



## **USMLE Step 1**

### **EXPLANATIONS TO RELEASED ITEMS**

## *2007 Edition*

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## BLOCK 1

**1. The correct answer is C.** During exercise with skeletal muscle, the dominant vascular control of the muscle is metabolic. With exercise, the muscle cells release numerous metabolites, including adenosine, lactic acid, and CO<sub>2</sub>. The effect of these is referred to as “metabolic vasodilation” via relaxation of vascular smooth muscle. The arteriolar dilation that results allows increased blood flow to the muscle during exercise.

Capillary hydrostatic pressure tends to increase rather than decrease (**choice A**) during intense dynamic exercise because of increased arterial blood pressure and arteriolar dilation.

Decreased metabolite concentration (**choice B**) is incorrect because exercising muscle releases higher levels of metabolites than quiescent muscle does.

Oxygen concentration in exercising muscle tends to decrease rather than increase (**choice D**) due to increased oxygen utilization, though it remains near resting level as long as the anaerobic threshold is not crossed.

Decreased vascular resistance occurs during dynamic exercise, such as an exercise stress test. During the active contraction of the muscle, compression of vessels does transiently increase resistance; but when the muscle relaxes, the metabolic vasodilation allows hyperemia. So during a stress test the average vascular resistance decreases, thus increased vascular resistance (**choice E**) is incorrect.

**2. The correct answer is D.** The child’s pain is of the outer ear, which is worsened by manipulation. This appearance is classic for otitis externa, a relatively common infection that is often caused by *Pseudomonas*. Seen more frequently in children, it occurs more often in regular swimmers secondary to water becoming trapped in the ear canal. Treatment is usually straightforward but has the potential for serious complications in the diabetic or immunocompromised patient.

Infections of the middle ear (**choice A**) are characterized by bulging of the tympanic membrane. In these cases the external ear is not painful.

In bullous myringitis (**choice B**), the tympanic membrane is inflamed and painful vesicles are present.

The new onset of pain in the external ear makes a chronic middle-ear infection (**choice C**) an unlikely diagnosis.

Middle-ear infections can spread to the mastoid air cells, leading to mastoiditis (**choice E**).

**3. The correct answer is C.** Halving the amount of enzyme will halve the velocity of the reaction at each higher substrate concentration. Therefore, curve 3 is correct. At very low substrate concentrations, the amount of enzyme is not limiting, and the curve resembles that of the control. This feature is also seen in curve 3.

Curve 1 (**choice A**) has the same maximum velocity as the control curve, but has a faster velocity at lower substrate concentrations. This pattern can be seen with enzymes with a lower Michaelis-Menten constant ( $K_m$ ).

Curve 2 (**choice B**) has the same maximal velocity, but has a slower velocity at lower substrate concentrations. This pattern can be seen with competitive inhibition or with enzymes with a higher  $K_m$ .

If the amount of enzyme is halved, the maximal velocity should be only one-half the maximal velocity indicated by the control curve (**choice D**).

**4. The correct answer is E.** The key in making the diagnosis is noting first that bile is not entering the bowel; and second, that the circulating bilirubin is conjugated. Occlusion of the biliary system can occur secondary to stones or masses, but in such a young patient, atresia should also be a concern.

Cholesterol synthesis (**choice A**) is required for the synthesis of bile acids; clearly, this is not the source of this neonate's problem.

A lack of glucuronosyltransferase (**choice B**) would result in an inability to conjugate bile salts.

Hemolysis (**choice C**) can certainly lead to a conjugated hyperbilirubinemia. However, bile would be excreted into the bowel.

Inflammation of the terminal ileum (**choice D**) would not lead to clay-colored stools.

**5. The correct answer is E.** The interosseous membrane holds the radius and ulna together; although it does permit the ulna and radius to move in pronation and supination, this membrane prevents the ulnar and radius from moving longitudinally apart. By preventing longitudinal movement, the interosseous membrane helps transmit force from the radius to the ulna.

