulomatous diseases, and excessive calcium intake (milk-alkali syndrome).

26. What are the symptoms and signs of hypocalcemia?

Symptoms: Paresthesias (the classic pattern is perioral or distal extremities), muscle aches, dementia, depression, and psychosis.

Signs: Prolonged QT interval on ECG, tetany, **Chvostek sign** (tetany elicited by tapping on the facial nerve to cause facial muscle contraction), **Trousseau sign** (carpopedal spasm caused by inflation of a blood pressure cuff or application of a tourniquet), dementia, depression, psychosis, seizures, and papilledema.

27. What causes hypocalcemia?

- Hypoparathyroidism (usually after thyroid gland surgery)
- Pseudohypoparathyroidism (genetic end-organ unresponsiveness to PTH with normal PTH levels, shortened metacarpal bones, short stature, and mental retardation)
- DiGeorge syndrome
- Vitamin D deficiency (osteomalacia, rickets)
- Renal failure of any cause and certain renal tubular problems
- Acute pancreatitis (one of the Ranson criteria)
- Secondary to hypomagnesemia

Hypoproteinemia of any cause may lead to low levels of total serum calcium, but levels of ionized calcium (the active form) are normal. In any patient with low serum calcium, the first step is to determine whether the serum albumin level is decreased. If it is, no treatment is required and no symptoms will develop.

28. What specific problems are caused by obesity?

Obesity causes an increase in overall mortality (at any age) and increases the risk for insulin resistance and diabetes, hypertension, hypertriglyceridemia, coronary artery disease, gallstones, sleep apnea and hypoventilation, osteoarthritis, thromboembolism, varicose veins, and cancer (especially endometrial cancer).

29. Define precocious puberty and pseudoprecocious puberty.

True precocious puberty is defined as activation of the hypothalamic-pituitary axis with sexual maturation before the age of 8 years in females and before the age of 9 years in males. In **pseudoprecocious puberty,** secondary sex characteristics develop prematurely because of high circulating levels of androgen or estrogen.

30. How is precocious puberty different from pseudoprecocious puberty?

True precocious puberty is usually idiopathic but can be caused by central nervous system (CNS) lesions. A general rule of thumb is that true precocious puberty causes testicular or ovarian enlargement, which

does not occur with pseudoprecocious puberty (ovarian cysts are not considered true ovarian enlargement). All patients with suspected precocious puberty should have a gonadotropin-releasing hormone (GnRH) stimulation test. If a dose of GnRH produces the typical pubertal response of increased follicle-stimulating hormone and luteinizing hormone, true precocious puberty is diagnosed. An MRI scan of the brain should be obtained to rule out CNS disease (e.g., hamartomas, tumors, cysts, trauma) as the cause.

31. What causes pseudoprecocious puberty?

Pseudoprecocious puberty may be caused by exogenous hormones, adrenal tumors, congenital adrenal hyperplasia (e.g., 21-hydroxylase deficiency), hormone-secreting tumors, or **McCune-Albright syndrome** in females (ovarian cysts, pseudoprecocious puberty, polyostotic fibrous dysplasia of bone, and café au lait spots) (Fig. 10-2; Plate 19).

32. How is precocious puberty treated?

Because premature puberty causes premature fusion of growth plates in the bone and can cause serious social problems for affected children, treatment is indicated. Treatment of any underlying disorders is indicated for pseudoprecocious puberty. For true idiopathic precocious puberty, treatment with long-acting GnRH agonists is indicated to suppress the pituitary-hypothalamic axis and to delay the onset of puberty until an appropriate age.

33. What is the difference between a primary and secondary endocrine disorder?

In **primary disorders**, the problem is in the gland; the hypothalamic-pituitary axis is functioning appropriately. In primary hypothyroidism, for example, the thyroid gland does not function properly for whatever reason, but the pituitary and hypothalamus respond appropriately. Therefore, thyroid hormone is low (as in all cases of hypothyroidism), but TSH and thyroid-releasing hormone (TRH) are high (the appropriate response from the pituitary and hypothalamus to low levels of thyroid hormone).

In **secondary disorders**, the true dysfunction is outside the gland itself. For example, in secondary hypothyroidism, thyroid hormone is low, but TSH and/or TRH is also low (inappropriate in the setting

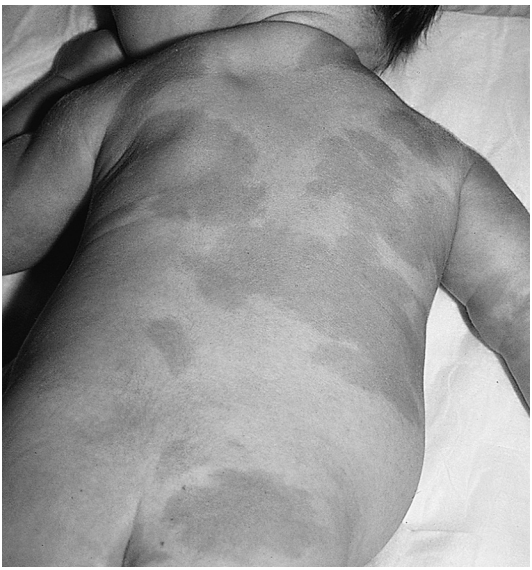

Figure 10-2. Multiple patterned café au lait spots in a child with McCune-Albright syndrome. See Plate 19. (From Eichenfield LF, Frieden IJ, Esterly NB. Neonatal Dermatology, 2nd ed. Philadelphia: Saunders, 2008, Fig. 22-3.)

of low thyroid hormone). If the pituitary is destroyed or surgically removed, secondary hypothyroidism results from low TSH; the thyroid gland functions well, but no TSH is available to stimulate it. To confuse the picture, the dysfunction also may be completely outside the endocrine axis (e.g., heart failure that causes secondary hyperaldosteronism).

This concept in endocrine gland dysfunction is quite important. Simple blood tests can localize the problem. You may be able to answer a USMLE question simply by reading through the various values for hormones and hormone-releasing factors and figuring out where in the hypothalamus-pituitary-target gland axis the problem lies.

34. What are the symptoms and signs of primary hyperaldosteronism (Conn syndrome)? What are the causes?

Symptoms: Weakness and edema.

Signs: Hypertension, hypokalemia, hypernatremia, and edema.

Conn syndrome is caused by an aldosterone-secreting adrenal neoplasm. Because it is a primary disease, renin levels are low; the rest of the endocrine axis responds appropriately to gland dysfunction. Order a CT scan of the abdomen to look for an adrenal mass. The treatment is surgical removal of the tumor.

35. What causes secondary hyperaldosteronism?

Secondary hyperaldosteronism is *much more common* than primary disease. It occurs because of low perfusion of the kidney, as in congestive heart failure, renal artery stenosis (bruit), dehydration, nephrotic syndrome, and cirrhosis. The key mechanism is that the kidney senses hypoperfusion and secretes renin; therefore, the renin level is high. Treatment of the underlying disorder (if possible) resolves the hyperaldosteronism. Potassium levels may be normal or even high. Of note, hyperkalemia may be the cause of increased aldosterone release just as hypocalcemia causes increased release of PTH. Both are normal physiologic responses.

36. Give the classic clinical description of a pheochromocytoma. How is it diagnosed?

Look for wild swings in blood pressure (with some measurements dangerously high), tachycardia, postural hypotension, headaches, sweating, flushing, dizziness, mental status changes, and/or a feeling of impending doom (like a panic attack). The screening test is a 24-hour urine collection for metanephrines, homovanillic acid, and/or vanillylmandelic acid (catecholamine breakdown products that are abnormally elevated in the urine). If levels are high, order an abdominal CT scan to look for an adrenal mass (Fig. 10-3). Surgical tumor removal is the treatment of choice after stabilization with alpha and then beta blockers.

37. Define diabetes insipidus (DI). What are the two types?

DI is a lack of antidiuretic hormone (ADH), or vasopressin, effect in the body. Patients with DI secrete inappropriately dilute urine because of the lack of ADH effect and may urinate up to 25 L of urine per day, resulting in dehydration and hypernatremia. Such patients die rapidly if they are unable to drink water. Normally, when the body is dehydrated, ADH causes urine to become highly concentrated through retention of free water. In DI, the urine remains dilute even though the serum osmolarity is quite high as a result of dehydration. The two types are **central** and **nephrogenic.**

38. What causes central DI?

Central DI is caused by a lack of ADH production by the posterior pituitary. Although it is often idiopathic, look for trauma, neoplasm, or sarcoid/granulomatous disease as the cause. Order a CT or MRI scan of the head, if indicated.

39. What causes nephrogenic DI?

Nephrogenic DI is caused by kidney unresponsiveness to ADH. Look for medications (e.g., lithium, demeclocycline) as the cause.

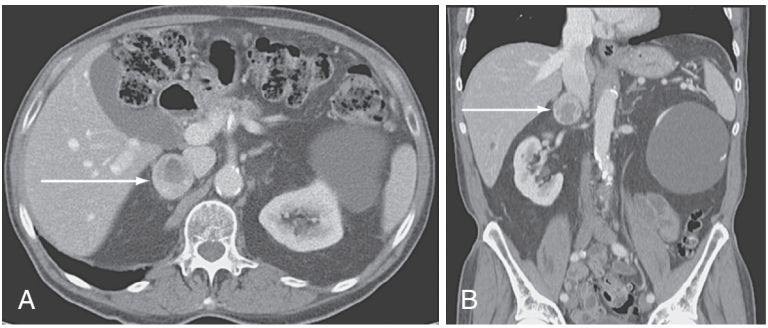

Figure 10-3. A computed tomographic (CT) scan of the abdomen with intravenous contrast agent of a 71-year-old man with an incidentally discovered right adrenal mass. The fractionated plasma free metanephrines were abnormal. **A,** The axial CT image shows a typical 3.8-cm heterogeneously enhancing right adrenal mass just lateral to the inferior vena cava and consistent with pheochromocytoma (*arrow*). **B,** Coronal view shows the location (*arrow*) of the mass superior to the right kidney and inferior and medial to the liver. After alpha- and beta-adrenergic blockade, a pheochromocytoma was removed laparoscopically. (From Kronenberg H, et al. Williams textbook of endocrinology. 11th ed. Philadelphia: Saunders, 2008, Fig. 15-3.)

40. What diagnostic test can reveal whether DI is central or nephrogenic? How are these conditions treated?

Give the patient a dose of ADH, and measure urine osmolarity. If central DI is the cause, urine osmolarity increases with ADH challenge. In nephrogenic DI, the urine remains inappropriately dilute after the patient is given ADH. Treatment for central DI is ADH replacement (given orally or as a nasal spray). Treatment for nephrogenic DI involves stopping any offending drug and giving a thiazide diuretic; ADH does not help. Although giving a diuretic to a patient with DI seems counterintuitive, it has the paradoxical effect of decreasing urine output.

41. Define the syndrome of inappropriate antidiuretic hormone secretion (SIADH). How is it diagnosed?

The name says it all: ADH is released inappropriately. SIADH is a consideration in patients with hyponatremia and normal volume status (euvolemic). In SIADH, serum osmolarity is low, but urine osmolarity is high (inappropriate urine concentration). Look for the values of all electrolytes and lab tests to be low (the classic example is uric acid) because of dilution of the serum with free water secondary to inappropriate ADH.

42. What causes SIADH?

Central nervous system causes: Stroke, hemorrhage, infection, trauma.

Medications: Narcotics, oxytocin (in pregnant patients), chlorpropamide, antiepileptic agents.

Trauma: Pain is a powerful stimulus for ADH. Watch for the postoperative patient who is receiving fluids (and often narcotics) and has pain.

Lung problems: Simple pneumonia or ADH-secreting small cell cancer of the lung.

43. How is SIADH treated?

Treat with water restriction. Stop intravenous fluids and restrict oral fluid intake. For Step 2 purposes, do not give hypertonic saline unless the patient has active seizures. You may cause brainstem damage or central pontine myelinolysis from too rapid correction of sodium level. **Demeclocycline** is sometimes used to treat SIADH if water restriction fails because it induces nephrogenic DI, which allows the patient to eliminate free water.

ETHICS

1. **True or false: Adult patients of sound mind are allowed to refuse life-saving treatments.**
   True. You should not force blood products, antibiotics, or any other treatments on a patient who does not want them.

2. **What should you do if a child has a life-threatening condition and the parents refuse a simple, curative treatment (e.g., antibiotics for meningitis)?**
   First try to persuade the parents to change their mind; if this fails, attempt get a court order to give the treatment. Do not treat until you have talked to the courts unless it is an emergency. Even with Jehovah's witnesses who do not want their children to receive a blood transfusion, you should seek the court's assistance in getting the transfusion if it is the only treatment option available.

3. **True or false: People with terminal illnesses can choose to die.**
   True. This is the rationale behind hospice care. Let competent people die if they want to do so. Do not commit active euthanasia, but respect a patient's wishes for passive euthanasia.

4. **What is the difference between active and passive euthanasia?**
   Active euthanasia is the intentional hastening of death, whereas passive euthanasia is withholding treatments and "letting nature take its course."

5. **With whom can you discuss your patient's condition?**
   Only with people who need to know because they are directly involved in the patient's care and with people authorized by the patient (e.g., authorized family members). Do not tell a medical colleague who is uninvolved with the patient's care how that patient is doing, even if the colleague is a friend of yours or the patient.

6. **In what situations are you allowed to breach patient confidentiality?**
   Break confidentiality only in the following situations:
   - The patient asks you to do so.
   - Child abuse is suspected.
   - The courts mandate you to do so.
   - You must fulfill the duty to warn or protect (if a patient says that he is going to kill someone or himself, you have to tell someone, the authorities, or both).
   - The patient has a reportable disease.
   - The patient is a danger to others (e.g., if a patient is blind or has seizures, let the proper authorities know so that they can revoke the patient's license to drive; if the patient is an airplane pilot and is paranoid, hallucinates, and suffers from schizophrenia, then authorities need to know).

7. **What are the components of informed consent?**
   Informed consent involves giving the patient information about the following:
   - Diagnosis (his or her condition and what it means).
   - Prognosis (the natural course of the condition without treatment).

- Proposed treatment (description of the procedure and what the patient will experience).
- Risks and benefits of the treatment.
- Alternative treatments.

The patient then must be allowed to make his or her own choice. The documents seen on the wards that patients are made to sign are not technically required or sufficient for informed consent. They are used for medicolegal purposes (i.e., lawsuit paranoia).

8. What should you do if a patient is incompetent to make decisions?

Get the family and/or courts to appoint a guardian (surrogate decision maker or health care power of attorney).

9. True or false: A living will should not be respected if the next of kin asks you not to follow it.

False. Such situations are tricky, but technically (and for the USMLE) living wills or patient-mandated "do-not-resuscitate" orders should be respected and followed if properly documented. The classic question involves a patient who says in a living will that if he or she is unable to breathe independently, a ventilator should not be used. Do not put the patient on a ventilator, even if the husband, wife, son, or daughter tells you to do so.

10. What should you do if a patient is in critical condition or in a coma and has made no advance directive or living will?

The wishes of the family, next of kin, or health care power of attorney should be followed. In cases of disagreement among family members, suspicion of ulterior motives, or uncertainty, involve the hospital's ethics committee. As a last resort, go to the courts for help.

11. What about depression in the context of end-of-life decisions?

Depression always should be evaluated as a reason for "incompetence." Patients who are suicidal may refuse all treatment, but their refusal should not be respected until the depression is treated.

12. True or false: In some circumstances, patients can be hospitalized against their will.

True. Psychiatric patients frequently are hospitalized against their will if they are deemed to be a danger to themselves or others. Patients can be held only for a limited time (1 to 3 days) before they must have a hearing before a court official to determine whether they must remain in custody. These decisions are based on the principle of **beneficence** (the principle of doing good for the patient and avoiding harm).

13. True or false: Restraints can be used on patients against their will.

True. Restraints can be used on an incompetent or violent (e.g., delirious, psychotic) patient if needed, but their use should be brief and reevaluated often (at least once every 24 hours). Be aware that the use of restraints in delirious or demented patients rarely helps prevent falls and may cause injury.

14. When do patients younger than 18 years of age not require parental consent for a medical decision?

In general, people younger than 18 years of age do not require parental consent if they are emancipated (married, living on their own and financially independent, raising children, or serving in the armed forces); have a sexually transmitted disease, want contraception, or are pregnant; want illicit drug treatment or counseling; or have psychiatric illness. Some states have exceptions to these rules, but for Step 2 purposes in such situations, let minors make their own decisions.

15. What should you do if a child has a medical emergency and the parents are unavailable for decision making?

Treat the child as you see fit; that is, act in the child's best interest.

16. True or false: It is acceptable to hide a diagnosis from a patient if the family asks you to do so.

False. Do not hide a diagnosis from a patient (including a child) if the patient wants to know (even if the family asks you to do so). Do not lie to any patient because the family asks you to do so. Conversely, you should not force patients to receive information against their will; if they do not want to know the diagnosis, do not tell them.

17. What should you do if a patient requires emergency care but the patient cannot communicate and no family members are available?

Treat the patient as you see fit unless you know that the patient wishes otherwise.

18. True or false: Withdrawing care and withholding care are the same in the eyes of the law.

True. It is important to communicate this principle to family members who feel guilty. The simple fact that a patient is on a respirator does not mean that you cannot turn the respirator off.

19. True or false: In terminally ill, noncurable patients, one of the primary goals is to relieve pain.

True. Opioids are commonly used, even though they may cause respiratory depression. It is more important to make patients comfortable and pain-free than to worry about respiratory depression in this setting.

CHAPTER 12

GASTROENTEROLOGY

1. Define gastroesophageal reflux disease (GERD). What causes it?

GERD means that stomach acid refluxes into the esophagus. It is caused by inappropriate, intermittent relaxation of the lower esophageal sphincter. The incidence is increased greatly in patients with a hiatal hernia (see question 4).

2. Describe the classic symptoms of GERD. How is it treated?

The main complaint is usually "heartburn," often related to eating and lying supine. GERD may also cause abdominal or chest pain. Initial treatment is to elevate the head of the bed and to avoid coffee, alcohol, tobacco, spicy and fatty foods, chocolate, and medications with anticholinergic properties. If this approach fails, antacids, histamine-2 blockers, and proton-pump inhibitors may be tried. Many patients have already tried over-the-counter remedies, and many physicians begin empirical treatment at the first visit because "lifestyle modifications" usually fail. Surgery (Nissen fundoplication) is reserved for severe or resistant cases.

3. What are the sequelae of GERD?

Sequelae of GERD include esophagitis, esophageal stricture (which may mimic esophageal cancer), esophageal ulcer, hemorrhage, Barrett esophagus, and esophageal adenocarcinoma (Fig. 12-1).

4. What is a hiatal hernia? How is it different from a paraesophageal hernia?

A hiatal hernia is a sliding hernia, which means that the whole gastroesophageal junction moves above the diaphragm, pulling the stomach with it. This common and benign finding may predispose to GERD. In a paraesophageal hernia, the gastroesophageal junction stays below the diaphragm, but the stomach herniates through the diaphragm into the thorax. This type of hernia is uncommon but serious; it may become strangulated and should be repaired surgically.

5. What are the signs of peptic ulcer disease (PUD)?

The classic symptoms of PUD are chronic, intermittent, epigastric pain (burning, gnawing, or aching) that is localized and often relieved by antacids or milk. Look for epigastric tenderness. Other signs and symptoms include occult blood in the stool and nausea or vomiting. PUD is more common in men. The two types of PUD are gastric and duodenal ulcers.

6. Explain the classic differences between duodenal and gastric ulcers.

	DUODENAL	GASTRIC
% of cases	75	25
Acid secretion	Normal to high	Normal to low
Main cause	*Helicobacter pylori*	Use of nonsteroidal antiinflammatory drugs (NSAIDs), including aspirin
Peak age	40s	50s
Blood type	O	A
Eating food	Pain gets better, then worse 2-3 hours later	Pain not relieved or made worse

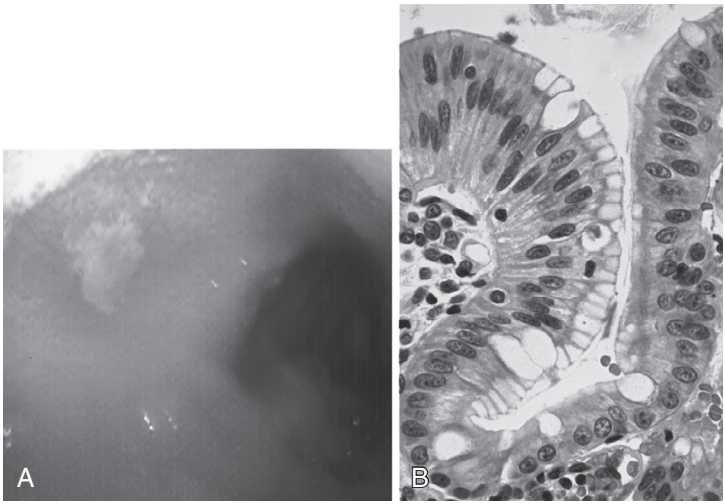

Figure 12-1. Barrett esophagus is defined by both endoscopic and histologic components. Endoscopically there must be visible pink columnar epithelium within the tubular esophagus **(A)** that histologically has intestinalized metaplastic columnar epithelium defined by the presence of true goblet cells (**B,** *arrows*) on hematoxylin and eosin staining. Barrett esophagus should not be diagnosed unless both components are present. (From Patterson GA. Pearson's thoracic and esophageal surgery. 3rd ed. Philadelphia: Churchill Livingstone, 2008, Fig. 36-2).

7. What is the diagnostic study of choice for PUD?

The gold standard is endoscopy (most sensitive test), but an upper gastrointestinal (GI) barium study is cheaper and less invasive. Empirical treatment with medications may be tried in the absence of diagnostic studies if the symptoms are typical. If endoscopy is done, a biopsy of any gastric ulcer is mandatory to exclude malignancy. Duodenal ulcers do not have to be biopsied initially because malignancy is rare.

8. What is the most feared complication of PUD? What should you suspect if an ulcer does not respond to treatment?

The most feared complication of PUD is **perforation.** Look for peritoneal signs, history of PUD, and free air on an abdominal radiograph (Fig. 12-2). Treat with antibiotics (e.g., ceftriaxone, metronidazole) and laparotomy with repair of the perforation. If ulcers are severe, atypical (e.g., located in the jejunum), or nonhealing, think about stomach cancer or Zollinger-Ellison syndrome (gastrinoma; check gastrin level). PUD is also a cause of GI bleeding, which can be severe in some cases.

9. How is PUD treated initially?

First, remember that diet changes are not thought to help heal ulcers, although reduced alcohol and tobacco use may speed healing. Stop all NSAID use. Start treatment with proton-pump inhibitors, test for *Helicobacter pylori* infection, and treat with antibiotics if positive. Many regimens exist, but the most commonly used is triple therapy with a proton-pump inhibitor, clarithromycin, and amoxicillin.

10. List the surgical options for ulcer treatment. What complications may occur?

Surgical options generally are considered only if medical treatment has failed or if complications are present (perforation, bleeding). Surgical procedures for PUD include antrectomy, vagotomy, and Billroth I or II procedures. After surgery (especially with Billroth procedures) watch for dumping

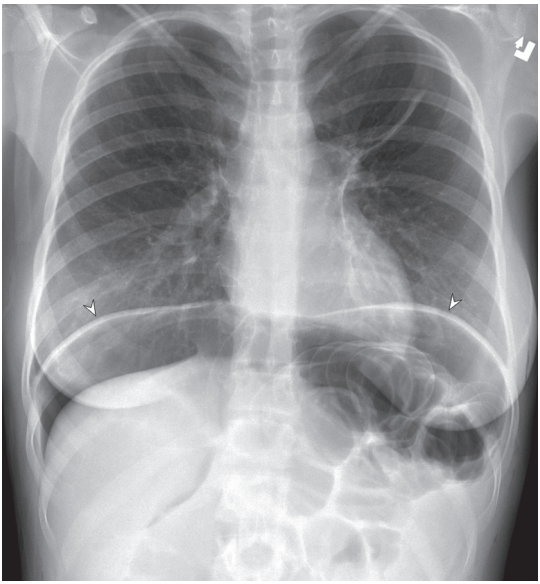

Figure 12-2. Pneumoperitoneum from bowel perforation on conventional radiographs. Upright radiograph shows the large amount of free intraperitoneal air (lucent area just inferior to the diaphragm). (From Goldman. Goldman's Cecil medicine. 24th ed. Philadelphia: Saunders, 2011, Fig. 135-1.)

syndrome (weakness, dizziness, sweating, and nausea or vomiting after eating). Patients also develop hypoglycemia 2 to 3 hours after a meal, which causes recurrence of the same symptoms, as well as afferent loop syndrome (bilious vomiting after a meal relieves abdominal pain), bacterial overgrowth, and vitamin deficiencies (vitamin B_{12} and/or iron, causing anemia).

11. Define achlorhydria. What causes it?

Achlorhydria is an absence of hydrochloric acid (HCl) secretion. It is caused most commonly by **pernicious anemia,** in which antiparietal cell antibodies destroy acid-secreting parietal cells and thus cause achlorhydria and vitamin B_{12} deficiency. It often is associated with other endocrine autoimmune disorders (e.g., hypothyroidism, vitiligo, diabetes, hypoadrenalism). Achlorhydria also may be caused by surgical gastric resection.

12. What are the classic differences between upper and lower GI bleeds?

	UPPER GI BLEED	LOWER GI BLEED
Location	Proximal to ligament of Treitz	Distal to ligament of Treitz
Common causes	Gastritis, ulcers, varices, esophagitis	Vascular ectasia, diverticulosis, colon cancer (Fig. 12-3; Plate 20), colitis, inflammatory bowel disease, hemorrhoids
Stool	Tarry, black stool (melena)	Bright red blood seen in stool (hematochezia)
NGT aspirate	Positive for blood	Negative for blood

GI, Gastrointestinal; *NGT*, nasogastric tube.

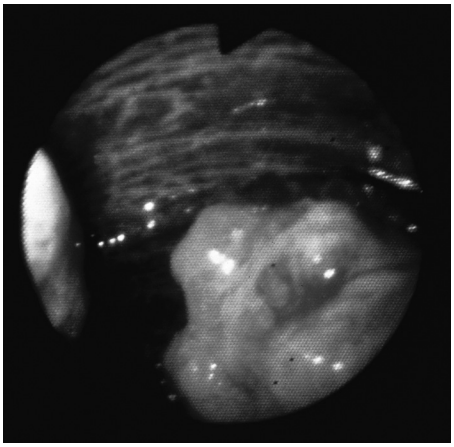

Figure 12-3. Colonoscopic photograph of a pale colon cancer easily seen against the dark background of pseudomelanosis coli. See Plate 20. (From Feldman M, Friedman LS, Brandt LJ, eds. Sleisenger and Fordtran's gastrointestinal and liver disease. 9th ed. Philadelphia: Saunders, 2010, Fig. 124-8. Courtesy Juergen Nord, MD, Tampa, Fla.).

13. How is a GI bleed treated?

The first step is to *make sure that the patient is stable* (ABCs [airways, breathing, circulation]); intravenous fluids and blood, if needed, before you try to reach a diagnosis. Next, place a nasogastric tube, and test the aspirate for blood to help determine whether the patient has an upper or lower GI bleed. **Endoscopy** is usually the first test performed (upper or lower, depending on symptoms and nasogastric tube aspirate). Endoscopically treatable lesions include ulcers, polyps, vascular ectasias, and varices.

14. What radiologic imaging studies can be done to localize a GI bleed? Does surgery have a role?

Radionuclide (i.e., nuclear medicine) scans can detect slow or intermittent bleeds if a source cannot be found with endoscopy. Angiography can detect more rapid bleeds, and embolization of bleeding vessels can be done during the procedure. Surgery is reserved for severe or resistant bleeds and typically involves resection of the affected bowel (usually colon).

15. Define diverticulosis. What are its complications?

Diverticulosis is characterized by saclike mucosal projections through the muscular layer of the colon and/or rectum. It is extremely common, and the incidence increases with age. It is thought to be caused in part by a low-fiber, high-fat diet. Complications include GI bleeding (common cause of painless lower GI bleeds) and diverticulitis (inflammation of a diverticulum), which can lead to abscess, fistula formation, sepsis, or large bowel obstruction.

16. How do you diagnose and treat diverticulitis? What test should a patient have after a treated episode of diverticulitis?

Signs and symptoms of diverticulitis include left lower quadrant pain or tenderness, fever, diarrhea or constipation, and increased white blood cell count. The pathophysiology is thought to be similar to appendicitis. Stool or other debris impacts within the diverticulum and causes obstruction, leading to bacterial overgrowth and inflammation. The diagnosis can be confirmed with a computed tomography (CT) scan (Fig. 12-4), if needed, which can also help rule out complications such as perforation or abscess. In the absence of complications, the treatment is antibiotics that cover bowel

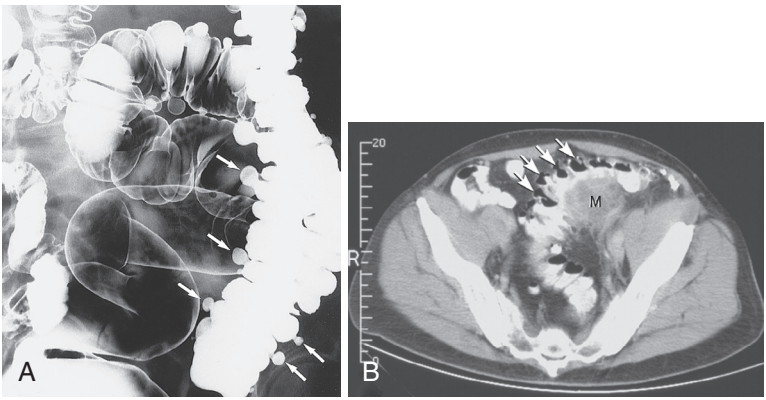

Figure 12-4. Diverticulosis of the colon is seen on this oblique view of the sigmoid colon **(A)** during a double-contrast barium enema showing multiple outpouchings *(arrows)* that represent diverticula. Diverticula also can be seen in a computed tomography scan **(B)** as outpouchings *(arrows),* but a developing focal inflammatory mass (M) also is compatible with a developing abscess. (From Mettler FA Jr. Essentials of radiology. 2nd ed. Philadelphia: Saunders, 2005, Fig. 6-73.)

flora (e.g., a fluoroquinolone plus metronidazole) and bowel rest (i.e., no oral intake). Surgery is needed for perforation or abscess.

After a treated episode of diverticulitis, all patients need colon cancer screening with colonoscopy (colon carcinoma with perforation can mimic diverticulitis clinically and on CT). These studies should be avoided during active diverticulitis, however, because of an increased risk for perforation.

17. How is diarrhea categorized according to etiology?

- Systemic. Any illness can cause diarrhea as a systemic symptom, especially in children (e.g., infection).
- Osmotic
- Secretory
- Malabsorptive
- Infectious
- Exudative
- Altered intestinal transit

18. Define osmotic diarrhea. How can an easy diagnosis be made?

Osmotic diarrhea is caused by nonabsorbable solutes that remain in the bowel, where they retain water (e.g., lactose or other sugar intolerance). When the patient stops ingesting the offending substance (e.g., avoidance of milk, a trial of not eating), the diarrhea stops—an easy diagnosis.

19. What causes secretory diarrhea?

Secretory diarrhea results when the bowel secretes too much fluid. It is often caused by bacterial toxins (cholera, some species of *Escherichia coli*), VIPoma (pancreatic islet cell tumor that secretes vasoactive intestinal peptide), or bile acids (after ileal resection). Secretory diarrhea continues when the patient stops eating.

20. What are the common causes of malabsorptive diarrhea?

Celiac disease (look for dermatitis herpetiformis, and avoid gluten in the diet; Fig. 12-5; Plate 21), Crohn disease, and postgastroenteritis (because of depletion of brush-border enzymes). Malabsorptive diarrhea improves when the patient stops eating.

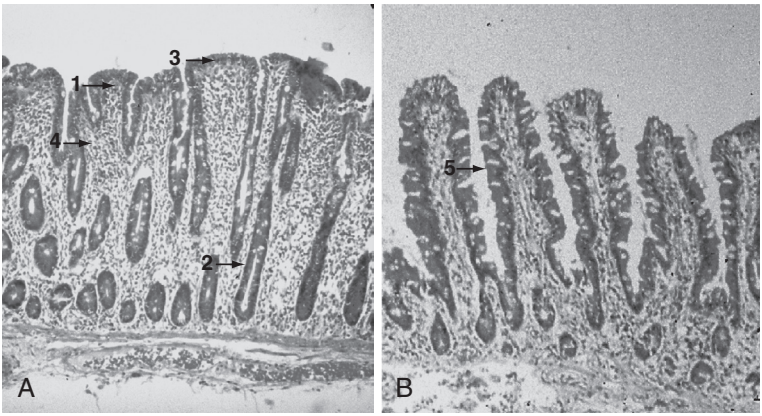

Figure 12-5. Mucosal pathology in celiac disease. **A,** Duodenal biopsy specimen of a patient with untreated celiac disease. The histologic features of severe villus atrophy *(arrow 1)*, crypt hyperplasia *(arrow 2)*, enterocyte disarray *(arrow 3)*, and intense inflammation of the lamina propria and epithelial cell layer *(arrow 4)* are evident. **B,** Repeat duodenal biopsy after 6 months on a strict gluten-free diet. There is marked improvement, with well formed villi *(arrow 5)* and a return of the mucosal architecture toward normal. See Plate 21. (From Feldman M, Friedman LS, Brandt LJ. Sleisenger and Fordtran's gastrointestinal and liver disease. 9th ed. Philadelphia: Saunders, 2010, Fig. 104-2.)

21. What are the common clues to infectious diarrhea? What are the common causes?

In patients with infectious diarrhea, look for fever and white blood cells in the stool (only with invasive bacteria such as *Shigella, Salmonella, Yersinia,* and *Campylobacter* spp.; not found with toxigenic bacteria). Travel history (Montezuma's revenge caused by *E. coli*) is also a tip-off. Hikers and stream-drinkers may have *Giardia* infection, which includes steatorrhea (fatty, greasy, malodorous stools that float) because of small bowel involvement and unique protozoal cysts in the stool. Treat with metronidazole. Also watch for *Clostridium difficile* diarrhea in patients with a history of antibiotic use. Test the stool for *C. difficile* toxin, and if the result is positive, treat with oral metronidazole (vancomycin is a second-line agent if metronidazole is not an option).

22. What causes exudative diarrhea?

Exudative diarrhea results from inflammation in the bowel mucosa that causes seepage of fluid. Mucosal inflammation is usually because of inflammatory bowel disease (Crohn disease or ulcerative colitis; see question 27) or cancer. Patients commonly have fever and white blood cells in the stool, as in infectious diarrhea, but a lack of pathogenic organisms, chronicity, and nonbowel symptoms are clues.

23. What are the common causes of diarrhea caused by altered intestinal transit?

This type of diarrhea is seen after bowel resections, in patients taking medications that interfere with bowel function, and in patients with hyperthyroidism or neuropathy (e.g., diabetic diarrhea). Watch for factitious diarrhea, which is caused by secret laxative abuse.

24. Define irritable bowel syndrome. How do you recognize it?

Irritable bowel syndrome is a common cause of GI complaints. Patients may be anxious or neurotic and have a history of diarrhea aggravated by stress; bloating; abdominal pain relieved by defecation; and/or mucus in the stool. Look for psychosocial stressors in the history and normal physical findings

and test results. Irritable bowel syndrome is a diagnosis of exclusion; you must do at least basic lab tests, rectal examination, stool examination, and sigmoidoscopy. Because it is so common, however, it is the most likely diagnosis if the question gives no positive findings, especially in young adults (female-to-male ratio = 3:1).

25. What should you do if a patient has diarrhea?

In all patients with diarrhea, watch for and treat dehydration and electrolyte disturbances, especially metabolic acidosis and hypokalemia. Diarrhea is a common and preventable cause of death in underdeveloped countries. Do a rectal examination, look for occult blood in stool, and examine the stool for bacteria (Gram stain and culture), ova and parasites, fat content (steatorrhea), and white blood cells.

26. What should you watch for in children after a bout of diarrhea?

After bacterial (especially *E. coli* or *Shigella* sp.) diarrhea in children, watch for **hemolytic uremic syndrome,** which is characterized by thrombocytopenia, hemolytic anemia (schistocytes, helmet cells, and fragmented red blood cells on peripheral blood smear), and acute renal failure. Treatment is supportive. Patients may need dialysis and/or transfusions.

27. Specify the classic differences between Crohn disease and ulcerative colitis.

	CROHN DISEASE	ULCERATIVE COLITIS
Place of origin	Distal ileum, proximal colon	Rectum
Thickness of pathology	Transmural	Mucosa/submucosa only
Progression	Irregular (skip lesions)	Proximal, continuous from rectum; no skipped areas
Location	From mouth to anus	Involves only colon, rarely extends to ileum
Bowel habit changes	Obstruction, abdominal pain	Bloody diarrhea
Classic lesions	Fistulas/abscesses, cobblestoning, string sign on barium x-ray (Fig. 12-6)	Pseudopolyps, lead-pipe colon on barium x-ray (Fig. 12-7), toxic megacolon
Colon cancer risk	Slightly increased	Markedly increased
Surgery	No (may make worse)	Yes (proctocolectomy with ileoanal anastomosis)

28. Describe the extraintestinal manifestations of inflammatory bowel disease.

Both forms of inflammatory bowel disease can cause uveitis, arthritis, ankylosing spondylitis, erythema nodosum, erythema multiforme, primary sclerosing cholangitis, failure to thrive or grow in children, toxic megacolon, anemia of chronic disease, and fever. Toxic megacolon is more common in ulcerative colitis; look for a markedly distended colon on abdominal radiograph.

29. How is inflammatory bowel disease treated?

Patients are treated with 5-aminosalicylic acid, with or without a sulfa drug (e.g., sulfasalazine), when stable. Steroids and other immune modulators (e.g., azathioprine) are used during severe disease flare-ups.

30. What causes toxic megacolon? How is it treated?

Toxic megacolon is classically seen with inflammatory bowel disease (especially ulcerative colitis) and infectious (especially *C. difficile*) colitis. It may be precipitated by the use of antidiarrheal medications, which for this reason are usually not given for infectious diarrhea. Most patients have a high fever, leukocytosis, abdominal pain, rebound tenderness, and a dilated segment of colon on

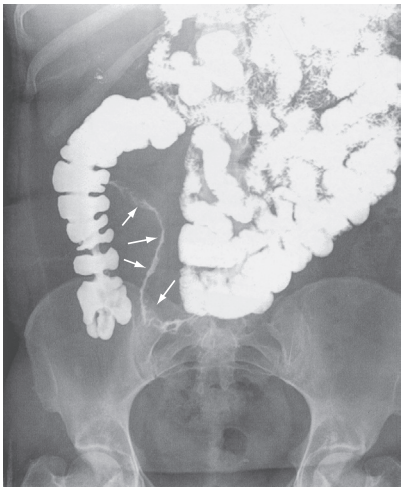

Figure 12-6. Small bowel follow through in a patient with Crohn disease that demonstrates a string sign in the right lower quadrant. The classic radiologic string sign *(arrows)* of a markedly narrowed bowel segment amidst widely spaced bowel loops is a result of spasm and edema associated with active inflammation. (From Feldman M, Friedman LS, Brandt LJ. Sleisenger and Fordtran's gastrointestinal and liver disease. 9th ed. Philadelphia: Saunders, 2010, Fig. 111-4. Courtesy of Dr. Jack Wittenberg, Boston, Mass.)

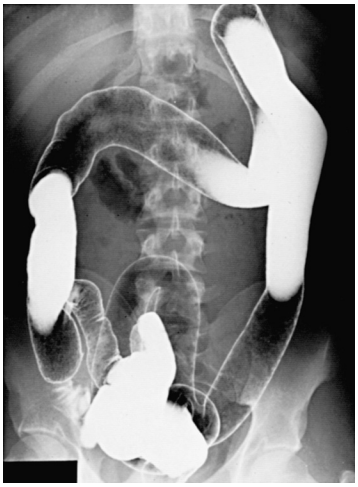

Figure 12-7. A double-contrast barium enema in a patient with longstanding ulcerative colitis demonstrates a marked loss of haustration. The terminal ileum is normal. (From Feldman M, Friedman LS, Brandt LJ. Sleisenger and Fordtran's gastrointestinal and liver disease. 8th ed. Philadelphia: Saunders, 2006, Fig. 109-9.)

abdominal radiograph. Toxic megacolon is an emergency. Start treatment by discontinuing all antidiarrheal medications. Do not allow the patient to eat, place a nasogastric tube, start intravenous fluids, and give antibiotics to cover bowel flora (e.g., ceftriaxone plus metronidazole) as well as steroids if the cause is inflammatory bowel disease. Surgery is required if perforation occurs (free air is seen on abdominal radiograph).

31. List the common findings of acute liver disease.

- Elevated liver function tests (aspartate aminotransferase [AST], alanine aminotransferase [ALT], bilirubin, alkaline phosphatase, and/or prothrombin time [PT] and international normalized ratio)
- Jaundice
- Nausea and vomiting
- Right upper quadrant pain or tenderness
- Hepatomegaly

32. List the common causes of acute liver disease.

- Alcohol
- Medications
- Infection (usually hepatitis)
- Reye syndrome
- Biliary tract disease
- Autoimmune disease

33. What is the classic abnormality on liver function tests in patients with alcoholic hepatitis?

An elevated AST that is more than twice the value of ALT, although both may be elevated.

34. What clues suggest hepatitis A? Describe the diagnostic serology.

Look for outbreaks from a foodborne source. There are no long-term sequelae of infection, although acute liver failure is a remote possibility. IgM anti-hepatitis A virus (HAV) is positive during jaundice or shortly thereafter. The incubation period for hepatitis A is about 4 weeks, although IgM may be detected by the time symptoms begin.

35. How is hepatitis B acquired? What is the best treatment?

Hepatitis B is acquired perinatally, by sexual transmission, or from contaminated needles. Transfused blood is now screened for hepatitis B, but risk of transmission is still about 1/200,000 according to the American Red Cross. A history of transfusion years ago is still a risk factor (screening by blood banks began in 1972 in the United States). Prevention is the best treatment (vaccination). Interferon alfa-2b, peginterferon alfa-2a, adefovir, dipivoxil, entecavir, telbivudine, or tenofovir can be tried in patients with chronic hepatitis and elevated liver enzymes.

36. Describe the serology of hepatitis B infection, including the surface, core, and "e" markers.

The hepatitis B surface antigen (HBsAg) is positive with any unresolved infection (acute or chronic). The hepatitis B "e" antigen (HBeAg) is a marker for infectivity; patients with the hepatitis B "e" antibody (HBeAb) have a low likelihood of spreading disease. The first antibody to appear is the IgM hepatitis B core antibody (HBcAb), which appears during the "window phase" when both HBsAg and hepatitis B surface antibody (HBsAb) are negative. Positive HBsAb means that the patient is immune (as a result of either recovery from infection or vaccination); HBsAb never appears if the patient has chronic hepatitis.

Make sure you know and understand Table 12-1. It is high yield.

37. What are the possible sequelae of chronic hepatitis B or C?

Cirrhosis and hepatocellular cancer (only with chronic, not acute, infection).

TABLE 12–1. SEROLOGIC MARKERS AT DIFFERENT STAGES OF DISEASE

	HBsAg	HBeAg	HBeAb	HBsAb	HBcAb
Incubation	+	+	-	-	-
Acute stage	+	+	-	-	+
Persistent carrier	+	±	±	-	+
Recovery (immune)	-	-	+	+	+
Immunization	-	-	-	+	-

The presence of HBeAg and antiHBe depends on degree of infectivity.
Adapted from Cohen J, Powderly WG, Berkley SF, et al. Infectious diseases, 2nd ed. Edinburgh: Mosby, 2004, p. 2015, with permission.

38. What should be given to persons acutely exposed to hepatitis B?

Hepatitis B immunoglobulin and hepatitis B vaccination or hepatitis B vaccination alone have been demonstrated to be effective in preventing transmission after exposure to hepatitis B virus.

39. Which type of viral hepatitis is the new king of chronic hepatitis?

Hepatitis C. The hepatitis C virus is the most likely cause of hepatitis after a blood transfusion. Although blood is now screened for hepatitis B and C, the hepatitis C test was developed later (screening in the United States began in 1972 for hepatitis B and 1992 for hepatitis C). Hepatitis C also is more likely than hepatitis B to progress to chronic hepatitis, cirrhosis, and cancer. Because of the relatively high prevalence in the "baby boomer" generation and lack of symptoms, the Centers for Disease Control and Prevention has recommended that all Americans born between 1945 and 1965 have a one-time screening test for hepatitis C.

40. Describe the serology and treatment for hepatitis C.

A positive hepatitis C antibody means that the patient has had an infection in the past, but does not mean the infection has been cleared. Many patients become chronic carriers of the virus. A test for hepatitis C virus RNA is available to detect and quantify the virus. Treatment is with pegylated interferon alfa and ribavirin (plus a protease inhibitor for those with genotype 1). Success rates depend on the type of infection. Genotype 1 is the most common in the United States, but treatment success rates are higher with genotypes 2 and 3.

41. When is hepatitis D seen? Describe the serology.

Hepatitis D is seen only in patients with hepatitis B. It may become chronic (with hepatitis B coinfection) and is acquired in the same ways as hepatitis B. IgM antibodies to the hepatitis D antigen demonstrate resolution of recent infection. Presence of the hepatitis D antigen, hepatitis D virus RNA, and high levels of IgM antibodies to hepatitis D indicates chronicity.

42. How is hepatitis E transmitted? What is special about the infection in pregnant women?

Hepatitis E is transmitted like hepatitis A (via food and water; no chronic state). It is often fatal in pregnant women (for unknown reasons).

43. What are the classic causes of drug-induced hepatitis?

Acetaminophen, isoniazid and other tuberculosis drugs (e.g., rifampin, pyrazinamide), halothane, HMG CoA-reductase inhibitors, and carbon tetrachloride. The first step in treatment is to stop the drug.

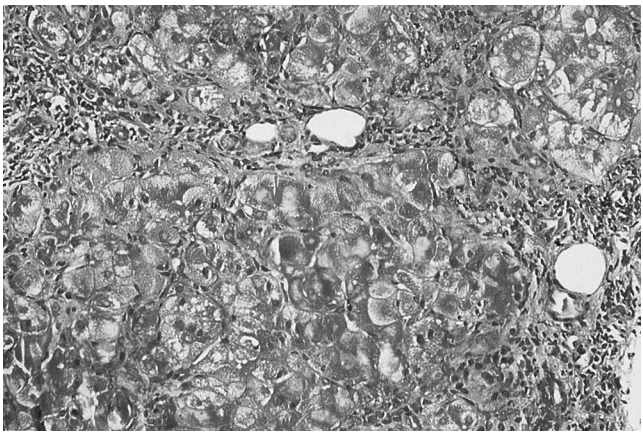

Figure 12-8. Chronic viral hepatitis. Portal-portal bridging fibrosis is seen in longstanding chronic hepatitis C. See Plate 22. (From Odze RD, Goldblum JR. Surgical pathology of the GI tract, liver, biliary tract, and pancreas. 2nd ed. Saunders, 2009, Fig. 38-10.)

44. When should you suspect idiopathic autoimmune hepatitis? What is the serologic marker?

Idiopathic autoimmune hepatitis is classically seen in 20- to 40-year-old women with antismooth muscle or antinuclear antibodies and no risk factors or lab markers for other causes of hepatitis. Treat with steroids.

45. What are the usual causes of chronic liver disease?

Alcohol, hepatitis, and metabolic diseases. Watch for the stigmata of chronic liver disease: gynecomastia, testicular atrophy, palmar erythema, spider angiomas on skin, and ascites.

46. Which species of viral hepatitis can lead to chronic liver disease?

Hepatitis B, C, and D. Hepatitis D can cause infection only in the setting of coexisting hepatitis B (Fig. 12-8; Plate 22).

47. Define hemochromatosis. How do you recognize it?

Hemochromatosis, in its primary form, is usually autosomal recessive; look for a family history. Nearly 1 in 250 people in the United States are homozygous for this condition, although penetrance and clinical expression are variable. The pathophysiology is incompletely understood but includes excessive iron absorption by the intestine. Excessive iron is deposited in the liver (potentially causing cirrhosis and/or hepatocellular carcinoma), pancreas (potentially causing diabetes), heart (resulting in dilated cardiomyopathy), skin (causing pigmentation classically known as **bronze diabetes**), and joints (arthritis). Men are symptomatic earlier and more often because women lose iron with menstruation. Treat with phlebotomy. Secondary iron overload can cause secondary hemochromatosis, which is classically because of an anemia that results in ineffective erythropoiesis (e.g., thalassemia) and excessive iron intake.

48. Define Wilson disease. How do you recognize it? How is it treated?

Wilson disease is an autosomal recessive disease caused by excessive serum copper. Serum **ceruloplasmin** (a copper transport protein) is usually low or absent, but serum copper may be normal. Biopsy shows excessive copper in the liver. Patients classically have liver disease with central nervous system (CNS) and psychiatric manifestations (caused by copper deposits in the basal

ganglia; another name for this disease is hepatolenticular degeneration) and **Kayser-Fleischer rings** in the eye. Treat with penicillamine (copper chelator).

49. What are the clues to a diagnosis of alpha-1 antitrypsin deficiency?

The classic description is a young adult who develops cirrhosis and/or emphysema without risk factors for either. Alpha-1 antitrypsin deficiency has an autosomal recessive inheritance pattern; look for a positive family history. Diagnosis requires a serum alpha-1 antitrypsin less than 11 μmol/L as well as a severe deficient genotype.

50. What metabolic derangements accompany liver failure?

Coagulopathy: Prolonged PT. In severe cases, partial thromboplastin time (PTT) may also be prolonged. Vitamin K does not solve the problem because it cannot be utilized by the damaged liver. Symptomatic patients must be treated with fresh frozen plasma.

Jaundice/hyperbilirubinemia: Elevated conjugated and unconjugated bilirubin with hepatic damage (vs. biliary tract disease).

Hypoalbuminemia: The liver synthesizes albumin.

Ascites: Because of portal hypertension and/or hypoalbuminemia. Ascites can be detected on physical examination by shifting dullness or a positive fluid wave. A possible complication is **spontaneous bacterial peritonitis** caused by infected ascitic fluid that can lead to sepsis. Look for fever and/or change in mental status in a patient with known ascites. Perform a paracentesis, examine the ascitic fluid for elevated white blood cell count (especially neutrophils), and do Gram stain, culture, and sensitivity tests, as well as glucose (low with infection), and protein (high with infection) tests. The usual causes are *E. coli, Streptococcus pneumoniae,* and other enteric bugs. Treat with broad-spectrum antibiotics (cefotaxime is a common choice).

Portal hypertension: Seen with cirrhosis (chronic liver disease); causes hemorrhoids, varices, and caput medusae (engorged veins on the abdominal wall).

Hyperammonemia: The liver clears ammonia. Treat with decreased protein intake (source of ammonia) and lactulose (prevents absorption of ammonia). The last choice is neomycin (which is not used as much as it once was), which kills bowel flora that make ammonia.

Hepatic encephalopathy: Mostly caused by hyperammonemia; often precipitated by protein intake, GI bleed, or infection. Look for asterixis and/or mental status changes.

Hepatorenal syndrome: Liver failure may cause kidney failure (idiopathic).

Hypoglycemia: The liver stores glycogen.

Disseminated intravascular coagulation: Activated clotting factors are cleared by the liver.

51. What signs and symptoms suggest biliary tract obstruction as a cause of jaundice?

- Elevated conjugated bilirubin. Conjugated bilirubin is more elevated than unconjugated bilirubin because the liver still functions and can conjugate bilirubin, but conjugated bilirubin cannot be excreted because of biliary tract disease.
- Markedly elevated alkaline phosphatase
- Pruritus
- Clay-colored stools
- Dark urine, which is strongly positive for conjugated bilirubin. Unconjugated bilirubin is not excreted in the urine because it is tightly bound to albumin.

52. What are the commonly tested types of biliary tract obstruction?

Bile duct obstruction, cholestasis, cholangitis, primary biliary cirrhosis, and primary sclerosing cholangitis.

53. What are the two major causes of common bile duct obstruction? How are they distinguished?

The most common cause is obstruction with a gallstone (choledocholithiasis). Look for a history of gallstones or the four Fs (female, forty, fertile, and fat). Ultrasound often images the stone; if not, use

magnetic resonance cholangiopancreatography or endoscopic retrograde cholangiopancreatography (MRCP). Treatment is endoscopic removal of the stone. The second major cause of common bile duct obstruction is cancer. Look for weight loss. Pancreatic cancer is the most common type; look for **Courvoisier sign** (jaundice with a palpably enlarged gallbladder). Sometimes cholangiocarcinoma or bowel cancer blocks the common bile duct.

54. What are the two common causes of cholestasis?

Medications (e.g., birth control pills, trimethoprim-sulfamethoxazole, phenothiazines, androgens) and pregnancy.

55. What clues suggest a diagnosis of primary biliary cirrhosis?

This condition usually is seen in middle-aged women with no risk factors for liver or biliary disease. It causes marked pruritus, jaundice, and positive **antimitochondrial antibodies.** The rest of the workup is negative. Cholestyramine helps with symptoms, but the only treatment is liver transplantation.

56. Who gets primary sclerosing cholangitis?

Primary sclerosing cholangitis usually occurs in young adults with inflammatory bowel disease (usually ulcerative colitis). The symptoms are similar to bacterial cholangitis: fever, chills, pruritus, and right upper quadrant abdominal pain are common.

57. What usually precipitates cholangitis? What is the tip-off to its presence? How is it treated?

Cholangitis usually is precipitated by a gallstone that blocks the common bile duct with subsequent infection of the bile duct system. The tip-off is the presence of **Charcot triad:** fever, right upper quadrant pain, and jaundice. Treat with antibiotics, and remove gallstones surgically or endoscopically.

58. What are the classic symptoms of esophageal disease?

Dysphagia (difficulty in swallowing) and/or odynophagia (painful swallowing). Patients may also have atypical chest pain.

59. Define achalasia. How is it diagnosed and treated?

Achalasia is caused by incomplete relaxation of a hypertensive lower esophageal sphincter and loss or derangement of peristalsis. It is usually idiopathic but may be secondary to **Chagas disease** (South America). Patients have intermittent dysphagia for solids and liquids, but no heartburn because the lower esophageal sphincter stays tightly closed and does not allow acid reflux. Barium swallow reveals a dilated esophagus with distal "bird-beak" narrowing (Fig. 12-9). The diagnosis often is confirmed with esophageal manometry. Treat with calcium channel blockers, pneumatic balloon dilatation, or botulism toxin injection. Surgery (myotomy) is a last resort. Patients have an increased risk for esophageal carcinoma.

60. What are the symptoms and signs of esophageal spasm? How is it treated?

Both diffuse esophageal spasm (Fig. 12-10) and nutcracker esophagus (best thought of as a special variant of esophageal spasm) are characterized by irregular, forceful, and painful esophageal contractions that cause intermittent chest pain. Diagnose with esophageal manometry. Treat with calcium channel blockers and, if needed, surgery (myotomy).

61. What clues suggest scleroderma as the cause of esophageal complaints?

Scleroderma may cause aperistalsis because of esophageal fibrosis and atrophy of smooth muscle. The lower esophageal sphincter often becomes incompetent, and many patients have heartburn (in contrast to achalasia). Look for positive antinuclear antibody and masklike facies as well as other autoimmune symptoms. Remember also the **CREST** syndrome, which consists of **c**alcinosis, **R**aynaud phenomenon, **e**sophageal dysmotility, **s**clerodactyly, and **t**elangiectasias.

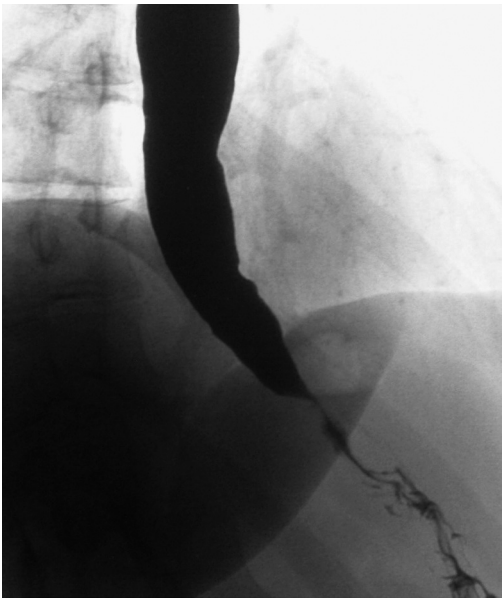

Figure 12-9. Classic appearances of achalasia. Note the tapered appearance of the gastroesophageal junction with the column of barium above. (From Adam A, Dixon AK. Grainger & Allison's diagnostic radiology. 5th ed. Churchill Livingstone, 2008, Fig. 30.21.)

62. What do you need to know about the epidemiology of esophageal cancer?

First, the epidemiology has recently changed because adenocarcinoma is now more common than squamous cell carcinoma. Adenocarcinoma is caused by the long-standing effects of gastric acid reflux and thus occurs in the distal esophagus. Squamous cell carcinoma is usually caused by alcohol and tobacco (synergistic effect) and classically is seen in black men older than 40 years who smoke and drink alcohol. Patients complain of weight loss and food "sticking" in the chest (solids more than liquids). The tumor is usually in the proximal esophagus.

63. What is the relationship between Barrett esophagus and esophageal cancer?

Barrett esophagus, which usually is caused by longstanding GERD, predisposes to esophageal adenocarcinoma. Barrett esophagus describes a columnar metaplasia of the normally squamous cell esophageal mucosa. Once Barrett esophagus is seen on endoscopy and confirmed with endoscopic biopsy, periodic biopsies must be done to monitor for the development of esophageal cancer.

64. What causes acute pancreatitis?

More than 80% of cases are caused by alcohol or gallstones. Other causes include hypertriglyceridemia, viral infections (mumps, coxsackie virus), trauma, hypercalcemia, PUD, medications (e.g., isoniazid, furosemide, simvastatin, steroids, azathioprine), and scorpion stings.

65. What are the signs and symptoms of acute pancreatitis?

Patients classically have epigastric abdominal pain that radiates to the back, nausea with vomiting that fails to relieve the pain, leukocytosis, and elevated amylase and lipase levels. Watch for **Grey Turner sign** (blue-black flanks) and **Cullen sign** (blue-black umbilicus), both of which are because of a hemorrhagic pancreatic exudate and indicate severe pancreatitis. Perforated ulcers

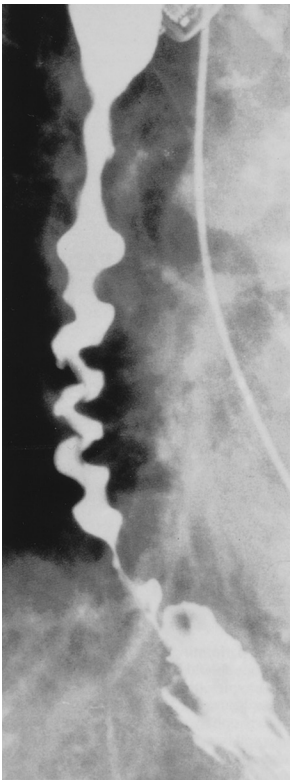

Figure 12-10. Barium esophagogram showing a "corkscrew" esophagus in a patient with diffuse esophageal spasm. The patient had dysphagia and chest pain. Upper endoscopy was normal. (From Feldman M, ed. Gastroenterology and hepatology: the comprehensive visual reference. New York: Churchill Livingstone, 1997, with permission.)

also are associated with elevated amylase and lipase levels and present similarly. However, patients usually have free air on abdominal radiographs and a history of peptic ulcer disease.

66. How is acute pancreatitis treated?

Patients are not allowed to eat, a nasogastric tube is often placed, and intravenous fluids and narcotics are given. For pain control, hydromorphone or fentanyl are often used. Other options include meperidine (which has a risk of seizures) or morphine (which causes sphincter of Oddi spasm, although clinical evidence of this is lacking).

67. What are the complications of acute pancreatitis?

Complications include pseudocyst formation (drain surgically if symptomatic and persistent for several weeks), abscess or infection (treat with antibiotics and drainage if needed), and chronic pancreatitis.

68. What causes chronic pancreatitis? How is it treated?

Chronic pancreatitis in the United States is almost always caused by alcoholism and usually results from repeated bouts of acute pancreatitis. Gallstones do not cause chronic pancreatitis. Chronic pancreatitis may lead to diabetes, steatorrhea (excessive fat in the stool caused by lack of pancreatic

enzymes), calcification of the pancreas (which may be seen on a plain abdominal radiograph), and fat-soluble vitamin deficiencies (because of malabsorption). The incidence of pancreatic cancer is slightly increased in patients with pancreatitis, although smoking is a greater risk factor than alcohol for pancreatic cancer.

Treat chronic pancreatitis with alcohol abstinence, oral pancreatic enzyme replacement, and fat-soluble vitamin supplements.

69. Distinguish between Mallory-Weiss and Boerhaave tears in the esophagus. How are they diagnosed?

Mallory-Weiss tears are superficial erosions in the esophageal mucosa, whereas Boerhaave tears are full-thickness esophageal ruptures. Both may cause a GI bleed and are usually seen with vomiting and retching (alcoholics and bulimic patients) if they are not iatrogenic (because of endoscopy). Diagnosis is usually made endoscopically (bleeding vessels should be sclerosed) and/or from contrast radiographs. Mallory-Weiss tears usually stop bleeding on their own or with endoscopic treatment, but Boerhaave tears require immediate surgical repair and drainage.

70. What is the rule about bowel contrast when a GI perforation is suspected?

For all GI studies, barium is preferred because it provides higher quality images. However, with suspected GI perforation, do not use barium because it can cause chemical peritonitis or mediastinitis when a perforation/leak is present. Instead, use water-soluble contrast (e.g., Gastrografin). Things get tricky in patients with a significant risk for aspiration because the lungs tolerate barium well but develop chemical pneumonitis from water-soluble contrast. When in doubt, give water-soluble contrast, followed by barium once perforation has been excluded.

71. Which GI malformations are common in children? How can they be distinguished?

NAME*	PRESENTING AGE	VOMIT DESCRIPTION	FINDINGS/KEY WORDS
Pyloric stenosis	0-3 mo	Nonbilious, projectile	Males > females; palpable olive-shaped mass in the epigastrium; low Cl/low K metabolic alkalosis
Intestinal atresia	0-1 wk	Bilious	"Double-bubble" sign, Down syndrome
TE fistula†	0-2 wk	Food regurgitation	Respiratory compromise with feeding, aspiration pneumonia, inability to pass a nasogastric tube into the stomach, gastric distention (from air)
Hirschsprung disease	0-1 yr	Feculent	Abdominal distention, obstipation, no nerve ganglia seen on rectal biopsy; males > females
Anal atresia	0-1 wk	Late, feculent	Detected on initial examination in the nursery; males > females
Choanal atresia	0-1 wk	—	Cyanosis with feeding, relieved by crying; inability to pass a nasogastric tube through nose

Cl, Chloride; *K*, potassium; *TE*, tracheoesophageal.
*Treat each of these conditions with **surgical repair**.
†The most common variant (85% of cases) has esophageal atresia with a fistula from the bronchus to the distal esophagus. The result is gastric distention, as each breath transmits air to the GI tract. Be able to recognize a sketch of this most common variant (Fig. 12-11; Plate 23).

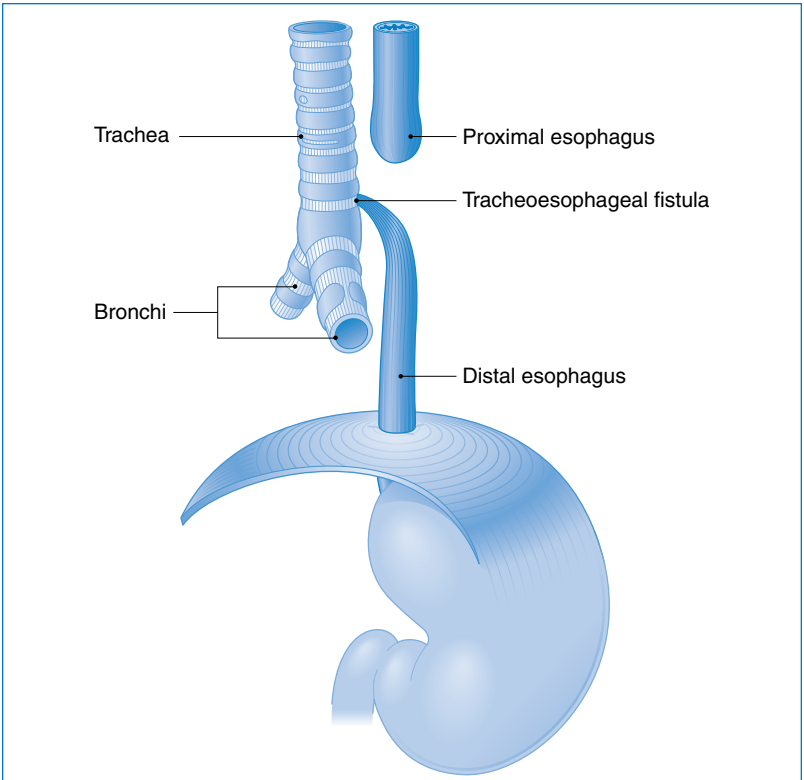

Figure 12-11. Tracheoesophageal fistula. Diagram of the most common type of esophageal atresia and tracheoesophageal fistula. See Plate 23. (From Gilbert-Barness E. Potter's pathology of the fetus, infant and child. 2nd ed. Mosby, 2007, Fig. 25.6.)

72. Describe other pediatric GI conditions that you need to know for the Step 2 USMLE.

NAME	PRESENTING AGE	VOMIT DESCRIPTION	FINDINGS/KEY WORDS
Intussusception	3 mo-2 yr	Bilious	Currant-jelly stools (blood and mucus), palpable sausage-shaped mass; treat with pneumatic or hydrostatic enema guided by fluoroscopy or ultrasound (diagnostic and therapeutic)
Necrotizing enterocolitis	0-2 mo	Bilious	Premature baby, fever, rectal bleeding, air in bowel wall. Treat with NPO, orogastric tube, IV fluids, and antibiotics
Meconium ileus	0-1 wk	Feculent, late	Cystic fibrosis manifestation (as is rectal prolapse)

NAME	PRESENTING AGE	VOMIT DESCRIPTION	FINDINGS/KEY WORDS
Midgut volvulus	0-2 yr	Bilious	Sudden onset of pain, distention, rectal bleeding, peritonitis, "bird's beak" on abdominal radiograph; treat with surgery
Meckel diverticulum	0-2 yr	Varies	Rule of 2s*; GI ulceration/bleeding; use Meckel scan to detect; treat with surgery
Strangulated hernia	Any age	Bilious	Physical examination detects bowel loops in inguinal canal

IV, Intravenous; *NPO*, nothing by mouth (no feedings).
*Rule of 2s for Meckel diverticulum: 2% of population affected (most common GI tract abnormality; remnant of omphalomesenteric duct), 2 inches long, within 2 feet of ileocolic junction, presents in the first 2 years of life. Meckel diverticulum can cause intussusception, obstruction, or volvulus.

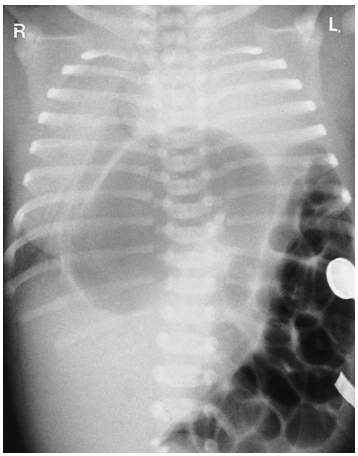

Figure 12-12. Diaphragmatic hernia shown in a newborn with significant respiratory difficulty. An antero-posterior view of the chest and abdomen demonstrates opacification of the left hemithorax, with bowel loops pushing up into the opacified left hemithorax. This condition carries a high fatality rate and should be recognized immediately. (From Mettler F. Essentials of radiology. 2nd ed. Philadelphia: Saunders, 2004, Fig. 9-13.)

73. Which GI malformation primarily causes respiratory problems?

Diaphragmatic hernia, which is more common in males. Ninety percent are on the left side. The main point to know is that bowel herniates into the thorax through the diaphragmatic defect, compressing the lung and impeding lung development (pulmonary hypoplasia develops). Patients come to the hospital with respiratory distress and have bowel sounds in the chest and bowel loops in the thorax on chest radiographs (Fig. 12-12). Treat with surgical correction of the diaphragm.

74. How are omphalocele and gastroschisis differentiated?

An **omphalocele** is in the midline, the sac contains multiple abdominal organs, the umbilical ring is absent, and other anomalies are common. **Gastroschisis** is to the right of the midline, only small bowel is exposed (no true hernia sac), the umbilical ring is present, and other anomalies are rare (Fig. 12-13; Plate 24).

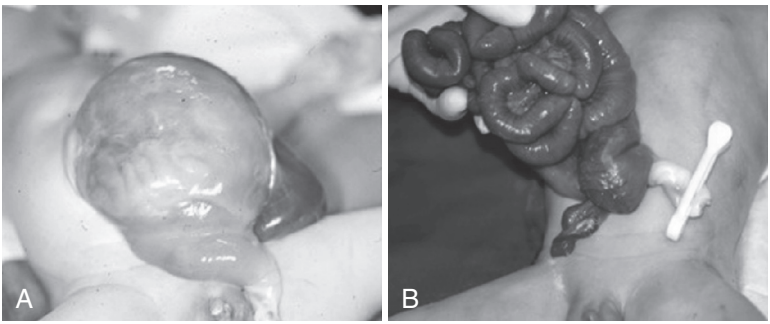

Figure 12-13. Abdominal wall defects. **A,** Omphalocele with intact sac. **B,** Gastroschisis with eviscerated multiple bowel loops to the right of the umbilical cord. See Plate 24. (From Sabiston DC, Townsend CM. Sabiston textbook of surgery: the biological basis of modern surgical practice. 19th ed. Philadelphia: Saunders, 2012, Fig. 67-20.)

75. What is Henoch-Schönlein purpura? Why is it mentioned in the GI section?

Henoch-Schönlein purpura is a vasculitis that may present with GI bleeding and abdominal pain. Look for a history of upper respiratory infection, characteristic rash on lower extremities and buttocks (Fig. 12-14; Plate 25), swelling in hands and feet, arthritis, and/or hematuria and proteinuria. Treat supportively with hydration, rest, and pain relief.

76. What is the most common cause of diarrhea in children?

As a primary cause, probably viral gastroenteritis (e.g., Norwalk virus, rotavirus). However, diarrhea is often a nonspecific sign of any systemic illness (e.g., otitis media, pneumonia, urinary tract infection).

77. True or false: Children may develop inflammatory bowel disease and irritable bowel syndrome.

True. Abdominal pain may be the result of inflammatory bowel disease or irritable bowel syndrome. Diarrhea, fever, bloody stools, anemia, joint pains, and poor growth are more concerning for inflammatory bowel disease. GI complaints may be caused by anxiety or psychiatric problems. Watch for separation anxiety, children who do not want to go to school, depression, and child abuse.

78. What is the first step in evaluating neonatal jaundice? Why is jaundice of concern in a neonate?

The first step is to determine whether the jaundice is physiologic or pathologic. Measure total, direct, and indirect bilirubin. The main concern is **kernicterus,** which is caused by high levels of unconjugated bilirubin with subsequent deposit in the basal ganglia. Look for poor feeding, seizures, flaccidity, opisthotonos, and apnea in the setting of severe jaundice.

79. What causes physiologic jaundice of the newborn? Who gets it?

Fifty percent of normal infants have physiologic jaundice, and it is even more common in premature infants. Bilirubin is mostly unconjugated because of incomplete maturation of liver function. In full-term infants, bilirubin is less than 12 mg/dL, peaks at day 2 to 4, and returns to normal by 2 weeks. In premature infants, bilirubin is less than 15 mg/dL, peaks at 3 to 5 days, and may be elevated for up to 3 weeks.

80. How is pathologic jaundice recognized? What are the causes?

In pathologic jaundice, bilirubin levels go higher than those mentioned above and continue to rise or fail to decrease appropriately. ***Any* jaundice present at birth is pathologic.** Causes include the following.

Breast milk jaundice: Breast-fed infants with peak bilirubin levels of 10 to 20 mg/dL at 2 to 3 weeks of age. Treat with temporary cessation of breastfeeding (switch to bottle) until jaundice resolves.

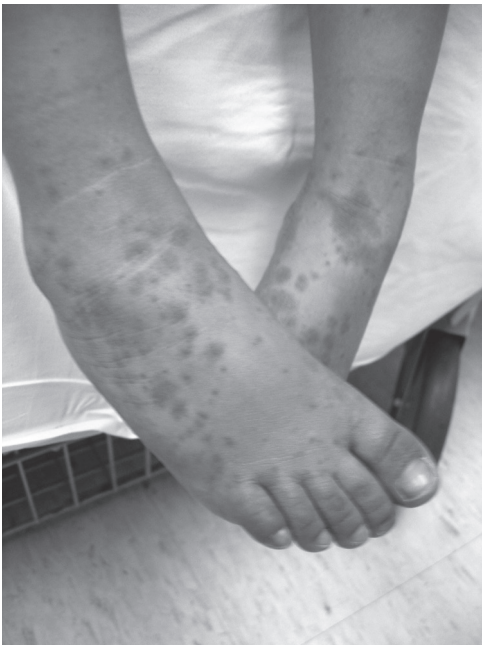

Figure 12-14. Henoch-Schönlein purpura in a 7-year-old child. Note typical red-purple rash on the lower extremities. See Plate 25. (From Marx JA, Hockberger RS, Walls RM. Rosen's emergency medicine: concepts and clinical practice. 7th ed. Mosby, 2009, Fig. 170-10. Courtesy Marianne Gausche-Hill, MD.)

Illness: Infection or sepsis, hypothyroidism, liver insult, cystic fibrosis, and other illnesses may prolong neonatal jaundice and lower the threshold for kernicterus. The youngest, sickest infants are at greatest risk for hyperbilirubinemia and kernicterus.

Hemolysis: From Rhesus (Rh) incompatibility or congenital red cell diseases that cause hemolysis in the neonatal period. Look for anemia, peripheral smear abnormalities, positive family history, and higher levels of unconjugated bilirubin.

Metabolic disorders: Crigler-Najjar syndrome causes severe unconjugated hyperbilirubinemia, whereas Gilbert syndrome causes a mild form. Rotor and Dubin-Johnson syndromes cause conjugated hyperbilirubinemia.

Biliary atresia: Full-term infants with clay- or gray-colored stools and high levels of conjugated bilirubin. Treat with surgery.

Medications: Avoid sulfa drugs in neonates; they displace bilirubin from albumin and may precipitate kernicterus.

81. How is pathologic jaundice treated?

Unconjugated hyperbilirubinemia that persists, rises above 15 mg/dL, or rises rapidly is treated with **phototherapy** to convert unconjugated bilirubin to a water-soluble form that can be excreted. A last resort is exchange transfusion, but should not be implemented unless the level of unconjugated bilirubin is greater than 20 mg/dL.

82. What should you do if an infant is born to a mother with active hepatitis B?

An infant born to a mother with active hepatitis B should receive the first immunization shot and hepatitis B immune globulin at birth.

CHAPTER 13

GENERAL SURGERY

1. Define the acute abdomen. What physical examination signs suggest its presence?

Acute abdomen generally refers to an inflamed peritoneum (peritonitis), which is often because of a surgically correctable problem. Patients with an acute abdomen often receive a laparotomy and/or laparoscopy because it signifies a potentially life-threatening condition. The best physical examination confirmations of peritonitis are **rebound tenderness** and **involuntary guarding.** Rebound tenderness is elicited by letting go quickly after deep palpation of the abdomen; acute pain occurs in the area of palpation (with generalized peritonitis) or at the location of localized inflammation (e.g., Rovsing sign in appendicitis). Involuntary guarding describes abdominal wall muscle spasms that cannot be controlled. Voluntary guarding (person reflexively or willfully tenses their abdomen during attempted palpation) and tenderness to palpation are softer signs often present in benign diseases.

2. What should you do if you are not sure whether a stable patient has an acute abdomen?

When you are in doubt and the patient is stable, use minimal as needed pain medications (to avoid masking symptoms before you have a diagnosis), perform serial abdominal examinations, and consider a computed tomography (CT) scan. If the patient becomes unstable, proceed to laparoscopy and/or laparotomy.

3. Name a few causes of peritonitis that do not require laparotomy or laparoscopy.

Pancreatitis, many cases of diverticulitis, and spontaneous bacterial peritonitis.

4. Specify which conditions are associated with pain and peritonitis in the listed abdominal areas.

AREA	ORGAN (CONDITIONS)
Upper right quadrant	Gallbladder/biliary (cholecystitis, cholangitis) or liver (abscess)
Upper left quadrant	Spleen (rupture with blunt trauma)
Lower right quadrant	Appendix (appendicitis), pelvic inflammatory disease (PID)
Lower left quadrant	Sigmoid colon (diverticulitis), PID
Epigastric area	Stomach (peptic ulcer) or pancreas (pancreatitis)

5. What are the classic symptoms and signs of gallstone disease?

Classic gallstone symptoms include postprandial, colicky pain in the right upper quadrant with bloating and/or nausea and vomiting. The pain usually begins 15 to 60 minutes after a meal (especially a fatty meal). Look for **Murphy sign** (palpation of the right upper quadrant under the rib cage causes arrest of inspiration as a result of pain) as the main physical examination finding for cholecystitis.

6. What are the six Fs of cholecystitis? How are the demographics of patients with pigment stones different from those with cholesterol stones?

The first five Fs summarize the demographics of people with cholesterol gallstones: **f**at, **f**orty, **f**ertile, **f**emale, and **f**latulent; the sixth F is **f**ebrile, which indicates that such patients have now developed acute cholecystitis. Patients with pigment (i.e., calcium bilirubinate) stones are classically young patients with hemolytic anemia (e.g., sickle cell disease, hereditary spherocytosis).

7. How is a clinical suspicion of cholecystitis confirmed and treated?

Ultrasound is the best first imaging study for suspected gallbladder disease (Fig. 13-1). It may show gallstones, a thin layer of fluid around the gallbladder, and/or a thickened gallbladder wall. A more specific ultrasonographic Murphy sign using direct visualization of the gallbladder can be obtained (variant anatomy and significant obesity can create uncertainty). A nuclear hepatobiliary scintigraphic study (e.g., hepato-iminodiacetic acid [HIDA] scan) clinches the diagnosis with nonvisualization of the gallbladder (Fig. 13-2). The treatment is pain control and cholecystectomy (antibiotics may be indicated if infection is suspected); a laparoscopic approach is generally preferred over an open procedure.

8. Define cholangitis. How does it differ from cholecystitis? How is it treated?

Cholangitis is an inflammation of the bile ducts, whereas cholecystitis is an inflammation of the gallbladder. Cholangitis is classically caused by biliary obstruction with subsequent bile stasis and infection. Choledocholithiasis (a gallstone in the common bile duct) and malignancy are common causes of obstruction. Autoimmune cholangitis (e.g., sclerosing cholangitis) and primary infection (e.g., *Clonorchis sinensis* and other parasite infections common in some parts of Asia) are other causes. Cholangitis classically presents with **Charcot triad:** (1) right upper quadrant pain, (2) fever or shaking chills, and (3) jaundice. Patients may have a history of gallstones. Start broad-spectrum antibiotics to cover bowel flora (e.g., piperacillin with tazobactam); then manage more definitively depending on the circumstances (e.g., cholecystectomy with evacuation of any common duct stones for gallstone disease, biliary stent placement for unresectable malignant obstruction).

9. Describe the classic presentation of appendicitis. How is it treated?

Appendicitis classically presents in 10- to 30-year-olds with a history of crampy, poorly localized periumbilical pain followed by nausea and vomiting. Then the pain localizes to the right lower quadrant, and peritoneal signs develop with worsening of nausea and vomiting. It is said that a patient

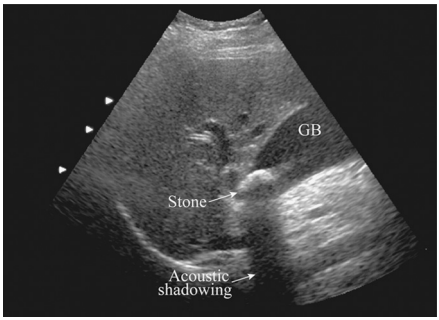

Figure 13-1. Typical ultrasonographic appearance of cholelithiasis. A gallstone is present within the lumen of the gallbladder (GB), casting an acoustic shadow. If the patient is repositioned, the stones will move, thereby excluding the possibility of a gallbladder polyp. (From Feldman M, Friedman L, Brandt L. Sleisenger and Fordtran's gastrointestinal and liver disease. 8th ed. Philadelphia: Saunders, 2006, Fig. 62-6A.)

who is hungry and asking for food does not have appendicitis (called the "hamburger" sign). A classic clue to the diagnosis is **Rovsing sign:** when you palpate a different quadrant and then quickly release your hand, the patient feels pain at McBurney point (two thirds of the way from the umbilicus to the anterior superior iliac spine). McBurney point is the area of maximal tenderness in the right lower quadrant and the site where an open appendectomy incision is made. CT is increasingly used to confirm the diagnosis before surgery in stable patients (Fig. 13-3).

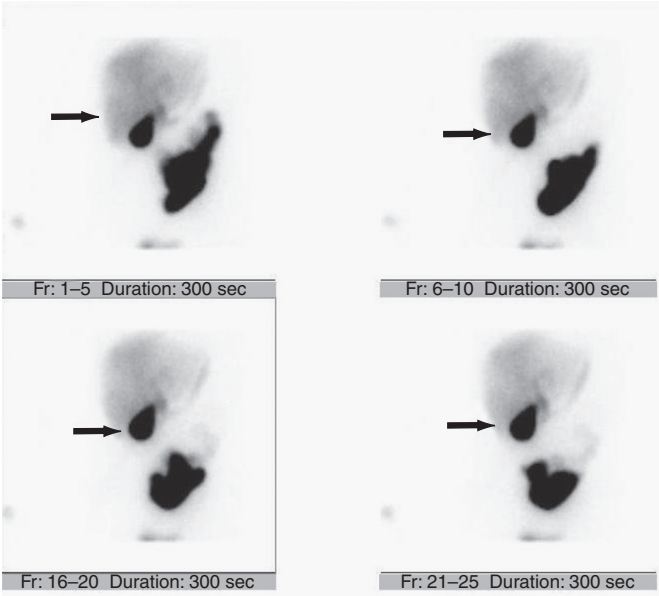

Figure 13-2. Hepato-iminodiacetic acid (HIDA) scan showing the filling of the gallbladder. With gallbladder filling *(arrows),* the diagnosis of acute cholecystitis is effectively eliminated. (From Sabiston DC, Townsend CM. Sabiston textbook of surgery. 19th ed. Philadelphia: Saunders, 2012, Fig. 55-13.)

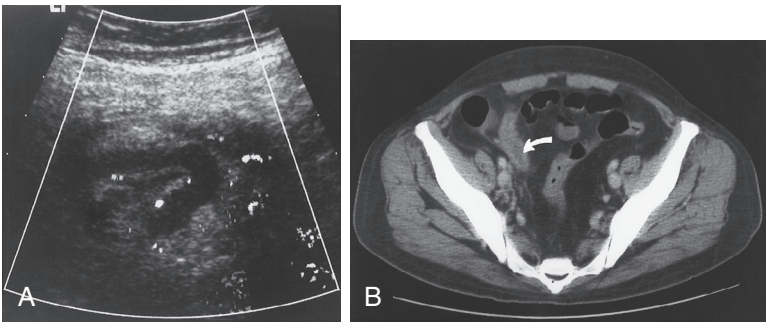

Figure 13-3. Appendicitis. **A,** Ultrasound shows a thickened hypoechoic tubular blind-ended structure in the right iliac fossa. The surrounding fat is hyperechoic. **B,** Computed tomography (CT) scan shows the thickened inflamed appendix *(arrow).* (Courtesy of Dr. A. McLean, St Bartholomew's Hospital, London.)

10. What is the cause of left lower quadrant pain and fever in a patient older than 50 years until proved otherwise? How is it treated?

Diverticulitis. Treat medically with broad-spectrum antibiotics (e.g., ciprofloxacin plus metronidazole), avoidance of eating, and a nasogastric tube if nausea and vomiting are present. For disease that recurs or is refractory to medical therapy, consider sigmoid colon resection.

11. What tests should and should not be done to confirm possible cases of diverticulitis? What test does every patient need after a treated episode of diverticulitis?

Colonoscopy should not be performed in the acute setting because colon rupture may occur; barium enema is also avoided for the same reason. However, one of these tests should be done in every patient after treatment to exclude colon carcinoma. Order a CT scan, if necessary, to confirm a diagnosis of diverticulitis (Fig. 13-4).

12. Describe the typical history, physical examination, and laboratory findings of pancreatitis. How is it treated?

Look for epigastric pain that radiates to the back in an alcohol abuser or a patient with a history of (or risk factors for) gallstones. Serum amylase and/or lipase should be elevated. If these values are not given, order them. Other common signs include decreased bowel sounds, localized ileus ("sentinel" loop of bowel on abdominal radiograph) and nausea, vomiting, and/or anorexia.