The annular ligament (**choice A**) binds the proximal (elbow) end of the radius to the ulna but is much smaller than the interosseous ligament and is not as important in transmitting longitudinal force.

The bicipital aponeurosis (**choice B**) arises from the distal tendon of the biceps and inserts into the ulna.

The flexor retinaculum (**choice C**) covers the carpal tunnel at the wrist.

The intermuscular septa (**choice D**) extend from the deep fascia to the radius and ulna.

**6. The correct answer is A.** In this question, the fact that the mutated peptide is much shorter than the normal suggests that an early stop codon has been encountered. Although a substitution mutation can generate a stop codon, the fact that amino acids 11–20 are all different suggests that a frameshift mutation occurs in the codon for amino acid 11, which results in the generation of an early stop codon after amino acid 20. The addition or deletion of a single nucleotide would lead to such a frameshift mutation. Therefore, a deletion in codon 11 would result in the changes described.

Nucleotide deletion in codon 20 (**choice B**) would cause a frameshift *after* codon 20, and will not affect codons 11–20.

A nucleotide deletion in the intervening sequence (**choice C**) would also have no effect on the codons upstream of the deletion. In this question, the deletion must have occurred in codon 11.

A nucleotide substitution in codon 11 (**choice D**) would change that amino acid itself but should not cause a frameshift or affect the identity of downstream amino acids.

A substitution mutation in codon 20 (**choice E**) would change only that amino acid, or may cause early termination, but would not affect the identity of amino acids 11–20.

**7. The correct answer is B.** In contrast to most other cell types, erythrocytes, as well as the brain, testes, and renal medulla, use glucose as the sole energy source. Even during starvation, when the brain can still derive energy from ketone bodies, erythrocytes will continue to rely on glucose due to the lack of mitochondria. As a result, red blood cells can produce energy only via glycolysis of glucose followed by lactic acid production.

Free fatty acids (**choice A**) must be hydrolyzed via beta-oxidation, a process that occurs in the mitochondrial matrix.

$\beta$ -hydroxybutyrate (**choice C**) is a ketone body. During starvation, the brain may derive its energy source from ketone bodies, which are converted to acetyl CoA inside the cell. However, energy derived from acetyl CoA occurs by aerobic respiration, which does not occur in erythrocytes.

Pyruvate (**choice D**) is generated as a product of glycolysis; but in erythrocytes, pyruvate is converted to lactic acid with no further energy production.

Triglycerides (**choice E**) may be released by fat cells and may produce fatty acids and glycerol for energy use. Erythrocytes cannot derive energy from triglycerides.

**8. The correct answer is B.** The question stem describes an intention tremor, which is an uncontrolled shaking of the affected extremity that is present only with purposeful movement and is worse at the end of the movement. A lesion of a cerebellar hemisphere will produce motor disorders, including intention tremor in the ipsilateral extremities. Other movement disorders that would be predicted in this patient include dysmetria (inability to stop movements at the desired point), adiadochokinesia (inability to perform rapid alternating movements smoothly and regularly), and decomposition of movements (inability to coordinate movements that require several joints).

Lesions of the basal ganglia (**choice A**) do not produce intention tremor. Basal ganglia lesions can produce (depending on where the lesion is) resting tremor (which improves with purposeful movement), chorea, athetosis, and dystonia.

A lesion of the cerebellar vermis (**choice C**) can produce truncal ataxia and dysarthria.

A lesion of the frontal eye field (**choice D**) results in deviation of the eyes ipsilateral to the lesion.

The motor nucleus of the thalamus (**choice E**) is an imprecise term, but probably refers to the ventral anterior and ventral lateral nuclei, which receive inputs from the basal ganglia and cerebellum. Lesion of this area could produce motor deficits, but would not cause an intention tremor.