Treat pancreatitis supportively; narcotics are often needed for pain control; hydromorphone or fentanyl are common choices these days; meperidine, which has a risk of seizures, has traditionally been favored over morphine because of the concern about sphincter of Oddi spasm, although clinical evidence of this is lacking. Do not feed the patient initially; place a nasogastric tube as needed for nausea and vomiting; and give intravenous (IV) fluids as well as other needed supportive care. Watch for the complications of pseudocyst and pancreatic abscess, both of which can be diagnosed by CT scan and may require surgical intervention.

13. Describe the usual history of a perforated ulcer. How is it treated?

Patients often have no history of alcohol abuse or gallstones (pancreatitis risk factors). Abdominal radiographs classically show free air under the diaphragm, and a history of peptic ulcer disease

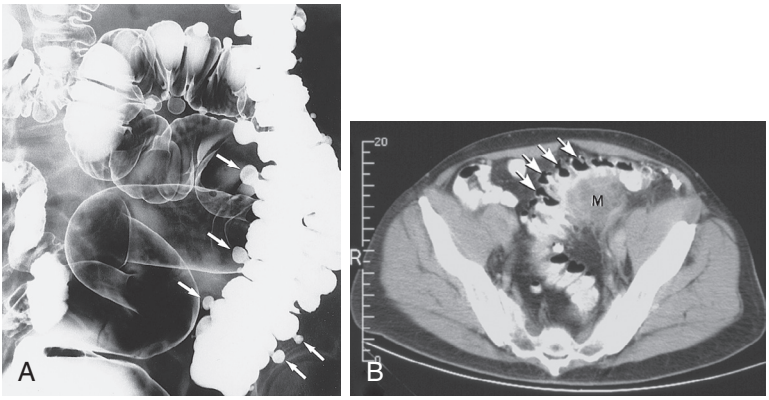

Figure 13-4. A, Diverticulosis of the colon is seen on this oblique view of the sigmoid colon during a double-contrast barium enema showing multiple outpouchings *(arrows)* that represent diverticula. **B,** Diverticula also can be seen in a computed tomography (CT) scan as outpouchings *(arrows),* but a developing focal inflammatory mass (M) also is compatible with a developing abscess. (From Mettler F. Essentials of radiology. 2nd ed. Philadelphia: Saunders, 2004, Fig. 6-73.)

(PUD) is often included in the patient description. Remember that a perforated bowel can cause an increased amylase and lipase levels. Treat with surgery.

14. What are the hallmarks of small bowel obstruction? How is it treated?

Small bowel obstruction commonly causes bilious vomiting (early symptom), abdominal distention, constipation, hyperactive bowel sounds (high-pitched, rushing sounds), and usually poorly localized abdominal pain. Radiographs show multiple air-fluid levels. Patients often have a history of previous surgery.

Start treatment by withholding food, placing a nasogastric tube, and giving IV fluids. If the obstruction does not resolve or if peritoneal signs develop, laparotomy is usually needed. CT scanning can confirm an uncertain diagnosis in stable patients and may reveal the underlying cause of obstruction.

15. What are the common causes of a small bowel obstruction?

In adults, the most common cause is **adhesions,** which usually develop from prior surgery. Incarcerated hernias and Crohn disease are other common causes. Other causes include Meckel diverticulum and intussusception (both typically seen in children).

16. Describe the signs and symptoms of large bowel obstruction. What causes it? How is it treated?

Large bowel obstruction usually presents with gradually increasing abdominal pain, abdominal distention, constipation, and feculent vomiting (late symptom). In older adults, the most common causes are diverticulitis, colon cancer, and volvulus. In children, watch for Hirschsprung disease. Treat early by withholding food and placing a nasogastric tube for nausea and vomiting. Sigmoid volvulus (Figs. 13-5 and 13-6) can often be decompressed with an endoscope. Other causes or refractory cases require surgery to relieve the obstruction.

17. List and differentiate the three common types of groin hernias.

1. **Indirect hernias** are the most common type in both sexes and all age groups. The hernia sac travels through the inner and outer inguinal rings (protrusion begins lateral to the inferior epigastric vessels) and into the scrotum or labia because of a patent processus vaginalis (congenital defect).
2. **Direct hernias** (no sac) protrude medial to the inferior epigastric vessels because of weakness in the abdominal musculature of Hesselbach's triangle.
3. **Femoral hernias** are more common in women. The hernia (no sac) goes through the femoral ring onto the anterior thigh (located below the inguinal ring).

Of the three types, femoral hernias are the most susceptible to incarceration and strangulation. All three types are treated with elective surgical repair if symptomatic.

18. Define incarcerated and strangulated hernias.

Incarceration occurs when a herniated organ is trapped and becomes swollen and edematous. Incarcerated hernias are the most common cause of small bowel obstruction in patients who have had no previous abdominal surgery and the second most common cause in patients who have had previous abdominal surgery (Fig. 13-7). Treatment is prompt surgery.

Strangulation occurs after incarceration when the entrapment becomes so severe that the blood supply is cut off. Strangulation can lead to necrosis and is a surgical emergency. Patients may come to the hospital with symptoms of small bowel obstruction and shock.

19. True or false: Generally, patients should not eat or drink for 8 hours or more before surgery.

True. This protocol reduces the chance of aspiration and subsequent pneumonia.

20. What is the best test (other than a good history) for preoperative evaluation of pulmonary function?

Spirometry, which gives functional vital capacity, forced expiratory volumes, and maximal voluntary ventilation. A good history (e.g., activity level, exercise tolerance) is also useful.

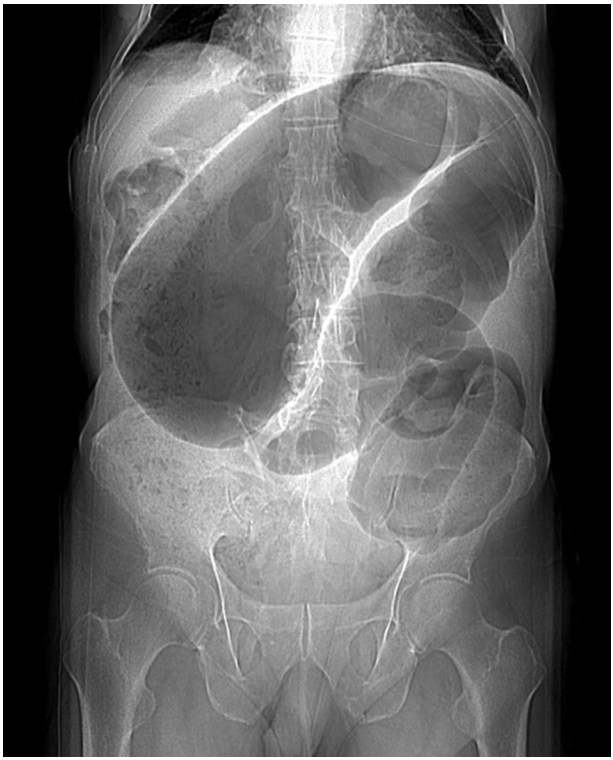

Figure 13-5. Plain abdominal radiograph of a sigmoid volvulus with a massively distended loop of colon under the left hemidiaphragm. (From Yeo CJ. Shackelford's surgery of the alimentary tract. 7th ed. Philadelphia: Saunders, 2012, Fig. 151-2.)

21. What measures help prevent intraoperative and postoperative deep venous thrombosis (DVT) and pulmonary embolus (PE)?

Compressive/elastic stockings, early ambulation, and/or low-dose heparins (unfractionated or low molecular weight).

22. What is the most common cause of fever in the first 24 hours after surgery?

Atelectasis. Prevent and treat atelectasis with early ambulation, chest physiotherapy/percussion, incentive spirometry, and proper pain control. Too much pain and too many narcotics (both can decrease respiratory effort) increase the risk of atelectasis.

23. What are the other common causes of postoperative fever?

The five Ws—**w**ater, **w**ind, **w**alk, **w**ound, and **w**eird drugs—summarize the common causes of postoperative fever. Water stands for urinary tract infection, wind for atelectasis and pneumonia, walk for DVT, wound for surgical wound infection, and weird drugs for drug fever. In patients with daily fever spikes that do not respond to antibiotics, think about an intraabdominal abscess. Order a CT scan to locate the abscess, and then drain it if present.

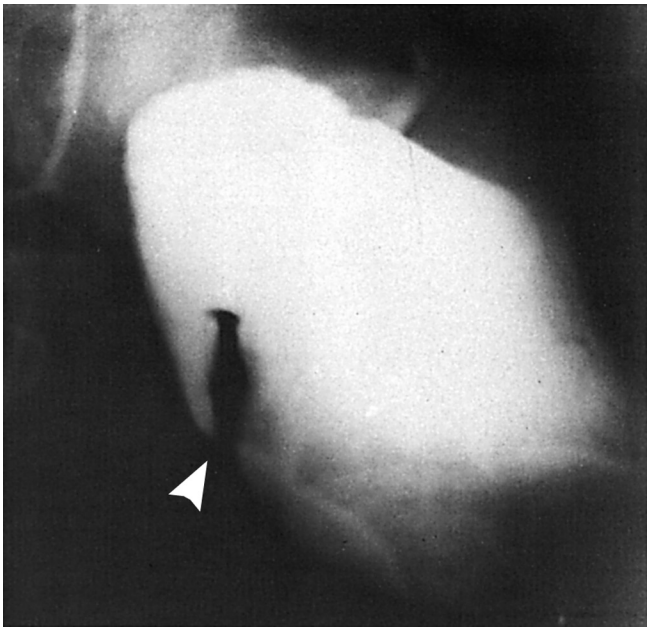

Figure 13-6. This barium enema shows the characteristic "bird's beak" sign of volvulus *(arrowhead).* (From Marx JA, Hockberger RS, Walls RM, eds. Rosen's emergency medicine: concepts and clinical practice. 7th ed. Philadelphia: Mosby, 2009, Fig. 93-3.)

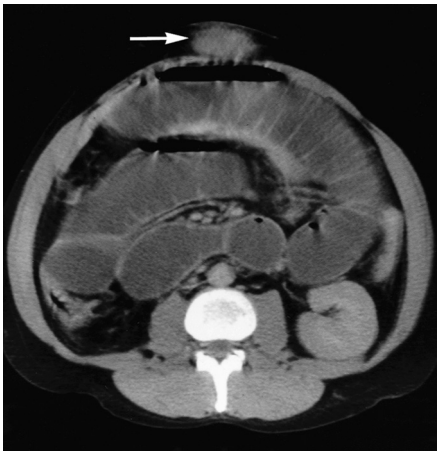

Figure 13-7. Small intestinal obstruction. A section through the mid-abdomen from a computed tomography (CT) scan shows dilated, mainly fluid-filled, small intestinal loops. The obstruction was because of an incarcerated paraumbilical hernia, the edge of which can be identified *(arrow).* (From Adam A, et al. Grainger and Allison's diagnostic radiology. 5th ed. Edinburgh: Churchill Livingstone, 2008, Fig. 32-37.)

24. Define fascial or wound dehiscence. How do you recognize it?

Fascial or wound dehiscence occurs when the surgical wound opens spontaneously, usually 5 to 10 days postoperatively. Look for leakage of serosanguineous fluid from the wound, particularly after the patient coughs or strains. Frequently the wound is infected. Surgical reclosure of the wound and treatment of infection are required.

25. Explain the ABCDEs of trauma. How are they used?

The ABCDEs of trauma are **a**irway, **b**reathing, **c**irculation, **d**isability, and **e**xposure. They are the keys to the initial management of trauma patients. Follow them in order if simultaneous management is not possible. For example, if a patient is bleeding to death and has a blocked airway, address airway management first.

26. What is the difference between airway and breathing in trauma protocol?

Airway means provision, protection, and maintenance of an adequate airway at all times. If the patient can speak, the airway is fine. You can use an oropharyngeal airway in uncomplicated cases and give supplemental oxygen. When you are in doubt or the patient's airway is blocked, intubate. If intubation fails, do a cricothyroidotomy.

Breathing is similar to airway, but even patients with an open airway may not be breathing spontaneously. The end result is the same. When you are in doubt or the patient is not breathing, intubate. If intubation fails, do a cricothyroidotomy.

27. Explain circulation, disability, and exposure.

Circulation refers to circulating blood volume. For practical purposes, it means that if the patient seems hypovolemic (tachycardic, bleeding, weak pulse, pale, diaphoretic, capillary refill more than 2 seconds), give IV fluids and/or blood products. Initially, you should start two large-bore IV lines and give a bolus of 10 to 20 mL/kg (roughly 1 L) of lactated Ringer solution or normal saline. Then reassess the patient after the bolus for improvement. Repeat the bolus, if needed.

Disability refers to the need to check neurologic function. In practical terms, this translates into doing a Glasgow coma scale assessment.

Exposure reminds you to expose and examine the entire body. In other words, remove all of the patient's clothes and "put a finger in every orifice" so that you do not miss any occult injuries.

28. What imaging films are routinely ordered for most patients with at least moderately severe trauma?

Cervical spine, chest, and pelvic radiographs.

29. What is the imaging study of choice for head trauma?

Noncontrast CT (better than magnetic resonance imaging [MRI] for acute trauma).

30. How do you manage a patient with blunt abdominal trauma?

In patients with blunt abdominal trauma, the initial findings determine the appropriate course of action. If the patient is awake and stable and your examination is "benign," observe the patient and repeat the abdominal examination later. You can also do a FAST (focused assessment by sonography in trauma) scan to check for free fluid in the abdomen and pelvis. Meanwhile, perform a CT scan of the abdomen and pelvis with oral and IV contrast.

If the patient is hemodynamically unstable (hypotension and/or shock that does not respond to fluid challenge), proceed directly to laparotomy.

If the patient has a positive FAST scan (i.e., there is free fluid, presumably blood, in the abdomen), proceed to laparotomy.

If the patient has altered mental status, the abdomen cannot be examined, or an obvious source of blood loss explains the hemodynamic instability, order a CT scan of the abdomen and pelvis (Fig. 13-8) with oral and IV contrast (also obtain a CT scan of the head and cervical spine if altered mental status is present). Diagnostic peritoneal lavage is no longer used because it is nonspecific and less sensitive than CT; it can also alter CT scan results.

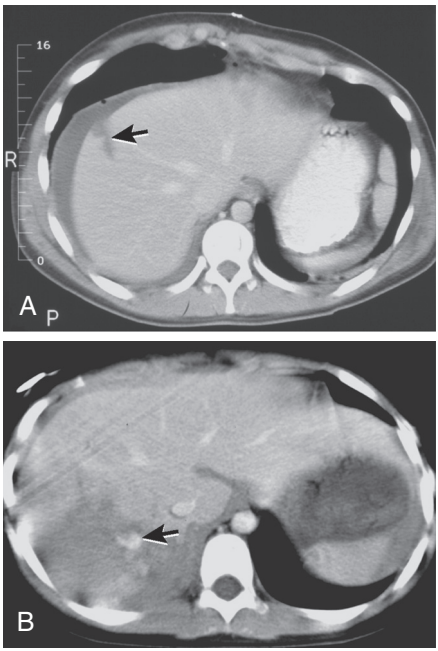

Figure 13-8. Small and large hepatic lacerations. **A,** A computed tomography (CT) scan was obtained through the upper abdomen in this patient after a motor vehicle accident. A small area of low density *(arrow)* is seen in the lateral portion of the right lobe, and blood surrounds the liver. **B,** A CT scan in another patient after a motor vehicle accident shows a much larger area of lacerated liver in the posterior aspect of the right lobe. A central area of increased density (the white area at the *tip of the arrow*) indicates acute hemorrhaging at the time of the scan. (From Mettler F. Essentials of radiology. 2nd ed. Philadelphia: Saunders, 2004, Fig. 6-47.)

31. How is penetrating abdominal trauma managed?

In patients with penetrating abdominal trauma (e.g., gunshot, stab wound), the type of injury and the initial findings determine the course of action. With any gunshot wound that may have violated the peritoneal cavity, proceed directly to laparotomy. With a wound from a sharp instrument, management is more controversial. Either proceed directly to laparotomy (your best choice if the patient is unstable) or perform a CT scan if the patient is stable. With nonoperative management, perform serial abdominal examinations.

32. Which six thoracic injuries can be rapidly fatal?

1. Airway obstruction
2. Open pneumothorax
3. Tension pneumothorax
4. Cardiac tamponade
5. Massive hemothorax
6. Flail chest

You may be asked to recognize and/or treat any of these six conditions on the USMLE.

33. How do you recognize and treat airway obstruction?

Patients with airway obstruction have no audible breath sounds, cannot answer questions even if awake, and may be gurgling. Treat with intubation. If intubation fails, do a cricothyroidotomy (or a tracheostomy in the operating room, if time allows).

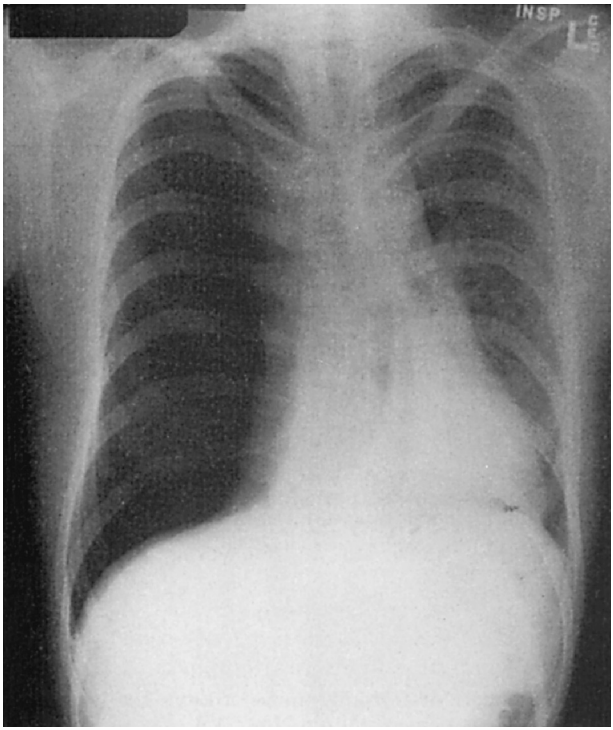

Figure 13-9. Radiograph of tension pneumothorax. The right hemithorax is dark (lucent) because the mediastinum has shifted to the left. (From Marx JA, Hockberger RS, Walls RM, eds. Rosen's emergency medicine: concepts and clinical practice. 7th ed. Philadelphia: Mosby, 2009, Fig. 75-3.)

34. How do you recognize and treat an open pneumothorax?

An open pneumothorax presents with an open defect in the chest wall and decreased or absent breath sounds on the affected side. This condition causes poor ventilation and oxygenation. Treat with intubation, positive-pressure ventilation, and closure of the defect in the chest wall. To close the defect, use gauze and tape it on three sides only. This approach allows excessive pressure to escape so that you do not convert an open pneumothorax into a tension pneumothorax.

35. How do you recognize and treat a tension pneumothorax?

A tension pneumothorax may occur after blunt or penetrating trauma to the chest. Air forced into the pleural space cannot escape and collapses the affected lung and then shifts the mediastinum and trachea to the opposite side of the chest (Fig. 13-9). Findings include absent breath sounds on the affected side and a hypertympanic percussion sound. Hypotension and/or distended neck veins may result from impaired cardiac filling. Treat with needle thoracentesis, followed by insertion of a chest tube.

36. Describe the usual presentation of cardiac tamponade. How is it diagnosed and treated?

Cardiac tamponade is classically associated with penetrating trauma to the left side of the chest. Patients have hypotension (caused by impaired cardiac filling), distended neck veins, muffled heart sounds, **pulsus paradoxus** (exaggerated fall in blood pressure on inspiration), and normal breath

sounds. If the patient is unstable, treat with pericardiocentesis; put a catheter through the skin and into the pericardial sac and aspirate blood and fluid. If the patient is stable, you can first do an echocardiogram to confirm the diagnosis.

37. Define massive hemothorax. How is it diagnosed and treated?

Massive hemothorax is defined as a loss of more than 1 L of blood into the thoracic cavity. Patients have decreased (not absent) breath sounds in the affected area, dull note on percussion, hypotension, collapsed neck veins (from blood leaving the vascular tree), and tachycardia. Placement of a chest tube allows the blood to come out. Give IV fluids and/or blood before you place the chest tube if the diagnosis is known in advance. If the bleeding stops after the initial outflow, order a chest radiograph or CT scan to check for remaining blood or pathology. Treat supportively. If the bleeding does not stop, emergent thoracotomy is required.

38. How do you recognize and treat flail chest?

Flail chest occurs when several adjacent ribs are broken in multiple places, causing the affected part of the chest wall to move paradoxically during respiration (inward during inspiration, outward during expiration). Almost all patients have an associated pulmonary contusion, which, combined with pain, may make respiration inadequate. When you are in doubt or the patient is not doing well, intubate and give positive pressure ventilation.

39. What is the most common cause of immediate death after an automobile accident or a fall from a great height?

Aortic rupture. Look for a widened mediastinum on chest radiograph and an appropriate history of trauma. Order a CT scan or angiogram if a contained aortic rupture (of those who survive to be admitted to the hospital, 50% will die in the first 24 hours) is suspected. Aortic laceration, traumatic aortic injury and traumatic pseudoaneurysm all describe the phenomenon seen in initial survivors: an aortic rupture contained by a hematoma or an inadequate amount of surrounding tissue (e.g., adventitia only). Treat with immediate surgical repair.

40. What do you need to know about splenic rupture?

The spleen is the most commonly injured organ in blunt trauma (Fig. 13-10). Patients with splenic rupture, the most severe form of injury, have a history of blunt abdominal trauma, hypotension, tachycardia, shock, and/or **Kehr sign** (referred pain in the left shoulder). Patients with Epstein-Barr

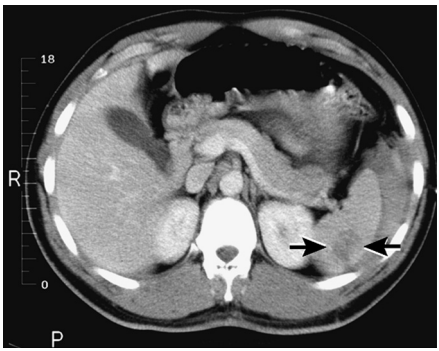

Figure 13-10. Splenic laceration. This computed tomography (CT) scan performed on a patient after a motor vehicle accident shows a dark area near the posterior aspect of the spleen *(arrows),* which is the laceration. Note also the blood surrounding the spleen. (From Mettler F. Essentials of radiology. 2nd ed. Philadelphia: Saunders, 2004, Fig. 6-60.)

virus infection or infectious mononucleosis and splenomegaly should avoid contact sports to prevent rupture. Make sure patients needing splenectomy have received the pneumococcal, meningococcal, and *H. influenzae* (i.e., encapsulated bacteria) vaccines.

41. What clues suggest a diagnosis of diaphragmatic rupture? How is it treated?

Diaphragm rupture usually occurs after blunt trauma and on the left side (because the liver protects the right side of the diaphragm). You may hear bowel sounds when listening to the chest or see bowel that has herniated into the chest on chest radiograph. Treatment is surgical repair of the diaphragm.

42. What are the three zones of the neck? How is trauma in each of the different zones managed?

Zone I is the base of the neck from 2 cm above the clavicles to the level of the clavicles.
Zone II is the midcervical region from 2 cm above the clavicle to the angle of the mandible.
Zone III is the top of the neck from the angle of the mandible to the base of the skull.
With zone I and III injuries, you generally should order an arteriogram before going to the operating room. With zone II injuries, proceed to the operating room for surgical exploration without an arteriogram. In patients with obvious bleeding or a rapidly expanding hematoma in the neck, proceed directly to operating room, no matter where the injury is.

43. How should a choking victim be managed?

Always leave choking patients alone if they are speaking, coughing, or breathing. If they stop doing all of these, perform the Heimlich maneuver.

44. What should you do if a tooth is knocked out?

Put the tooth back in place with no cleaning (or only saline to rinse it off) and stabilize the tooth in place. The sooner this is done, the better the prognosis for salvage of the tooth.

GENETICS

1. Specify how the following disorders are *usually* transmitted genetically. The choices are autosomal dominant or recessive, X-linked recessive, chromosomal disorder, or polygenic disorder.

DISORDER	INHERITANCE PATTERN
von Willebrand disease	Autosomal dominant
Neurofibromatosis	Autosomal dominant
MEN I/II syndrome	Autosomal dominant
Achondroplasia	Autosomal dominant
Sphingolipidoses (Tay-Sachs disease, Gaucher disease)	Autosomal recessive
Fabry disease*	X-linked recessive
Mucopolysaccharidoses (e.g., Hurler disease)	Autosomal recessive
Hunter disease†	X-linked recessive
Glycogen storage diseases (e.g., McArdle disease)	Autosomal recessive
Cystic fibrosis	Autosomal recessive
Marfan syndrome	Autosomal dominant
Huntington disease	Autosomal dominant
Pyloric stenosis	Polygenic disorder
Cleft lip/palate	Polygenic disorder
Type 2 diabetes	Polygenic disorder
Down syndrome	Chromosomal disorder (trisomy 21)
Familial hypercholesterolemia	Autosomal dominant
Galactosemia	Autosomal recessive
Amino acid disorders (e.g., phenylketonuria)	Autosomal recessive
Edward syndrome	Chromosomal disorder (trisomy 18)
Sickle cell disease	Autosomal recessive
Hemophilia	X-linked recessive
Glucose-6-phosphatase deficiency	X-linked recessive
Patau syndrome	Chromosomal disorder (trisomy 13)
Lesch-Nyhan syndrome	X-linked recessive
Obesity	Polygenic disorder

DISORDER	INHERITANCE PATTERN
Neural tube defects	Polygenic disorder
Turner syndrome	Chromosomal disorder (XO)
Schizophrenia	Polygenic disorder
Duchenne muscular dystrophy	X-linked recessive
Wiskott-Aldrich syndrome	X-linked recessive
Bruton agammaglobulinemia	X-linked recessive
Fragile X syndrome	X-linked recessive
Children's polycystic kidney disease	Autosomal recessive
Wilson disease	Autosomal recessive
Bipolar disorder	Polygenic disorder
Ischemic heart disease	Polygenic disorder
Alcoholism	Polygenic disorder
Hemochromatosis	Autosomal recessive
Adrenogenital syndrome (e.g., 21-hydroxylase deficiency)	Autosomal recessive
Familial polyposis coli	Autosomal dominant
Adult polycystic kidney disease	Autosomal dominant
Hereditary spherocytosis	Autosomal dominant
Tuberous sclerosis	Autosomal dominant
Myotonic dystrophy	Autosomal dominant

MEN, Multiple endocrine neoplasia.
*Fabry disease is the exception to the rule that the sphingolipidosis disorders are autosomal recessive.
†Hunter disease is the exception to the rule that the mucolipopolysaccharidase disorders are autosomal recessive.

2. What is the likelihood that a mother with an autosomal dominant condition will pass the condition to the child if the father does not have the disease?

50%. The father is not a carrier (because autosomal dominant diseases express themselves in carriers), and it is reasonable to assume that the mother has one copy of the diseased gene and one normal gene (unless told otherwise). It is exceedingly rare to find two diseased genes.

3. Genetic testing reveals that both mother and father are carriers of a diseased gene for an autosomal recessive condition but do not have the condition themselves. What are the odds that their first child will develop the condition or be an asymptomatic carrier?

The child has a 25% risk of developing the condition, a 50% risk of being an asymptomatic carrier, and a 25% chance of not inheriting the diseased gene at all.

4. The father has an X-linked recessive disorder. What are the chances that he will pass the disease to his son or daughter if the mother does not have the diseased gene?

There is no chance that he will pass the condition to his son; he will give his son a Y chromosome. On the other hand, there is a 100% chance he will pass the diseased gene to his daughter, but because

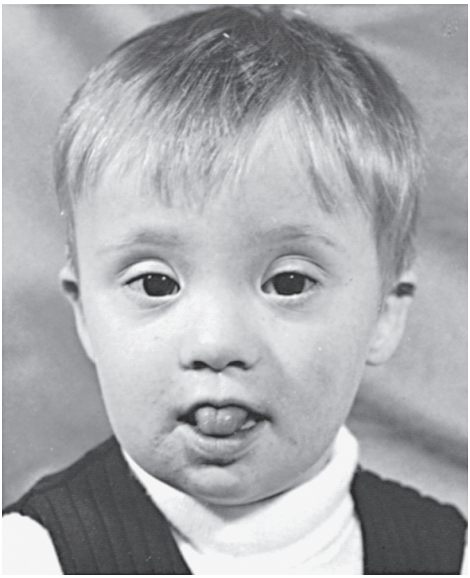

Figure 14-1. Child with Down syndrome. Note the flat facial profile, flat nasal bridge, open mouth, protruding tongue, folded ears, and epicanthic folds. (From Kliegman RM. Nelson textbook of pediatrics. 19th ed. Philadelphia: Saunders, 2011, Fig. 76-8A.).

it is X-linked recessive, she has no chance of developing the condition. She will get a diseased X chromosome from the father and a healthy X chromosome from the mother.

5. The mother is a carrier for an X-linked recessive disorder and the father is healthy. What are the odds that a son or daughter will develop the disease?

There is a 50% chance for a son and no chance for a daughter. However, there is a 50% chance that the daughter will become a carrier.

6. How do you recognize Down syndrome?

Down syndrome (trisomy 21) is the most common known cause of mental retardation in the United States. The biggest risk factor is maternal age (1 in 1500 offspring of 16-year-old mothers and 1 in 25 offspring of 45-year-old mothers). At birth look for hypotonia, transverse palmar crease, and characteristic facies (Fig. 14-1). Congenital cardiac defects (especially ventricular septal defects) are common, and affected persons have an increased risk for leukemia, duodenal atresia, and early Alzheimer disease.

7. What is the second most common known cause of inherited mental retardation?

Fragile X syndrome (X-linked recessive). Affected males often have large testicles.

8. How do you recognize Edward syndrome?

Edward syndrome (trisomy 18) affects females more than males. Characteristics include mental retardation, small size for age, a small head with hypoplastic mandible and low-set ears, and clenched fist with the index finger overlapping the third and fourth fingers (almost pathognomonic; Fig. 14-2; Plate 26).

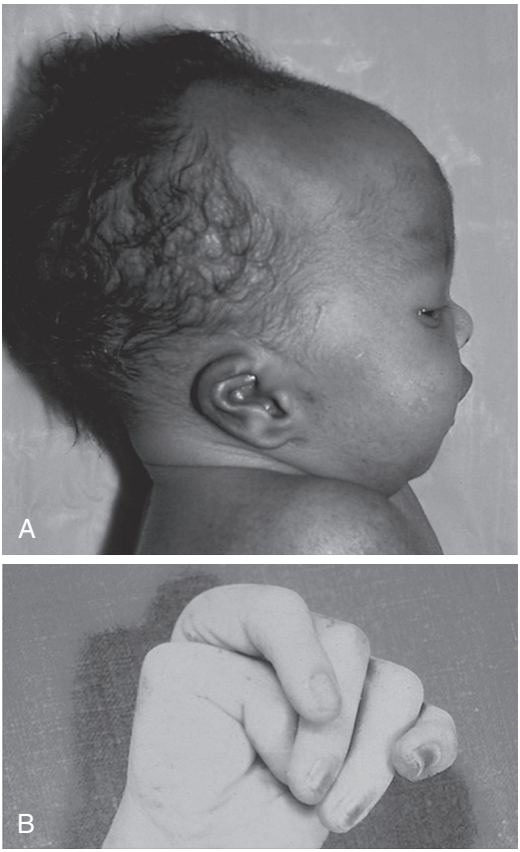

Figure 14-2. Edward syndrome. **A,** Note the small head, prominent occiput, and low-set, malformed ears. **B,** Clenched hand with overlapping fingers. See Plate 26. (Kanski JJ. Clinical diagnosis in ophthalmology. 1st ed. Philadelphia: Mosby, 2006, Fig. 15.10. Courtesy BJ Zitelli and HW Davis).

9. What is Patau syndrome?

Patau syndrome (trisomy 13) presents with mental retardation, apnea, deafness, holoprosencephaly (fusion of cerebral hemispheres), myelomeningocele, cardiovascular abnormalities, and rocker-bottom feet.

10. How do you recognize Turner syndrome?

Patients with Turner syndrome (females with XO instead of XX) have nuchal (neck) lymphedema at birth, short stature, webbed neck, widely spaced nipples, amenorrhea, and lack of breast development (caused by primary ovarian failure; Fig. 14-3; Plate 27). Coarctation of the aorta is common, and you may see horse-shoe kidneys or cystic hygroma. A buccal smear classically reveals absent Barr bodies.

11. Describe Klinefelter syndrome.

Patients with Klinefelter syndrome (males who are XXY instead of XY) are tall with small testes (less than 2 cm in length), gynecomastia, sterility, and a slightly decreased IQ (on average). The classic case on the Step 2 examination is a man who complains of infertility.

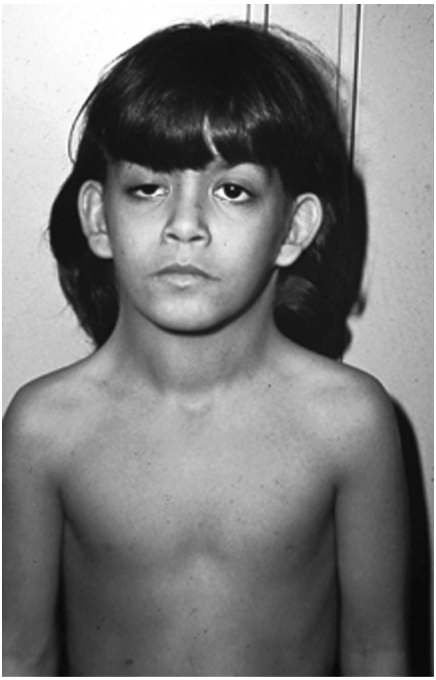

Figure 14-3. Turner syndrome. This 13-year-old female demonstrates the classic webbed neck and triangular facies of Turner syndrome. She has sexual infantilism and short stature. See Plate 27. (Moshang T, ed. Pediatric endocrinology: the requisites in pediatrics. 1st ed. St. Louis: Mosby 2005, Plate 8-2.)

12. What is the hallmark of cri du chat syndrome?

Cri du chat (French for cry of the cat) syndrome is caused by a deletion on the short arm of chromosome 5. Look for a high-pitched cry in an infant that sounds like the cry of a cat along with severe mental retardation.

13. What presentation suggests galactosemia?

Congenital cataracts and neonatal sepsis with vomiting after breast-feeding. Patients should avoid foods containing galactose and lactose.

14. Describe the clinical findings in tuberous sclerosis.

This autosomal dominant disorder presents with hypopigmented skin macules, seizures, mental retardation, central nervous system (CNS) hamartomas (tubers), and an increased risk for cardiac rhabdomyomas and renal tumors known as angiomyolipomas. Look for a positive family history.

15. What causes Lesch-Nyhan syndrome? What classic behavior do patients exhibit?

This syndrome is caused by a deficiency of hypoxanthine-guanine phosphoribosyltransferase (HGPRT), which causes congenital hyperuricemia. Patients have mental retardation and self-mutilating behavior. The classic example is the patient who bites off his or her own fingers.

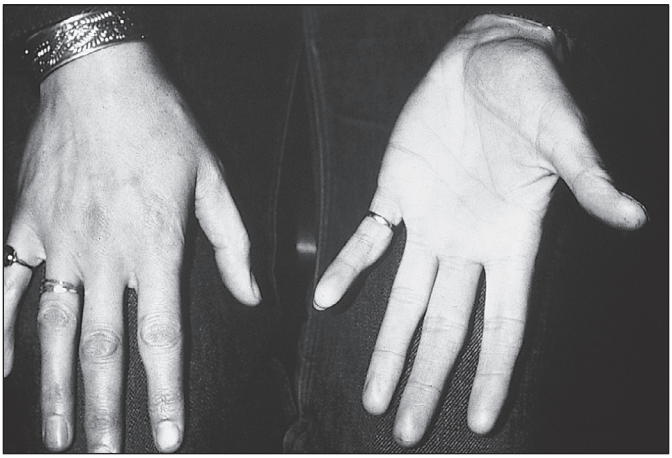

Figure 14-4. Marfan syndrome. Arachnodactyly in a patient with Marfan syndrome. See Plate 28. (Stamper RL, Lieberman MF, Drake MV. Becker-Shaffer's diagnosis and therapy of the glaucomas. 8th ed. Philadelphia: Mosby 2009, Fig. 19.41.)

16. What causes Marfan syndrome? How do you recognize it?

Marfan syndrome is an autosomal dominant connective tissue disorder caused by abnormal microfibrillin protein and is associated with ocular, skeletal, and cardiovascular problems. Look for a positive family history. Patients are tall and have arachnodactyly (long, thin fingers; Fig. 14-4; Plate 28), hyperextensible joints, mitral valve prolapse, dislocation of the lens of the eye, and a high risk for thoracic aortic dissection.

CHAPTER 15

GERIATRICS

1. What age group constitutes the most rapidly growing segment of the population?

Persons older than 85 years of age.

2. True or false: An 80-year-old person needs more calories than a 30-year-old person.

False. An 80-year-old person has half the lean body mass of a 30-year-old person and thus needs fewer calories. The basal metabolic rate is based on lean body mass. Older patients, however, need more sodium, vitamin B_{12}, vitamin D (and/or calcium), folate, and nonheme iron than younger patients.

3. True or false: Hearing and vision changes are a normal part of aging.

True. **Presbyopia** (hardening of the lens that decreases the ability to accommodate) becomes almost universal after age 50, thus the common need for reading glasses after age 50. **Presbyacusis,** the loss of ability to discriminate between sounds, also is part of the normal process of aging.

4. True or false: Brain atrophy is a normal part of aging.

True. Decreased brain weight, enlarged ventricles and sulci, and a slightly decreased ability to learn new material are normal parts of aging.

5. Describe the normal changes in male sexual function that occur with aging.

- Increased refractory period (after ejaculation, it takes longer to achieve another erection)
- Increased time to achieve an erection
- Delayed ejaculation (e.g., an older man may ejaculate only once every three times that he has sex)

6. Describe the normal changes in female sexual function that occur with aging.

- Decreased vaginal lubrication (women not on hormone replacement therapy may use estrogen cream or water-soluble lubricants)
- Dyspareunia caused by atrophy of clitoral, labial, and vaginal tissues (treated with estrogen cream)
- Delayed orgasm

7. True or false: Impotence and lack of sexual desire are normal in older people.

False. Impotence in men and lack of sexual desire in either sex are not normal and should be investigated. Look for psychiatric disorders (e.g., depression) as well as physical causes, such as medications (selective serotonin reuptake inhibitors and antihypertensives are notorious culprits), vascular disease (watch for atherosclerosis risk factors), and neurologic disease (especially in patients with diabetes).

8. What is the best prophylaxis for pressure ulcers in an immobilized patient?

Frequent turning and the use of special air mattresses.

9. Describe the normal changes in sleep habits in older people.
Older persons require less sleep, sleep less deeply, wake up more frequently during the night, and awaken earlier in the morning. It also takes longer for older persons to fall asleep (longer sleep latency), and they have less stage 3 and 4 and rapid eye movement sleep.

10. Define pseudodementia. How do you recognize it?
Depression in older adults can resemble dementia. On the Step 2 examination, look for a history that would trigger depression (e.g., loss of a spouse, terminal or debilitating disease) and other symptoms of depression (e.g., frequent crying, suicidal thoughts).

11. True or false: Roughly 2% of the population is older than age 65.
False. Approximately 15% of people are older than age 65, and this number is increasing.

12. True or false: Almost 50% of patients older than age 65 suffer from some type of dementia.
False. Roughly 15% of people older than 65 suffer from dementia. The most common causes of dementia are Alzheimer dementia, dementia with Lewy bodies, vascular dementia, Parkinson dementia, and frontotemporal dementia. Other disorders that can cause dementia include infection with human immunodeficiency virus (HIV) and Pick disease. Test for reversible causes of dementia such as hypothyroidism, depression, and vitamin B_{12} deficiency.

13. Describe the characteristics of Alzheimer dementia.
Alzheimer dementia is a neurodegenerative disorder primarily affecting older adults and characterized by memory impairment, particularly memory for facts and events. Memory loss develops insidiously and progresses slowly over time. Language function, visuospatial skills, and executive function tend to be affected early in the disease process.

14. Describe the characteristics of dementia with Lewy bodies.
Dementia with Lewy bodies is an increasingly recognized clinical entity characterized by dementia plus two of the three following distinctive clinical features: visual hallucinations, parkinsonism (bradykinesia, limb rigidity, and gait disorders), and cognitive fluctuations. In contrast to Alzheimer dementia, the memory loss in dementia with Lewy bodies presents later in the course of the disease. Early symptoms include driving difficulties (e.g., getting lost) and impaired job performance. Sleep disorders such as acting out dreams are common in patients with dementia with Lewy bodies.

15. Describe a scenario that would make you suspect vascular dementia.
Look for a patient with vascular risk factors (e.g., hypertension, diabetes, dyslipidemia, coronary artery disease) whose presenting symptoms include a dementia with abrupt onset and a stepwise deterioration.

16. True or false: Dementia is common in patients with Parkinson disease.
True. Dementia is a common feature of Parkinson disease. Factors that influence the incidence of dementia include older age, age 60 ears or older at onset of Parkinson disease, longer duration of Parkinson disease, and severity of parkinsonism.

17. Describe the characteristics of frontotemporal dementia.
Frontotemporal dementia is characterized by focal deterioration of the frontal and/or temporal lobes leading to changes in personality or social behavior, with an eventual progression to dementia. Age of onset is typically in the 50s or 60s.

18. True or false: Only 5% of people older than age 65 live in nursing homes.
True. On the Step 2 examination, beware of old-fashioned stereotypes. Not all older persons are demented and living in nursing homes.

CHAPTER 16

GYNECOLOGY

1. What is the most common cause of preventable infertility in the United States?
Pelvic inflammatory disease (PID).

2. What is the most likely cause of infertility in a normally menstruating woman younger than age 30 years?
PID.

3. What is PID? How do you recognize it?
PID is typically caused by an ascending sexually transmitted infection of the upper female genital tract that may involve the endometrial cavity (endometritis), fallopian tubes (salpingitis), ovaries (oophoritis), parametrial tissues/ligaments (parametritis), and/or peritoneal cavity (peritonitis). Look for a female aged 13 to 35 years with the following symptoms: (1) abdominal pain, (2) adnexal tenderness, *and* (3) **cervical motion tenderness.** All three criteria must be present. In addition, one or more of the following should be present: elevated erythrocyte sedimentation rate/C-reactive protein (CRP) level, leukocytosis, fever, or purulent cervical discharge.

4. How is PID treated? What are the common sequelae?
Treat PID with more than one antibiotic to cover multiple organisms, especially *Neisseria gonorrhoeae* and *Chlamydia trachomatis* (the most common organisms). There are several different regimens recommended by the Centers for Disease Control and Prevention, but the following are good choices: ceftriaxone plus doxycycline for outpatients; cefoxitin or cefotetan plus doxycycline for inpatients to cover multiple organisms. Also consider *Escherichia coli,* anaerobes, and, with a history of intrauterine device use, *Actinomyces israelii.*

Common sequelae include infertility caused by scarring of the fallopian tubes and progression to tuboovarian abscess (palpable on examination, may respond to antibiotics alone) that may rupture. Treat rupture with emergent laparotomy and excision of the affected tube (unilateral disease) or total abdominal hysterectomy and bilateral salpingo-oophorectomy for bilateral disease.

5. Define endometriosis. What are the symptoms and signs?
Endometriosis is defined as endometrial glands outside the uterus (ectopic). Patients are usually nulliparous and older than 30 years with the following symptoms: **dysmenorrhea** (painful menstruation), **dyspareunia** (painful intercourse), **dyschezia** (painful defecation), and/or perimenstrual spotting. The most common site for the ectopic endometrial glands is the ovaries; look for tender adnexa in an afebrile patient. Other sites include the broad (uterosacral) ligament and peritoneal surface. Nodularities on the broad ligament are classic findings on physical examination; the classic sequela is a retroverted uterus.

6. How is endometriosis diagnosed and treated?
The gold standard of diagnosis is laparoscopy with visualization of the endometriosis. Treat first with birth control pills (if acceptable to the patient); danazol and gonadotropin-releasing hormone agonists (e.g., leuprolide) are second-line agents. Surgery and cautery can be used to destroy the endometriomas, a procedure that often improves fertility. In an older patient, consider hysterectomy and bilateral salpingo-oophorectomy for severe symptoms.

7. What is the most likely cause of infertility in a menstruating woman older than age 30 without a history of PID?
Endometriosis.

8. Cover the right-hand columns and specify the findings and treatment for the following vaginal infections:

INFECTIOUS AGENT	FINDINGS	TREATMENT
Candida sp.	"Cottage cheese" appearance; pseudohyphae seen on KOH preparation; history of diabetes, antibiotic treatment, or pregnancy	Topical or oral antifungal
Trichomonas vaginalis	Trichomonads can be seen swimming under microscope; pale green, frothy, watery discharge; "strawberry" cervix	Metronidazole
Gardnerella vaginalis	Malodorous discharge; fishy smell on KOH preparation; clue cells	Metronidazole
HPV	Venereal warts, koilocytosis on Pap smear	Many (acid, cryo therapy, laser, podophyllin)
Herpes virus	Multiple shallow, painful ulcers; recurrence and resolution	Acyclovir, valacyclovir
Syphilis (stage I)	Painless chancre, spirochete on dark-field microscopy	Penicillin
Syphilis (stage II)	Condyloma lata, maculopapular rash on palms, serology	Penicillin
Chlamydia trachomatis	Most common STD; dysuria, positive culture and antibody tests	Doxycycline or azithromycin*
Neisseria gonorrhoeae	Mucopurulent cervicitis; gram-negative bacteria on Gram stain	Ceftriaxone
Molluscum	Characteristic appearance of lesions, intracellular inclusions	Curette, cryotherapy, or electrocauterization/ coagulation
Pediculosis	"Crabs"; look for itching; lice can be seen on pubic hairs	Permethrin cream (or malathion)

KOH, Potassium hydroxide; STD, sexually transmitted disease; HPV, Human papillomavirus.
*Chlamydia can be treated with erythromycin if the patient is pregnant. If compliance is an issue (alcoholic, drug abuse, homeless, or unreliable patient), give azithromycin 1 g orally in a single dose so that you can watch the patient take it. Patients with gonorrhea should be treated for presumed chlamydial co-infection (but the opposite is not true).

9. True or false: With all of the infections listed in the previous table, you should seek out and treat the patient's sexual partners.
False. *Candida* and *Gardnerella* species are not typically STDs; they are usually caused by disturbances in the normal vaginal flora. You should treat the patient's sexual partners and give counseling (e.g., condoms) for the other infections, which are sexually transmitted.

10. True or false: Patients with gonorrhea usually are treated for presumed chlamydial infection.

True. A common current treatment strategy is to give both ceftriaxone (for gonorrhea) and doxycycline (for chlamydia) together to patients with gonorrhea. The reverse is not true; do *not* automatically give gonorrhea treatment to patients with chlamydial infection.

11. Define adenomyosis. How does it classically present? What is the treatment?

Adenomyosis is defined as endometrial glands within the uterine musculature. Patients are usually older than 40 with dysmenorrhea and menorrhagia and have a large, boggy uterus on physical examination. Do dilation and curettage first to rule out endometrial cancer. Consider hysterectomy to relieve severe symptoms; gonadotropin-releasing–hormone agonists may also relieve symptoms.

12. What are fibroids? How common are they? How often do they become malignant?

Fibroids (i.e., leiomyomas) are benign uterine tumors (Fig. 16-1). They are the most common tumors in women and the most common indication for hysterectomy (when they grow too large or cause symptoms). Up to 40% of women have fibroids by age 40 years. Malignant transformation is rare (<1%).

13. Explain the relationship between uterine leiomyomas and hormones. How do leiomyomas present? What is the treatment?

Leiomyomas of the uterus are estrogen-dependent. Therefore, you may see rapid growth during pregnancy or use of oral contraceptive pills and regression after menopause. Leiomyomas may cause infertility, pain, and menorrhagia or metrorrhagia. Anemia due to leiomyoma is an indication for hysterectomy. Rare patients present with a polyp protruding through the cervix. Dilation and curettage are needed to rule out endometrial cancer in women who present after the age of 35 years.

Treatment is usually surgical (the levonorgestrel-releasing intrauterine device is seeing more widespread use, although randomized trials are lacking). Myomectomy can sometimes maintain or even restore fertility; the alternative is hysterectomy.

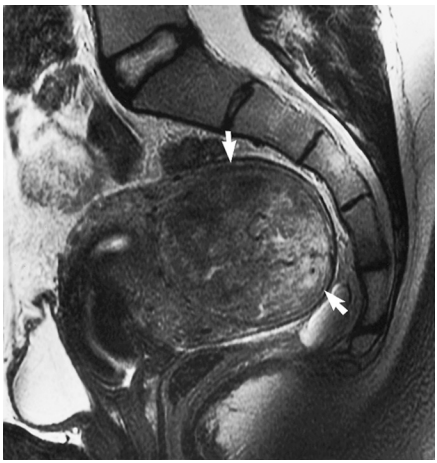

Figure 16-1. This T2-weighted sagittal magnetic resonance imaging (MRI) scan shows a subserosal leiomyoma *(arrows)* that distends the posterior aspect of the uterus, displacing the endometrium. (From Adam A, et al. Grainger and Allison's diagnostic radiology. 5th ed. Edinburgh: Churchill Livingstone, 2008, Fig. 54-12.)

14. What is the first test to order in any woman of reproductive age with abnormal uterine bleeding?

A pregnancy test.

15. Define dysfunctional uterine bleeding (DUB). When is it physiologic?

DUB is defined as abnormal uterine bleeding not associated with a tumor, inflammation, or pregnancy. It is the most common cause of abnormal uterine bleeding and is a diagnosis of exclusion. More than 70% of cases are associated with anovulatory cycles (unopposed estrogen). The age of the patient is important because after menarche and immediately before menopause, DUB is extremely common and, in fact, is considered physiologic. Most other women have polycystic ovary syndrome (PCOS), the most common nonphysiologic cause of DUB.

16. Why is dilation and curettage done in women older than age 35 years with DUB? What other test should be ordered in all women with DUB (regardless of age)?

To rule out endometrial cancer. Hemoglobin and hematocrit (or complete blood count) should be ordered for all women with DUB to make sure that the patient is not anemic from excessive blood loss.

17. What causes DUB other than PCOS? How is DUB treated?

Causes of DUB include infections, endocrine disorders (thyroid, adrenal, pituitary/prolactin), coagulation defects, and estrogen-producing neoplasms. In the absence of treatable pathology, treat first with nonsteroidal anti-inflammatory drugs (NSAIDs), which are first-line agents for DUB and dysmenorrhea. Oral contraceptive pills are also a first-line agent for menorrhagia and DUB if the patient does not desire pregnancy and menstrual cycles are irregular. Monotherapy with progesterone is used for severe bleeding.

18. Define PCOS. How do you recognize it?

PCOS is an endocrine imbalance characterized by androgen excess as well as a ratio of leuteinizing hormone (LH) to follicle-stimulating hormone (FSH) greater than 2:1. Patients also frequently develop enlarged ovaries with multiple peripherally oriented cysts, which can be seen on ultrasound (Figs. 16-2 and 16-3). On the Step 2 exam, watch for an overweight woman who has acne, hirsutism, amenorrhea, and/or infertility.

19. What is the most likely cause for infertility in a woman younger than 30 years with abnormal menstruation?

PCOS.

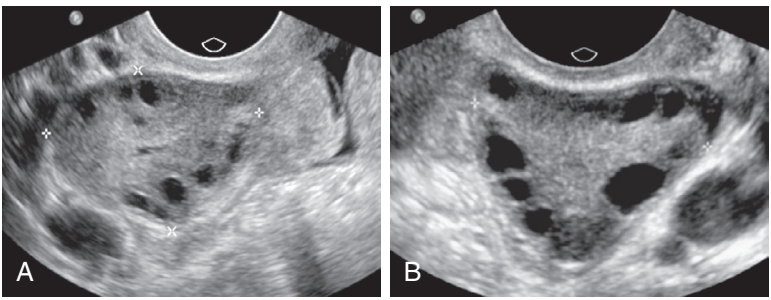

Figure 16-2. Polycystic ovaries. Sagittal **(A)** and transverse **(B)** transvaginal ultrasound of the left ovary depicting enlarged ovaries with multiple subcentimeter peripherally placed follicles and echogenic central stroma. (From Adam A, et al. Grainger and Allison's diagnostic radiology. 5th ed. Edinburgh: Churchill Livingstone, 2008, Fig. 54-22.)

20. How is PCOS treated? With what risk is it associated?

Treat with oral contraceptive pills or cyclic progesterone. If the patient desires pregnancy, you can use **clomiphene** to induce ovulation. Chronic unopposed estrogen (i.e., not enough progesterone; hence, infrequent menses) increases the risk of **endometrial cancer** in affected patients. Spironolactone can be used to treat hirsutism associated with PCOS. Metformin sometimes is used to treat the insulin resistance associated with PCOS and to help restore ovulation. However, metformin is not FDA-approved for this use, and oral contraceptive pills or cyclic progesterone are the preferred agents for endometrial protection.

21. Is infertility usually a male or a female problem?

Two thirds of cases are due to a female problem, one third to a male problem.

22. Assuming that the history and physical exam offer no clues, what is the first step in evaluating a couple for infertility?

Semen analysis, which is cheap, easy, and noninvasive.

23. List the relevant characteristics of normal semen.

- Ejaculate volume > 1 mL
- Sperm concentration > 20 million/mL
- Initial forward motility > 50% of sperm
- Normal morphology > 60% of sperm

24. What is the next step after semen evaluation?

Documentation of ovulation. The history may suggest an ovulatory problem (irregular menstrual cycle length, duration, or amount of flow; lack of premenstrual syndrome symptoms). Basal body temperature, luteal phase progesterone levels, and/or endometrial biopsy can be done to check for ovulation.

25. What radiologic test is commonly used to examine the fallopian tubes and uterus? What points in the history may lead you to suspect a uterine or tube problem?

A hysterosalpingogram is commonly used to examine the uterus and tubes. The history may suggest a tubal problem (PID, previous ectopic pregnancy) or a uterine problem (previous dilation and curettage that caused intrauterine synechiae, history of fibroids, or symptoms of endometriosis).

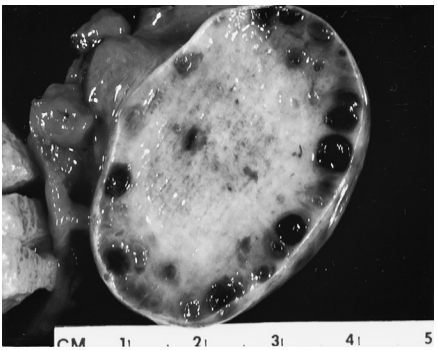

Figure 16-3. This sagittal section of a polycystic ovary demonstrates a large number of follicular cysts and thickened stroma. (From Katz V, et al. Comprehensive gynecology. 5th ed. Philadelphia: Mosby, 2007, Fig. 40-7.)

26. What test is the last resort in the work-up for infertility?

Laparoscopy can be done as a last resort or with a history suggestive of endometriosis. Lysis of adhesions and destruction of endometriosis lesions often restore fertility.

27. Which two medications can be used to restore female fertility? In what situations are they effective?

Medical therapy usually consists of clomiphene citrate to induce ovulation, but this approach requires adequate production of estrogen. If the woman is hypoestrogenic, use human menopausal gonadotropin, which is a combination of FSH and LH. If medications fail, in vitro fertilization can be attempted.

28. What is the main risk associated with medical induction of ovulation?

Multiple gestation pregnancies.

29. Distinguish between primary and secondary amenorrhea.

A patient with primary amenorrhea has never menstruated or had a menstrual period, whereas a patient with secondary amenorrhea used to menstruate but has stopped.

30. Until proved otherwise, what is the cause of secondary amenorrhea in a previously menstruating woman of reproductive age?

Pregnancy. Always order a human chorionic gonadotropin (hCG) test to rule out pregnancy as the first step in your evaluation of secondary amenorrhea.

31. True or false: Excessive exercise may cause amenorrhea.

True. It is not uncommon to find amenorrhea (or hypomenorrhea) in hard-training athletes. It results from an exercise-induced depression of gonadotropin-releasing hormone.

32. What are other common causes of secondary amenorrhea?

- PCOS
- Anorexia (amenorrhea is required for a diagnosis of anorexia)
- Endocrine disorders (headaches, galactorrhea, and visual field defects may indicate a pituitary tumor)
- Antipsychotics (due to increased prolactin)
- Previous chemotherapy (causes premature ovarian failure and menopause)

Although not considered secondary amenorrhea, **menopause** should be kept in mind as a cause for cessation of menstruation.

33. After ruling out pregnancy, if the cause of secondary amenorrhea is not obvious from the history and physical exam, what is the next step in your evaluation?

Administer progesterone to assess the patient's estrogen status. If vaginal bleeding develops within 2 weeks of administering progesterone, the patient has sufficient estrogen. In this case, check the LH level. If it is high, consider PCOS. If it is low or normal, check the levels of prolactin and thyroid-stimulating hormone (TSH). The high TSH level in hypothyroidism causes high prolactin levels. If the prolactin is high with a normal TSH level, order a magnetic resonance imaging (MRI) scan of the brain to rule out pituitary prolactinoma. If the prolactin level is normal, look for low levels of gonadotropin-releasing hormone, which may be induced by drugs, stress, or exercise. In these patients, clomiphene can be used in an attempt to facilitate pregnancy.

34. What if the patient fails to have vaginal bleeding after receiving progesterone?

If the patient has no vaginal bleeding, estrogen levels are inadequate. Check the FSH level next. If it is elevated, premature ovarian failure is the problem; check for autoimmune disorders, karyotype abnormalities, and a history of chemotherapy. If the FSH level is low or normal, the problem may be a brain tumor (e.g., craniopharyngioma). Order an MRI scan of the brain. Clomiphene is ineffective in these patients.

35. True or false: Pregnancy can present as primary amenorrhea.

True. Always assess the hCG level in the evaluation of any type of amenorrhea.

36. At what age can primary amenorrhea be diagnosed? What is the first step in evaluation?

A diagnosis of primary amenorrhea is made when a girl has not menstruated by age 16 years. Patients also should be evaluated in the absence of secondary sexual characteristics by age 14 years or in the absence of menstruation within 2 years of developing secondary sex characteristics (breast development, axillary and pubic hair). The first step is to rule out pregnancy.

37. In a patient older than 14 years with no secondary sexual characteristics or development, what is the most likely cause of amenorrhea?

The most likely cause in this setting is a congenital problem. In a phenotypically normal female with normal breast development but no axillary or pubic hair, think of **androgen insensitivity syndrome.** In such patients, the uterus is absent. In the presence of normal breast development and a uterus, the first step is to assess the prolactin level to rule out pituitary adenoma. If the prolactin level is high, order an MRI scan. If it is normal, administer progesterone and follow the same procedure as in the evaluation of secondary amenorrhea.

38. When in doubt, what is the best way to evaluate any type of amenorrhea?

First, order a pregnancy test. If it is negative, administer progesterone. Further testing depends on the results of the progesterone challenge (bleeding or no bleeding). A TSH level and/or prolactin level should also be ordered, especially with symptoms of hypothyroidism or pituitary tumor.

39. When does menopause occur? What are the symptoms and signs?

The average age of menopause is around 51 years. Patients have irregular cycles or amenorrhea, hot flashes and mood swings, and an elevated FSH level. Patients also may complain of dysuria, dyspareunia, incontinence, and/or vaginal itching, burning, or soreness. Vaginal symptoms often are due to atrophic vaginitis; look for the vaginal mucosa to be thin, dry, and atrophic with increased parabasal cells on cytology. Topical estrogen improves vaginal symptoms, but other symptoms require oral therapy.

40. What is the current state of hormone replacement therapy?

Hormone replacement therapy is currently recommended short-term for the management of moderate-to-severe vasomotor flushing. Long-term use for the prevention of disease (e.g., osteoporosis, cardiovascular disease) is no longer recommended based on the results of the Women's Health Initiative and the Heart and Estrogen/Progestin Replacement Study (HERS) trial.

41. When a woman presents with a nipple discharge, what historical points are important?

A history of using oral contraceptive pills, hormone therapies, antipsychotic medications, or symptoms suggestive of hypothyroidism, which can all cause nipple discharge. The color of the discharge and whether the discharge is unilateral or bilateral is also very important. For example, if nipple discharge is bilateral and nonbloody, it is not due to breast cancer, but it may be due a prolactinoma (check prolactin level) or endocrine disorder (check a thyroid stimulating hormone level). Alternatively, when nipple discharge is unilateral and bloody (nipple discharge secondary to carcinoma generally contains hemoglobin), and/or associated with a mass, this should raise concern about possible breast cancer. Do a biopsy of any mass if present.

42. What are the most likely causes of a breast mass in a woman younger than age 35 years?

Fibrocystic disease: Bilateral, multiple, cystic lesions that are tender to the touch, especially premenstrually. This is the most common of all breast diseases. Generally, no work-up is needed other than routine follow-up. Oral contraceptive pills, progesterone, or danazol may help relieve symptoms.

Fibroadenoma: A painless, discrete, sharply circumscribed, unilateral, rubbery, mobile mass. This is the most common benign tumor of the female breast. Patients may be observed for one or more menstrual cycles in the absence of symptoms. Because tumors are estrogen-dependent, pregnancy and oral contraceptive pills may stimulate growth, whereas menopause causes regression. Excision is curative but not required except for cosmetic reasons.

Mastitis/abscess: Typically in the first few months postpartum, lactating women may develop a painful, swollen, erythematous breast. The nipple may be cracked or fissured. The patient should be treated with analgesics (e.g., acetaminophen, ibuprofen) and instructed to continue breastfeeding with the affected breast(s) even though it is painful (use a breast pump to empty the breast if needed) to prevent further milk duct blockage and abscess formation. An antistaphylococcal antibiotic (e.g., dicloxacillin, cephalexin) should be given when symptoms are more than mild. If there is risk for methicillin-resistant *Staphylococcus aureus* (MRSA) or if MRSA is cultured, use trimethoprim-sulfamethoxazole or clindamycin. If a fluctuant mass develops or there is no response to antibiotics within a few days, an abscess is likely present and must be drained.

Fat necrosis: Patients have a history of trauma in the area of the mass.

43. True or false: Mammography should be done for any suspicious breast lesion in a woman younger than age 30 years.

False. Mammography is usually not done in women younger than age 30 years because breast tissue is often too dense to discern a mass. If you are suspicious of breast cancer, which is very rare in this age group, proceed to ultrasound imaging or directly to biopsy.

44. What are the likely causes of a breast mass in a woman older than age 35 years?

Fibrocystic disease: As mentioned previously, but aspiration of cyst fluid and baseline mammography are recommended. If the cyst fluid is nonbloody and the mass resolves after aspiration, the patient needs only reassurance and follow-up (with a baseline mammogram). If the fluid is bloody or the cyst recurs quickly, do a biopsy to rule out cancer.

Fibroadenoma: Get a baseline mammogram. Observe briefly if the mass is small and seems benign clinically *and* if the woman is premenopausal and has no risk factors for breast cancer. Otherwise, do a biopsy. Phyllodes tumors (minority are malignant) may masquerade as a fibroadenoma.

Fat necrosis: As mentioned previously.

Mastitis/abscess: As mentioned previously.

Breast cancer: On the Step 2 exam, you may not get the classic presentation of nipple retraction and/or peau d'orange in a nulliparous woman with a strong family history. In a woman 35 years old or older, you will never be faulted for doing a biopsy of any mass. In the absence of a classic benign presentation (e.g., trauma to the breast with fat necrosis, bilateral masses with premenstrual syndrome mastalgia), always consider biopsy. Also get a baseline mammography.

45. True or false: If a patient is postmenopausal or older than age 50 years and a new breast mass develops, you should assume cancer "until proven otherwise."

True. After menopause, the risk of breast cancer begins to increase sharply, and the incidence of benign disorders begins to decrease sharply. Most benign disorders are caused by reproductive hormones that are present in younger women.

46. True or false: Mammography is best used as a tool to evaluate a palpable breast mass.

False. Mammography is best used as a tool to detect nonpalpable breast masses (as a screening tool). A suspicious lesion found on mammography should be biopsied, even if it seems benign or is inapparent on physical exam. Additionally, a clinically suspicious mass should be biopsied unless imaging demonstrates unequivocally benign findings (e.g., a cyst).

47. What causes pelvic relaxation or vaginal prolapse? What are the symptoms and signs?

Pelvic relaxation is due to a weakening of pelvic supporting ligaments. Look for a history of several vaginal deliveries, feeling of heaviness or fullness in the pelvis, backache, worsening of symptoms with standing, and resolution of symptoms with lying down.

48. What types of pelvic relaxation are seen clinically? How are they treated?

Cystocele: The bladder bulges into the *upper anterior vaginal wall.* Common symptoms include urinary urgency, frequency, and/or incontinence.

Rectocele: The rectum bulges into the *lower posterior vaginal wall.* Watch for difficulty with defecation.

Enterocele: Loops of bowel bulge into the *upper posterior vaginal wall.*

Urethrocele: The urethra bulges into the *lower anterior vaginal wall.* Common symptoms include urinary urgency, frequency, and/or incontinence.

Conservative treatment for all types of pelvic relaxation involves pelvic strengthening exercises and/or a pessary (artificial device to provide support). Surgery is used for refractory or severe cases or by patient choice.

49. Other than abstinence, what are the most effective forms of birth control (when used properly)?

The most effective forms of birth control are sterilization (e.g., tubal ligation, vasectomy), implants (etonogestrel implant), or an intrauterine device, followed by injectable hormone depot preparations (progesterone), birth control pills/patch, and then hormonal vaginal ring.

50. Which forms of birth control prevent STDs?

Abstinence and condoms.

51. What are the major problems with intrauterine devices?

They increase the risk of ectopic pregnancies and PID (watch for *Actinomyces* spp. to be the cause). For these reasons, they are most appropriate for older, monogamous women.

52. What is the classic cause of ambiguous genitalia on the Step 2 exam?

Adrenogenital syndrome, also known as congenital adrenal hyperplasia. Ninety percent of cases are caused by **21-hydroxylase deficiency.** Girls present as neonates with ambiguous genitalia. Boys present as neonates with salt-losing adrenal crisis or as toddlers with precocious sexual development. Patients with 21-hydroxylase deficiency have salt-wasting (low sodium), hyperkalemia, hypotension, and elevated 17-hydroxyprogesterone. Treat with steroids and intravenous fluids immediately to prevent death.

53. What should you tell the parents of a child with ambiguous genitalia?

Tell the parents the truth: you do not know the child's gender. No patient with ambiguous genitalia should be assigned a sex until the work-up is complete. A karyotype must be done.

54. What is indicated by a “bunch of grapes” protruding from a pediatric vagina?

Sarcoma botryoides, a malignant tumor (a type of embryonal rhabdomyosarcoma).

55. Define precocious puberty. What causes it? How should it be treated?

By definition, precocious puberty occurs in girls younger than 8 years old or boys younger than 9 years old. Premature or precocious puberty is usually idiopathic, but it may be caused by a hormone-secreting tumor (e.g., Leydig cell tumor) or central nervous system (CNS) disorder (e.g., hamartoma, astrocytoma), both of which must be ruled out. Treat the underlying cause. If the condition is idiopathic, treat with a gonadotropin-releasing hormone analog to prevent premature epiphyseal closure and arrest or reverse puberty until an appropriate age.

56. What causes vaginitis or discharge in prepubescent girls?

Most cases are nonspecific or physiologic, but look for a vaginal foreign body, sexual abuse (especially if an STD is present), or candidal infection. A candidal infection may be a presentation of diabetes; check the serum glucose level and/or the urine for glycosuria.

57. How do you recognize and treat an imperforate hymen?

Imperforate hymen classically presents at menarche with hematocolpos (blood in the vagina) that cannot escape; thus, the hymen bulges outward. Treatment is surgical opening of the hymen.

58. What is the usual cause of vaginal bleeding in neonates? How is it treated?

Vaginal bleeding in neonates is usually physiologic and due to maternal estrogen withdrawal. No treatment is needed because the bleeding resolves on its own.

59. Which women are candidates for hormone replacement therapy?

Hormone replacement therapy (i.e., estrogen with or without progesterone) is now controversial and probably best used only as a means of symptom relief. Observation during therapy is necessary because estrogen and progesterone are not harmless. Every woman should make the decision on her own after weighing the risks and benefits. See questions 60-64 for more details.

60. What are the known benefits of estrogen therapy?

- Decreased osteoporosis and decreased fractures
- Reduced hot flashes and genitourinary symptoms of menopause (dryness, urgency, atrophy-induced incontinence, frequency)
- Decreased risk of colorectal cancer (according to the Women's Health Initiative, when combined estrogen and progesterone therapy is used)

61. What are the known risks of estrogen therapy?

- Increased risk of endometrial cancer (eliminated by coadministration of progesterone)
- Small increase in risk of coronary heart disease with combined estrogen and progesterone therapy, although the risk is not increased in women who are less than 10 years postmenopausal or 50 to 59 years of age
- Increased risk of venous thromboembolism
- Increased risk of breast cancer (according to the Women's Health Initiative when combined estrogen and progesterone therapy is used. There was a slightly decreased risk of breast cancer with estrogen only, although this decrease was not statistically significant.)
- Increased risk of stroke (according to the Women's Health Initiative, with either estrogen only or combined estrogen and progesterone therapy)
- Increased risk of gallbladder disease

62. What are the most common side effects of estrogen therapy?

- Endometrial bleeding
- Bloating
- Breast tenderness
- Headaches
- Nausea

63. What are the absolute contraindications to estrogen therapy?

- Unexplained vaginal bleeding
- Active liver disease
- History of thromboembolism
- Coronary artery disease
- History of endometrial or breast cancer
- Pregnancy

64. What are the relative contraindications to estrogen therapy?

- Seizure disorder
- Hypertension
- Uterine leiomyomas
- Familial hyperlipidemia
- Migraine headaches
- Thrombophlebitis
- Endometriosis
- Gallbladder disease

65. What test is often done before starting estrogen therapy?

Women classically undergo an endometrial biopsy, ultrasound, or dilation and curettage at the beginning of treatment to rule out endometrial hyperplasia and/or cancer; evaluation of any unexplained bleeding is done, even while on therapy, unless such an evaluation yielded normal results within the past 6 months.

66. True or false: Women without a uterus do not need to take progesterone with estrogen.

True. The main reason for giving progesterone with hormone replacement therapy is to eliminate the increased risk of endometrial cancer that accompanies unopposed estrogen therapy. If a woman has no uterus, then she has no need for progesterone.

67. What are the absolute contraindications to oral contraceptive pills?

- Venous thromboembolism, current or past (deep venous thrombosis [DVT] or pulmonary embolism [PE])
- Cerebrovascular disease (stroke)
- Coronary artery disease
- Complicated valvular heart disease
- Diabetes with complications
- Breast cancer
- Pregnancy
- Lactation (fewer than 6 weeks postpartum)
- Liver disease
- Headaches with focal neurologic symptoms
- Major surgery with prolonged immobilization
- Age older than 35 years and smoking of 15 or more cigarettes per day
- Hypertension (blood pressure greater than 160/100 mm Hg or with concomitant vascular disease)

68. What are the relative contraindications to oral contraceptive pills?

- Postpartum fewer than 21 days
- Lactation (6 weeks to 6 months)
- Undiagnosed vaginal or uterine bleeding
- Age older than 35 years and smoking of fewer than 15 cigarettes per day
- History of breast cancer but no recurrence in past 5 years
- Interacting drugs (certain anticonvulsants, rifampin)
- Gallbladder disease
- Headaches without aura, age 35 years or older
- Hypertension (well-controlled or blood pressure 140-159/90-99 mm Hg)

69. What is the relationship between oral contraceptive pills and hypertension?

Oral contraceptive pills are one of the most common causes of secondary hypertension. Any patient taking birth control pills who is noted to have an increased blood pressure should discontinue the pills, then have her blood pressure rechecked at a later date.

70. What do you need to know about oral contraceptive pills and surgery?

Because of the risks of thromboembolism, oral contraceptive pills should be stopped 1 month before elective surgery and not restarted until 1 month after surgery.

71. What are the side effects of oral contraceptive pills?

The side effects include glucose intolerance (check for diabetes mellitus annually in women at high risk), depression, edema (bloating), weight gain, cholelithiasis, **benign liver adenomas,** melasma ("the mask of pregnancy"), nausea, vomiting, headache, hypertension, and drug interactions. Drugs such as rifampin and antiepileptics may induce metabolism of oral contraceptive pills and reduce their effectiveness.

72. What is the relationship between oral contraceptive pills and breast and cervical cancer?

Oral contraceptive pills have little, if any, effect on the risk of developing breast cancer. Cervical neoplasia may be increased in users of birth control pills, but this effect also may be due to the confounding factor of increased sexual relations or number of partners. Nonetheless, users of birth control pills should have regular Pap smears.

73. What is the relationship between oral contraceptive pills and ovarian and endometrial cancer?

Oral contraceptive pills have been shown to reduce the incidence of ovarian cancer by 50%; they also reduce the incidence of endometrial cancer.

74. What are the other beneficial effects of oral contraceptive pills?

They decrease the incidence of menorrhagia, dysmenorrhea, benign breast disease, functional ovarian cysts (often prescribed for the previous four effects), premenstrual tension, iron-deficiency anemia, ectopic pregnancy, and salpingitis.

CHAPTER 17

HEMATOLOGY

1. Define anemia.

Hemoglobin less than 12 mg/dL in women or less than 14 mg/dL in men.

2. What are the symptoms and signs of anemia?

Symptoms: Fatigue, dyspnea on exertion, light-headedness, dizziness, syncope, palpitations, angina, and claudication.

Signs: Tachycardia, pallor (especially of the sclera and mucous membranes), systolic ejection murmurs (from high flow), and signs of the underlying cause (e.g., jaundice, pigment **gallstones** (Fig. 17-1; Plate 29) in hemolytic anemia, positive stool guaiac with a gastrointestinal [GI] bleed).

3. What are the important elements of the history when anemia is present?

Important points include medications, blood loss (e.g., trauma, surgery, melena, hematemesis, menorrhagia), chronic diseases (anemia of chronic disease), family history (e.g., hemophilia, thalassemia, sickle cell disease, glucose-6-phosphatase deficiency), and alcoholism (which may lead to iron, folate, and B_{12} deficiencies as well as GI bleeds).

4. What medications can cause anemia? How?

Many medications can cause anemia through various mechanisms. Methyldopa, penicillins, and sulfa drugs can cause red blood cell (RBC) antibodies with subsequent hemolysis; chloroquine and sulfa drugs cause hemolysis in patients with glucose-6-phosphatase deficiency; phenytoin causes megaloblastic anemia through interference with folate metabolism; and chloramphenicol, cancer drugs, and zidovudine cause aplastic anemia and bone marrow suppression. Other drugs also are implicated, but this list should be sufficient for answering questions on the USMLE.

5. What test should be ordered first to help determine the cause of anemia?

The complete blood count (CBC) with red blood cell indices. First and foremost, the hemoglobin must be below normal to diagnose anemia. The mean corpuscular volume (MCV) tells you whether the anemia is microcytic (MCV < 80), normocytic (MCV = 80-100), or macrocytic (MCV > 100).

6. What test should be ordered next?

Peripheral blood smear. There are many "classic" findings that can help make the diagnoses:

- Sickled cells (sickle cell disease; Fig. 17-2; Plate 30).
- Hypersegmented neutrophils (folate/B_{12} deficiency; Fig. 17-3; Plate 31).
- Hypochromic and microcytic RBCs (iron deficiency; Fig. 17-4; Plate 32).
- Basophilic stippling (lead poisoning; Fig. 17-5; Plate 33).
- Heinz bodies (glucose-6-phosphatase deficiency; Fig. 17-6; Plate 34).
- "Bite cells" (classically, glucose-6-phosphatase deficiency; other hemolytic anemias; Fig. 17-6; Plate 34).
- Howell-Jolly bodies (asplenia; Fig. 17-7; Plate 35).
- Teardrop-shaped RBCs (myelofibrosis; Fig. 17-8; Plate 36).
- Schistocytes, helmet cells, and fragmented RBCs (intravascular hemolysis; Fig. 17-9; Plate 37).
- Spherocytes and elliptocytes (hereditary spherocytosis and elliptocytosis; Fig. 17-10; Plate 38).
- Acanthocytes and spur cells (abetalipoproteinemia; Fig. 17-11; Plate 39).

- Target cells (thalassemia, liver disease; Fig. 17-12; Plate 40).
- Echinocytes, including "burr" cells and acanthocytes (uremia; Fig. 17-13; Plate 41).
- Polychromasia (from **reticulocytosis**; should alert you to the possibility of hemolysis; Fig. 17-14; Plate 42).
- Rouleaux formation (multiple myeloma; Fig. 17-15; Plate 43).
- Parasites inside red blood cells (RBCs) (malaria [Fig. 17-16; Plate 44], babesiosis).
- Iron inclusions in RBCs of the bone marrow (sideroblastic anemia; Fig. 17-17; Plate 45).

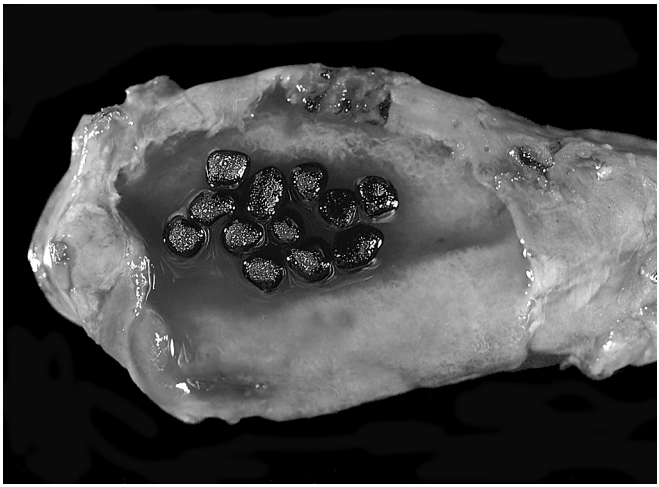

Figure 17-1. Pigment gallstones within an otherwise unremarkable gallbladder are a marker for hemolytic anemia. See Plate 29. (From Kumar V, Abbas AK, Fausto N, Aster JC. Robbins and Kotran pathologic basis of disease, professional edition. 8th ed. Philadelphia: Saunders, 2009, Fig. 18-53.)

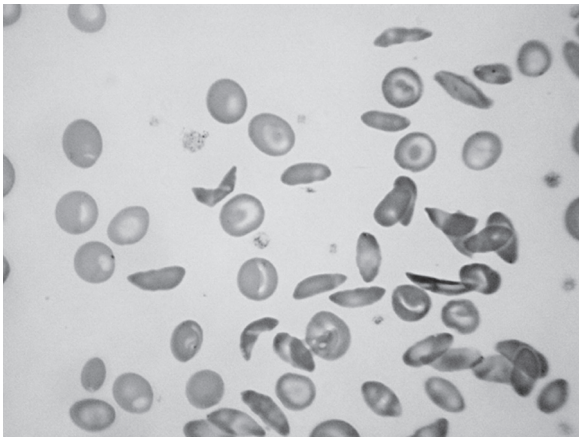

Figure 17-2. Sickle cells show a sickle or crescent shape resulting from the polymerization of hemoglobin S. This smear also shows target cells and boat-shaped cells with a lesser degree of polymerization of hemoglobin S than in a classic sickle cell. See Plate 30. (From Goldman L, Schafer AI. Goldman's Cecil medicine. 24th ed. Philadelphia: Saunders, 2011, Fig. 160-7.)

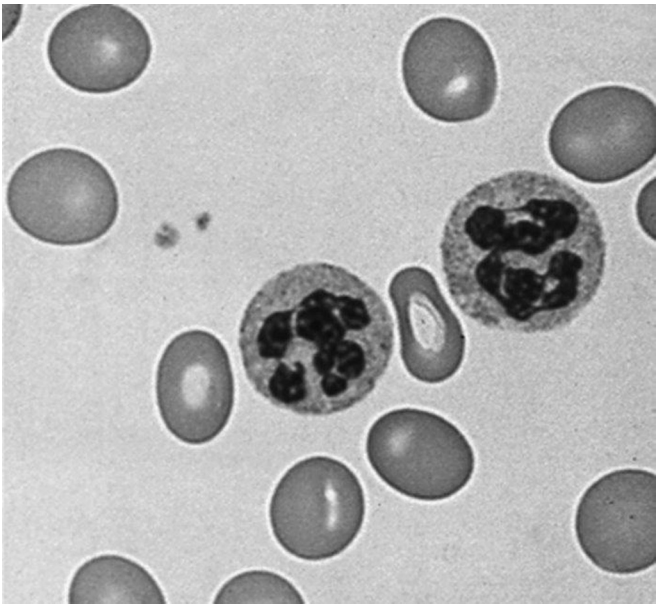

Figure 17-3. Megaloblastic changes of macrocytosis and a hypersegmented neutrophil. See Plate 31. (From Rakel RE, Rakel DP. Textbook of family medicine. 8th ed. Philadelphia: Saunders, 2011, Fig. 39-4; The American Society of Hematology Image Bank image #2611. Copyright 1996 American Society of Hematology, used with permission.)

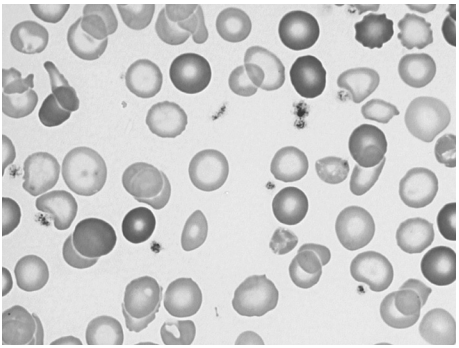

Figure 17-4. Iron-deficiency anemia. Pale red blood cells (RBCs) with enlarged central pallor. See Plate 32. (From McPherson R, Pincus M. Henry's clinical diagnosis and management by laboratory methods. 21st ed. Philadelphia: Saunders, 2006, Fig. 31-2.)

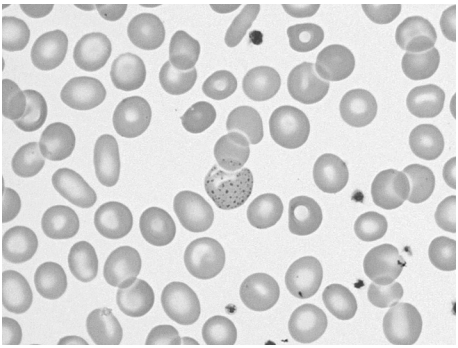

Figure 17-5. Basophilic stippling. Irregular basophilic granules in red blood cells (RBCs); often associated with lead poisoning and thalassemia. See Plate 33. (From McPherson R, Pincus M. Henry's clinical diagnosis and management by laboratory methods. 21st ed. Philadelphia: Saunders, 2006, Fig. 29-23.)

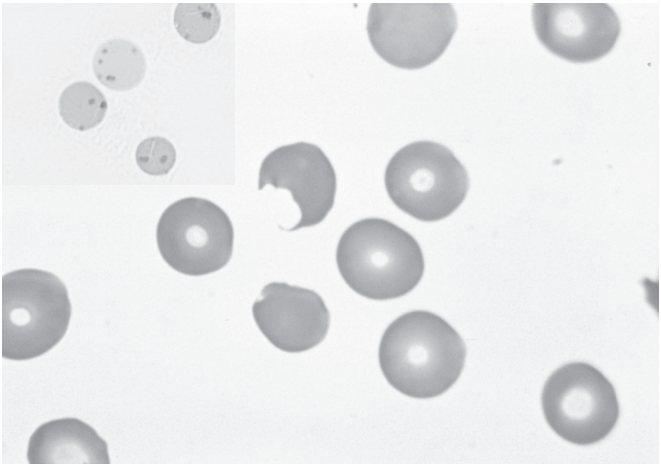

Figure 17-6. Bite cells with Heinz bodies. See Plate 34. (Courtesy Dr. Robert W. McKenna, Department of Pathology, University of Texas Southwestern Medical School, Dallas, Texas.)

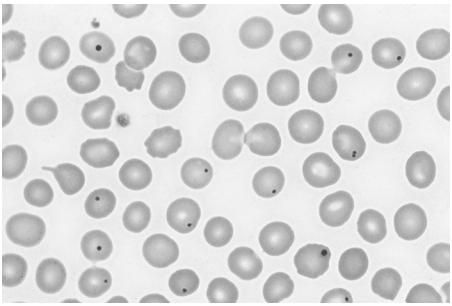

Figure 17-7. Howell-Jolly bodies in peripheral blood erythrocytes. These nuclear remnants indicate lack of splenic filtrative function. See Plate 35. (From Orkin SH, et al. Nathan and Oski's hematology of infancy and childhood. 7th ed. Philadelphia: Saunders: 2009, Fig. 14-4.)

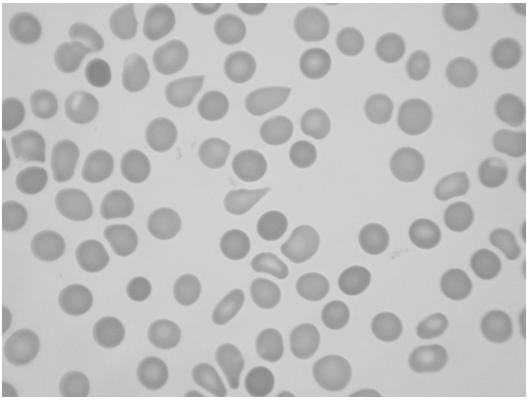

Figure 17-8. Teardrop red blood cells (RBCs), usually seen in myelofibrosis. See Plate 36. (From Goldman L, Ausiello D. Cecil medicine. 23rd ed. Philadelphia: Saunders, 2008, Fig. 161-13.)