**9. The correct answer is D.** The organism in question is *Clostridium difficile*, the cause of pseudomembranous colitis (antibiotic-associated colitis). *C. difficile* is an anaerobic Gram-positive rod that forms spores, necessitating sterilization with wet heat at 121 C for at least 15 minutes. None of the other procedures listed would effectively eliminate spores from the bedpan.

**10. The correct answer is E.** Choice E displays typical blood gases for a patient who has metabolic alkalosis with compensatory respiratory acidosis. Metabolic alkalosis tends to develop for several reasons when there is persistent vomiting. First, the loss of hydrochloric acid with vomiting is amplified by the addition of bicarbonate to the blood when stomach acid production increases in response to the vomiting. Also, the clinical scenario is consistent with dehydration. Volume-contracted states tend to cause metabolic alkalosis; renal compensation for volume depletion includes increased reabsorption of bicarbonate with sodium in the proximal tubule.

**Choices A and B** are acidotic states—metabolic and respiratory, respectively.

**Choice C** is normal acid–base status.

**Choice D** is uncompensated respiratory alkalosis; reduced CO<sub>2</sub> is responsible for the increased pH.

**11. The correct answer is A.** In periods of severe stress, such as this case of burns, cortisol is secreted in large amounts. Cortisol has many metabolic actions, including increasing protein turnover (for synthesizing new proteins). A side effect of this is an increase in nitrogen loss.

Erythropoietin (**choice B**) stimulates erythrocyte production from the marrow. Insulin (**choice C**) acts principally on glucose and fat metabolism.

Parathyroid hormone (**choice D**) regulates calcium and phosphate metabolism.

Thyroxine (T<sub>4</sub>) (**choice E**) increases metabolic rate, but would not specifically be expected to increase nitrogen loss.

**12. The correct answer is C.** Separation anxiety is a normal feature of childhood emotional development, occurring between the ages of 8 and 18 months, when the infant is separated from the mother. Between the ages of 2 months and 2 years, children might show preference for a comforting “transitional object” (e.g., teddy bear), which is usually discarded by age 4, when the transition from dependence on the mother to independence is more complete. Separation anxiety *disorder* is characterized by excess anxiety for at least 2 weeks following separation from persons to whom the child is attached. At separation, anxiety may be experienced to the point of panic. Physical complaints such as stomachaches and headaches are common. These children often have problems falling asleep, and frequently experience nightmares. Often, they will go into the parents’ room and try to sleep with them.

In childhood schizophrenia (**choice A**), schizophrenic symptoms occur before puberty. Schizophrenia may present with grossly immature behavior, failure to develop a separate identity from the mother, and withdrawal, and may include autistic behaviors.

According to Freud, the latency phase (**choice B**) occurs between 5 and 12 years of age, and is characterized by a quiescent sexual drive because of the resolution of the Oedipal complex. Sexual energy is sublimated into socially acceptable options such as schoolwork and sports. During this phase, the superego, responsible for moral and ethical development, is formed.

In socialized conduct disorder (**choice D**), conduct problems manifest as antisocial activity (stealing, fighting, cruelty to animals, etc.) with peers. These children are very loyal to their group and have an ethical code, although it may differ from that of the rest of society. They are likely to be diagnosed with antisocial personality disorder in adulthood.

Symbiotic psychosis (**choice E**) is a developmental disorder of early childhood. It is characterized by profound reaction to separation, but also by severe developmental and social retardation.

**13. The correct answer is E.** The patient is hypokalemic and alkalotic, yet is still spilling abnormal amounts of potassium into the urine. A plausible explanation is that she is taking a diuretic drug. Athletes often use diuretics to reduce weight, and diuretic use can trigger a metabolic alkalosis with increased bicarbonate levels and significant potassium loss.

Aldosterone deficiency (**choice A**) would produce hyponatremia and hyperkalemia.

Hyperventilation (**choice B**) would produce a respiratory alkalosis with decreased bicarbonate.