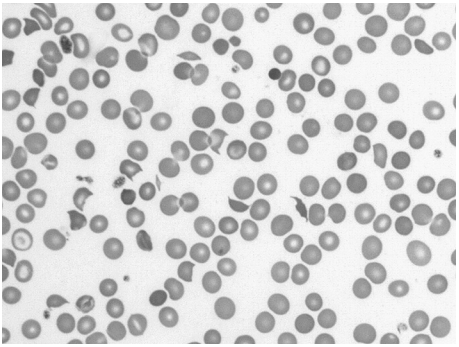

Figure 17-9. Schistocytes and helmet cells. Red blood cell (RBC) fragments seen with microangiopathic hemolytic anemia and disseminated intravascular coagulation (DIC). See Plate 37. (From McPherson R, Pincus M. Henry's clinical diagnosis and management by laboratory methods. 21st ed. Philadelphia: Saunders, 2006, Fig. 29-19.)

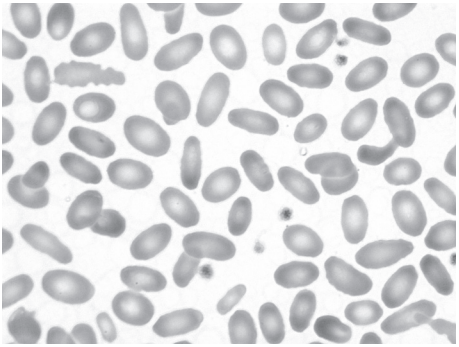

Figure 17-10. Hereditary elliptocytosis. Blood film reveals characteristic elliptical red blood cells (RBCs). See Plate 38. (From McPherson RA, Pincus MR. Henry's clinical diagnosis and management by laboratory methods. 22nd ed. Philadelphia: Saunders, 2011, Fig. 30-16.)

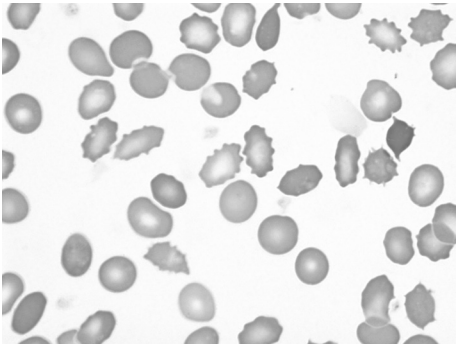

Figure 17-11. Acanthocytes. Irregularly spiculated red blood cells (RBCs), frequently seen in abetalipoproteinemia or liver disease. See Plate 39. (From McPherson R, Pincus M. Henry's clinical diagnosis and management by laboratory methods. 21st ed. Philadelphia: Saunders, 2006, Fig. 29-20.)

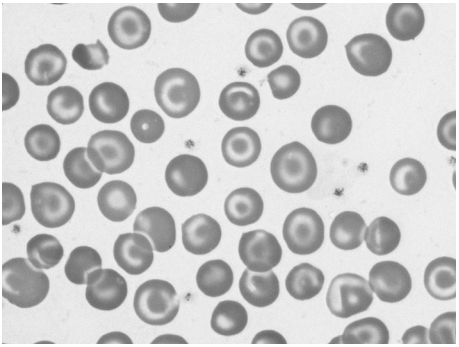

Figure 17-12. Target cells are frequently seen in hemoglobin C disease and liver disease. See Plate 40. (From McPherson R, Pincus M. Henry's clinical diagnosis and management by laboratory methods. 21st ed. Philadelphia: Saunders, 2006, Fig. 29-18.)

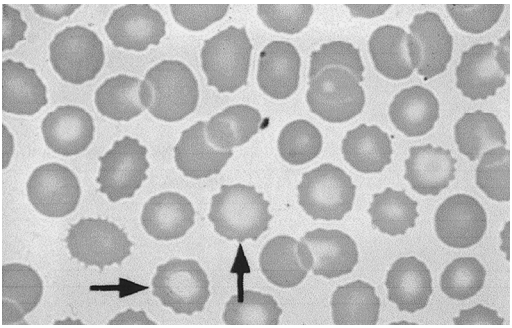

Figure 17-13. Echinocytes, or burr cells *(arrows),* are the hallmark of uremia. See Plate 41. (Hoffman R, et al. Hematology: basic principles and practice. 5th ed. Philadelphia: Churchill Livingstone, 2008, Fig. 156-1.)

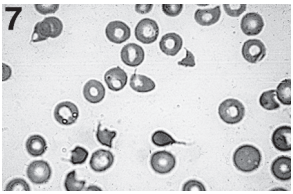

Figure 17-14. Microangiopathic hemolytic anemia demonstrating red blood cell (RBC) fragments, anisocytosis, polychromasia, and decreased platelets. See Plate 42. (From Tschudy MM, Arcara KM, editors. The Harriet Lane handbook. 19th ed. Philadelphia: Mosby, 2011, Plate 7.)

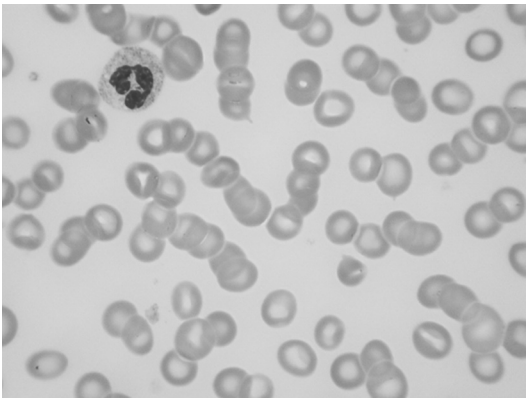

Figure 17-15. Rouleaux formation of stacked red blood cells (RBCs) seen in multiple myeloma. See Plate 43. (From Goldman L, Ausiello D. Cecil Medicine. 23rd ed. Philadelphia: Saunders, 2008, Fig. 161-19.)

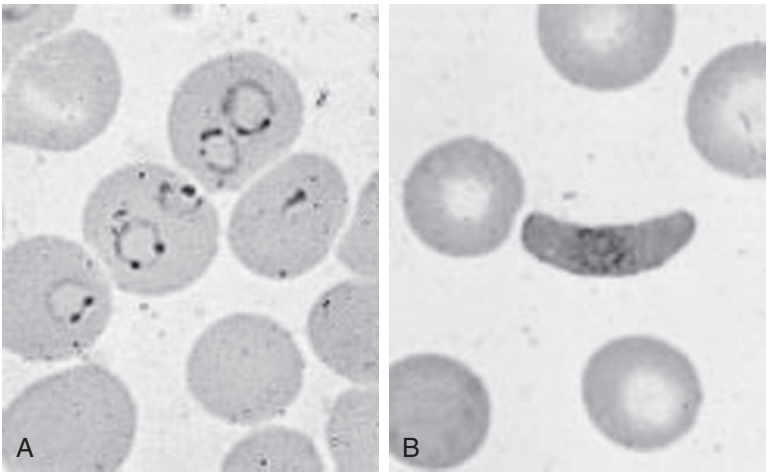

Figure 17-16. Malaria. Peripheral blood film examples of various stages of *Plasmodium falciparum*. **A,** Small ring forms. **B,** A crescentic gametocyte with centrally placed chromatin. See Plate 44. (From Hoffman R, et al. Hematology: basic principles and practice. 5th ed. Philadelphia: Churchill Livingstone, 2008, Fig. 159-5.)

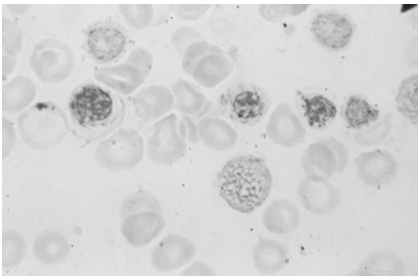

Figure 17-17. Ringed sideroblasts seen in sideroblastic anemia. See Plate 45. (From Goldman L, Ausiello D. Cecil medicine. 23rd ed. Philadelphia: Saunders, 2008, Fig. 163-5.)

7. What are reticulocytes? Why is a reticulocyte count routinely ordered in an anemia workup?

Reticulocytes are immature RBCs. If their count is abnormally decreased in the setting of anemia, the marrow is not responding properly and is the problem. A high reticulocyte count should make you think of hemolysis or blood loss as the cause (the marrow is responding properly and is not the problem).

8. Which test comes next?

At this point, it depends. If you have a complete history and results of the other three tests (CBC with red blood cell indices, peripheral smear, and reticulocyte count), most possibilities will be eliminated and you can order a confirmatory test. If the answer is still not clear, consider a bone marrow biopsy. For the Step 2 examination, biopsy is unlikely to be necessary unless malignancy is the cause of the anemia.

9. What are the classic causes of microcytic, normocytic, and macrocytic anemia? Which of these tends to have an inappropriately low reticulocyte count?

MICROCYTIC	NORMOCYTIC
With normal or elevated reticulocyte count	*With normal or elevated reticulocyte count*
Thalassemia/hemoglobinopathy (e.g., sickle cell disease)	Acute blood loss Hemolytic (multiple causes) Medications (antibody-causing)
With low reticulocyte count	*With low reticulocyte count*
Lead poisoning Sideroblastic anemia Anemia of chronic disease (some cases) Iron deficiency	Cancer/dysplasia (e.g., myelophthisic anemia, acute leukemia) Anemia of chronic disease (some cases) Aplastic anemia/medications causing bone marrow suppression Endocrine failure (thyroid, pituitary) Renal failure
MACROCYTIC	
All types have low reticulocyte count	
Folate deficiency Vitamin B_{12} deficiency Medications (methotrexate, phenytoin) Alcohol abuse (interferes with folate use) Cirrhosis, liver disease	

10. What clues point to hemolysis as the cause for anemia?

- Elevated lactate dehydrogenase (LDH)
- Elevated bilirubin (unconjugated as well as conjugated if the liver is functioning)
- Jaundice
- Low or absent haptoglobin (intravascular hemolysis only)
- Urobilinogen, bilirubin, and hemoglobin in urine (only conjugated bilirubin shows up in the urine, and hemoglobin shows up in the urine only when haptoglobin has been saturated, as in brisk intravascular hemolysis)
- Pigmented gallstones or history of cholecystectomy (usually at a young age)

11. What is the most common cause of anemia in the United States?

Iron deficiency anemia.

12. Why do people get iron deficiency?

Iron deficiency is common in women of reproductive age because of menstrual blood loss. In all patients older than age 40 (men and especially postmenopausal women), it is important to rule out colon cancer as a cause of chronic, asymptomatic blood loss. Increased requirements also may lead to iron deficiency in children and pregnant or breast feeding women. Give iron-containing formula or iron supplements to all infants except full-term infants who are exclusively breastfed. Start iron supplementation (iron-fortified cereal or daily iron supplement) at 4 to 6 months for full-term infants and at 2 months for preterm infants. Giving cow's milk before 1 year of age may lead to anemia by causing GI bleeding, so avoidance of cow's milk in the first year is essential. Iron supplements are also commonly given during pregnancy and lactation (because of the increased demand).

13. What are the classic laboratory abnormalities in iron deficiency anemia? What weird cravings may occur with iron deficiency?

Look for low iron and low ferritin levels, elevated total iron-binding capacity (TIBC; also known as transferrin), and low TIBC saturation. Rare patients may develop a craving for ice or dirt (**pica**).

14. What is Plummer-Vinson syndrome?

A triad of unknown etiology: esophageal web resulting in dysphagia; iron deficiency anemia; and glossitis.

15. How is iron deficiency treated?

First you must determine the cause. In a menstruating woman, a presumptive diagnosis of menstrual blood loss is often made. In patients older than 40 years, be sure to test the stool for occult blood and strongly consider colonoscopy to detect occult colon cancer. Postmenopausal vaginal bleeding may also cause anemia and warrants screening for gynecologic cancer. Treat with iron supplements for 3 to 6 months in uncomplicated cases to replete body iron stores.

16. What causes folate deficiency? In what patient populations is it commonly seen?

Folate deficiency is commonly seen in alcoholics (poor intake) and pregnant women (increased need). All women of reproductive age should take folate supplements (ideally before pregnancy occurs) to prevent neural tube defects in their offspring. Rare causes of folate deficiency include poor diet (e.g., tea and toast), methotrexate, prolonged therapy with trimethoprim-sulfamethoxazole, anticonvulsant therapy (especially phenytoin), and malabsorption. Look for macrocytes and **hypersegmented neutrophils** (either one should make you think of folate deficiency) with no neurologic symptoms or signs and low folate levels in serum or RBCs. Treat with oral folate.

17. What is the most common cause of vitamin B_{12} deficiency?

Pernicious anemia. This megaloblastic anemia is caused by **antiparietal cell antibodies.** Remember the physiology of B_{12} absorption with intrinsic factor secretion by parietal cells and absorption of the B_{12}—intrinsic factor complex in the ileum. Achlorhydria (no stomach acid secretion and elevated stomach pH) and antibodies to parietal cells are generally present in pernicious anemia.

18. What else may cause vitamin B_{12} deficiency? How is B_{12} deficiency diagnosed?

Gastrectomy, terminal ileum resection or disease (e.g., Crohn disease), strict vegan diet, chronic pancreatitis, and the infamous *Diphyllobothrium latum* (fish tapeworm) infection. The peripheral smear looks the same as in folate deficiency (macrocytes, hypersegmented neutrophils), but patients have **neurologic deficiencies** (e.g., loss of sensation and position sense, paresthesias, ataxia, spasticity, hyperreflexia, positive Babinski sign, dementia). Diagnosis is confirmed by a low serum B_{12} level. The presence of anti-intrinsic factor antibodies is highly confirmatory for pernicious anemia. The Schilling test is of historical interest but is no longer commonly employed in the diagnosis of B_{12} deficiency.

19. How is vitamin B_{12} deficiency treated?

Vitamin B_{12} supplements are given. The usual replacement is via parenteral (intramuscular) injection or high-dose oral replacement. Because of the potential for erratic absorption, oral replacement may be best utilized after levels have been normalized via the parenteral route. Supplementation may be required for life.

20. How is thalassemia differentiated from iron deficiency?

Both cause microcytic, hypochromic anemia, but thalassemia must be differentiated from iron deficiency because iron levels are normal in thalassemia. Iron supplementation is contraindicated in patients with thalassemia because it may cause iron overload. Look for elevations in hemoglobin A2 or hemoglobin F (beta thalassemia only); target cells, nucleated RBCs, and diffuse basophilia

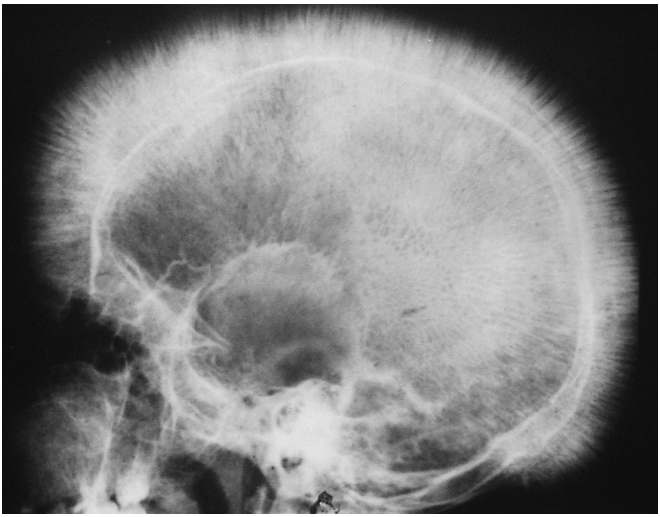

Figure 17-18. Thalassemia: x-ray film of the skull showing new bone formation on the outer table, producing perpendicular radiations resembling a crewcut. (From Kumar V, Abbas AK, Fausto N, Aster JC. Robbins and Cotran pathologic basis of disease, professional edition. 8th ed. Philadelphia: Saunders, 2009, Fig. 14-13. Courtesy of Dr. Jack Reynolds, Department of Radiology, University of Texas Southwestern Medical School, Dallas, Texas.)

on peripheral smears; skull radiograph with "crew-cut" appearance (Fig. 17-18); extramedullary hematopoiesis; splenomegaly; and positive family history. Thalassemia is more common in black persons, as well as persons of Mediterranean and Asian descent.

21. What diagnostic test confirms a diagnois of thalassemia? How is it treated?

Diagnosis is made by hemoglobin electrophoresis. There are four gene loci for the alpha chain of hemoglobin but only two for the beta chain. Patients with alpha thalassemia are symptomatic at birth or die in utero (fetal hydrops), whereas patients with beta thalassemia are not symptomatic until 6 months of age.

No treatment is required for minor thalassemia. Patients are often asymptomatic because they are used to living with a lower level of hemoglobin. Thalassemia major is more dramatic and severe. Treat with transfusions, as needed, and iron chelation therapy to prevent secondary hemochromatosis.

22. What two clues on the Step 2 examination often point to a diagnosis of sickle cell disease?

For the Step 2 examination, peripheral smear and race. Eight percent of African Americans are heterozygous for sickle cell trait. Know what sickled RBCs look like. Patients usually have a high percentage of reticulocytes (8%-20%).

23. What are the clinical manifestations and complications of sickle cell disease?

- Aplastic crises (caused by parvovirus B19 infection)
- Bone pain (because of infarcts; the classic example is avascular necrosis of the femoral head)
- Dactylitis (also known as hand-foot syndrome, seen in children)
- Renal papillary necrosis
- Splenic sequestration crisis

- Autosplenectomy (increased infections with encapsulated bugs such as *Pneumococcus, Haemophilus,* and *Neisseria* species)
- Acute chest syndrome (mimics pneumonia)
- Pigment cholelithiasis
- Priapism
- Stroke

24. How is sickle cell disease diagnosed and treated?

Diagnosis is made by hemoglobin electrophoresis. Screening is done at birth, but symptoms usually do not appear until around 6 months of age because of the lack of adult hemoglobin production. Treat with prophylactic penicillin until at least 5 years of age and perhaps longer, beginning as soon as the diagnosis is made. Proper vaccination includes the pneumococcal, meningococcal, and *H. influenzae* vaccines (given to all children anyway), as well as yearly influenza vaccination. Other strategies include folate supplementation, early treatment of infections, and proper hydration.

A sickle cell crisis involves severe pain in various sites caused by RBC sickling. Treat with oxygen, lots of intravenous (IV) fluids, and analgesics (do not be afraid to use narcotics). Consider transfusions if symptoms and/or findings are severe.

25. What findings help you manage anemia in the setting of acute blood loss?

The important point is that immediately after blood loss the hemoglobin may be normal; it takes at least 3 to 4 hours, often more, for reequilibration. Look for signs of hypovolemic shock: obvious bleeding; pale, cold skin; tachycardia; and hypotension. Transfuse if indicated, even with a normal hemoglobin in the acute setting. Consider internal hemorrhage in the setting of trauma and abdominal aortic aneurysm in patients with a pulsatile abdominal mass.

26. What are the commonly tested causes of autoimmune hemolytic anemia?

- Lupus erythematosus (or medications that cause lupus-like syndromes, such as procainamide, hydralazine, and isoniazid) and other autoimmune disorders
- Drugs (the classic example is methyldopa, but penicillins, cephalosporins, sulfa drugs, and quinidine also have been implicated)
- Leukemia or lymphoma
- Infection (the classic examples are mycoplasmosis, Epstein-Barr virus, and syphilis)

27. What laboratory test is often positive in patients with autoimmune anemia?

The **Coombs test** is positive in most autoimmune anemias. You also may see spherocytes on peripheral smear because of incomplete macrophage destruction (extravascular hemolysis) of RBCs.

28. What clues point to lead poisoning as a cause of anemia?

Lead poisoning causes a hypochromic, microcytic anemia, almost always in a child. With acute lead poisoning, look for vomiting, ataxia, colicky abdominal pain, irritability (aggressive behavior, behavioral regression), and encephalopathy, cerebral edema, or seizures. Usually, however, poisoning is chronic and low level with minimal nonspecific symptoms. Watch for basophilic stippling on peripheral smear and elevated free erythrocyte protoporphyrin or lead level, and consider risk factors for lead exposure (a child who eats paint chips or lives in an old, run-down building).

29. True or false: Children with risk factors should be screened for lead poisoning.

True. Screening all asymptomatic children with a serum lead level at 1 and 2 years old, regardless of risk, is becoming controversial. However, in children with risk factors, screening is very important because chronic low-level exposure may lead to permanent neurologic sequelae. Screening should start at 6 months in children with risk factors, such as pica (especially paint chips and dust in old buildings that may have lead paint), residence in an old or neglected building, and/or residence near

or family members who work at a lead-smelting or battery-recycling plant. Screen and measure symptomatic exposure with serum lead levels (normal value < 10 μg/dL).

30. How is lead poisoning treated?

Treat initially with decreased exposure (best strategy) as well as lead chelation therapy, if needed. Use succimer in children and dimercaprol in adults; in severe cases, use dimercaprol plus ethylenediamine tetraacetic acid (EDTA) for children or adults.

31. How can sideroblastic anemia be recognized? Should the presence of sideroblastic anemia raise concern about other conditions?

On the Step 2 examination, the typical description is a microcytic, hypochromic anemia with increased or normal iron, ferritin, and total iron-binding capacity (transferrin). This description should immediately steer you away from iron deficiency. Look for polychromatophilic stippling and the classic "ringed sideroblast" in the bone marrow (know what it looks like). Sideroblastic anemia may be related to myelodysplasia or future blood dyscrasia. Although you will probably not be asked about management, treatment is supportive. In rare cases, the anemia responds to **pyridoxine.** Do not give iron.

32. How do you recognize anemia of chronic disease?

First, look for the presence of a disease that causes chronic inflammation (e.g., rheumatoid arthritis, lupus erythematosus, cancer, tuberculosis). The anemia is either normocytic or microcytic. Serum iron is low, but so is total iron-binding capacity. Thus the percent saturation may be near normal. Serum ferritin is elevated (because ferritin is an acute-phase reactant, the level should be increased). Treat the underlying disorder to correct the anemia. Do not give iron.

33. Describe the hallmarks of spherocytosis.

This normochromic, normocytic anemia is associated with spherocytes on peripheral smear, positive family history (autosomal dominant), splenomegaly, positive osmotic fragility test, and an increased **mean corpuscular hemoglobin concentration** (the only occasion when this RBC index is useful for the Step 2 examination). Treatment often involves splenectomy. Spherocytes may also be seen in extravascular hemolysis, but the osmotic fragility test is normal.

34. Why does anemia develop in patients with chronic renal disease? How do you treat it?

Normocytic, normochromic anemia with decreased reticulocyte count develops in all patients with chronic renal failure because of decreased erythropoietin production. If necessary, give erythropoietin to correct the anemia.

35. What clues point to a diagnosis of aplastic anemia?

Although aplastic anemia may be idiopathic, on the Step 2 examination watch for chemotherapy, radiation, malignancy affecting the bone marrow (especially leukemias), benzene, and implicated medications (e.g., chloramphenicol, carbamazepine, sulfa drugs, zidovudine, gold). Decreased white blood cells and platelets accompany the anemia. Treat first by stopping any possible causative medication; then try antithymocyte globulin, colony-stimulating factors (e.g., erythropoietin, sargramostim, filgrastim, pegfilgrastim), or bone marrow transplant.

36. Define myelophthisic anemia. What clues on the peripheral smear suggest its presence?

Myelophthisic anemia is caused by a space-occupying lesion in the bone marrow. The common causes are malignant invasion that destroys bone marrow (most common) and myelodysplasia or myelofibrosis. On the peripheral smear, look for marked anisocytosis (different size), poikilocytosis (different shape), nucleated RBCs, giant and/or bizarre-looking platelets, and **teardrop-shaped** RBCs. A bone marrow biopsy may reveal no cells ("dry tap" if the marrow is fibrotic) or malignant-looking cells.

37. How do you recognize glucose-6-phosphatase deficiency?

This genetic disorder is X-linked recessive, affecting males. It is most common in black persons as well as persons of Mediterranean descent. Look for sudden hemolysis or anemia after exposure to fava beans or certain drugs (antimalarials, salicylates, sulfa drugs) or after infection. You may see **Heinz bodies** and "bite cells" on peripheral smear. The diagnosis is made with a red blood cell enzyme assay, which should not be done immediately after hemolysis because of the potential for a false-negative result (all of the older RBCs have already been destroyed, and the younger RBCs are not affected in most patients). Treat with avoidance of precipitating foods and medications; discontinue the triggering medication first.

38. Name some other causes of anemia.

- Endocrine failure (especially pituitary and thyroid; look for endocrine symptoms)
- Mechanical heart valves (hemolyzed RBCs)
- Disseminated intravascular coagulation (DIC), thrombotic thrombocytopenic purpura, and hemolytic uremic syndrome (look for schistocytes and red blood cell fragments on smear and other appropriate findings)
- Other hemoglobinopathies (the hemoglobin C and E varieties are fairly common)
- Paroxysmal nocturnal or cold hemoglobinuria
- *Clostridium perfringens* infection, malaria, and babesiosis (cause intravascular hemolysis and fever)
- Hypersplenism (associated with splenomegaly and often with low platelets and white blood cells)

39. When is transfusion indicated for anemia (at what hemoglobin level)?

Always transfuse on clinical grounds; observe the symptoms. In other words, treat the patient, not the laboratory value. There is no such thing as a "trigger value" for transfusion. Even so, most clinicians would give transfusion when hemoglobin levels are less than 7 or 8 g/dL in the acute setting, particularly when the patient has heart disease.

40. What are the indications for the use of various blood products?

Whole blood: Used only for rapid, massive blood loss or exchange transfusions (poisoning, thrombotic thrombocytopenic purpura).

Packed red blood cells: Used for routine transfusions.

Washed red blood cells: Free of traces of plasma, white cells, and platelets; good in IgA deficiency as well as for allergic or previously sensitized patients.

Platelets: Given for symptomatic thrombocytopenia (usually $< 10{,}000/\mu L$).

Granulocytes: Used on rare occasions for neutropenia.

Fresh frozen plasma: Contains all clotting factors; used for bleeding diathesis when vitamin K will take too long to take effect (e.g., DIC, severe warfarin poisoning) or when vitamin K will not work (liver failure).

Cryoprecipitate: Contains fibrinogen and factor VIII; used in hemophilia, von Willebrand disease, and DIC.

41. What is the most common cause of a blood transfusion reaction? What blood type can be given in an emergency to avoid a reaction?

The most common cause of a blood transfusion reaction is laboratory error. Type O negative blood can be used to avoid a reaction when you cannot wait for blood typing or when the blood bank does not have the patient's blood type.

42. Describe the signs and symptoms of a blood transfusion reaction.

Look for **febrile reaction** (e.g., chills, fever, headache, back pain) from antibodies to white blood cells; **hemolytic reaction** (e.g., anxiety or discomfort, dyspnea, chest pain, shock, jaundice) from antibodies to RBCs; or **allergic reaction** (e.g., urticaria, edema, dizziness, dyspnea, wheezing, anaphylaxis) to an unknown component in donor serum. Oliguria may be an associated finding.

43. What should you do if you suspect a transfusion reaction?

The first step is to *stop the transfusion.* If oliguria is present, treat with IV fluids and diuresis (mannitol or furosemide).

44. What are the other risks of transfusion?

There is a small but real risk of infection (usually viral infections such as hepatitis B and C, human immunodeficiency virus (HIV), and cytomegalovirus) and hyperkalemia (from hemolysis). With large transfusions (greater than 5 units of packed RBCs), bleeding diathesis may result from dilutional thrombocytopenia and citrate (a blood preservative and calcium chelator that prevents clotting). Look for oozing from puncture or IV sites.

45. What are the most common causes of DIC?

The most common cause is pregnancy and obstetric complications (roughly 50% of cases), followed by malignancy (33%), sepsis, and trauma (especially head trauma, prostate surgery, and snake bites).

46. How do you recognize and treat DIC in a classic at-risk patient?

DIC usually manifests with bleeding diathesis but may have thrombotic tendencies. Look for the classic oozing or bleeding from puncture and IV sites; prolonged prothrombin time (PT), partial thromboplastin time (PTT), and bleeding time (BT). DIC is the only disorder on the Step 2 examination that prolongs all three tests. Other clues include positive D-dimer, increased fibrin degradation products, thrombocytopenia, decreased fibrin, and decreased clotting factors (including factor VIII, which is normal in hepatic necrosis).

Treat the underlying cause (e.g., evacuate the uterus, give antibiotics). You may need to give transfusions with fresh frozen plasma or, in rare cases, heparin (only if thrombosis occurs).

47. With what conditions is eosinophilia associated?

- Allergic or atopic diseases (allergic rhinitis, asthma, allergic bronchopulmonary aspergillosis, eczema, urticaria, atopic dermatitis, milk-protein allergy, drug reactions)
- Parasitic infections
- Fungal infections
- HIV infection
- Malignancies (lymphoma, leukemia, lung cancer, gastric cancer, pancreatic cancer, colon cancer, ovarian cancer)
- Connective tissue/autoimmune diseases (Churg-Strauss vasculitis, rheumatoid arthritis, lupus, scleroderma, eosinophilic fasciitis, Dressler syndrome, inflammatory bowel disease)
- Granulomatous disorders (sarcoidosis)
- Skin disorders (psoriasis, pemphigus)
- Immune disorders (Wiskott-Aldrich syndrome, hyper-IgE syndrome, IgA deficiency, thymoma)
- Adrenal insufficiency
- Pulmonary eosinophilia (Löffler syndrome)
- Cirrhosis
- Atheroembolic disease
- Familial eosinophilia
- Eosinophilia-myalgia syndrome (from using L-tryptophan)

48. With what conditions is basophilia associated?

Allergies or neoplasm/blood dyscrasia.

49. True or false: The lupus anticoagulant causes a clotting tendency.

True. Although the lupus anticoagulant may cause a prolonged PTT, the patient has a tendency toward thrombosis. Look for associated lupus symptoms, positive results on the Venereal Disease Research Laboratory (VDRL) or rapid plasma reagin (RPR) tests for syphilis, or a history of miscarriages to help you recognize this condition.

50. What are genetic and acquired causes of an increased tendency toward clot-forming?

The list keeps growing. Watch for factor V Leiden mutation (or activated protein C resistance), prothrombin G20210A mutation, hyperhomocysteinemia, elevated factor VIII level, and deficiencies in protein C, protein S, or antithrombin III as genetic causes of an increased tendency toward thrombosis. Acquired causes include antiphospholipid syndrome (lupus anticoagulant and anticardiolipin antibody), hyperhomocysteinemia, pregnancy, cancer, and estrogen-containing medications. Note that hyperhomocysteinemia can be genetic or acquired. All are treated with anticoagulant therapy to prevent deep venous thrombosis (DVT) and pulmonary embolus (PE). Suspect these conditions when recurrent clots develop or when a clot develops in the absence of risk factors for clot development.

51. Which clotting tests measure which portions of the coagulation cascade? Which medications affect these tests?

PT measures the function of the extrinsic clotting pathway (prolonged by warfarin), activated PTT measures the function of the intrinsic clotting pathway (prolonged by heparin), and BT measures platelet function (prolonged by aspirin).

52. How do specific diseases affect clotting tests? What are the main differential points?

DISEASE	PT	PTT	BT	PLATELET COUNT	RBC COUNT	OTHER
von Willebrand disease	Normal	High	High	Normal	Normal	Autosomal dominant (look for family history)
Hemophilia A/B	Normal	High	Normal	Normal	Normal	X-linked recessive, A = low factor VIII, B = low factor IX
DIC	High	High	High	Low	Normal/low	Appropriate history, low level of factor VIII
Liver failure	High	High	Normal	Normal/low	Normal/low	Jaundice, normal factor VIII level; do not give vitamin K (ineffective); use FFP
Heparin	Normal	High	Normal	Normal/low	Normal	Watch for thrombocytopenia and thrombosis
Warfarin	High	Normal	Normal	Normal	Normal	Vitamin K antagonist (factors II, VII, IX, and X)
ITP	Normal	Normal	High	Low	Normal	Watch for preceding URI

Continued

DISEASE	PT	PTT	BT	PLATELET COUNT	RBC COUNT	OTHER
TTP	Normal	Normal	High	Low	Low	Hemolysis (smear), CNS symptoms (hallucinations, altered mental status, headache, stroke); treat with plasmapheresis; do not give platelets!
Scurvy	Normal	Normal	Normal	Normal	Normal	Fingernail and gum hemorrhages, bone hemorrhages; caused by vitamin C deficiency

BT, Bleeding time; *CNS*, central nervous system; *DIC*, disseminated intravascular coagulation; *FFP*, fresh frozen plasma; *ITP*, idiopathic thrombocytopenic purpura; *PT*, prothrombin time; *PTT*, partial thromboplastin time; *RBC*, red blood cell; *TTP*, thrombotic thrombocytopenic purpura; *URI*, upper respiratory infection.

53. What are the common causes of thrombocytopenia? What kind of bleeding problems are caused by low platelet counts?

Common causes of thrombocytopenia include purpura (idiopathic or thrombotic), hemolytic uremic syndrome, DIC, HIV, splenic sequestration, heparin (including heparin-induced thrombocytopenia [HIT]; treat by first stopping heparin), other medications (especially quinidine and sulfa drugs), autoimmune disease, and alcohol. Bleeding from thrombocytopenia is in the form of petechiae, nose bleeds, and easy bruising.

54. What causes petechiae or "platelet-type" bleeding in the setting of normal platelets?

Vitamin C deficiency (scurvy) causes bleeding similar to that seen with low platelets (splinter and gum hemorrhages, petechiae); perifollicular and subperiosteal hemorrhages are unique to scurvy. Patients have a poor dietary history (the classic example is hot dogs and soda or tea and toast), myalgias and arthralgias, and capillary fragility (bleeding is caused by collagen problems in the vessels). Treat with oral vitamin C.

Other causes include uremia (results in platelet dysfunction), inherited connective tissue disorders (Ehlers-Danlos syndrome, Marfan syndrome), and chronic corticosteroid use (causes capillary fragility).

HYPERTENSION

1. How often should you screen for hypertension?

Although there is no absolutely correct answer, all people should be screened roughly every 2 years, starting at the age of 3 years.

2. Define hypertension.

Persistent blood pressure greater than 140/90 mm Hg. Individuals with a systolic blood pressure of 120 to 139 mm Hg or a diastolic pressure of 80 to 89 mm Hg should be considered as prehypertensive. Remember that 145/60 mm Hg is hypertension, as is 115/95 mm Hg (isolated systolic or diastolic hypertension, respectively). Treatment is needed. In grading the severity of hypertension, use the worst number, whether diastolic or systolic. See Table 18-1 for the 2003 Joint National Committee (JNC-7) classification.

TABLE 18-1. 2003 JOINT NATIONAL COMMITTEE (JNC-7) HYPERTENSION CLASSIFICATION

SYSTOLIC BP* (MM HG)	DIASTOLIC BP* (MM HG)	CLASSIFICATION
<120	<80	Normal
120-139	80-89	Prehypertension
140-159	90-99	Stage I hypertension
≥160	≥100	Stage II hypertension

**Classification is based on the worst number* (e.g., 168/60 mm Hg is considered stage II hypertension even though diastolic pressure is normal).

3. What is the "two-measurement" rule in the diagnosis of hypertension?

The blood pressure should be measured two times on each of two separate office visits before the diagnosis and pharmacologic treatment of hypertension. However, if asked, institute conservative measures (see question 4) and address associated comorbidities (e.g., obesity, diabetes) after the first abnormal measurement. There are a few important exceptions to the "start conservative and remeasure" strategy, however, and more aggressive approaches are gaining favor. Patients with marked blood pressure elevations (generally > 200/120 mm Hg) and acute target-organ damage (e.g., encephalopathy, myocardial infarction (MI), unstable angina, pulmonary edema, stroke) require hospitalization and parenteral drug therapy. Patients with markedly elevated blood pressure but without target organ damage usually do not require hospitalization but should be given immediate combination oral antihypertensive therapy. See question 7 for more details. In pregnant woman, preeclampsia may be the cause of hypertension. Waiting to treat in this setting can have devastating consequences to mother and fetus.

4. What are the conservative (i.e., nonpharmacologic) treatments for hypertension?

Dietary changes (i.e., low salt, low fat, low calorie), reduced smoking and alcohol intake, weight loss, and exercise may each have a positive effect on blood pressure and, in some cases, get the patient back into the normotensive range. For stage I hypertension, it is reasonable to give a 1- to 2-month

trial of lifestyle modifications before starting medication. In patients with stage II hypertension or those with diabetes or renal disease, early pharmacologic treatment is often preferred.

5. List the first-line medications for treatment of hypertension.

Thiazide-type diuretics should be used as initial therapy for most patients with hypertension, either alone or in combination with one of the following classes: angiotensin-converting enzyme (ACE) inhibitors, angiotensin receptor blockers, beta blockers, or calcium channel blockers. Which medication class you should use often depends on the individual patient and his or her other medical problems. In some cases, medications from multiple classes may be needed to reach blood pressure goals.

DRUG CLASS	USE IN PATIENTS WITH:	AVOID IN PATIENTS WITH:
Thiazides	Heart failure, diabetes, high risk for coronary artery disease or stroke, osteoporosis	Gout, electrolyte disturbances (e.g., hyponatremia), pregnancy
Beta blockers	Stable angina, acute coronary syndrome/unstable angina, acute or prior MI, high risk for coronary artery disease, atrial tachycardia/fibrillation, thyrotoxicosis (short-term), essential tremor, migraines	Asthma, chronic obstructive pulmonary disease, heart block, sick sinus syndrome
ACE inhibitors	Heart failure, diabetes, acute coronary syndrome/unstable angina, acute or prior MI, high risk for coronary artery disease or stroke, chronic kidney disease	Pregnancy (and generally women of childbearing age), angioedema, renovascular hypertension (may cause renal failure)
ARBs	Heart failure, diabetes, chronic kidney disease	Pregnancy (and generally women of childbearing age), renovascular hypertension (may cause renal failure)
Calcium channel blockers	Raynaud syndrome, atrial tachyarrhythmias	Heart block, sick sinus syndrome, congestive heart failure (all related to central-acting agents), pregnancy

ACE, Angiotensin-converting enzyme; *ARB*, angiotensin receptor blocker; *MI*, myocardial infarction.

Note: ACE inhibitors are first-line agents for congestive heart failure because they reduce mortality rates. In diabetes, ACE inhibitors reduce progression to nephropathy and neuropathy. All patients with stable congestive heart failure or diabetes should take an ACE inhibitor (if they can tolerate it), even in the absence of hypertension.

6. What are the preferred treatments for women of reproductive age and pregnant women with hypertension?

Labetalol, hydralazine, and alpha-methyldopa are safe. If preeclampsia is present, remember that magnesium sulfate lowers blood pressure.

7. Define hypertensive urgency. How is it different from hypertensive emergency?

Hypertensive urgency is defined as blood pressure greater than 200/120 mm Hg without symptoms. Hypertensive emergency is defined as blood pressure greater than 200/120 mm Hg with symptoms

or evidence of end-organ damage. Examples include acute left ventricular failure, chest pain or angina, MI, encephalopathy (watch for headaches, confusion, retinal hemorrhages, papilledema, mental status changes, vomiting, blurry vision, dizziness, and/or seizures), or acute renal failure (from necrotizing arteriolitis). Both require immediate treatment, but hypertensive emergency is more worrisome. Hypertensive urgency typically is treated orally with furosemide, clonidine, or captopril. There are many treatment options for hypertensive emergency, but intravenous nitroprusside, labetalol, or nicardipine are the most common.

8. What causes hypertension?

Roughly 90% to 95% of cases are idiopathic, multifactorial, or essential hypertension. About 5% to 10% of cases are a result of secondary (known) causes.

9. What are the common causes of secondary hypertension in younger men and women?

In younger men, a common cause of secondary hypertension is excessive alcohol intake (get the patient to quit). In younger women, common and classic causes are birth control pills (stop them) and renal artery stenosis (RAS) from fibromuscular dysplasia (which may cause a bruit and should be treated with balloon angioplasty).

10. List less common causes of secondary hypertension.

- Pheochromocytoma. Look for wild swings in blood pressure with diaphoresis and confusion. As a screening test, order 24-hour urine collection to assess catecholamine products (metanephrines, vanillylmandelic acid, homovanillic acid).
- RAS. Unlike young patients with fibromuscular dysplasia, older patients typically have RAS because of atherosclerosis. A renal artery bruit is classically present (although not sensitive); magnetic resonance or conventional angiography makes the definitive diagnosis (Fig. 18-1). Giving ACE inhibitors to patients with RAS may precipitate acute renal failure (sometimes the first diagnostic clue to its presence).
- Polycystic kidney disease. Look for flank mass, positive family history (autosomal dominant pattern of inheritance), and elevations in creatinine and blood urea nitrogen.
- Cushing syndrome. Look for stigmata of Cushing syndrome on examination. Order a 24-urine collection to assess free cortisol or a dexamethasone suppression test.
- Conn syndrome. The cause is an aldosterone-secreting adrenal neoplasm. Look for high aldosterone levels, low renin levels, hypernatremia, hypokalemia, metabolic alkalosis, and/or an adrenal mass on computed tomography (CT). The screening test of choice is the plasma aldosterone to plasma renin activity ratio; a ratio of greater than 30 is indicative of primary hyperaldosteronism.

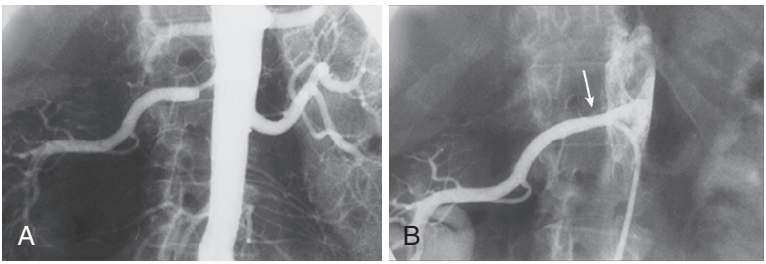

Figure 18-1. A, Baseline aortogram showing 70% diameter stenosis of the right renal artery. **B,** After stenting. Note the mild residual narrowing *(arrow).* (From Libby LS: Braunwald's heart disease: a textbook of cardiovascular medicine. 8th ed. Philadelphia: Saunders, 2008, Fig. 59-12.)

- Coarctation of the aorta. Look for hypertension in the upper extremities only, with unequal pulses, radiofemoral delay, and rib notching on chest radiograph; associated with Turner syndrome. Magnetic resonance imaging (MRI) or angiography makes a definitive diagnosis.
- Renal failure from any cause. In children, watch for poststreptococcal glomerulonephritis or hemolytic uremic syndrome.

11. What does lowering blood pressure accomplish?

Hypertension is the number-one modifiable risk factor for strokes. Lowering blood pressure decreases the risk for heart disease, myocardial infarction, atherosclerosis, stroke, renal failure, and dissecting aortic aneurysm.

12. What is the most common cause of death among untreated patients with hypertension?

The same as for the general population—coronary artery disease.

13. Which tests should be ordered for every patient with a diagnosis of hypertension? Why?

1. Electrocardiogram (ECG): To determine whether the heart has been affected (e.g., left ventricular hypertrophy).
2. Chemistry 7 panel (i.e., basic metabolic panel): Clues to possible secondary cause of hypertension (e.g., electrolyte disturbances in Conn syndrome) and evaluation for diabetes.
3. Urinalysis: Clues to possible secondary cause of hypertension (e.g., red blood cell [RBC] casts in poststreptococcal glomerulonephritis) and to kidney damage (proteinuria).
4. Hemoglobin and hematocrit: To evaluate for anemia or polycythemia.
5. Lipid panel: To evaluate for dyslipidemia as an additional risk factor for coronary artery disease.

IMMUNOLOGY

1. List the four classic types of hypersensitivity reactions.

- Anaphylactic (type I)
- Cytotoxic (type II)
- Immune complex-mediated (type III)
- Cell-mediated/delayed (type IV)

2. What causes type I hypersensitivity? Give the classic clinical examples.

Type I (anaphylactic) hypersensitivity is a result of preformed IgE antibodies that cause release of vasoactive amines (e.g., histamine, leukotrienes) from mast cells and basophils. Examples are anaphylaxis, atopy, hay fever, urticaria, allergic rhinitis, and some forms of asthma. Anaphylaxis may be caused by bee stings, food allergy (especially peanuts and shellfish), medications (especially penicillins and sulfa drugs), or rubber glove allergy.

3. Describe the clinical findings with chronic type I hypersensitivity.

Look for eosinophilia, elevated IgE levels, positive family history, and seasonal exacerbations. Patients also may have allergic "shiners" (bilateral infraorbital edema) and a transverse nasal crease (caused by frequent nose rubbing). Pale, bluish, edematous nasal turbinates with many eosinophils in clear, watery nasal secretions are also classic.

4. What medication should be avoided in patients with nasal polyps?

Do not give aspirin, which may precipitate a severe asthma attack.

5. How do you recognize and treat true anaphylaxis?

Look for the classic triggers mentioned above just before the patient becomes agitated and flushed and develops itching (urticaria), facial swelling (angioedema), and difficulty in breathing. Symptoms tend to develop rapidly and dramatically.

Treat immediately by securing the airway (laryngeal edema may prevent intubation, in which case do a cricothyroidotomy, if needed) and give subcutaneous epinephrine. Antihistamines are only useful for cutaneous reactions and itching, not for more severe reactions. Use corticosteroids only if the initial treatment options are not available (not a first-line agent).

6. What usually causes hereditary angioedema?

A deficiency of **C1 esterase inhibitor** (complement) is the usual cause of hereditary angioedema. Patients have diffuse swelling of the lips, eyelids, and possibly the airway, unrelated to allergen exposure. The disease is autosomal dominant; look for a positive family history. C4 complement levels are low. Acute treatment is the same as for anaphylaxis. Androgens are used for long-term treatment because they increase liver production of C1 esterase inhibitor.

7. What type of testing can identify an allergen if it is not obvious?

Skin or patch testing (Fig. 19-1; Plate 46).

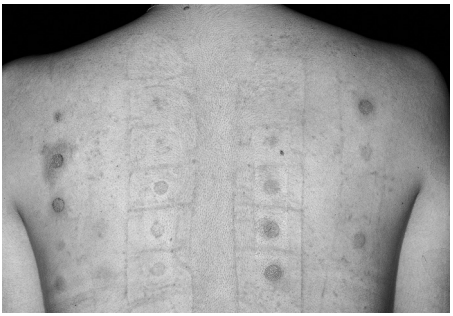

Figure 19-1. Patch testing. A battery of common and suspected allergens is applied to the back with a patch for 48 hours and then removed. The skin is then examined at 96 hours. Irritant reactions disappear, allergic ones do not. This patient has many positive reactions of varying intensity. See Plate 46. (From Habif TP. Clinical dermatology. 5th ed. St. Louis: Mosby, 2009, Fig. 4-30.)

8. What causes type II hypersensitivity? List some classic clinical examples.

Type II (cytotoxic) hypersensitivity is a result of preformed IgG and IgM antibodies that react with the antigen and cause secondary inflammation. Examples include the following:

- Autoimmune hemolytic anemia (classically caused by methyldopa, penicillins, or sulfa drugs) or other cytopenias caused by antibodies (e.g., idiopathic thrombocytopenic purpura).
- Transfusion reactions.
- Erythroblastosis fetalis (Rh incompatibility).
- Goodpasture syndrome (watch for linear immunofluorescence on kidney biopsy).
- Myasthenia gravis.
- Graves disease.
- Pernicious anemia.
- Pemphigus vulgaris.
- Hyperacute transplant rejection (as soon as the anastomosis is made at transplant surgery, the transplanted organ deteriorates in front of the surgeon's eyes).

9. What laboratory test is usually positive with a type II hypersensitivity that causes anemia?

Coombs test (usually the direct Coombs test).

10. What causes type III hypersensitivity? List some classic clinical examples.

Type III (immune complex-mediated) hypersensitivity is caused by antigen-antibody complexes that are usually deposited in vessels and cause an inflammatory response. Examples include serum sickness, lupus erythematosus, rheumatoid arthritis, polyarteritis nodosa, cryoglobulinemia, and certain types of glomerulonephritis (e.g., from chronic hepatitis).

11. What causes type IV hypersensitivity? How is it related to tuberculosis testing?

Type IV (cell-mediated/delayed) hypersensitivity is caused by sensitized T lymphocytes that release inflammatory mediators. The tuberculosis skin test (purified protein derivative [PPD]) exploits this immune system reaction. Other examples include contact dermatitis (especially poison ivy, nickel earrings, cosmetics, and medications), chronic transplant rejection, and granulomas (e.g., sarcoidosis).

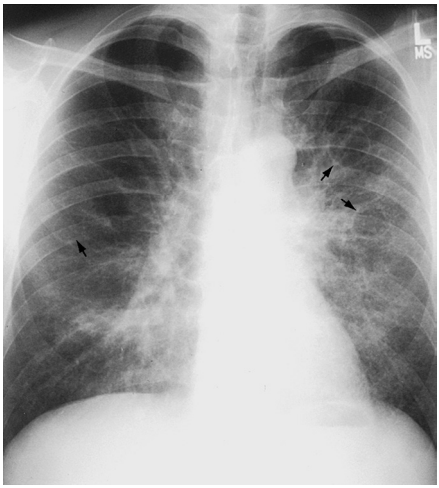

Figure 19-2. Posteroanterior chest radiograph of an HIV-seropositive patient with *Pneumocystis* pneumonia showing bilateral, predominantly perihilar granular opacities and three pneumatoceles *(arrows).* Pneumatoceles may predispose patients to pneumothorax. (From Mason RJ, et al. Murray and Nadel's textbook of respiratory medicine. 4th ed. Philadelphia: Saunders, 2005, Fig. 75-5. Reproduced with permission from L. Huang.)

12. What sexually transmitted infectious disease should be considered when a patient's presenting symptoms include a sore throat and mononucleosis-like syndrome?

Human immunodeficiency virus (HIV) infection because initial seroconversion may present as a mononucleosis-like syndrome (e.g., fever, malaise, pharyngitis, rash, lymphadenopathy).

13. How is HIV diagnosed? How long after exposure does the HIV test become positive?

Diagnosis is made with the enzyme-linked immunosorbent assay (ELISA), which, if positive, is confirmed with a Western blot test. All of these tests should be done before making a diagnosis. It takes 6 to 12 weeks for antibodies to develop in the majority of patients. Antibodies are present by 6 months in 95% of patients. Therefore, if a patient wants testing because of recent risk-taking behavior, you should retest the patient in 6 months if the initial test is negative.

Rapid tests are available, but the predictive accuracy varies with the prevalence of HIV infection in the population. Positive tests require confirmatory testing with ELISA and Western blot. Negative test results are reliable unless the patient is in the window period of acute HIV infection.

14. Are "control" tests needed when a PPD tuberculosis test is done in HIV-positive patients?

Most authorities no longer recommend "control" (also known as anergy) testing when a PPD test is done in HIV-positive patients.

15. How do you recognize *Pneumocystis jiroveci* pneumonia (PCP)?

For the Step 2 examination, think of PCP first in any patient with HIV and pneumonia, even though community-acquired pneumonia is more common even in patients with AIDS. Look for severe hypoxia with normal radiographs or diffuse bilateral interstitial infiltrates (Fig. 19-2).

Patients usually have a dry, nonproductive cough. PCP may be detected with silver stains (Wright-Giemsa, Giemsa, or methenamine silver) applied to induced sputum; if not, you can use bronchoscopy with bronchoalveolar lavage and brush biopsy to make the diagnosis. High levels of lactate dehydrogenase are suspicious in the appropriate setting. PCP is now usually treated presumptively (typically with trimethoprim-sulfamethoxazole with corticosteroids), with diagnostic testing reserved for those in whom the diagnosis is unclear or initial treatment fails.

16. What is the most common primary immunodeficiency? How do you recognize it?

IgA deficiency, which causes recurrent respiratory and gastrointestinal (GI) infections. IgA levels are always low, and levels of IgG subclass 2 may be low. Do not give immunoglobulins, which may cause anaphylaxis because of development of anti-IgA antibodies. Alternatively, if any patient develops anaphylaxis after immunoglobulin exposure, you should think of IgA deficiency.

17. How do you recognize Bruton agammaglobulinemia?

Bruton agammaglobulinemia (X-linked agammaglobulinemia) is an X-linked recessive disorder with low or absent B cells that affects males. Infections begin after 6 months of age when maternal antibodies disappear. Look for recurrent lung or sinus infections with *Streptococcus* and *Haemophilus* species.

18. What causes DiGeorge syndrome? How do you recognize it?

DiGeorge syndrome is caused by hypoplasia of the third and fourth pharyngeal pouches. Look for hypocalcemia and tetany (from hypocalcemia caused by absent parathyroid glands) in the first 24 to 48 hours of life. The thymus may also be absent or hypoplastic, and congenital heart defects and typical facies are often present.

19. What is the classic cause of severe combined immunodeficiency? How does it present?

Severe combined immunodeficiency may be autosomal recessive or X-linked. The classic cause is **adenosine deaminase deficiency** (autosomal recessive). Patients have B- and T-cell defects and severe infections in the first few months of life. Other symptoms include cutaneous anergy and absent or dysplastic thymus and lymph nodes.

20. What triad indicates the diagnosis of Wiskott-Aldrich syndrome?

Wiskott-Aldrich deficiency is an X-linked recessive disorder that affects males. The classic triad consists of eczema, thrombocytopenia (look for bleeding), and recurrent infections (usually respiratory).

21. How do you recognize Chediak-Higashi syndrome?

Chediak-Higashi syndrome is usually an autosomal recessive disorder characterized by giant granules in neutrophils, infections, and often oculocutaneous albinism. It is caused by a defect in microtubule polymerization.

22. Describe the pathophysiology of chronic granulomatous disease (CGD).

CGD is usually an X-linked recessive disorder that affects males. Because of a defect in the activity of the enzyme nicotinamide adenine dinucleotide phosphate oxidase, patients have recurrent infections with catalase-positive organisms (e.g., *Staphylococcus aureus, Pseudomonas* species). Diagnosis is clinched if the question mentions deficient nitroblue tetrazolium (NBT) dye reduction by granulocytes. This test measures the respiratory burst, which patients with chronic granulomatous disease lack. If you see "CGD" on a USMLE question, then look for "NBT" in the answer.

23. Cover the right-hand column, and answer the questions about HIV management on the left.

QUESTION	ANSWER
After HIV diagnosis, how often do you check the CD4 count?	Every 3-4 months. Every 6 months for patients who are adherent to therapy with sustained viral suppression and stable clinical status for more than 2-3 years.
When do you start antiretroviral therapy?	When the CD4 count is less than 350/mm^3 or if there is a history of an AIDS-defining illness. Also should be initiated in pregnant women, in patients with HIV-associated nephropathy, and in patients with hepatitis B coinfection.
What are the AIDS-defining illnesses?	*Pneumocystic jiroveci* pneumonia Esophageal candidiasis Wasting Kaposi sarcoma Disseminated *Mycobacterium avium* infection Tuberculosis Cytomegalovirus disease HIV-associated dementia Recurrent bacterial pneumonia Toxoplasmosis Immunoblastic lymphoma Chronic cryptosporidiosis Burkitt lymphoma Disseminated histoplasmosis Invasive cervical cancer Chronic herpes simplex
When do you start PCP prophylaxis?	When the CD4 count is less than 200/mm^3 or a history of oropharyngeal candidiasis
What is the drug of choice for PCP prophylaxis?	Trimethoprim-sulfamethoxazole (Bactrim)
What other agents are used in patients with allergy or intolerance to Bactrim?	Dapsone, aerosolized pentamidine, and atovaquone
When should you start *Mycobacterium avium* complex (MAC) prophylaxis?	When the CD4 count is less than 50/mm^3
What drugs are used for MAC prophylaxis?	Clarithromycin or azithromycin (rifabutin is an alterative)
True or false: Once the CD4 count is less than 200/mm^3, the patient is automatically considered to have AIDS (even without opportunistic infections).	True
True or false: Give the measles-mumps-rubella vaccine.	True (CD4 count must be greater than 200/mm^3)
True or false: Give the varicella vaccine.	True, if patient does not have evidence of immunity (CD4 count must be greater than 200/mm^3)
True or false: Do not give annual influenza vaccines.	False (give every year to all HIV-infected patients)

QUESTION	ANSWER
True or false: Pneumococcal vaccine should be given.	True. It should be given to all HIV-infected patients, and revaccination every 5 years should be considered
True or false: Give hepatitis A vaccine.	True, if the patient has chronic liver disease or is at increased risk for hepatitis A infection
True or false: Give hepatitis B vaccine.	True
True or false: PPD testing should be done annually.	True, if the initial test is negative and the patient is high-risk
True or false: Oral polio vaccine should be given to patients who are at risk of exposure through travel or work.	False (use inactive polio vaccine injection)
The risk of which cancer is increased on skin and in the mouth?	Kaposi sarcoma
The risk of which type of blood cell cancer is increased?	Non-Hodgkin lymphoma (usually primary B-cell lymphomas of central nervous system [CNS])
What do positive India ink preparations of the cerebrospinal fluid mean?	*Cryptococcus neoformans* meningitis
What do ring-enhancing lesions in the brain on CT or MR scans usually mean?	Toxoplasmosis, cysticercosis/*Taenia solium,* or lymphoma
True or false: HIV may cause thrombocytopenia.	True
True or false: HIV can cause dementia.	True
True or false: HIV protects against peripheral neuropathies.	False (HIV can cause them)
True or false: HIV-positive mothers may breast-feed their infants.	False (breast milk transmits HIV)
What is the first-choice agent for cytomegalovirus retinitis?	Valganciclovir
What are the second-choice agents for cytomegalovirus retinitis?	Ganciclovir, foscarnet, or cidofovir
True or false: Pregnant patients should receive anti-retroviral therapy.	True. Three-drug therapy is currently recommended (no different for the pregnant female; earlier administration is best)
True or false: Infants born to HIV-positive mothers should take zidovudine (ZDV).	True (for at least 6 weeks after delivery)
True or false: Cesarean section increases maternal HIV transmission.	False (it may decrease transmission to the infant)
What is the most likely cause of pneumonia in HIV-positive patient?	*Streptococcus pneumoniae*
What is the most likely cause of opportunistic pneumonia in HIV-positive patient?	*Pneumocystis jiroveci*
What is the stain used on sputum to detect PCP?	Silver (Wright-Giemsa or Giemsa)
What are the two pathogens that cause chronic diarrhea only in AIDS?	*Cryptosporidium* and *Isospora* spp.

QUESTION	ANSWER
True or false: Herpes-zoster infection in young adults = possible HIV infection.	True (suggests immunodeficiency)
True or false: Thrush in young adults may mean HIV infection.	True (also associated with diabetes, leukemia, and steroids)
True or false: A positive HIV antibody test in a newborn is unreliable.	True (maternal antibodies in the neonate can give a false-positive result for the first 6 months)

24. Complement deficiencies of C5 through C9 cause recurrent infections with which genus of bacteria?

Neisseria species.

25. Define chronic mucocutaneous candidiasis.

Chronic mucocutaneous candidiasis is a cellular immunodeficiency specific for candidal infection. Patients have thrush and candidal infections of the scalp, skin, and nails as well as anergy to *Candida* sp. with skin testing. It is often associated with hypothyroidism. The rest of the immune function is intact; no other types of infections are present.

26. Give the classic description of hyper-IgE syndrome (Job-Buckley syndrome).

Patients with hyper-IgE syndrome have recurrent staphylococcal infections (especially of the skin) and have extremely high IgE levels. They also commonly have fair skin, red hair, and eczema.

INFECTIOUS DISEASES

1. Cover the middle and right-hand columns and specify which bugs are associated with each type of infection and what type of empirical antibiotic should be used while waiting for culture results.

CONDITION	MAIN ORGANISM(S)	EMPIRICAL ANTIBIOTICS
Urinary tract infection	*Escherichia coli*	Trimethoprim-sulfamethoxazole, nitrofurantoin, amoxicillin, quinolones
Bronchitis	Virus, *Haemophilus influenzae, Moraxella* spp.	Usually no benefit from antibiotics. May consider macrolides or doxycycline
Pneumonia (classic)	*Streptococcus pneumoniae, H. influenzae*	Third-generation cephalosporin, azithromycin
Pneumonia (atypical)	*Mycoplasma, Chlamydia* spp.	Macrolide antibiotic, doxycycline
Osteomyelitis	*Staphylococcus aureus, Salmonella* spp.	Oxacillin, cefazolin, vancomycin
Cellulitis	Streptococci, staphylococci	Cephalexin or dicloxacillin. Trimethoprim-sulfamethoxazole, doxycycline, or clindamycin are often used as first-line agents because of the emergence of methicillin-resistant *S. aureus* (MRSA)
Meningitis (neonate)	Streptococci B, *E. coli, Listeria* spp.	Ampicillin + aminoglycoside (usually gentamicin); an expanded spectrum third-generation cephalosporin (cefotaxime) should be added if a gram-negative organism is suspected
Meningitis (child/adult)	*S. pneumoniae, Neisseria meningitidis**	Cefotaxime or ceftriaxone + vancomycin
Endocarditis (native valve)	Staphylococci, streptococci,	Antistaphylococcal penicillin† (or vancomycin if allergic to penicillin) + aminoglycoside
Endocarditis (prosthetic valve)	Numerous different organisms	Vancomycin + gentamicin + cefepime or a carbapenem
Sepsis	Gram-negative organisms, streptococci, staphylococci	Third-generation penicillin/cephalosporin + aminoglycoside, or imipenem
Septic arthritis‡	*S. aureus* Gram negative bacilli Gonococci	Vancomycin Ceftazidime or ceftriaxone Ceftriaxone, ciprofloxacin, or spectinomycin

**H. influenzae* is no longer as common a cause of meningitis in children because of widespread vaccination. In a child with no history of immunization, *H. influenzae* is the most likely cause of meningitis.
†Examples: Oxacillin, nafcillin.
‡Think of staphylococci if the patient is monogamous or not sexually active. Think of gonorrhea for younger adults who are sexually active.

2. Cover the middle and right-hand columns and specify the empirical antibiotic of choice for each organism.

ORGANISM*	ANTIBIOTIC	OTHER CHOICES
Streptococcus A or B	Penicillin, cefazolin	Erythromycin
S. pneumoniae	Third-generation cephalosporin + vancomycin	Fluoroquinolone
Enterococcus	Penicillin or ampicillin + aminoglycoside	Vancomycin + aminoglycoside
Staphylococcus aureus	Antistaphylococcus penicillin (e.g., methicillin)	Vancomycin, trimethoprim-sulfamethoxazole, doxycycline, clindamycin, or linezolid for MRSA
Gonococcus†	Ceftriaxone	Cefixime or high-dose azithromycin followed by test of cure in 1 week
Meningococcus	Cefotaxime or ceftriaxone	Chloramphenicol or penicillin G if proven to be penicillin susceptible
Haemophilus	Second- or third-generation cephalosporin	Amoxicillin
Pseudomonas	Antipseudomonal penicillin (ticarcillin, piperacillin) +/- beta lactamase inhibitor (clavulanate, tazobactam)	Ceftazidime, cefepime, aztreonam, imipenem, ciprofloxacin
Bacteroides	Metronidazole	Clindamycin
Mycoplasma	Erythromycin, azithromycin	Doxycycline
Treponema pallidum	Penicillin	Doxycycline
Chlamydia	Doxycycline, azithromycin	Erythromycin, ofloxacin
Lyme disease (*Borrelia* spp.)	Cefuroxime, doxycycline, amoxicillin	Erythromycin

*Always use culture sensitivities to guide therapy once available.
†With genital infections, always treat for presumed *Chlamydia* coinfection with azithromycin or doxycycline.

3. Cover the right-hand column and specify what each Gram stain most likely represents.

GRAM STAIN RESULT	MEANING
Blue/purple color	Gram-positive organism
Red color	Gram-negative organism
Gram-positive cocci in chains	Streptococci
Gram-positive cocci in clusters	Staphylococci
Gram-positive cocci in pairs (diplococci)	*Streptococcus pneumoniae*
Gram-negative coccobacilli (small rods)	*Haemophilus* sp.
Gram-negative diplococci	*Neisseria* sp. (sexually transmitted disease, septic arthritis, meningitis) or *Moraxella* sp. (lungs, sinusitis)
Plump gram-negative rod with thick capsule (mucoid appearance)	*Klebsiella* sp.

GRAM STAIN RESULT	MEANING
Gram-positive rods that form spores	*Clostridium* sp., *Bacillus* sp.
Pseudohyphae	*Candida* sp.
Acid-fast organisms	*Mycobacterium* (usually *M. tuberculosis*), *Nocardia* sp.
Gram-positive with sulfur granules	*Actinomyces* sp. (pelvic inflammatory disease [PID] in intrauterine device users; rare cause of neck mass/cervical adenitis)
Silver-staining	*Pneumocystis jiroveci* and cat-scratch disease
Positive India ink preparation (thick capsule)	*Cryptococcus neoformans*
Spirochete	*Treponema* sp., *Leptospira* sp. (both seen only on dark-field microscopy), *Borrelia* sp. (seen on regular light microscope)

4. What is the gold standard for diagnosis of pneumonia?

Sputum culture. Obtain the culture before starting antibiotics, although many physicians treat empirically without culture in routine cases. Obtain blood cultures as well because bacteremia is common with pneumonia.

5. What is the most common cause of pneumonia? How does it classically present?

Streptococcus pneumoniae. Look for rapid onset of shaking chills after 1 to 2 days of upper respiratory infection symptoms (sore throat, runny nose, dry cough), followed by fever, pleurisy, and productive cough (yellowish-green or rust-colored from blood), especially in older adults. Chest radiograph shows lobar consolidation (Fig. 20-1), and the white blood cell count is high with a large percentage of neutrophils. Treat with a macrolide (e.g., azithromycin, clarithromycin), doxycycline, third-generation cephalosporin with a macrolide or doxycycline, or a fluoroquinolone that provides atypical coverage (e.g., levofloxacin, moxifloxacin).

6. What is the best prevention against *S. pneumoniae*?

Vaccination. Give pneumococcal vaccine to all children as well as adult patients over 65 years old, splenectomized patients, patients with sickle-cell disease (who have autosplenectomy) or splenic dysfunction, immunocompromised patients (human immunodeficiency virus (HIV), malignancy, organ transplant), and all patients with chronic disease (e.g., diabetes, cardiac disease, asthma and other pulmonary disease, renal disease, liver disease, or tobacco use).

7. How do you recognize and treat *Haemophilus influenzae* pneumonia?

H. influenzae is now uncommon in children because of vaccination, but is still an important cause of pneumonia in older adults and in those with underlying lung disease such as chronic obstructive pulmonary disease. Often it resembles pneumococcal pneumonia clinically, but look for gram-negative coccobacilli on sputum Gram stain. Treat with amoxicillin or a second- or third-generation cephalosporin.

8. Describe the hallmarks of *Staphylococcus aureus* pneumonia.

S. aureus tends to cause hospital-acquired (nosocomial) pneumonia and pneumonia in patients with cystic fibrosis (along with *Pseudomonas* sp.), patients who abuse intravenous drugs, and patients with chronic granulomatous disease (look for recurrent lung abscesses). Empyema and lung abscesses are relatively common with *S. aureus* pneumonia.

9. In what clinical situations do you tend to see gram-negative pneumonias?

Pseudomonas infection is classically associated with cystic fibrosis, *Klebsiella* infection may be found in patients who are homeless and/or suffer from alcoholism (watch for classic description of currant

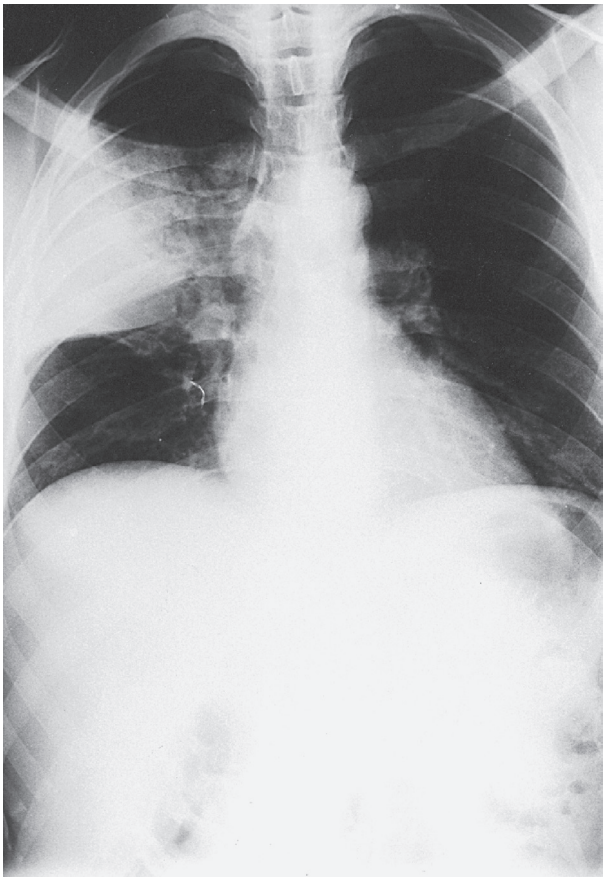

Figure 20-1. Pneumococcal pneumonia presenting with lobar consolidation. (From Mason RJ. Murray and Nadel's textbook of respiratory medicine. 5th ed. Philadelphia: Saunders, 2010, Fig. 32-1.)

jelly sputum), and enteric gram-negative organisms (e.g., *Escherichia coli*) are associated with aspiration, neutropenia, and hospital-acquired pneumonia. These pneumonias often have a high mortality rate because often patients are already in poor health and the severity of the pneumonia (abscesses are common). Treat empirically with an antipseudomonal penicillin (e.g., ticarcillin, piperacillin) with or without a beta lactamase inhibitor (e.g., clavulanate, tazobactam). Alternatives include ceftazidime or ciprofloxacin.

10. How do you recognize *Mycoplasma* pneumonia?

Mycoplasma infection is most common in adolescents and young adults (the classic patient is a college student or soldier who lives in a dormitory/barracks and has sick contacts). It is one of the atypical pneumonias because it presents differently than a typical pneumonia due to *S. pneumoniae.* For example, it has a long prodrome with gradual worsening of malaise, headaches, dry, nonproductive cough, and sore throat; the fever tends to be low-grade. Chest radiograph shows a patchy, diffuse bronchopneumonia and classically looks impressive, although the patient often does

not feel that bad. Look for positive **cold-agglutinin antibody titers,** which may cause hemolysis or anemia. Atypical pneumonia is treated empirically with a macrolide antibiotic (azithromycin), doxycycline, or broad-spectrum fluoroquinolone (e.g., levofloxacin, moxifloxacin).

11. What about chlamydial pneumonia?

Chlamydophila sp. is second only to *Mycoplasma* sp. as the cause of atypical pneumonia in adolescents and young adults. It presents similarly but has negative cold-agglutinin antibody titers. Treat with erythromycin in children younger than 8 years of age and either azithromycin or doxycycline in children older than 8 years of age, adolescents, and adults.

12. In what setting do you see *Pneumocystis jiroveci* pneumonia (PCP) and cytomegalovirus (CMV) pneumonia?

In HIV-positive patients with CD4 counts less than 200/mm^3 (AIDS) and other severely immunosuppressed patients (e.g., organ transplant recipients taking powerful immunosuppressants, patients on cancer chemotherapy). In AIDS, PCP is the most common opportunistic pneumonia and may require bronchoalveolar lavage for diagnosis. PCP can be seen with silver stains and typically causes bilateral interstitial lung infiltrates. Treat with trimethoprim-sulfamethoxazole plus corticosteroids. CMV pneumonia is characterized by intracellular inclusion bodies. Treat with valganciclovir.

13. What is the best time to treat PCP?

Before it happens. PCP is acquired when the CD4 count is below 200/mm^3. At that point you should institute PCP prophylaxis in an HIV-positive patient with trimethoprim-sulfamethoxazole. Alternatives include dapsone or atovaquone.

14. Cover the middle and right-hand columns and specify the organism after looking at the scenario associated with it.

SCENARIO	ORGANISM(S)	COMMENTS
Stuck with thorn or gardening	*Sporothrix schenckii*	Treat with itraconazole
Aplastic crisis in sickle cell disease	Parvovirus	B19
Sepsis after splenectomy	*Streptococcus pneumoniae, Haemophilus influenzae, Neisseria meningitis* (encapsulated bacteria)	
Pneumonia in the Southwest (California, Arizona)	*Coccidioides immitis*	Treat with itraconazole or fluconazole; amphotericin B for severe disease
Pneumonia after cave exploring or exposure to bird droppings in Ohio and Mississippi River valleys	*Histoplasma capsulatum*	
Pneumonia after exposure to a parrot or exotic bird	*Chlamydophila psittaci*	
Fungus ball/hemoptysis after tuberculosis or cavitary lung disease	*Aspergillus* sp.	Treat with voriconazole (Fig. 20-2)
Pneumonia in a patient with silicosis	Tuberculosis	
Diarrhea after hiking/drinking from a stream	*Giardia lamblia*	Stool cysts; treat with metronidazole
Pregnant woman with cats	*Toxoplasma gondii*	Treat infected pregnant women with spiramycin

SCENARIO	ORGANISM(S)	COMMENTS
B_{12} deficiency and abdominal symptoms	*Diphyllobothrium latum* (intestinal tapeworm)	
Seizures with ring-enhancing brain lesion on computed tomography (CT)	*Taenia solium* (cysticercosis) or toxoplasmosis	Treat neurocysticercosis with albendazole or praziquantel, usually with steroids; consider anticonvulsants
Squamous cell bladder cancer in Middle East or Africa	*Schistosoma haematobium*	
Worm infection in children	*Enterobius* sp.	Perianal itching, positive tape test; treat with mebendazole or albendazole
Fever, muscle pain, eosinophilia, and periorbital edema after eating raw meat	*Trichinella spiralis* (trichinosis)	
Gastroenteritis in young children	Rotavirus, Norwalk virus	
Food poisoning after eating reheated rice	*Bacillus cereus*	Infection is usually self-limited
Food poisoning after eating raw seafood	*Vibrio parahaemolyticus*	
Diarrhea after travel to Mexico	*Escherichia coli* (Montezuma revenge)	Treat with ciprofloxacin
Diarrhea after antibiotics	*Clostridium difficile*	Use oral metronidazole or oral vancomycin
Baby paralyzed after eating honey	*Clostridium botulinum*	Toxin blocks acetylcholine release
Genital lesions in children in the absence of sexual abuse or activity	Molluscum contagiosum	
Cellulitis after cat/dog bites	*Pasteurella multocida*	Treat animal bite wounds with prophylactic amoxicillin-clavulanate
Slaughterhouse worker with fever	Brucellosis	
Pneumonia after being in hotel or near air conditioner or water tower	*Legionella pneumophila*	Treat with azithromycin or levofloxacin
Burn wound infection with blue/green color	*Pseudomonas* sp.	*S. aureus* is also a common burn infection, but it lacks blue-green color

15. How is syphilis diagnosed?

Screen for syphilis with a rapid plasma reagin (RPR) or Venereal Disease Research Laboratory (VDRL) test. Confirm a positive test with a fluorescent treponemal antibody absorbed (FTA-ABS) or microhemagglutination (MHA-TP) test because false-positive results occur with the RPR and VDRL tests, classically in patients with lupus erythematosus. Once syphilis is treated, the RPR and VDRL tests become negative, whereas the FTA-ABS and MHA-TP tests often remain positive for life. You also can scrape the base of a genital chancre or condyloma lata and look for spirochetes on dark-field microscopy.

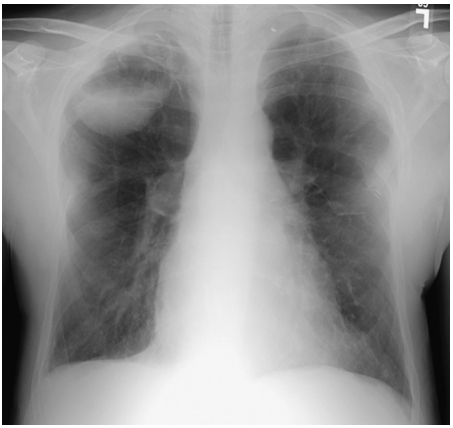

Figure 20-2. Invasive aspergillosis. Large right upper lobe cavity containing an air-fluid level. Transthoracic needle biopsy demonstrated fungal elements morphologically consistent with Aspergillus species. (From Mason RJ. Murray and Nadel's Textbook of Respiratory Medicine. 5th ed. Philadelphia: Saunders, 2010, Fig. 95-3.)

16. Which group of patients should always be screened for syphilis?

Pregnant women. Early treatment can prevent birth defects.

17. How is syphilis treated?

With penicillin. Use doxycycline for penicillin-allergic patients.

18. Describe the three stages of syphilis.

Primary stage: Look for a painless chancre that resolves on its own within 8 weeks (Fig. 20-3; Plate 47).

Secondary stage: Roughly 6 weeks to 18 months after infection; look for condyloma lata, maculopapular rash (classically involves palms and soles of feet; Fig. 20-4; See Plate 48.), and lymphadenopathy.

Tertiary stage: Years after initial infection (between the secondary and tertiary stages is the latent phase, in which the disease is quiet and asymptomatic). Look for gummas (granulomas in many different organs), neurologic symptoms and signs (e.g., neurosyphilis, Argyll-Robertson pupil, dementia, paresis, tabes dorsalis, Charcot joints), and thoracic aortic aneurysms.

19. How do you recognize measles (rubeola) infection in a child?

Look for a lack of immunization. Pathognomonic Koplik spots (tiny white spots on buccal mucosa) are seen 3 days after high fever, cough, runny nose, and conjunctivitis with or without photophobia. On the next day, a maculopapular rash begins on the head and neck and spreads downward to cover the trunk (cephalocaudal progression). Treat supportively.

20. Describe the complications of measles.

Complications include giant-cell pneumonia, especially in very young and immunocompromised patients; otitis media; and encephalitis, either acute or late (**subacute sclerosing panencephalitis,** which usually occurs years later).

21. Why is rubella infection (German measles) an important disease?

Rubella is important mainly because infection in pregnant mothers can cause severe birth defects in the fetus. Screen all women of reproductive age and immunize those without evidence of rubella

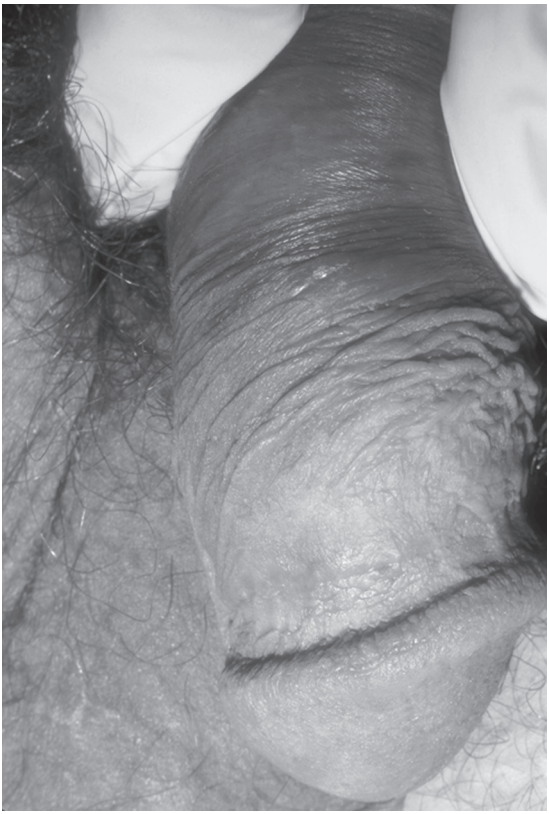

Figure 20-3. Penile chancre in a patient with primary syphilis. See Plate 47. (From Wein WS, et al, editors. Campbell-Walsh urology. 10th ed. Philadelphia: Saunders, 2011, Fig. 13-7.)

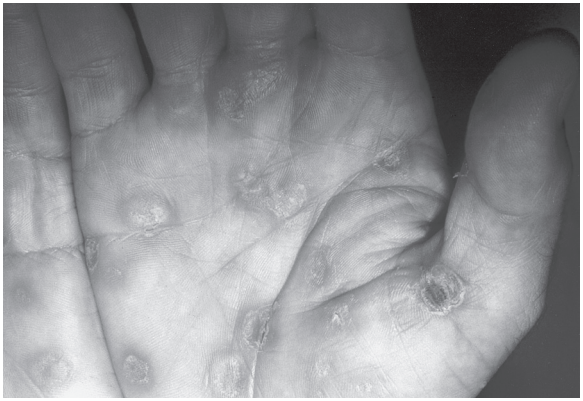

Figure 20-4. Palmar lesions of secondary syphilis. See Plate 48. (From Mandell GL, Bennett JE, Dolin R. Mandell, Douglas, and Bennett's principles and practice of infectious diseases. 7th ed. Philadelphia: Churchill and Livingstone, 2009, Fig. 238-5.)

antibodies before pregnancy to avoid this complication. However, the vaccine is contraindicated in pregnant women.

22. How do you recognize a rubella infection in children? What are the complications?

Rubella is milder than measles. Signs and symptoms include low-grade fever, malaise, and tender swelling of the suboccipital and postauricular nodes; arthralgias are common. After a 2- to 3-day prodrome, a faint maculopapular rash appears on the face and neck and spreads to the trunk (cephalocaudal progression), just as in measles. Complications include encephalitis and otitis media.

23. How do you recognize roseola infantum (exanthem subitum)? What causes it?

Roseola infantum is often easy to recognize because of the progression: high temperature (may be greater than 40°C) with no apparent cause for 4 days, which may result in febrile seizures, followed by an abrupt return to normal temperature just as a diffuse macular/maculopapular rash appears on the chest and abdomen. The disease is rare in children older than 3 years. It is caused by the human herpesvirus type 6 (a herpes family DNA virus).

24. How do you recognize erythema infectiosum (fifth disease) in children? What causes it?

Look for the classic "slapped-cheek" rash (Fig. 20-5; Plate 49, confluent erythema over the cheeks looks like someone slapped the child across the face) accompanied by mild constitutional symptoms (e.g., low-grade fever, malaise). One day later, a maculopapular rash appears on the arms, legs, and trunk. The disease is caused by parvovirus B19, the same virus that causes aplastic crisis in sickle cell disease.

25. How do you recognize chickenpox? What causes it?

The description and progression of the rash should lead you to the diagnosis: discrete macules (usually on the trunk) turn into papules, which turn into vesicles that rupture and crust over. Such

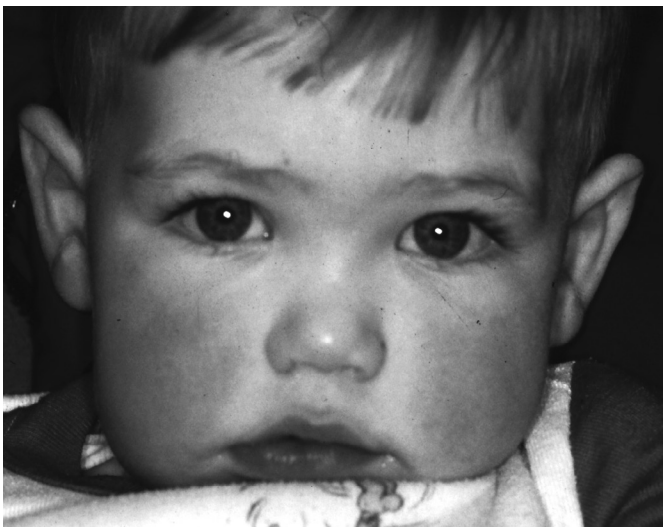

Figure 20-5. "Slapped cheek" appearance of erythema infectiosum. See Plate 49. (From Baren JM, Rothrock SG, Brennan JA, Brown, L: Pediatric emergency medicine. 1st ed. Philadelphia: Saunders, 2007, Fig 123-5.)

changes occur within 1 day. Because the lesions appear in successive crops, the rash will be in different stages of progression in different areas. The cause is the varicella virus.

26. How can you make a definitive diagnosis of chickenpox? At what point is a patient with chickenpox no longer infectious?

A Tzanck smear of tissue from the base of a vesicle shows multinucleated giant cells. A presumptive diagnosis can be made if the rash is classic. Infectivity ceases only when the last lesion crusts over.

27. What are the complications of chickenpox?

A major complication is infection of the lesions with streptococci or staphylococci, which cause erysipelas, cellulitis, and/or sepsis. The patient should be instructed to keep clean to avoid infection. Other complications include pneumonia (especially in very young children, adults, and immunocompromised patients), and encephalitis. Do not give aspirin to a child with a fever unless you have a diagnosis that requires its use because of the risk of **Reye syndrome.** The varicella-zoster virus can reactivate years later to cause herpes zoster (also known as shingles, see Fig. 20-6; Plate 50), a rash that develops in a dermatomal distribution, often with preceding pain and paresthesias. A child who has not been immunized or exposed to chickenpox can catch the disease from someone with shingles.

28. Describe the treatment and prophylaxis for chickenpox.

In most cases, no treatment is needed except supportive care (e.g., acetaminophen, fluids, avoidance of infecting others). Acyclovir can be used in severe cases. Routine vaccination with the varicella vaccine is now recommended for all children in the United States. Varicella zoster immune globulin is available for prophylaxis in patients with debilitating illness (e.g., leukemia, AIDS) within 4 days of exposure and for newborns of mothers with chickenpox. Intravenous immunoglobulin can be given if varicella zoster immune globulin is not available.

29. What is scarlet fever? What causes it? How is it recognized and treated?

Scarlet fever is a febrile illness with a rash caused by certain *Streptococcus* species. Look for a history of untreated streptococcal pharyngitis; only streptococcal species that produce erythrogenic toxin can cause scarlet fever. Pharyngitis is followed by a sandpaper-like rash on the abdomen and trunk with classic circumoral pallor and strawberry tongue. The rash tends to desquamate once the fever subsides. Oral penicillin V is the treatment of choice for streptococcal pharyngitis to

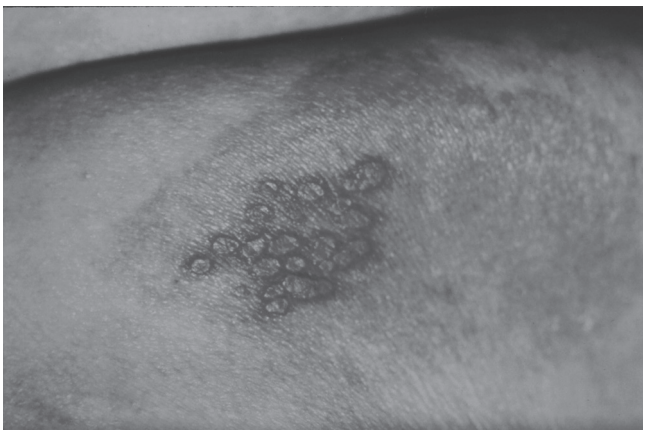

Figure 20-6. Herpes zoster. Grouped vesicopustules on an erythematous base. See Plate 50. (From Marx JA. Rosen's emergency medicine. 7th ed. Philadelphia: Mosby, 2009, Fig. 118-28. Courtesy David Effron, MD.)

prevent rheumatic fever. Alternative therapies include amoxicillin, cephalosporins, macrolides, or clindamycin.

30. What are the diagnostic criteria for Kawasaki disease (mucocutaneous lymph node syndrome)?

For the Step 2 examination, this rare disease is seen in patients younger than 5 years old. The diagnostic criteria include fever of more than 5 days' duration (mandatory for diagnosis); bilateral conjunctival injection; changes in the lips, tongue, or oral mucosa (e.g., strawberry tongue, fissuring, injection); changes in the extremities (e.g., skin desquamation, edema, erythema); polymorphous truncal rash, which usually begins 1 day after the fever starts; and cervical lymphadenopathy. Also look for arthralgia or arthritis.

31. What is the most feared complication of Kawasaki disease? How do you prevent it?

The most feared complications involve the heart (coronary artery aneurysms, congestive heart failure, arrhythmias, myocarditis, and even myocardial infarction [MI]). Include Kawasaki disease in the differential diagnosis of any child who has an MI. If Kawasaki disease is suspected, give aspirin and intravenous immunoglobulins. Both have been proven to reduce cardiac lesions. Kawasaki disease is one of the few indications for giving aspirin to a child. Follow the child with echocardiography to detect heart involvement.

32. Describe the classic findings of Epstein-Barr virus (EBV) infection (infectious mononucleosis).

Look for fatigue, fever, pharyngitis, and cervical lymphadenopathy in a young adult. The signs and symptoms are similar to those of streptococcal pharyngitis, but malaise tends to be prolonged and pronounced in EBV infection. To differentiate from streptococcal pharyngitis, look for the following:

- Splenomegaly (patients are at increased risk for splenic rupture and should avoid contact sports and heavy lifting).
- Hepatomegaly.
- Atypical lymphocytes (bizarre forms that may resemble leukemia) with lymphocytosis, anemia, or thrombocytopenia.
- Positive serology (heterophile antibodies [e.g., Monospot test]) or specific EBV antibodies (viral capsid antigen, Epstein-Barr nuclear antigens).

33. What is an important differential diagnosis of EBV infection?

Acute HIV infection, which can cause a mononucleosis-type syndrome.

34. What is the association between EBV and cancer?

EBV is associated with nasopharyngeal cancer, African Burkitt lymphoma, and posttransplant lymphoproliferative disorder.

35. Describe the classic clinical vignette for Rocky Mountain spotted fever. What causes it? What is the treatment?

Look for history of a tick bite (especially in a patient on the East Coast) 1 week before development of high temperature/chills, severe headache, and prostration or severe malaise. A rash appears roughly 4 days later on the palms/wrists and soles/ankles and spreads rapidly to the trunk and face (unique pattern of spread). Patients often look quite ill (e.g., disseminated intravascular coagulation, delirium). The infection is caused by *Rickettsia rickettsii*. Treat with doxycycline; chloramphenicol is a second choice.

36. How do you recognize and treat the rash of impetigo? What causes it?

In patients with impetigo, which is caused by *Streptococcus* and *Staphylococcus* species, look for a history of a break in the skin (e.g., previous chickenpox, insect bite, scabies, cut). The rash starts as

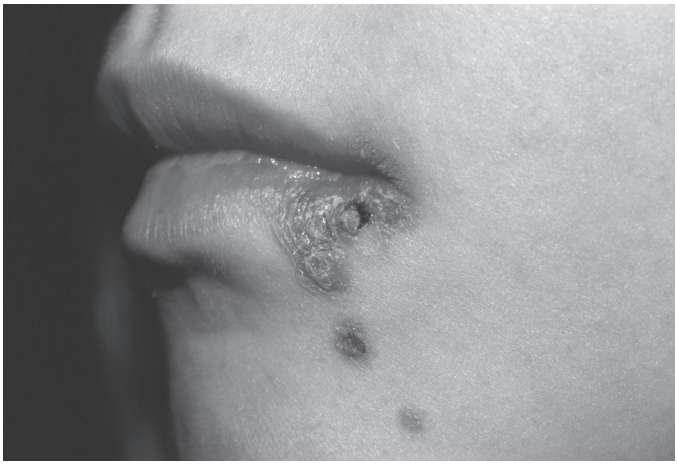

Figure 20-7. Impetigo. Multiple crusted and oozing lesions. See Plate 51. (From Kliegman RM, Stanton BF, St. Geme JW III, Schor NF. Nelson textbook of pediatrics. 19th ed. Philadelphia: Saunders, 2011, Fig. 657-1.)

thin-walled vesicles that rupture and form yellowish crusts (Fig. 20-7; Plate 51). The skin is classically described as "weeping." Typical lesions appear on the face and tend to be localized. The rash is infectious; look for a history of sick contacts. Treat with dicloxacillin, cephalexin, or clindamycin to cover both *Streptococcus* and *Staphylococcus* species. Topical mupirocin also may be used.

37. Describe the two clinical types of endocarditis. What are the causative organisms?

- **Acute** (fulminant) endocarditis, which typically affects normal heart valves and most commonly is caused by *S. aureus.*
- **Subacute,** which has an insidious onset and typically affects previously damaged or prosthetic valves. The most common cause is *Streptococcus viridans,* but other streptococcal and staphylococcal species may also cause endocarditis (e.g., *Staphylococcus epidermis, Streptococcus bovis,* enterococci). Suspect colon cancer if *S. bovis* is found on blood culture.

38. How is endocarditis diagnosed and treated?

The diagnosis generally is made by blood cultures. Empirical treatment is begun until the culture and sensitivity results are known. An antistaphylococcal penicillin (e.g., oxacillin, nafcillin) plus an aminoglycoside is a good choice for native valve endocarditis. A third-generation penicillin or cephalosporin plus an aminoglycoside is a reasonable choice. Empirical treatment for prosthetic valve endocarditis is vancomycin plus gentamicin plus either cefepime or a carbapenem.

39. What are the classic signs and symptoms of endocarditis?

Look for general signs of infection (e.g., fever, tachycardia, malaise) plus new-onset heart murmur, embolic phenomena (stroke and other infarcts), **Osler nodes** (painful nodules on tips of fingers), **Janeway lesions** (*nontender,* erythematous lesions on palms and soles), **Roth spots** (round retinal hemorrhages with white centers), and septic shock (more likely with acute than subacute disease).

40. What elements of the history point to endocarditis?

Look for patients who are more likely to be affected by endocarditis:

- Intravenous drug abusers, who usually have right-sided lesions, although left-sided lesions are much more common in the general population.

- Patients with abnormal heart valves (e.g., prosthetic valves, rheumatic valvular disease, congenital heart defects such as ventricular septal defects or tetralogy of Fallot).
- Postoperative patients (especially after dental surgery).

41. What are the recommendations for endocarditis prophylaxis?

The 2008 American Heart Association recommendations conclude that only an extremely small number of cases of infective endocarditis might be prevented by antibiotic prophylaxis for dental procedures. Cardiac conditions for which prophylaxis with dental procedures is recommended includes prosthetic cardiac valve, previous infectious endocarditis, congenital heart disease, and cardiac transplant recipients who develop valvulopathy. Antibiotic prophylaxis is no longer recommended for genitourinary or gastrointestinal procedures.

If a prophylactic antibiotic is indicated, it should be administered in a single dose before the procedure. Amoxicillin is the preferred choice for oral therapy. Cephalexin, clindamycin, azithromycin, or clarithromycin may be used in patients with penicillin allergy. Ampicillin, cefazolin, ceftriaxone, or clindamycin may be used for patients unable to take oral medication.

42. What is the classic age group for meningitis? Describe the physical findings.

Neonates are the classic age group for meningitis; 75% of all cases occur in children younger than 2 years. Deciding when to do a lumbar tap is difficult because patients often do not have classic physical findings (Kernig sign and Brudzinski sign). Look for lethargy, hyperthermia or hypothermia, poor muscle tone, bulging fontanelle, vomiting, photophobia, altered consciousness, and signs of generalized sepsis (e.g., hypotension, jaundice, respiratory distress). Seizures may also be seen, but simple febrile seizures are common in the absence of meningitis if the patient is between 5 months and 6 years old and has a temperature greater than 102°F.

43. What should you do if you suspect meningitis?

In the absence of trauma, do a lumbar puncture immediately and begin broad-spectrum antibiotics and intravenous fluids. Do *not* wait for culture or other results before starting antibiotics.

44. What is the most common neurologic sequela of meningitis?

Hearing loss. All pediatric and many adult patients need formal hearing evaluation after a bout of meningitis. Vision testing also is recommended. Other sequelae include mental retardation, motor deficits/paresis, epilepsy, and learning/behavioral disorders.

45. What are the common viral (aseptic) causes of meningitis in children?

Mumps and measles meningitis may be seen in children who are not immunized. The best treatment is prevention via immunization. Watch for neonatal herpes encephalitis (HSV-2) if the mother has genital lesions of herpes simplex virus at the time of delivery. Other children and adults can develop HSV-1 herpes encephalitis, which classically affects the **temporal lobes** on a head computed tomography (CT) or magnetic resonance imaging (MRI) scan. Give intravenous acyclovir.

46. Which types of bacterial meningitis require antibiotic prophylaxis in contacts?

N. meningitidis and *H. influenzae*. If a case of meningitis is caused by *Neisseria* sp., give all contacts rifampin, ciprofloxacin, ceftriaxone, or azithromycin as prophylaxis; rifampin is used for *H. influenzae* meningitis prophylaxis.

47. What are the "big three" respiratory infections in patients younger than 5 years old?

Croup, epiglottitis, and respiratory syncytial virus infection (RSV; bronchiolitis). These three diseases are high yield on the USMLE.

48. How do you recognize croup (acute laryngotracheitis)? Describe the cause and treatment.

Look for a child 1 to 2 years of age. Croup usually occurs in the fall or winter. Fifty percent to 75% of cases are caused by infection with parainfluenza virus; the other common causative agent is influenza virus. The disease begins with symptoms of viral upper respiratory infection (e.g., rhinorrhea, cough, fever). Roughly 1 to 2 days later patients develop a "barking" cough, hoarseness, and inspiratory stridor. The **"steeple sign"** (describes subglottic narrowing of the trachea; Fig. 20-8) is classic on a frontal radiograph of the chest or neck. Treat with dexamethasone, racemic epinephrine, a mist tent, and humidified oxygen.

49. How do you recognize epiglottitis? Describe the cause and treatment.

Epiglottitis usually occurs in children 2 to 5 years old. The main cause is *H. influenzae* type b, thus widespread vaccination has significantly reduced the incidence of this condition. *S. aureus, S. pyogenes*, and *S. pneumoniae* are other potential causes. Look for little or no prodrome with rapid progression to high temperature, toxic appearance, drooling, and respiratory distress with no coughing. The **thumb sign** (describes a swollen, enlarged epiglottis; Fig. 20-9) is classic on lateral radiographs of the neck. Do not examine the throat or irritate the child in any way. You may precipitate airway obstruction. When a case of epiglottitis is diagnosed, the first step is to be prepared to establish an airway (intubation and, if needed, tracheostomy). Treat with a combination of oxacillin or cefazolin or clindamycin or vancomycin plus cefotaxime or ceftriaxone.

50. Describe the classic clinical vignette for bronchiolitis. What is the cause? How is it treated?

Bronchiolitis generally affects children aged 0 to 18 months and usually occurs in the fall or winter. More than 75% of cases are caused by RSV; other causes are parainfluenza and influenza viruses.

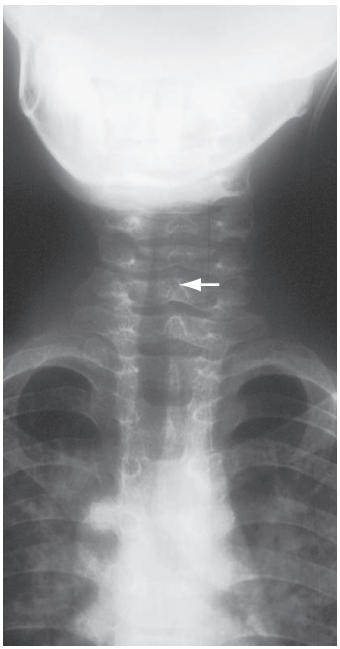

Figure 20-8. Anteroposterior radiograph of the neck region of child with croup. Note the steeple sign *(white arrow).* (From Wetmore RF. Pediatric otolaryngology: the requisites in pediatrics. 1st ed. Philadelphia: Mosby, 2007, Fig. 11-1.)

Patients first develop symptoms of viral upper respiratory infection, followed 1 to 2 days later by rapid respirations, intercostal retractions, and expiratory wheezing. The child may have crackles on auscultation of the chest. Diffuse hyperinflation of the lungs is classic on chest radiograph; look for flattened diaphragms. Treat supportively (e.g., oxygen, mist tent, bronchodilators, intravenous fluids). Use ribavirin only in patients with severe symptoms or who are at high risk (e.g., patients with cyanosis or other chronic health problems).

51. What "old-school" pediatric infection causes pseudomembranes and myocarditis? What about whooping cough?

Diphtheria (*Corynebacterium diphtheriae*) and pertussis (*Bordetella pertussis*), respectively. Diphtheria is quite uncommon in the United States because of mandatory vaccination. Pertussis was uncommon, but the incidence has been increasing significantly over the past 20 years. If a child is unimmunized (e.g., child of immigrants), don't forget these two entities. Diphtheria causes grayish pseudomembranes (necrotic epithelium and inflammatory exudate) on the pharynx, tonsils, and uvula as well as myocarditis. Pertussis is associated with severe paroxysmal coughing and a high-pitched whooping inspiratory noise (traditionally called "whooping cough"), particularly in children and especially those younger than 1 year of age. Treat diphtheria with antitoxin and either penicillin or erythromycin. Treat pertussis with azithromycin or erythromycin.

52. In what clinical scenario does rabies occur in the United States? Describe the classic physical findings.

Rabies in the United States is caused by to bites from infected animals, such as bats, skunks, raccoons, or foxes; rabies as a result of bites from dogs is rare because of vaccination. The incubation period is usually around 1 to 2 months. The classic findings are hydrophobia (fear of water as a result of painful swallowing) and central nervous system (CNS) signs (e.g., paralysis).

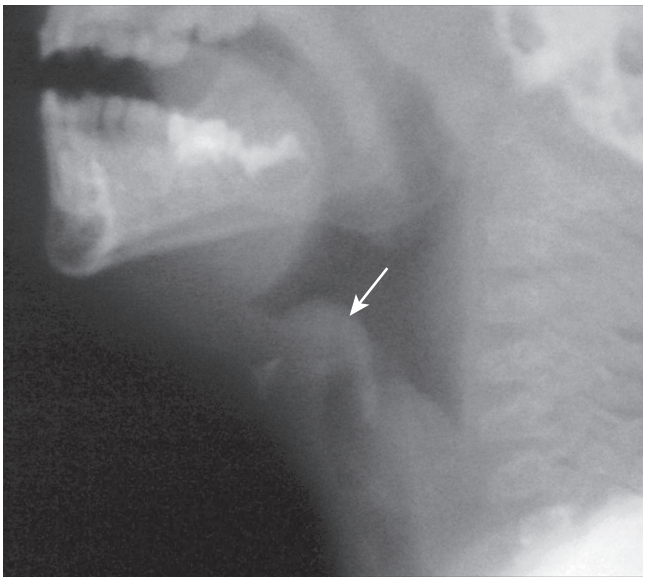

Figure 20-9. Lateral neck radiograph demonstrating epiglottis with the "thumb sign." (From Zaoutis LB, Chiang VW. Comprehensive pediatric hospital medicine. 1st ed. Philadelphia: Mosby, 2007, Fig. 66-3.)

53. What should you do after a patient is bitten by an animal?

- Treat the local wound. Cleanse thoroughly with soap. Do *not* cauterize or suture the wound. Amoxicillin-clavulanate is often given for cellulitis prophylaxis.
- Observe the animal. If possible, capture and observe the dog or cat to see if it develops rabies. If a wild animal is caught, it should be killed and the brain tissue examined for rabies.
- If the wild animal escapes or has rabies, give rabies immunoglobulin and rabies vaccine. In cases of a dog or cat bite, do *not* give immunoglobulin or vaccine unless the animal acted strangely or bit the patient without provocation and rabies is prevalent in the area (rare). Do not give prophylaxis or vaccine for rabbit or small rodent bites (e.g., rats, mice, squirrels, chipmunks).

54. What are the two main infections caused by *S. pyogenes* (group A streptococci)? What are the common sequelae?

S. pyogenes causes pharyngitis and skin infections. Sequelae include rheumatic fever, scarlet fever, and poststreptococcal glomerulonephritis.

55. How does streptococcal pharyngitis present? How do you diagnose and treat it?

Look for sore throat with fever, tonsillar exudate, enlarged tender cervical nodes, and leukocytosis. A positive streptococcal throat culture confirms the diagnosis. Elevated titers of antistreptolysin O (ASO) and anti-DNase antibody can be used for a retrospective diagnosis in patients with rheumatic fever or poststreptococcal glomerulonephritis. Treat streptococcal pharyngitis with penicillin, amoxicillin, cephalosporin, macrolide, or clindamycin to avoid rheumatic fever and scarlet fever.

56. What are the major and minor Jones criteria for rheumatic fever? Why is rheumatic fever less common today?

The five major Jones criteria include migratory polyarthritis, carditis, chorea, erythema marginatum, and subcutaneous nodules. The minor Jones criteria include elevations in erythrocyte sedimentation rate, C-reactive protein (CRP), white blood cell count, and ASO titer; prolonged PR interval on electrocardiogram (ECG); and arthralgia. The diagnosis of rheumatic fever requires a history of streptococcal infection and the presence of two of the major criteria or one major criterion plus two minor criteria. Treatment of streptococcal pharyngitis with antibiotics markedly reduces the incidence of rheumatic fever; thus it is less common today. Give all patients affected by rheumatic fever endocarditis prophylaxis before surgical procedures.

57. How do you recognize poststreptococcal glomerulonephritis? How is it treated?

Poststreptococcal glomerulonephritis occurs most commonly after a streptococcal skin infection, but it may also occur after pharyngitis. Patients are usually children and generally present with a history of infection with a nephritogenic strain of *Streptococcus* species 1 to 3 weeks earlier, as well as abrupt onset of hematuria, proteinuria (mild, not in nephrotic range), red blood cell (RBC) casts, hypertension, edema (especially periorbital), and elevated blood urea nitrogen and creatinine. Treat supportively. Control blood pressure and use diuretics for severe edema. Treatment of streptococcal infections does not reduce the incidence of poststreptococcal glomerulonephritis.

58. Distinguish between impetigo and erysipelas.

Both are superficial skin infections caused by streptococci or *S. aureus* and often occur after a break in the skin (e.g., trauma, scabies, insect bite). **Impetigo** (see Fig. 20-7) classically changes first from maculopapules to vesicopustules and bullae and then to honey-colored, crusted lesions. Staphylococci are a more frequent cause than streptococci. Definitely think of staphylococci if a furuncle or carbuncle is present; think of streptococci if glomerulonephritis develops. Impetigo is contagious; watch for sick contacts. If there are a limited number of lesions without bullae, topical mupirocin may be used. If there are bullous or many lesions, treat with dicloxacillin, cephalexin, or clindamycin. **Erysipelas** (Fig. 20-10; Plate 52) is a superficial cellulitis that appears red, shiny, and

swollen; it is tender and may be associated with vesicles and bullae, fever, and lymphadenopathy. Treat with penicillin or amoxicillin, although erysipelas may require parenteral therapy with a cephalosporin (ceftriaxone or cefazolin) if systemic symptoms such as fever and chills are present.

59. What organisms typically cause cellulitis? What special circumstances should make you think of atypical causes?

Streptococci and staphylococci cause most cases. Think of *Pseudomonas* species with burns or severe trauma; *Pasteurella multocida* after dog or cat bites (treat with ampicillin); *Vibrio vulnificus* in fishermen or other patients exposed to salt water (treat with tetracycline). Diabetic patients with foot ulcers tend to have polymicrobial infections and need powerful, broad-spectrum antibiotic coverage.

60. Describe the physical findings of cellulitis.

In patients with cellulitis, the involved overlying skin is red, hot, and frequently tender. It looks like erysipelas but involves deeper subcutaneous tissues. Antibiotic selection depends on whether the cellulitis is purulent or nonpurulent. These are newer terms and are designations within the 2011 Infectious Diseases Society of America clinical practice guidelines for MRSA. The idea is that a purulent infection may be caused by *Staphylococcus aureus*. Oral treatment options for purulent cellulitis are trimethoprim-sulfamethoxazole, doxycycline, clindamycin, and linezolid. Oral treatment options for nonpurulent cellulitis are dicloxacillin, cephalexin, and clindamycin.

61. Define necrotizing fasciitis. How is it treated?

Necrotizing fasciitis is defined as the progression of cellulitis to necrosis and gangrene. Watch for crepitus and signs of systemic toxicity (e.g., tachycardia, fever, hypotension). Often multiple organisms are involved (aerobes and anaerobes). Treat with intravenous fluids, incision and drainage/surgical debridement, and broad-spectrum antibiotics. This includes a carbapenem (imipenem or meropenem) plus clindamycin.

62. What is the most common cause of endometritis (puerperal fever)? How do you recognize and treat it?

Watch for endometritis, an infection of the endometrial lining, as a cause of postpartum fever. The hallmark is uterine tenderness, and the most common cause is *Streptococcus* species. Treat with clindamycin plus gentamicin after local cultures are obtained.

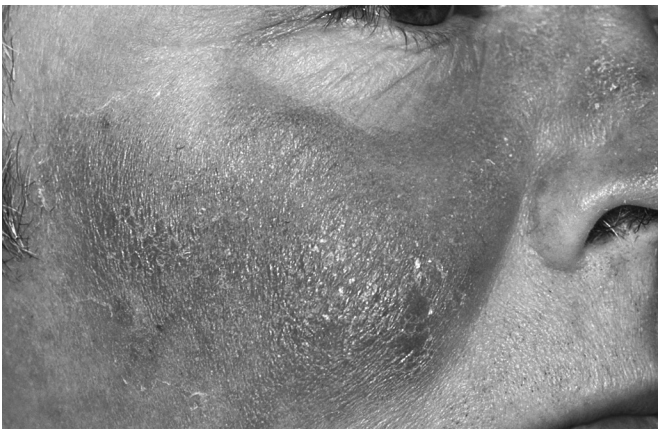

Figure 20-10. Sharply defined erythema and edema, characteristic of erysipelas. See Plate 52. (From Zaoutis LB, Chiang VW. Comprehensive pediatric hospital medicine. 1st ed. Philadelphia: Mosby, 2007, Fig. 156-2.)

63. What infection in neonates is caused by *Streptococcus agalactiae* (group B streptococci)?

S. agalactiae is the most common cause of neonatal meningitis or sepsis. The organism is often part of normal vaginal flora and may be acquired from the birth canal. Group B streptococci are penicillin-sensitive. Expectant mothers are cultured for group B strep, and if it is present around the time of delivery, then prophylactic intravenous penicillin (preferred) or intravenous ampicillin is given to the mother to prevent meningitis in the newborn.

64. Other than pneumonia, what infections does *S. pneumoniae* commonly cause?

Otitis media, meningitis, sinusitis, and spontaneous bacterial peritonitis.

65. What are the main infections caused by *S. aureus?*

The list is long. *S. aureus* is a common cause of the following infections:

- Skin and soft-tissue abscesses (especially in the breast after breast feeding or in the skin after a furuncle).
- Endocarditis (especially in drug users).
- Osteomyelitis (the most common cause unless sickle cell disease is present).
- Septic arthritis.
- Food poisoning (via a preformed toxin).
- Toxic shock syndrome (via a preformed toxin).
- Scalded skin syndrome (via a preformed toxin; affects younger children who often present with impetigo, then desquamate; Fig. 20-11; Plate 53).
- Impetigo.
- Cellulitis.
- Wound infections.
- Pneumonia (often forms lung abscess or empyema).
- Furuncles and carbuncles.

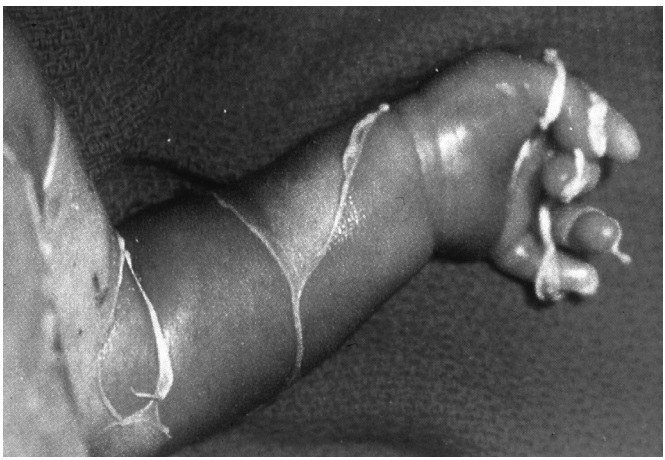

Figure 20-11. Scalded appearance from widespread desquamation seen in staphylococcal scalded skin syndrome. See Plate 53. (From Baren JM, Rothrock SG, Brennan JA, Brown L. Pediatric emergency medicine. 1st ed. Philadelphia: Saunders, 2007, Fig. 126-4.)

66. What is the treatment of choice for staphylococcal infections?

On the USMLE, treatment of choice is an antistaphylococcal penicillin (e.g., methicillin, dicloxacillin). Use vancomycin, clindamycin, doxycycline, trimethoprim-sulfamethoxazole, or linezolid if the staphylococcal species is known to be methicillin-resistant or if MRSA is suspected. MRSA is a rapidly growing problem. Most abscesses (regardless of the causative organism) must be treated first with surgical incision and drainage because antibiotics cannot penetrate through the walls of an abscess cavity.

67. Cover up the right-hand column in the table below and describe the preferred treatment for tuberculosis based on the clinical scenario.

CLINICAL SETTING/FINDINGS	TREATMENT
Exposed adult with negative PPD skin test	None
Exposed child younger than 5 years old with negative PPD	INH for 3 months, then repeat PPD
Prophylaxis for PPD conversion (negative to positive), no active disease	INH for 9 months
Active pulmonary disease/positive culture	INH/rifampin/pyrazinamide/ethambutol for 2 months, then INH/rifampin for 4 months in most patients

INH, Isoniazid; *PPD*, purified protein derivative.

68. Name some other important tuberculosis treatment issues.

Multidrug resistant strains are an increasing problem and require four-drug therapy (pyrazinamide, isoniazid, ethambutol, and rifampin) in most circumstances.

If the patient is noncompliant, directly observed therapy (someone watches the patient take medications every day) is recommended.

Consider supplementation with vitamin B_6 (pyridoxine) for patients on isoniazid (INH), or watch for signs of deficiency, such as neuropathy, confusion, angular chilitis, or a seborrheic dermatitis-like rash.

Watch for liver dysfunction in patients on therapy. Patients should be advised to abstain from alcohol while on treatment and should have their transaminase levels monitored.

LABORATORY MEDICINE

1. **What may cause a false lab report of hyperkalemia?**
   Hemolysis of the blood sample. Repeat the test if a high value does not make sense (e.g., high level with no electrocardiogram [ECG] changes or symptoms).

2. **What can cause a "false" hyponatremia (pseudohyponatremia)?**
   Pseudohyponatremia may be caused by hyperglycemia, hyperproteinemia, or hyperlipidemia. The hyponatremia resolves with correction of the glucose, lipid, or protein levels.

3. **What may result from rapid correction of hyponatremia?**
   Brainstem damage **(central pontine myelinolysis)**. For this reason you should generally not give hypertonic saline to correct hyponatremia except in severe or symptomatic cases, and then it should be given in limited quantities.

4. **What effect do serum acidosis and serum alkalosis have on potassium and calcium levels?**
   Alkalosis may cause hypokalemia and symptoms of hypocalcemia (perioral numbness, tetany) as a result of cellular shift, whereas acidosis may cause hyperkalemia by the same mechanism. Correction of acid-base status will correct the potassium and calcium derangements.

5. **Other than pancreatic disease, what else can cause elevated levels of amylase and lipase?**
   Damage of the salivary glands or bowel, renal failure, and ruptured tubal pregnancy may cause amylase and lipase elevations. Elevation of both amylase and lipase in the same patient, however, is usually caused by pancreatitis. The boards may try to trick you with an isolated elevation of amylase.

6. **Which diseases can cause elevated levels of alkaline phosphatase? What laboratory test is used to distinguish among these diseases?**
   Alkaline phosphatase can be elevated in biliary disease, bone disease, or pregnancy (the placenta produces alkaline phosphatase). If the elevation is a result of biliary disease, gamma-glutamyltranspeptidase (GGT) and/or 5′-nucleotidase (5′-NT) also should be elevated; both values, however, are normal in bone disease and pregnancy.

7. **True or false: Hypothyroidism can cause elevated cholesterol.**
   True. Thyroid hormone replacement corrects the elevated cholesterol.

8. **Injury to what organ (other than the heart) causes elevated levels of creatine kinase (CK)?**
   Muscle. Watch for trauma, rhabdomyolysis, HMG-CoA reductase inhibitors (which can cause muscle damage), and burns.

9. **What is the relationship of low calcium and potassium levels to low levels of magnesium?**

Hypokalemia and/or hypocalcemia may be caused by hypomagnesemia. In addition, if hypomagnesemia is present, it is often impossible to correct the hypokalemia or hypocalcemia until you correct the hypomagnesemia. If a patient has hypokalemia that does not correct with potassium supplements, check the magnesium level.

10. Which two electrolytes are classically depleted in the setting of diabetic ketoacidosis or diabetic hyperosmolar, hyperglycemic state?
Potassium and phosphorus.

11. What does a blood urea nitrogen (BUN)-to-creatinine ratio greater than 15 or 20 generally imply?
Dehydration.

12. What disease classically causes a false-positive result on the rapid plasma reagin (RPR) or venereal disease research laboratory (VDRL) syphilis test?
Systemic lupus erythematosus (SLE). A false-positive result on the RPR or VDRL test is actually one of the diagnostic criteria for SLE.

13. Define isosthenuria. What condition does it suggest?
Isosthenuria is the inability to concentrate or dilute the urine. The specific gravity of urine and serum is the same—classically 1.010. Isosthenuria is often associated with sickle cell trait or disease.

14. What does an elevated erythrocyte sedimentation rate mean in pregnancy?
Nothing. This is a normal finding in pregnancy (i.e., it is not a good test to order in a pregnant patient).

15. True or false: A high-normal level of BUN or creatinine during pregnancy often indicates renal disease.
True. BUN and creatinine are decreased significantly in pregnancy after the first trimester in women with normal renal function.

NEPHROLOGY

1. What are the symptoms and signs of acute renal failure?

Symptoms: Fatigue, nausea and vomiting, anorexia, shortness of breath, mental status changes.

Signs: Increased levels of blood urea nitrogen (BUN) and creatinine, metabolic acidosis, hyperkalemia, tachypnea (caused by acidosis and hypervolemia), and hypervolemia (bilateral rales on lung examination, elevated jugular venous pressure, dilutional hyponatremia).

2. What are the three broad categories of renal failure?

Prerenal, renal/intrarenal, and postrenal.

3. Define prerenal failure. What are the causes? How do you recognize it?

In prerenal failure, the kidney is not adequately perfused. The most common cause is hypovolemia (dehydration, hemorrhage). Look for a BUN-to-creatinine ratio greater than 20 and signs of hypovolemia (e.g., tachycardia, weak pulse, depressed fontanelle). Give intravenous fluids and/or blood. Other common prerenal causes are sepsis (treat the sepsis and give intravenous fluids), heart failure (give digoxin and diuretics), liver failure (hepatorenal syndrome; treat supportively), and renal artery stenosis (RAS).

4. Define postrenal failure. What causes it?

In postrenal failure, urine is blocked from being excreted at some point beyond the kidneys (ureters, prostate, urethra). The most common cause is benign prostatic hypertrophy (BPH). Patients are men older than age 50 with BPH symptoms (e.g., hesitancy, dribbling); ultrasound demonstrates bilateral hydronephrosis. Treat with catheterization (suprapubic, if necessary) to relieve the obstruction and prevent further renal damage. Then consider surgery (transurethral resection of the prostate). Other causes are nephrolithiasis (but remember that stones generally have to be bilateral to cause renal failure), retroperitoneal fibrosis (watch for a history of methysergide, bromocriptine, methyldopa, or hydralazine use), and pelvic malignancies.

5. What is the most common cause of intrarenal failure?

Intrarenal failure, which results from a problem within the kidney itself, is most commonly caused by **acute tubular necrosis** from various causes.

6. What do you need to know about intravenous contrast and renal failure?

Intravenous contrast can precipitate renal failure, usually in diabetic patients and patients with preexisting renal disease. Avoid contrast in such patients if possible. If you must give intravenous contrast, give lots of intravenous hydration before and after the contrast is given to decrease the chance of renal failure. Also consider the use of oral acetylcysteine on the day before and the day of contrast administration.

7. True or false: Muscle breakdown can cause renal failure.

True. Myoglobinuria or rhabdomyolysis caused by strenuous exercise (e.g., marathon runners), alcohol, burns, muscle trauma, muscle compression (e.g., prolonged immobilization after a fall), heat stroke, and neuroleptic malignant syndrome may cause renal failure. The cellular debris that results from muscle breakdown plugs the renal filtration system. Look for very high levels of creatine phosphokinase (CPK). Treat with hydration and diuretics.

8. What medications commonly cause renal insufficiency or failure?

Chronic use of nonsteroidal antiinflammatory drugs (NSAIDs; may cause acute tubular necrosis or papillary necrosis), cyclosporine, aminoglycosides, and methicillin.

9. Define Goodpasture syndrome. How does it present?

Goodpasture syndrome is caused by the presence of measurable antiglomerular basement membrane antibodies, which cause a linear immunofluorescence pattern on renal biopsy. These antibodies react with and damage both kidneys and lungs. Look for a young man with hemoptysis, dyspnea, and renal failure. Treat with steroids and cyclophosphamide.

10. Define Wegener granulomatosis. How does it present?

Wegener granulomatosis is a vasculitis that also affects the lungs and kidneys. Look for nasal involvement (bloody nose, nasal perforation) or hemoptysis and pleurisy as presenting symptoms, along with renal disease. Patients test positive for titers of **antineutrophil cytoplasmic antibody (ANCA).** Treat with cyclophosphamide and glucocorticoids. Methotrexate is an alternative.

11. What is the prototypical cause of glomerulonephritis? How does it present?

Poststreptococcal glomerulonephritis is the classic example on board examinations. It usually affects children with a history of upper respiratory infection or strep throat 1 to 3 weeks earlier. Presenting symptoms include edema, hypervolemia, hypertension, hematuria, and oliguria. *Red blood cell (RBC) casts* on urinalysis clinch the diagnosis. Treat supportively. Also watch for lupus erythematosus as a cause of glomerulonephritis. Renal failure is a major cause of morbidity and mortality in patients with lupus.

12. What are the indications for dialysis in patients with renal failure?

Whenever renal failure is present, first try to determine the cause and fix it, if possible, to correct the renal failure. Indications for acute dialysis include uremic encephalopathy, pericarditis, severe metabolic acidosis (roughly pH < 7.25), heart failure, and hyperkalemia severe enough to cause arrhythmia.

13. Define nephrotic syndrome. What causes it? How is it diagnosed?

Nephrotic syndrome is defined by proteinuria (>3.5 g/day), hypoalbuminemia, edema (the classic pattern is morning periorbital edema), and hyperlipidemia with lipiduria. In children it is usually caused by minimal change disease (podocytes with missing "feet" on electron microscopy), which often follows an infection. Measure 24-hour urine protein or spot urine protein-to-creatinine ratio to clinch the diagnosis. Treat with steroids. Causes in adults include diabetes, hepatitis B, amyloidosis, lupus erythematosus, and drugs (e.g., gold, penicillamine, captopril).

14. Define nephritic syndrome. What is the classic cause? How is it treated?

Nephritic syndrome generally is defined as oliguria, azotemia (rising BUN/creatinine), hypertension, and hematuria. The patient may have some degree of proteinuria, but not in the nephrotic range. The classic cause is poststreptococcal glomerulonephritis. Treatment is supportive, including control of hypertension and maintenance of urine output with intravenous fluids and diuretics.

15. What causes chronic kidney disease (CKD)?

Any of the causes of acute renal failure can cause chronic renal failure if the insult is severe or prolonged. Most cases of CKD are a result of diabetes mellitus (number one cause) or hypertension (number two cause). A popular Step 2 cause is polycystic kidney disease. Watch for multiple cysts in the kidney and a positive family history (usually autosomal dominant; autosomal recessive form presents in children), hypertension, hematuria, palpable renal masses, berry aneurysms in the circle of Willis, and cysts in liver (Fig. 22-1).

16. What metabolic derangements are seen in CKD?

- Azotemia (high levels of BUN and creatinine)
- Metabolic acidosis

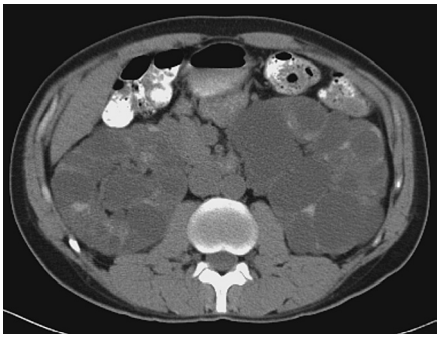

Figure 22-1. This noncontrast computed tomography (CT) image demonstrates autosomal dominant polycystic kidney disease. The kidneys are markedly enlarged bilaterally with multiple low-density cysts throughout both kidneys. The little remaining renal parenchyma is noted by the sparse higher density material squeezed by the cysts. (From Brenner B. Brenner and Rector's the kidney. 8th ed. Philadelphia: Saunders, 2008, Fig. 27-30.)

- Hyperkalemia
- Fluid retention (may cause hypertension, edema, congestive heart failure, and pulmonary edema)
- Hypocalcemia and hyperphosphatemia (impaired vitamin D production; bone loss leads to renal osteodystrophy)
- Anemia (cause by lack of erythropoietin; give synthetic erythropoietin to correct)
- Anorexia, nausea, vomiting (from build-up of toxins)
- Central nervous system (CNS) disturbances (mental status changes and even convulsions or coma from toxin build-up)
- Bleeding (as a result of disordered platelet function)
- Uremic pericarditis (friction rub may be heard)
- Skin pigmentation and pruritus (skin turns yellowish-brown and itches because of metabolic byproducts)
- Increased susceptibility to infection (as a result of decreased cellular immunity)

17. How is CKD treated?

Treat CKD with regular hemodialysis (usually 3 times/week), water-soluble vitamins (which are removed during dialysis), phosphate restriction and binders (calcium carbonate, calcium acetate, or sevelamer), erythropoietin as needed, and hypertension control. The only cure is renal transplant.

18. What are the signs and symptoms of urinary tract infection (UTI)? What are the most likely organisms?

Symptoms and signs include urgency, dysuria, suprapubic and/or low back pain, and low grade fever. UTIs usually are caused by *Escherichia coli* (75% to 85% of cases) but may also be caused by *Staphylococcus saprophyticus* or *Proteus, Pseudomonas, Klebsiella, Enterobacter,* and/or *Enterococcus* species (or other enteric organisms). Patients who acquire UTIs in the hospital or from a chronic, indwelling Foley catheter are more likely to have organisms other than *E. coli.*

19. What factors increase the likelihood of UTIs?

Female gender and conditions that promote urinary stasis (BPH, pregnancy, stones, neurogenic bladder, vesicoureteral reflux) or bacterial colonization (indwelling catheter, fecal incontinence, surgical instrumentation) predispose to UTI.

20. How do you diagnose and treat UTIs?

The gold standard for diagnosis is a positive urine culture with at least 100,000 colony-forming units (measure of bacterial load) of specific bacteria. At the least, get a midstream sample; the best

method is a catheterized sample or suprapubic tap. Urinalysis shows white blood cells, bacteria (on Gram stain of the urine), positive leukocyte esterase, and/or positive nitrite.

Empirical treatment usually is based on symptoms and urinalysis while awaiting culture results. Commonly used antibiotics include trimethoprim-sulfamethoxazole, amoxicillin, nitrofurantoin, ciprofloxacin, or a first-generation cephalosporin for about 5 days.

21. Why are UTIs in children of special concern?

In children, a UTI is cause for concern because it may be the presenting symptom of a genitourinary malformation. The most common examples are vesicoureteral reflux and posterior urethral valves. Urine culture should be obtained. Order an ultrasound and either a voiding cystourethrogram or radionuclide cystogram to evaluate the urinary tract in any child 2 months to 2 years old with a first UTI. Recommendations for imaging in older children are less clear-cut.

22. True or false: You should treat asymptomatic bacteriuria in most patients.

False. The exception is the pregnant patient, in whom asymptomatic bacteriuria is treated because of the high risk of progression to pyelonephritis. Use antibiotics that are safe in pregnancy, such as penicillins.

23. How does pyelonephritis usually occur? What are the signs and symptoms? How is it treated?

Pyelonephritis most often is a result of an ascending UTI caused by *E. coli* (>80% of cases). Presenting symptoms include high fever, shaking chills, costovertebral angle tenderness, flank pain, and/or UTI symptoms. Order urinalysis and urine and blood cultures to establish the diagnosis, but treat this life-threatening infection on an inpatient basis with intravenous antibiotics while awaiting results. A typical regimen consists of an oral fluoroquinolone or intravenous ceftriaxone or fluoroquinolone in uncomplicated pyelonephritis. Always choose an antibiotic regimen with good *E. coli* coverage.

24. How do you differentiate among the common pediatric hematologic disorders that affect the kidney?

	HUS	HSP	TTP	ITP
Most common age	Children	Children	Young adults	Children or adults
Previous infection	Diarrhea (*Escherichia coli*)	URI	None	Viral (especially in children)
RBC count	Low	Normal	Low	Normal
Platelet count	Low	Normal	Low	Low
Peripheral smear	Hemolysis	Normal	Hemolysis	Normal
Kidney effects	ARF, hematuria	Hematuria	ARF, proteinuria	None
Treatment	Supportive*	Supportive*	Plasmapheresis, NSAIDs; no platelets‡	Steroids,† splenectomy if drugs fail
Key differential points	Age, diarrhea	Rash, abdominal pain, arthritis, melena (Fig. 22-2; Plate 54)	CNS changes, age	Antiplatelet antibodies

ARF, Acute renal failure; *CNS*, central nervous system; *HSP*, Henoch-Schönlein purpura; *HUS*, hemolytic uremic syndrome; *ITP*, idiopathic thrombocytopenia; *NSAIDs*, nonsteroidal antiinflammatory drugs; *RBC*, red blood cell; *TTP*, thrombotic thrombocytopenic purpura; *URI*, upper respiratory infection.

*In HUS and HSP, patients may need dialysis and transfusions.

†Give steroids only if the patient is bleeding or platelet counts are very low (<20,000-30,000/μL).

‡Do not give platelet transfusions to patients with TTP; clots may form.

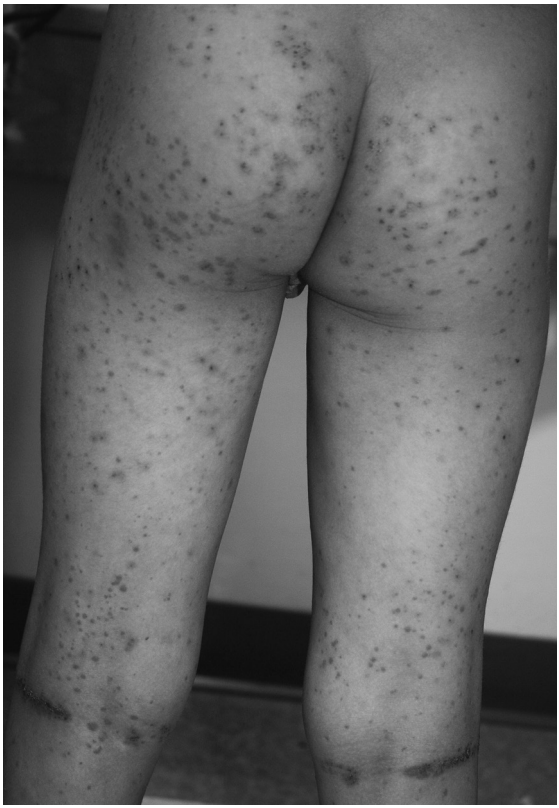

Figure 22-2. Henoch-Schönlein purpura. Nonblanchable macules and papules on the buttocks and lower extremities. See Plate 54. (From Taal MW. Brenner and Rector's the kidney. 9th ed. Philadelphia: Saunders: 2011, Fig. 59-20.)

25. Which is more likely to be seen on a plain abdominal radiograph: kidney stones or gallbladder stones?

Kidney stones (85%), which more commonly calcify (Fig. 22-3), are more likely to be seen than gallstones (15%).

26. What are the signs and symptoms of renal stones? How are they diagnosed and treated?

Kidney stones (nephrolithiasis) generally present with severe, intermittent, unilateral flank and/or groin pain when the stone dislodges and gets stuck in the ureter (ureterolithiasis). Most stones can be seen on abdominal radiographs and are composed of calcium. Renal ultrasound or computed tomography (CT) scan can be used to detect a stone if clinical suspicion is high but plain abdominal radiographs are negative. Symptomatic urolithiasis should be treated with lots of hydration and pain control (to see if the stone will pass). If the stone does not pass, it needs to be removed surgically (preferably endoscopically) or by lithotripsy.

27. What causes kidney stones?

Nephrolithiasis is often idiopathic, but on the Step 2 examination watch for one of the following underlying disorders that predispose to the development of kidney stones:

- **Hypercalcemia** as a result of hyperparathyroidism or malignancy (calcium stones).

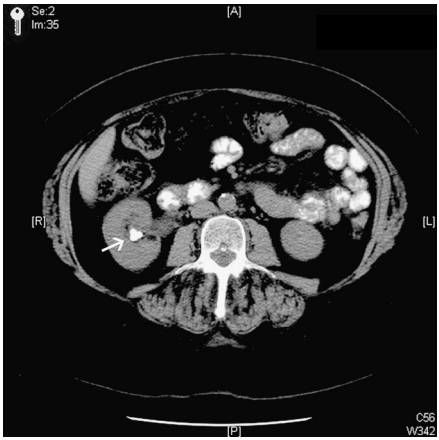

Figure 22-3. Computed tomography (CT) image of a urinary calculus in the right kidney. All stones (with the exception of some medication calculi) appear as dense, white objects within the urinary collecting system. (From Wein A, et al. Campbell-Walsh urology. 9th ed. Philadelphia: Saunders, 2007, Fig. 43-2.)

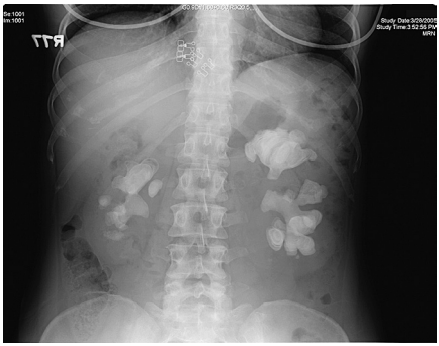

Figure 22-4. Plain film of a patient with bilateral staghorn calculi composed entirely of struvite. This patient had a 15-year history of recurrent urinary tract infections (UTIs). (From Wein A, et al. Campbell-Walsh urology. 9th ed. Philadelphia: Saunders, 2007, Fig. 43-9.)

- **Infection** from ammonia-producing organisms (*Proteus* spp., staphylococci). Look for **staghorn calculi** (large stones composed of magnesium, ammonia, and phosphate [struvite] that fill the renal calyceal system; Fig. 22-4).
- **Hyperuricemia** from uric acid stones caused by gout or leukemia treatment (allopurinol and intravenous hydration are given before leukemia chemotherapy to prevent this complication).
- **Cystinuria/aminoaciduria** should be suspected if the stone is made of cystine or in a repetitive stone-forming patient.

Note: Send any recovered stones to the laboratory for stone analysis to determine its type.

NEUROLOGY

1. In what common situation is a lumbar puncture contraindicated?

In the setting of acute head trauma, signs of intracranial hypertension (e.g., papilledema), or suspicion for subarachnoid hemorrhage. Do a lumbar tap only after you have a negative computed tomography (CT) or magnetic resonance imaging (MRI) scan of the head in these settings. Otherwise, you may cause uncal herniation and death.

2. Cover all but the left-hand column and describe the classic findings of cerebrospinal fluid (CSF) analysis in the following conditions.

CONDITION	CELLS (ML)*	GLUCOSE (MG/DL)	PROTEIN (MG/DL)	PRESSURE (MM HG)
Normal CSF	0-3 (L)	50-100	20-45	100-200
Bacterial meningitis	>1000 (PMN)	<50	Around 100	>200
Viral/aseptic meningitis	>100 (L)	Normal	Normal/slightly increased	Normal/slightly increased
Pseudotumor cerebri	Normal	Normal	Normal	>200
Guillain-Barré syndrome	0-100 (L)	Normal	>100	Normal
Cerebral hemorrhage†	Bloody (RBC)	Normal	>45	>200
Multiple sclerosis‡	Normal/slightly increased (L)	Normal	Normal/slightly increased	Normal

CSF, cerebrospinal fluid; *L*, lymphocytes; *PMN*, neutrophils; *RBC*, red blood cells.
*Main cell type is in parentheses after number.
†Think of subarachnoid hemorrhage, but this pattern may also occur after an intracerebral bleed.
‡On electrophoresis of CSF, look for oligoclonal bands as a result of increased IgG production and an increased level of myelin basic protein in the CSF during active demyelination.
Note: Tuberculous and fungal meningitis have low glucose (<50) with increased cells (>100), which are predominantly lymphocytes. In patients with fungal meningitis, a positive India ink preparation equals *Cryptococcus neoformans*.

3. Give a classic case description of multiple sclerosis.

Multiple sclerosis classically presents with an insidious onset of neurologic symptoms in white women aged 20 to 40 years with exacerbations and remissions. Common presentations include paresthesias and numbness, weakness and clumsiness, visual disturbances (decreased vision and pain caused by optic neuritis, diplopia as a result of cranial nerve involvement), gait disturbances, incontinence and urgency, and vertigo. Also look for emotional lability or other mental status changes. Internuclear ophthalmoplegia (a disorder of conjugate gaze in which the affected eye shows impairment of adduction) and scanning speech (spoken words are broken up into separate syllables separated by a noticeable pause and sometimes with stress on the wrong syllable) are classic; the patient may have a positive Babinski sign.

4. What is the most sensitive test for diagnosis of multiple sclerosis? How is it treated?

MRI is the most sensitive diagnostic tool and shows demyelination plaques. Also look for increased IgG/oligoclonal bands and possibly myelin basic protein in the CSF. Treatment is not highly effective

but includes interferon, glatiramer, mitoxantrone, natalizumab, cyclophosphamide, and methotrexate. Acute exacerbations are treated with glucocorticoids.

5. Define Guillain-Barré syndrome.

Guillain-Barré syndrome is a postinfectious polyneuropathy. Look for a history of mild infection (especially upper respiratory infection) or immunization roughly 1 week before onset of symmetric, distal weakness or paralysis with mild paresthesias that start in the feet and legs with loss of deep tendon reflexes in affected areas. The hallmark of the disease is that motor function is often affected with intact or only minimally impaired sensation. As the ascending paralysis or weakness progresses, respiratory paralysis may occur. Watch carefully; usually spirometry is performed to follow inspiratory ability. Intubation may be required. Diagnosis is by clinical presentation. CSF is usually normal except for markedly increased protein. Nerve conduction velocities are slowed. The disease usually resolves spontaneously. Plasmapheresis (for adults) and intravenous immune globulin (for children) reduce the severity and length of disease. Do *not* use steroids; they no longer have a role in the treatment of Guillain-Barré syndrome.

6. What causes nerve conduction velocity to be slowed?

Demyelination. Watch for Guillain-Barré syndrome and multiple sclerosis as causes.

7. What causes an electromyography (EMG) study to show fasciculations or fibrillations at rest?

A lower motor neuron lesion (i.e., a peripheral nerve problem).

8. What causes an EMG study with no muscle activity at rest and decreased amplitude of muscle contraction upon stimulation?

Intrinsic muscle disease such as the muscular dystrophies or inflammatory myopathies (e.g., polymyositis). You now know enough about EMG for the USMLE.

9. What is the most common cause of syncope? What other conditions should you consider?

Vasovagal syncope is the most common cause and classically is seen after stress or fear. Arrhythmias and orthostatic hypotension are also common. Consider hypoglycemia as a cause. The other main categories include:

- Cardiac problems (arrhythmias, hypertrophic cardiomyopathy, valvular disease, tamponade). Always check an electrocardiogram (ECG). Further testing with echocardiography or treadmill stress testing can be performed based on the ECG findings and degree of suspicion.
- Neurologic disorders (e.g., seizures, migraine headache, brain tumor). Consider an electroencephalogram or CT/MRI scan if history suggests seizures or intracranial lesion.
- Vascular disease (consider transient ischemic attacks (TIAs) or carotid stenosis, which can be ruled out with carotid artery ultrasound/duplex scanning, although this is not a common cause of syncope).
- Medication effects (e.g., anticholinergic agents, beta blockers, narcotics, vasodilators, alpha-agonists, antipsychotics).

As many as half of patients have syncope of unknown cause after a standard diagnostic evaluation.

10. Cover the right-hand column and localize the neurologic lesion for each of the following symptoms and signs.

SYMPTOM/SIGN	AREA
Decreased or no reflexes, fasciculations, atrophy	Lower motor neuron disease (or possibly muscle problem)
Hyperreflexia, clonus, increased muscle tone	Upper motor neuron lesion (cord or brain)

SYMPTOM/SIGN	AREA
Apathy, inattention, disinhibition, labile affect	Frontal lobes
Broca (motor) aphasia	Dominant frontal lobe*
Wernicke (sensory) aphasia	Dominant temporal lobe*
Memory impairment, hyperaggression, hypersexuality	Temporal lobes
Inability to read, write, name, or do math	Dominant parietal lobe*
Ignoring one side of body, trouble with dressing	Nondominant parietal lobe*
Visual hallucinations/illusions	Occipital lobes
Cranial nerves III and IV	Midbrain
Cranial nerves V, VI, VII, and VIII	Pons
Cranial nerves IX, X, XI, and XII	Medulla
Ataxia, dysarthria, nystagmus, intention, tremor, dysmetria, scanning speech	Cerebellum

*The left side is dominant in more than 95% of the population (99% of right-handed people and 60% to 70% of left-handed people).

11. For delirious or unconscious patients in the emergency department with no history of trauma, for what three common causes should you think about giving empirical treatment?

- Hypoglycemia (give glucose)
- Opioid overdose (give naloxone)
- Thiamine deficiency (give thiamine before giving glucose in a suspected alcoholic patient)

Other common causes are alcohol, illicit drugs, prescription drugs, diabetic ketoacidosis, stroke, and epilepsy or postictal state.

12. What are the classic differential points between delirium and dementia?

	DELIRIUM	DEMENTIA
Onset	Acute and dramatic	Chronic and insidious
Common causes	Illness, toxin, withdrawal	Alzheimer disease, multi-infarct dementia, HIV/AIDS
Reversible	Usually	Usually not
Attention	Poor	Usually unaffected
Arousal level	Fluctuates	Normal

13. What symptoms and signs do delirium and dementia have in common?

Both may have hallucinations, illusions, delusions, memory impairment (usually global in delirium, whereas remote memory is spared in early dementia), orientation difficulties (unawareness of time, place, person), and "sundowning" (worse at night).

14. Define pseudodementia.

Depression can cause some clinical symptoms and signs of dementia, classically in older adults. This type of "dementia" is reversible with treatment. Step 2 questions will address other signs and symptoms of depression (e.g., sadness, loss of loved one, weight or appetite loss, suicidal ideation, poor sleep, feelings of worthlessness).

15. What treatable causes of dementia must be ruled out?

The American Academy of Neurology recommends screening for B_{12} deficiency and hypothyroidism. Other treatable causes of dementia that you might consider screening for but which do not have clear data to support or refute screening in all patients with dementia include hyperhomocysteinemia, endocrine disorders (thyroid and parathyroid), uremia, liver disease, hypercalcemia, syphilis, Lyme disease, brain tumors, and normal-pressure hydrocephalus. Treatment of Parkinson disease may reverse dementia if it is present.

16. Define Wernicke encephalopathy and Korsakoff syndrome. What causes them?

Thiamine deficiency, classically in alcoholic patients, causes the acute delirium of **Wernicke encephalopathy,** which results in ataxia, ophthalmoplegia, nystagmus, and confusion. If untreated, this acute encephalopathy may progress to **Korsakoff syndrome,** which is characterized by memory loss with confabulation; because patients cannot remember, they make things up. Korsakoff syndrome usually is irreversible. Always give thiamine before glucose in an alcoholic patient to prevent precipitating Wernicke encephalopathy.

17. Differentiate among tension, cluster, and migraine headaches. How is each treated?

Tension headaches are the most common; look for a long history of headaches and stress, plus a feeling of tightness or stiffness, usually frontal or occipital and bilateral. Treat with stress reduction and acetaminophen/nonsteroidal antiinflammatory drugs (NSAIDs).

Cluster headaches are unilateral, severe, and tender; they occur in clusters (e.g., three in 1 week, then none for 2 months) and are usually accompanied by autonomic symptoms such as ptosis, lacrimation, rhinorrhea, and nasal congestion. Supplemental oxygen and subcutaneous sumatriptan are first-line therapy for acute attacks.

Migraine headaches classically are associated with an aura (a peculiar sensation, such as a noise or a flash of light, that lets the patient know that an attack is about to start). Often signs and symptoms include photophobia, nausea/vomiting, and a positive family history. Occasionally neurologic symptoms are seen during attacks. Migraines usually begin between the ages of 10 and 30 years. Medications used for the acute treatment of migraines include NSAIDs, triptans, ergotamine, and antiemetics. Prophylaxis can be achieved with beta blockers, tricyclic antidepressants, topiramate, valproic acid, and calcium channel blockers.

18. How do you recognize a headache secondary to brain tumor or intracranial mass?

By the presence of associated neurologic symptoms and signs of intracranial hypertension (papilledema; nausea/vomiting, which may be projectile; and mental status changes or ataxia). The classic headache occurs every day and is worse in the morning. Watch for a headache that wakes the patient from sleep. Headaches from an intracranial mass get worse with a Valsalva maneuver, exertion, or sex. Obtain a CT or MRI scan of the head.

19. Define pseudotumor cerebri. How is it diagnosed and treated?

Pseudotumor cerebri is a fairly benign condition that can mimic a tumor because both cause intracranial hypertension with papilledema and daily headaches that classically are worse in the morning and may be accompanied by nausea and vomiting. The difference, however, is that pseudotumor cerebri usually is found in young, obese females who are unlikely to have a brain tumor. Negative CT and MRI scans rule out a tumor or mass. The main worrisome sequela is vision loss. Treatment is supportive; weight loss usually helps, and repeated lumbar punctures or a CSF shunt may be needed. Large doses of vitamin A, tetracyclines, and withdrawal from corticosteroids are possible causes of pseudotumor cerebri.

20. How do you recognize a headache as a result of meningitis?

The adult patient has a fever, **Brudzinski sign** or **Kernig sign,** and positive CSF findings (the classic findings in bacterial meningitis are significantly elevated white blood cells, decreased glucose,

protein around 100 mg/dL, and increased opening pressure) if a lumbar tap is done. Photophobia is also common.

21. What causes the "worst headache" of a patient's life?

This is a classic description for a subarachnoid hemorrhage. The most common causes are ruptured congenital berry aneurysm or trauma. Look for blood around the brain or within sulci on a CT or MRI scan or grossly bloody CSF on lumbar puncture. Treatment is supportive. Aneurysms require surgical treatment to prevent rebleeding and death.

22. What are the common extracranial causes of headache?

- Eye pain (optic neuritis, eye strain from refractive errors, iritis, glaucoma)
- Middle ear pain (otitis media, mastoiditis)
- Sinus pain (sinusitis)
- Oral cavity pain (toothache)
- Herpes zoster infection with cranial nerve involvement
- Nonspecific headache (malaise from any illness, studying for the Step 2 examination)

23. What does a lesion of the first cranial nerve (CN I) cause? What exotic syndrome should you watch for clinically?

CN I lesions cause anosmia (inability to smell). Watch for **Kallmann syndrome,** which is anosmia plus hypogonadism caused by gonadotropin-releasing hormone deficiency.

24. True or false: Brain lesions can be localized based on the visual field defect.

True. Remember this stuff from basic science? Review it again for at least one easy point on the USMLE Step 2 (Fig. 23-1). If you really hate this stuff, at least remember bitemporal hemianopsia caused by an optic chiasm lesion, usually caused by a pituitary tumor.

VISUAL FIELD DEFECT	LOCATION OF LESION
Right anopsia (monocular blindness)	Right optic nerve
Bitemporal hemianopsia	Optic chiasm (classically caused by pituitary tumor)
Left homonymous hemianopsia	Right optic tract
Left upper quadrant anopsia	Right optic radiations in the right temporal lobe
Left lower quadrant anopsia	Right optic radiations in the right parietal lobe
Left homonymous hemianopsia with macular sparing	Right occipital lobe (from posterior cerebral artery occlusion)

25. How do you distinguish between a benign and serious cause of CN III deficit?

With benign causes (i.e., hypertension, diabetes) of a CN III palsy, the pupil is normal in size and reactive; no treatment is needed. With serious causes (i.e., aneurysm, tumor, uncal herniation), the pupil is dilated and nonreactive ("blown"). Urgent diagnosis and treatment are required. Additional neurologic symptoms also indicate a serious cause.

The first step in serious cases is to obtain a CT or MRI scan of the head. Careful observation is preferred in benign cases. If the patient does not improve within a few months or does not have hypertension or diabetes, order a CT or MRI scan of the head to be sure.

26. What does CN V (trigeminal nerve) innervate? What classic peripheral nerve disorder affects its function?

CN V innervates the muscles of mastication and facial sensation, including the afferent limb of the corneal reflex. Watch for **trigeminal neuralgia** (tic douloureux), which classically is described as

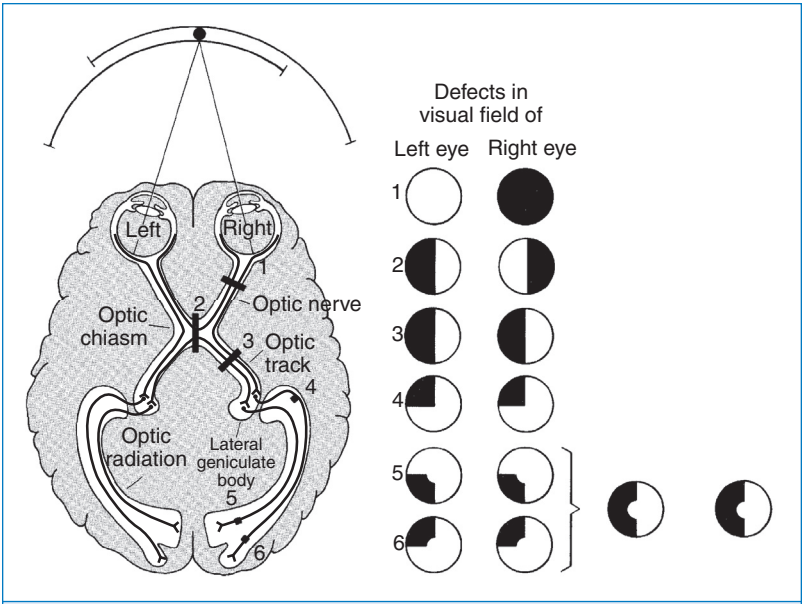

Figure 23-1. Visual field defects produced by lesions at various levels of the visual pathway. 1, Right optic nerve; 2, optic chiasm; 3, optic tract; 4, Meyer's loop; 5, cuneus; 6, lingual gyrus; *bracket,* occipital lobe (with macular sparing). (From Berne R. Physiology. 5th ed. Philadelphia: Mosby, 2003.)

unilateral shooting pains in the face in older adults and often triggered by activity (e.g., brushing the teeth). This condition is best treated with antiepilepsy medications (e.g., carbamazepine). If the patient is younger and female or the symptoms are bilateral, consider multiple sclerosis and rule out other causes, such as tumor or stroke.

27. What structures does CN VII innervate? What is the difference between an upper and lower motor neuron lesion of the facial nerve?

CN VII (facial nerve) innervates the muscles of facial expression, taste in the anterior two thirds of the tongue, skin of the external ear, lacrimal and salivary glands (except the parotid gland), and stapedius muscle. With an upper motor neuron lesion of CN VII, the forehead is spared on the affected side, and the cause is usually a stroke or tumor. With a lower motor neuron lesion, the forehead is involved on the affected side, and the cause is usually Bell palsy or tumor.

28. What problems other than facial droop affect patients with a CN VII lesion?

Patients may be unable to close their eyes. Give artificial tears to prevent corneal ulceration. Also watch for **hyperacusis** (quiet noises sound extremely loud) in Bell palsy as a result of stapedius muscle paralysis.

29. What rare tumor is a classic cause of lower motor neuron lesions of CN VII and CN VIII?

Cerebellopontine angle tumors (e.g., acoustic neuroma, classically seen in patients with neurofibromatosis).

30. Describe the function of the vestibulocochlear nerve (CN VIII). What symptoms do lesions cause?

CN VIII is needed for hearing and balance. Lesions can cause deafness, tinnitus, and/or vertigo. In children, think of meningitis as a cause. In adults, symptoms may be caused by a toxin or medication (e.g., aspirin, aminoglycosides, loop diuretics, cisplatin), infection (labyrinthitis), tumor, or stroke.

31. What does the glossopharyngeal nerve (CN IX) innervate? What physical findings are associated with a lesion?

CN IX innervates the pharyngeal muscles and mucous membranes (afferent limb of gag reflex), parotid gland, taste in the posterior third of the tongue, skin of the external ear, and the carotid body/sinus. With lesions (cause by stroke or tumor) look for loss of gag reflex and loss of taste in the posterior third of the tongue.

32. Describe the function of the vagus nerve (CN X). Specify the physical findings and causes of lesions.

CN X innervates muscles of the palate, pharynx, and larynx (efferent limb of gag reflex); taste buds in the base of the tongue; abdominal viscera; and skin of the external ear. Look for hoarseness, dysphagia, and loss of gag or cough reflex. Lesions are commonly a result of stroke, but do not forget aortic aneurysms or tumors (especially apical/Pancoast lung tumors) as a cause of recurrent laryngeal nerve palsy and hoarseness.

33. What muscles does the spinal accessory nerve (CN XI) innervate? How do you know on which side the lesion is located?

CN XI innervates the sternocleidomastoid and trapezius muscles. Patients with CN XI lesions have trouble turning their heads to the side opposite the lesion and have ipsilateral shoulder droop.

34. What does a lesion of the hypoglossal nerve (CN XII) cause?

CN XII innervates the muscles of the tongue. A protruded tongue deviates to the same side as the lesion.

35. Which vitamin deficiencies may present with neurologic signs or symptoms?

- Vitamin B_{12}: Dementia, peripheral neuropathy, loss of vibration sense in lower extremities, loss of position sense, ataxia, spasticity, hyperactive reflexes, and positive Babinski sign.
- Thiamine: Peripheral neuropathy, confusion, ophthalmoplegia, nystagmus, ataxia, confusion, delirium, dementia.
- Vitamin E: Loss of proprioception/vibratory sensation, areflexia, ataxia, and gaze palsy.
- Vitamin A: Vision loss.
- Vitamin B_6: Peripheral sensory neuropathy (watch for isoniazid as a cause, and give prophylactic B_6 to patients taking isoniazid, if given the choice).

36. What are the six general types of seizures that you should be able to recognize?

- Simple partial
- Complex partial
- Absence (petit mal)
- Tonic-clonic
- Febrile
- Secondary

37. Describe a simple partial seizure. How is it treated?

Simple partial (local or focal) seizures may be motor (e.g., Jacksonian march), sensory (e.g., hallucinations), or psychic (cognitive or affective symptoms). The key point is that consciousness is *not*

impaired. The first-line agents for treatment are carbamazepine, lamotrigine, oxcarbazepine, and levetiracetam.

38. Describe complex partial seizures. How are they treated?

Complex partial (psychomotor) seizures are any simple partial seizure followed by impairment of consciousness. Patients perform purposeless movements and may become aggressive if restraint is attempted (however, people who get in fights or kill other people are not having a seizure). The first-line agents for treatment are valproate, lamotrigine, and levetiracetam.

39. Give the classic description of an absence seizure.

Absence (petit mal) seizures do not begin after the age of 20 years. They are brief (10 to 30 seconds in duration), generalized seizures in which the main manifestation is loss of consciousness, often with eye or muscle fluttering. The classic description is a child in a classroom who stares into space in the middle of a sentence, then 20 seconds later resumes the sentence where he left off. The child is *not* daydreaming; he or she is having a seizure. There is no postictal state (an important differential point). The first-line treatment agents are ethosuximide and valproate.

40. How do you recognize a tonic-clonic seizure?

Tonic-clonic (grand mal) seizures are the classic seizures that we knew about before we went to medical school. They may be associated with an aura. Tonic muscle contraction is followed by clonic contractions, usually lasting 2 to 5 minutes. Associated symptoms may include incontinence and tongue lacerations. The postictal state is characterized by drowsiness, confusion, headache, and muscle soreness. The first-line agents for treatment are valproate, lamotrigine, or levetiracetam.

41. Define febrile seizure.

Children between the ages of 6 months and 5 years may have a seizure caused by fever. Always assume another cause outside this age range. The seizure is usually of the tonic-clonic, generalized type. No specific seizure treatment is required, but you should treat the underlying cause of the fever, if possible, and give acetaminophen to reduce fever. Such children do *not* have epilepsy, and the chances of their developing it are just barely higher than in the general population. Make sure that the child does not have meningitis, tumor, or another serious cause of the seizure. The Step 2 question will give clues in the case description if you should pursue work-up for a serious condition.

42. What are the common causes of secondary seizures? How are they treated?

- Mass effect (tumor [Fig. 23-2], hemorrhage)
- Metabolic disorder (hypoglycemia, hypoxia, phenylketonuria, hyponatremia)
- Toxins (lead, cocaine, carbon monoxide poisoning)
- Drug withdrawal (alcohol, barbiturates, benzodiazepines, withdrawing anticonvulsants too rapidly)
- Cerebral edema (severe or malignant hypertension; also watch for pheochromocytoma and eclampsia)
- Central nervous system (CNS) infections (meningitis, encephalitis, toxoplasmosis [Fig. 23-3], cysticercosis)
- Trauma
- Stroke

Treat the underlying disorder and use a benzodiazepine (lorazepam or diazepam) and/or phenytoin or fosphenytoin acutely to control seizures. For all seizures (primary or secondary), secure the airway, and, if possible, roll the patient onto his or her side to prevent aspiration.

43. Define status epilepticus. How is it treated?

Status epilepticus is defined as a seizure that lasts for a sufficient length of time (usually 30 minutes or longer) or is repeated frequently enough that the individual does not regain consciousness between seizures. Status epilepticus may occur spontaneously or result from withdrawing

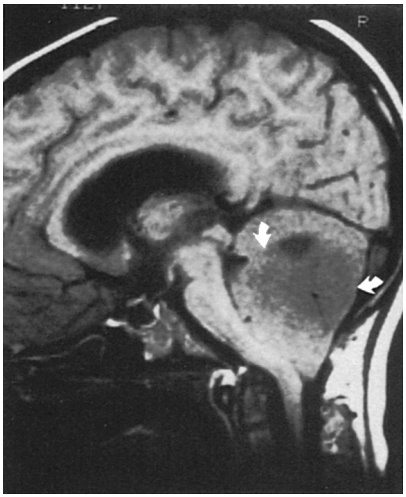

Figure 23-2. Magnetic resonance imaging (MRI) scan of medulloblastoma. Sagittal T1-weighted image shows a hypointense mass involving the vermis *(arrows)*. (From Kuhn JP, Slovis TL, Haller JO. Caffey's pediatric diagnostic imaging. 10th ed. Philadelphia: Mosby, 2004, p. 574.)

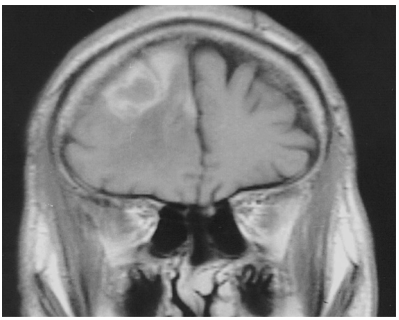

Figure 23-3. Magnetic resonance imaging (MRI) scan (post-contrast T1-weighted image) demonstrating a focal mass-like lesion with ring enhancement within the right frontoparietal area in a 30-year-old HIV-positive patient whose presenting symptoms included mental status changes. The primary differential diagnosis is between lymphoma and toxoplasmosis. (From Goetz C. Textbook of clinical neurology. 3rd ed. Philadelphia: Saunders, 2007, Fig. 23-34.)

anticonvulsants too rapidly. Treat with intravenous lorazepam. Give fosphenytoin if the seizures persist. As with all seizures, remember your ABCs (**a**irway, **b**reathing, **c**irculation). Protect the airway. Intubate if necessary, and roll the patient on his or her side to prevent aspiration.

44. True or false: Hypertension can cause seizures.

True. Remember hypertension as a cause of seizures or convulsions, headache, confusion, stupor, and mental status changes.

45. What do you need to remember when giving anticonvulsants to women?

All anticonvulsants are teratogenic, and women of reproductive age need counseling about the risks of pregnancy. Do a pregnancy test before starting an anticonvulsant and offer birth control. Valproic acid is a major contributor to the risk. Polypharmacy increases the risk. There is limited human information of the risks to the fetus with the newer antiepileptic medications.

46. What causes strokes? How common are they?

Cerebrovascular disease (stroke) is the most common cause of neurologic disability in the United States—and the third leading cause of death. Ischemia as a result of atherosclerosis (atherothrombotic ischemia) is by far the most common type of stroke (more than 85% of cases). Hypertension is another cause of stroke and typically causes hemorrhagic stroke, most commonly in the basal ganglia, thalamus, or cerebellum. With this in mind, be aware of more exotic causes of stroke, such as atrial fibrillation with resultant clot formation and emboli to the brain, septic emboli from endocarditis, and sickle cell disease.

47. How is an acute stroke treated?

Treatment for an acute stroke in evolution is supportive (e.g., airway, oxygen, intravenous fluids). The first step is to obtain a CT scan of the head without contrast to evaluate for bleeding or mass (Fig. 23-4). If no blood is seen on the CT scan, aspirin is usually the medication of choice. Heparin is not recommended for the treatment of acute ischemic stroke and should be avoided as a choice on the USMLE. Chapter 39 ("Vascular Surgery") discusses the role of carotid endarterectomy, which is not done emergently. Thrombolysis with tPA (tissue plasminogen activator) can be attempted if patients come to the hospital within 3 hours (up to 4.5 hours in certain circumstances) and meet strict criteria for its use.

48. Define TIA. How is it managed?

TIA is a brief episode of neurologic dysfunction resulting from temporary cerebral ischemia not associated with cerebral infarction. This newer definition is tissue-based rather than time-based. TIA is often a precursor to stroke and is caused by ischemia. The classic presentation is ipsilateral blindness (amaurosis fugax) and/or unilateral hemiplegia, hemiparesis, weakness, or clumsiness that lasts less than 5 minutes.

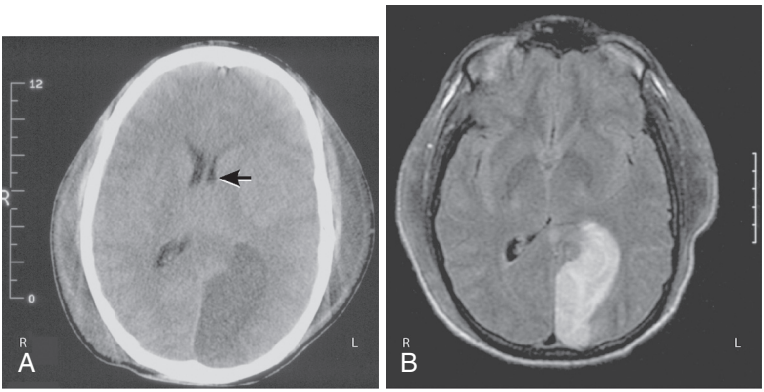

Figure 23-4. Stroke on computed tomography (CT) and magnetic resonance imaging (MRI) scans. **A,** The CT scan done 3 days after a stroke shows a low-density area posteriorly on the left with mass effect and clear midline shift (*arrow*). **B,** The MRI scan done on the same day shows the infarcted area much more clearly. (From Mettler F. Essentials of radiology. 2nd ed. Philadelphia: Saunders, 2004.)

Order a carotid duplex scan to look for carotid stenosis. The correct choice for long-term therapy is aspirin and antiplatelet medications. Choose carotid endarterectomy over aspirin if the degree of carotid stenosis is 70% to 99%.

49. Describe the signs and symptoms of Huntington disease. How is it acquired? What is the classic CT finding?

Huntington disease is an autosomal dominant condition that usually presents between the ages of 35 and 50 years. Look for choreiform movements (irregular, spasmodic, involuntary movements of the limbs or facial muscles) and progressive intellectual deterioration, dementia, or psychiatric disturbances. **Atrophy of the caudate nuclei** may be seen on CT or MRI scan. Treatment is supportive; tetrabenazine or atypical neuroleptics (olanzapine, risperidone, or aripiprazole) may help with the chorea and agitation/psychosis.

50. Define Parkinson disease. How do you recognize it on the Step 2 examination?

Parkinson disease has a classic tetrad of (1) slowness or poverty of movement, (2) muscular ("lead pipe" and "cog-wheel") rigidity, (3) "pill-rolling" tremor at rest (which disappears with movement and sleep), and (4) postural instability (manifested by the classic shuffling gait and festination). Patients may also have dementia and depression. The mean age of onset is around 60 years.

51. Describe the pathophysiology of Parkinson disease. How is it treated pharmacologically?

The cause is thought to be a loss of dopaminergic neurons, especially in the **substantia nigra,** which project to the basal ganglia. The result is decreased dopamine in the basal ganglia. Drug therapy, which aims to increase dopamine, includes dopamine precursors (levodopa with carbidopa), dopamine agonists (bromocriptine, apomorphine, pergolide, pramipexole, and ropinirole), monoamine oxidase-B inhibitors (selegiline), COMT inhibitors (entacapone and tolcapone), anticholinergics (trihexyphenidyl and benztropine), and amantadine.

52. What is the classic iatrogenic cause of parkinsonian signs and symptoms?

Antipsychotics may cause parkinsonian symptoms in schizophrenic patients. This is a favorite Step 2 question. Treat this side effect of antipsychotic medication with anticholinergics (benztropine, trihexyphenidyl) or antihistamines (diphenhydramine).

53. What brain lesions cause a resting tremor and an intention tremor? What about hemiballismus?

A resting tremor, if caused by a brain lesion, is generally a sign of basal ganglia disease, as is chorea. An intention tremor is usually a result of cerebellar disease. Hemiballismus (random, violent, unilateral flailing of the limbs) is classically caused by a lesion in the **subthalamic nucleus.**

54. What conditions other than Parkinson disease cause a resting tremor?

A resting tremor may be caused by hyperthyroidism, anxiety, drug withdrawal or intoxication, or benign (essential) hereditary tremor. Benign hereditary tremor is usually autosomal dominant; look for a positive family history and use beta blockers to reduce the tremor. Also watch for Wilson disease (hepatolenticular degeneration), which can cause chorea-like movements; asterixis (slow, involuntary flapping of outstretched hands) may be seen in patients with liver failure.

55. What diseases should come to mind in children with cerebellar findings?

- Brain tumor (cerebellar astrocytoma, medulloblastomas)
- Hydrocephalus (enlarging head in an infant younger than age 6 months, Arnold-Chiari or Dandy-Walker malformations)
- Friedreich ataxia (starts between ages 5 and 15 years; autosomal recessive; look for areflexia, loss of vibration/position sense, and cardiomyopathy)

- Ataxia-telangiectasia (progressive cerebellar ataxia, oculocutaneous telangiectasias, and immune deficiency)

56. What diseases should come to mind in adults with cerebellar findings?

Alcoholism, brain tumor, ischemia or hemorrhage, and multiple sclerosis.

57. How do you recognize amyotrophic lateral sclerosis (ALS) on the Step 2 examination?

ALS (Lou Gehrig disease) is the only condition that you are likely to be asked about that causes both upper and lower motor neuron lesion signs and symptoms. This idiopathic neurodegenerative disease is more common in men, and the mean age at onset is 55 years. The key is to notice a combination of upper motor neuron lesion signs (spasticity, hyperreflexia, positive Babinski sign) and lower motor neuron lesion signs (fasciculations, atrophy, flaccidity) present at the same time. Treatment is supportive. Fifty percent of patients die within 3 years of disease onset.

58. What are the two classic causes of a "floppy" (flaccid) baby? How do you differentiate the two?

Genetic disorders, the most common of which is Werdnig-Hoffmann disease (WHD), and infant botulism. History easily differentiates the two. WHD is an autosomal recessive degeneration of anterior horn cells in the spinal cord and brainstem (lower motor neuron disease). Most infants are hypotonic at birth, and all are affected by 6 months. Look for a positive family history and a long, slowly progressive disease course. Treatment is supportive only.

Infant botulism is caused by a *Clostridium botulinum* toxin. Look for sudden onset and a history of ingesting honey or other home-canned foods. Diagnosis is made by finding *C. botulinum* toxin or organisms in the feces. Treatment involves inpatient monitoring and support with a close watch of respiratory status. The child may need intubation for respiratory muscle paralysis. Spontaneous recovery usually occurs within 1 week, and supportive care is all that is needed.

59. List the causative categories of peripheral neuropathy and give examples of each.

- Metabolic/endocrine: Diabetes mellitus (autonomic and sensory neuropathy), uremia, hypothyroidism.
- Nutritional: Deficiencies of vitamin B_{12}, vitamin B_6 (look for history of isoniazid), thiamine ("dry" beriberi), and vitamin E.
- Toxins/medications: Lead (the classic symptom is wrist drop or foot drop; look for coexisting CNS or abdominal symptoms) or other heavy metals, isoniazid, vincristine, ethambutol (optic neuritis), aminoglycosides (especially CN VIII).
- Immunization and autoimmune disorders: Guillain-Barré syndrome, lupus erythematosus, polyarteritis nodosa, scleroderma, sarcoidosis, amyloidosis.
- Trauma: Carpal tunnel syndrome (entrapment of the median nerve at the wrist; usually caused by repetitive physical activity but may be a presentation of acromegaly or hypothyroidism; look for positive Tinel and Phalen signs), pressure paralysis (radial nerve palsy in alcoholics), fractures (causing nerve compression).
- Infectious: Lyme disease, diphtheria, HIV, leprosy.

60. What test can be used to prove the presence of a peripheral neuropathy, regardless of etiology?

Nerve conduction velocity is slowed with a peripheral neuropathy.

61. Describe the pathophysiology of myasthenia gravis (MG). Who is affected? What are the classic physical findings?

MG is an autoimmune disease that destroys acetylcholine receptors. Most patients have antibodies to acetylcholine receptors in their serum. The disease usually presents in women between the ages of

20 and 40 years. Look for ptosis, diplopia, and general muscle fatigability, especially toward the end of the day or with repetitive use.

62. How is MG diagnosed? What tumor is associated with it?

Diagnosis is made with the Tensilon test. After injection of edrophonium (Tensilon), a short-acting anticholinesterase inhibitor, muscle weakness improves. Nerve stimulation studies can also be used. Watch for associated **thymomas** (a tumor of the thymus). Thymectomy is generally recommended for patients younger than age 60 years without thymoma. Long-term medical treatment consists of long-acting anticholinesterase inhibitors (pyridostigmine) and immunotherapy (glucocorticoids, mycophenolate, azathioprine, and cyclosporine).