Diabetes mellitus with ketoacidosis (**choice C**) would cause a metabolic acidosis, characterized by a decreased serum bicarbonate.

Anabolic steroid use (**choice D**) would probably not produce any marked changes in electrolytes.

**14. The correct answer is D.** The suprachiasmatic nucleus is a hypothalamic nucleus involved, along with the pineal gland, with generation of circadian rhythms. A lesion of this nucleus would disrupt the regulation of circadian rhythms, producing the symptoms described in the question stem.

The accessory optic nucleus (**choice A**) is involved in eye movements rather than circadian rhythms.

The lateral preoptic nucleus (**choice B**) is an interstitial nucleus of the medial forebrain bundle rostral to the lateral hypothalamic area. This nucleus is not involved in the generation or maintenance of circadian rhythms.

The pretectal nucleus (**choice C**) is thought to be involved in the pupillary light reflex and some types of eye movements, rather than in circadian rhythms.

The supraoptic nucleus (**choice E**) is one of the magnocellular hypothalamic nuclei involved in oxytocin and vasopressin secretion.

**15. The correct answer is B.** The dashed curve is shifted to the right along the  $x$ -axis, indicating an increase in volume of the cells. The volume of the cells is greater in solution Y because of cellular swelling as water flows into the relatively hypertonic cells from the relatively hypotonic solution (osmosis).

If solution Y were relatively hypertonic (**choice A**), the cells would shrink as water flowed out of the cells into the solution, and curve Y would be left-shifted with respect to curve X.

If solution Y were isoosmotic (**choice C**) with solution X, there would be no volume change and the two distributions would be identical. Another way of saying this is that the two solutions are isotonic (**choice D**) with respect to each other.

**16. The correct answer is C.** The input–output relationship between a motor neuron and the muscle cells that it innervates is one-to-one. Each action potential in the neuron causes an action potential in all of the muscle cells that are innervated by the motoneuron. With increased frequency of muscle action potentials, accumulation of calcium causes summation of force, potentially leading to tetanic contraction. Thus, increased action potential frequency in a motoneuron increases force developed in the muscle.

Choices A and B are incorrect because both the amplitude (**choice A**) and duration (**choice B**) of muscle action potentials are constant in normal conditions; these are referred to as the all-or-none properties of the action potential.

There is only a single endplate on a muscle fiber, so the number of active endplates on the muscle fiber (**choice D**) is incorrect.

Increasing the rate of synthesis of acetylcholine (**choice E**) would increase the amount of acetylcholine released by the axon terminal; however, the amount of acetylcholine released by the nerve terminal at a normal neuromuscular junction is always sufficient to bring the skeletal muscle membrane to threshold. So increasing the amplitude of the endplate potential would not affect muscle force.

**17. The correct answer is E.** Elderly women are particularly prone to develop varying degrees of prolapse of the bladder and uterus. In the early stages, this problem can present with incontinence in situations that raise intra-abdominal pressure, including coughing, sneezing, and laughing (stress incontinence). Exercises that strengthen the urogenital diaphragm can sometimes ameliorate the problem.

The detrusor muscle (**choice A**) is the intrinsic muscle of the bladder that contracts during urination, expelling the urine into the urethra.

The obturator internus (**choice B**) and the piriformis muscles (**choice C**) stabilize the hip.

The rectus abdominis (**choice D**) is a major muscle of the abdominal wall.

**18. The correct answer is D.** The human immunodeficiency virus (HIV) attaches to CD4 receptors on cells and thus infects T-helper lymphocytes and cells of macrophage lineage. Granulomas are pathologic lesions that involve the stimulation of TH1 cells and their attraction

and activation of monocytes from the blood into the area. Because TH1 cells are killed by the virus, HIV-infected individuals lose their ability to form granulomas in response to a number of intracellular pathogens.