63. What three conditions may cause an MG-like clinical picture?

1. **Eaton-Lambert syndrome** is a paraneoplastic syndrome (classically seen with small cell lung cancer) associated with muscle weakness. The extraocular muscles are spared, whereas MG almost always is characterized by prominent involvement of extraocular muscles. Eaton-Lambert syndrome has a different mechanism of action (impaired release of acetylcholine from nerves) and a differential response to repetitive nerve stimulation. The weakness in MG worsens with repetitive use or stimulation, whereas the weakness in Eaton-Lambert syndrome improves.
2. **Organophosphate poisoning** also causes MG-like muscle weakness. Poisoning usually is caused by agricultural exposure. Look for symptoms of parasympathetic excess (e.g., miosis, excessive bronchial secretions, urinary urgency, diarrhea). Edrophonium causes worsening of the muscular weakness. Treat with atropine and pralidoxime.
3. **Aminoglycosides in high doses** may cause MG-like muscular weakness and/or prolong the effects of muscular blockade after anesthesia.

64. What is the most common type of muscular dystrophy? How is it inherited? What are the classic findings?

The most common type is Duchenne muscular dystrophy, an X-linked recessive disorder of dystrophin that usually presents in boys between the ages of age 3 and 7. Look for muscle weakness, markedly elevated levels of creatine phosphokinase, pseudohypertrophy of the calves (caused by fatty and fibrous infiltration of the degenerating muscle), and often a lower-than-normal IQ. Gower sign is also classic: the patient "walks" his hands and feet toward each other to rise from a prone position (Fig. 23-5). Muscle biopsy establishes the diagnosis. Treatment is supportive. Most patients die by age 20.

65. List the five less common types of muscular dystrophies.

1. Becker muscular dystrophy: Also an X-linked recessive dystrophin disorder but milder.
2. Facioscapulohumeral dystrophy: An autosomal dominant disorder that affects the areas in the name (face, shoulder girdle). Symptoms begin between the age of 7 and 20 years. Life expectancy is normal.
3. Limb-girdle dystrophy: Affects pelvic and shoulder muscles; begins in adulthood.
4. Mitochondrial myopathies: Of interest because they are inherited mitochondrial defects (passed only from mother to offspring; cannot be transmitted by men). The key phrase is "ragged red fibers" on biopsy specimen. Ophthalmoplegia is usually present.
5. Myotonic dystrophy: An autosomal dominant disorder that presents between the ages of 20 and 30 years. Myotonia (inability to relax muscles) classically presents as an **inability to relax the grip or release a handshake.** Look for coexisting mental retardation, baldness, and testicular or ovarian atrophy. Treatment is supportive, including genetic counseling. The diagnosis is clinical.

66. What class of inherited metabolic disorders affects muscle and may resemble muscular dystrophy?

The rare glycogen storage diseases (autosomal recessive inheritance) can cause muscular weakness, especially **McArdle disease,** a deficiency in glycogen phosphorylase that is relatively mild and presents with weakness and cramping after exercise as a result of lactic acid build-up.

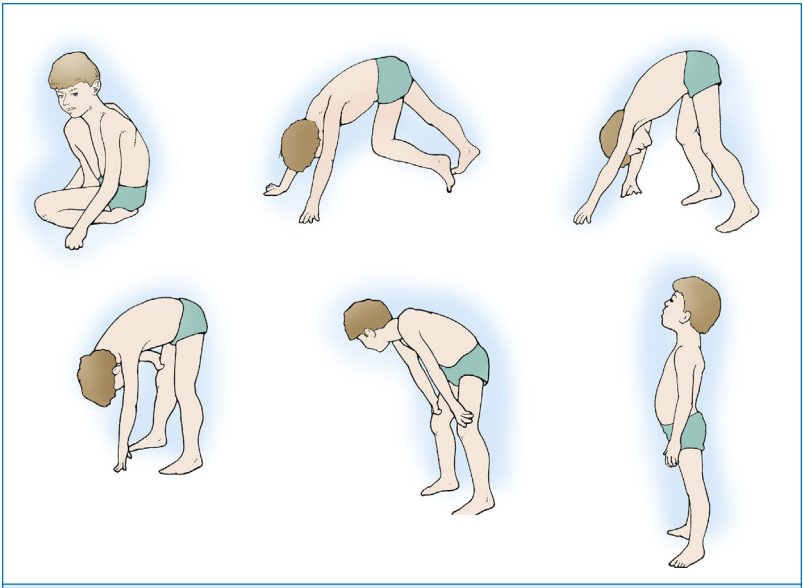

Figure 23-5. Gower sign. Child must use hands to rise from sitting position. (From Canale ST, Beaty JH. Campbell's operative orthopaedics. 11th ed. Philadelphia: Mosby, 2011, Fig. 32-5. Redrawn from Siegel IM. Clinical management of muscle disease. London: William Heinemann, 1977.)

NEUROSURGERY

1. List the four major types of intracranial hemorrhage.

- Subdural hematoma
- Epidural hematoma
- Subarachnoid hemorrhage
- Intracerebral hemorrhage

2. What causes a subdural hematoma? How do you recognize and treat it?

Subdural hematomas are caused by bleeding from veins that bridge the cortex and dural sinuses. On a computed tomography (CT) scan, the hematoma is crescent-shaped (Fig. 24-1). Subdural hematomas are common in alcoholic patients and victims of head trauma. They may present immediately after trauma or as long as 1 to 2 months later. If the patient has a history of head trauma, always consider the diagnosis of subdural hematoma. If large, expanding, or accompanied by neurologic deficits, treat with surgical evacuation.

3. What causes an epidural hematoma? How do you recognize and treat it?

Epidural hematomas are caused by bleeding from meningeal arteries (classically, the middle meningeal artery). On a CT scan, the hematoma is lenticular in shape (Fig. 24-2). At least 85% of epidural hematomas are associated with a skull fracture (classically, a temporal bone fracture), and many patients have an ipsilateral "blown" pupil (dilated, fixed, nonreactive pupil on the side of the hematoma). The classic history includes head trauma with loss of consciousness, followed by a lucid interval of minutes to hours, then neurologic deterioration. Treatment usually includes surgical evacuation.

4. Define subarachnoid hemorrhage. What causes it? How is it treated?

A subarachnoid hemorrhage is bleeding between the arachnoid and pia mater. The most common cause is trauma, followed by ruptured berry aneurysms. Blood can be seen in the cerebral ventricles and surrounding the brain or brainstem on a CT scan. Classically, the patient describes the "worst headache of my life," although many die or are unconscious before they reach the hospital. Patients who are awake have signs of meningitis (positive Kernig sign and Brudzinski sign). Remember the association between polycystic kidney disease and berry aneurysms. CT is the test of choice and should be performed before performing lumbar puncture (see question 12). A lumbar puncture shows grossly bloody cerebrospinal fluid (CSF).

Treat with support of vital functions, anticonvulsants, and observation. Once the patient is stable, do a CT or magnetic resonance (MR) angiogram to look for aneurysms or arteriovenous malformations, which may be treatable with surgical clipping or catheter-directed angiographic procedures.

5. What causes an intracerebral hemorrhage? How do you recognize and treat it?

Intracerebral hemorrhage describes bleeding into the brain parenchyma (Fig. 24-3). The most common cause is hypertension, but it may also be a result of other forms of stroke, trauma, arteriovenous malformations, coagulopathies, or tumors. Two thirds of intracerebral hemorrhages occur in the basal ganglia (especially with hypertension). The patient may come to the hospital with coma or, if awake, contralateral hemiplegia and hemisensory deficits. Blood (which appears white on a CT scan) can be seen in the brain parenchyma and may extend into the ventricles. Surgery is reserved for large, accessible hemorrhages, although usually it is not helpful.

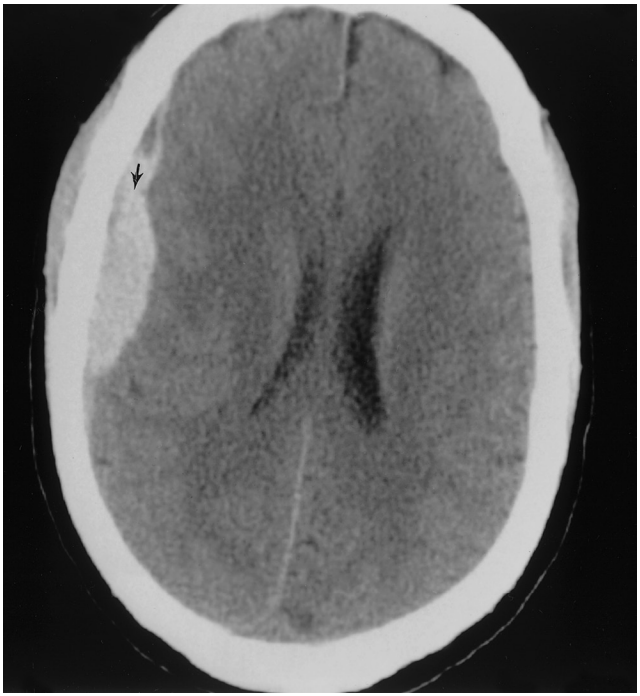

Figure 24-1. Subdural hematoma. An axial nonenhanced computed tomography (CT) scan of the brain demonstrates acute extra-axial hematoma. There is hyperdense blood *(arrow)* layered along the lateral aspect of the right brain margin separating brain from the inner table of the skull consistent with an acute subdural hematoma. (From Layon AJ, Gabrielli A, Friedman WA. Textbook of neurointensive care. Philadelphia: Saunders, 2003.)

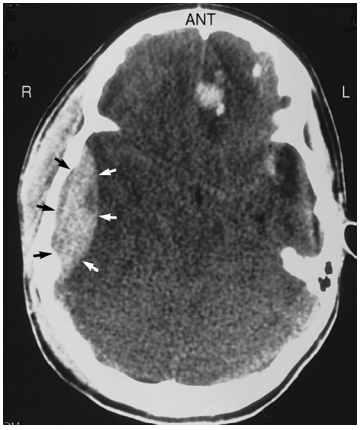

Figure 24-2. Epidural hematoma. In this patient, who was in a motor vehicle accident, a lenticular area of increased density is seen on a noncontrasted axial computed tomography (CT) scan in the right parietal region. Areas of hemorrhage also are seen in the left frontal lobe. (From Mettler F. Essentials of radiology. 2nd ed. Philadelphia: Saunders, 2004.)

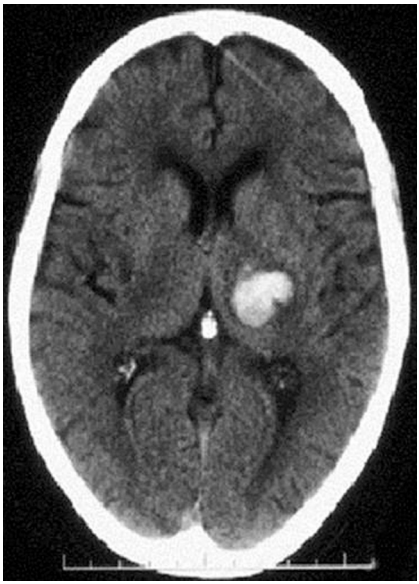

Figure 24-3. Intracerebral hemorrhage. A computed tomography (CT) scan shows a parenchymal hemorrhage involving the left thalamus and posterior internal capsule. (From Goldman. Goldman's Cecil medicine. 24th ed. Philadelphia: Saunders, 2011. Courtesy of Gregory W. Albers, Stanford University, Stanford, Calif.)

6. After a history of head trauma, what does a dilated, unreactive pupil on one side mean until proved otherwise?

In the setting of head trauma, a dilated, unreactive pupil on one side most likely represents impingement of the ipsilateral third cranial nerve and impending uncal herniation caused by increased intracranial pressure. Of the different intracranial hemorrhages, this scenario is seen most commonly with epidural hemorrhages. Do *not* perform a lumbar puncture in any patient with a "blown" pupil because you may precipitate uncal herniation and death. Instead, order a CT or magnetic resonance imaging (MRI) scan of the head.

7. List the four classic signs of a basilar skull fracture.

1. Periorbital ecchymosis ("raccoon eyes")
2. Postauricular ecchymosis (Battle sign)
3. Hemotympanum (blood behind the eardrum)
4. CSF otorrhea or rhinorrhea (leakage of CSF, which is clear in appearance, from the ears or nose)

8. What is the imaging test of choice for skull fractures of the calvarium? How are they managed?

Skull fractures of the calvarium (roof of the skull) are best seen on a CT scan (preferred over plain x-rays). Surgical indications include contamination (surgical cleaning and debridement), depression with impingement on brain parenchyma, or open fracture with CSF leak. Otherwise, such fractures can be observed and generally heal on their own.

9. True or false: Severe, permanent neurologic deficits may occur after head trauma, even with a negative CT or MR scan of the head.

True. Head trauma can cause cerebral contusion or shear injury of the brain parenchyma, both of which may not show up on a CT or MR scan but may cause temporary or permanent neurologic deficits.

10. What finding suggests increased intracranial pressure?

Increased intracranial pressure (intracranial hypertension) is highly suggested in the setting of bilaterally dilated and fixed pupils. Normal intracranial pressure is between 5 and 15 mm Hg. Less specific symptoms include headache, papilledema, nausea and vomiting, and mental status changes. Look also for the classic Cushing triad, which consists of increasing blood pressure, bradycardia, and respiratory irregularity.

11. How should increased intracranial pressure be managed?

The first step is to intubate the patient in reverse Trendelenburg position (head up). Once intubated, the patient should be hyperventilated for rapid lowering of intracranial pressure through decreased intracranial blood volume (caused by cerebral vasoconstriction). For longer term treatment, **mannitol** diuresis may decrease cerebral edema. Furosemide is also used but is less effective. Ventriculostomy should be performed if hydrocephalus is identified. Barbiturate coma and decompressive craniotomy (burr holes) are last-ditch measures. Anticonvulsant therapy should be started if seizures are suspected; prophylactic anticonvulsants are controversial but may be warranted in some cases.

Remember that cerebral perfusion pressure equals blood pressure minus intracranial pressure. In other words, do *not* treat hypertension initially in a patient with increased intracranial pressure because hypertension is the body's way of trying to increase cerebral perfusion. Lowering blood pressure in this setting may worsen symptoms or even cause a stroke.

12. True or false: Lumbar puncture is the first test that should be performed in a patient with increased intracranial pressure.

False. *Never* do a lumbar puncture in any patient with signs of increased intracranial pressure until a CT scan is done first. If the CT is totally negative, you can proceed to a lumbar puncture, if needed. If you do a lumbar puncture first, you may precipitate uncal herniation and death.

13. How do patients with spinal cord trauma present? How are they managed?

Patients with spinal cord trauma often come to the hospital with “spinal shock” (loss of reflexes and motor function, hypotension). Order standard trauma radiographs (cervical spine, chest, pelvis) as well as additional spine radiographs or CT scans based on physical examination. Also give corticosteroids (proven to improve outcome). Moderate hypothermia is increasingly being used in the management of patients with spinal cord trauma. Surgery is performed for incomplete neurologic injury (some residual function maintained) with external compression (e.g., subluxation, bone chip). An MRI can show cord injury noninvasively.

14. What causes spinal cord compression? How do patients present?

Spinal cord compression usually is defined as acute or subacute. Most cases of acute cord compression result from trauma. Look for the appropriate history. Subacute compression is often caused by metastatic cancer but may also result from a primary neoplasm, subdural or epidural abscess (classically seen in diabetics and caused by *Staphylococcus aureus*), or hematoma (especially after a lumbar tap or epidural/spinal anesthesia in a patient with a bleeding disorder or a patient taking anticoagulation).

Patients present with local spinal pain (especially with bone metastases) and neurologic deficits below the lesion (e.g., hyperreflexia, positive Babinski sign, weakness, sensory loss).

15. How should patients with subacute spinal cord compression be diagnosed and treated?

The first step in the emergency department is to give high-dose corticosteroids and order an MRI scan (preferred over CT; Fig. 24-4). If the cause is cancer or tumor, give local radiation if the metastases are from a known primary tumor that is radiosensitive. Surgical decompression can be used if the tumor is not radiosensitive. For a hematoma or subdural/epidural abscess, surgery is indicated for decompression and drainage. Prognosis is related most closely to pretreatment function; the longer you wait to treat, the worse the prognosis.

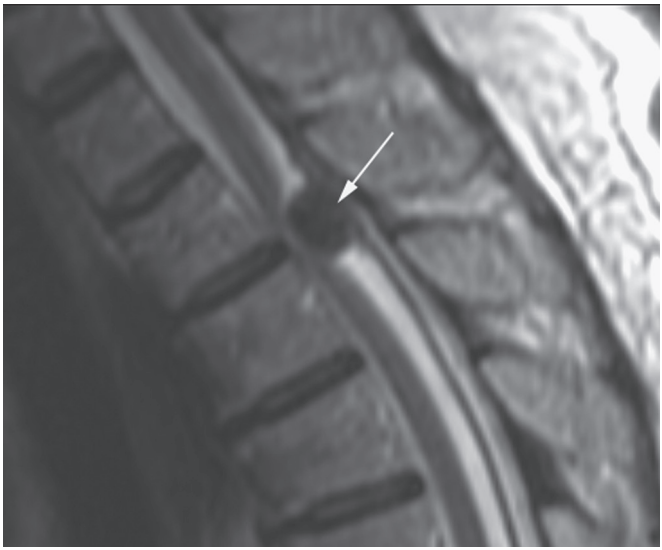

Figure 24-4. Meningioma. Sagittal T2-weighted image demonstrates a hypointense extramedullary dural based mass lesion that causes marked spinal cord compression *(arrow)*. (From Daroff RB, Fenichel GM, Jankovic J, Mazziotta J. Bradley's neurology in clinical practice. 6th ed. Philadelphia: Saunders, 2012.)

16. Define syringomyelia. What causes it? How does it usually present?

Syringomyelia is a central pathologic cavitation of the spinal cord, usually in the cervical or upper thoracic region. Most cases are idiopathic, but syringomyelia may also follow trauma or be related to congenital cranial base malformations (e.g., Arnold-Chiari malformation). The classic presentation, caused by involvement of the lateral spinothalamic tracts, is bilateral loss of pain and temperature sensation below the lesion in the distribution of a "cape." The cavitation in the cord gradually widens to involve other tracts, causing motor and sensory deficits. MRI scan is the diagnostic imaging study of choice. The primary treatment available is surgical creation of a shunt.

17. Define spina bifida. How can it be prevented?

Spina bifida is a congenital abnormality in which lack of fusion of the spinal column, specifically the posterior vertebral arches, allows protrusion of spinal membranes, with or without spinal cord. Spina bifida occulta, the mildest form of the disease (bone deficiency without dural membrane or cord protrusion), is often asymptomatic and should be suspected in patients with a triangular patch of hair over the lumbar spine. More serious defects are usually obvious and occur most often in the lumbosacral region. A **meningocele** is protrusion of the meninges outside the spinal canal, whereas a **myelomeningocele** is protrusion of meninges plus central nervous system (CNS) tissue outside the spinal canal. Patients with a myelomeningocele almost always have an associated Arnold-Chiari malformation. Giving folate supplementation to women contemplating pregnancy reduces the incidence of spina bifida and other neural tube defects.

18. Define hydrocephalus. How is it recognized in children?

Hydrocephalus is excessive accumulation of CSF in the cerebral ventricles. In children, look for increasing head circumference, increased intracranial pressure, bulging fontanelle, scalp vein engorgement, and paralysis of upward gaze. The most common causes include congenital malformations, tumors, and inflammation (e.g., hemorrhage, meningitis). Treat the underlying cause, if possible; otherwise a surgical shunt is created to decompress the ventricles.

19. In what setting does dural venous sinus thrombosis occur? How is it diagnosed and treated?

The risk factors are similar to those for deep venous thrombosis (DVT) in other areas, including hypercoagulable state, trauma, dehydration, pregnancy, oral contraceptive use, infections (e.g., extension of sinusitis or mastoiditis intracranially), nephrotic syndrome, and local tumor invasion. The diagnostic test of choice is MRI (Fig. 24-5). Even though hemorrhagic infarcts are common with dural venous thrombosis, treatment with anticoagulation improves outcomes.

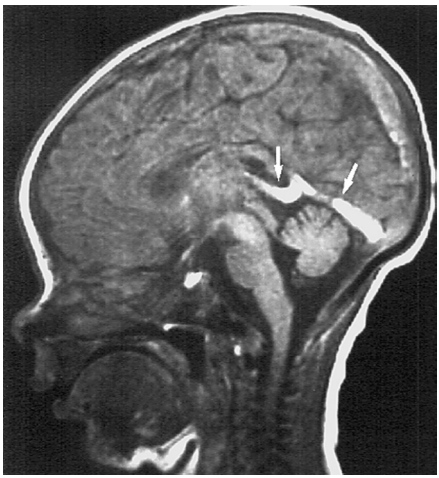

Figure 24-5. Venous thrombosis is seen as a high signal area on magnetic resonance imaging (MRI; sagittal image). The great vein of Galen and straight sinus are involved *(white arrows)*. (From Katz DS, Math KR, Groskin SA. Radiology secrets. Philadelphia: Hanley & Belfus, 1998, with permission.)

OBSTETRICS

1. A patient who is taking birth control pills presents with amenorrhea. What is the likely cause?

Pregnancy. No form of contraception is 100% effective (including tubal ligation), especially when patient compliance is required.

2. List the symptoms and signs of pregnancy.

- Amenorrhea
- Morning sickness
- Weight gain
- Hegar sign (softening and compressibility of the lower uterine segment)
- Chadwick sign (dark discoloration of the vulva and vaginal walls)
- Linea nigra
- Melasma (also known as chloasma or the "mask of pregnancy")
- Auscultation of fetal heart tones
- Gestational sac or fetus seen on ultrasound
- Uterine contractions
- Palpation/ballottement of fetus

3. Which vitamin should all pregnant women take? Why?

Give all pregnant patients folate to prevent neural tube defects. Ideally, all women of reproductive age should take folate because it is most effective in the first trimester, before most women know that they are pregnant. Iron supplements frequently are given to pregnant women to help prevent anemia.

4. Define macrosomia. What is the likely cause?

Macrosomia is defined as a newborn that weighs more than 4 kg (roughly 9 lb). The cause is maternal diabetes mellitus until proven otherwise.

5. What routine tests should be obtained for all pregnant patients?

Pap smear: If the patient is due for a pap smear. Pregnancy does not change the frequency of screening.

Urinalysis: At the first visit and every visit thereafter (to screen for proteinuria, preeclampsia, and bacteriuria; not a good screen for diabetes).

Urine culture: Obtained at 12 to 16 weeks to screen for asymptomatic bacteriuria.

Hemoglobin and hematocrit: At the first visit to determine whether the patient is anemic (because pregnancy may worsen anemia); repeat in the third trimester.

Blood type, rhesus (Rh) type, and antibody screen: At first visit (for identification of possible isoimmunization).

Syphilis test: At first visit (mandated in most states) and subsequent visits (for high-risk patients).

Rubella antibody screen: If the patient is found to be nonimmune, counsel her to get postpartum immunization. Rubella vaccine should not be given during pregnancy.

Glucose screen for gestational diabetes: At first visit in patients with risk factors for diabetes mellitus (obesity, positive family history, or age older than 30 years); otherwise, screen

at 24 to 28 weeks. Use fasting serum glucose and serum glucose levels 1 or 2 hours after an oral glucose load (oral glucose tolerance test).

Serum alpha-fetoprotein: Performed at 15 to 20 weeks, primarily to detect open spina bifida and anencephaly.

Hepatitis B antigen testing: To prevent perinatal transmission.

Varicella: All pregnant women should be tested for immunity to varicella.

Thyroid function: Maternal hypothyroidism may affect fetal neurologic development. Maternal hyperthyroidism can lead to fetal and maternal complications.

HIV test: The American College of Obstetrics and Gynecology (ACOG) advocates an "opt-out" approach to screening rather than an "opt-in" approach to increase screening.

Chlamydia screening: The Centers for Disease Control and Prevention (CDC) and ACOG advocate testing all pregnant women at the first prenatal visit.

Down syndrome screening: Should be offered to all pregnant patients. There are multiple ways to screen. See questions 21 to 27.

Group B beta-hemolytic streptococcus (GBS): Screen at 35 to 37 weeks with a swab of the lower vagina and rectum.

Others: Tuberculosis skin test for women at higher risk. Testing for gonorrhea for women at higher risk of infection. Testing for toxoplasmosis is controversial. If asked, you should do chlamydia and gonorrhea cultures for any pregnant teenager. Testing for sexually transmitted infections should be repeated in the third trimester for women who continue to be at risk or for women who acquire a risk factor during pregnancy.

6. On every prenatal visit, listen to fetal heart tones and evaluate uterine size. When can these factors first be noticed? What constitutes a size/date discrepancy?

Fetal heart tones can be heard with Doppler ultrasound at 10 to 12 weeks and with a normal stethoscope at 16 to 20 weeks. At 12 weeks of gestation, the uterus enters the abdomen and is palpable at the symphysis pubis; at roughly 20 weeks, it reaches the umbilicus. **Uterine size** is evaluated by measuring the distance from the symphysis pubis to the top of the fundus in centimeters. At roughly 20 to 35 weeks, the measurement in centimeters should equal the number of weeks of gestation. A discrepancy greater than 2 to 3 cm is called a **size/date discrepancy.** Ultrasound should be done for further evaluation (e.g., intrauterine growth retardation, multiple gestations).

7. When is ultrasound most accurate at estimating the fetal age?

At 16 to 20 weeks, the biparietal diameter (measured on ultrasound) gives the most accurate estimate of fetal age.

8. What is a hydatiform mole? What are the clues to its presence?

A hydatiform mole is one form of gestational trophoblastic neoplasia, in which the products of conception basically become a tumor. Look for the following clues:

- Preeclampsia before the third trimester.
- An hCG level that does not return to zero after delivery (or abortion/miscarriage) or one that rises rapidly during pregnancy.
- First- or second-trimester bleeding with possible expulsion of "grapes" from the vagina (grossly, the tumor looks like a "bunch of grapes") and excessive nausea/hyperemesis.
- Uterine size/date discrepancy.
- "Snowstorm" pattern on ultrasound.

9. Distinguish between complete and partial moles. How are hydatiform moles treated?

Complete moles have a karyotype of 46 XX (with all chromosomes from the father) and no fetal tissue. **Incomplete moles** usually have a karyotype of 69 XXY with fetal tissue in the tumor.

Treat hydatiform moles with uterine dilation and curettage. Then follow with serial measurements of hCG levels until they fall to zero. If the hCG level does not fall to zero or rises, the patient has either an invasive mole or a choriocarcinoma (increasingly aggressive forms of gestational trophoblastic neoplasia) and needs chemotherapy (usually methotrexate or dactinomycin, both of which are extremely effective).

10. How is intrauterine growth retardation (IUGR) defined? What causes it?

IUGR is defined as fetal size below the tenth percentile for age. Causes are best understood in broad terms as maternal (e.g., smoking, alcohol or drug use, lupus erythematosus), fetal (e.g., TORCH infections, congenital anomalies), or placental (e.g., hypertension, preeclampsia). For a discussion of TORCH infections, see question 36.

11. When should ultrasound be used to evaluate the fetus?

The indications for ultrasound are now quite liberal. Order ultrasound for all patients who have a size/date discrepancy greater than 2 to 3 cm or risk factors for pregnancy-related problems (e.g., hypertension, diabetes, renal disease, lupus erythematosus, smoking, alcohol or drug use, history of previous pregnancy-related problems). Ultrasound also is used when fetal death, distress, or abortion or miscarriage is suspected (e.g., a baby that stops kicking, vaginal bleeding, slow fetal heartbeat on auscultation).

12. How is fetal well-being evaluated?

A **nonstress** test is the easiest initial screen. It is performed with the mother at rest. A fetal heart rate tracing is obtained for 20 minutes. A normal strip has at least 2 accelerations of heart rate, each at least 15 beats per minute above baseline and lasting at least 15 seconds.

A **biophysical profile** is slightly more involved and includes a nonstress test as well as a measure of amniotic fluid (to determine whether oligohydramnios or polyhydramnios is present), a measure of fetal breathing movements, and a measure of general fetal movements.

If the fetus scores poorly on the biophysical profile, the next test is the **contraction stress test,** which looks for uteroplacental dysfunction. Oxytocin is given, and a fetal heart strip is monitored. If late decelerations are seen on the fetal heart strip with each contraction, the test is positive. In most cases of a positive contraction stress test, a cesarean section is performed.

13. True or false: A biophysical profile often is used in high-risk pregnancies in the absence of obvious problems.

True. A biophysical profile may be done once or twice a week from the start of the third trimester until delivery to monitor for potential problems.

14. True or false: Aspirin should be avoided during pregnancy.

True. Use acetaminophen instead. One important exception is in patients with antiphospholipid syndrome, in whom aspirin may improve pregnancy outcome (subcutaneous unfractionated heparin or low molecular weight heparin also can be used to treat antiphospholipid syndrome in pregnancy).

15. Define postterm pregnancy. Why is it a major concern? How is it treated?

Postterm pregnancy is defined as more than 42 weeks of gestation. Both prematurity and postmaturity increase perinatal morbidity and mortality rates. With postmaturity, **dystocia** (or difficult delivery) becomes more common because of the increased size of the infant.

In general, if the gestational age is known to be accurate and the cervix is favorable, labor is induced (e.g., with oxytocin). If the cervix is not favorable or the dates are uncertain, twice-weekly biophysical profiles are done. At 41 weeks, most obstetricians advise induction of labor. A 2012 meta-analysis demonstrated that routine labor induction at greater than 41 weeks compared with expectant management resulted in lower perinatal mortality and a lower rate of meconium aspiration syndrome.

16. What two rare disorders are associated with prolonged gestation?
Anencephaly and placental sulfatase deficiency.

17. What are the normal changes and complaints in pregnancy?
Normal changes in pregnancy include nausea or vomiting (morning sickness), amenorrhea, heavy (possibly even painful) feeling of the breasts, increased pigmentation of the nipples and areolae, Montgomery tubercles (sebaceous glands in the areola), backache, linea nigra, melasma (chloasma), striae gravidarum, and mild ankle edema. Heartburn and increased frequency of urination are also common problems.

18. What test is used to screen for neural tube defects? At what time during pregnancy is it measured? Explain the significance of a low or high alpha-fetoprotein (AFP) level in maternal serum.
Maternal AFP is most accurate when measured between 15 and 20 weeks of gestation. A low AFP may represent **Down syndrome,** fetal demise, or inaccurate dates. A high AFP may represent **neural tube defects** (e.g., anencephaly, spina bifida), **ventral wall defects** (e.g., omphalocele, gastroschisis), multiple gestation, or inaccurate dates.

19. What should be done if the AFP is elevated?
Repeat the test. As many as 30% of elevated maternal serum AFP test results may be elevated but are normal upon repeat testing. The initial elevation is not associated with an increased risk of neural tube defects.

20. What further testing should a patient undergo if the AFP remains elevated?
If the AFP remains elevated, the patient is advised first to undergo ultrasound to determine whether a neural tube defect or other anomaly is present. The ultrasound is also used to confirm gestational age, number of fetuses, and fetal viability. Further evaluation with amniocentesis may be required if the ultrasound findings are uncertain or there is a concern for nonvisualized neural tube defects (via elevated AFP level in amniotic fluid or detection of acetylcholinesterase in amniotic fluid). There is a small risk of miscarriage after amniocentesis.

21. What prenatal tests are available to screen for Down syndrome?
The first trimester combined test, integrated tests, sequential testing, contingent testing, the quadruple test, and maternal plasma-based tests. The ACOG recommends that all women be offered screening before 20 weeks of gestation.

22. What is the first trimester combined test? When is it performed?
The first trimester combined test is performed at 11 to 13 weeks of gestation. The test involves determination of nuchal translucency (NT) by ultrasound, combined with serum pregnancy-associated plasma protein-A (PAPP-A) and serum human chorionic gonadotropin (hCG). Chorionic villus sampling (CVS) is used for women who have this first trimester screening and test positive.

23. Describe the integrated tests.
The full integrated test includes an ultrasound measurement of nuchal translucency at 10 to 13 weeks of gestation, PAPP-A at 10 to 13 weeks of gestation, and AFP, unconjugated estradiol (uE3), hCG, and inhibin A at 15 to 18 weeks of gestation. Results of the full integrated test are not available until the second trimester.

The serum integrated test is the same as the full integrated test but without the ultrasound evaluation of nuchal translucency. This test is used in areas where expertise in the ultrasound measurement of nuchal translucency is not available. Results of the serum integrated test are not available until the second trimester.

24. Describe sequential testing.
Step-wise sequential testing has been developed to provide a risk estimate during the first trimester. The first trimester portion of the integrated screen is performed. If the tests indicate a very high risk

of having an affected fetus, CVS is offered. Those women whose results do not place them at very high risk of having an affected fetus go on to have the second trimester portion of the screening.

25. Describe contingent testing.

Contingent testing has not yet been proven efficacious in a prospective clinical trial and probably will not be tested on the USMLE; however, contingent screening is defined in terms of three risk cut-offs: (1) women at very high risk of having a fetus with Down syndrome after first trimester testing are offered immediate invasive prenatal diagnosis, (2) women at very low risk are provided with their risk estimate and require no additional testing, and (3) women at intermediate risk receive second trimester marker testing.

26. What is the quadruple test? For whom is it typically used? When is it performed?

The quadruple test includes the serum markers AFP, uE3, hCG, and inhibin A. The quadruple test is the best available test for women who receive prenatal care in the second trimester, but can be used for women who receive earlier prenatal care. It is performed at 15 to 18 weeks of gestation.

27. What is a maternal plasma-based test?

This is the newest option that is just becoming widely available and may someday make many of these other tests obsolete. This test, also called cell-free fetal DNA testing, detects fetal DNA in the circulation and has a detection rate more than 98% and a false-positive rate of less than 0.5% for Down syndrome and Edward syndrome (trisomy 18). It is used after 10 weeks of gestation. Cell-free fetal DNA testing is not yet validated in low-risk women, but can be used in higher risk women (i.e., women who will be older than 35 at the time of delivery; presence of sonographic findings associated with fetal aneuploidy; history of previous pregnancy with fetal trisomy; or positive screening results on tests such as the first trimester combined test, the integrated test, or the quadruple test).

28. What is the next step if a woman has a positive screening test for Down syndrome?

Offer fetal karyotype determination. This is done by CVS in the first trimester and by amniocentesis in the second trimester.

29. Why is CVS done instead of amniocentesis in some cases?

CVS can be done at 9 to 12 weeks of gestation (earlier than amniocentesis) and generally is reserved for women with previously affected offspring or known genetic disease. It offers the advantage of a first-trimester abortion if the fetus is affected. CVS is associated with a slightly higher miscarriage rate than amniocentesis.

30. True or false: CVS can detect neural tube defects but not genetic disorders.

False. CVS can detect genetic or chromosomal disorders but not neural tube defects.

31. Cover the right-hand column and specify the effects of the following classic teratogens on an exposed fetus.

AGENT DEFECT(S)	CAUSED
Thalidomide	Phocomelia (absence of long bones and flipperlike appearance of hands)
Antineoplastics	Many
Tetracycline	Yellow or brown teeth
Aminoglycosides	Deafness
Valproic acid	Spina bifida, hypospadias

Continued

AGENT DEFECT(S)	CAUSED
Progesterone	Masculinization of female fetus
Cigarettes	Intrauterine growth retardation, low birth weight, prematurity
Oral contraceptive pills	VACTERL syndrome
Lithium	Cardiac (Ebstein) anomalies
Radiation	Intrauterine growth retardation, CNS defects, eye defects, malignancy (e.g., leukemia)
Alcohol	Fetal alcohol syndrome
Phenytoin	Craniofacial, limb, and cerebrovascular defects; mental retardation
Warfarin	Craniofacial defects, intrauterine growth retardation, CNS malformation, stillbirth
Carbamazepine	Fingernail hypoplasia, craniofacial defects
Isotretinoin*	CNS, craniofacial, ear, and cardiovascular defects
Iodine	Goiter, neonatal hypothyroidism
Cocaine	Cerebral infarcts, mental retardation
Diazepam	Cleft lip and/or palate
Diethylstilbestrol	Clear cell vaginal cancer, adenosis, cervical incompetence

CNS, Central nervous system; *VACTERL*, **V**ertebral anomalies, imperforate **A**nus, **C**ardiac anomalies, **T**racheo**E**sophageal fistula, **R**enal anomalies, Limb anomalies
*Vitamin A in general is considered teratogenic when recommended intake levels are exceeded.

32. List the teratogenic effects of maternal diabetes mellitus. What is the best way to reduce these complications?

- Cardiovascular malformations
- Cleft lip and/or palate
- Caudal regression (lower half of the body is incompletely formed)
- Neural tube defects
- Left colon hypoplasia/immaturity
- Macrosomia (most common and classic)
- Microsomia (can occur if the mother has long-standing diabetes)

Tight control of glucose during pregnancy dramatically reduces these complications.

33. What other problems does maternal diabetes cause in pregnancy?

In the mother, diabetes can result in polyhydramnios and preeclampsia (as well as the complications of diabetes). Problems in infants born to a diabetic mother (other than birth defects) include an increased risk of respiratory distress syndrome and postdelivery hypoglycemia (from fetal islet-cell hypertrophy caused by maternal and thus fetal hyperglycemia). After birth, the infant is cut off from the mother's glucose and the hyperglycemia resolves, but the infant's islet cells still overproduce insulin and cause hypoglycemia. Treat with intravenous glucose.

34. True or false: Oral hypoglycemic agents should not be used during pregnancy.

True. Use insulin to treat diabetes if diet and exercise cannot control glucose levels. Oral hypoglycemics, unlike insulin, may cross the placenta and cause fetal hypoglycemia.

35. What commonly used drugs are generally considered safe in pregnancy?

A short list of drugs that are generally safe in pregnancy includes acetaminophen, penicillins, cephalosporins, erythromycin, nitrofurantoin, histamine-2 receptor blockers, antacids, heparin, hydralazine, methyldopa, labetalol, insulin, and docusate.

36. What are the TORCH syndromes? What do they cause?

TORCH is an acronym for several maternal infections that can cross the placenta and can cause intrauterine fetal infections that may result in birth defects. Most TORCH infections can cause mental retardation, microcephaly, hydrocephalus, hepatosplenomegaly, jaundice, anemia, low birth weight, and IUGR.

T = ***T****oxoplasma gondii:* Look for exposure to cats. Specific defects include intracranial calcifications and chorioretinitis.

O = **O**ther: Varicella-zoster causes limb hypoplasia and scarring of the skin. Syphilis causes rhinitis, saber shins, Hutchinson teeth, interstitial keratitis, and skin lesions.

R = **R**ubella: Worst in the first trimester (some recommend abortion if the mother has rubella in the first trimester). Always check antibody status on the first visit in patients with a poor immunization history. Look for cardiovascular defects, deafness, cataracts, and microphthalmia.

C = **C**ytomegalovirus: Most common infection of the TORCH group. Look for deafness, cerebral calcifications, and microphthalmia.

H = **H**erpes: Look for vesicular skin lesions (with positive Tzanck smears) and history of maternal herpes lesions.

37. True or false: With most in utero infections that can cause birth defects, obvious clues are present in the mother and/or fetus at birth.

False. Although the USMLE probably will give clues, the mother may be asymptomatic (i.e., she may have a subclinical infection), and the infant may be asymptomatic at birth, developing only later such symptoms as learning disability, mental retardation, or autism.

38. Describe therapy to reduce HIV transmission from an infected mother to the fetus. When should an infant born to an HIV-infected mother be tested?

In untreated HIV-positive patients, HIV is transmitted to the fetus in roughly 25% of cases. When three-drug therapy is given to the mother prenatally and zidovudine is given to the infant for 6 weeks after birth, HIV transmission is reduced to roughly 2%. A noninfected infant may still have a positive HIV antibody test at birth because maternal antibodies can cross the placenta. Within 6 to 18 months, however, the test reverts to negative. This is why infants of infected mothers are tested using a direct HIV DNA PCR (polymerase chain reaction) test at birth, at 4 to 6 weeks of age, and 2 months after the second test. Babies who have these three negative tests should have an HIV antibody test at 12 and 18 months of age. Cesarean section may reduce HIV transmission to the child.

39. What should you do if a pregnant woman has genital herpes?

A decision is generally made when the mother goes into labor (not beforehand). If, at the time of true labor, the mother has active, visible genital herpes lesions, do a cesarean section to prevent transmission to the fetus. If, at the time of true labor, the mother has no visible genital herpes lesions, the child can be delivered vaginally.

40. What should you do for the child if the mother has chronic hepatitis B or chickenpox?

If the mother has chronic hepatitis B, give the infant the first hepatitis B vaccine shot and hepatitis B immunoglobulin at birth. If the mother contracts chickenpox in the last 5 days of pregnancy or the first 2 days after delivery, give the infant varicella-zoster immunoglobulin.

41. How do you treat gonorrheal and chlamydial genital infections during pregnancy?

The treatment for gonorrhea remains unchanged because ceftriaxone is safe during pregnancy. For chlamydial infection, give azithromycin, amoxicillin, or erythromycin base instead of doxycycline or erythromycin estolate.

42. How is tuberculosis treated in pregnancy?

In a similar way as for a nonpregnant patient. Use isoniazid, rifampin, and ethambutol if the risk of a drug-resistant organism is low. Pyrazinamide should be used with caution because of a lack of data on the risk of teratogenicity. However, pyrazinamide should be added if a drug-resistant organism is suspected. Streptomycin, which is a rarely used second-line agent, should be avoided. Give vitamin B_6 to pregnant patients treated with isoniazid to avoid a deficiency.

43. What are the signs of placental separation during delivery?

The signs of placental separation include a fresh show of blood from the vagina, lengthening of the umbilical cord, and a rising fundus that becomes firm and globular.

44. True or false: After cesarean section, a patient may have a vaginal delivery in the future.

It depends. After a classic (vertical) uterine incision, patients must have cesarean sections for all future deliveries because of the increased rate of uterine rupture with vaginal delivery. After a lower (horizontal) uterine incision (the incision of choice), a patient may deliver future pregnancies vaginally with only a slightly increased (i.e., acceptable) risk of uterine rupture.

45. Define lochia. When is it a problem?

For the first several days after delivery, some vaginal discharge (known as lochia) is normal. It is red for the first few days and gradually turns white or yellowish-white by day 10. If the lochia is foul smelling, suspect endometritis.

46. What treatment may be given to a woman who does not want to breastfeed?

Because the breasts can become engorged with milk and thus quite painful, you may prescribe tight-fitting bras, ice packs, and analgesia to reduce symptoms. Medications for the suppression of lactation (e.g., bromocriptine, estrogens, oral contraceptive pills) are generally no longer recommended because of risks of thromboembolism and stroke.

47. List the common contraindications for breastfeeding.

- Use of alcohol or illicit drugs (with a few caveats that won't be tested on the USMLE)
- HIV infection, although the World Health Organization recommends breastfeeding in developing countries if replacement feeding is not possible
- Some medications, including antineoplastic agents, antimetabolic agents (cyclophosphamide, mercaptopurine), some anticonvulsants (topiramate), amiodarone

48. What is the preferred method of anesthesia in obstetric patients? Why?

Epidural anesthesia. General anesthesia involves a higher risk of aspiration and its resulting pneumonia because the gastroesophageal sphincter is relaxed in pregnancy and patients usually have not refrained from eating before going into labor. There also is concern about the effect of general anesthetic agents on the fetus. Spinal anesthesia can interfere with the mother's ability to push and is associated with a higher incidence of hypotension than epidural anesthesia.

49. True or false: Asymptomatic bacteriuria, detected on routine urinalysis, should be treated during pregnancy.

True. Up to 20% of patients develop cystitis or pyelonephritis if untreated. This rate is much higher than in nonpregnant patients, who should not be treated for asymptomatic bacteriuria. In pregnancy, the gravid uterus can compress the ureters, and increased progesterone can decrease the tone of the ureters, increasing urinary stasis and the risk for urinary tract infection.

50. What do you need to know about vaginal group B streptococcal colonization and pregnancy?

Pregnant women should be tested for vaginal group B streptococci. Women who are carriers should be treated during labor with penicillin G or ampicillin. Earlier treatment (e.g., second trimester) is

ineffective because group B streptococci frequently return—and usually they are dangerous only during labor and delivery. The reason for treating asymptomatic carriers is to prevent neonatal sepsis and endometritis, both of which are commonly caused by group B streptococci.

51. When does mastitis occur? How do you recognize and treat it?

Mastitis (inflammation of the breast) usually develops in the first 2 months postpartum. Breasts are red, indurated, painful, and nipple cracks or fissuring may be seen. *Staphylococcus aureus* is the usual cause. Treat with analgesics (e.g., acetaminophen, ibuprofen), warm and/or cold compresses, and continued breastfeeding with the affected breast(s) even though it is painful (use a breast pump to empty breast if needed) to prevent further milk duct blockage and abscess formation. An antistaphylococcal antibiotic (e.g., cephalexin, dicloxacillin) is usually given for more than mild symptoms. If a fluctuant mass develops or there is no response to antibiotics within a few days, an abscess is likely present and must be drained.

52. What are the diagnostic signs and symptoms of preeclampsia? When does it occur?

Preeclampsia causes **hypertension,** defined as a greater than 30-point increase in systolic or a greater than 15-point increase in diastolic blood pressure over baseline. Other signs and symptoms include **proteinuria** (2+ or more protein on urinalysis), oliguria, edema of the hands or face, headache, visual disturbances, or the HELLP syndrome (**h**emolysis, **e**levated **l**iver enzymes, **l**ow **p**latelets, and right upper quadrant or epigastric pain). Preeclampsia usually occurs in the third trimester.

53. What are the main risk factors for preeclampsia? How is it treated?

The risk factors (in decreasing order of importance) include chronic renal disease, chronic hypertension, family history of preeclampsia, multiple gestations, nulliparity, extremes of reproductive age (the classic patient is a young woman with her first child), diabetes, and black race. The definitive treatment is delivery. This is the treatment of choice if the patient is at term. In a preterm patient with mild disease, the hypertension can be treated with hydralazine, labetalol, or methyldopa. Advise bed rest and observe. If the patient has severe disease (defined as oliguria, mental status changes, headache, blurred vision, pulmonary edema, cyanosis, HELLP syndrome, blood pressure greater than 160/110 mm Hg, or progression to eclampsia [seizures]), deliver the infant once the mother's condition is stabilized. Otherwise, both mother and infant may die.

54. True or false: The combination of hypertension and proteinuria during pregnancy means preeclampsia until proven otherwise.

True.

55. When is edema normal during pregnancy? When is it not?

Mild ankle edema is normal in pregnancy, but moderate-to-severe edema of the ankles or edema of the hands is likely to be preeclampsia.

56. What should you consider if preeclampsia develops before the third trimester?

The possibility of gestational trophoblastic disease (i.e., hydatiform mole, choriocarcinoma).

57. Distinguish between preeclampsia and eclampsia. How can eclampsia be prevented?

Preeclampsia plus seizures equals eclampsia. Eclampsia can be prevented by regular prenatal care so that you catch the disease in the preeclamptic stage and treat appropriately.

58. What should you use to treat seizures in eclampsia? What are the toxic effects?

Use **magnesium sulfate** for eclamptic seizures; it also lowers blood pressure. Toxic effects include hyporeflexia (first sign of toxicity), respiratory depression, central nervous system (CNS) depression, coma, and death. If toxicity occurs, the first step is to stop the magnesium infusion.

59. True or false: When eclampsia occurs, you must deliver the infant immediately, regardless of maternal status.

False. Do *not* try to deliver the infant until the mother's condition is stable (e.g., do not perform a cesarean section while the mother is having seizures).

60. Why are preeclampsia and eclampsia so important?

Preeclampsia and eclampsia cause uteroplacental insufficiency, IUGR, fetal demise, and increased maternal morbidity and mortality.

61. True or false: Preeclampsia and eclampsia are risk factors for development of future hypertension.

False.

62. What are the major causes of maternal mortality associated with childbirth?

In decreasing order: pulmonary embolism (PE), pregnancy-induced hypertension (preeclampsia/eclampsia), and hemorrhage.

63. How do you recognize an amniotic fluid PE?

Look for a recently postpartum mother who develops sudden shortness of breath, tachypnea, chest pain, hypotension, and disseminated intravascular coagulation. Treatment is supportive.

64. Define oligohydramnios. What causes it? Why is it worrisome?

Oligohydramnios means a deficiency of amniotic fluid (<500 mL or an amniotic fluid index < 5). Causes include IUGR, premature rupture of the membranes, postmaturity, and renal agenesis (Potter disease). Oligohydramnios may cause fetal problems, including pulmonary hypoplasia, cutaneous or skeletal abnormalities caused by compression, and hypoxia caused by cord compression.

65. Define polyhydramnios. What causes it? Why is it worrisome?

Polyhydramnios means an excess of amniotic fluid (>2 L or an amniotic fluid index > 25). Causes include maternal diabetes, multiple gestation, neural tube defects (anencephaly, spina bifida), gastrointestinal (GI) anomalies (omphalocele, esophageal atresia), and hydrops fetalis. Polyhydramnios can cause maternal problems, including postpartum uterine atony (with resultant postpartum hemorrhage) and maternal dyspnea (an overdistended uterus compromises pulmonary function).

66. How early can a standard home pregnancy test diagnose pregnancy?

Roughly 2 weeks after conception (about the time when the woman realizes that her period is late).

67. Define the characteristics and duration of the normal stages of labor.

STAGE	CHARACTERISTICS	NULLIGRAVIDA	MULTIGRAVIDA
First stage	Onset of true labor to full cervical dilation	<20 hr	<14 hr
Latent phase	From 0 to 3-4 cm dilation (slow, irregular)	Highly variable	Highly variable
Active phase	From 3-4 cm to full dilation (rapid, regular)	>1 cm/hr dilation	>1.2 cm/hr dilation
Second stage	From full dilation to birth of baby	30 min-3 hr	5-30 min
Third stage	Delivery of baby to delivery of placenta	0-30 min	0-30 min
Fourth stage	Placental delivery to maternal stabilization	Up to 48 hr	Up to 48 hr

68. Distinguish between a protraction disorder and an arrest disorder. What should you do when either occurs?

A **protraction disorder** occurs once true labor has begun if the mother takes longer than the previous chart indicates, but labor nonetheless is progressing slowly. An **arrest disorder** (failure to progress) occurs once true labor has begun if no change in dilation is seen over 2 hours or no change in descent is seen over 1 hour.

In either situation, first rule out an abnormal lie and cephalopelvic disproportion. If neither is present, the mother can be treated with labor augmentation (e.g., oxytocin, prostaglandin). If these steps fail, manage expectantly and do a cesarean section at the first sign of fetal distress.

69. What is the most common cause of protraction or arrest disorder?

Cephalopelvic disproportion, defined as a disparity between the size of the infant's head and the mother's pelvis. Labor augmentation is contraindicated in this setting.

70. Distinguish between true labor and false labor.

In true labor, normal contractions occur at least every 3 minutes, are fairly regular, and are associated with cervical changes (effacement and dilation). In false labor (Braxton-Hicks contractions), contractions are irregular and no cervical changes occur.

71. What problems may be encountered when oxytocin is used to augment labor?

On the Step 2 examination, watch for uterine hyperstimulation (painful, overly frequent, and poorly coordinated uterine contractions), uterine rupture, fetal heart rate decelerations, and water intoxication/hyponatremia (because of the antidiuretic hormone effect of oxytocin). Treat all of these complications first by discontinuing the oxytocin infusion; the half-life is less than 10 minutes.

72. What problems are associated with the use of intravaginal prostaglandin and amniotomy?

Prostaglandin E2 (dinoprostone) or misoprostol may be used locally to induce the cervix (a process sometimes called "ripening") and is highly effective in combination with (or before) oxytocin. It also may cause uterine hyperstimulation. **Amniotomy** (creating a manual opening in the amniotic membrane) also hastens labor but exposes the fetus and uterine cavity to possible infection if labor does not occur promptly.

73. What are the contraindications to labor induction or augmentation?

The list is almost the same as the list of contraindications to vaginal delivery: Placenta or vasa previa, umbilical cord prolapse, prior classic (vertical) cesarean section, transverse fetal lie, active genital herpes, cephalopelvic disproportion, and cervical cancer.

74. Define abortion.

Abortion is defined as the termination (intentional or not) of a pregnancy at less than 20 weeks of gestation or when the fetus weighs less than 500 g. Miscarriage describes a spontaneous abortion.

75. What are the different terms for an unintentional abortion?

Threatened abortion: Uterine bleeding without cervical dilation and no expulsion of tissue. Treat with bed rest and pelvic rest.

Inevitable abortion: Uterine bleeding with cervical dilation and crampy abdominal pain and no tissue expulsion.

Incomplete abortion: Passage of some products of conception through the cervix.

Complete abortion: Expulsion of all products of conception from the uterus. Treat with serial testing of hCG level to make sure that it goes down to zero.

Missed abortion: Fetal death with no expulsion of tissue (in some cases not for several weeks). Treat with dilation and curettage if less than 14 weeks of gestation, attempted delivery if more than 14 weeks of gestation.

All of the above terms imply less than 20 weeks of gestation. Treat all abortions with intravenous fluids (and blood transfusions if necessary) and consider dilation and curettage (once the fetus is confirmed as dead or expelled). Give the mother RhoGAM if she has an Rh-negative blood type.

76. Define induced and recurrent abortions. What do recurrent abortions suggest?

- **Induced abortion** is an intentional termination of pregnancy at less than 20 weeks of gestation; it may be elective (requested by patient) or therapeutic (done to maintain the health of the mother).
- **Recurrent abortion** is defined as two or three successive, unplanned abortions. History and physical examination may suggest the cause:
  - Infection (*Listeria, Mycoplasma,* or *Toxoplasma* species, syphilis).
  - Inherited thrombophilia (factor V Leiden, G20210A gene mutation, antithrombin deficiency, deficiency of protein C or protein S).
  - Environmental factors (alcohol, tobacco, drugs).
  - Diabetes.
  - Hypothyroidism.
  - Systemic lupus erythematosus (especially with positive antiphospholipid/lupus anticoagulant antibodies, sometimes an isolated syndrome without coexisting lupus).
  - Cervical incompetence (watch for a history of exposure to diethylstilbestrol [DES] in the patient's mother during pregnancy and/or a patient with recurrent painless second-trimester abortions; treat future pregnancies with cervical cerclage).
  - Congenital female tract abnormalities (if possible, correct to restore fertility).
  - Fibroids (remove them).
  - Chromosomal abnormalities (e.g., maternal or paternal translocations).

77. True or false: hCG roughly doubles every 2 days in the first trimester.

True. An hCG level that stays the same or increases only slowly with serial testing indicates a fetus in trouble (e.g., threatened abortion, ectopic pregnancy) or fetal demise. A rapidly increasing hCG level or one that does not decrease after delivery may indicate hydatiform mole or choriocarcinoma.

78. When can ultrasound detect an intrauterine gestational sac? Why do you need to know this information?

At roughly 5 weeks after the last menstrual period (or when hCG is greater than 2000 mIU), evidence of intrauterine pregnancy can be detected by transvaginal sonography. A definite fetus and fetal heartbeat can be detected by transvaginal ultrasound at 5 to 6 weeks of gestation.

Use this information when trying to determine the possibility of an ectopic pregnancy. For example, if the patient's last menstrual period was 4 weeks ago and a pregnancy test is positive, you cannot rule out an ectopic pregnancy with ultrasound. If, however, the patient's last menstrual period was 10 weeks ago with a positive pregnancy test and an ultrasound of the uterus does not show a gestational sac, be suspicious of an ectopic pregnancy.

79. What are the risk factors for developing an ectopic pregnancy?

The major risk factor for ectopic pregnancy is a previous history of pelvic inflammatory disease (10-fold increase in ectopic pregnancy rate). Other risk factors include a previous ectopic pregnancy, history of tubal sterilization or tuboplasty, pregnancy that occurs with an intrauterine device in place, and a history of DES exposure, which can cause tubal abnormalities in women who were exposed in utero.

80. What are the classic symptoms and signs of a ruptured ectopic pregnancy?

A recent history of amenorrhea with current vaginal bleeding and abdominal pain. Patients also have a positive hCG pregnancy test. If you palpate an adnexal mass, it may be an ectopic pregnancy or a corpus luteum cyst.

81. What should you do if you suspect an ectopic pregnancy?

Order an ultrasound to look for a gestational sac or fetus. When the diagnosis is in doubt and the patient is doing poorly (e.g., hypovolemia, shock, severe abdominal pain, rebound tenderness), do a laparoscopy for definitive diagnosis and treatment, if necessary. Culdocentesis is rarely performed in a stable patient to check for blood in the pouch of Douglas (with a ruptured ectopic pregnancy) because it has a high false-negative rate.

82. How is symptomatic ectopic pregnancy managed?

Surgically. A tubal pregnancy, if stable and less than 3 cm in diameter, can be treated with salpingostomy and removal of the products of conception. The tube is left open to heal on its own; this strategy retains normal tubal function and fertility. If the patient's condition is unstable or the ectopic pregnancy has ruptured or is greater than 3 cm in diameter, a salpingectomy is required. In Rh-negative patients, give RhoGAM after treatment. Methotrexate (causes fetal demise) is an alternative treatment for small (<3 cm), unruptured tubal pregnancies.

83. What are the problems with preexisting maternal hypertension in pregnancy?

Preexisting hypertension (present before conception) increases the risk for IUGR and preeclampsia.

84. What does a basic fetal heart monitoring strip contain?

The fetal heart rate and the uterine contraction pattern over time.

85. In fetal heart monitoring, what is the difference between early decelerations, late decelerations, and variable decelerations?

In **early decelerations** (Fig. 25-1), the peaks match up (nadir of fetal heart deceleration and peak of uterine contraction). This pattern signifies **head compression** (probably a vagal response) and is normal.

Variable decelerations (Fig. 25-2) are so-called because fetal heart rate deceleration varies in relation to uterine contractions. This is the most commonly encountered type of deceleration pattern and signifies **cord compression.** If it is seen, place the mother in the lateral decubitus position, administer oxygen by face mask, and stop any oxytocin infusion. If the fetal bradycardia is severe (<80-90 beats/min) or fails to resolve, check the fetal oxygen saturation or scalp pH.

Late decelerations (Fig. 25-3) occur when fetal heart rate deceleration comes after uterine contraction. This pattern signifies **uteroplacental insufficiency** and is the most worrisome. If it is seen, first place the mother in the lateral decubitus position; then give oxygen by face mask and stop oxytocin, if applicable. Next, give a tocolytic ($beta_2$ agonist such as ritodrine or magnesium sulfate) if the mother is not in active labor and intravenous fluids if the mother is hypotensive. If the late decelerations persist, measure the fetal oxygen saturation or scalp pH. Consider preparing for operative delivery.

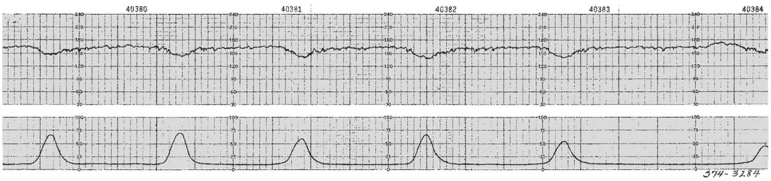

Figure 25-1. Early decelerations are caused by compression of the fetal head. They are shallow, symmetric, uniform decelerations that begin early in the contraction, have their nadir coincident with the peak of the contraction, and return to the baseline by the time the contraction is over. (From Gabbe S, et al. Obstetrics: normal and problem pregnancies. 5th ed. Philadelphia: Churchill Livingstone, 2007, Fig. 15-13.)

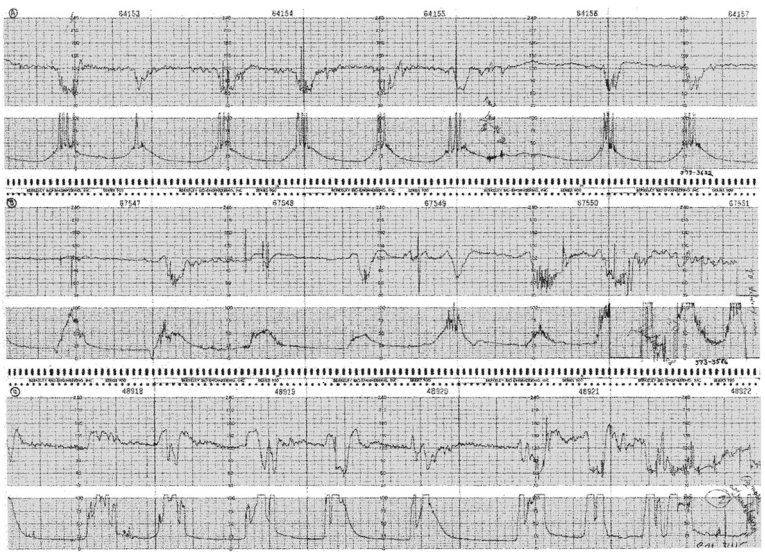

Figure 25-2. These are typical variable decelerations. Variable decelerations are often recognized by the accelerations that precede and follow the decelerations. (From Gabbe S, et al. Obstetrics: normal and problem pregnancies. 5th ed. Philadelphia: Churchill Livingstone, 2007, Fig. 15-18.)

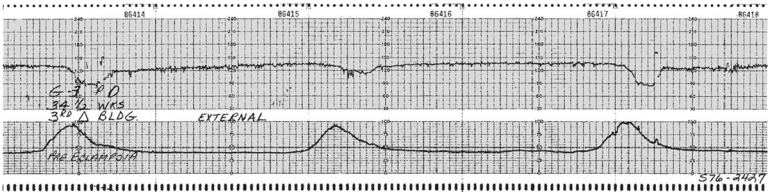

Figure 25-3. Late decelerations are seen in a case complicated by third-trimester bleeding. Note the presence of persistent late decelerations with only three contractions in 20 minutes as well as the apparent loss of variability of the fetal heart rate. The rise in baseline tone of the uterine activity channel cannot be evaluated with the external system. (From Gabbe S, et al. Obstetrics: normal and problem pregnancies. 5th ed. Philadelphia: Churchill Livingstone, 2007, Fig. 15-14.)

86. What other patterns of fetal distress may be seen on a fetal heart tracing? What is a normal fetal heart rate?

Loss of short-term (beat-to-beat) variability, loss of long-term variability (or normal baseline changes in heart rate over 1 minute), and prolonged fetal tachycardia (>160 beats/min). The normal fetal heart rate is 120 to 160 beats/min.

87. What if the question gives you a value for fetal oxygen saturation or scalp pH?

Any fetal scalp pH less than 7.2 or abnormally decreased oxygen saturation is an indication for immediate cesarean delivery. If the pH is greater than 7.2 or oxygenation is normal, you can generally continue to observe the mother and fetus.

88. What should you do if shoulder dystocia or impaction occurs during vaginal delivery?

The first step is to try the McRoberts maneuver. Have the mother sharply flex her thighs against her abdomen, which may free the impacted shoulder. Other maneuvers include applying suprapubic pressure, Woods screw maneuver (rotates the fetus so the anterior shoulder emerges from behind the maternal symphysis), delivery of the posterior arm, and fracture of the clavicle (risky). If these maneuvers fail, options are limited. A cesarean section is usually the procedure of choice (after pushing the infant's head back into the birth canal).

89. What causes third-trimester bleeding?

- Placenta previa
- Abruptio placentae
- Uterine rupture
- Fetal bleeding
- Cervical or vaginal infections (e.g., herpes simplex virus, gonorrhea, chlamydial or candidal infection)
- Cervical or vaginal trauma (usually from sexual intercourse)
- Bleeding disorders (rare before delivery; more common after delivery)
- Cervical cancer (which may occur in pregnant patients)
- "Bloody show"

90. True or false: The initial workup of third-trimester bleeding, like most conditions, requires a history and thorough physical examination, including a good pelvic examination.

False. You should do a history and partial physical examination, but *always* do an ultrasound before a pelvic examination.

91. Why do an ultrasound before a pelvic examination for third-trimester bleeding?

When placenta previa is present, disturbing the placenta may make the bleeding worse and turn a worrisome case into an emergency.

92. Define placenta previa. How does it present? How is it diagnosed and treated?

True placenta previa occurs when the placenta implants in an area where it covers the cervical opening (os). Predisposing factors include multiparity, increasing maternal age, multiple gestation, and a history of prior placenta previa. *Always* do an ultrasound before a pelvic examination for third-trimester bleeding. The bleeding is painless and may be profuse. Ultrasound is 95% to 100% accurate in diagnosis. Mandatory cesarean section is required for delivery, but patients may be admitted to the hospital for bed and pelvic rest and tocolysis if they are preterm and stable and if the bleeding has stopped.

93. Define abruptio placentae. How does it present? How is it treated?

Abruptio placentae is premature detachment of a normally situated placenta. Predisposing factors include hypertension (with or without preeclampsia), trauma, polyhydramnios with rapid decompression after membrane rupture, cocaine or tobacco use, and preterm premature rupture of membranes. Patients can have this condition without visible vaginal bleeding; the blood may be contained behind the placenta. Usual symptoms include pain, uterine tenderness, increased uterine tone with a hyperactive contraction pattern, and fetal distress. Abruptio placentae also may cause disseminated intravascular coagulation if fetal products enter the maternal circulation. Ultrasound detects only a small percentage of cases. Treat with intravenous fluids (and blood if needed) and rapid delivery (vaginal preferred).

94. What factors predispose to uterine rupture? How does it present? How is it treated?

Predisposing factors include previous uterine surgery (especially prior cesarian section with vertical incision), trauma, oxytocin, grand multiparity (several previous deliveries), excessive uterine distention (e.g., multiple gestation, polyhydramnios), abnormal fetal lie, cephalopelvic disproportion, and

shoulder dystocia. Uterine rupture is very painful, has a sudden and dramatic onset, and often is accompanied by maternal hypotension or shock. Other classic signs are the ability to feel fetal body parts on abdominal examination and a change in the abdominal contour. Maternal distress usually is more pronounced than fetal distress (unlike abruptio placentae, in which fetal distress is greater). Treat with immediate laparotomy and delivery. Hysterectomy usually is required after delivery.

95. What causes fetal bleeding to present as third-trimester vaginal bleeding?

Visible fetal bleeding usually is caused by vasa previa or velamentous insertion of the cord, which occurs when umbilical vessels present in advance of the fetal head, usually traversing the membranes and crossing the cervical os. The biggest predisposing risk factor is multiple gestation (the greater the number of fetuses, the higher the risk). Bleeding is painless, and the mother's condition is completely stable, whereas the fetus shows worsening distress (tachycardia initially, then bradycardia as the fetus decompensates). An Apt test performed on vaginal blood is positive for fetal blood (this test differentiates fetal from maternal blood). Treat with immediate cesarean section.

96. Explain the term "bloody show." How is it diagnosed?

With cervical effacement, a blood-tinged mucous plug may be released from the cervical canal and heralds the onset of labor. This normal occurrence is a diagnosis of exclusion in the evaluation of third-trimester bleeding.

97. Describe the initial management of third-trimester bleeding.

For all cases of third-trimester bleeding, start intravenous fluids, give blood if needed, start the patient on oxygen, and start fetal and maternal monitoring. Then order a complete blood count, coagulation profiles, ultrasound, and drug screen if drug use is suspected because cocaine causes placental abruption. Give RhoGAM if the mother is Rh-negative. A Kleihauer-Betke test can quantify fetal blood in the maternal circulation and can be used to calculate the dose of RhoGAM.

98. Define preterm labor. How is it treated?

Preterm labor is defined as labor between 20 and 37 weeks of gestation. Put the mother in the lateral decubitus position, order bed and pelvic rest, and give oral or intravenous fluids and oxygen. In some cases these maneuvers stop the contractions. If they fail, you can give a tocolytic ($beta_2$ agonist or magnesium sulfate) if no contraindications (heart disease, hypertension, diabetes, hemorrhage, ruptured membranes, cervix dilated more than 4 cm) are present. The mother can be managed as an outpatient with an oral tocolytic once she is stable.

99. What are tocolytics? When is it not appropriate to give them?

Tocolytics stop uterine contractions. Common examples are $beta_2$ agonists (terbutaline, ritodrine) and magnesium sulfate. Do not give tocolytics to the mother in the presence of preeclampsia, severe hemorrhage, chorioamnionitis, IUGR, fetal demise, or fetal anomalies incompatible with survival.

100. What is fetal fibronectin? When is a test for this substance useful? Is the test more helpful when positive or negative?

Fetal fibronectin (an extracellular matrix protein that helps attach the amniotic membranes to the uterine lining) can be detected in the vaginal secretions of some women presenting with signs and symptoms of preterm labor. The test is most helpful when negative between 22 and 34 weeks of gestation because it indicates a very low likelihood of delivery in the next 2 weeks. Thus a more conservative, observational approach can be used. When fetal fibronectin is positive in this setting, the woman remains at a higher risk for delivery in the next 2 weeks and a more aggressive approach to tocolysis and fetal lung maturity hastening is typically employed.

101. When should fetal lung maturity be evaluated?

Evaluation of fetal lung maturity is indicated before elective deliveries that are, or may be, less than 39 weeks' gestation. Testing is not necessary for well-documented pregnancies that are 39 or more

weeks' gestation, pregnancies that are less than 32 weeks' gestation (because fetal lung maturity is unlikely), or when delaying delivery because of fetal lung immaturity will place the mother or fetus at significant risk.

102. What tests can be used to assess fetal lung maturity?

- Lamellar body count
- Lecithin/sphingomyelin ratio
- Phosphatidylglycerol
- Surfactant/albumin ratio
- Optical density at 650 nm
- Foam stability index

For the purposes of the USMLE, it is not necessary to know the details of these tests. No test performs better than another. All of these tests are better at predicting the absence, rather than the presence, of respiratory distress.

103. What is the role of steroids in preterm labor?

Often steroids are given with tocolytics (at 24 to 34 weeks of gestation) to hasten fetal lung maturity and thus decrease the risk of respiratory distress syndrome in the neonatal period.

104. Define quickening. When does it occur?

Quickening is the term used to describe when the mother first detects fetal movements, usually at 18 to 20 weeks of gestation in a primigravida and 16 to 18 weeks of gestation in a multigravida.

105. Give the order of fetal positions during normal labor and delivery.

- Descent
- Flexion
- Internal rotation
- Extension
- External rotation
- Expulsion

106. What subtype of maternal antibody can cross the placenta?

IgG is the only type of maternal antibody that crosses the placenta. This may be an important diagnostic point: an elevated neonatal IgM concentration is never normal, whereas an elevated neonatal IgG often represents maternal antibodies.

107. Explain Rh incompatibility. In what situations does it occur?

Rh (or rhesus factor) blood-type incompatibility is of concern because it can lead to hemolytic disease of the newborn. Rh incompatibility occurs when the mother is Rh-negative and her infant is Rh-positive. The boards assume an understanding of inheritance of the Rh factor. If both the mother and the father are Rh-negative, there is nothing to worry about because their infant will be Rh-negative. If the father is Rh-positive, the infant has a 50/50 chance of being Rh-positive.

108. How do you detect and manage potential hemolytic disease of the newborn?

If indicated by maternal and potential fetal blood type, check maternal titers of Rh antibody every month, starting in the seventh month of gestation. Give RhoGAM automatically at 28 weeks and within 72 hours after delivery as well as after any procedures that may cause transplacental hemorrhage (see question 110).

109. True or false: The first child is usually the most severely affected by Rh incompatibility.

False. Previous maternal sensitization is required for disease to occur. In other words, if a nulliparous Rh-negative mother has never received blood products, her first Rh-positive infant will not be

affected by hemolytic disease—except in the rare case of sensitization during the first pregnancy from undetected fetomaternal bleeding, which commonly occurs later in the pregnancy and in most instances can be prevented by RhoGAM administration at 28 weeks. The second Rh-positive infant, however, will be affected—unless you, the astute board taker, administer RhoGAM at 28 weeks and within 72 hours after delivery during the first pregnancy. Any history of blood transfusion, abortion, ectopic pregnancy, stillbirth, or delivery can cause sensitization.

110. How much RhoGAM should you give if the maternal Rh antibody titer is extremely high?

In this setting RhoGAM is worthless because sensitization has already occurred. RhoGAM administration is a good example of primary prevention. Close fetal monitoring for hemolytic disease is required.

111. How do you recognize, monitor, and treat hemolytic disease of the newborn?

Hemolytic disease of the newborn in its most severe form causes fetal hydrops (edema, ascites, pleural and/or pericardial effusions) and death. Amniotic fluid spectrophotometry and ultrasound can help gauge the severity of fetal hemolysis. Treatment of hemolytic disease involves (1) delivery, if the fetus is mature (check lung maturity with a lecithin-to-sphingomyelin ratio); (2) intrauterine transfusion; and (3) phenobarbital, which helps the fetal liver break down bilirubin by inducing enzymes.

112. True or false: ABO blood group incompatibility can cause hemolytic disease of the newborn.

True. ABO blood group incompatibility can cause hemolytic disease of the newborn when the mother is type O and the infant is type A, B, or AB. This condition does not require previous sensitization because IgG antibodies (which can cross the placenta) occur naturally in mothers with blood type O—but not in mothers with other blood types. The hemolytic disease is usually less severe than with Rh incompatibility, but treatment is the same. In rare instances, other minor blood antigens also may cause a reaction.

113. When should RhoGAM be given?

To reiterate, give RhoGAM only when the mother is Rh-negative and the father is Rh-positive or his blood type is unknown. During routine prenatal care, check for Rh antibodies at the first visit. If the test is positive, do not give RhoGAM—you are too late. Otherwise, give RhoGAM routinely at 28 weeks and immediately after delivery. Also give RhoGAM after an abortion, stillbirth, ectopic pregnancy, amniocentesis, CVS, and any other invasive procedure that may cause transplacental bleeding during pregnancy.

114. Define premature rupture of membranes (PROM). How is it diagnosed?

PROM is rupture of the amniotic sac before the onset of labor. Diagnosis of rupture of membranes (whether premature or not) is based on history, sterile speculum examination, and/or a positive nitrazine test. The sterile speculum examination shows pooling of amniotic fluid and a fern pattern when the fluid is placed on a microscopic slide and allowed to dry. Nitrazine paper turns blue in the presence of amniotic fluid. Ultrasound should be done in cases of PROM to assess amniotic fluid volume as well as gestational age and any anomalies that may be present.

115. What usually follows membrane rupture? What should you do if it does not occur?

Spontaneous labor usually follows membrane rupture; for this reason, an amniotomy may be done in an attempt to induce labor if membranes do not rupture spontaneously. If labor does not occur within 6 to 8 hours of membrane rupture, the mother is term, and if the cervix is favorable, labor should be induced.

Labor is induced because the main risk of PROM is infection, which may occur in the mother (chorioamnionitis) and/or the infant (neonatal sepsis, pneumonia, meningitis). The usual culprits are group B streptococci, *Escherichia coli,* or *Listeria* sp.

116. Define preterm premature rupture of membranes (PPROM). How is it managed?

PPROM is defined as premature rupture of membranes before 36 to 37 weeks of gestation. The risk of infection increases with the duration of ruptured membranes. Do a culture and Gram stain of the amniotic fluid. If it is negative, treatment simply involves pelvic and bed rest with frequent follow-up. If the culture is positive for group B streptococci, treat the mother with penicillin G or ampicillin, even if she is asymptomatic.

117. How does chorioamnionitis present and how is it treated?

Patients with chorioamnionitis have presenting symptoms of fever and a tender, irritable uterus, usually after delivery. Antepartum chorioamnionitis may occur in patients with PROM. Do a culture and Gram stain of the cervix and amniotic fluid, and treat with antibiotics such as ampicillin plus gentamicin while awaiting culture results.

118. Define postpartum hemorrhage. What are the common causes?

Postpartum hemorrhage is defined as a blood loss greater than 500 mL during vaginal delivery or greater than 1 L during cesarean section. The most common cause is **uterine atony** (75%-80% of cases). Other causes include lacerations, retained placental tissue, coagulation disorders, low placental implantation, and uterine inversion. Retained placental tissue results from placenta accreta (penetration of the placenta through the endometrium into the myometrium), increta (deeper penetration of the placenta into the myometrium), or percreta (penetration of the placenta through the myometrium to the uterine serosa); in all three conditions, the placenta grows more deeply into the uterine wall than it should. The major risk factor for this condition is previous uterine surgery or cesarean section, and the usual treatment is hysterectomy.

119. What causes uterine atony? How is it treated?

Uterine atony is caused by overdistention of the uterus (as a result of multiple gestation, polyhydramnios, or macrosomia), prolonged labor, oxytocin usage, grand multiparity (a history of five or more deliveries), and precipitous labor (too fast or less than 3 hours). Treat with a dilute oxytocin infusion, and use bimanual compression to massage the uterus while the oxytocin infusion is running. If this approach fails, use ergonovine (contraindicated with maternal hypertension), prostaglandin f_2-alpha, or misoprostol. If these strategies also fail, the patient may need a hysterectomy; ligation of the uterine vessels can be attempted if the patient wants to retain fertility.

120. What is the treatment for retained products of conception?

With retained products of conception (which is probably the most common cause of a *delayed* postpartum hemorrhage), remove the placenta manually to stop the bleeding. Next try curettage in the operating room under anesthesia. If placenta accreta, increta, or percreta is present, hysterectomy is usually necessary to stop the bleeding.

121. What causes uterine inversion? How is it treated?

When the uterus inverts, it usually can be seen outside the vagina. It is usually iatrogenic, a result of *pulling too hard on the cord.* If it occurs, put the uterus back in place manually; you may need to use anesthesia because of pain. Give intravenous fluids and oxytocin.

122. Define postpartum fever. What are the common causes?

Postpartum fever is defined as a temperature greater than 100.4°F (38°C) for at least 2 consecutive days and is classically caused by endometritis. However, do not forget easy causes of

postpartum fever, such as a urinary tract infection or atelectasis/pneumonia. Pulmonary problems are especially common after a cesarean section. Other causes include pelvic abscess and pelvic thrombophlebitis.

123. What should you do if a patient has postpartum fever?

Look for clues in the history and physical examination. For example, in a patient with a history of PROM and a tender uterus on examination, endometritis is almost certainly the cause of the fever. Next, get cultures of the endometrium, vagina, blood, and urine. Start empirical antibiotics if indicated. Clindamycin plus gentamicin is a good choice; add "big-gun" antibiotics if the patient is crashing.

124. What should you do if postpartum fever does not improve with antibiotics?

If a postpartum fever does not resolve with broad-spectrum antibiotics, there are two main possibilities: progression to pelvic abscess or pelvic thrombophlebitis. A computed tomography (CT) scan will show a pelvic abscess, which needs to be drained, and sometimes demonstrates thrombophlebitis. Pelvic thrombophlebitis presents with persistent spiking fevers, lack of response to antibiotics, and no abscess on CT. Give heparin or low molecular weight heparin for a cure (and diagnosis in retrospect).

125. What should you consider if a postpartum patient goes into shock without evident bleeding?

- Amniotic fluid embolism
- Uterine inversion
- Concealed hemorrhage (e.g., uterine rupture with bleeding into the peritoneal cavity)

126. List normal laboratory changes of pregnancy.

- The erythrocyte sedimentation test becomes markedly elevated; hence this test is essentially worthless in pregnancy.
- Total thyroxine (T_4) and thyroid-binding globulin increase, but free T_4 remains normal.
- Hemoglobin increases, but plasma volume increases even more; thus the net result is a decrease in hemoglobin and hematocrit.
- Blood urea nitrogen (BUN) and creatinine decrease because of an increase in glomerular filtration rate. BUN and creatinine levels at the high end of normal indicate renal disease in pregnancy.
- Alkaline phosphatase increases markedly.
- Mild proteinuria and glycosuria are normal in pregnancy.
- Electrolytes and liver function tests remain normal.

127. What cardiovascular and pulmonary changes occur in a normal pregnancy?

Normal cardiovascular changes: Blood pressure decreases slightly, heart rate increases by 10 to 20 beats/min, stroke volume increases, and cardiac output increases (by up to 50%).

Normal pulmonary changes: Minute ventilation increases because of increased tidal volume, but respiratory rate remains the same or increases only slightly; residual volume and carbon dioxide decrease. Collectively these changes cause the physiologic hyperventilation/respiratory alkalosis of pregnancy.

128. What is the average weight gain during pregnancy? What commonly causes weight gain to be more or less?

The average weight gain in pregnancy is roughly 28 pounds (12.5 kg). A larger weight gain may mean maternal diabetes. A smaller weight gain may mean hyperemesis gravidarum or psychiatric or major systemic diseases.

129. Define hyperemesis gravidarum. How do you recognize and treat it?

Hyperemesis gravidarum is intractable nausea and vomiting leading to dehydration and possible electrolyte disturbances. It presents in the first trimester, usually in younger patients with their first pregnancy and underlying social stressors or psychiatric problems. Treat with supportive care as well

as small, frequent meals and antiemetic medications such as pyridoxine-doxylamine, diphenhydramine, meclizine, dimenhydrinate, prochlorperazine, metoclopramide, or ondansetron. Patients may need intravenous fluids and correction of electrolyte abnormalities.

130. Define cholestasis of pregnancy. How is it treated?

Cholestasis of pregnancy presents with itching (often severe) and/or abnormal liver function tests, usually in the second and third trimester. In rare cases, jaundice may coexist. The only known definitive treatment is delivery, but ursodeoxycholic acid or cholestyramine may help with symptoms.

131. What is acute fatty liver of pregnancy? How is it treated?

Acute fatty liver of pregnancy is a more serious disorder than cholestasis. It presents in the third trimester or after delivery and usually progresses to hepatic coma. Treat with intravenous fluids, glucose, and fresh frozen plasma to correct coagulopathies. Vitamin K does not work, because the liver is in temporary failure. If the patient survives with supportive care, liver dysfunction usually resolves on its own with time.

132. True or false: In terms of surgery, the usual rule of thumb is to treat the disease in a pregnant woman the same as you would treat it in a nonpregnant woman.

It definitely is true in the case of an acute surgical abdomen. Pregnant women can develop appendicitis, which may present with right upper quadrant pain caused by displacement of the appendix by the pregnant uterus. Just as in nonpregnant patients, a laparotomy or laparoscopy is perfectly appropriate when the diagnosis is unsure and the patient has peritoneal signs.

For semiurgent conditions (e.g., ovarian neoplasm), it is best to wait until the second trimester to perform surgery (when the pregnancy is most stable). Purely elective cases are avoided during pregnancy.

133. How do you manage fetal malpresentation?

External cephalic version can be used to rotate the fetus from the breech to the cephalic position. If this fails, whether to attempt vaginal delivery or do a cesarean section must be decided. Although under specific guidelines some frank and complete breeches may be delivered vaginally, it is acceptable to do a cesarean section for any breech presentation. With shoulder presentation or incomplete/footling breech, cesarean section is mandatory. For face and brow presentations, watchful waiting is best because most cases convert to vertex presentations. If they do not convert, do a cesarean section.

134. What is the "poor man's way" to distinguish between monozygotic and dizygotic twins?

If the sex or blood type is different, the twins are dizygotic (i.e., fraternal). If the placentas are monochorionic, the twins are monozygotic (i.e., identical). These three simple points differentiate monozygotic from dizygotic twins in 80% of cases. In the remaining 20%, human leukocyte antigen typing studies are required to determine the type of twins.

135. What are the maternal and fetal complications of multiple gestations?

Maternal complications include anemia, hypertension, premature labor, postpartum uterine atony, postpartum hemorrhage, and preeclampsia.

Fetal complications include polyhydramnios, malpresentation, placenta previa, abruptio placentae, velamentous cord insertion/vasa previa, premature rupture of the membranes, prematurity, umbilical cord prolapse, IUGR, congenital anomalies, and increased perinatal morbidity and mortality.

The higher the number of fetuses, the higher the risk of most of the conditions mentioned for both mother and offspring.

136. How are multiple gestations delivered?

With vertex-vertex presentations of twins (both infants are head first), you can try vaginal delivery for both infants, but with any other twin presentation combination or more than two infants, perform cesarean section.

ONCOLOGY

1. What are the key differential points for the commonly tested blood dyscrasias?

TYPE	AGE	WHAT TO LOOK FOR IN CASE DESCRIPTION/ TRIGGER WORDS
ALL	Children (peak age: 3-5 yr)	Pancytopenia (bleeding, fever, anemia), history of radiation therapy, Down syndrome
AML	>30 yr	Pancytopenia (bleeding, fever, anemia), Auer rods (Fig. 26-1; Plate 55), DIC
CML (Fig. 26-2; Plate 56)	30-50 yr	White blood cell count greater than 50,000, Philadelphia chromosome, blast crisis, splenomegaly
CLL	>50 yr	Male gender, lymphadenopathy, lymphocytosis, infections, smudge cells, splenomegaly
Hairy cell leukemia	Adults	Blood smear (hairlike projections), splenomegaly
Mycosis fungoides/ Sézary syndrome	>50 yr	Plaquelike, itchy skin rash that does not improve with treatment, blood smear (cerebriform nuclei known as "butt cells"), Pautrier abscesses in epidermis
Burkitt lymphoma (Fig. 26-3; Plate 57)	Children	Associated with EBV (in Africa)
CNS B-cell lymphoma	Adults	Seen in patients with HIV infection, AIDS
T-cell leukemia	Adults	Caused by HTLV-1 virus
Hodgkin disease	15-34 yr	Reed-Sternberg cell, cervical lymphadenopathy, night sweats
Non-Hodgkin lymphoma	Any age	Small follicular type has best prognosis, large diffuse type has worst; primary tumor may be located in GI tract
Myelodysplasia/ myelofibrosis	>50 yr	Anemia, teardrop cells, "dry tap" on bone marrow biopsy, high MCV and RDW; associated with CML
Multiple myeloma	>40 yr	Bence-Jones protein (IgG = 50%, IgA = 25%), osteolytic lesions, high serum calcium
Waldenström macroglobulinemia	>40 yr	Hyperviscosity, IgM spike, cold agglutinins (Raynaud phenomenon with cold sensitivity)

TYPE	AGE	WHAT TO LOOK FOR IN CASE DESCRIPTION/ TRIGGER WORDS
Polycythemia vera	>40 yr	High hematocrit/hemoglobin, pruritus (especially after hot bath or shower); use phlebotomy
Primary thrombocythemia	>50 yr	Platelet count usually greater than 1,000,000; may have bleeding or thrombosis

ALL, Acute lymphoblastic leukemia; *AML*, acute myelogenous leukemia; *CLL*, chronic lymphocytic leukemia; *CML*, chronic myelogenous leukemia; *CNS*, central nervous system; *DIC*, disseminated intravascular coagulation; *EBV*, Epstein-Barr virus; *GI*, gastrointestinal; *MCV*, mean corpuscular volume; *RDW*, red cell distribution width.

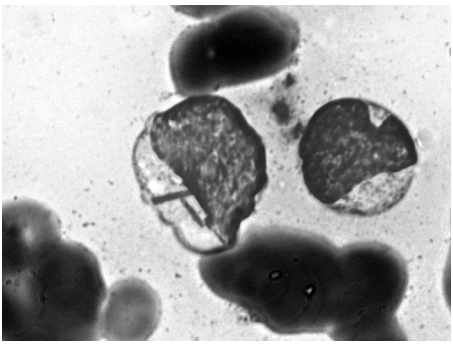

Figure 26-1. Auer rods vary from prominent, as in this cell, to thin and delicate. See Plate 55. (From McPherson RA, Pincus MR. Henry's clinical diagnosis and management by laboratory methods. 22nd ed. Philadelphia: Saunders, 2011, Fig. 33-25.)

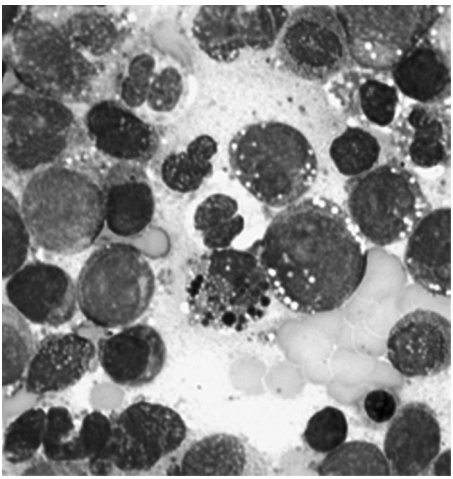

Figure 26-2. Chronic myelogenous leukemia showing myeloid blast phase. See Plate 56. (From Hoffman R, Benz EJ Jr, Shattil SJ, et al. Hematology: basic principles and practice. 5th ed. Philadelphia: Churchill Livingstone, 2008, Figure 69-5A.)

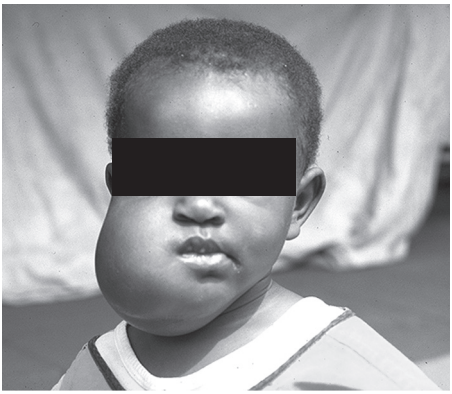

Figure 26-3. A young boy from South America with typical endemic Burkitt lymphoma presenting in the mandible. See Plate 57. (From Jaffe ES, Harris NL, Vardiman JW, et al. Hematopathology. 1st ed. St. Louis: Saunders, 2010, Fig. 24-1. Courtesy Prof. Georges Delsol, Toulouse, France.)

2. Which cancers have the overall highest incidence and mortality rate in men and women in the United States?

Overall highest incidence.

MALE	FEMALE
Prostate	Breast
Lung	Lung
Colon	Colon

Overall highest mortality rate.

MALE	FEMALE
Lung	Lung
Prostate	Breast
Colon	Colon

3. What are the most common types of cancer in children and young adults (<30 yr)?

Leukemia and lymphoma.

4. What is the major risk factor for cancer? What is the major modifiable risk factor for cancer?

Age is the biggest risk factor (the incidence of cancer in the United States roughly doubles every 5 years after age 25), and smoking is the biggest modifiable risk factor.

5. What is the most common cancer in most organs?

Metastatic cancer (Fig. 26-4). On the Step 2 examination, do *not* assume that the question is looking for the most common primary cancer unless the word "primary" is specified.

6. Metastatic cancer to the spine can cause spinal cord compression. How do you recognize and treat this medical emergency?

Spinal cord compression causes local spinal pain and neurologic symptoms (reflex changes, weakness, sensory loss, paralysis, incontinence, urinary retention). In rare cases it may be the first

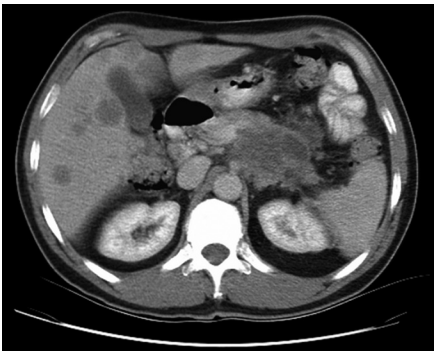

Figure 26-4. Pancreatic carcinoma with liver metastases. Portal venous phase computed tomography (CT) shows poorly enhancing liver deposits from a primary mass in the pancreatic body. (From Adam A, et al. Grainger & Allison's diagnostic radiology. 5th ed. Edinburgh: Churchill Livingstone, 2008, Fig. 37-33.)

indication of a malignancy. The first step is to start high-dose corticosteroids; then order a magnetic resonance (MRI) scan. The next step is to treat with radiation. Surgical decompression is used if radiation fails or the tumor is known not to be radiosensitive. Prompt intervention is essential, and outcome is closely linked to pretreatment function.

7. Name the mode of inheritance and types of cancer found in the following conditions.

DISEASE/SYNDROME	INHERITANCE	TYPE OF CANCER (IN ORDER OF MOST LIKELY)/OTHER INFORMATION
Retinoblastoma	Autosomal dominant	Retinoblastoma, osteogenic sarcoma (later in life)
MEN, type I	Autosomal dominant	Parathyroid, pituitary, pancreas (islet cell tumors)
MEN, type IIa	Autosomal dominant	Thyroid (medullary cancer), parathyroid, pheochromocytoma
MEN, type IIb	Autosomal dominant	Thyroid (medullary cancer), pheochromocytoma, mucosal neuromas
Familial polyposis coli	Autosomal dominant	Hundreds of colon polyps that always become cancer
Gardner syndrome	Autosomal dominant	Familial polyposis plus osteomas and soft tissue tumors
Turcot syndrome	Autosomal dominant	Familial polyposis plus CNS tumors
Peutz-Jeghers syndrome	Autosomal dominant	Look for perioral freckles and multiple noncancerous GI polyps; increased incidence of noncolon cancer (stomach, breast, ovaries); no increased risk of colon cancer

Continued

DISEASE/SYNDROME	INHERITANCE	TYPE OF CANCER (IN ORDER OF MOST LIKELY)/OTHER INFORMATION
Neurofibromatosis, type I (Fig. 26-5; Plate 58)	Autosomal dominant	Multiple neurofibromas, café-au-lait spots; increased number of pheochromocytomas, bone cysts, Wilms tumor, leukemia
Neurofibromatosis, type II	Autosomal dominant	Bilateral acoustic neuromas
Tuberous sclerosis	Autosomal dominant	Adenoma sebaceum, seizures, mental retardation, glial nodules in brain; increased renal angiomyolipomas and cardiac rhabdomyomas
Von Hippel-Lindau disease	Autosomal dominant	Hemangioblastomas in cerebellum, renal cell cancer; cysts in liver and/or kidney
Xeroderma pigmentosa	Autosomal recessive	Skin cancer
Albinism	Autosomal recessive	Skin cancer
Down syndrome	Trisomy 21	Leukemia

CNS, Central nervous system; *GI*, gastrointestinal; *MEN*, multiple endocrine neoplasia.

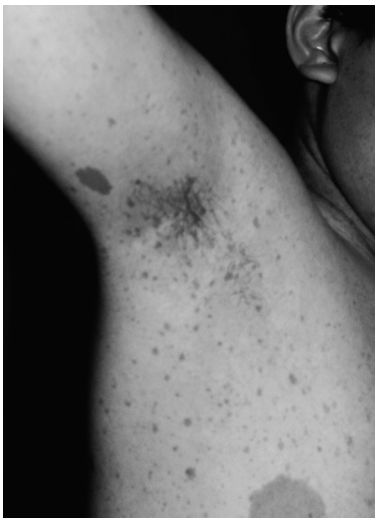

Figure 26-5. Café-au-lait patches as well as multiple axillary freckles in a 14-year-old boy. See Plate 58. (From Hoyt CS, Taylor D. Pediatric ophthalmology and strabismus. 4th ed. Saunders, 2012, Figure 65.4.)

8. What other conditions are associated with an increased risk of malignancy?

Other diseases with an increased incidence of cancer include dermatomyositis, polymyositis, immunodeficiency syndromes, Bloom syndrome, and Fanconi anemia. Breast, ovarian, and colon cancers are well known to have familial tendencies (as well as some other types of cancer), but rarely can a Mendelian inheritance pattern be demonstrated (e.g., BRCA-1 and BRCA-2 account for about 5% of breast cancers).

9. Cover the right-hand column and specify the major environmental risk factors for the following cancers.

CANCER TYPE	ENVIRONMENTAL RISK FACTORS*
Lung	Smoking, asbestos (also nickel, radon, coal, arsenic, chromium, uranium)
Mesothelioma	Asbestos and smoking
Leukemia	Chemotherapy/radiotherapy, other immunosuppressive drugs, benzene
Bladder	Smoking, aniline dyes (rubber and dye industry), schistosomiasis (in immigrants)
Skin	Ultraviolet light exposure (e.g., sun), coal tar, arsenic
Liver	Alcohol, vinyl chloride (liver angiosarcomas), aflatoxins (Africa)
Oral cavity	Smoking, alcohol
Pharynx/larynx	Smoking, alcohol
Esophagus	Smoking, alcohol
Pancreas	Smoking
Renal cell	Smoking
Stomach	Alcohol, nitrosamines/nitrites (from smoked meats and fish)
Clear cell cancer†	In utero exposure to diethylstilbestrol (DES)
Colon/rectum	High-fat and low-fiber diet, smoking, alcohol, obesity
Breast	Chest radiation, hormone replacement therapy, alcohol
Cervix	Sex/HPV infection, smoking, high parity
Thyroid	Childhood neck or chest irradiation, low dietary iodine
Endometrium	Unopposed estrogen stimulation, obesity, tamoxifen, high fat diet
All cancer overall	Smoking (number two is probably alcohol)

*The factor with the greatest impact is listed first.
†Of cervix and vagina.

10. What clinical vignette should make you suspect lung cancer?

The classic clue is a change in the chronic cough of a smoker. The more pack years of tobacco use, the more suspicious you should be. Patients also may have presenting symptoms such as hemoptysis, pneumonia, or weight loss. The chest radiograph may show a mass or pleural effusion. Withdraw fluid and examine for malignant cells.

11. How do you diagnose and treat lung cancer?

As with all cancers, you need a tissue biopsy (e.g., via bronchoscopy, computed tomography [CT]-guided biopsy, open lung biopsy) to confirm malignancy and to define the histologic type. Non–small cell lung cancer may be treated with surgery if the cancer remains within the lung parenchyma (i.e., without involvement of the opposite lung, pleura, chest wall, spine, or mediastinal structures). Early metastases of small cell lung cancer make surgery inappropriate. Small cell lung cancer and extensive non–small cell lung cancer (Fig. 26-6) are treated with chemotherapy with or without radiation. Usually a platinum-containing chemotherapy regimen (e.g., cisplatin) is used.

12. What consequences can result from an apical (Pancoast) lung cancer?

Horner syndrome: From invasion of the cervical sympathetic chain. Look for unilateral ptosis, miosis, and anhidrosis (no sweating).

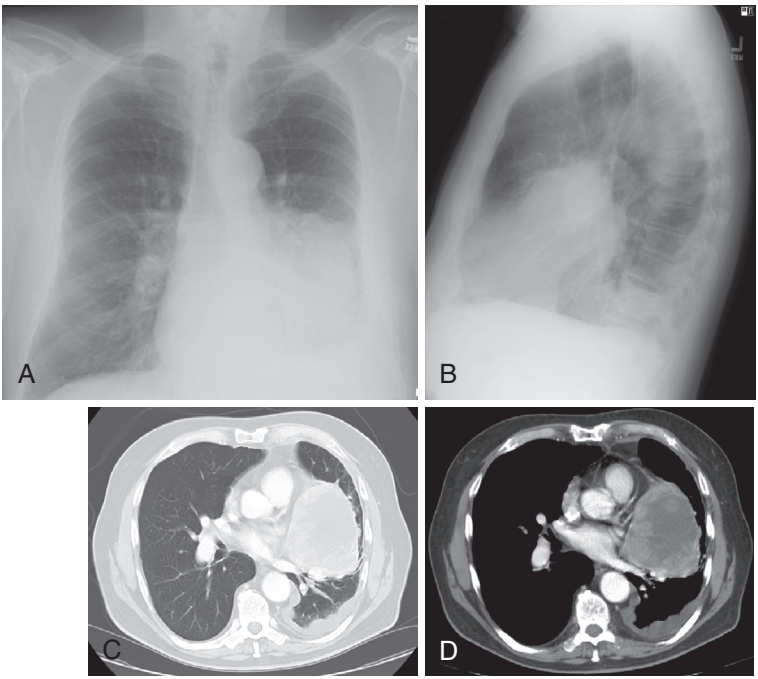

Figure 26-6. Imaging non–small cell lung cancer. **A,B,** Posteroanterior and lateral chest radiogram of patients with non–small cell lung cancer which is locally advanced. **C,D** Computed tomography (CT) imaging using lung and mediastinal windows. (From Abeloff M, et al. Abeloff's clinical oncology. 4th ed. Philadelphia: Churchill Livingstone, 2008, Fig. 76-12.)

Superior vena cava syndrome: Caused by compression of superior vena cava with impaired venous drainage. Look for edema and plethora (redness) of the neck and face (Fig. 26-7; Plate 59) and central nervous system (CNS) symptoms (headache, visual symptoms, and altered mental status).

Unilateral diaphragm paralysis: From phrenic nerve involvement (apical tumor not required) will result in an elevated hemidiaphragm on chest x-ray.

Hoarseness: From recurrent laryngeal nerve involvement (apical tumor not required).

13. What is a paraneoplastic syndrome? What are the commonly tested paraneoplastic syndromes of lung cancer?

A paraneoplastic syndrome is a condition caused by a malignancy but not related directly to destruction or invasion by the tumor. Classic examples in lung cancer are as follows:

Cushing syndrome: From production of adrenocorticotropic hormone (histologic type: small cell carcinoma).

Syndrome of inappropriate antidiuretic hormone secretion (SIADH): From production of antidiuretic hormone (histologic type: small cell carcinoma).

Hypercalcemia: From production of parathyroid-like hormone (histologic type: squamous cell carcinoma).

Eaton-Lambert syndrome: Myasthenia gravis-like disease from lung cancer that spares the ocular muscles. The muscles become stronger with repetitive stimulation, which is the opposite of myasthenia gravis (histologic type: small cell carcinoma).

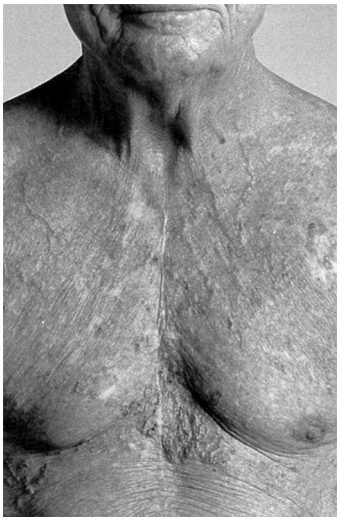

Figure 26-7. A patient with superior vena cava syndrome and the characteristic venous dilation and facial edema. See Plate 59. (From Abeloff MD, Armitage JO, Niederhuber JE, et al. Abeloff's clinical oncology. 4th ed. Philadelphia: Churchill Livingstone, 2008, Fig. 54-3.)

14. How should you manage a patient with a solitary pulmonary nodule on chest radiograph?

The first step is comparison with previous chest radiographs. If the nodule has remained the same size for more than 2 years, it is very unlikely to be cancer. If no old films are available and the patient is older than 35 years or has more than a 5-year history of smoking, get a CT scan (and possibly a positron emission tomography [PET] scan). If these are not definitely benign, get a biopsy of the nodule (via bronchoscopy or transthoracic needle biopsy, if possible) for tissue diagnosis.

If the patient is younger than 35 years or has no smoking history, the cause is most likely infection (tuberculosis or fungi), hamartoma, or collagen vascular disease. The patient should undergo CT scan and careful observation with follow-up imaging in 3 to 6 months. Investigate for infection if the history is suspicious.

15. Over the course of their lifetime, how many women in the United States will develop breast cancer?

Roughly 1 in 8.

16. What are the risk factors for breast cancer?

A personal history of breast cancer (major risk factor); female sex; family history in first-degree relatives; age older than 40 years (rare before age 30, incidence steadily increases with age); early menarche, late menopause, late first pregnancy, or nulliparity (more menstrual cycles = higher risk); atypical hyperplasia of the breast; radiation exposure before age 30 years; inherited gene mutations (e.g., BRCA1, BRCA2); dense breast tissue; high-fat diet; diethylstilbestrol (DES) exposure; recent oral contraceptive use; combined postmenopausal hormone replacement therapy; excessive alcohol consumption; obesity; and possibly not breastfeeding.

17. What classic signs and symptoms indicate that a breast mass is cancer until proved otherwise?

- Fixation of the breast mass to the chest wall or overlying skin
- Satellite nodules or ulcers on the skin

- Lymphedema (peau d'orange)
- Matted or fixed axillary lymph nodes
- Inflammatory skin changes (red, hot skin with enlargement of the breast caused by inflammatory carcinoma)
- Prolonged unilateral scaling erosion of the nipple with or without discharge (may be Paget disease of the nipple)
- Microcalcifications on mammography
- Any new breast mass in a postmenopausal woman

18. What is the conservative approach to ensure that you do not miss a breast cancer?

When in doubt, biopsy every palpable breast mass in women older than age 35 years that is not clearly a cyst (ultrasound is needed make the determination), especially if the patient has any of the risk factors mentioned in the previous question. If the Step 2 question does not want you to biopsy the mass, it will give definite clues that the mass is not a cancer (e.g., bilateral lumpy breasts that become symptomatic with every menses and have no dominant mass, patient younger than age 30 years).

19. What should you do with a breast mass in a woman younger than age 30 years?

In women younger than 30, breast cancer is rare. With a discrete breast mass in this age group, you should think of fibroadenoma. Consider ultrasound of the breast and observe the patient over a few menstrual cycles before considering biopsy unless the ultrasound is suspicious. Fibroadenomas are usually roundish, rubbery-feeling, and freely movable.

20. What is the most common histologic type of breast cancer?

Invasive (infiltrating) ductal carcinoma (Fig. 26-8) accounts for about 70% of breast cancer.

21. What is the role of mammography in deciding whether to biopsy a breast mass?

When a palpable breast mass is detected, the decision to biopsy is made on *clinical* grounds. A mammogram that looks benign should not deter you from doing a biopsy if you are clinically suspicious. On the other hand, a lesion that is detected on mammography and looks suspicious should be biopsied, even if it is not palpable. Needle localization biopsy can be used.

22. True or false: A mammogram should not be done in women younger than age 30 years.

True in most cases. The breast tissue is too dense for current techniques to be of value. Mammograms in women younger than age 30 years are rarely helpful.

23. How does tamoxifen affect breast cancer? What other therapies may be used?

Tamoxifen (often with endocrine therapy) improves outcomes in premenopausal women with estrogen receptor positive breast cancer. Tamoxifen has also been shown to decrease the risk of breast cancer in women at high risk for developing disease.

Raloxifene has also been shown to be as effective as tamoxifen in reducing breast cancer risk in postmenopausal women at increased risk of the disease. However, raloxifene did not reduce the risk of noninvasive breast cancers, such as ductal carcinoma in situ (DCIS) and lobular carcinoma in situ (LCIS).

Aromatase inhibitors (e.g., anastrozole, exemestane, letrozole) are used for the treatment of hormone-sensitive breast cancer in postmenopausal women. Aromatase inhibitors generally are not used in premenopausal women.

Trastuzumab is used after surgery and chemotherapy for HER-2/neu breast cancer and targets the HER-2 protein.

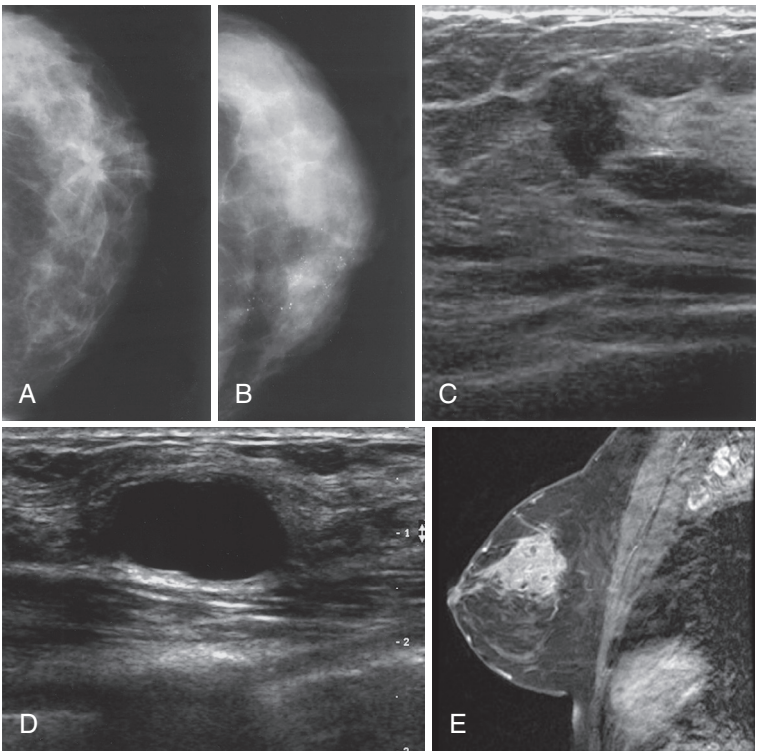

Figure 26-8. Mammographic, ultrasonographic, and magnetic resonance imaging (MRI) findings in breast disease. **A,** Stellate mass in the breast. A density with spiculated borders in combination with distortion of surrounding breast architecture suggests a malignancy. **B,** Clustered microcalcifications. Fine, pleomorphic, and linear calcifications that cluster together suggest the diagnosis of ductal carcinoma in situ. **C,** Ultrasound image of breast cancer. The mass is solid, contains internal echoes, and displays an irregular border. Most malignant lesions are taller than they are wide. **D,** Ultrasound image of a simple cyst. The cyst is round with smooth borders, there is a paucity of internal sound echoes, and there is increased through-transmission of sound with enhanced posterior echoes. **E,** Breast MRI showing gadolinium enhancement of a breast cancer. Rapid and intense gadolinium enhancement reflects increased tumor vascularity. (From Townsend C, et al. Sabiston textbook of surgery. 18th ed. Philadelphia: Saunders, 2008, Fig. 34-6.)

24. True or false: Mastectomy and breast-conserving surgery with radiation are considered equal in efficacy.

True. In either case, do an axillary node dissection (or a sentinel node biopsy) to determine spread to the nodes. If nodes are positive, give chemotherapy.

25. What are the three main risk factors for prostate cancer?

- **Age:** Prostate cancer is rare in men younger than 40 years old. The incidence increases with age, and about 60% of men older than 80 years have at least microscopic prostate cancer.
- **Race:** Black greater than white greater than Asian.
- **Family history:** Men who have a family history of prostate cancer are more likely to develop the disease at a younger age and to die of it than men who do not have a family history.

26. How do you recognize prostate cancer?

On the Step 2 examination, look for patients older than age 50 years. Patients often present late because early prostate cancer is asymptomatic. Look for symptoms typical of benign prostatic hyperplasia (hesitancy, dysuria, frequency) with hematuria and/or elevated prostate-specific antigen (PSA). Look for prostate irregularities (nodules) on rectal examination. Patients also may have back pain from vertebral metastases, which are osteoblastic.

27. How is prostate cancer treated?

Local prostate cancer is treated with surgery (prostatectomy) or local radiation. With metastases, the patient has several options for hormonal therapy: Orchiectomy, gonadotropin-releasing hormone agonist (leuprolide, goserelin, buserelin, triptorelin), androgen-receptor antagonist (flutamide), and GnRH antagonists (degarelix). Radiation therapy is used for local disease or pain from bony metastases; standard chemotherapy is usually ineffective.

28. List the primary risk factors for colon cancer.

- **Age** (incidence begins to increase after age 40; peak incidence between 60 and 75 years)
- **Family history** (especially with familial polyposis or Gardner, Turcot, Peutz-Jeghers, or Lynch syndrome)
- **Inflammatory bowel disease** (ulcerative colitis more than Crohn disease, but both are associated with increased risk)
- **Low-fiber, high-fat diet**

29. What are the classic symptoms for patients with colon cancer?

Patients may have presenting symptoms such as asymptomatic blood in the stool (visible streaks of blood on stool or positive occult blood test). Anemia is classic with right-sided colon cancer. Change in stool caliber ("pencil stool") or frequency (alternating constipation and frequency) is a classic presentation of left-sided colon cancer. Colon cancer is also a common cause of large bowel obstruction in adults. As with any cancer, look for weight loss.

30. What is the rule about occult blood in the stool of a patient older than age 40 years?

Occult blood in the stool of a person older than 40 years should be considered colon cancer until proven otherwise. To rule out colon cancer, do a colonoscopy.

31. How is colon cancer treated?

Treatment is primarily surgical, with resection of involved bowel. Adjuvant chemotherapy is sometimes given (e.g., 5-fluorouracil with leucovorin; irinotecan; oxaliplatin; cetuximab and panitumumab; bevacizumab) for lymph node involvement. Distant metastases frequently go to the liver first (as with all gastrointestinal [GI] tumors). Surgical resection of a solitary liver metastasis is often attempted. With metastases elsewhere, chemotherapy is the only option, and prognosis is poor.

32. What is the classic tumor marker for colon cancer? How is it used clinically?

Carcinoembryonic antigen (CEA) may be elevated with colon cancer, and if a patient is found to have colon cancer, the CEA level is usually measured before surgery. If it is elevated preoperatively (not always), the CEA level should return to normal after surgical removal of the tumor. Periodic monitoring of CEA after surgery may then help to detect recurrence before it is clinically apparent. CEA is *not* used as a screening tool for colon cancer; it is used only to follow known cancer because it is neither sensitive nor specific (can be elevated with other visceral tumors).

33. Describe the classic presentation of pancreatic cancer. How is it treated? What is the cell of origin?

The classic patient is a smoker in the 40- to 80-year-old range who has lost weight and is jaundiced. Other signs and symptoms include depression, epigastric pain, migratory thrombophlebitis

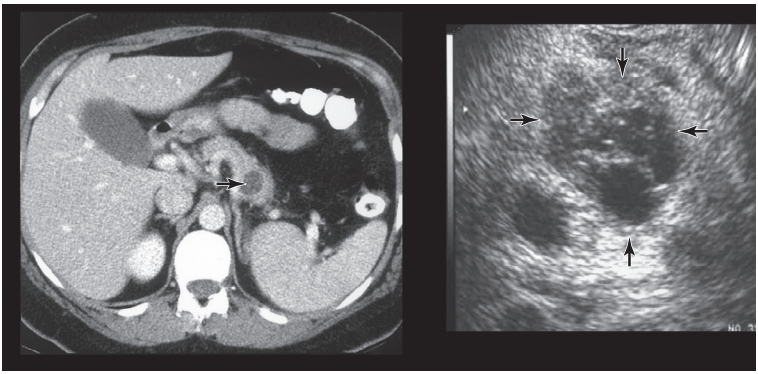

Figure 26-9. A mucinous cystic neoplasm of the tail of the pancreas. The endoscopic ultrasonogram (right) demonstrates septa and loculations not seen on the computed tomography scan (CT; left) and also allows for sampling of cyst fluid. The arrow on the left panel points to the cystic neoplasm on the CT image, and the arrows on the right image delineate the neoplasm on the ultrasonographic image. (From Feldman M, Friedman L, Brandt L. Sleisenger and Fordtran's gastrointestinal and liver disease. 8th ed. Philadelphia: Saunders, 2006, Fig. 58-11.)

(**Trousseau syndrome,** which also may be seen with other visceral cancers), and a palpable, nontender gallbladder (**Courvoisier sign**). Pancreatic cancer is more common in men than in women, in diabetics than in nondiabetics, and in blacks than in whites. Surgery (Whipple procedure) is rarely curative, and the prognosis generally is dismal. Chemotherapy is minimally successful at prolonging survival. The cell of origin in pancreatic cancer is ductal epithelium (Fig. 26-9).

34. What is the most common islet cell tumor of the pancreas? How is it diagnosed?

Insulinomas (beta cell tumor) are the most common islet cell tumors. Look for two-thirds of the **Whipple triad:** Hypoglycemia (glucose less than 50 mg/dL) and central nervous symptoms caused by hypoglycemia (confusion, stupor, loss of consciousness). As a good doctor, you provide the third part of the Whipple triad: Administration of glucose to relieve symptoms. Ninety percent of insulinomas are benign; they should be cured with resection, if possible. In your work-up, take a history and check the C-peptide level first to make sure that the patient is not a diabetic who is taking too much insulin or a patient with factitious disorder. C-peptide levels are high with insulinoma and low with the other disorders.

35. Define Zollinger-Ellison syndrome. What clues point to the diagnosis?

Zollinger-Ellison syndrome is a gastrinoma that causes acid hypersecretion (gastrin stimulates acid secretion) and peptic ulcer disease. Peptic ulcers are often multiple and resistant to therapy and may be found in unusual locations (distal duodenum or jejunum). More than one half of these pancreatic islet cell tumors are malignant. Diagnosis is made with an elevated fasting serum gastrin level or a secretin stimulation test.

36. Name the other two islet cell tumors. What should islet cell tumors make you think about?

- **Glucagonomas** (alpha cell tumor) cause hyperglycemia with high glucagon levels and migratory necrotizing skin erythema.
- **VIPomas** (tumors that secrete vasoactive intestinal peptide [VIP]) cause watery diarrhea, hypokalemia, and achlorhydria.

Watch for multiple endocrine neoplasia (MEN) syndromes in patients with islet cell tumors.

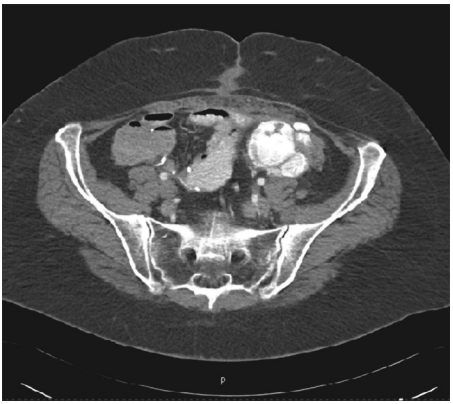

Figure 26-10. Axial computed tomography (CT) image shows a dense, calcified mass in the left pelvis, compatible with a metastatic implant from ovarian cancer. (From Abeloff MD, Armitage JO, Niederhuber JE, et al. Abeloff's clinical oncology. 4th ed. Philadelphia: Churchill Livingstone, 2008, Fig. 21-11.)

37. How does ovarian cancer classically present? How are ovarian masses evaluated?

Female patients classically present late with weight loss, pelvic mass, ascites, and/or bowel obstruction. Any ovarian enlargement in a postmenopausal female is cancer until proven otherwise. In women of reproductive age, most ovarian enlargements are benign. Ultrasound is a good first test to evaluate an ovarian lesion.

38. How is ovarian cancer treated? What is the cell of origin? What is the most common type of ovarian cancer?

Ovarian cancer (Fig. 26-10) usually is treated with debulking surgery and chemotherapy. The prognosis is usually poor because of a late presentation. Most ovarian cancers arise from ovarian epithelium. Serous cystadenocarcinoma is the most common type; histopathologic studies classically reveal psammoma bodies. Mucinous cystadenocarcinoma is also common. When physicians use the term "ovarian cancer" without a qualifier, they are talking about epithelial malignancies (i.e., cystadenocarcinomas).

39. List the three commonly tested germ-cell tumors. What clues suggest their presence?

- **Teratoma/dermoid cyst** (most common and most tested type). Look for a description of the tumor to include skin, hair, and/or teeth or bone; it may show up as calcifications on radiograph.
- **Sertoli-Leydig cell tumor,** which causes virilization (hirsutism, receding hairline, deepening voice, clitoromegaly).
- **Granulosa/theca-cell tumors,** which cause feminization and precocious puberty.

Female patients with germ cell tumors of the ovary are classically younger than age 30 years.

40. What is Meigs syndrome?

An ovarian fibroma that causes ascites and right hydrothorax.

41. What is a Krukenberg tumor?

A stomach cancer (or other GI malignancy) with metastases to the ovaries.

42. What commonly used medication has been shown to reduce the risk of ovarian cancer?

Oral contraceptive pills, which also reduce the incidence of endometrial cancer.

43. What is the best available screening method to reduce the incidence and mortality of cervical cancer?

Papanicolaou (Pap) smears. Give all female patients a Pap smear if they are due, even if they come to the hospital for a totally unrelated complaint. Screening should start at age 21 years. The frequency of screening depends on whether human papillomavirus (HPV) testing is also being used as well as the patient's age and results of previous Pap smears. See Chapter 31 for additional details.

44. What should you do if a Pap smear is abnormal?

The follow-up required for an abnormal Pap smear depends on the cervical cytologic results. Lower grade lesions may be evaluated with HPV testing and colposcopy/endocervical curettage, if needed. Higher grade lesions require colposcopy with biopsy and/or loop electrosurgical excision (LEEP). Invasive cancer requires surgery (at least a hysterectomy) and may include radiation with cisplatin-based chemotherapy.

45. List the main risk factors for cervical cancer.

- Age younger than 20 years old at first coitus, pregnancy, or marriage
- Multiple sexual partners (role of HPV and possibly herpes virus)
- Coitus with a promiscuous partner
- Smoking
- Low socioeconomic status
- High parity (which protects against endometrial and breast cancer)

46. Where does cervical cancer begin? How does it present? How is it treated?

Invasive cervical cancer begins in the transformation zone and usually presents with vaginal bleeding or discharge (postcoital bleeding, intermenstrual spotting, or abnormal menstrual bleeding). Treat with surgery and/or radiation.

47. What do you need to know about DES and cancer?

Maternal exposure to DES during pregnancy increases a daughter's risk of developing clear cell cancer of the cervix and/or vagina.

48. What is the rule of thumb for postmenopausal vaginal bleeding?

Postmenopausal vaginal bleeding is cancer until proved otherwise. Endometrial cancer is the most common type to present in this fashion; it is also the fourth most common cancer overall in women. Do an endometrial biopsy (generally preferred) or a transvaginal ultrasound for any woman with postmenopausal bleeding (as well as a Pap smear).

49. List the main risk factors for endometrial cancer.

- Obesity
- Nulliparity
- Late menopause
- Diabetes, hypertension, and gallbladder disease (probably related to obesity)
- Chronic, unopposed estrogen stimulation (e.g., polycystic ovary syndrome, estrogen-secreting neoplasm [granulosa-theca cell tumor], estrogen replacement therapy without progesterone)

50. What is the most common type of endometrial cancer? How is it treated?

Most uterine cancers are adenocarcinomas and spread by direct extension. Treat with surgery and radiation.

51. What commonly prescribed medication reduces the risk of endometrial cancer?

Oral contraceptive pills, which also decrease the risk for ovarian cancer.

52. Describe the common presentations of brain tumors.

CNS tumors are the second most common tumors in children (second to leukemia); be suspicious in this age group. In adults, two-thirds of primary tumors are supratentorial (i.e., above the tentorium cerebelli, a portion of dura that separates the cerebellum from the cerebral hemispheres), whereas in children two-thirds are infratentorial (i.e., lower brainstem or cerebellum [posterior fossa]). In either group, look for new-onset seizures, neurologic deficits or signs of intracranial hypertension (headache, blurred vision, papilledema, nausea, projectile vomiting). In children, also look for hydrocephalus (manifested as an inappropriately increasing head circumference), new clumsiness, ataxia, loss of developmental milestones, or a change in school performance or personality.

53. What are the most common histologic types of primary CNS tumors in children and adults? How are primary brain tumors treated?

The most common primary type in **adults** is **glioma** (Fig. 26-11). Most gliomas are astrocytomas, which are intraparenchymal and have little or no calcification. The second most common type in adults is **meningioma**, which often is calcified and is external to the brain substance. In **children** the most common types are **cerebellar astrocytoma** (benign pilocytic astrocytoma) and **medulloblastoma**, followed by **ependymoma**. Treat with surgical removal (if possible), followed by radiation and/or chemotherapy, depending on the tumor.

54. Which cancers tend to metastasize to the brain?

Lung cancer, breast cancer, and melanoma are the most common; together they account for 75% of brain metastases.

55. What tumor is most likely in a young, obese woman with headaches, papilledema, vomiting, and a negative CT/MRI scan?

A pseudotumor, as in **pseudotumor cerebri.** Pseudotumors are not actual tumors, but reflect idiopathic increased intracranial pressure. Symptoms and signs include headache, papilledema,

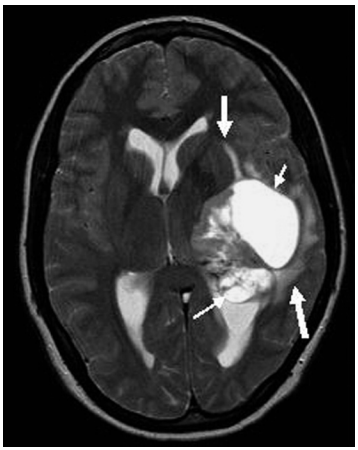

Figure 26-11. A malignant glioma is seen on this T2-weighted magnetic resonance image (MRI) demonstrating edema *(large arrows)* and necrosis (uniform high signal regions, *small arrows*). (From Goldman L, Ausiello D. Cecil medicine. 23rd ed. Philadelphia: Saunders, 2008, Fig. 419-5.)

vision loss, elevated intracranial pressure with normal CSF, and no other evident cause of intracranial hypertension. Weight loss may help; acetazolamide or topiramate also may help. Repeated lumbar punctures or a CSF shunt may be needed to prevent vision loss.

56. What tumor should you suspect in an adult with signs of eighth cranial nerve damage and increased intracranial pressure?

An acoustic neuroma (especially in the setting of neurofibromatosis). Co-involvement of the facial nerve is not uncommon (Fig. 26-12).

57. What tumor should you suspect in children with intracranial calcifications on skull radiographs?

Craniopharyngioma (benign tumors that arise from remnants of the Rathke pouch and grow slowly from birth).

58. What should you know about testicular cancer?

It is the most common solid malignancy in adult men younger than 30 years old. The main risk factor is **cryptorchidism.** Transillumination and ultrasound help to distinguish a hydrocele, which is filled with fluid and transilluminates, from cancer, which is solid and does not transilluminate. The most common histologic type is seminoma, which is radiosensitive and highly curable. Use ultrasound to make the diagnosis.

59. What tumor resembles "a bunch of grapes" coming out of the vagina?

Sarcoma botryoides, a type of embryonal rhabdomyosarcoma usually seen in children.

60. What is the classic physical finding of a pituitary tumor? What is the most common type?

The classic physical finding is **bitemporal hemianopsia.** Order an MRI of the brain in any patient with this finding. Patients also may have signs and symptoms of increased intracranial pressure.

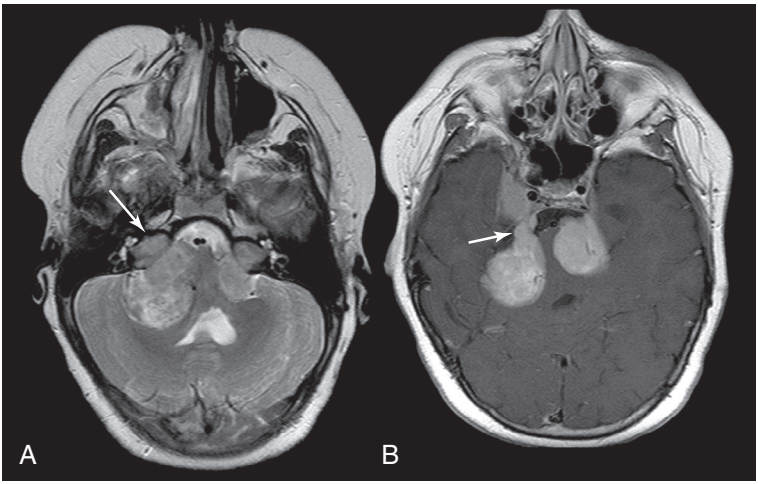

Figure 26-12. Neurofibromatosis type 2 (NF2). **A,** Bilateral cerebellopontine angle masses extending into the internal auditory meatus and causing expansion *(arrow)* in a child with NF2 and bilateral acoustic neuromas. **B,** Trigeminal schwannomas extending into the cavernous sinus on the right. The arrow indicates the cisternal segment of the right trigeminal nerve. (From Adam A, et al. Grainger & Allison's diagnostic radiology. 5th ed. Edinburgh: Churchill Livingstone, 2008, Fig. 70-24.)

The most common type is a prolactinoma, which is associated with high prolactin levels, galactorrhea, and menstrual or sexual dysfunction. Other types of pituitary tumors may cause hyperthyroidism, Cushing disease, or acromegaly, or they may be nonfunctional (i.e., they do not secrete hormones).

61. What two points do you need to know about nasopharyngeal cancer?

It usually is seen in Asian patients (particularly those who are from Asia), and it is associated with **Epstein-Barr virus (EBV).**

62. Describe the classic presentation of esophageal cancer. What is the most common cell type?

The presentation depends on the histologic type. The classic patient with squamous cell carcinoma is a chronic smoker and alcohol drinker between the ages of 40 and 60 years (black patients more than white patients) who presents with weight loss, anemia, and the complaint that "my food is sticking," which progresses to dysphagia for liquids. The other cell type is adenocarcinoma, which is typically caused by malignant degeneration of Barrett esophagus (columnar metaplasia of esophageal squamous epithelium caused by acid reflux); thus patients have a long history of acid reflux and heartburn. Prognosis usually is quite poor in either type because of late presentation. Squamous cell carcinomas used to predominate, but squamous cell carcinoma and adenocarcinoma now occur with almost equal frequency.

63. What physical and laboratory findings suggest thyroid cancer? What is the most common type of thyroid cancer? What historical point is of concern with thyroid cancer?

Patients often have a single, stony-hard nodule or mass in the thyroid gland that may be rapidly enlarging. The nodule is "cold" on a nuclear scan (i.e., it fails to take up radioactive tracer). The most common type is papillary thyroid cancer. Other worrisome findings are hoarseness, which indicates recurrent laryngeal nerve invasion, and increased calcitonin level, which indicates the rare medullary thyroid cancer. Patients with medullary thyroid cancer may have MEN syndrome. Historically, irradiation to the head or neck is of concern as a result of its association with thyroid cancer.

64. How should you evaluate a thyroid mass for possible malignancy?

To evaluate a nodule in the thyroid, order thyroid function tests. Thyroid-stimulating hormone (TSH) is the best screening test; "toxic" or functional nodules are unlikely to be cancer. If the TSH is normal, get a fine needle aspiration of the mass. If the TSH is decreased, then order a nuclear scan. A "cold" nodule or area of decreased uptake is more suspicious than a nodule with normal or increased uptake. Ultrasound is also commonly used to help evaluate a thyroid mass. If the history is suspicious (radiation to neck, MEN syndrome, hoarseness, "stony hard" nodule), obtain a biopsy even if the other tests are normal.

65. What clinical vignette is suspicious for bladder cancer?

Persistent, painless hematuria, especially in patients older than 40 years who smoke or work in the rubber or dye industry (exposure to aniline dye). CT scan to evaluate the upper urinary tract and cystoscopy should be performed to evaluate for potential bladder cancer (as well as other causes of hematuria, including renal cell carcinoma).

66. What increases the risk for hepatocellular cancer of the liver? What is the classic tumor marker for liver cancer?

The same factors that increase the risk for cirrhosis. The "big three" are alcohol, chronic hepatitis (hepatitis C is now a more likely culprit than hepatitis B), and hemochromatosis. **Alpha-fetoprotein (AFP)** is often elevated and can be measured postoperatively to detect recurrences. It also is used for screening in high-risk populations (e.g., those with cirrhosis).

67. What are the presenting symptoms in patients with liver cancer? How is liver cancer treated?

Patients often have a history of alcoholism, hepatitis, hemochromatosis, or other causes of cirrhosis. Their presenting symptoms include weight loss, right upper quadrant pain, and an enlarged liver. Surgery is the only hope for cure. The prognosis is poor.

68. What other tumors of the liver may appear on the USMLE? What clues suggest their presence?

- **Hemangioma:** Most common primary tumor of the liver; benign and generally left alone. Surgery is performed only if symptoms (pain, bleeding) are present.
- **Hepatic adenoma:** Benign tumor in women of reproductive age who take **birth control pills.** Stop the birth control pills; the tumor may regress. If not, surgery is usually preferred to prevent hemorrhage and rare malignant transformation.
- **Cholangiocarcinoma:** Malignant. Fifty percent of patients have inflammatory bowel disease (especially ulcerative colitis); liver flukes (*Clonorchis* sp.) increase the risk in some immigrant populations (China, Japan, Taiwan, Vietnam, Korea, far eastern Russia).
- **Angiosarcoma:** Malignant. Look for industrial exposure to vinyl chloride.
- **Hepatoblastoma:** Malignant; the most common primary liver malignancy in children.

69. What is the significance of adrenal tumors?

Most are benign, but they may be functional and cause primary hyperaldosteronism (Conn syndrome) or hyperadrenalism (Cushing syndrome). Another possibility is pheochromocytoma, which is associated with intermittent, severe hypertension, mental status changes, headaches, and diaphoresis.

70. What are the risk factors for stomach cancer? What are the symptoms?

Risk factors include Asian race, increasing age, smoking history, ingestion of smoked meat, and *Helicobacter pylori* infection. Symptoms and signs include anemia, weight loss, early satiety, abdominal pain, and a nonhealing gastric ulcer. All gastric ulcers must be biopsied to exclude malignancy. Consider follow-up endoscopy to document resolution of an ulcer, though this is somewhat controversial. Be especially suspicious if the question describes a nonhealing ulcer in a patient with weight loss.

71. What is a Virchow node?

A Virchow node is a left supraclavicular node enlargement caused by the spread of visceral cancer (classically stomach cancer).

72. What do you need to know about osteosarcomas for the Step 2 examination?

Osteosarcomas most commonly are seen around the knee in 10- to 30-year-old patients. The classic x-ray finding is a "sunburst" periosteal reaction (Fig. 26-13) in the distal femur or proximal tibia associated with a mass. In older adults, the risk is increased in bones with long-standing Paget disease or osteomyelitis.

73. What are the symptoms of carcinoid tumors? Where are they most commonly found?

Carcinoid tumors secrete serotonin-like products that can cause symptoms, but the liver breaks down serotonin and other vasoactive secretions to make the tumor initially asymptomatic. Once a carcinoid tumor metastasizes to the liver and vasoactive products reach the systemic circulation, symptoms begin (carcinoid syndrome): Episodic cutaneous flushing, abdominal cramps, diarrhea, and right-sided heart valve damage. The most common location is in the small bowel, but carcinoid tumors are also the most common appendiceal tumor (sometimes found at the time of appendectomy in patients with appendicitis).

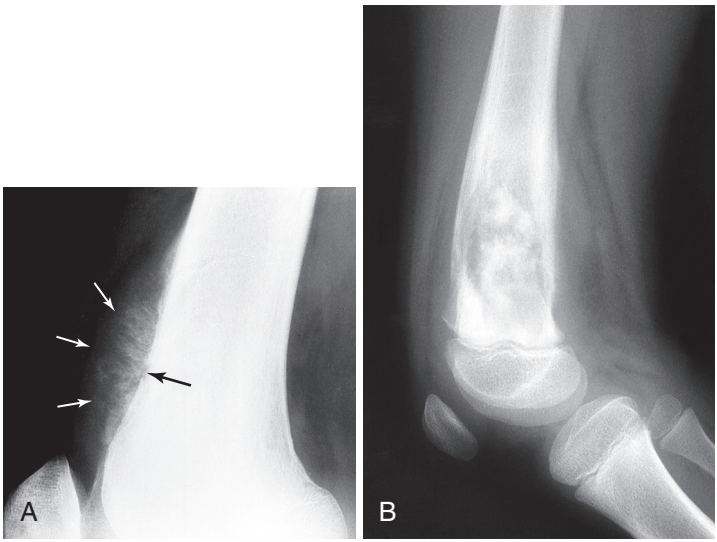

Figure 26-13. Osteogenic sarcoma of the knee. **A,** A lateral view of the knee in a 19-year-old man shows a sunburst-type periosteal reaction *(arrows).* Knowing that the distal femur is the most common site of osteogenic sarcoma, that periosteal reaction is a feature, and that this patient is a teenager should make osteogenic sarcoma very high on your differential diagnostic list. **B,** A destructive central lesion is seen here in the distal femur of an 8-year-old girl. (From Mettler F. Essentials of radiology. 2nd ed. Philadelphia: Saunders, 2004, Fig. 8-113.)

74. What laboratory test detects carcinoid tumors?

Urinary levels of 5-hydroxyindoleacetic acid (5-HIAA, a serotonin breakdown product) are increased.

75. What is the classic clinical manifestation of Kaposi sarcoma?

A rash that does not respond to multiple treatments in an HIV-positive patient. Kaposi sarcoma is a vascular skin tumor that commonly begins as a papule or plaque on the upper body or in the oral cavity (Fig. 26-14; Plate 60). It is highly associated with herpes virus (human herpesvirus-8 [HHV-8]) infection.

76. What is the main risk factor for skin cancer?

Ultraviolet light exposure.

77. Explain the ABCDEs of melanoma. What should you do if they are present?

The ABCDEs of melanoma (Fig. 26-15; Plate 61) are characteristics of a mole that should make you suspicious of malignant transformation: **A**symmetry, **b**orders (irregular), **c**olor (change in color or multiple colors), **d**iameter (lesions greater than 6 mm are more likely to be malignant), and **e**volving changes (lesions that change over time). Do an excisional biopsy of a lesion with any of these characteristics because melanomas commonly metastasize if not caught early. The risk of metastasis correlates most closely with depth of invasion into the skin.

78. What do you need to know about basal cell and squamous cell skin cancers?

Both of these cancers usually appear on sun-exposed areas (classically the head and neck area). The classic description of a basal cell cancer is a pearly, umbilicated nodule with telangiectasias; it is extremely common and almost never metastasizes (see Fig. 6-12; Plate 62). Squamous cell cancer sometimes metastasizes and often has a red, scaly, inflamed appearance or presents

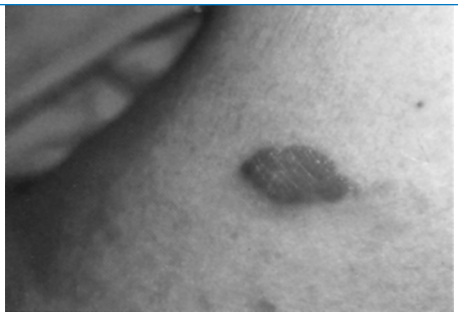

Figure 26-14. Kaposi sarcoma. See Plate 60. (From Hoffman R, Benz EJ Jr, Shattil SJ, et al. Hematology: basic principles and practice. 5th ed. Philadelphia: Churchill Livingstone, 2008, Fig. 121-35.)

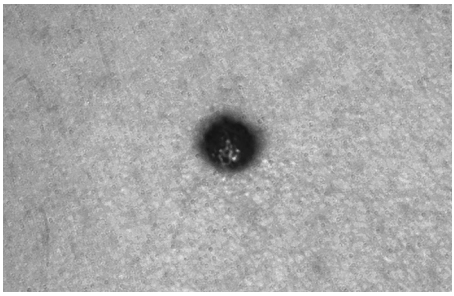

Figure 26-15. Primary nodular malignant melanoma found on back of patient. See Plate 61. (From Yanoff M, Sassani JW. Ocular pathology. 6th ed. Mosby, 2008, Fig. 17.8A.)

as an area of skin ulceration (see Fig. 6-13). Excisional biopsy is appropriate for all suspicious lesions.

79. How can you differentiate a Wilms tumor from a neuroblastoma?

Both present as flank masses in children (peak age: around 2 years). Neuroblastomas most commonly arise from the adrenal gland and often contain calcifications, whereas Wilms tumors arise from the kidney and rarely calcify, thus imaging (CT scan) can usually distinguish the two. In rare cases, neuroblastomas regress spontaneously (for unknown reasons).

80. What factors increase the risk for oral cancers? Describe the typical appearance.

Smoking or chewing tobacco and alcohol are the main risk factors for oral cancer; their effect is synergistic. Also look for poor oral hygiene. Lesions often begin as leukoplakia (white patch; Fig. 26-16; Plate 62) or malakoplakia (red patch). Oral hairy leukoplakia can resemble leukoplakia somewhat but is an unrelated condition affecting HIV-positive patients that is associated with the EBV. The clinical setting should help you distinguish the two.

81. What are the two major cytologic clues for histiocytosis?

CD1 positive cells and Birbeck granules (cytoplasmic inclusion bodies that look like tennis rackets; Fig. 26-17).

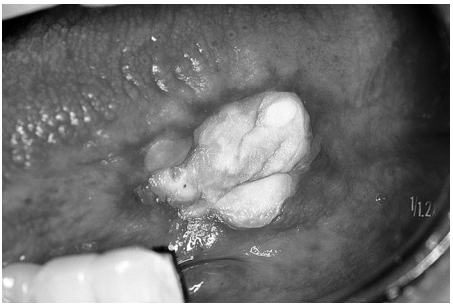

Figure 26-16. A thick, sharply marginated focal leukoplakia of the ventral/lateral tongue with a uniform erythematous periphery. See Plate 62. (From Flint PW, Haughey BH, Niparko JK, et al. Cummings otolaryngology: head & neck surgery. 5th ed. Philadelphia: Mosby, 2010, Fig. 91-5C.)

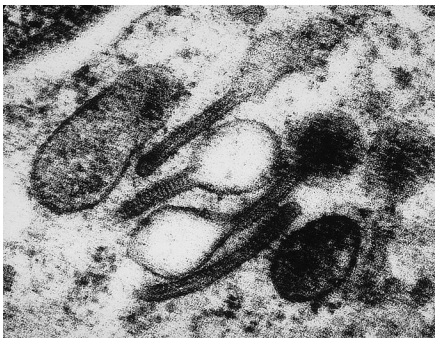

Figure 26-17. Birbeck granules. These characteristic racquet-shaped cytoplasmic inclusions are a marker for Langerhans cells of the skin. (From du Vivier A. Atlas of clinical dermatology. 3rd ed. New York: Churchill Livingstone, 2002, p 27, with permission.)

82. What is a unicameral bone cyst? Who gets it? Describe the classic presentation.

It is an expansile, lytic, well-demarcated benign lesion in the proximal portion of the humerus in children and adolescents (Fig. 26-18). Although benign, it may weaken bone enough to cause a pathologic fracture of the humerus (the classic presentation).

83. Describe the classic presentation of a retinoblastoma.

Retinoblastoma classically presents in a child younger than 3 years old with leukocoria (the pupillary red reflex changes to white) and/or unilateral exophthalmos. It may be bilateral in the inherited form.

84. True or false: All patients with metastatic cancer should be encouraged to receive chemotherapy.

False. The risks and side effects of chemotherapy can be enormous, and sometimes minimal prolongation of life is achieved. The risks and benefits must be weighed. Patients with cancer (like all other patients) have the right to refuse any treatment. However, watch for and treat depression, even in terminal patients.

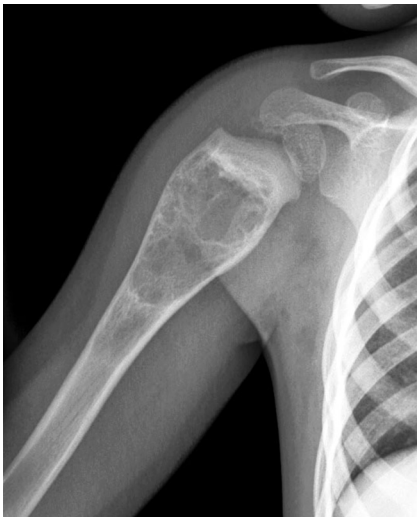

Figure 26-18. Plain film of unicameral bone cyst manifesting as a large expansile completely cystic intramedullary lesion that has well-defined focally sclerotic borders. (From Gilbert-Barness E. Potter's pathology of the fetus, infant and child. 2nd ed. Philadelphia: Mosby, 2007, Fig. 34.1.2).

85. Cover the right-hand column and name the cancer(s) associated with the following tumor markers.

MARKER	CANCER(S)
AFP	Liver (hepatocellular carcinoma), gonad (yolk-sac tumors)
CEA	Colorectal, lung, breast, ovary, pancreas, thyroid, liver, stomach, bladder, prostate
PSA	Prostate
HCG	Hydatiform moles, choriocarcinoma, testicular
CA-125	Ovary
S-100	Melanoma
CA 19-9	Pancreas, colorectal
CA 27-29	Breast
CA 15-3	Breast
Hormone receptors (estrogen and progesterone)	Breast
HER2	Breast
Beta-2-microglobulin	Multiple myeloma, CLL, and some lymphoma
BTA	Bladder
Calcitonin	Medullary thyroid carcinoma

AFP, Alpha fetoprotein; *BTA*, bladder tumor antigen; *CEA*, carcinoembryonic antigen; *CLL*, chronic lymphocytic leukemia; *HCG*, human chorionic gonadotropin; *PSA*, prostate specific antigen.

CHAPTER 27

OPHTHALMOLOGY

1. What is the hallmark of conjunctivitis?
Hyperemia of the conjunctival vessels.

2. Distinguish among allergic, viral, and bacterial conjunctivitis in terms of signs and symptoms and treatment.

ETIOLOGY	SIGNS AND SYMPTOMS	TREATMENT
Allergic	Itching, bilateral, seasonal, long duration	Vasoconstrictors or topical antihistamines/mast cell stabilizers
Viral*	Preauricular adenopathy, highly contagious (look for affected contacts); clear, watery discharge	Supportive, hand washing to prevent spread
Bacterial	Purulent discharge; classic in neonates	Topical antibiotics ± systemic antibiotics

*The number-one viral cause is adenovirus.

3. What are the three common causes of neonatal conjunctivitis?
Chemical, *Neisseria gonorrhoeae*, and *Chlamydia trachomatis*.

4. What causes chemical conjunctivitis? How do you recognize it?
Chemical conjunctivitis is caused by the silver nitrate (or erythromycin) drops that are given to all newborns to prevent gonorrhea conjunctivitis. The drops may cause a chemical conjunctivitis (with no purulent discharge) that appears within 12 hours of instilling the drops and resolves within 48 hours. Chemical conjunctivitis is always the best guess if the conjunctivitis develops in the first 24 hours of life.

5. How can you distinguish gonorrheal from chlamydial conjunctivitis?
In cases of suspected **gonorrheal conjunctivitis,** look for symptoms of gonorrhea in the mother. The infant has an extremely purulent discharge starting between 2 and 5 days after birth. Infants who were given prophylactic drops should not develop gonorrheal conjunctivitis. Treatment involves systemic ceftriaxone or cefotaxime.

In cases of **chlamydial (inclusion) conjunctivitis,** the mother often reports no symptoms. The infant has mild-to-severe conjunctivitis beginning between 5 and 14 days after birth. Oral erythromycin is recommended for chlamydial conjunctivitis or pneumonia; topical therapy for chlamydial conjunctivitis is not effective.

6. If you forget everything else about neonatal conjunctivitis, what point should you remember to help you distinguish among the three discussed causes?
The varying time frames during which they present.

7. True or false: Conjunctivitis frequently causes loss of vision.

False. Other than transient blurriness (caused by tear film debris) that resolves with blinking, conjunctivitis should not affect vision. If vision is affected, think of other, more serious conditions.

8. Define glaucoma. What are the risk factors for developing it? What are the two general types?

Glaucoma is best thought of as ocular hypertension (or elevated intraocular pressure, measured with a tonometer); its effects include visual field defects and blindness. The risk factors are age older than 40 years, black race, and positive family history. The two main types are open-angle and closed-angle glaucoma.

9. Describe the physical findings of open-angle glaucoma. How common is it? How is it treated?

Open-angle glaucoma causes 90% of the cases of glaucoma; it is painless and does not have acute attacks. The only signs are elevated intraocular pressure (usually 20 to 30 mm Hg), a gradually progressive visual field loss, and optic nerve changes (increased cup-to-disc ratio on funduscopic examination). Treatment may involve several different classes of medications, including beta blockers, prostaglandins, alpha adrenergic agonists, carbonic anhydrase inhibitors, cholinergic agonists, as well as laser therapy and surgery.

10. How does closed-angle glaucoma present? What should you do if you recognize it?

Closed-angle glaucoma presents with sudden ocular pain, seeing halos around lights, red eye, high intraocular pressure (greater than 30 mm Hg), nausea and vomiting, sudden decreased vision, and a fixed, mid-dilated pupil. It is an ophthalmologic emergency. Treat the patient immediately with **pilocarpine**, oral glycerin, and/or acetazolamide to break the attack. Definitive surgery (peripheral iridectomy) is used to prevent further attacks. In rare cases, anticholinergic medications can trigger an attack of closed-angle glaucoma in a susceptible, previously untreated patient. Medications do not cause acute attacks in patients with open-angle glaucoma or in patients with surgically treated closed-angle glaucoma.

11. How do steroids affect the eye?

Steroids, whether topical or systemic, can cause glaucoma and cataracts. Topical ocular steroids can worsen ocular herpes and fungal infections. For the Step 2 examination, do *not* give topical ocular steroids, especially if the patient has a dendritic corneal ulcer that stains green by fluorescein. Such an ulcer represents herpes.

12. Define ultraviolet keratitis. How is it treated?

Exposure to ultraviolet light can cause keratitis (corneal inflammation) with pain, foreign body sensation, red eye, tearing, and decreased vision. Patients have a history of welding, using a tanning bed or sunlamp, or snow-skiing ("snow-blindness"). Treat with an eye patch (for 24 hours) and topical antibiotic. You can reduce pain with an anticholinergic eye drop that causes paralysis of the ciliary muscle (cycloplegia).

13. What pediatric rheumatologic condition is commonly associated with uveitis?

Uveitis is common in juvenile rheumatoid arthritis (especially the pauciarticular form). Patients with juvenile rheumatoid arthritis need periodic ophthalmologic examination to check for uveitis.

14. What is the most common cause of painless, slowly progressive loss of vision?

Cataracts, especially in older adults. Treatment is surgical removal of the affected lens and replacement with an artificial lens.

15. What should cataracts in a neonate suggest?

Cataracts in a neonate may indicate a TORCH (**t**oxoplasmosis, **o**ther, **r**ubella, **c**ytomegalovirus, and **h**erpes simplex virus) infection or an inherited metabolic disorder (the classic example is galactosemia).

16. What changes in the retina and fundus are seen in diabetes and hypertension?

Diabetes is associated with dot-blot hemorrhages, microaneurysms, and neovascularization of the retina. **Hypertension** is associated with arteriolar narrowing, copper/silver wiring, and cotton-wool spots. Papilledema may be seen with severe hypertension and should alert you to the presence of a hypertensive emergency.

17. What is the most common cause of blindness in patients younger than age 55 years? Older than age 55 years? In black patients?

In the United States, diabetes is the number-one cause of blindness in younger adults, and senile macular degeneration (look for macular drusen) is the most common cause of blindness in adults older than age 55 years. Glaucoma is the number-one cause of blindness in black patients of any age and the number-three overall cause of blindness in the United States.

18. Define proliferative diabetic retinopathy. How is it treated? How is nonproliferative diabetic retinopathy treated?

Proliferative diabetic retinopathy occurs after many years of established diabetes and is defined by the development of neovascularization (new, abnormal growth of vessels in the retina). Treatment involves application of a laser beam to the periphery of the entire retina (**panretinal photocoagulation**). Surgical or medical vitrectomy is used in some cases. Medical therapy for proliferative diabetic retinopathy is investigational but is used in some circumstances. The most promising are the vascular endothelial growth factor (VEGF) inhibitors (bevacizumab, ranibizumab, pegaptanib).

Focal laser treatment is common for nonproliferative (background) retinopathy when macular edema is present; the laser is applied only to the affected area. In severe cases, panretinal photocoagulation may be used. Otherwise, nonproliferative retinopathy is treated supportively—primarily with tight control of blood glucose and follow-up eye examinations to watch for development of macular edema or neovascularization.

19. Distinguish between preorbital (preseptal) and orbital cellulitis.

Both conditions may present with swollen lids; fever; a history of facial laceration, trauma, insect bite, or sinusitis; and chemosis (edema of the conjunctiva). However, if ophthalmoplegia, proptosis, severe eye pain, or decreased visual acuity is present, the patient has orbital cellulitis (Fig. 27-1; Plate 63). Orbital cellulitis is an ophthalmologic emergency because it may extend into the skull, causing meningitis, venous thrombosis, and/or blindness.

20. What are the common bacterial causes of preorbital and orbital cellulitis? How are they treated?

The most common pathogens in both cases are *Streptococcus pneumoniae, Haemophilus influenzae* type b, and *Staphylococcus aureus* or streptococcal species (in patients with a history of trauma). Treat either condition by obtaining blood cultures and administering broad-spectrum antibiotics until culture results are known. A typical regimen for preorbital cellulitis is monotherapy with clindamycin or combination therapy with trimethoprim-sulfamethoxazole plus either amoxicillin or amoxicillin-clavulanic acid or cefpodoxime or cefdinir. A typical regimen for orbital cellulitis is vancomycin plus either ceftriaxone or cefotaxime or ampicillin-sulbactam, or piperacillin-tazobactam. Although preorbital cellulitis may be treated on an outpatient basis with close follow-up, orbital cellulitis requires hospital admission and intravenous antibiotics.

21. What is the key to managing chemical burns to the eye? Which is worse, acid or alkaline burns?

With chemical burns to the eye (acid or alkaline), the key to management is copious irrigation with the closest source of water. The longer you wait, the worse the prognosis. Do not wait to get additional history. Alkali burns have a worse prognosis because they tend to penetrate more deeply into the eye.

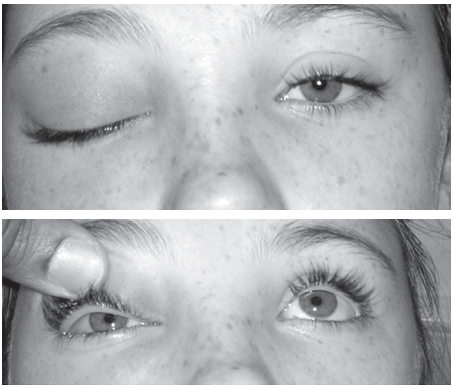

Figure 27-1. A 12-year-old boy with orbital cellulitis. Note the poor elevation of the affected eye. See Plate 63. (From Hoyt CS, Taylor D. Pediatric ophthalmology and strabismus. 4th ed., Philadelphia: Saunders, 2012, Fig. 13.10Ai, Aii.)

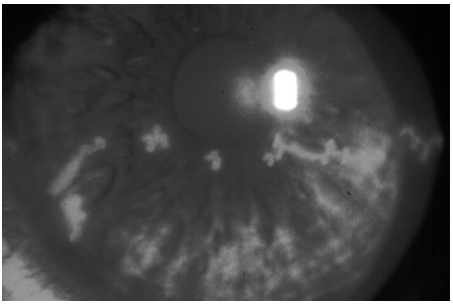

Figure 27-2. Varicella dendritic keratitis. Numerous dendrites are seen in this slit lamp photograph with fluorescein staining of the dendritic lesions from active viral growth in the corneal epithelium. See Plate 64. (From Krachmer JH, Mannis MJ. Cornea. 3rd ed., St. Louis: Mosby, 2010, Fig. 80.2.)

22. Distinguish between a hordeolum (stye) and a chalazion. How are they treated?

A hordeolum is a painful red lump near the lid margin. A chalazion is a painless lump away from the lid margin. Treat both with warm compresses. For chalazion, use intralesional steroid injection or incision and drainage if warm compresses do not work.

23. How do you recognize and treat herpes simplex keratitis?

Herpes simplex keratitis usually begins with conjunctivitis and vesicular lid eruption, then progresses to the classic dendritic keratitis (seen with fluorescein stain; Fig. 27-2; Plate 64). Treat with topical antivirals (e.g., idoxuridine, trifluridine). Corticosteroids are generally contraindicated with dendritic keratitis because they may make the condition worse.

24. What findings suggest an ophthalmic herpes zoster infection?

Ophthalmic herpes zoster infection should be suspected in patients with involvement of the tip of the nose (Hutchinson sign) and/or medial eyelid, a typical zoster dermatomal skin rash, and eye complaints. Treat with oral acyclovir. Complications include uveitis, keratitis, and glaucoma.

25. How do you recognize a central retinal artery occlusion? What causes it?

Central retinal artery occlusion presents with sudden (within a few minutes), painless, unilateral loss of vision. The classic funduscopic appearance includes a pale, opaque fundus with a cherry red spot in the fovea (center) of the macula. No satisfactory treatment is available. The most common cause is emboli (from carotid plaque or heart), but watch for temporal arteritis as a cause on the Step 2 examination.

26. Describe the symptoms of temporal arteritis. What should you do if you suspect it?

Temporal arteritis is a vasculitis seen in older adults. Symptoms include jaw claudication, loss of vision (caused by central retinal artery occlusion), tortuous temporal artery (as seen or palpated on examination), markedly elevated erythrocyte sedimentation rate, and coexisting **polymyalgia rheumatica** (in 50%; causes proximal muscle pain and stiffness). If temporal arteritis is suspected in the setting of vision complaints, administer corticosteroids immediately before confirming the diagnosis with a temporal artery biopsy. Withholding treatment until a formal diagnosis can be made may cause the patient to lose vision in the other eye.

27. How do you recognize central retinal vein occlusion? Describe the cause and treatment.

Central retinal vein occlusion also presents with sudden (within a few hours), painless, unilateral loss of vision. The classic funduscopic appearance includes distended, tortuous retinal veins, retinal hemorrhages, and a congested, edematous fundus. No satisfactory treatment is available. The most common causes are hypertension, diabetes, glaucoma, and increased blood viscosity (e.g., leukemia). Complications are related to neovascularization, which commonly develops and leads to vision loss and glaucoma.

28. Describe the classic history of a patient with retinal detachment.

The classic history of a patient with retinal detachment includes a sudden (instant), painless, unilateral loss of vision with "floaters" (little black spots that are seen no matter where the patient looks), and flashes of light. It is sometimes described as a curtain or veil coming down in front of the eye. This history should prompt immediate referral to an ophthalmologist. Surgery may save the patient's vision by reattaching the retina.

29. True or false: Cataracts and macular degeneration are common causes of bilateral, painless loss of vision in older adults.

True. Although one side may be worse than the other, bilateral complaints are not uncommon. The red reflex typically becomes black with a significant cataract. Those with macular degeneration typically have focal yellow-white deposits called **drusen** in and around the macula on funduscopic examination. Treat cataracts with surgery; most cases (90%) of macular degeneration are the "dry" or nonexudative subtype, which is treated supportively (e.g., magnification aids). "Wet" or exudative macular degeneration is treated with intravitreal vascular endothelial growth factor (VEGF) inhibitors, thermal laser photocoagulation in selected patients, and photodynamic therapy.

30. How do optic neuritis and papillitis present? What are the common causes?

Optic neuritis and papillitis typically present with a fairly quick (over hours to days), painful, unilateral or bilateral loss of vision. The optic disc margins may appear blurred on funduscopic examination with papillitis, just as in papilledema.

Multiple sclerosis (which can also cause internuclear ophthalmoplegia) is a very common cause of optic neuritis, especially in 20- to 40-year-old women. Lyme disease, malignancy, and syphilis are other causes.

31. What causes bitemporal hemianopsia until proven otherwise?

A pituitary tumor (or other neoplasm) pressing on the optic chiasm.

32. Use the visual field defect to localize the sight of the brain lesion (Fig. 27-3).

VISUAL FIELD DEFECT	LOCATION OF LESION
Right anopsia (monocular blindness)	Right optic nerve
Bitemporal hemianopsia	Optic chiasm
Left homonymous hemianopsia	Right optic tract
Left upper quadrant anopsia	Right optic radiations in the right temporal lobe
Left lower quadrant anopsia	Right optic radiations in the right parietal lobe
Left homonymous hemianopsia with macular sparing	Right occipital lobe (from posterior cerebral artery occlusion)

33. What two diseases commonly cause isolated palsies of cranial nerves III, IV, and VI? How do you recognize them?

Isolated palsies of cranial nerve III, IV, and VI usually are caused by vascular complications from diabetes mellitus and hypertension. Symptoms generally resolve on their own within 2 months. In patients older than age 40 years with a history of diabetes or hypertension and no other neurologic deficits or pain, observation is generally all that is required because hypertension and/or diabetes is the most likely cause. If resolution does not occur within 8 weeks, the patient is younger than age 40 years, neither hypertension nor diabetes is present, or the patient starts to develop pain or other neurologic deficits, order a magnetic resonance imaging (MRI) scan of the head to rule out tumor or aneurysm (i.e., benign cause less likely).

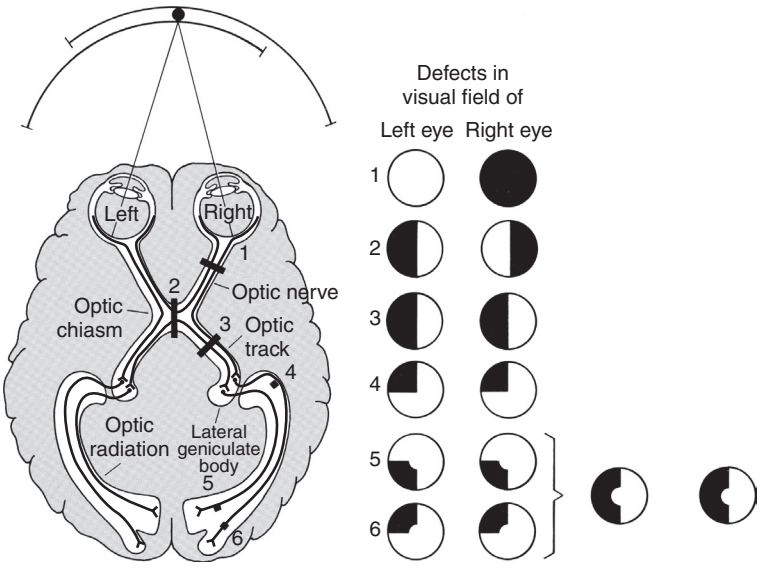

Figure 27-3. Visual field defects produced by lesions at various levels of the visual pathway. 1, Right optic nerve; 2, optic chiasm; 3, optic tract; 4, Meyer loop; 5, cuneus; 6, lingual gyrus; *bracket*, occipital lobe (with macular sparing). (From Berne R. Physiology. 5th ed. Philadelphia: Mosby, 2003, Fig. 8-10.)

34. What are the physical exam findings of a third cranial nerve palsy? What should you remember when trying to determine the cause?

With an oculomotor (cranial nerve III) lesion, the eye is down and out, and the patient can move the eye only laterally. If a third cranial nerve palsy is a result of benign vascular causes (i.e., hypertension, diabetes), the pupil is normal, and close observation is all that is needed because the condition typically resolves on its own in several weeks. A "blown" (dilated, nonreactive) pupil is a medical emergency. The most likely cause is an aneurysm or tumor. Order an MRI scan and/or a cerebral angiogram.

35. What are the physical findings in palsies of cranial nerves IV and VI? How do lesions of cranial nerves V and VII affect the eye?

With a trochlear (cranial nerve IV) lesion, the affected eye cannot look down when the gaze is medial because of superior oblique muscle paralysis. With an abducens (cranial nerve VI) lesion, the patient cannot look laterally with the affected eye because of lateral rectus muscle paralysis. Cranial nerves V (afferent, sensory limb) and VII (efferent, motor limb) are involved in the corneal blink reflex. Lesions can produce corneal drying, which can be treated with saline eye drops.

36. What is strabismus? Beyond what age is it abnormal in children?

Strabismus is the medical term for a "lazy eye." The affected eye deviates, most commonly inward. Strabismus is normal only if intermittent and during the first 3 months of life. When strabismus is constant or persistent beyond 3 months, it requires ophthalmologic referral to prevent blindness (known as amblyopia) in the affected eye.

37. Why does blindness develop in patients with strabismus?

The visual system is still developing until the age of 7 or 8 years. For this reason, visual screening of both eyes is important in children. If one eye does not see well or is turned outward, the brain cannot fuse the two different images that it sees. Thus, it suppresses the "bad" eye, which does not develop the proper neural connections. This eye will never see well and cannot be corrected with glasses because the problem is neural rather than refractive. This problem is treatable with special glasses or surgery if it is caught in time; the goal of treatment is to allow normal neural connections (and thus vision) to develop.

38. What is presbyopia? When does it occur?

Presbyopia occurs between the ages of 40 and 50 years, when the lens loses its ability to accommodate. Patients then need bifocals or reading glasses for near vision. Presbyopia is a normal part of aging.

ORTHOPEDIC SURGERY

1. What orthopedic fractures are associated with the highest mortality rate?

Pelvic fractures because patients can bleed to death. If the patient's condition is unstable, consider heroic measures such as military antishock trousers (MAST trousers) and an external fixator.

2. Why should areas distal to the fracture site be assessed by physical examination?

Areas distal to the fracture site should be assessed for neurologic and vascular compromise, either of which may be an emergency.

3. Distinguish between an open and a closed fracture.

With an open (compound) fracture, the skin is broken over the fracture site. In closed fractures, the skin is intact over the fracture site.

4. Explain the difference in management of open and closed fractures.

With closed fractures, closed reduction and casting generally can be done. With open fractures, you should give antibiotics with coverage for gram-positive and gram-negative organisms (cefuroxime is appropriate; fluoroquinolones are an alternative). If the patient is at risk for methicillin-resistant *Staphylococcus aureus* (MRSA) infection, add vancomycin. Do surgical debridement, give a tetanus vaccine booster, lavage fresh wounds (if less than 8 hours old), and perform **open reduction and internal fixation** (ORIF). The main risk in open fractures is infection, which usually is not a problem with closed fractures because the skin is intact.

5. What are the indications for open reduction other than an open fracture?

- Intraarticular fractures or articular surface malalignment
- Nonunion or failed closed reduction
- Compromise of blood supply
- Multiple trauma (to allow mobilization at the earliest possible point)
- Need for perfect reduction to optimize extremity function (e.g., professional athletes)

6. What type of radiographs should you order if you suspect a fracture?

For any suspected fracture, order two views (usually anteroposterior and lateral) of the site, and consider radiographs of the joints above and below the fracture site.

7. How should you treat a patient with severe pain after trauma and negative x-rays?

Treat the patient conservatively. Assume that there is a fracture and have the patient rest the injured area. Splinting may be appropriate for distal extremity injuries. Obtain follow-up radiographs 7 to 14 days after the injury if symptoms persist; many occult fractures become visible at that time. The exception to waiting is a suspected hip fracture in an older adult—proceed to computed tomography (CT) or magnetic resonance imaging (MRI) of the hip to allow earlier diagnosis and treatment (Fig. 28-1), which decrease operative morbidity and length of hospital stay compared with delayed diagnosis and treatment.

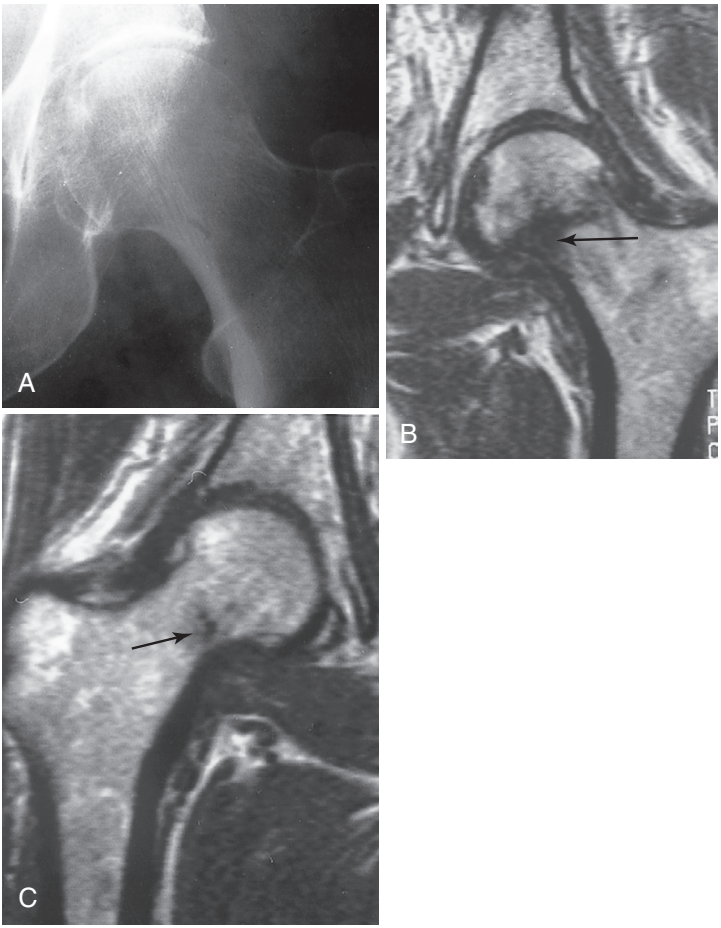

Figure 28-1. Imaging of occult hip fracture. **A,** Anteroposterior radiograph of the left hip demonstrates no evidence of fracture. **B,** Coronal T1-weighted magnetic resonance imaging (MRI) clearly shows a well-demarcated line of decreased signal in the subcapital region of the left femoral neck consistent with a nondisplaced fracture *(arrow).* **C,** MRI of the right hip shows a subtle medial femoral neck fracture *(arrow)* not demonstrated on the conventional radiograph. (From Adam A, et al. Grainger & Allison's diagnostic radiology. 5th ed. Edinburgh: Churchill Livingstone, 2008, Fig. 46-73.)

8. Define compartment syndrome. What is the cause?

Compartment syndrome is a problem of muscle compartments, which are limited by the fascia in which they are contained. It is seen in the extremities (most commonly in the calf) when edema or hemorrhage causes swelling inside a muscle compartment. Rising pressure inside the fascial compartment can result in permanent nerve damage and muscle necrosis.

The three common clinical scenarios in which compartment syndrome is seen are fractures (classically midshaft tibial fractures or supracondylar fractures of the humerus in children), burns (especially electrical and circumferential burns), and vascular compromise (or after vascular surgery procedures).

9. What are the symptoms and signs of compartment syndrome? How is it treated?

- Pain (especially pain on passive movement out of proportion to the injury)
- Paresthesias, hypesthesia, and numbness (decreased sensation and two-point discrimination)
- Cyanosis or pallor
- Firm-feeling muscle compartment
- Paralysis (late, ominous sign)
- Elevated compartment pressure (>30-40 mm Hg)

On the USMLE, the diagnosis of compartment syndrome often has to be made clinically without a pressure reading. Although pulses may be slightly decreased, they usually are palpable (or detectable with Doppler ultrasound) with compartment syndrome. Lack of palpable pulses is an ominous, late sign. Compartment syndrome is an emergency, and quick action can save an otherwise doomed limb. Treatment is immediate fasciotomy; incising the fascial compartment relieves the pressure.

10. Cover the right-hand columns of the following table and specify the motor and sensory functions of the following peripheral nerves. In what common clinical scenarios are they often damaged?

NERVE	MOTOR FUNCTION	SENSORY FUNCTION	CLINICAL SCENARIO
Radial	Wrist extension (watch for wrist drop)	Back of forearm, back of hand (first 3 digits)	Humeral fracture
Ulnar	Finger abduction (watch for "claw hand")	Front and back of last 2 digits	Elbow dislocation or fracture
Median	Pronation, thumb opposition	Palmar surface of hand (first 3 digits)	Carpal tunnel syndrome, humeral fracture
Axillary	Abduction, lateral rotation	Lateral shoulder	Upper humeral dislocation or fracture
Peroneal	Dorsiflexion, eversion (watch for foot drop)	Dorsal foot and lateral leg	Knee dislocation, fibula fracture

11. What is the difference between insufficiency stress fracture and fatigue stress fracture? How are stress fractures diagnosed and treated?

A stress fracture (Fig. 28-2) is an incomplete or small fracture that develops because of repeated or prolonged forces against the bone. In fatigue fractures, abnormal stresses are applied to normal bones (e.g., overuse injury, as in military recruits or marathon runners). In insufficiency fractures, normal/physiologic stresses are applied to an abnormal bone (e.g., osteoporotic bone). Diagnosis is made using x-rays; MRI or nuclear medicine scan may be used if x-rays are negative but strong clinical suspicion remains. The treatment is rest to allow healing and to prevent progression to a complete fracture. In the setting of insufficiency fractures, treatment of osteoporosis (e.g., alendronate, calcium, vitamin D) is also needed to help prevent future fractures.