Clonal deletion of T lymphocytes reactive to mycobacterial antigens (**choice A**) refers to the elimination of specific clones (cells derived from a single original precursor) but HIV destroys all CD4-bearing T lymphocytes, regardless of their clonal origin.

Decreased production of tumor necrosis factor- $\alpha$  by macrophages (**choice B**) is not correct because although HIV infects macrophages, they are not as susceptible to its killing effects as are T-helper lymphocytes. Tumor necrosis factor (TNF)- $\alpha$  is indeed a cytokine produced by macrophages in granulomatous lesions during normal conditions, but the decreased elaboration of this cytokine in HIV infection would be the result of the declining T-helper cell population, and not a cause of decreased granuloma formation.

Inability of T lymphocytes to provide helper functions for B lymphocytes (**choice C**) is not correct because B lymphocytes are not involved in the formation of granulomas.

Poor phagocytic activity of macrophages (**choice E**) is not correct because HIV has not been shown to affect the process of phagocytosis. The number of macrophages in a patient may ultimately decline due to the cytopathic effect of the virus, but their phagocytic activities are not affected.

**19. The correct answer is B.** The drop in blood pressure is consistent with decreased effective circulating volume. A key observation is the increased hemoglobin concentration, which strongly suggests decreased total body water; this is reinforced by the elevated serum sodium. Evaporative loss of water causes decreased extracellular fluid volume; hematocrit, hemoglobin, serum sodium, and urea nitrogen increase.

Acute renal failure (**choice A**) causes a profound increase of serum creatinine; this patient's creatinine is at the upper end of normal.

Diabetic ketoacidosis (**choice C**) is eliminated as an answer choice by the observation that the serum glucose is within the normal range.

Gastrointestinal hemorrhage (**choice D**) would be expected to cause decreased hemoglobin; in this patient, hemoglobin is actually increased.

SIADH (**choice E**) causes volume expansion and is not expected to increase blood urea nitrogen; most importantly, it causes hyponatremia.

**20. The correct answer is A.** Clumping of latex beads coated with antibody (usually IgG) and fibrinogen can be used to identify certain bacterial species, including Gram-positive cocci. These tests depend on the availability of very specific antibodies directed against bacterial antigens. Coating the beads with fibrinogen, as well as antibody, allows detection of fibrinogen receptors on some bacteria (e.g., staphylococcal clumping factor). Staphylococci also express protein A, which binds IgG.

In **choice B**, interleukin-1 is a chemotactic factor and factor VIII is a blood-clotting factor.

In **choice C**, properdin is a factor that helps to activate complement and platelet factor 3 helps to aggregate platelets.

In **choice D**, prothrombin is the precursor for thrombin and C3b is a complement factor.

In **choice E**, transferrin is an iron transport protein and plasminogen is the precursor for the clot-dissolving enzyme plasmin.

**21. The correct answer is B.** The photograph shows a diverticulum in which a mucosal outpouching penetrates through a defect in the muscular wall of the small intestine. Diverticular disease can cause abdominal pain, constipation, and bleeding.

Adenocarcinoma (**choice A**) forms an irregular mass grossly resembling the covering mucosa.

A polypoid adenoma (**choice C**) or a villous adenoma (**choice D**) would protrude into the lumen above the level of the mucosa.

Grossly, a volvulus (**choice E**) would appear as a twisted loop of bowel.

**22. The correct answer is A.** The description of gram-positive cocci in pairs and chains that agglutinate with group B antiserum in blood cultures from a 1-day-old newborn child secures the diagnosis of *Streptococcus agalactiae* (group B streptococcus, GBS) sepsis. This organism is the most common cause of neonatal septicemia and meningitis, and is acquired during passage through the birth canal of colonized mothers.

*S. agalactiae* would not be a normal flora organism in the digestive system of a neonate (**choice B**) at 1 week after birth.

Newborn's nasopharynx (**choice C**) is not a correct choice because the organism is not transmitted by respiratory means.

The organism is not transplacentally transmitted (**choice D**).

Most organisms that could enter the umbilical stump (**choice E**) would be anaerobic.

**23. The correct answer is C.** This child has Gaucher disease, caused by a defect in the body's ability to degrade glucocerebrosides within lysosomes. Hepatomegaly and mental retardation are characteristic of type II, or the acute neuropathic form of Gaucher disease. Lysosomal hydrolase is the best answer of those listed, and is a generic term for a lysosomal enzyme that hydrolyzes a chemical. The specific enzyme deficient in Gaucher disease is glucosylceramide  $\beta$ -D-glucosidase.

Lipases (**choices A, B, and E**) are not involved in the critical parts of the degradation of glucocerebrosides.

This problem is not a disorder of synthesis, so sphingolipid synthase (**choice D**) is wrong.

**24. The correct answer is A.** While the measles virus contains a variety of proteins against which antibodies can be formed, the hemagglutinin proteins, which are located on the viral

surface, are most likely to be clinically protective. Measles, mumps, and parainfluenza viruses all have hemagglutinin spikes on their outer lipoprotein envelopes.

Matrix antigens (**choice B**), nonstructural antigens (**choice C**), nucleocapsid antigens (**choice D**), and polymerase antigens (**choice E**) are not exposed, and the antibody would not be as effective.

**25. The correct answer is B.** This patient's poor cardiac function is most likely related to his excessive alcohol intake. Alcoholic cardiomyopathy is a common type of dilated cardiomyopathy that is, at least initially, reversible. There is impaired systolic function with an increased end-systolic volume. Furthermore, the dilated heart is predisposed to arrhythmias.

An aerobic exercise program (**choice A**) does not address the underlying cause for the impaired function.

There is no evidence for atherosclerotic coronary heart disease. Although a healthy diet (**choice C**) is of benefit, it is not the primary concern in this patient.

Isometric exercises (**choice D**) are recommended as part of a healthy lifestyle although, as with the other factors, isometric exercise is not the primary concern.

The patient's weight (**choice E**) is appropriate. The approximate ideal weight for a male is 106 lb plus 6 lb for every inch in height over 5 feet.

**26. The correct answer is C.** Grapefruit juice contains active components that inhibit intestinal and hepatic CYP3A4 activity. Therefore, grapefruit juice can increase the peak serum concentration of drugs that are metabolized by CYP3A4, such as felodipine, midazolam, saquinavir, and verapamil, and can lead to potentially toxic side effects.

Hepatic CYP3A4 activity would decrease, rather than increase (**choice A**), in the presence of grapefruit juice.

Intestinal drug metabolism would decrease, rather than increase (**choice B**), in the presence of grapefruit juice.

Grapefruit juice has its primary effect on inhibiting metabolism, thus total body clearance would not increase (**choice D**).

Grapefruit juice would not increase the volume of distribution (the amount of drug in the body divided by drug concentration) of a drug (**choice E**). If anything, the volume of distribution would decrease because of increased drug concentration resulting from decreased metabolism.

**27. The correct answer is B.** Finasteride is an inhibitor of 5- $\alpha$ -reductase, the enzyme that converts testosterone (**choice E**) to dihydrotestosterone (dihydrotestosterone causes prostate growth). Therefore, use of this agent would inhibit dihydrotestosterone synthesis.

Androstenedione (**choice A**) is the precursor to testosterone. Androstenedione synthesis would be unaffected by finasteride administration.

Testosterone is also a precursor to estradiol (**choice C**). Testosterone synthesis would not be decreased by finasteride administration.

Estradiol is the precursor to estrone (**choice D**). Estradiol synthesis would not be decreased by finasteride administration.