12. What fracture usually is diagnosed in trauma patients with pain in the anatomic snuffbox?

Scaphoid bone fracture (Fig. 28-3), classically after a fall onto an outstretched hand. X-rays may not show a fracture initially, so if the patient has a fall onto an outstretched hand and has pain in the anatomic snuffbox, treat these injuries as a fracture. Repeat x-rays can be performed 1 to 2 weeks later.

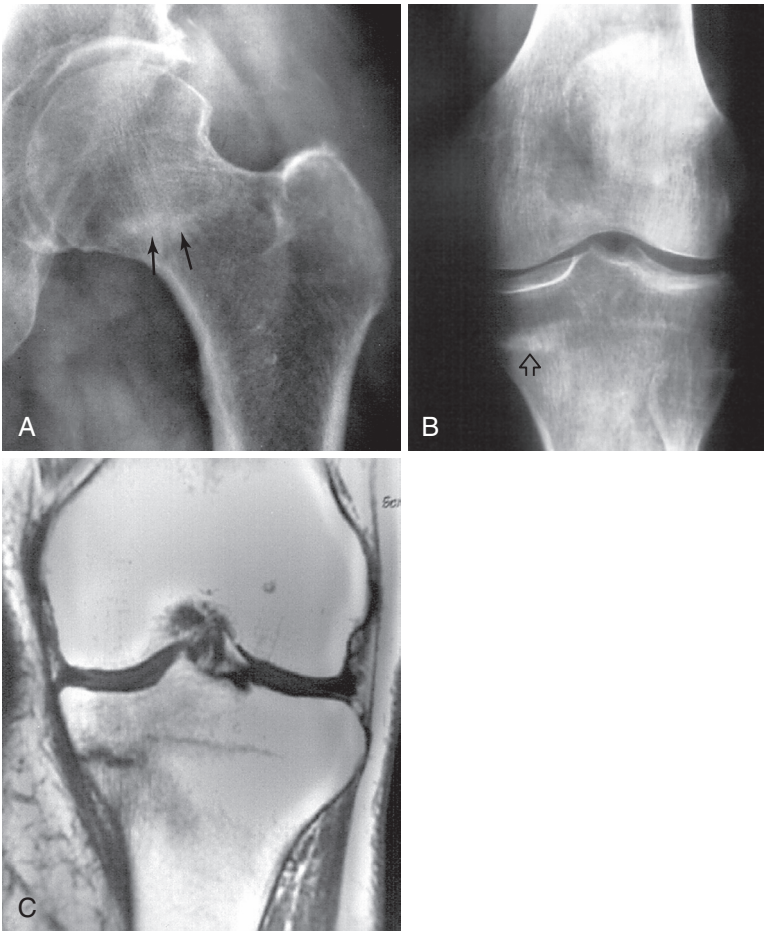

Figure 28-2. A, Stress fracture involving cancellous bone of the subcapital region of the femoral neck has the appearance of a band of sclerosis *(arrows).* **B,** A more subtle stress fracture at the medial tibial plateau *(open arrow).* **C,** Magnetic resonance imaging (MRI) was ordered to confirm the fracture, clearly showing the low signal fracture line. (From Katz DS, Math KR, Groskin SA, eds. Radiology secrets. Philadelphia: Hanley & Belfus, 1998, p. 438, with permission.)

13. What are the most common locations of intervertebral disc herniations? What symptoms do they cause?

Lumbar disc herniation is a common, often correctable cause of low back pain. The most common location is the L5-S1 disc, which affects the S1 nerve root. Look for decreased ankle jerk, weakness of plantar flexors in the foot, pain from the midgluteal area to the posterior calf, and a positive straight leg-raise test. The second most common location for herniation is the L4-L5 disc, which affects the L5 nerve root. Look for decreased biceps femoris reflex, weakness of foot extensors, and pain in the hip or groin.

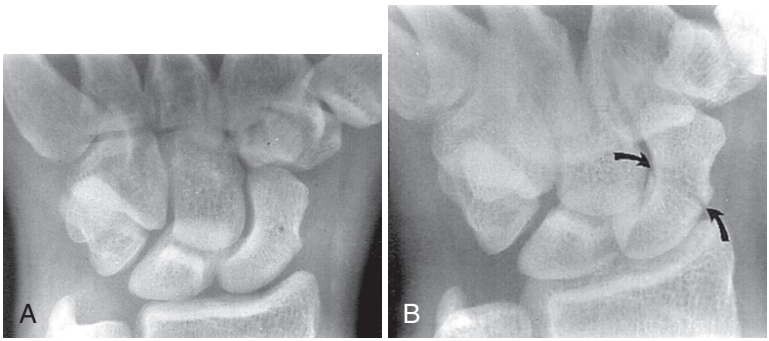

Figure 28-3. Delayed study showing occult scaphoid fracture. **A,** Patient with snuffbox tenderness presents with normal radiograph of the wrist. **B,** A film obtained 10 days later clearly shows the fracture line at the mid-waist of the scaphoid *(curved arrows).* (From Katz DS, Math KR, Groskin SA, eds. Radiology secrets. Philadelphia: Hanley & Belfus, 1998, p. 436, with permission.)

After the lumbar area, the second most common location is the cervical spine. The classic symptom of cervical disc disease is neck pain. Herniation is most common at the C6-C7 disc, which affects the C7 nerve root. Look for decreased triceps reflex/strength and weakness of forearm extension.

14. How is intervertebral disc herniation diagnosed and treated?

Diagnosis is made with MRI scan (preferred) or by CT scan or myelography. Conservative treatment, including bed rest and analgesics, usually is attempted first because roughly 90% of cases resolve with conservative management. Epidural steroid injection may help. Surgery (discectomy) may be required if conservative treatment fails or significant neurologic deficit is present (to prevent permanent nerve damage).

15. Define Charcot joint. What causes it? How is it managed?

Charcot joints (neuropathic joints) are seen in patients with diabetes mellitus or other conditions causing peripheral neuropathy (e.g., tertiary syphilis). Lack of proprioception causes gradual arthritis or arthropathy and joint deformity. Patients should get radiographs for any (even minor) trauma because they may not feel even a severe fracture.

16. What is the most common bacterial cause of osteomyelitis? In what clinical scenarios should you think of other causes?

Osteomyelitis is caused most commonly by *Staphylococcus aureus.* Think of gram-negative bacteria in immunocompromised patients or intravenous drug abusers. *Salmonella* species is the most likely cause in patients with sickle cell disease. Think *Pseudomonas aeruginosa* if there is a puncture wound through a tennis shoe. Diabetic patients who develop a "diabetic foot" with subsequent osteomyelitis usually have a polymicrobial infection. Aspirate and biopsy the affected joint or bone, and order a Gram stain, culture, and cell count of the fluid or tissue if osteomyelitis is suspected. Check a serum ESR or C-reactive protein.

17. Which bacteria are the most common cause of septic arthritis? In what scenario should you think of another cause?

Septic arthritis is most commonly caused by *Staphylococcus aureus,* but in sexually active adults (especially when young and/or promiscuous), suspect *Neisseria gonorrhoeae.* Aspirate the joint and order a Gram stain, culture, and cell count with differential if infection is suspected.

18. What is reflex sympathetic dystrophy (RSD)? How do patients present?

RSD is a poorly understood disorder that generally occurs in an extremity and is characterized by pain, swelling, and signs of autonomic dysfunction (vasomotor instability with alternating warmth and coolness and/or sweating and dryness of the area). In most (but not all) cases it is posttraumatic in origin. The associated trauma is classically mild, and symptoms may begin days or several weeks after the injury. Patients classically have severe, intermittent pain, often described as burning, with associated temperature changes and sweating during episodes. A minor stimulus (e.g., light touch) may trigger severe pain symptoms. The diagnosis can be confirmed with radiographs or nuclear medicine scan. A presumptive diagnosis is often made in the appropriate setting if a sympathetic nerve block (i.e., injection of local anesthetic into the involved nerve) relieves symptoms. This procedure can be repeated as part of therapy if it is initially successful.

19. True or false: There is a high incidence of vascular injury with posterior knee dislocations.

True. Order an angiogram if pulses are asymmetric (i.e., weaker or absent on the affected side) to check for injury.

20. What is the most common type of bone tumor?

Metastatic (especially from breast, lung, or prostate cancer).

21. What is a pathologic fracture? What is the most common cause of a pathologic fracture?

A pathologic fracture is one that occurs in bone previously weakened by another disease. Osteoporosis (especially in elderly, thin women) is the most common cause, but you should always think about the possibility of malignancy.

22. To what site is pain from hip inflammation or dislocation/fracture classically referred?

The knee (especially in children).

23. Specify age at presentation, epidemiology, symptoms and signs, and treatment for the three classically tested pediatric hip disorders.

NAME	AGE	EPIDEMIOLOGY	SYMPTOMS/SIGNS	TREATMENT
CHD	At birth	Female, first-borns, breech delivery	Barlow and Ortolani signs	Observation, abduction splint, or open or closed reduction
LCPD	4-10 yr	Short male with delayed bone age	Knee, thigh, groin pain, limp	Orthoses
SCFE	9-13 yr	Overweight male adolescent	Knee, thigh, groin pain, limp	Surgical pinning

CHD, Congenital hip dysplasia; *LCPD*, Legg-Calvé-Perthes disease; *SCFE*, slipped capital femoral epiphysis.
Note: All of these conditions may present in an adult as arthritis of the hip.

24. If you forget everything else about differentiating the three pediatric hip disorders, what historical point will help you the most on the USMLE?

Age at onset of symptoms.

25. Define Osgood-Schlatter disease. How is it recognized and treated?

Osgood-Schlatter disease is osteochondritis of the tibial tubercle. It is often bilateral and usually presents in boys between 10 and 15 years of age. Symptoms and signs include pain, swelling, and tenderness in the knee (remember, the pediatric hip problems above have referred pain in the knee, but no knee swelling or tenderness upon palpation of the knee). Treat with rest, activity restriction, and nonsteroidal antiinflammatory drugs (NSAIDs). Most cases resolve on their own.

26. How do you check for scoliosis? Who is usually affected? What is the treatment?

Check for scoliosis by having patients touch their toes while you look at the spine. If scoliosis is present, you will see an abnormal lateral curvature of the spine. Scoliosis usually affects prepubertal girls and is idiopathic. Treat with a brace for anything other than very minor (less than 15 degrees) curvature. If the deformity is severe (e.g., respiratory compromise, rapid progression), surgery should be considered.

27. What are the common findings with ligament injuries of the knee? How do you distinguish injuries of the anterior cruciate, posterior cruciate, medial collateral, and lateral collateral ligaments on physical examination?

Ligament injuries in the knee commonly cause pain, joint effusions, instability of the joint, and history of the joint *popping, buckling,* or *locking up.*

- **Anterior cruciate ligament (ACL)** tears are the most common. Watch for the *anterior* drawer test. The knee is placed in 90 degrees of flexion and pulled forward (like opening a drawer). If the tibia pulls forward more than normal (e.g., more than the unaffected side), the test is positive, and the patient has an ACL tear.
- **Posterior cruciate ligament (PCL)** tears can be diagnosed with the *posterior* drawer test. Push the tibia back with the knee in 90 degrees of flexion. If the tibia pushes back more than normal, the test is positive and a PCL tear is present.
- **Medial collateral ligament (MCL)** tears are suggested during the *abduction* or *valgus* stress test. With the knee in 30 degrees of flexion, abduct the ankle while holding the knee. If the knee joint abducts to an abnormal degree, the test is positive and a medial compartment injury is present.
- **Lateral collateral ligament (LCL)** tears are suggested during the *adduction* or *varus* stress test. Adduct the ankle while holding the knee. If the knee joint adducts to an abnormal degree, the test is positive, and a lateral compartment injury is present.

MRI (Fig. 28-4) and/or arthroscopy can be used to confirm suspected tears and look for other injuries.

28. What are the risk factors for avascular necrosis (AVN)? What is the best test to make the diagnosis?

Avascular necrosis describes local intravascular coagulation with subsequent bone ischemia and necrosis of cancellous bone and marrow. Patients have pain in the affected area. There are many potential causes/associations, including:

- Trauma (usually in the setting of a fracture).
- Corticosteroid excess (endogenous or iatrogenic).
- Sickle cell disease or other hemoglobinopathy.
- Alcohol abuse.
- Lupus and other connective tissue disorders.
- Decompression sickness.
- Slipped capital femoral epiphysis.
- Pancreatitis.

The best test to make the diagnosis is MRI (Fig. 28-5), which becomes positive before regular x-rays.

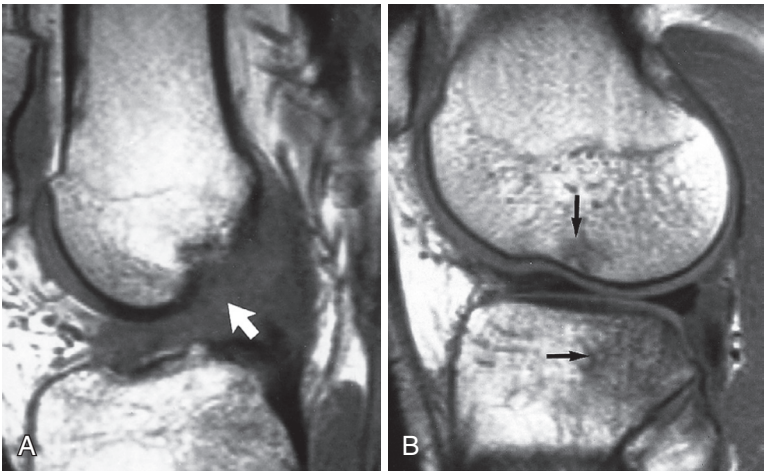

Figure 28-4. Magnetic resonance imaging (MRI) appearance of acute ACL rupture. **A,** Sagittal T1-weighted MRI of the knee demonstrates a mass of intermediate amorphous signal in the expected location of the anterior cruciate ligament (ACL) *(arrow)*, consistent with a complete tear of the ACL. **B,** Further laterally, low signal in the posterior tibia and lateral femoral condyle represents typical contusions seen in association with ACL injury *(small arrows)*. (From Adam A, et al. Grainger & Allison's diagnostic radiology. 5th ed. Edinburgh: Churchill Livingstone, 2008, Fig. 46-81.)

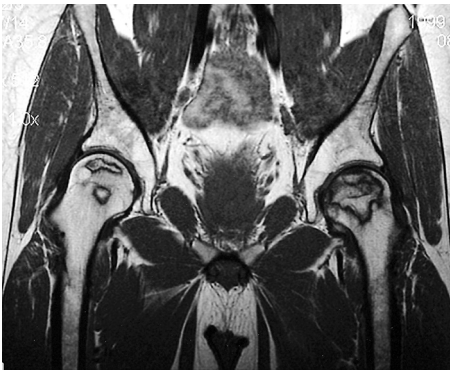

Figure 28-5. Avascular necrosis (AVN) of the hip. Coronal T1-weighted magnetic resonance image (MRI) through both hips confirms the presence of geographic areas of abnormality in both femoral heads which are well demarcated from the adjacent normal bone by a thin rim of low signal material. (From Adam A, et al. Grainger & Allison's diagnostic radiology. 5th ed. Edinburgh: Churchill Livingstone, 2008, Fig. 50-21.)

PEDIATRICS

1. Give the average ages at which the following commonly tested milestones are achieved.

MILESTONE	AGE*
Social smile	1-2 mo
Cooing	2-4 mo
While prone, lifts head up 90°	3-4 mo
Rolls front to back	4-5 mo
Voluntary grasp (no release)	5 mo
Stranger anxiety	6-9 mo
Sits with no support	7 mo
Pulls to stand	9 mo
Waves "bye-bye'"	10 mo
Voluntary grasp with voluntary release	10 mo
Plays pat-a-cake	9-10 mo
First words	9-12 mo
Imitates others' sounds	9-12 mo
Separation anxiety	12-15 mo
Walks without help	13 mo
Can build tower of 2 cubes	13-15 mo
Understands 1-step commands (no gesture)	15 mo
Good use of cup and spoon	15-18 mo
Can build tower of 6 cubes	2 yr
Runs well	2 yr
Ties shoelaces	5 yr

*Reduce the age of premature infants in the first 2 years for assessing development. For example, for children born after 6 months of gestation, subtract 3 months from their chronologic age. Therefore, they should be expected to perform only at the 6-month-old level when they are 9 months old.

2. True or false: The overall pattern of development is more important than the age at which individual milestones are reached.

True. The exact age is not as important as the overall pattern in looking for dysfunctional development. When in doubt, use a formal developmental test.

3. What screening and preventive care measures should be done at every pediatric visit?

Height, weight, blood pressure, developmental/behavioral assessment, and anticipatory guidance (counseling/discussion about age-appropriate concerns) should be done at every pediatric visit.

4. True or false: Screening and preventive care are important mainly during a well checkup.

False. Screening and preventive care are an important part of every encounter with a patient (adult or child). USMLE questions may try to fool you on this point. For example, a mother complains that her 4-year-old child sleeps 11 hours every night. This is normal behavior. The answer to the question, "What should you do next?" may be to give an objective hearing examination, which is a routine screening procedure in a 4-year-old child.

5. What are the commonly performed screening tests for metabolic and congenital disorders?

States vary widely in their policies regarding newborn screening. All states screen for hypothyroidism and phenylketonuria at birth; screens must be done within the first month of life. Most states screen for galactosemia and hemoglobinopathies such as sickle cell disease. Some states include screening for homocystinuria, maple syrup urine disease, congenital adrenal hyperplasia, cystic fibrosis, biotinidase deficiency, tyrosinemia, and toxoplasmosis. If any of these screens are positive, the first step is to order a confirmatory test to make sure that the screening test gave a true-positive result.

6. What are the frequently tested items under the umbrella of primary prevention using "anticipatory guidance"?

Tell parents the following:

- Keep the water heater under 110°F to 120°F.
- Use proper car restraints (e.g., child safety seat, booster seat).
- Put the infant to sleep on his or her side or back to help prevent sudden infant death syndrome (SIDS), the most common cause of death in children aged 1 to 12 months.
- Do not use infant walkers because they cause injuries.
- Watch out for small objects, which may be aspirated.
- Do not give honey before 1 year of age.
- Do not give cow's milk before 1 year of age.
- Introduce solid foods gradually, starting at 6 months of age.
- Supervise children in bathtubs and swimming pools.

7. How often should height, weight, and head circumference be measured? What do they signify?

Head circumference should be measured at every visit in the first 2 years; height and weight should be measured routinely until adulthood. All three parameters are markers of general well-being; abnormal values may suggest disease.

8. What if a child has low height, weight, or head circumference compared with peers?

The pattern of growth along plotted growth curves over time (which you may be asked to interpret) tells you more than any single measurement. If a child has always been low or high compared with peers, generally the pattern is benign. A patient who goes from a normal to an abnormal curve is much more worrisome. Parents commonly bring in a child with delayed physical growth or delayed puberty. You need to know when to reassure and when to do further testing and questioning.

9. Define failure to thrive. What causes it?

There is no consensus definition for failure to thrive, but commonly used definitions include a head circumference, height, or weight less than the fifth percentile for age; a weight less than 80% of ideal weight for age; or a weight gain that causes a decrease in two or more major percentage lines on the growth curve. Failure to thrive is most commonly a result of psychosocial or functional problems. Watch for signs of neglect and child abuse. Organic causes usually have specific clues to trigger your suspicion.

10. What conditions are suggested by obesity in children?

Obesity usually is caused by overeating and too little activity (>95% of cases). Less than 5% of cases are a result of organic causes (e.g., Cushing syndrome, Prader-Willi syndrome).

11. What conditions should you consider in a child with an abnormal head circumference?

Increased head circumference may mean hydrocephalus or tumor, whereas decreased head circumference may mean microcephaly (e.g., from congenital TORCH infection). Again, the pattern of head circumference over time (plotted on a growth curve) is most helpful in defining pathology.

12. How are hearing and vision screened?

Hearing and vision should be measured objectively at least once by 4 years of age. After the initial screen, measure every few years until adulthood or more often if the history so dictates.

13. In what situations should you worry about hearing loss?

- After a bout of meningitis (hearing loss is the most common neurologic complication)
- With congenital toxoplasmosis, other (e.g., syphilis, HIV), rubella, cytomegalovirus, herpes simplex (TORCH) infections
- With measles or mumps
- With chronic middle ear effusions or chronic or recurrent otitis media
- With the use of ototoxic drugs (e.g., aminoglycosides)

14. What is the red reflex? What should an abnormal reflex suggest?

Check for loss of the red reflex at birth and routinely thereafter to detect congenital cataracts or ocular tumors. When a penlight is shined at the pupil, you usually see red because of the underlying fundus. If a cataract (or tumor) is present in the eye, the red reflex disappears and you see white (known as leukocoria and classically caused by retinoblastoma; Fig. 29-1; Plate 65).

15. True or false: Before a certain age, intermittent strabismus is normal.

True. It is normal for infants to have occasional ocular misalignment (strabismus) until 3 months of age. After 3 months (or with constant eye deviation), strabismus should be evaluated and managed by an ophthalmologist to prevent possible blindness in the affected eye.

16. How is screening for anemia done?

Recommendations of routine screening for anemia (with a complete blood count or hemoglobin/hematocrit) vary and are changing. Hemoglobin or hematocrit measurement is recommended at 12 months of age, but may be required at other times as dictated by history and risk assessment. Recommendations for screening during adolescence vary, but adolescents should be screened at least once. If any risk factors for iron deficiency are present during infancy (prematurity, low birth weight, ingestion of cow's milk before 1 year of age, low dietary intake, low socioeconomic status), screen with a complete blood count or hemoglobin and hematocrit if given the option.

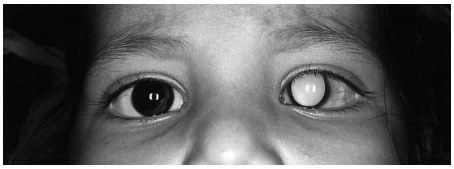

Figure 29-1. Leukocoria (white pupillary reflex) is the most common presenting feature of retinoblastoma and may be first noticed in family photographs. See Plate 65. (From Kanski JJ. Clinical diagnosis in ophthalmology. 1st ed. Philadelphia: Mosby, 2006, Fig. 9.94. Courtesy of U. Raina.)

17. True or false: All children should be given prophylactic iron supplements.

False. Exclusively breastfed infants do not require supplementation. All other children should receive supplementation. Start iron supplements in full-term infants at 4 to 6 months of age and in preterm infants at 2 months of age. Most infant formulas and cereals contain iron, thus separate supplements are usually not required.

18. How and when do you screen for lead exposure?

Screening for lead toxicity is controversial. Routine screening is no longer recommended. However, all Medicaid-eligible children must be screened. Consider screening high-risk children (those who live in old buildings, have a sibling or playmate with lead toxicity, eat paint chips, live near a battery recycling plant, or have a parent who works at a battery recycling plant). Screen for lead exposure by doing a serum lead level. If the initial lead level is abnormally high, closer follow-up and intervention are needed. The best first step is to stop the exposure.

19. True or false: Most children need fluoride supplementation.

False. Because most water is fluoridated, supplementation is not needed. However, if a child lives in an area where the water is inadequately fluoridated (rare) or the child is fed exclusively from premixed, ready-to-eat formulas (which use nonfluoridated water), fluoride supplements should be given.

20. True or false: Breastfed infants are more likely to require vitamin D supplements than formula-fed infants.

True. The American Academy of Pediatrics recommends that exclusively and partially breastfed infants receive vitamin D supplements shortly after birth and continue until they are weaned and consume formula or whole milk. Formula-fed infants do not require supplements in the United States because all formulas contain vitamin D supplements.

21. When should children be screened for tuberculosis?

Universal screening for tuberculosis is not recommended. There is no need to screen children who have no risk factors. Risk assessment should occur regularly until 2 years of age, then annually. Test those at high risk (family member with tuberculosis, family member with a positive tuberculosis test, a child born in a high-risk country, a child who has traveled to a high-risk country, or a child who has consumed unpasteurized milk or cheese).

22. True or false: Screening children for renal disease with a urinalysis is not recommended.

True. However, you should screen for congenital/anatomic abnormalities (e.g., vesicoureteral reflux) after a febrile urinary tract infection in children 2 months to 2 years of age by getting an ultrasound and either voiding cystourethrogram (VCUG) or radionuclide cystogram (RNC). Screening after the age of 2 years is more controversial and likely won't be a question on the USMLE.

23. True or false: Current vaccine recommendations and schedules are always provided on the USMLE.

False. However, because the timing of normal immunizations is being updated constantly, the administration schedule for common vaccines may be provided on the Step 2 examination. Higher yield information relates to special patient populations (e.g., give pneumococcal vaccine to patients with sickle cell disease or splenectomy) and vaccine contraindications (no measles-mumps-rubella or influenza vaccines for egg-allergic patients, no live vaccines for immunocompromised patients).

24. True or false: Sexually active teenaged girls need screening for chlamydial infection and gonorrhea.

True. There are high numbers of reported cases of chlamydia and gonorrhea in younger women. The Centers for Disease Control and Prevention (CDC) recommends annual screening for chlamydia for

all sexually active females aged 25 and younger. The CDC recommends screening high-risk sexually active females for gonorrhea.

25. When should you recommend that a child see a dentist for the first time?
Around 2 to 3 years of age.

26. What are the Tanner stages? When do they occur?
The Tanner stages measure the stages of puberty. Stage 1 is preadolescent, stage 5 is adult. Advancing stages are assigned for testicular and penile growth in boys and breast growth in girls. Both male and female stages also use pubic hair development. The average age of puberty (when a patient first has changes from the preadolescent stage 1) is 10.5 years in girls and 11.5 years in boys. The classic first events of puberty are testicular enlargement in boys and breast development in girls.

27. Define delayed puberty. What is the most common cause?
Delayed puberty is defined by a lack of testicular enlargement in boys by age 14 years or a lack of breast development or pubic hair in girls by age 12 years. The most common cause is constitutional delay, a normal variant. Watch for parents with a similar history of being "late bloomers." The child's growth curve consistently lags behind that of peers, but the line representing the child's growth curve is parallel to the normal growth curve. Treatment is reassurance only.

28. What are other causes for delayed puberty?
Rarely, delayed puberty is caused by primary testicular failure (Klinefelter syndrome, cryptorchidism, history of chemotherapy, gonadal dysgenesis) or ovarian failure (Turner syndrome, gonadal dysgenesis). Even more rarely, delayed puberty is caused by a hypothalamic/pituitary defect, such as Kallmann syndrome or tumor.

29. What causes precocious puberty?
Precocious puberty is usually idiopathic but may be caused by the McCune-Albright syndrome (in girls), ovarian tumors (granulosa, theca-cell, or gonadoblastoma), testicular tumors (Leydig-cell tumors), central nervous system (CNS) disease or trauma, adrenal neoplasm, or congenital adrenal hyperplasia, which causes precocious puberty only in boys and usually is caused by 21-hydroxylase deficiency.

30. True or false: If the underlying cause for precocious puberty is uncorrectable or idiopathic after diagnostic workup, patients should receive treatment.
True. Most patients are given long-acting gonadotropin-releasing hormone agonists to suppress the progression of puberty. This approach helps prevent premature epiphyseal closure with short stature.

31. How are cavernous hemangiomas treated?
Cavernous hemangiomas are benign vascular tumors that often are first noticed a few days after birth. They tend to increase in size after birth (sometimes becoming quite large) and gradually resolve within the first 2 years of life (Fig. 29-2; Plate 66). The best treatment is to do nothing but observe and follow.

32. Distinguish between caput succedaneum and cephalohematoma. How are these conditions treated?
Both conditions are noted in newborns after vaginal delivery. Caput succedaneum defines diffuse swelling or edema of the scalp that crosses the midline, is benign, and requires no further investigation or treatment. Cephalohematomas are subperiosteal hemorrhages that are sharply limited by sutures and do not cross the midline. Cephalohematomas are usually benign and self-resolving, but in rare

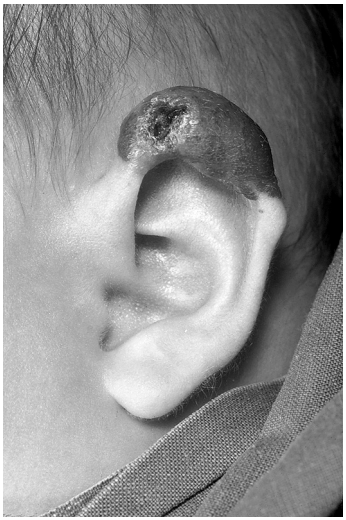

Figure 29-2. Infantile hemangioma. These lesions grow rapidly during the first few months of life once they appear (20% at birth), but they are asymptomatic unless they bleed, become infected, or obstruct a vital structure. Complete resolution is typical before the age of 7 years, and no treatment is usually required. See Plate 66. (From du Vivier A. Atlas of clinical dermatology. 3rd ed. New York: Churchill Livingstone, 2002, p. 117, with permission.)

cases they may indicate an underlying skull fracture. Order a radiograph or computed tomography (CT) scan to rule out fracture if given the option.

33. When does the anterior fontanelle usually close? What disorder should you suspect if it fails to close?

The anterior fontanelle usually is closed by 18 months of age. Delayed closure or an unusually large anterior fontanelle may indicate hypothyroidism, hydrocephalus, rickets, or intrauterine growth retardation.

34. How many vessels does a normal umbilical cord have? What disorder should you suspect if one of the vessels is absent?

The umbilical cord is checked at birth for the presence of the normal three vessels: two arteries and one vein. If only one artery is present, consider the possibility of congenital renal malformations.

35. True or false: Milky-white and possibly blood-tinged vaginal discharge is usually abnormal in the first week of life for a female newborn.

False. This discharge is usually physiologic and caused by maternal hormone withdrawal.

36. What findings should make you suspect child abuse?

- Failure to thrive
- Multiple fractures, bruises, or injuries in different stages of healing
- Metaphyseal "bucket handle" or "corner" fractures (Fig. 29-3)
- Shaken baby syndrome (retinal hemorrhages or subdural hematomas with no external signs of trauma)
- Behavioral, emotional, or interactional problems
- Sexually transmitted diseases

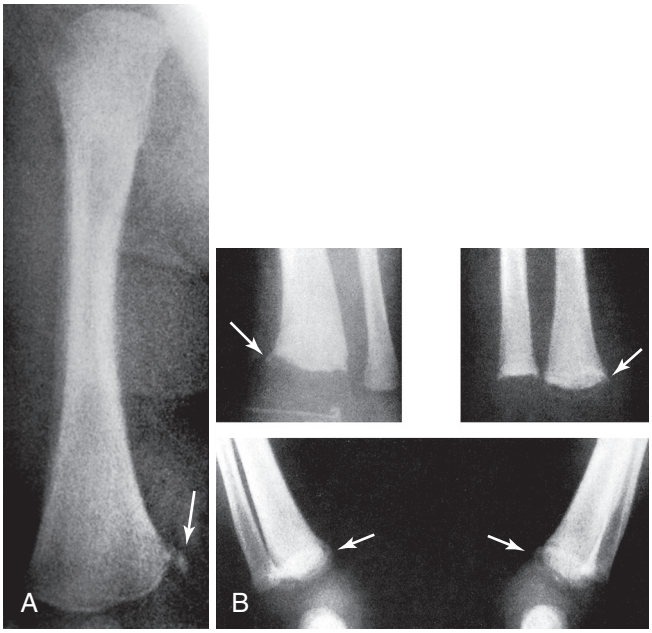

Figure 29-3. Metaphyseal fractures. Radiographs of the right femur **(A)** and both ankles **(B)** of a 2-month-old abused infant demonstrating metaphyseal corner fractures of the distal femur and both distal tibia *(arrows).* The angled tangential view reveals the "bucket handle" appearance of the fracture. (From Adam A, et al. Grainger & Allison's diagnostic radiology. 5th ed. Edinburgh: Churchill Livingstone, 2008, Fig. 68-24.)

- Multiple personality disorder (classically a result of sexual abuse)
- Whenever a parent's story does not fit the child's injury

37. True or false: You do not need proof to report child abuse.

True. In fact, reporting any suspicion of child abuse is mandatory. You do not need proof and cannot be sued for reporting your suspicion.

38. True or false: Children have the same range of normal vital signs as adults.

False. Children have lower blood pressure and higher heart and respiratory rates than adults. In addition, children often have different laboratory values. For example, a child's hemoglobin/hematocrit value is normally higher at birth and lower throughout childhood compared with an adult. Normal laboratory value ranges should be provided on the USMLE. In addition, the renal, pulmonary, hepatic, and central nervous systems are not fully mature or functional at birth.

39. What is an APGAR score? When is it measured?

The APGAR score is a general measure of well-being in newborns. It is commonly assessed at 1 and 5 minutes after birth if values are normal. If the score is less than 7, continue to assess every 5 minutes until the infant reaches a score of 7 or more (while resuscitating the child as needed). There are five categories of the APGAR score with a maximal score of 2 points per category and a possible total of 10 points. Remember the APGAR pneumonic: Appearance skin color), pulse (heart rate), grimace (reflex irritability), activity (muscle tone), and respiration (breathing).

	NUMBER OF POINTS GIVEN		
CATEGORY	**0**	**1**	**2**
Color	Pale, blue	Body pink, extremities blue	Completely pink
Heart rate	Absent	<100 beats/min	>100 beats/min
Reflex irritability*	None	Grimace	Grimace and strong cry, cough, and sneeze
Muscle tone	Limp	Some flexion of extremities	Active motion
Respiratory effort	None	Slow, weak cry	Good, strong cry

*Reflex irritability usually is measured by the infant's response to stimulation of the sole of the foot or a catheter put into the nose.

40. True or false: The APGAR score is important because it is the first assessment of how a child is doing.

False. Do not wait until the 1-minute mark to evaluate the infant. You may have to suction or intubate the infant seconds after delivery.

41. What should you always remember when a question mentions that a child was given aspirin?

Reye syndrome, which causes encephalopathy and/or liver failure. It usually occurs after aspirin is given for influenza or varicella infection. Use acetaminophen in children to avoid this rare (but often tested) condition.

42. When should the Moro and palmar grasp reflex disappear?

By 6 months of age.

PHARMACOLOGY

1. On the USMLE, bizarre, unique, and fatal side effects are tested as well as common side effects of common drugs. Cover the right-hand column and name the side effects of the listed drugs.

DRUG	SIDE EFFECT
Trazodone	Priapism
Aspirin	Gastrointestinal (GI) bleeding, hypersensitivity
Bleomycin	Pulmonary fibrosis
Cyclophosphamide	Hemorrhagic cystitis
Bupropion	Seizures
Isoniazid	Vitamin B_6 deficiency, lupus-like syndrome, liver toxicity
Cyclosporine	Renal toxicity
Penicillins	Anaphylaxis; rash with Epstein-Barr virus (EBV)
Angiotensin-converting enzyme (ACE) inhibitors	Cough, angioedema
Demeclocycline	Diabetes insipidus
Lithium	Diabetes insipidus, thyroid dysfunction
Sulfa drugs	Allergies, kernicterus in neonates
Halothane	Liver necrosis
Local anesthetic	Seizures
Phenytoin	Folate deficiency, teratogen, hirsutism
Vincristine	Peripheral neuropathy
Amiodarone	Thyroid dysfunction, pulmonary toxicity
Valproic acid	Neural tube defects in offspring
Isotretinoin	Terrible teratogen
Thioridazine	Retinal deposits, cardiac toxicity
Heparin	Thrombocytopenia, thrombosis
Vancomycin	Red man's syndrome
Clofibrate	Increased GI neoplasms
Tetracyclines	Photosensitivity, teeth staining in children
Quinolones	Teratogens (cartilage damage)
Quinine	Cinchonism (tinnitus, vertigo), thrombocytopenia, QT prolongation
Morphine	Sphincter of Oddi spasm
Clindamycin	Pseudomembranous colitis (can be caused by any broad-spectrum antibiotic)

Continued

DRUG	SIDE EFFECT
Chloramphenicol	Aplastic anemia, gray-baby syndrome
Doxorubicin	Cardiomyopathy
Busulfan	Pulmonary fibrosis
Monoamine oxidase (MAO) inhibitors	Tyramine crisis (after eating cheese or wine)
Hydralazine	Lupus-like syndrome
Procainamide	Lupus-like syndrome
Minoxidil	Hirsutism
Aminoglycoside	Hearing loss, renal toxicity
Acetaminophen	Liver toxicity (in high doses)
Chlorpropamide	Syndrome of inappropriate antidiuretic hormone (SIADH)
Oxytocin	SIADH
Opiates	SIADH
Didanosine (ddI)	Pancreatitis, peripheral neuropathy
Halogen anesthesia	Malignant hyperthermia
Succinylcholine	Malignant hyperthermia
Zidovudine (AZT)	Bone marrow suppression
Digitalis	GI disorders, vision changes, arrhythmias
Acetazolamide	Metabolic acidosis
Clozapine	Agranulocytosis
Selective serotonin reuptake inhibitors (e.g., fluoxetine)	Anxiety, agitation, insomnia, sexual dysfunction
Warfarin	Necrosis, teratogen
Niacin	Skin flushing, pruritus
HMG CoA reductase inhibitors (e.g., simvastatin)	Liver and muscle toxicity
Ethambutol	Optic neuritis
Metronidazole	Disulfiram-like reaction with alcohol
Cisplatin	Nephrotoxicity
Methyldopa	Hemolytic anemia (Coombs test-positive)

2. What are the side effects of diuretics?

- **Thiazide diuretics** cause calcium retention, hyperglycemia, hyperuricemia, hyperlipidemia, hyponatremia, hypokalemic metabolic alkalosis, and hypovolemia; because they are sulfa drugs, watch out for sulfa allergy.
- **Loop diuretics** cause hypokalemic metabolic alkalosis, hypovolemia (more potent than thiazides), ototoxicity, and calcium excretion; with the exception of ethacrynic acid, they also are sulfa drugs.
- **Carbonic anhydrase inhibitors** cause metabolic acidosis.
- **Potassium-sparing diuretics** (e.g., spironolactone) may cause hyperkalemia.

3. What are the side effects of beta blockers?

Like many antihypertensive agents, beta blockers can cause sedation, depression, and sexual dysfunction. They also cause bradycardia and heart block in susceptible patients and should be

avoided in patients with these conditions, as should central-acting calcium channel blockers (e.g., verapamil, diltiazem). Beta blockers also can precipitate asthmatic attacks and mask the symptoms of hypoglycemia, thus they should be avoided or used with caution in asthmatics and those with chronic obstructive pulmonary disease. A $beta_1$ selective beta blocker (atenolol, metoprolol) or a combined beta and alpha blocker (carvedilol) is preferred if a beta blocker is needed to treat another condition such as heart disease. Use in diabetic patients requires an analysis of the risks and benefits; if other equivalent medications are available, use them instead.

4. What class of antihypertensive agents is best known for severe, first-dose orthostatic hypotension?

$Alpha_1$ antagonists.

5. What antihypertensive is best known for causing depression?

Methyldopa. Beta blockers may also cause depression.

6. Cover the right-hand column of the following table and give the antidote(s) for overdose or toxic exposure to the drugs in the left-hand column.

POISON OR MEDICATION	ANTIDOTE
Acetaminophen	Acetylcysteine
Benzodiazepines	Flumazenil
Beta blockers	Glucagon
Carbon monoxide	Oxygen (hyperbaric in cases of severe poisoning)
Cholinesterase inhibitors	Atropine, pralidoxime
Copper or gold	Penicillamine
Digoxin	Normalize potassium and other electrolytes; digoxin antibodies
Iron	Deferoxamine
Lead	Edetate (EDTA); use succimer in children
Methanol or ethylene glycol	Fomepizole, ethanol
Muscarinic blockers	Physostigmine
Opioids	Naloxone
Quinidine or tricyclic antidepressants	Sodium bicarbonate (cardioprotective)

7. If the following medications are given at the same time, what may happen?

MEDICATIONS	POSSIBLE EFFECT OF SIMULTANEOUS ADMINISTRATION
MAO inhibitor plus meperidine	Coma
Aminoglycoside plus loop diuretic	Enhanced ototoxicity
Thiazide plus lithium	Lithium toxicity
MAO inhibitor plus SSRI	Serotonin syndrome (hyperthermia, rigidity, myoclonus, and autonomic instability)

MAO, Monoamine oxidase; *SSRI*, serotonin specific reuptake inhibitor.

8. What prophylactic medication should be given to contacts of a patient with *Neisseria* meningitis?

Rifampin, ciprofloxacin, or ceftriaxone.

9. Name three medications that cause hepatic enzyme induction and two that cause hepatic enzyme inhibition.

Barbiturates, antiepileptics, and rifampin are the classic enzyme inducers; cimetidine, erythromycin, and ketoconazole are classic enzyme inhibitors. The end result may be ineffectiveness or toxicity of other administered drugs (e.g., warfarin, oral contraceptives, antiepileptics).

10. True or false: If a patient responds to placebo, a psychosomatic condition can be diagnosed.

False. Response to placebo means only that the patient responded to placebo. Normal patients with real diseases often have an improvement in symptoms with a placebo medication or treatment.

11. Describe the mechanism of action for aspirin and other nonsteroidal antiinflammatory drugs (NSAIDs). How do they differ?

Aspirin and other NSAIDs inhibit cyclooxygenase centrally and peripherally, an action that gives them antiinflammatory, antipyretic, analgesic, and antiplatelet effects. The difference between aspirin and other NSAIDs is that aspirin binds to and inhibits cyclooxygenase *irreversibly,* whereas the cyclooxygenase inhibition of other NSAIDs is reversible. The net result of this difference is in platelets, which cannot make new cyclooxygenase. One dose of aspirin causes antiplatelet effects for the entire life of the platelet, whereas the antiplatelet effects of other NSAIDs last only for several hours.

12. How is acetaminophen different from aspirin and other NSAIDs?

Acetaminophen is thought to inhibit cyclooxygenase primarily in the brain; it does not act well in the periphery of the body. Thus it has analgesic and antipyretic effects but no antiplatelet or significant antiinflammatory effects.

13. What are the side effects and toxic effects of aspirin?

Aspirin causes GI upset and bleeding; it is the most important preventable risk factor for the development of gastric ulcers. Always consider GI bleeding and ulcers in any patient taking aspirin. In addition, aspirin can cause renal damage or aggravate gout. Toxic doses of aspirin can cause tinnitus, vertigo, respiratory alkalosis and metabolic acidosis, hyperthermia, coma, and death. Severe overdoses of aspirin can be removed by dialysis.

14. What are the side effects of nonaspirin NSAIDs?

NSAIDs also cause GI upset, bleeding, and ulcers. Consider GI bleeding and ulcer in all patients taking aspirin or other NSAIDs. NSAIDs may also cause renal damage (interstitial nephritis, acute tubular necrosis, and/or papillary necrosis), especially in patients who take them long term and have preexisting renal disease.

15. What two developments in NSAID therapy may reduce GI and bleeding complications?

Cyclooxygenase-2 (COX-2) inhibitors and new combinations of NSAIDs with prostaglandin E_1. Normal NSAIDs inhibit type 1 cyclooxygenase (in addition to type 2), which is thought to be the main culprit in causing GI problems. Prostaglandin E_1 protects the stomach by supplying what NSAIDs take away. COX-2 inhibitors avoid the problem altogether, but are not as protective against GI bleeding as initially thought. Two of the three COX-2 inhibitors initially approved in the United States have been removed from the marked because of adverse cardiovascular effects.

16. What happens with an overdose of acetaminophen?

High doses of acetaminophen cause liver toxicity as a result of depletion of glutathione. Treat with **acetylcysteine** to decrease liver injury.

17. What age group should not be given aspirin? What finding on physical examination is a contraindication to aspirin use?

Children younger than 15 years of age (especially with a fever or viral infection) should not be given aspirin because of concern about causing Reye syndrome. Do not give aspirin to people with **nasal polyps** because hypersensitivity reactions involving an asthmatic attack are extremely common. People with asthma may have an asthma attack after taking aspirin even in the absence of nasal polyps.

18. What is the relationship between aspirin and myocardial infarction?

Low-dose aspirin has been proved to be of benefit in reducing the risk of myocardial infarction in both patients who have had a previous myocardial infarction and patients with stable or unstable angina who have not had an infarction. The 2012 American College of Chest Physicians (ACCP) clinical practice guidelines on antithrombotic and thrombolytic therapy recommends that all patients with chronic stable angina or other clinical or laboratory evidence of coronary artery disease receive aspirin indefinitely. There is strong medical literature support for the net benefit of aspirin for the primary prevention of first myocardial infarction in individuals at moderate to high risk. Aspirin is recommended in all patients with diabetes with cardiovascular disease and for primary prevention in diabetic patients with one or more risk factors (e.g., age older than 40 years, cigarette smoking, hypertension, hyperlipidemia, obesity, albuminuria, family history of cardiovascular disease). The risks of aspirin prophylaxis may outweigh the benefits in patients with a history of liver disease, kidney disease, peptic ulcer disease or GI bleeding, poorly controlled hypertension, or a bleeding disorder.

19. Discuss the relationship between aspirin and strokes.

Low-dose aspirin is of proven benefit in reducing strokes in patients with transient ischemic attacks (TIAs) and/or known carotid artery stenosis. However, risks may outweigh benefits (see question 18), especially in patients with uncontrolled hypertension, which, coupled with aspirin, can increase the risk of a hemorrhagic stroke.

20. True or false: Patients should be given an aspirin as soon as possible in the emergency department for a suspected myocardial infarction or unstable angina.

True, but beware of the patient whose symptoms include chest pain caused by aortic dissection (aspirin should be avoided in such patients).

21. True or false: In the setting of an acute neurologic deficit, you should give aspirin before ordering brain imaging.

False. When patients come to the hospital with an acute neurologic deficit, you do not know whether they are having a stroke or TIA. TIA is a retrospective diagnosis made once the symptoms subside and imaging has ruled out tissue injury. First you should order a computed tomography (CT) scan or magnetic resonance imaging (MRI) to rule out hemorrhagic stroke. If the CT scan or MRI is negative for blood, the patient should be given aspirin (160-325 mg) within 24 to 48 hours of TIA or stroke onset.

PREVENTIVE MEDICINE

1. Cover all but the left-hand column, and give the appropriate screening recommendations. Although other guidelines for cancer screening are in clinical use, the recommendations from the American Cancer Society (below) are a good guideline to use for the USMLE.

CANCER	PROCEDURE	AGE	FREQUENCY
Colorectal	Colonoscopy or	>50 yr for all studies	Every 10 yr
	Flexible sigmoidoscopy or		Every 5 yr
	Double contrast barium enema or		Every 5 yr
	Computed tomography (CT) colonography or		Every 5 yr
	Fecal occult blood test or		Annually
	Fecal immunochemical test or		Annually
	Stool DNA test		Interval uncertain
Colon, prostate	Digital rectal examination	>40 yr	Annually
Prostate	Prostate specific antigen test	>50 yr*	Controversial, but offer annually
Cervical	Pap smear	Beginning at age 21 years regardless of sexual activity	If conventional Pap test is used, test annually, then every 2-3 yr for women 30 yr or older who have had three negative cytology test results If Pap and HPV testing are used, test every 3 years if both HPV and cytology results are negative
Gynecologic	Pelvic examination	21-64 yr	Annually; every 2-3 yr after 3 normal examinations
		≥65 yr	Annually; when to stop is not clearly established
Endometrial	Endometrial biopsy	Menopause	No recommendation for routine screening in the absence of symptoms

Continued

CANCER	PROCEDURE	AGE	FREQUENCY
Breast	Breast self-examination	>20 yr	Benefits and limitations should be discussed, but breast self-examination is no longer recommended by the American Cancer Society
Breast	Physical exam by doctor	20-40 yr	Every 3 yr
		>40 yr	Annually
Breast	Mammography	>40 yr	Annually
Lung	Sputum, chest x-ray		Testing is not recommended for asymptomatic individuals, even if they are high-risk
	CT scan		Annual CT scan is controversial but may be indicated for smokers and former smokers aged 55-74 yr who have smoked at least one pack of cigarettes per day for at least 30 yr

This table is intended for the screening of asymptomatic, healthy patients, which is adequate for review for the USMLE. Controversial areas usually are not tested on the USMLE.
*Start at age 45 yr in African Americans and at age 40 yr for patients with a first-degree relative diagnosed at an early age.

2. True or false: Tumor markers are generally not used for cancer screening.

True. Prostate-specific antigen is the exception to this rule. Alpha-fetoprotein (AFP; liver and testicular cancer), carcinoembryonic antigen (CEA), CA-125, and other serum markers are not appropriate for screening the general population. However, look for abnormal laboratory values to show up in questions as a clue to diagnosis.

3. True or false: Urinalysis should not be used to screen the general population for bladder cancer.

True. Screening with urinalysis for urinary tract cancer (which causes hematuria) is not recommended. However, look for persistent, painless hematuria as a clue that urinary tract cancer may be present.

4. Cover the right-hand column and give the indications for each of the following vaccines in adults.

VACCINE	WHICH ADULTS SHOULD RECEIVE AND OTHER INFORMATION
Hepatitis B	Adolescents though 18 years of age and adults at increased risk of hepatitis B virus infection (children are vaccinated as well).
Influenza	Anyone who wants to reduce their chances of getting the flu can get vaccinated. It is recommended for people who are at high risk for serious flu complications or people who live with or care for people at high risk for serious complications. People who should get vaccinated each year are children ages 6 months to 18 years, women who will be pregnant during the flu season, people who are immunosuppressed, adults aged 50 and older, people with chronic medical conditions (pulmonary, cardiovascular, renal, hepatic, hematologic, or metabolic disorders including diabetes), people who live in nursing homes and other long-term care facilities, health care personnel, household contacts and caregivers of children younger than 5 years old and adults over age 50, and household contacts and caregivers for those at high risk for serious flu complications.

VACCINE	WHICH ADULTS SHOULD RECEIVE AND OTHER INFORMATION
Pneumococcus	All adults 65 years of age and older; people aged 2 to 64 years with chronic cardiovascular disease, chronic pulmonary disease, chronic liver disease, or diabetes mellitus; people aged 2 years and older with functional or anatomic asplenia; people aged 2 years and older living in environments in which the risk for disease is high; and immunocompromised persons aged 2 years and older who are at high risk for infection.
Rubella	All women of child-bearing age who lack immunity or history of immunization. Do not give to pregnant women. Women should avoid pregnancy for 4 weeks after receiving the vaccine. Also give to health care workers (to protect pregnant women's unborn children). Give to susceptible adolescents and adults without evidence of rubella immunity. Do not give to immunocompromised patients (except patients who test HIV-positive).
Tetanus	All people should be given a tetanus booster every 10 years. Give tetanus prophylaxis for any wound if vaccination history is unknown or if patient has received fewer than three total dosages. Give tetanus booster in people with full vaccination history if more than 5 years have passed since last dosage for all wounds other than clean, minor wounds (including burns). Give tetanus immunoglobulin with vaccine for patients with unknown/incomplete vaccination and unclean or major wounds. Adults (11 years and older) should receive a single dose of Tdap to replace a single dose of Td if they received their last dose of Td 10 or more years earlier (this is a new recommendation from the CDC in June 2012 that now includes adults 65 years and older). Adults who have or anticipate having close contact with an infant younger than 12 months old should receive a single dose of Tdap. Health care workers should receive Tdap. Tdap is preferred to Td if prophylaxis is indicated for a wound. It is now recommended that Tdap be given to women with every pregnancy regardless of their prior immunization history, preferably in the late second or in the third trimester (recommended by the CDC in October 2012).

CDC, Centers for Disease Control and Prevention.

5. Define the following rates that are commonly seen on the USMLE.

RATE	DEFINITION
Birth rate	Live births/1000 population
Fertility rate	Live births/1000 population of women aged 15 to 45 yr
Death rate	Deaths/1000 population
Neonatal mortality rate	Neonatal deaths (first 28 days of life)/1000 live births
Perinatal mortality rate	Neonatal deaths + stillbirths/1000 total births
Infant mortality rate	Deaths (from 0 to 1 year old)/1000 live births
Maternal mortality rate	Maternal pregnancy-related deaths (deaths while pregnant or in the first 42 days after delivery)/100,000 live births

6. Define stillbirth.

A stillbirth (fetal death) is defined as a prenatal or natal (during delivery) death after 20 weeks of gestation.

7. Name the major cause of neonatal mortality. What is the neonatal mortality rate in the United States?

The major cause of neonatal mortality is prematurity. The neonatal mortality rate in the United States is roughly 6/1000 (higher in blacks).

8. List the top three causes of infant mortality in the United States.

- Congenital abnormalities
- Prematurity/low birth weight
- Sudden infant death syndrome

9. List the top three causes of maternal mortality in the United States.

- Pulmonary embolus
- Hypertension/pregnancy-induced hypertension (preeclampsia/eclampsia)
- Hemorrhage

The rate increases with age and is higher among black women.

10. What is the basic difference between Medicare and Medicaid?

Medicare is health insurance for people who are eligible for Social Security (primarily people older than 65 years as well as people who are permanently or totally disabled with end-stage renal disease). Nursing home fees are paid by Medicare only for a short time after a hospital admission; then they are paid by the patient. If the patient has no money, the state usually pays.

Medicaid covers the indigent and poor who are deemed eligible according to the criteria of individual states.

CHAPTER 32

PSYCHIATRY

1. What are the five main diagnostic criteria for schizophrenia?

- Delusions
- Hallucinations
- Disorganized speech
- Grossly disorganized or catatonic behavior
- Negative symptoms (i.e., flat affect, avolition)

2. Why is the duration of symptoms important with psychosis?

The time frame is important because, given the same symptoms, a patient is given one of three different diagnoses based only on their duration:

- Less than 1 month = acute psychotic disorder.
- 1 to 6 months = schizophreniform disorder.
- More than 6 months = schizophrenia.

3. List the positive symptoms of schizophrenia.

- Delusions
- Bizarre behavior
- Hallucinations
- Thought disorder (e.g., tangentiality, clanging)

These symptoms respond well to all currently used antipsychotics.

4. List the negative symptoms of schizophrenia.

- Flat affect
- Anhedonia
- Alogia (no speech)
- Poor attention
- Avolition (apathy)

These symptoms respond poorly to traditional antipsychotics (e.g., haloperidol) but may respond to "atypical" agents such as risperidone, olanzapine, aripiprazole, paliperidone, quetiapine, or ziprasidone.

5. What features of schizophrenia suggest a poor prognosis?

- Poor premorbid functioning (most important)
- Family history of schizophrenia
- Early onset
- Negative symptoms
- No precipitating factors
- Poor support system
- Single, divorced, or widowed status

6. What features suggest a good prognosis?

- Good premorbid functioning (most important)
- Family history of mood disorders

- Late onset
- Positive symptoms
- Obvious precipitating factors
- Good support system
- Married status

7. What is the difference in age of onset for schizophrenia in males and females?
The typical age of onset is 15 to 25 years for males (look for someone going to college and deteriorating) and 25 to 35 years for females.

8. True or false: Roughly 1% of the population has schizophrenia in almost every country in the world.
True.

9. True or false: In the United States, most schizophrenic people are born in the summer months.
False. Most schizophrenic patients in the United States are born in the winter (reason unknown).

10. Roughly what percentage of patients with schizophrenia commit suicide?
In the United States, roughly 10% of patients with schizophrenia eventually commit suicide (a past attempt is the best predictor of eventual success).

11. True or false: Psychosocial treatment has been shown to improve outcome in schizophrenia.
True. Antipsychotic medications are the mainstay of therapy, but psychosocial treatment has been shown to improve outcome. Medications are needed first, but the best treatment (as in most psychiatric illnesses) is medications plus therapy.

12. Differentiate among the classes of antipsychotic drugs.

	HIGH POTENCY	LOW POTENCY	ATYPICAL AGENTS*
Prototype drug	Haloperidol	Chlorpromazine	Risperidone, olanzapine, aripiprazole, paliperidone, quetiapine, ziprasidone
EPS side effects	High incidence	Low incidence	Low incidence
ANS side effects†	Low incidence	High incidence	Medium incidence
Positive symptoms	Works well	Works well	Works well
Negative symptoms	Works poorly	Works poorly	Works fairly well

ANS, Autonomic nervous system; *EPS*, extrapyramidal system.
*Atypical, newer antipsychotics are generally first-line treatment and maintenance therapy as a result of reduced extrapyramidal side effects and efficacy with negative symptoms. Choose them over older agents.
†ANS side effects include anticholinergic effects (dry mouth, urinary retention, blurry vision, mydriasis), alpha$_1$ blockade (orthostatic hypotension), and antihistamine effects (sedation).

13. What are the four commonly tested extrapyramidal side effects of antipsychotics?
Acute dystonias, akathisia, parkinsonism, and tardive dyskinesia.

14. Define acute dystonia. How is it treated?
Acute dystonia is an extrapyramidal movement disorder that occurs in the first few hours or days of treatment with an antipsychotic medication. Patients develop muscle spasms or stiffness

(e.g., torticollis, trismus), tongue protrusions and twisting, opisthotonos, and/or oculogyric crisis (forced sustained deviation of the head and eyes). Acute dystonia is most common in young men. Treat with antihistamines (e.g., diphenhydramine) or anticholinergics (e.g., benztropine, trihexyphenidyl).

15. Define akathisia.

Akathisia occurs in the first few days of treatment with an antipsychotic medication (or other medications such as antidepressants). The patient has a subjective feeling of restlessness and may pace constantly, alternate sitting and standing, and be unable to sit still. Beta blockers can be tried for treatment.

16. Describe the relationship between antipsychotics and parkinsonism.

Parkinsonism usually occurs in patients taking antipsychotics within the first few months of treatment. Parkinsonism is thought to develop because of dopamine depletion, whereas psychosis is thought to develop because of too much dopamine in the brain (a gross oversimplification). Thus antipsychotics create an iatrogenic lowering of effective dopamine in the brain by blocking dopamine receptors. The patient develops stiffness, cogwheel rigidity, shuffling gait, masklike facies, and drooling. Parkinsonism is most common in older women. Treat with antihistamines (e.g., diphenhydramine) or anticholinergics (e.g., benztropine, trihexyphenidyl).

17. Define tardive dyskinesia. When does it occur?

Tardive dyskinesia appears after years of treatment with antipsychotics. Most commonly the patient develops perioral movements (darting, protruding movements of the tongue, chewing, grimacing, and puckering). The patient may also have involuntary, choreoathetoid movements of the head, limbs, and trunk. There is no known treatment for tardive dyskinesia. If you are asked to make a choice when the patient develops tardive dyskinesia, discontinue the current antipsychotic and consider switching to a second generation agent (e.g., clozapine, risperidone).

18. What is neuroleptic malignant syndrome? How do you recognize and treat it?

Neuroleptic malignant syndrome is a life-threatening condition that can occur at any time during antipsychotic treatment. Patients classically develop rigidity, mutism, obtundation, agitation, high temperature (up to 107°F), very **high levels of creatine phosphokinase** (more than 10 times the normal range), sweating, and myoglobinuria. Treat by first discontinuing the antipsychotic; then give supportive care for fever and potential renal failure caused by myoglobinuria (primarily intravenous fluids). Lastly, consider dantrolene (just as in malignant hyperthermia, which is thought to be a similar condition).

19. Describe the relationship between antipsychotics and prolactin.

Dopamine blockade causes increases in prolactin levels because dopamine is a prolactin-inhibiting factor in the tuberoinfundibular tract of the brain. The end result may be high serum prolactin levels, resulting in **galactorrhea** and impotence, menstrual dysfunction, and/or decreased libido.

20. What are the classic side effects of thioridazine, chlorpromazine, and clozapine?

- Thioridazine: Retinal pigment deposits
- Clozapine: Agranulocytosis (white blood cell counts must be monitored)
- Chlorpromazine: Jaundice and photosensitivity

21. What are the side effects of the atypical antipsychotics?

- Olanzapine: Weight gain, sedation, hypotension, dry mouth
- Quetiapine: Sedation, orthostatic hypotension, akathisia, weight gain, dry mouth
- Ziprasidone: Nausea, weakness, mild QT prolongation
- Aripiprazole: Headache, nausea, akathisia, tremor, constipation
- Paliperidone: Parkinsonism, dystonia, dyskinesia, akathisia, QT prolongation
- Clozapine: Orthostatic hypotension, weight gain, metabolic syndrome, sedation, constipation

22. Define bipolar disorder. What are the classic symptoms?

Mania is the only criterion required for a diagnosis of bipolar disorder, but a history of or future episodes of depression are classically present. Classic symptoms of mania include decreased need for sleep, pressured speech, sexual promiscuity, shopping sprees, and an exaggerated self-importance or delusions of grandeur. Look for initial onset between 16 and 30 years old.

23. How is bipolar disorder treated?

Both lithium and valproic acid are mood stabilizers and first-line agents. Typical antipsychotics (haloperidol), atypical antipsychotics (risperidone, quetiapine, clozapine, ziprasidone, and aripiprazole), carbamazepine, and gabapentin are second-line agents. Antipsychotics or antidepressants may be needed if the patient becomes psychotic or depressed; use at the same time as the mood stabilizer.

24. What are the side effects of lithium, valproic acid, and carbamazepine?

- Lithium: Renal dysfunction (diabetes insipidus), thyroid dysfunction, tremor, and central nervous system (CNS) effects at toxic levels
- Valproic acid: Liver dysfunction
- Carbamazepine: Bone marrow suppression

25. Define bipolar II disorder and cyclothymia.

Bipolar II disorder is hypomania (mild mania without psychosis that does not cause occupational dysfunction) plus major depression. Cyclothymia is at least 2 years of hypomania alternating with depressed mood, but there are *no* full-blown episodes of mania or major depression.

26. List the major risk factors for suicide.

- Age older than 45 years
- Prior psychiatric history
- Alcohol or substance abuse
- Depression
- History of rage or violence
- Recent loss or separation
- Prior suicide attempts
- Loss of health
- Male gender (men commit suicide three times more often than women, but women attempt it four times more often than men)
- Unemployed or retired status
- Single, widowed, or divorced status

27. What is the best predictor of future suicide?

A past attempt.

28. True or false: Be careful in asking about suicide because you may plant the idea in the patient's head.

False. Always ask a patient about suicidal thoughts; it does not make them more likely to commit suicide. If necessary, you should temporarily hospitalize an acutely suicidal patient against his or her will.

29. True or false: When patients are just emerging from a deep depression, they are at increased risk for suicide.

True. When the antidepressant begins to work, the patient gets a little more energy—possibly just enough to carry out a suicide plan.

30. True or false: The highest suicide rates are in people aged 15 to 24 years.

False. Suicide rates are rising most rapidly in 15 to 24 year olds, but the greatest absolute risk is in people older than age 65 years.

31. True or false: Patients with depression often do not complain about it directly.

True. Patients often do not come out and say, "I'm depressed." You must watch for the clues: Change in sleep habits (classically insomnia), vague somatic complaints, anxiety, low energy or fatigue, change in appetite (classically decreased appetite), poor concentration, psychomotor retardation, and/or anhedonia (loss of pleasure). The history may or may not reveal obvious precipitating factors, such as loss of loved one, divorce or separation, unemployment or retirement, or chronic or debilitating disease.

32. How do you treat depression?

As with most psychiatric illnesses, the treatment of choice is both medications (antidepressants) and psychotherapy. The combination is more effective than medications alone. Serotonin-specific reuptake inhibitors (SSRIs) usually are the preferred first-line agents. Other options include serotonin-norepinephrine reuptake inhibitors (SNRIs) and the tricyclic antidepressants. Bupropion and mirtazapine have unique modes of action.

33. Is depression more common in males or females?

Depression is more common in females.

34. What is an adjustment disorder with depressed mood?

A diagnosis that you must be able to distinguish from major depression. With adjustment disorder, a patient goes through a normal life experience (e.g., relationship break-up, failing grade, loss of job) but does not handle it well. There is marked distress that is in excess of what would be expected from exposure to the stressor or causes significant impairment in social or occupational functioning. Although patients may have a depressed mood, they do not meet the criteria for full-blown major depression. For example, a woman divorces her husband, seems to cry a lot for the next few weeks, and leaves work early on most days. Or a high-school boy doesn't make the basketball team and mopes around the house, crying and not wanting to go to school or out with his friends for a few weeks.

35. Define dysthymia.

Dysthymia is a depressed mood on most days for more than 2 years without episodes of major depression, mania/hypomania, or psychosis.

36. True or false: Antidepressants can trigger mania or hypomania.

True—especially in bipolar patients.

37. How do tricyclic antidepressants work? What are their side effects?

Tricyclic antidepressants (e.g., nortriptyline, amitriptyline) prevent reuptake of norepinephrine and serotonin. They also block alpha-adrenergic receptors (watch for orthostatic hypotension, dizziness, or falls) and muscarinic receptors (watch for anticholinergic effects, such as dry mouth, blurred vision, constipation, and urinary retention), cause sedation (antihistamine effect), and lower the seizure threshold (especially bupropion, which technically is not a tricyclic). Tricyclic antidepressants are dangerous in overdose primarily because of **cardiac arrhythmias,** which may respond to bicarbonate.

38. How do SSRIs work? Why are they preferred over tricyclics?

SSRIs (e.g., fluoxetine, citalopram, paroxetine, sertraline, fluvoxamine, escitalopram) prevent reuptake of serotonin only. They have less serious side effects (insomnia, anorexia, jitteriness, headache, sexual dysfunction) and are not dangerous with overdose. Tricyclics used to be the number-one cause of prescription drug overdose in the United States.

39. How do SNRIs work?

SNRIs (e.g., venlafaxine, duloxetine, desvenlafaxine) prevent reuptake of serotonin and norepinephrine. The side effects of SNRIs are similar to those of SSRIs but also include noradrenergic symptoms such as sweating and dizziness.

40. What are monoamine oxidase (MAO) inhibitors? Describe their side effects.

MAO inhibitors (e.g., phenelzine, tranylcypromine) are older medications that are not used as first-line agents for treatment of depression. They may be good for atypical depression (look for hypersomnia and hyperphagia—the opposite of classic depression) that fails to respond to other agents. When patients taking MAO inhibitors eat tyramine-containing foods (especially wine and cheese), they may get a hypertensive crisis. Do *not* give MAO inhibitors at the same time as SSRIs or meperidine; severe reactions can occur, possibly even death.

41. What is the most notorious side effect of trazodone?

Priapism (persistent, painful erection in the absence of sexual desire that may lead to permanent impotence if not treated).

42. Distinguish between normal grief and pathologic grief (i.e., depression).

Initial grief after a loss (e.g., death of a loved one) may include a state of shock, feeling of numbness or bewilderment, distress, crying, sleep disturbances, decreased appetite, difficulty in concentrating, weight loss, and guilt (survivor guilt) for up to 1 year—in other words, the same symptoms as depression. It is normal to have an illusion or hallucination about the deceased, but a normal grieving person knows that it is an illusion, whereas a depressed person believes that it is real. Intense yearning (even years after the death) and even searching for the deceased are normal. Feelings of worthlessness, psychomotor retardation, and suicidal ideation are not signs of normal grief; they are signs of depression.

43. How do you recognize and treat panic disorder?

Panic disorder classically affects 20- to 40-year-old patients, who often think that they are dying or having a heart attack, although in fact they are healthy and have a negative work-up for organic disease. Patients often hyperventilate and are extremely anxious. Remember the association between panic disorder and agoraphobia (fear of leaving the house). Treat with SSRIs (e.g., fluoxetine), which are favored over benzodiazepines.

44. What is generalized anxiety disorder? How is it treated?

Patients with generalized anxiety disorder worry about everything (e.g., career, family, future, relationships, money) at the same time. Symptoms are not as dramatic as in panic disorder; the patient is simply a severe worrier. Treat with cognitive behavioral therapy and medications: buspirone (nonaddictive, nonsedating but slow onset of action), SSRIs (especially if depressive symptoms coexist), or benzodiazepines (addictive, sedating).

45. Give the classic examples of simple phobias. How are they treated?

Classic examples of simple phobias include fear of needles, blood products, animals, and heights. Treat with behavioral therapy, including flooding (sudden, intense exposure to the feared object without chance for escape), systematic desensitization (gradual increase in intensity and type of exposure until the person is comfortable with intense exposure to the feared object), and biofeedback (learning to control autonomic variables like heart rate during anxiety-inducing maneuvers).

46. What is social phobia?

Social phobia, also known as social anxiety disorder, is a specific type of simple phobia (fear of social situations) that is best treated with behavioral therapy. Beta blockers may be used before a public appearance that cannot be avoided to reduce symptoms, and SSRIs are increasingly being used as a primary treatment, though SNRIs and benzodiazepines may also be used.

47. How do you recognize and treat posttraumatic stress disorder?

Look for someone who has been through a life-threatening event (e.g., war, severe accident, rape), repeatedly experiences the event (nightmares, flashbacks), and tries to avoid thinking about it. As a result, patients have depression or poor concentration. Treat with peer group therapy; if you have to choose a medication, use an antidepressant, usually an SSRI.

48. True or false: Homosexuality is not considered a psychiatric disorder.

True. Homosexuality and homosexual experimentation are not considered a disease at any age; they are normal variants. Having kinky fantasies and occasionally doing kinky things (e.g., a man wearing women's underwear, mild foot fetish) also are considered normal.

49. Explain the concept of somatoform disorders.

A patient with somatoform disorder experiences psychiatric stress and expresses it through physical symptoms. Patients do not do so on purpose.

50. Describe the four major somatoform disorders.

Somatization disorder: The patient has multiple different complaints in multiple different organ systems over many years and has had extensive work-ups in the past.

Conversion disorder: The patient has an obvious precipitating factor (e.g., fight with boyfriend), then develops unexplainable neurologic symptoms (e.g., blindness, stocking-glove numbness).

Hypochondriasis: The patient continues to believe that he or she has a disease despite extensive negative work-up.

Body dysmorphic disorder: The patient is preoccupied with an imagined physical defect; for example, a teenager who thinks that his or her nose is too big when it is normal size.

51. How are somatoform disorders treated?

Treat all somatoform disorders with frequent return visits to the clinic and/or psychotherapy. Screen for and treat any coexisting depression.

52. Distinguish among somatoform disorders, factitious disorders, and malingering.

In **somatoform disorders,** the patient does not intentionally create symptoms (unconscious process). In **factitious disorders,** patients intentionally create an illness or symptoms (e.g., they inject insulin to create hypoglycemia) and subject themselves to procedures in order to assume the role of a patient (no financial or other secondary gain). In **malingering,** patients intentionally create their illness for secondary gain (e.g., money, release from work or jail).

53. How do you recognize dissociative fugue (also called psychogenic fugue or fugue state)?

Dissociative fugue is a reversible amnesia for personal identity including the memories, personality, and other identifying characteristics of individuality. It usually involves unplanned travel or wandering. There is complete amnesia for the fugue episode. The classic patient develops amnesia, travels, and assumes a new identity, but does not remember the event upon returning.

54. What psychiatric disorder is most likely to be associated with childhood sexual abuse?

Dissociative identity disorder (formerly known as multiple personality disorder).

55. Define personality disorders.

Personality disorders are lifelong disorders that affect the way in which a person interacts with the world. Look for a history dating back to childhood or teenage years. No real treatment is available, although psychotherapy can be tried.

56. Give a one- or two-sentence description of each of the following 10 personality disorders below.

Paranoid: Patients are paranoid and think that everyone (friends, too) is out to get them; they often start law suits.

Schizoid: Patients are classic loners who have no friends and no interest in having friends.

Schizotypal: Patients have bizarre beliefs (cults, superstition, or illusions) and manner of speaking but no psychosis.

Avoidant: Patients have no friends but want them; they avoid others out of fear of criticism and rejection (inferiority complex).

Histrionic: Patients are overly dramatic, attention-seeking, and inappropriately seductive; they must be the center of attention.

Narcissistic: Patients are egocentric, lack empathy, and use others for their own gain; they have a sense of entitlement.

Antisocial: The most frequently tested personality disorder. Patients have long criminal records (e.g., con men) and tortured animals or set fires as children. A history of pediatric conduct disorder is required for this diagnosis. Patients are aggressive and do not pay their bills or support their children. They lie and have no remorse or conscience. Antisocial personality disorder has a strong association with alcoholism, drug abuse, and somatization disorder. Most patients are male.

Borderline: Patients have unstable moods, behaviors, relationships (many are bisexual), and self-image. Look for splitting; that is, they identify other individuals as all good or all bad and may frequently change categories. Other clues include suicide attempts, micropsychotic episodes (2 minutes of psychosis), impulsiveness, and constant crisis.

Dependent: Patients cannot be or do anything alone. For example, a wife may stay with her abusive husband despite continued abuse.

Obsessive-compulsive: Patients are obsessed with rules, perfection, and organization. They may seem anal-retentive and stubborn. Rules are more important than objectives. Affect is restricted. Money is a frequent concern and is often hoarded.

57. Define obsessive-compulsive disorder. How is it treated?

Obsessive-compulsive disorder describes patients with recurrent thoughts or impulses (obsessions) or recurrent behaviors or actions (compulsions) that cause marked dysfunction in their occupational and interpersonal lives. It is not the same as obsessive-compulsive personality disorder. Look for washing rituals (washing of hands 30 times per day) or checking rituals (checking to see if the door is locked 30 times per day). The onset usually is in adolescence or early adulthood. Treat with SSRIs or clomipramine and psychotherapy. Behavioral therapy (e.g., flooding) may also be effective.

58. True or false: Some psychiatric patients can be hospitalized against their will.

True. Patients can be hospitalized against their will if they are a danger to themselves (suicidal or unable to take care of themselves) or others (homicidal).

59. Describe the hallmark findings of narcolepsy. How is it treated?

Narcolepsy is a sleep disorder characterized by daytime sleepiness in spite of a normal daily sleep regimen. Patients have decreased latency for rapid-eye-movement (REM) sleep (patients go into REM as soon as they fall asleep); cataplexy (random loss of muscle tone that causes patients to fall down); and hallucinations as they awaken (hypnopompic) or fall asleep (hypnagogic). Treat with **modafinil** (a nonamphetamine stimulant), methylphenidate, or amphetamines.

60. What is the difference between objective and subjective psychological tests?

Objective tests are generally multiple-choice tests that are scored by a computer; the classic example is the IQ test. **Subjective tests** have no "right" answers and are scored by the test-giver (the classic example is the Rorschach test).

61. Characterize each of the following psychological tests as objective or subjective and briefly describe its use.

NAME OF TEST	DESCRIPTION
Stanford-Binet	Objective IQ test for adults
Wechsler Intelligence Scale for Children	Objective IQ test for children (4-17 years old)

NAME OF TEST	DESCRIPTION
Rorschach test	Subjective test in which patients describe what they see in an inkblot
Thematic Apperception Test	Subjective test in which the patient describes what is going on in a cartoon drawing of people
Beck Depression Inventory	Objective test to look for depression
Minnesota Multiphasic Personality Inventory	Objective test to measure personality type
Halstead-Reitan Battery	Objective test used to determine the location and effects of specific brain lesions
Luria-Nebraska Neuropsychological Battery	Objective test that assesses many cognitive functions as well as cerebral dominance (left-side or right-side)

Note: Psychological tests can be used to aid in a difficult diagnosis; they are not used or needed for a straightforward case.

62. True or false: Roughly 85% of cases of mental retardation are mild.

True. Patients with mild mental retardation can have a reasonable level of independence, with assistance or guidance during periods of stress.

63. What are the common causes of mental retardation?

Although mental retardation is usually idiopathic, look for fetal alcohol syndrome (the number-one preventable cause of mental retardation), Down syndrome (number-one overall known cause of mental retardation), and fragile X syndrome (in males).

64. How do you recognize autism?

Autism symptoms start at a very young age, beginning as early as 6 months and becoming well established by age 2 or 3 years. Look for impaired social interaction (isolative, unaware of surroundings), impaired verbal and nonverbal communication (strange words, babbling, repetition), and restricted activities and interests (head banging, strange movements). Autism can be thought of as a spectrum of disorders in which patients may range from very highly functioning (e.g., Asperger syndrome) to severely mentally retarded. Most individuals with autism manifest some degree of mental retardation, which typically is moderate in severity.

If you get a patient with normal language development who has impaired social interactions and restricted activities and interests, think Asperger syndrome.

No single cause has been identified for the development of autism. Genetic origins are suspected by twin studies and an increased incidence among siblings. Possible contributing factors include fetal alcohol exposure, infections (congenital rubella infection), other perinatal factors, or immunologic causes.

65. What is a learning disorder?

Learning disorders describe isolated impairment in math, reading, writing, speech, language, or coordination. All other skills are normal; no mental retardation is present (e.g., "Johnny just can't do math").

66. Define conduct disorder. With what adult disorder is it associated?

Conduct disorder is the pediatric form of **antisocial personality disorder.** Look for fire setting, cruelty to animals, lying, stealing, and/or fighting. As adults, patients often have antisocial disorder. Note: Conduct disorder as a child is required for a diagnosis of antisocial personality disorder in adults.

67. Define attention-deficit/hyperactivity disorder (ADHD).

As the name implies, patients are hyperactive and have short attention spans. ADHD is more common in males than females. Look for a fidgety child who is impulsive and cannot pay attention, but is not cruel. Treat with stimulants (paradoxical calming effect) such as methylphenidate (Ritalin), an amphetamine, or atomoxetine. Stimulants and amphetamines may cause insomnia, abdominal pain, anorexia, weight loss, and growth suppression. Atomoxetine is an SNRI and alternative to stimulant therapy but has serious potential side effects including cardiovascular events and suicidal thinking.

68. Describe the behavior of a child who has oppositional-defiant disorder.

The child displays negative, hostile, and defiant behavior toward authority figures (e.g., parents, teachers). He or she displays behavioral issues around adults but behaves normally around peers and is *not* a cruel, lying criminal.

69. Give the classic description of children with separation anxiety disorder.

Affected children refuse to go to school. Basically, they think that something will happen to them or their parents if they separate. They will do anything to avoid separation (e.g., stomach ache, headache, temper tantrum).

70. How do you recognize anorexia?

Classic is a female adolescent who is a good athlete or student with a perfectionistic personality. Three criteria are required for the diagnosis: (1) body weight at least 15% below normal; (2) intense fear of gaining weight or "feeling fat" despite emaciation; and (3) amenorrhea. Roughly 10% to 15% of patients die of complications of starvation or coexisting bulimia (electrolyte imbalances, cardiac arrhythmias, infections). Although more "positive" therapies are preferred, patients sometimes need to be hospitalized against their wills for intravenous nutrition. Roughly one half of patients with anorexia also have bulimia.

71. Define bulimia. What are the classic findings of the mouth and fingers?

Bulimic patients have binge-eating episodes, during which they feel a lack of control, and then engage in purging behavior (vomiting, laxatives, exercise, fasting). Those affected are typically normal weight or overweight (unless coexisting anorexia is present) adolescent females. Patients may require hospitalization for electrolyte disturbances. Classic findings include eroded tooth enamel as a result of frequent vomiting and eroded skin over the knuckles from putting fingers in the throat.

72. Describe Tourette syndrome. How is it treated?

Tourette syndrome is a motor tic disorder (eye-blinking, grunting, throat-clearing, grimacing, barking, or shoulder shrugging) that is exacerbated by stress and remits during activity or sleep. Although part of the classic description, coprolalia (swearing) affects only 10% to 30% of patients. Males are affected more often than females. Of interest, Tourette syndrome can be caused or unmasked by the use of stimulants (e.g., for presumed ADHD). Antipsychotics (haloperidol) or dopamine receptor blockers (e.g., fluphenazine, pimozide) can be used if the symptoms are severe. Tourette syndrome tends to be a lifelong problem.

73. True or false: A diagnosis of encopresis or enuresis cannot be made before a certain age.

True. Encopresis is normal until age 4 years and enuresis is normal until age 5 years. This diagnostic point is obviously important when the parent complains because both are normal findings in a 3-year-old child. Rule out physical problems (e.g., Hirschsprung disease, urinary tract infection), then treat with behavioral therapy ("gold-star for being good" charts, alarms, biofeedback). Desmopressin and imipramine may be used for refractory cases of enuresis.

74. True or false: Depression in children frequently presents as an irritable rather than a depressed mood.

True.

75. What are the three leading causes of death in adolescents?

Accidents, homicide, and suicide. Together they cause about 75% of teenage deaths.

76. What is the most commonly abused illicit drug? Describe its effects on users.

Marijuana. Watch for a teenager who is withdrawn and has a decline in school performance. Other symptoms include amotivational syndrome (chronic use results in laziness and lack of motivation), time distortion, and "munchies" (eating binges during intoxication). No physical symptoms have been reported with withdrawal, but psychological cravings may be present. Marijuana is not dangerous in overdose (although patients may experience temporary dysphoria) and is a controversial teratogen (evidence weak).

77. What symptoms are associated with cocaine intoxication? Cocaine withdrawal?

Cocaine causes sympathetic stimulation (insomnia, tachycardia, mydriasis, hypertension, sweating) with hyperalertness and possible paranoia, aggressiveness, delirium, psychosis, or formications ("cocaine bugs"; patients think that bugs are crawling on them). Overdose can be fatal as a result of arrhythmia, myocardial infarction (MI), seizure, or stroke. During withdrawal the patient is sleepy, hungry (vs. anorexic with intoxication), and irritable with possible severe depression. Cocaine withdrawal is not dangerous, but psychological cravings usually are severe. Cocaine is teratogenic, causing vascular disruptions in the fetus.

78. Describe the symptoms of amphetamine intoxication.

Amphetamines are longer acting and associated more commonly with psychotic symptoms (patients may appear to be full-blown schizophrenics), but their effects are similar to those of cocaine.

79. Describe the effects of opioids. What symptoms are seen in withdrawal?

Heroin and other opioids cause euphoria, analgesia, drowsiness, miosis, constipation, and CNS depression. Overdoses can be fatal because of respiratory depression, which should be treated with **naloxone.** Because the drug often is taken intravenously, associated morbidity and mortality include endocarditis, HIV infection, hepatitis, cellulitis, and talc damage. Withdrawal is not life-threatening, but patients act as though they are going to die. Symptoms of withdrawal include gooseflesh, diarrhea, insomnia, abdominal cramping, and pain. Methadone or buprenorphine can be used to reduce acute withdrawal symptoms.

80. How do you recognize intoxication with lysergic acid diethylamide (LSD) or hallucinogenic mushrooms?

Symptoms of intoxication with LSD or mushrooms include hallucinations (usually visual vs. auditory in schizophrenia), mydriasis, tachycardia, diaphoresis, and perception and mood disturbances. Neither is dangerous in overdose—unless the patient thinks that he or she can fly and jumps out a window. No withdrawal symptoms or teratogenic effects have been reported. Users may experience "flashbacks" (brief feelings of being on the drug again even though none was taken) months to years later or a "bad trip" (acute panic reaction or dysphoria), which should be treated with reassurance or a benzodiazepine or antipsychotic, if needed.

81. How do you recognize phencyclidine (PCP) intoxication?

PCP intoxication causes LSD/mushroom symptoms plus confusion, agitation, and aggressive behavior. Also look for vertical and/or horizontal nystagmus, possible schizophrenic-like symptoms (e.g., paranoia, auditory hallucinations, disorganized behavior, speech). Overdose can be fatal because of convulsions, coma, and respiratory arrest. Treat with supportive care and urine acidification to hasten elimination. No withdrawal symptoms have been reported.

82. Describe the symptoms and signs of inhalant intoxication. Who is likely to abuse inhalants?

Inhalant intoxication (e.g., gasoline, glue, varnish remover) causes euphoria, dizziness, slurred speech, a feeling of floating, ataxia, or a sense of heightened power. It usually is seen in younger

teenagers (11 to 15 years old) because these substances are cheap, legal to buy, and readily available. Inhalants can be fatal in overdose as a result of respiratory depression, cardiac arrhythmias, or asphyxiation and may cause severe permanent sequelae (CNS, liver or kidney toxicity, peripheral neuropathy). There is no known withdrawal syndrome.

83. True or false: Benzodiazepines and barbiturates can be fatal in overdose but not in withdrawal.

False. Both can be fatal in overdose and withdrawal.

84. Describe the symptoms and signs of benzodiazepine or barbiturate intoxication.

Benzodiazepines and barbiturates cause sedation and drowsiness as well as disinhibition and reduced anxiety. They can be fatal in overdose as a result of respiratory depression; treat overdoses of a benzodiazepine with **flumazenil.** In withdrawal, death may result from seizures and/or cardiovascular collapse. Treat withdrawal on an inpatient basis with a long-acting benzodiazepine and gradually taper the dose over several days. Benzodiazepines and barbiturates are especially dangerous when mixed with alcohol because all three are CNS depressants.

85. What are the symptoms of caffeine withdrawal?

Headaches and fatigue.

86. What is the basic rule of thumb about the difference in symptoms between intoxication and withdrawal for the same drug?

The symptoms are usually the opposite of each other. For example, stimulants (e.g., cocaine, amphetamines) cause insomnia with intoxication and hypersomnolence in withdrawal, whereas depressants (e.g., alcohol, benzodiazepines, barbiturates) cause sedation with intoxication and insomnia in withdrawal.

CHAPTER 33

PULMONOLOGY

1. Describe the difference between obstructive and restrictive pulmonary disease on pulmonary function testing.

In chronic obstructive pulmonary disease (COPD), the functional expiratory volume in 1 second divided by the total forced vital capacity (FEV_1/FVC) is less than normal (the normal value [0.75 to 0.80] should be given in the question). In restrictive lung disease, FEV_1/FVC is often normal. FEV_1 may be equal in both conditions, but the ratio of FEV_1/FVC is always different.

2. What causes emphysema?

Emphysema is almost always a result of smoking (even second-hand smoke). If you have a young person with minimal smoke exposure (fewer than 5 years), then think of $alpha_1$-antitrypsin deficiency.

3. How do you recognize and treat asthma?

Watch for chronic wheezing in "allergic" children with a family history of asthma or allergies. In the acute setting, treat with $beta_2$ agonists. Use steroids if the attack is severe or does not respond to $beta_2$ agonists. Inhaled glucocorticoids (preferred agent), leukotriene modifiers (zafirlukast, montelukast, zileuton), long-acting beta-agonists, and cromolyn are prophylactic agents and are not used for acute attacks. Phosphodiesterase inhibitors (theophylline, aminophylline) are older agents that are now infrequently used. Do *not* prescribe beta blockers for asthmatics or patients with COPD; they block the $beta_2$ receptors that are needed to open the airways.

4. What is the concern with the use of long-acting beta-agonists (LABAs) in the treatment of asthma?

The bottom line is that the United States Federal Drug Administration (FDA) has recommended that LABAs not be used as solo agents in the treatment of asthma in children or adults because of an increased risk of death. The advisory recommends that LABAs not be used alone as initial therapy for asthma of any severity, that they not be added when asthma control is actively deteriorating, that they only be used long-term in patients whose asthma cannot be adequately controlled with other asthma controller medications, and that the LABA be discontinued, if possible, once asthma control is achieved.

5. What is a common cause of wheezing in children younger than age 2 years?

Respiratory syncytial virus (RSV) infection, which classically occurs in the winter and causes a fever. Asthma may also be the cause but usually is associated with a chronic history.

6. What should you think if a patient with acute asthma stops hyperventilating or has a normal carbon dioxide (CO_2) level?

Beware the asthmatic who is no longer hyperventilating or whose CO_2 is normal or rising. The patient should be hyperventilating, which causes low CO_2. If the patient seems calm or sleepy, do *not* assume that he or she is "okay." Such patients probably are crashing; they need an immediate arterial blood gas analysis and possible intubation. Fatigue alone is sufficient reason to intubate. Remember also that any patient with COPD may normally live with a higher CO_2 and lower oxygen (O_2) level. Treat the patient, not the laboratory value. If the patient is asymptomatic and talking to you, the laboratory value should not cause panic.

7. When should you intubate?

As a rough rule of thumb, think about intubation in any patient whose CO_2 is greater than 50 mm Hg or whose O_2 is less than 50 mm Hg, especially if the pH in either situation is less than 7.3 while the patient is breathing room air. Usually, unless the patient is crashing rapidly, a trial of oxygen by nasal cannula or face mask is given first. If it does not work or if the patient becomes too tired (use of accessory muscles is a good clue to the work of breathing), intubate. Clinical correlation is always required; patients with chronic lung disease may be asymptomatic at laboratory value levels that seem to defy reason. Alternatively, laboratory values may look great, but if the patient is becoming tired from increased work of breathing, intubation may be needed.

8. What should you do if a patient has a solitary pulmonary nodule on chest radiograph?

The first step is to compare the current film with old films (if available). If the lesion has not changed in more than 2 to 3 years, it is very likely to be benign. A nodule that has increased in size on serial imaging should be biopsied or excised. Computed tomography (CT) scans are used to evaluate and follow a solitary pulmonary nodule. A nodule that has a low probability of being malignant can be followed with serial CT scans. Positron emission tomography (PET) scan is used to evaluate intermediate probability nodules. A nodule that has a high probability of being malignant should be excised.

9. What classic clues point to the cause of a solitary pulmonary nodule?

- Immigrant: Think of tuberculosis; do a skin test.
- Southwest United States exposure: Think of *Coccidioides immitis.*
- Cave explorer, exposure to bird droppings; Ohio/Mississippi River valleys (Midwest): Think of histoplasmosis.
- Smoker older than age 50 years: Think of lung cancer; order bronchoscopy and biopsy.
- Person younger than 40 years with none of the previous: Think of hamartoma.

10. What should you know about pulmonary function in the setting of surgery?

A baseline chest radiograph is not part of the standard preoperative evaluation, but is often used for patients older than age 60 years or patients with known pulmonary or cardiovascular disease. Preoperative pulmonary function testing is somewhat controversial, and the question probably will not appear on the Step 2 examination. Overall, the best indicator of possible postoperative pulmonary complications is preoperative pulmonary function. The best way to reduce pulmonary complications postoperatively is to **stop smoking** preoperatively, especially when stopped at least 8 weeks before surgery. Aggressive pulmonary toilet, incentive spirometry, minimal narcotics, and early ambulation help prevent or minimize postoperative pulmonary complications. Lastly, remember that the most common cause of a postoperative fever in the first 24 hours is atelectasis.

11. How do you recognize and treat adult respiratory distress syndrome (ARDS)?

ARDS results from acute lung injury and causes noncardiogenic pulmonary edema, respiratory distress, and hypoxemia. Common causes are sepsis, major trauma, pancreatitis, shock, near-drowning, and drug overdose. Look for ARDS to develop within 24 to 48 hours of the initial insult. Classically, the patient has mottled/cyanotic skin, intercostal retractions, rales or rhonchi, and no improvement of hypoxia with oxygen administration. Radiographs show pulmonary edema with a normal cardiac silhouette (no cardiomegaly). Treat with intubation, mechanical ventilation with high percentage oxygen, and positive end-expiratory pressure while addressing the underlying cause (if possible).

12. How is pneumonia diagnosed?

The diagnosis of pneumonia usually is based on clinical findings (fever, rales or rhonchi) plus elevated white blood cell count and an abnormal chest radiograph consistent with pneumonia. Sputum and blood cultures usually are obtained before empirical antibiotic therapy is begun.

13. What is the difference between typical and atypical pneumonia?

Typical pneumonia is usually caused by bacteria such as *Streptococcus pneumoniae* or *Staphylococcus aureus*, the most common causes of pneumonia. Atypical pneumonia may be caused by influenza virus, *Mycoplasma*, *Chlamydia* spp., *Legionella*, *Haemophilus*, or adenovirus.

	TYPICAL PNEUMONIA	ATYPICAL PNEUMONIA
Prodrome	Short (<2 days)	Long (>3 days) (headache, malaise, body aches)
Fever	High (>102°F)	Low (<102°F)
Age	>40 yr	<40 yr
Chest radiograph	One distinct lobe involved	Diffuse or multilobe involvement
Pathogen	*Streptococcus pneumoniae*	Many (*Haemophilus, Mycoplasma, Chlamydia* spp.)
Antibiotic*	Ceftriaxone, broad-spectrum	Macrolides (e.g., azithromycin), doxycycline, or certain fluoroquinolones (e.g., levofloxacin, moxifloxacin)

*Avoid the temptation to pull out the "bigger-gun" antibiotics (very wide spectrum, potent) unless the patient is crashing or unstable.

14. What are the classic clinical clues for the different causative pathogens in pneumonia?

- **College student:** Think of *Mycoplasma* sp. (look for cold agglutinins) or *Chlamydia* sp.
- **Alcoholic:** Think of *Klebsiella* sp. ("currant jelly" sputum), *Staphylococcus aureus,* other enteric bugs (aspiration).
- **Cystic fibrosis:** Think of *Pseudomonas* sp. or *Staphylococcus aureus.*
- **Immigrant:** Think of tuberculosis.
- **COPD:** Think of *Haemophilus influenzae, Moraxella* sp.
- **Known tuberculosis with pulmonary cavitation:** Think of *Aspergillus* sp.
- **Silicosis** (metal, granite, pottery workers): Think of tuberculosis.
- **Exposure to air conditioner or aerosolized water:** *Legionella* sp.
- **HIV/AIDS:** Think of *Pneumocystis jiroveci* or cytomegalovirus (if you are shown koilocytosis).
- **Exposure to bird droppings:** Think of *Chlamydia psittaci* or histoplasmosis.
- **Child younger than 1 year of age:** Think of RSV.
- **Child 2 to 5 years of age:** Think of parainfluenza (croup).

15. What should you suspect if a child has recurrent pneumonias?

If the pneumonia always occurs in the same spot (especially the right middle and/or right lower lobe), it most likely is caused by foreign body aspiration. Remember that a foreign body is most likely to go down the right mainstem bronchus. This diagnosis should be considered especially if the child has no other signs of immunodeficiency (e.g., other types of infections, symptoms of cystic fibrosis) before or during the episodes. If immunodeficiency is the cause of recurrent pneumonias, the child should have a history of chronic bilateral lung problems and other types of infection.

16. What is "round" pneumonia?

Pneumonia may appear round, typically in children, which causes it to simulate a mass. In such cases involving children, assume pneumonia and treat appropriately. A follow-up x-ray can be obtained to confirm resolution, which is not usually required in children, who almost never develop lung malignancies. In an adult, a round pneumonia should be viewed with suspicion (more likely to be a malignancy) and further work-up with a CT scan is typically employed.

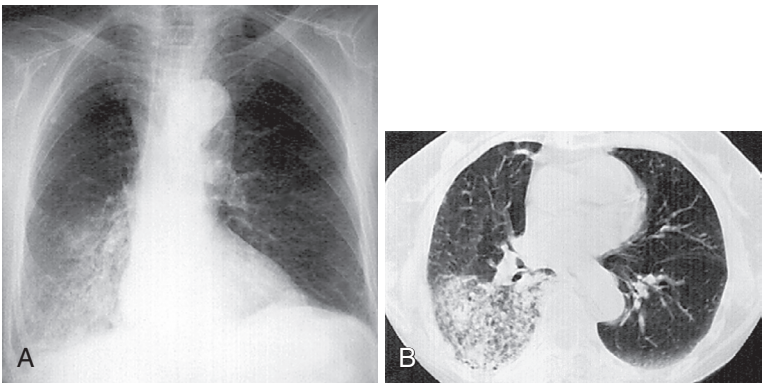

Figure 33-1. A and **B,** Consolidation in the right lower lobe, seen on front chest radiograph and computed tomography (CT), progressed despite antibiotic therapy. Biopsy proved bronchoalveolar carcinoma. (From Katz DS, Math KR, Groskin SA [eds]. Radiology secrets. Philadelphia: Hanley & Belfus, 1998, p 80, with permission.)

17. Why should you get a follow-up chest x-ray in all people older than age 40 years who develop pneumonia?

A follow-up chest x-ray is routine in those older than 40 years who develop pneumonia to make sure it clears after appropriate antibiotic treatment. If pneumonia does not clear by 4 to 6 weeks, suspect something other than bacterial pneumonia. The classic culprit is malignancy, specifically, **bronchoalveolar carcinoma,** which is a subtype of adenocarcinoma (Fig. 33-1). In addition, recurrent pneumonias in the same location in an adult may be caused by an endobronchial mass, whether benign or malignant.

18. What should you know about infant respiratory distress syndrome?

Infant respiratory distress syndrome is caused by atelectasis from a deficiency of surfactant; it is seen almost exclusively in premature infants and infants of diabetic mothers. Look for rapid, labored respirations, substernal retractions, cyanosis, grunting, and/or nasal flaring. Arterial blood gas shows hypoxemia and hypercarbia; radiograph shows diffuse atelectasis (described as diffuse, granular infiltrates). Treat with oxygen, give surfactant, and intubate if necessary. Complications include intraventricular hemorrhage and pneumothorax or bronchopulmonary dysplasia (complications of acute or chronic mechanical ventilation).

19. What prenatal tests help determine whether respiratory distress syndrome will occur?

Measurement of amniotic fluid in the pregnant mother can determine whether the fetus is producing adequate surfactant. A lecithin-to-sphingomyelin ratio greater than 2:1 or the presence of **phosphatidylglycerol** in the amniotic fluid indicates fetal lung maturity and a low likelihood of infant respiratory distress syndrome. The fluorescence polarization test reflects the ratio of surfactant to albumin in amniotic fluid and is a direct measurement of surfactant concentration. An elevated ratio indicates fetal lung maturity.

20. Define diaphragmatic hernia. How is it recognized clinically?

A defect in the diaphragm allows bowel to herniate into the chest. Diaphragmatic hernia is mentioned in the pulmonary section because it presents with respiratory difficulty, not gastrointestinal (GI) problems. Herniated bowel pushes on the developing lung and causes lung hypoplasia on the affected side. Look for a scaphoid abdomen and bowel sounds in the chest. Herniated bowel can be seen on the chest radiograph; 90% are left-sided.

21. How do you recognize and diagnose a tracheoesophageal fistula? How is it treated?

The most common type (85% of cases) of tracheoesophageal fistula is an esophagus with a blind pouch proximally and a fistula between a bronchus/carina and the distal esophagus (see Fig. 12-11). Look for a neonate with excessive oral secretions, coughing or cyanosis with attempted feedings, abdominal distention, and aspiration pneumonia. The diagnosis is made by the inability to pass a nasogastric tube; alternatively, an injection of air via a nasogastric tube under x-ray (i.e., fluoroscopy) shows only the proximal esophagus. Treatment is early surgical correction.

22. What is the most common lethal genetic disease in Caucasians? How do you recognize it?

Cystic fibrosis, which is an autosomal recessive disease. Always suspect cystic fibrosis in pediatric patients with rectal prolapse, meconium ileus, esophageal varices, recurrent pulmonary infections, or failure to thrive. The classic complaint from the mother is a "salty-tasting" baby. Patients also commonly have pancreatic insufficiency and infertility (98% of affected males and 50% of females); they may also develop cor pulmonale (right-heart failure).

23. How is cystic fibrosis diagnosed and treated?

Diagnosis is made by an abnormal increase in the electrolytes of the patient's sweat (sodium and chloride) and/or DNA testing. Treat with chest physical therapy, annual influenza vaccine, fat-soluble vitamin supplements, pancreatic enzyme replacement, bronchodilators, dornase alfa, and aggressive treatment of infections with antibiotics that cover *Staphylococcus, Haemophilus influenzae,* and *Pseudomonas* spp.

24. What should you do if a patient has a pleural effusion?

If you do not know the cause of the effusion (Fig. 33-2), consider thoracocentesis to examine the fluid in an attempt to determine its etiology. Common tests ordered on pleural fluid include Gram stain, culture and sensitivity testing (including tuberculosis culture), cell count with differential, glucose (low with infection), protein (high with infection), cytology (to look for malignancy), amylase (if pancreatitis is a suspected cause of effusion), triglycerides (if a chylous effusion is suspected), albumin, and lactate dehydrogenase (the last two tests help to determine whether the fluid is an exudate or transudate).

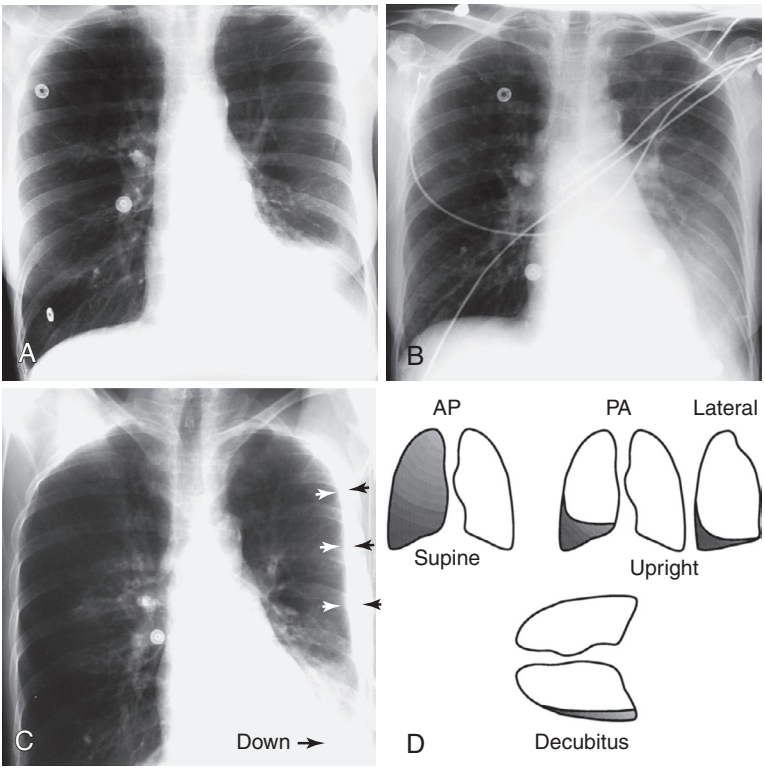

Figure 33-2. The appearance of pleural effusions depends on patient position. **A,** On an upright posteroanterior (PA) chest x-ray**,** a large left pleural effusion obscures the left hemidiaphragm, the left costophrenic angle, and the left cardiac border. **B,** On a supine anteroposterior (AP) view**,** the fluid runs posteriorly, causing a diffuse opacity over the lower two thirds of the left lung while the left hemidiaphragm remains obscured. This can easily mimic left lower lobe infiltrate or left lower lobe atelectasis. **C,** With a left lateral decubitus view**,** the left side of the patient is dependent, and the pleural effusion can be seen to be freely moving and layering *(arrows)* along the lateral chest wall. **D,** These findings are shown diagrammatically as well for a right pleural effusion**.** (From Mettler F. Essentials of radiology. 2nd ed., Philadelphia: Saunders, 2004, Fig. 3-80.)

RADIOLOGY

1. Cover the right-hand columns and specify what imaging study you should order for the following conditions.

TABLE 34–1. SCREENING AND/OR CONFIRMATORY RADIOLOGIC TESTS FOR DIFFERENT DISEASES

CONDITION	SCREENING (OR ONLY) TEST TO ORDER	CONFIRMATORY TEST	COMMENTS
Cardiovascular			
Aortic aneurysm	Abdominal US	CT with contrast	Screening US recommended for male smokers aged 65-75 years
Aortic dissection	CT with contrast	MRA or TEE	
Aortic trauma (tear)	CT with contrast	MRA or TEE	
Carotid stenosis	Duplex US	MRA	
Gastrointestinal			
Abdominal abscess	CT scan with contrast		
Abdominal trauma	FAST scan (Focused assessment with Sonography for Trauma) to assess for hemoperitoneum	CT with contrast	Laparotomy is the gold standard
Appendicitis	US (particularly in pregnant patients and children)	CT with contrast	Never truly confirmed until surgery
Bowel obstruction	Abdominal x-ray	CT with contrast	
Bowel perforation	Upright abdominal film/ chest x-ray	CT with contrast	
Cholecystitis	US	Nuclear hepatobiliary study (HIDA scan)	Look for gallbladder wall thickening and pericholecystic fluid on US
Choledocholithiasis	US	ERCP or MRCP	
Cholelithiasis	US		

TABLE 34-1. SCREENING AND/OR CONFIRMATORY RADIOLOGIC TESTS FOR DIFFERENT DISEASES —cont'd

CONDITION	SCREENING (OR ONLY) TEST TO ORDER	CONFIRMATORY TEST	COMMENTS
Diverticulitis	CT with contrast		No endoscopy acutely as there is a risk of perforation
Esophageal disease	Gastrografin or barium x-ray	CT with contrast (for rupture)	Endoscopy usually necessary as a follow-up study
GI bleeding	Endoscopy	Tagged red cell scan if unable to visualize on endoscopy	
Hematemesis	Endoscopy		
Meckel diverticulum	Meckel scan (nuclear medicine)		
Peptic ulcer disease	Endoscopy		
Pyloric stenosis	US	Barium x-ray	
Gynecologic			
Fibroids	US	MRI	
Ovarian disease	US	MRI	Laparoscopy may be needed
Pelvic mass (female)	US	MRI or CT with contrast or laparoscopy	
Pregnancy evaluation	US		Transvaginal US for early pregnancy; transabdominal for the remainder
Neurologic			
Acute stroke	Noncontrast CT	MRI	
Brain tumor	CT with contrast	MRI with contrast	
Head trauma	Noncontrast CT		
Intracranial hemorrhage	Noncontrast CT		
Multiple sclerosis	MRI		
Skull fracture	Noncontrast CT		
Orthopedic			
Arthritis	X-ray	MRI if more detailed evaluation is needed	
Bone metastases	Bone scan	PET scan	Plain x-rays for multiple myeloma

Continued

TABLE 34-1. SCREENING AND/OR CONFIRMATORY RADIOLOGIC TESTS FOR DIFFERENT DISEASES —cont'd

CONDITION	SCREENING (OR ONLY) TEST TO ORDER	CONFIRMATORY TEST	COMMENTS
Fracture	X-ray	Noncontrast CT	CT can pick up many fractures not seen on x-ray
Osteomyelitis	X-ray	Bone scan or tagged white blood cell nuclear scan	MRI without contrast can be helpful
Pelvic trauma	X-ray	Noncontrast CT	
Scaphoid fracture	X-ray	MRI	
Respiratory			
Chest mass	Chest x-ray	CT with contrast	
Chest trauma	Chest x-ray	CT with contrast	
Hemoptysis	Chest x-ray	Bronchoscopy or CT with contrast	
Pneumonia	Chest x-ray	CT with contrast	
Pulmonary embolism	CT with contrast	Pulmonary angiogram	Ventilation/perfusion nuclear scan if unable to tolerate radiation (pregnancy) or contrast
Pulmonary nodule	Chest x-ray	CT with contrast	May need PET scan to assess for malignancy
Urologic			
Hematuria (persistent)	CT scan with contrast (without contrast if *painful* hematuria)	Cystoscopy	
Hydronephrosis	US	CT with contrast	
Nephrolithiasis	Noncontrast CT	Intravenous pyelography rarely indicated or used	
Ureteral reflux	Voiding cystourethrogram (VCUG)		
Suspected urethral trauma	Retrograde urethrogram		

Note: With suspected GI perforation, do not use barium (it can cause a chemical peritonitis); use water-soluble contrast (e.g., Gastrografin).

CT, Computed tomography; *ERCP*, endoscopic retrograde cholangiopancreatography; *GI*, gastrointestinal; *hCG*, human chorionic gonadotropin; *HIDA*, hepatoiminodiacetic acid; *MRA*, magnetic resonance angiogram (an MRI test); *MRCP*, magnetic resonance cholangiopancreatography; *MRI*, magnetic resonance imaging; *PET*, positron emission tomography; *TEE*, transesophageal echocardiography; *US*, ultrasound.

RHEUMATOLOGY

1. What is the most common form of arthritis?

Osteoarthritis (at least 75% of cases), which is also called degenerative joint disease (Fig. 35-1).

2. If the cause of arthritis is in doubt, what should you do?

When in doubt, or if you suspect something other than osteoarthritis, obtain a radiograph of the affected joint and aspirate fluid. Examine the fluid for cell count and differential, glucose, bacteria (Gram stain and culture), and crystals.

3. How do you distinguish among the common causes of arthritis?

	OA	RA	GOUT	PSEUDOGOUT	SEPTIC
Usual age/sex	Older adults	Women 20-45 yr	Older men	Older adults	Any age
Classic joints	DIP, PIP, hip, knee	PIP, MCP, wrist	Big toe	Knees, elbows	Knee
Joint fluid WBC	<2000	>2000	>2000	>2000	>50,000
% Neutrophils	<25%	>50%	>50%	>50%	>75%

DIP, Distal interphalangeal joints; *MCP*, metacarpophalangeal joints; *OA*, osteoarthritis; *PIP*, proximal interphalangeal joints; *RA*, rheumatoid arthritis; *WBC*, white blood cells.

4. What other clues point to a diagnosis of osteoarthritis?

Osteoarthritis typically occurs in those older than age 40 years and has few signs of inflammation on examination, thus the joints are not hot, red, or tender like in the other four types of arthritis listed earlier. Look for Heberden nodes (visible and palpable distal interphalangeal [DIP] joint osteophytes; Fig. 35-2) and Bouchard nodes (proximal interphalangeal [PIP] joint osteophytes), worsening of symptoms after use and in the evening, bony spurs, and increasing incidence with age. Treat with weight reduction and as-needed nonsteroidal antiinflammatory drugs (NSAIDs) or acetaminophen.

5. What clues point to a diagnosis of rheumatoid arthritis?

Rheumatoid arthritis often causes systemic symptoms (fever, malaise, subcutaneous nodules, pericarditis, pleural effusion, uveitis), prolonged morning stiffness, and swan neck and boutonnière deformities. The diagnosis is often made by an elevated sedimentation rate or C-reactive protein (CRP) and positive rheumatoid factor, which is present in most adults but often negative in children. Radiographs and magnetic resonance imaging (MRI) can also support the diagnosis. General treatment strategies reflect the fact that the destruction of affected joints caused by inflammation occurs early in the course of rheumatoid arthritis. The patient should be offered treatment with disease modifying antirheumatic drugs (DMARDs) as soon as possible after the onset of disease. Escalate the intensity of treatment until synovitis and inflammation have improved.

There are five general classes of medications used for the treatment of rheumatoid arthritis, with DMARDs forming the backbone of treatment. Treatment options include the following: analgesics (from acetaminophen to narcotics), NSAIDs, glucocorticoids, nonbiologic DMARDs (methotrexate, sulfasalazine,

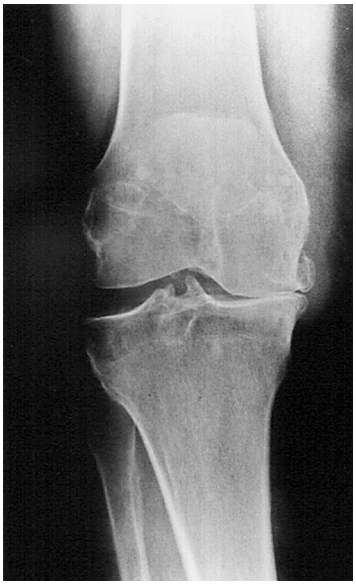

Figure 35-1. Degenerative joint disease of the knee. Significant joint space narrowing at the medial compartment of the knee is combined with osteophyte formation at the medial tibial plateau and femoral condyle. The joint space narrowing results in varus alignment at the knee (normal = slight valgus alignment). (From Katz DS, Math KR, Groskin SA [eds]. Radiology secrets. Philadelphia: Hanley & Belfus, 1998, p. 271, with permission.)

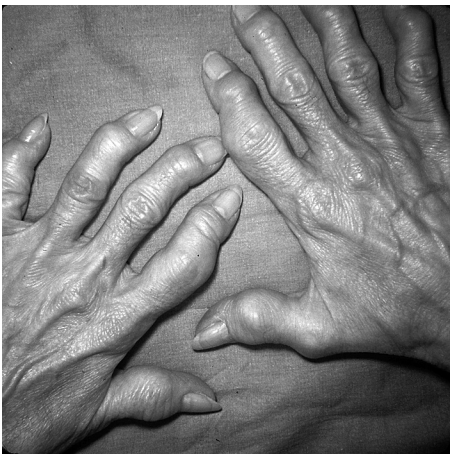

Figure 35-2. Osteoarthritic hands with Heberden (distal interphalangeal) and Bouchard (proximal interphalangeal) nodes on both index fingers and thumbs. See Plate 67. (From Canale ST, Beaty JH. Campbell's operative orthopaedics. 11th ed. Philadelphia: Mosby, 2007, Fig. 70-4.)

leflunomide, hydroxychloroquine, and minocycline), and biologic DMARDs. Biologic DMARDs include tumor necrosis factor (TNF) inhibitors (etanercept, infliximab, and adalimumab), an interleukin-1 receptor antagonist (anakinra), a monoclonal antibody (rituximab), and biologic response modifiers (abatacept).

6. What clues point to a diagnosis of gout?

Gout classically begins with podagra (gout in the big toe). Also look for high uric acid levels (not always present), tophi (subcutaneous uric acid deposits that look like punched-out lesions on bone radiographs), **needle-shaped crystals with negative birefringence** in the joint fluid, and male gender (more commonly affected than female gender). Alcohol and protein-rich foods may precipitate an attack. Colchicine or NSAIDs (but *not* aspirin, which causes decreased excretion of uric acid by the kidney) are used for acute attacks. For maintenance therapy, high fluid intake, alkalinization of the urine, and/or allopurinol or probenecid (neither drug is for acute attacks) may be used.

7. What causes pseudogout? How is it diagnosed?

Pseudogout is caused by deposition of calcium pyrophosphate crystals into joints. Look for **rhomboid crystals** with **weakly positive birefringence** (vs. negative birefringence with gout crystals in the joint fluid).

8. What clues point to a diagnosis of septic arthritis? What are the common causes?

In septic arthritis, Gram stain usually reveals bacteria in the synovial fluid. *Staphylococcus aureus* is the most common organism except in sexually active young adults, in whom the most common pathogen is *Neisseria gonorrhoeae.* Obtain blood cultures in addition to synovial fluid cultures because the pathogen usually reaches the joint via the hematogenous route. Also obtain urethral swabs and cultures in appropriate patients.

9. Name some other causes of arthritis.

- Prior trauma
- Lupus and other collagen vascular diseases (e.g., scleroderma)
- Psoriasis
- Inflammatory bowel disease
- Lyme disease
- Ankylosing spondylitis
- Reactive arthritis
- Hemophilia
- Paget disease
- Hemochromatosis, Wilson disease
- Neuropathy (i.e., Charcot joint)

10. True or false: Psoriasis can cause an arthritis that resembles osteoarthritis.

False. The arthritis resembles rheumatoid arthritis. On the Step 2 examination, look for psoriatic skin lesions to make an easy diagnosis (Fig. 35-3). The arthritis usually affects the hands and feet, and though it resembles rheumatoid arthritis, the rheumatoid factor is negative. NSAIDs are first-line therapy. Other treatments include nonbiologic DMARDS (methotrexate, PUVA, retinoic acid derivatives, and cyclosporine) and biologic DMARDS, including TNF inhibitors (etanercept, infliximab, adalimumab, and golimumab).

11. Describe the hallmarks of ankylosing spondylitis.

Ankylosing spondylitis is associated with human leukocyte antigen B27 (**HLA-B27**). Most often a 20- to 40-year-old man with a positive family history presents complains of back pain and morning stiffness. Patients may assume a bent-over posture. The sacroiliac joints are primarily affected, and radiographs may reveal a **"bamboo" spine** (Fig. 35-4). Patients have other autoimmune type symptoms, such as fever, elevations in erythrocyte sedimentation rate and CRP, and anemia. Some develop

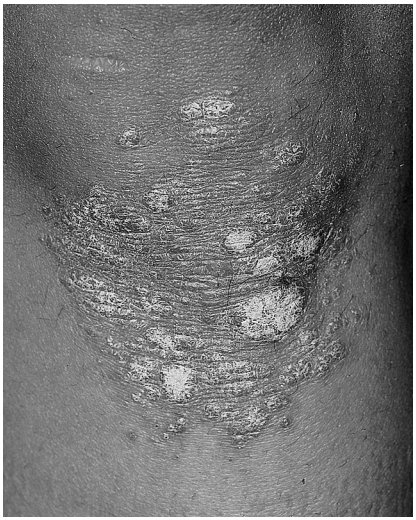

Figure 35-3. Psoriasis. Typical oval plaque with well-defined borders and silvery scale. See Plate 68. (From Habif TP. Clinical dermatology. 5th ed. Mosby, 2009, Fig. 8-1).

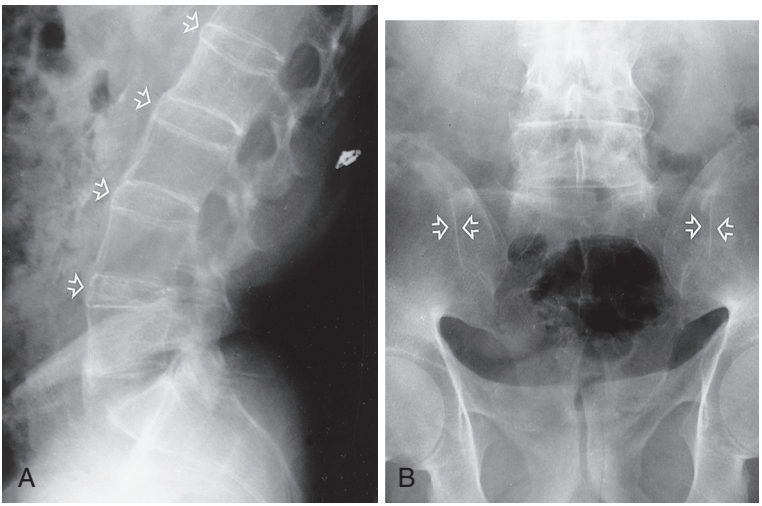

Figure 35-4. Ankylosing spondylitis. **A,** A lateral view of the lumbar spine demonstrates calcific bridging across the disk spaces (*arrows*), causing the typical "bamboo spine" appearance. **B,** Anteroposterior view of the pelvis shows that the sacroiliac joints *(arrows)* are not easily visualized as a result of fusion of both sacroiliac joints. (From Mettler F. Essentials of radiology. 2nd ed. Philadelphia: Saunders, 2004, Fig. 8-39.)

uveitis. Treat with NSAIDs, methotrexate, sulfasalazine, or TNF antagonists (etanercept, infliximab, adalimumab).

12. How do you recognize reactive arthritis as the cause of arthritis?

Reactive arthritis also is associated with HLA-B27. The classic triad of symptoms consists of **urethritis** (caused by chlamydial infection), **conjunctivitis,** and **arthritis** ("*can't pee, can't see, can't climb a tree*"). Reactive arthritis may also follow enteric bacterial infections. Superficial oral and penile ulcers are common. Diagnose and treat the sexually transmitted disease, and use NSAIDs for arthritis. Also treat the patient's sexual partners.

13. Why do patients with hemophilia get arthritis?

Recurrent hemarthroses (bleeding into the joints) can cause a debilitating arthritis. Treat with acetaminophen. Avoid aspirin and other NSAIDs because of bleeding concern.

14. What clues point to Lyme disease as the cause of arthritis?

Look for a history of a tick bite or hiking in the woods, **erythema chronicum migrans** rash (Fig. 35-5), and migratory arthritis (later). Treat *Borrelia burgdorferi,* the causative bacteria of Lyme disease, with doxycycline, amoxicillin, or cefuroxime. Avoid doxycycline in children younger than age 8 years and in pregnant or lactating women.

15. True or false: One of the major Jones criteria for the diagnosis of rheumatic fever is arthritis.

True. Migratory polyarthritis is one of the major Jones criteria. Look for a history of strep throat. The other major criteria are carditis, chorea, erythema marginatum, and subcutaneous nodules.

16. Why do patients with sickle cell disease often have arthritis?

Patients frequently experience arthralgias (pain) from ischemic sickle crises, but the classic cause of arthritis is avascular necrosis (e.g., hip arthritis from avascular necrosis of the femoral head).

17. Define Charcot joint. What clues point to its presence?

A Charcot joint is seen most commonly in diabetes but also occurs in other neuropathies. A lack of sensation causes the patient to overuse or misuse joints, which become deformed and painful. The best treatment is prevention. After even seemingly mild trauma, patients with neuropathy in the area of the trauma need radiographs to rule out fractures.

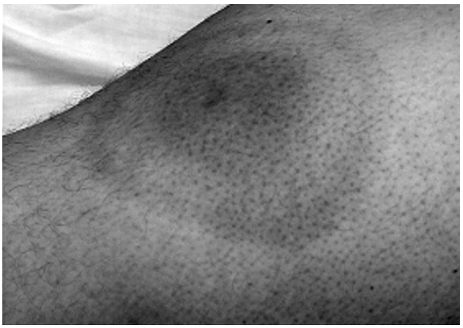

Figure 35-5. Erythema migrans rash of Lyme disease. Bull's eye lesion on lateral thigh. See Plate 69. (From Firestein GS, Budd RC, Gabriel SE, et al. Kelley's textbook of rheumatology. 9th ed. Philadelphia: Saunders, 2012, Fig. 110-1.Courtesy Juan Salazar, MD, University of Connecticut Health Center.)

18. What about lupus erythematosus and other autoimmune disorders as a cause of arthritis?

With lupus erythematosus, inflammatory bowel disease, and other autoimmune diseases, symptoms of the primary disease help make these diagnoses on the USMLE examination.

19. How do hemochromatosis and Wilson disease cause arthritis?

Via deposition of excessive iron (hemochromatosis) or copper (Wilson disease) into the joints.

20. What generalized systemic signs of inflammation may suggest an autoimmune disorder?

Systemic signs and symptoms of inflammation include elevations in erythrocyte sedimentation rate and CRP, fever, anemia of chronic disease, fatigue, and weight loss. If these symptoms are present (especially in a woman of reproductive age), consider the possibility of an autoimmune disease.

21. Describe the hallmarks of systemic lupus erythematosus (SLE).

SLE can cause malar rash, discoid rash, photosensitivity, kidney damage, arthritis, pericarditis and pleuritis, positive **antinuclear antibody (ANA),** positive anti-Smith antibody, positive syphilis results (on the Venereal Disease Research Laboratory and rapid plasmin reagin screening tests), positive lupus anticoagulant, blood disorders (thrombocytopenia, leukopenia, anemia, or pancytopenia), neurologic disturbances (depression, psychosis, seizures), and oral ulcers. Any of these may be presenting symptoms. Use the ANA titer as a screening test, and confirm with the **anti-Smith antibody** test. Treat with NSAIDs, hydroxychloroquine, corticosteroids, or immunosuppressive/immunomodulating agents (methotrexate, cyclophosphamide, cyclosporine, azathioprine, mycophenolate, tacrolimus, leflunomide, or belimumab).

22. Describe the hallmarks of scleroderma.

Scleroderma (also known as progressive systemic sclerosis) classically presents with **CREST** symptoms (**c**alcinosis, **R**aynaud phenomenon, **e**sophageal dysmotility with dysphagia, **s**clerodactyly, and **t**elangiectasia), heartburn, and masklike, leathery facies. Use the ANA test for screening; confirm the diagnosis with the **anticentromere antibody** test (for CREST symptoms only) and the **antitopoisomerase antibody** (for full-blown scleroderma). Treatment depends on the symptoms. Sclerotic skin lesions can be treated with topical glucocorticoids, calcipotriol, or methotrexate. Systemic therapy depends on the organs affected.

23. What are the hallmarks of Sjögren syndrome?

Sjögren syndrome causes dry eyes (keratoconjunctivitis sicca) and dry mouth (xerostomia) and often is associated with other autoimmune diseases. Treat with eye drops and good oral hygiene.

24. What are the signs and symptoms of dermatomyositis?

Dermatomyositis causes polymyositis (see question 29) plus skin involvement (a **heliotrope rash around the eyes** with associated periorbital edema is classic; Fig. 35-6). Patients usually have trouble rising from a chair or climbing steps because of the effects on proximal muscles. Muscle enzymes are elevated, and electromyography is irregular. Muscle biopsy establishes the diagnosis. Affected patients have an increased incidence of malignancy.

25. With what is polyarteritis nodosa associated? How is it diagnosed?

Polyarteritis nodosa is a type of vasculitis classically associated with hepatitis B infection and cryoglobulinemia. Symptoms include fever, abdominal pain, weight loss, renal disturbances, and/or peripheral neuropathies. Laboratory abnormalities include elevations in erythrocyte sedimentation rate and CRP, leukocytosis, anemia, and hematuria or proteinuria. Patients often have a positive **antineutrophil cytoplasmic antibody (ANCA)** titer. The vasculitis involves medium-sized vessels. Biopsy of an affected organ is the gold standard for diagnosis.

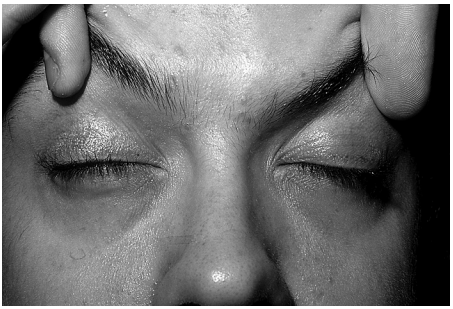

Figure 35-6. Dermatomyositis. Heliotrope (violaceous) discoloration around the eyes and periorbital edema. See Plate 70. (From Habif TP. Clinical dermatology. 5th ed. Philadelphia: Mosby, 2009, Fig. 17-19.)

26. Describe the usual presentation of Kawasaki disease. How is it treated?

Kawasaki disease usually affects children younger than 5 years; it is more common in Japanese and female children. Symptoms include truncal rash, high fever (which lasts longer than 5 days), conjunctival injection, cervical lymphadenopathy, strawberry tongue, late skin desquamation of palms and soles, and/or arthritis. Patients may develop coronary vessel vasculitis and subsequent aneurysms, which may thrombose and cause a myocardial infarction (MI). Kawasaki disease should be suspected in any child who has a heart attack. Treat during the acute stage with aspirin and intravenous immunoglobulins to reduce the risk of coronary aneurysm.

27. How does Takayasu arteritis present?

Takayasu arteritis tends to affect Asian women between the ages of 15 and 30 years. It is called the "pulseless disease" because you may not be able to feel the pulse or measure blood pressure on the affected side. The vasculitis affects the aortic arch and its branches. Carotid involvement may cause neurologic signs or stroke, and congestive heart failure is not uncommon. Angiogram shows the characteristic lesions. Treat with steroids.

28. How do you recognize Behçet syndrome?

On the Step 2 examination, Behçet syndrome classically presents in young men in their 20s with painful oral and genital ulcers. Patients may also have uveitis, arthritis, and other skin lesions (especially erythema nodosum). Steroids are the mainstay of therapy.

29. How do you distinguish among fibromyalgia, polymyositis, and polymyalgia rheumatica?

	FIBROMYALGIA	POLYMYOSITIS	POLYMYALGIA RHEUMATICA
Classic age/sex	Young adult women	Female aged 40-60 yr	Female >50 yr
Location	Various	Proximal muscles	Pectoral and pelvic girdles, neck
ESR	Normal	Elevated	Markedly elevated (often >100)
EMG/biopsy	Normal	Abnormal	Normal

Continued

	FIBROMYALGIA	POLYMYOSITIS	POLYMYALGIA RHEUMATICA
Classic findings	Anxiety, stress, insomnia, point tenderness over affected muscles	Elevated CPK, abnormal EMG/ biopsy, higher risk for cancer	Temporal arteritis, great response to steroids, very high ESR, older patients
Treatment	Antidepressants, NSAIDs, pregabalin, rest	Steroids	Steroids

CPK, Creatine phosphokinase; *EMG*, electromyography; *ESR*, erythrocyte sedimentation rate; *NSAIDS*, nonsteroidal antiinflammatory drugs.

30. Give the basic facts of Paget disease. How is it linked with cancer?

In Paget disease, bone is broken down and regenerated, often simultaneously. It usually is seen in persons older than 40 years and is more common in men. Often it is discovered in an asymptomatic patient through a radiograph. Classic cases involve the pelvis and skull; watch for a person who has had to buy larger-sized hats. Patients may complain of bone pain, arthritis, or hearing loss. **Alkaline phosphatase** is markedly elevated in the presence of normal calcium and phosphorus levels. The risk of osteosarcoma is increased in affected bones. The main treatment is the antiresorptive agents (e.g., zoledronic acid, alendronate, risedronate, pamidronate).

31. If a pediatric patient has uveitis and an inflammatory arthritis, but the rheumatoid factor is negative, what disease should you suspect?

Rheumatoid arthritis. The rheumatoid factor is often negative in the pauciarticular variant. Affected patients commonly develop uveitis.

SHOCK

1. Define shock.

Shock is a state in which blood flow to and perfusion of peripheral tissues is inadequate to sustain life. Although they are not included in a rigid definition of shock, for USMLE purposes, hypotension and oliguria or anuria are associated findings. Tachycardia is also usually present.

2. List the five primary clinical types of shock.

Hypovolemic, cardiogenic, septic, anaphylactic, and neurogenic.

3. What should you do if a patient is in shock?

Keep the patient alive with the ABCs (airways, breathing, and circulation) while you look for the cause of the shock. Give oxygen and fluids unless the patient is in congestive heart failure. If congestive heart failure is present, avoid fluids.

4. How should fluids be given if a patient is in shock?

Many patients in shock need fluid. The standard intravenous bolus is 10 to 20 mL/kg of normal saline or lactated Ringer solution; infuse 1 to 2 L as fast as it will go. Then reassess the patient to determine whether the bolus helped; positive signs include increases in blood pressure and urine output. Do *not* be afraid to give a second bolus if the first bolus leads to no improvement. Watch for fluid overload, which may cause congestive heart failure. Make sure that no bilateral crackles can be heard on lung examination. Place a Foley catheter to ensure accurate monitoring of urine output.

5. What should you do if fluid challenges fail to raise the blood pressure?

Use invasive hemodynamic monitoring (i.e., Swan-Ganz catheter) to help determine the cause of the shock and to guide therapeutic decisions.

6. What are the classic parameters of each type of shock?

TYPE OF SHOCK	CO	PCWP	SVR	SVO_2
Septic (early)	High	Low	Low	High
Hypovolemic	Low	Low	High	Low
Cardiogenic	Low	High	High	Low
Neurogenic	Low	Low	Low	Low
Anaphylactic	High (but can be variable)	Low	Low	Low

CO, Cardiac output; *PCWP*, pulmonary capillary wedge pressure; *SVR*, systemic vascular resistance; SVO_2, systemic venous oxygen saturation.

With anaphylactic shock, the cause is usually obvious because of a temporal relation to a common culprit (see question 11).

7. Specify the usual findings in patients with neurogenic shock.

Patients usually have a history of severe central nervous system (CNS) trauma or hemorrhage and flushed skin. The heart rate may be normal.

8. How do you recognize septic shock?

Look for fever, leukocytosis (unless the patient is on chemotherapy or has an immunosuppressive condition such as AIDS), skin that is flushed and warm to the touch, and extremes of age. Start broad-spectrum antibiotics after "pan-culturing" (blood, sputum, and urine cultures plus others as dictated by history).

9. What clues suggest cardiogenic shock?

Look for a history of myocardial infarction (MI), congestive heart failure, or chest pain. Assess patients for risk factors for coronary artery disease. Most patients have cold, clammy skin and look pale. Distended neck veins and pulmonary congestion (as demonstrated by physical examination and/or chest radiograph) are usually present.

10. How do you recognize hypovolemic shock?

Look for a history of fluid loss (hemorrhage, diarrhea, vomiting, sweating, use of diuretics, inability to drink water). Patients have cold, clammy skin and look pale. Fluid loss may be internal, as with a ruptured abdominal or thoracic aortic aneurysm and obstruction or infarction of the spleen, pancreas, or bowel. The postoperative state may also lead to hypovolemic shock. Patients usually have orthostatic hypotension, tachycardia, sunken eyes, tenting of the skin, and sunken fontanelle (young children).

11. What clues suggest anaphylactic shock?

Look for a history of recent exposure to the common culprits: Bee stings, peanuts, shellfish, penicillins, sulfa drugs, or any new medication. Treat with **epinephrine** and fluids. Administer oxygen, and intubate if necessary. A tracheostomy or cricothyroidotomy should be performed if laryngeal edema prevents intubation. Antihistamines are helpful primarily when the reaction is mild. Use corticosteroids when the reaction is prolonged or severe, but note that they are not first-line drugs in the treatment of anaphylaxis. Monitor all patients for at least 6 hours after the initial reaction.

12. What clues suggest pulmonary embolus as a cause of shock?

Look for deep venous thrombosis (positive **Homan sign** with painful, swollen leg) or risk factors for deep venous thrombosis. Remember the **Virchow triad:** Endothelial damage, stasis, and hypercoagulable state. Watch for postoperative status (especially after orthopedic or pelvic surgery) or a history of recent delivery (amniotic fluid embolus) or bone fractures (fat emboli). Patients classically have chest pain, tachypnea, shortness of breath, right-axis shift on electrocardiogram (ECG), and positive computed tomography (CT) pulmonary angiography or ventilation/perfusion scan. Heparin or a low molecular weight heparin should be administered to prevent further clotting and emboli.

13. How do you recognize pericardial tamponade as a cause of shock?

Look for a history of a stab wound in the left side of the chest and distended neck veins. Perform pericardiocentesis emergently in the setting of shock.

14. Explain toxic shock syndrome.

Toxic shock syndrome usually presents in a woman of reproductive age who leaves her tampon in place too long. Look for skin desquamation. It is caused by a *Staphylococcus aureus* toxin.

15. What clues suggest Addison disease as a cause of shock?

Patients usually have a history of steroid use, hyperkalemia, and hyponatremia. Treat with steroids and large volumes of normal saline.

16. What is the most important point to remember if a patient is in shock?

The ABCs. Patients in shock often need heroic measures to survive and are among the exceptions to the "wait-and-see" and "be conservative" rules that are usually favored by USMLE examiners. Intubate at the drop of a hat, do not feed the patient, and avoid narcotics if possible. Mental status changes are often an important clue to impending doom. Also monitor the ECG, vital signs, Swan-Ganz parameters (although this is not being used as much anymore), urine output, arterial blood gas, and hemoglobin and hematocrit.

17. Discuss the use of dobutamine, dopamine, norepinephrine, and isoproterenol to support blood pressure in the setting of shock.

- **Dobutamine** is a beta_1 agonist used to increase cardiac output by increasing contractility; it is the intensive care equivalent of digoxin.
- **Dopamine** affects dopamine receptors at low doses and results in selective vasodilation (the traditional use for renal perfusion is questionable). At higher doses, its beta_1 agonist effects increase contractility. At the highest doses, dopamine has alpha_1 agonist effects and causes vasoconstriction. Note that this differential effect is debated but still could be tested.
- **Norepinephrine** is used for its alpha_1 agonist effects, but it also has beta_1 effects. It is given primarily to patients with hypotension to increase peripheral resistance so that perfusion to vital organs can be maintained.
- **Isoproterenol** is used for its beta_1 and beta_2 effects in hypovolemic, septic, and cardiogenic shock.

18. Discuss the use of phenylephrine, epinephrine, and milrinone in the setting of shock.

- **Phenylephrine** is used for its alpha_1 agonist effects; it is similar to norepinephrine but has no beta effects.
- **Epinephrine** is used in patients with cardiac arrest and anaphylaxis for its alpha and beta effects.
- **Milrinone** and **amrinone** are phosphodiesterase inhibitors. They are used in patients with refractory heart failure (they are not first-line agents) because they have a positive inotropic effect via potentiation of cyclic adenosine monophosphate, but they cannot be used in hypotensive patients.

CHAPTER 37

SMOKING

1. Does smoking really deserve its own chapter in this book?

Smoking is the single most significant source of preventable morbidity and premature death in the United States. This is a recurrent theme on the USMLE, so whenever you are not sure which risk factor to choose to reduce morbidity or mortality, smoking is a safe guess.

2. How is smoking related to heart disease?

Smoking is the best risk factor to eliminate for prevention of deaths related to heart disease; it is responsible for 30% to 45% of such deaths in the United States. This risk is decreased by 50% within 1 year of quitting, and by 15 years after quitting, the risk is the same as for someone who has never smoked.

3. What cancers are more likely in smokers?

Smoking increases the risk for cancers of the lung (smoking causes 85%-90% of cases), oral cavity (90% of cases), esophagus (70%-80% of cases), larynx, pharynx, bladder (30%-50% of cases), kidney (20%-30%), pancreas (20%-25%), cervix, stomach, colon, and rectum.

4. Describe the effect of smoking on the lung.

Lung cancer and chronic obstructive pulmonary disease (COPD; emphysema, chronic bronchitis, and bronchiectasis) are a result of smoking. Emphysema almost always results from smoking; if the patient is very young or has no smoking history, you should consider **alpha$_1$-antitrypsin deficiency.** Although the changes of emphysema are irreversible, the risk of death still decreases if the patient stops smoking.

5. What about second-hand smoke?

Second-hand smoke has been proved to be a risk factor for lung cancer and other lung disease. The risk increases linearly with increasing exposure. When parents smoke, their exposed children are at an increased risk for asthma and upper respiratory infections, including otitis media.

6. What other bad things does smoking do?

Smoking retards the healing of peptic ulcer disease, and cessation stops the development of **Buerger disease** (Raynaud symptoms in a young male smoker). Smoking by a pregnant woman increases the risk of low birth weight, prematurity, spontaneous abortion, stillbirth, and infant mortality. Cessation of smoking preoperatively is the best way to decrease the risk of postoperative pulmonary complications, especially if it is stopped at least 8 weeks before surgery.

7. True or false: Women who smoke cannot take birth control pills.

True—if the woman is older than age 35 years and smokes or is younger than 35 years and smokes 15 or more cigarettes per day. The risk of thromboembolism is increased sharply in women who smoke and take birth control pills. Postmenopausal women, however, can take estrogen therapy regardless of smoking status.

8. So what is the bottom line for the boards?

Smoking is a very dangerous habit that should be avoided.

UROLOGY

1. Cover the right-hand columns and specify the classic differences between testicular torsion and epididymitis. What imaging test can diagnose and distinguish these two conditions?

	TESTICULAR TORSION	EPIDIDYMITIS
Age	Younger than 30 yr (usually prepubertal)	Older than 30 yr*
Appearance	Testis may be elevated into the inguinal canal; swelling	Swollen testis, overlying erythema, urethral discharge/urethritis, prostatitis
Prehn sign	Pain stays the same or worsens	Pain decreases with testicular elevation
Treatment	Immediate surgery to salvage testis; surgical orchiopexy for both testes	Antibiotics*

*In men younger than 50 years, epididymitis is commonly caused by sexually transmitted disease (chlamydial infection and gonorrhea). Treat accordingly. In men older than age 50 years, epididymitis is commonly caused by urinary tract infection (e.g., *Escherichia coli*). Treat with trimethoprim-sulfamethoxazole or ciprofloxacin.

Ultrasound is the diagnostic test of choice in the setting of testicular/scrotal pain. It can easily differentiate between these two conditions as well as visualize testicular tumors (which sometimes present with pain, although classically they are painless).

2. How does testicular cancer usually present? Describe the major risk factors, histology, and treatment.

Testicular cancer usually presents as a painless testicular mass in a young man (15-35 years old). The main risk factor is cryptorchidism. Roughly 90% are germ cell tumors; the most common type is **seminoma.** Testicular cancer generally is treated with orchiectomy and radiation; if disease is widespread, use chemotherapy. Alpha-fetoprotein (AFP) is a marker for yolk sac tumors; human chorionic gonadotropin is a marker for choriocarcinoma. Leydig cell tumors may secrete androgens and cause precocious puberty.

3. How is renal cell carcinoma diagnosed and treated?

Painless hematuria (gross or microscopic) is the most typical presenting sign. Patients rarely complain of the classic triad of hematuria, flank pain, and a palpable flank mass. Computed tomography (CT) scan (preferred over intravenous pyelography) is a good initial diagnostic test (Fig. 38-1). Treatment for disease confined to the kidney or with extension limited to renal vein invasion (classic) is surgical resection. With other organ invasion or distant metastatic disease (usually to lung or bone), immunotherapy (e.g., interleukin-2) is the preferred treatment.

4. What is the classic cause of orchitis? How is it treated? Does it usually cause infertility?

Mumps can cause orchitis, which classically presents with a painful, swollen testis in a postpubertal male. The best treatment is prevention (immunization against the mumps virus). Mumps orchitis

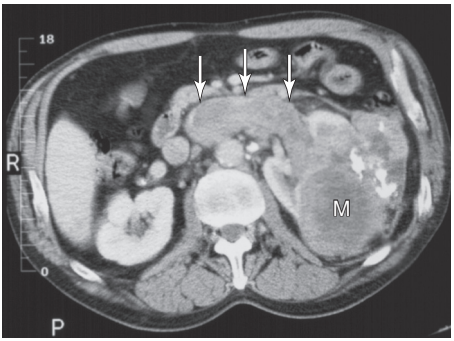

Figure 38-1. Renal cell carcinoma. A computed tomography (CT) scan at the mid portion of the kidneys demonstrates M, a large left renal mass that extends into the renal vein and into the inferior vena cava *(arrows).* (From Mettler F. Essentials of radiology. 2nd ed. Philadelphia: Saunders, 2004, Fig. 7-25.)

rarely causes sterility because it is usually unilateral. Epididymo-orchitis is more common and typically caused by spread from adjacent bacterial epididymitis.

5. What are the symptoms and sequelae of benign prostatic hyperplasia (BPH)?

BPH can cause urinary hesitancy, intermittency, terminal dribbling, decreased size and force of the urinary stream, sensation of incomplete emptying, nocturia, urgency, dysuria, and frequency. It may result in acute urinary retention, urinary tract infections, hydronephrosis, and even kidney damage or failure in severe cases.

6. How is BPH treated?

Medical therapy, which is started when the patient becomes symptomatic, includes long-acting alpha$_1$ blockers (e.g., terazosin, doxazosin, tamsulosin, alfuzosin, silodosin) and 5-alpha-reductase inhibitors (finasteride, dutasteride). Transurethral resection of the prostate (TURP) is used for more advanced cases, especially with repeated urinary tract infections, urosepsis, urinary retention, and/or hydronephrosis or kidney damage caused by reflux. Surgical prostatectomy is used in some patients, but is associated with a higher complication rate.

7. How do you recognize and manage acute urinary retention?

Acute urinary retention generally presents with abdominal pain; palpation of a full, distended bladder on abdominal examination; a history of BPH in men; and a lack of urination in the past 24 hours or longer. The first step is to empty the bladder. If you cannot pass a regular Foley catheter, consider the use of a larger catheter with a firm Coude tip, or alternatively do a suprapubic tap to drain the bladder. Then address the underlying cause—usually BPH, which in this setting is generally treated with TURP.

8. What are the common causes of impotence?

Impotence is caused most commonly by vascular problems and atherosclerosis. Medications are also a common culprit (especially antihypertensive and antidepressant agents). Diabetes can cause impotence through vascular (increased atherosclerosis) or neurogenic (diabetic autonomic neuropathy) compromise. Patients undergoing dialysis are often impotent. Remember "**p**oint and **s**hoot": Parasympathetics mediate erection; **s**ympathetics mediate ejaculation.

The history often gives you a clue if the cause of impotence is psychogenic. Look for a normal pattern of nocturnal erections, selective dysfunction (the patient has normal erections when masturbating but not with his partner), and a history of stress, anxiety, or fear.

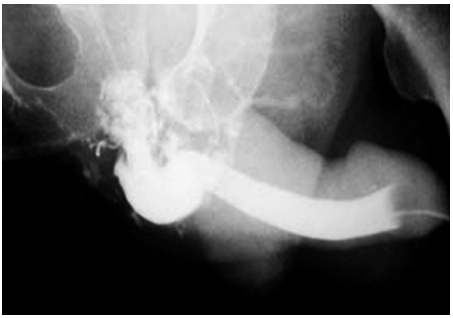

Figure 38-2. Retrograde urethrogram in pelvic fracture patient demonstrates complete disruption of posterior urethra. (From Wein A, et al. Campbell-Walsh urology. 9th ed. Philadelphia: Saunders, 2007, Fig. 83-10.)

9. What are the signs of urethral injury?

Usually urethral injury occurs in the context of pelvic trauma. The four hallmark warning signs are a boggy, movable prostate on examination, blood at the urethral meatus, severe pelvic fracture, and scrotal/perineal ecchymosis.

10. True or false: Urethral injury is a contraindication to passing a Foley catheter.

True. Always look for the four warning signs of urethral injury. If even one of these signs is present, do not attempt to pass a Foley catheter. Order a retrograde urethrogram to rule out urethral injury in this setting (Fig. 38-2).

11. Distinguish between hydrocele and varicocele.

A **hydrocele** represents a remnant of the processus vaginalis (remember embryology?) and transilluminates. It generally causes no symptoms and needs no treatment. A **varicocele** is a dilatation of the pampiniform venous plexus ("bag of worms," usually on the left). It does not transilluminate, disappears in the supine position, and becomes prominent with standing or the Valsalva maneuver. Varicoceles may cause infertility or pain; in either case, they can be treated surgically.

12. Describe the classic findings of nephrolithiasis.

Nephrolithiasis (kidney stones) can cause severe flank pain that often radiates to the groin and is colicky in nature. It may cause hematuria (gross or microscopic), and often an abdominal radiograph reveals the stone (85% of stones are radiopaque). A noncontrast helical CT scan is the diagnostic test of choice.

13. What are the different types of stones? What causes them?

Roughly 75% to 85% of stones contain calcium. Look for hypercalcemia (usually caused by hyperparathyroidism) or small bowel bypass, which increases oxalate absorption and thus calcium stone formation. Roughly 10% to 15% of stones are struvite (magnesium-ammonium-phosphate) stones, which are caused by urinary tract infection (usually with *Proteus* species). The classic example is the staghorn calculus (a stone that fills the entire calyceal system). About 5% to 10% of stones are uric acid. Look for gout or leukemia. The remaining 1% to 3% are cystine stones, which suggest hereditary cystinuria.

14. How is nephrolithiasis treated?

The cornerstones of nephrolithiasis treatment are large amounts of fluid hydration, narcotics for pain, and observation because most stones pass spontaneously. Stones less than or equal to 4 mm in diameter pass spontaneously. Stones 4 to 10 mm in diameter may or may not pass. Spontaneous

passage is unlikely with stones greater than or equal to 10 mm in diameter. If a stone does not pass, treat with lithotripsy, uteroscopy with stone retrieval, or open surgery (last resort).

15. Define cryptorchidism. When does it occur?

Cryptorchidism is arrested descent of the testicle(s) between the renal area and the scrotum. The more premature the infant, the greater the likelihood of cryptorchidism. Many arrested testes eventually descend on their own within the first year. Intramuscular hCG may be used to induce testicular descent. After 1 year, surgical intervention (orchiopexy) is warranted in an attempt to preserve fertility as well as to facilitate future testicular examinations. Affected testes have an increased risk for testicular cancer.

16. True or false: It is important to place abdominal testes in the scrotum surgically to decrease the risk of cancer.

False. Cryptorchidism is a major risk factor for testicular cancer (40 times increased risk), but bringing the testis into the scrotum probably does not alter the increased risk. The higher the testicle is found (the further away from the scrotum), the higher the risk for testicular cancer development and the lower the likelihood of retaining fertility.

17. Where do the left and right ovarian/testicular veins drain?

The right ovarian/testicular vein drains into the inferior vena cava, whereas the left ovarian/testicular vein drains into the left renal vein.

18. When is kidney transplant considered for patients with renal disease?

Kidney transplant is an option for patients with end-stage renal disease (glomerular filtration rate less than 10 to 15 mg/min), unless they have active infections or other life-threatening conditions (e.g., AIDS, malignancy). Lupus erythematosus and diabetes are not contraindications to transplantation.

19. Who makes the best donor for patients who need a kidney transplant?

Living, related donors are best (siblings or parents), especially when human leukocyte antigens (HLA) are similar, but cadaveric kidneys are more commonly used because of availability. Before transplant, perform ABO blood typing and lymphocytotoxic (HLA) cross-matching to ensure a reasonable chance at success.

20. Describe unacceptable kidney donors.

Unacceptable kidney donors include newborns (most centers set an age younger than 18 years as an exclusion criterion) and patients with a history of generalized or intraabdominal sepsis, malignancy, or any disease with possible renal involvement (e.g., diabetes, hypertension, lupus erythematosus).

21. Where is the transplanted kidney placed? What happens to the native kidneys?

A transplanted kidney is placed in the iliac fossa or pelvis (for easy biopsy access in case of later problems as well as for technical reasons). Usually the recipient's kidneys are left in place to reduce the morbidity of the surgery.

22. What are the three basic types of rejection with kidney transplantation?

Hyperacute, acute, and chronic.

23. What causes hyperacute rejection? What is the classic clinical description?

Hyperacute rejection is caused by preformed cytotoxic antibodies against the donor kidney; it occurs with ABO blood-type mismatch as well as other preformed antibodies. In the classic clinical description, the surgery is completed, the vascular clamps are released to allow blood flow, and the transplanted kidney quickly turns bluish-black. Treat by removing the kidney.

24. What causes acute rejection? How does it present? How is it treated?

Acute rejection is T-cell–mediated. It presents *days to weeks* after the transplant with fever, oliguria, weight gain, tenderness and enlargement of the graft, hypertension, and/or laboratory derangements. Increases in creatinine are more reliable than increases in blood urea nitrogen. Treatment involves pulse corticosteroids, anti–T-cell antibody therapies, (polyclonal antibodies, OKT3), other antibody therapies (basiliximab, daclizumab) and other immunosuppressants (tacrolimus, mycophenolate, cyclosporine). **Accelerated rejection** occurs over the *first few days* and is thought to reflect reactivation of previously sensitized T cells.

25. What causes chronic rejection? How does it present? How is it treated?

Chronic rejection can be T-cell– or antibody-mediated. This late cause (months to years after transplant) of renal deterioration presents with gradual decline in kidney function, proteinuria, and hypertension. Treatment is supportive and not effective, but the graft may last several years before it gives out completely. A new kidney can be transplanted if this occurs.

26. Discuss the mechanism of action of the commonly used immunosuppressant drugs in transplant medicine.

- Steroids inhibit interleukin-1 production.
- Methotrexate is a folic acid antagonist, but the precise mechanism in immunosuppression is unclear.
- Cyclosporine inhibits interleukin-2 production.
- Tacrolimus inhibits signaling through the T-cell receptor.
- Mycophenolate prevents T-cell activation.
- Azathioprine is an antineoplastic that is cleaved into mercaptopurine and inhibits DNA/RNA synthesis (which causes decreased production of B cells and T cells).
- Antithymocyte globulin is an antibody against T cells.
- OKT3 is an antibody to the CD3 receptor on T cells.
- Thalidomide: Mechanism of action is not known.
- Hydroxychloroquine interferes with antigen presentation.
- Basiliximab is a monoclonal antibody against the interleukin-2 receptor.
- Daclizumab is a monoclonal antibody against the interleukin-2 receptor.

27. How do you distinguish the nephrotoxicity of cyclosporine from rejection?

Cyclosporine is a well-known cause of nephrotoxicity that can be difficult to distinguish from graft rejection clinically. When in doubt, a percutaneous needle biopsy of the graft should be done if the patient is taking cyclosporine because in most cases the two can be distinguished histologically. Renal ultrasound also helps. Practically speaking, if you increase the immunosuppressive dose, acute rejection should decrease, whereas cyclosporine toxicity stays the same or worsens.

28. What risks are associated with immunosuppression?

Immunosuppression carries the risk of infection (with common as well as rare pathogens that infect patients with AIDS) and an increased risk of cancer (especially lymphomas and epithelial cell cancers).

29. Define epispadias and hypospadias. How are they treated?

Both are congenital penile anomalies. In **hypospadias** the urethra opens on the dorsal (under) side of the penis. In **epispadias** the urethra opens on the ventral (top) side of the penis. Epispadias is associated with exstrophy of the bladder. Both are treated with surgical correction.

30. Define Potter syndrome. With what is it associated?

Potter syndrome is bilateral renal agenesis, which causes oligohydramnios in utero (because the fetus swallows fluid but cannot excrete it). It is also associated with limb deformities, abnormal facies, and hypoplasia of the lungs. It is incompatible with life because of the severe associated lung hypoplasia.

CHAPTER 39

VASCULAR SURGERY

1. What clues suggest carotid stenosis? How is it diagnosed?

The classic presentation of carotid stenosis is a transient ischemic attack—especially amaurosis fugax, which is the sudden onset of transient, unilateral blindness, sometimes described as a "shade pulled over one eye." Physical examination may reveal a carotid bruit. Ultrasound of the carotid arteries (duplex scan of the carotids) is used to diagnose and quantify the degree of stenosis.

2. How is carotid stenosis managed?

In symptomatic patients, if the stenosis is **70% to 99%**, patients usually are advised to undergo carotid endarterectomy (CEA) for the best long-term prognosis—if their state of health allows them to tolerate the surgery. If stenosis is 50% to 69%, the data are less clear, and patient factors affect the decision. CEA is generally recommended for men, patients aged 75 or older, patients with recent stroke (not transient ischemic attack), and patients with hemispheric symptoms other than transient monocular blindness (amaurosis fugax). Female patients, patients younger than 75 years, and those with mild symptoms generally do better with medical management if stenosis is 50% to 69%. If stenosis is less than 50%, medical management is indicated.

Patients should not undergo carotid endarterectomy after a stroke that leaves them severely disabled, but small, nondisabling strokes are not contraindications to surgery. Carotid endarterectomy should not be performed during a transient ischemic attack or stroke in evolution. Surgery is always done electively, not on an emergent basis.

In asymptomatic patients, if the stenosis is 60% to 99%, CEA is indicated. If stenosis is less than 60%, medical management is indicated. Medical management includes antihypertensive agents, statins, and antiplatelet therapy.

The role of carotid angioplasty and carotid stenting in carotid stenosis is not yet clearly defined. Carotid endarterectomy remains the treatment of choice for suitable carotid stenosis.

Because medical therapy has improved since the initial studies comparing CEA with medical management were performed, medical management of lower grade carotid stenosis and asymptomatic carotid stenosis is gaining favor. This is an area that is still being clarified in the medical literature and likely will not be tested on the USMLE.

3. What is the most common cause of death during vascular surgery?

Myocardial infarction (MI), regardless of the procedure performed. Peripheral vascular and aortic disease are generalized markers for atherosclerosis, and almost all patients have significant coronary artery disease. Always evaluate patients for modifiable and treatable atherosclerosis risk factors (i.e., cholesterol, hypertension, smoking, diabetes).

4. What are the classic findings in a patient with an abdominal aortic aneurysm? How is it evaluated?

Abdominal aortic aneurysm (Fig. 39-1) classically presents as a pulsatile abdominal mass that may cause abdominal pain. If pain is present, rupture/leak of the aneurysm should be suspected, although an unruptured aneurysm may cause some degree of pain. Ultrasound or computed tomography (CT) scan is used for initial evaluation and diagnostic confirmation in stable patients, as well as for serial monitoring.

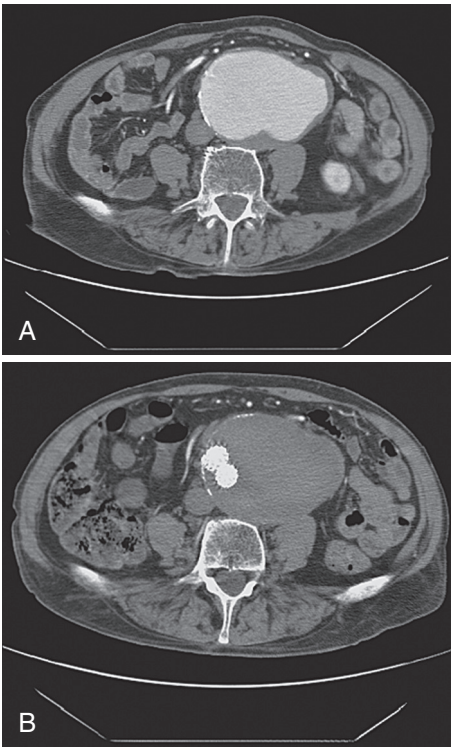

Figure 39-1. A, Cross sectional computed tomography (CT) image of an 11-cm abdominal aortic aneurysm. **B,** CT image 3 months after endovascular repair. Note the thrombosed aneurysm and patent limbs of the stent-graft. (From Townsend C, et al. Sabiston textbook of surgery. 18th ed. Philadelphia: Saunders, 2008, Fig. 65-4.)

5. How is an abdominal aortic aneurysm managed? What clues indicate that the aneurysm has ruptured?

If the aneurysm is smaller than 5 cm, you can follow it with serial ultrasound examinations to ensure that it is not enlarging. These smaller aneurysms should be managed with risk factor reduction (smoking cessation and treatment of hypertension and dyslipidemia). If the aneurysm is larger than 5 cm (or if you are told that it is enlarging rapidly), surgical correction should be advised if the patient can tolerate the surgery.

A **pulsatile abdominal mass plus hypotension** requires emergent laparotomy for a presumed ruptured aneurysm, which carries a mortality rate of roughly 90%. The management of an abdominal aortic aneurysm dissection depends on the location of the dissection. Patients who survive the initial tear typically complain of a severe sharp or tearing sensation in the back or chest. Acute dissections involving the ascending aorta are considered surgical emergencies. Dissections confined to the descending aorta are treated medically unless the dissection progresses or continues to bleed.

6. Define Leriche syndrome. For what is it a marker?

Leriche syndrome is the combination of claudication in the buttocks, buttock atrophy, and impotence in men caused by aortoiliac occlusive disease. Most patients need an aortoiliac bypass graft.

7. Define claudication. What are the associated physical findings?

Claudication is pain, usually in the lower extremity, brought on by exercise and relieved by rest. It occurs with severe atherosclerotic disease and is the equivalent of angina for the extremities. Associated physical findings include cyanosis (with dependent rubor), atrophic changes (thickened nails, loss of hair, shiny skin), decreased temperature, and decreased (or absent) distal pulses.

8. How are patients with claudication managed?

The best treatment is conservative: Cessation of smoking, exercise, and good control of cholesterol, diabetes, and hypertension. Antiplatelet agents are warranted in patients with claudication. Aspirin is preferred, but clopidogrel may be used for patients who cannot tolerate aspirin. Cilostazol may be used for the treatment of intermittent claudication. Beta blockers may worsen claudication (as a result of $beta_2$ receptor blockade), but benefits may outweigh the risks in some patients (e.g., prior MI). If claudication progresses to rest pain (forefoot pain, generally at night, which is classically relieved by hanging the foot over the edge of the bed) or interferes with lifestyle or work obligations, perform an arterial duplex for diagnosis and use angioplasty or surgical revascularization procedure for treatment. Because claudication and peripheral vascular disease are generalized markers for atherosclerosis, check for other atherosclerosis risk factors.

9. What is the probable cause of severe, sudden onset of foot pain in patients with no previous history of foot pain, trauma, or associated chronic physical findings?

This scenario may indicate an embolus (look for atrial fibrillation; the pulse may be absent in the affected area) or compartment syndrome (common after revascularization procedures).

10. Describe the classic presentation of chronic mesenteric ischemia.

The classic patient has a long history of postprandial abdominal pain (also known as intestinal angina; eating is "exercise" for the intestines), which causes "fear" of food and extensive weight loss. This diagnosis is difficult because, like all atherosclerotic disease, it presents in patients older than 40 years who have other conditions that may cause the same problem (e.g., peptic ulcer disease, pancreatic cancer, stomach cancer). Look for a history of extensive atherosclerosis (known coronary artery disease, peripheral vascular disease, stroke, or multiple risk factors), abdominal bruit, Hemoccult-positive stool, and lack of jaundice (jaundice suggests pancreatic cancer). In most patients, a CT scan of the abdomen is done; negative results raise the suspicion of ischemia. Diagnosis can be made with selective angiography of the superior mesenteric artery. Magnetic resonance angiography and CT angiography are emerging tools, but angiography is still the preferred modality. Patients are treated with surgical revascularization because of the risks of bowel infarction and malnutrition.

11. How does an acute bowel infarction present?

Classically, a patient with a history of extensive atherosclerosis or multiple atherosclerosis risk factors complains of abdominal pain or tenderness, bloody diarrhea, and possibly peritoneal signs (e.g., rebound tenderness, guarding). Watch for "thumbprinting" (thickened bowel walls that resemble thumb prints) on abdominal radiographs. Patients may also have tachycardia, hypotension, and/or shock.

12. What causes arteriovenous fistulas and pseudoaneurysms in the extremities? How do you recognize them?

Penetrating trauma in an extremity or iatrogenic catheter damage may be followed by the development of an arteriovenous fistula or pseudoaneurysm. Watch for bruits over the area or a palpable pulsatile mass. Small fistulas can be left alone, but larger fistulas require surgical or angiographic intervention.

13. What are the signs and symptoms of venous insufficiency? How is it treated?

Venous insufficiency generally occurs in the lower extremities. Patients may have a history of deep venous thrombosis, varicose veins, and/or swelling in the extremity with pain, fatigability, or

heaviness. Symptoms are relieved by elevating the extremity. Patients may also have increased skin pigmentation around the ankles with possible skin breakdown and ulceration.

Treatment is at first conservative, including elastic compression stockings, elevation with minimal standing, and treatment of ulcers with cleaning, wet-to-dry dressings, and antibiotics, if cellulitis occurs.

14. True or false: A superficial palpable cord is a fairly specific sign of deep venous thrombosis.

False. A superficial palpable cord usually represents superficial thrombophlebitis.

15. Describe the usual history of a patient with superficial thrombophlebitis. How is it treated?

Patients often have a history of varicose veins and complain of localized leg pain with superficial cordlike induration, reddish discoloration, and mild fever. Superficial thrombophlebitis is not a significant risk factor for pulmonary embolus, and patients do not need anticoagulation. Treatment is usually conservative, including nonsteroidal antiinflammatory drugs (NSAIDs) and warm compresses. The condition generally subsides on its own within a few days. A thrombectomy under local anesthesia can be done for severe or nonresolving symptoms.

16. Define subclavian steal syndrome. What symptoms does it cause? How is it treated?

Subclavian steal syndrome is usually caused by left subclavian artery obstruction proximal to the vertebral artery origin. To perfuse an exercising arm, blood is "stolen" from the vertebrobasilar system; that is, it flows backward into the distal subclavian artery instead of forward into the brainstem. Patients complain of central nervous system (CNS) symptoms (e.g., syncope, vertigo, confusion, ataxia, dysarthria) and upper extremity claudication during exercise. Treat with surgical bypass.

17. What are the symptoms of thoracic outlet syndrome? How is it treated?

Thoracic outlet obstruction refers to symptoms caused by obstruction of the nerves or blood vessels that serve the arm as the neurovascular bundle passes from the thoracocervical region to the axilla. Affected patients have upper extremity paresthesias (nerve impingement), weakness, cold temperature (arterial compromise), edema, and/or venous distention (venous compromise). The absence of central nervous system symptoms helps differentiate this condition from subclavian steal syndrome. Causes include cervical ribs (ribs arising from a cervical vertebrae that are usually asymptomatic but may compromise subclavian blood flow) or muscular hypertrophy (classic in young male weight lifters). Treat with surgical intervention (e.g., cervical rib resection).

CHAPTER 40

VITAMINS AND MINERALS

1. Specify the signs and symptoms of the various vitamin deficiencies and toxicities.

VITAMIN	DEFICIENCY	TOXICITY
A	Night blindness, scaly rash, xerophthalmia (dry eyes), Bitot spots (debris on conjunctiva); increased infections	Pseudotumor cerebri, bone thickening, teratogenic
C	Scurvy (hemorrhages/skin petechiae, bone, gums; loose teeth; gingivitis), poor wound healing, hyperkeratotic hair follicles, bone pain (from periosteal hemorrhages)	
D	Rickets, osteomalacia, hypocalcemia	Hypercalcemia, nausea, renal toxicity
E	Anemia, peripheral neuropathy, ataxia	Necrotizing enterocolitis (infants)
K	Hemorrhage, prolonged prothrombin time	Hemolysis (kernicterus)
B_1 (thiamine)	Wet beriberi (high-output cardiac failure), dry beriberi, (peripheral neuropathy), Wernicke and Korsakoff syndromes	
B_2 (riboflavin)	Angular stomatitis, dermatitis	
B_3 (niacin)	Pellagra (dementia, dermatitis, diarrhea), stomatitis	
B_6 (pyridoxine)	Peripheral neuropathy, stomatitis, convulsions in infants, microcytic anemia, seborrheic dermatitis	Peripheral neuropathy (only B vitamin with toxicity)
B_{12} (cobalamin)	Megaloblastic anemia *plus* neurologic symptoms	
Folic acid	Megaloblastic anemia *without* neurologic symptoms	

2. Specify the signs and symptoms of the various mineral deficiencies and toxicities.

MINERAL	DEFICIENCY	TOXICITY
Iron	Microcytic anemia, koilonychia (spoon-shaped fingernails)	Hemochromatosis
Iodine	Goiter, cretinism, hypothyroidism	Myxedema
Fluoride	Dental caries (cavities)	Fluorosis with mottling of teeth and bone exostoses

Continued

MINERAL	DEFICIENCY	TOXICITY
Zinc	Hypogeusia (decreased taste), rash, slow wound healing	
Copper	Menkes syndrome (X-linked; kinky hair, mental retardation)	Wilson disease
Selenium	Cardiomyopathy and muscle pain	Loss of hair and nails
Manganese		"Manganese madness" in miners of ore (behavioral changes/psychosis)
Chromium	Impaired glucose tolerance	

3. What are the fat-soluble vitamins? In what general category of patients are they deficient?

Vitamins A, D, E, and K are fat-soluble. Deficiency of any of these vitamins may be a result of malabsorption (e.g., cystic fibrosis, cirrhosis, celiac disease, duodenal bypass, bile-duct obstruction, pancreatic insufficiency, chronic giardiasis). In such patients, parenteral supplements are required if high-dose oral supplements fail.

4. What vitamin, mineral, and electrolyte deficiencies are classically seen in alcoholics?

Any can be seen, but watch especially for folate, thiamine, phosphorus, and magnesium deficiencies.

5. What is the most common cause of vitamin B_{12} deficiency?

Pernicious anemia, in which antiparietal cell antibodies destroy the ability to secrete intrinsic factor. Conditions associated with pernicious anemia include hypothyroidism, type 1 diabetes, and vitiligo (Fig. 40-1). The tapeworm *Diphyllobothrium latum* and removal of the ileum are exotic causes of B_{12} deficiency. Diagnosis of pernicious anemia is clinched by a low serum B_{12} level. The presence of anti-intrinsic factor antibodies is highly confirmatory for pernicious anemia. The Schilling test is of historical interest but is no longer commonly employed in the diagnosis of B_{12} deficiency.

6. What is the classic iatrogenic cause of vitamin B_6 deficiency?

Prolonged therapy with isoniazid (especially in young people). Pyridoxine supplementation is recommended for patients on isoniazid therapy for tuberculosis.

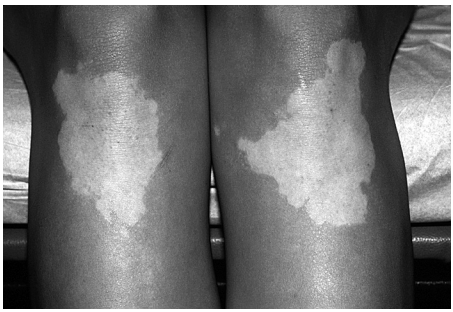

Figure 40-1. Sharply demarcated, symmetric, depigmented areas of vitiligo. See Plate 71. (From RM Kliegman RM, Stanton BF, St. Geme III JW, et al. Nelson textbook of pediatrics. 19th ed. Philadelphia: Saunders, 2011, Fig. 645-4.)

7. Which medications may cause folate deficiency?

Anticonvulsants (especially phenytoin), methotrexate, and trimethoprim.

8. Which vitamin is a known teratogen?

Vitamin A. Female patients taking one of the vitamin A analogs as treatment for acne must have a negative pregnancy test before the medication is started and should be counseled about the risks of teratogenicity. Some form of birth control should be used, and periodic pregnancy tests should be offered.

Isotretinoin is such a significant teratogen that access to this medication is very restricted. All patients and prescribers must be in a special program designed to eliminate fetal exposure to isotretinoin. There are strict qualification criteria, including monthly pregnancy testing, and two forms of contraception are recommended.

9. Which vitamin should be taken by all sexually active women of reproductive age?

Folate, which reduces the risk of neural tube defects in the fetus. The maximal benefit occurs before the woman knows that she is pregnant.

10. What are the physical findings of rickets (vitamin D deficiency in children)?

- Craniotabes (poorly mineralized skull; bones feel like a ping-pong ball)
- Rachitic rosary (costochondral beading; small round masses on anterior rib cage)
- Delayed fontanelle closure
- Bossing of the skull
- Kyphoscoliosis
- Bow-legs and knock-knees
- Bone changes appear first at the lower ends of the radius and ulna

11. Which vitamin is given to all newborns?

Vitamin K is given as prophylaxis against hemorrhagic disease of the newborn.

12. Which clotting factors are affected by vitamin K? What is the interaction of vitamin K and the liver?

Vitamin K is needed for hepatic synthesis of factors II, VII, IX, and X as well as proteins C and S. Chronic liver disease (cirrhosis) can cause prolongation of the prothrombin time and international normalized ratio because of the liver's inability to synthesize clotting factors even in the presence of adequate vitamin K levels. This problem should be corrected with fresh frozen plasma; vitamin K is ineffective in the setting of severe liver disease.

13. Describe the relationship between vitamin K and broad-spectrum antibiotics.

Prolonged therapy with broad-spectrum antibiotics is a potential cause of vitamin K deficiency. These medications can eliminate the normal gut bacteria that synthesize much of the vitamin K required daily.

14. What is the classic Step 2 description of a vitamin C–deficient patient?

An older adult with a diet of “hot dogs and soda” or “tea and toast” whose symptoms include bleeding gums and bone pain.

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F

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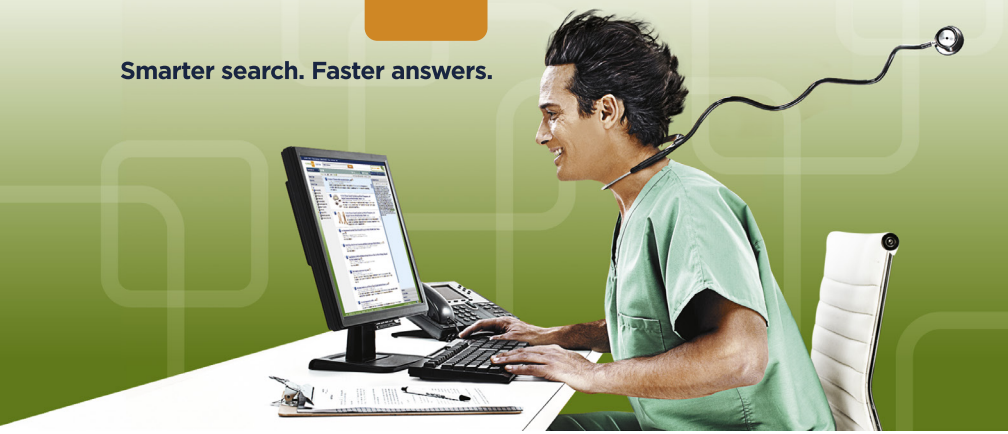

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