**28. The correct answer is B.** Hydatidiform mole is a form of gestational trophoblastic disease (GTD). In GTD, there is proliferation of trophoblastic tissue; the proliferation may be benign, invasive, or frankly malignant. Hydatidiform mole is a benign proliferation of trophoblastic tissue with cystic (hydropic) swelling of chorionic villi. Therapy consists of removing the mole by curettage or hysterectomy. hCG levels should be monitored in this disorder; persistent or rising levels of beta-hCG indicate molar remnants, or the development of an invasive mole or choriocarcinoma.

An adrenal adenoma (**choice A**) would not be expected to produce hCG.

Hydatidiform mole is essentially a failed pregnancy; a second, ectopic pregnancy (**choice C**) would be unlikely.

Pituitary insufficiency (**choice D**) would not lead to hCG production because trophoblast cells make hCG.

A second, noninvasive mole (**choice E**) would denote a second molar pregnancy, which would be unlikely compared with choriocarcinoma, which develops in about 4% of molar pregnancies. An invasive mole or remnants of the first mole are possible causes of the rising hCG levels, but they are not included in the alternatives.

**29. The correct answer is D.** The physical findings are consistent with volume depletion (e.g., dizziness and hypotension on standing, sinus tachycardia). Adult diarrhea is isotonic; therefore, there is an equal loss of total body sodium ( $TBNa^+$ ) and total body water (TBW). An isotonic loss of fluid does not alter the serum sodium concentration ( $\text{serum } Na^+ = TBNa^+/TBW$ ), and there is no gradient for water movement either into or out of the intracellular fluid. However, the patient has lost isotonic fluid from the extracellular fluid compartment, causing volume depletion in both the plasma compartment and the interstitial fluid compartment. When she stands up, the effect of gravity further reduces the return of blood to the right side of her heart, producing postural hypotension and dizziness. The increased pulse rate is a result of her baroreceptor reflex.

The only fluids that can increase blood pressure in a volume-depleted patient are those that remain in the extracellular (ECF) compartment and have a tonicity similar to that of plasma. The least expensive method is the intravenous infusion of crystalloid solutions (0.9% normal saline or Ringer's lactate). Because plasma volume accounts for one-third of the ECF (interstitial fluid accounts for the remaining two-thirds), it requires infusion of 3 L of normal saline to add 1 L to the plasma.

Desmopressin (**choice A**) is a vasoconstrictor and can raise blood pressure; however, it is an ancillary rather than a primary treatment for volume depletion (particularly blood loss in esophageal varices).

Infusion of 5% dextrose in water (**choice B**) cannot raise the blood pressure, since water is distributed between the ECF and ICF compartments by gradients established in the ECF by sodium. Because the ICF compartment is two-thirds of the TBW and the ECF compartment accounts for one-third of the TBW, most of the water infused in 5% dextrose solution will shift into the ICF compartment.

Fresh frozen plasma (FFP, **choice C**) would theoretically be an ideal fluid to infuse because it contains appropriate amounts of sodium and albumin. However, it is very expensive and also has the potential for transmitting infectious diseases (e.g., hepatitis C), so it is rarely used.

Methoxamine (**choice E**) is a direct-acting alpha-receptor agonist, and like desmopressin, can raise the blood pressure. However, it is only an ancillary treatment for volume depletion.

Verapamil (**choice F**) is a calcium channel blocker and is most often used in treating hypertension and supraventricular tachycardias. It would be contraindicated in this patient with volume depletion and postural hypotension.

**30. The correct answer is E.** This patient has symptoms of nonproductive cough with dyspnea on exertion and signs of consolidation in the right lower lobe. Sounds in the lungs are always transmitted better in areas of consolidation than in areas where infiltrates are primarily interstitial and spare the alveoli (e.g., atypical pneumonia due to *Mycoplasma pneumoniae*). Lung consolidation signs detected by the clinician include: 1) decreased percussion, 2) increased tactile fremitus (increased vibrations as compared with normal findings transmitted to the chest wall when the patient speaks), 3) bronchial breath sounds (short inspiratory phase and long expiratory phase from compression of the bronchi by an infiltrate), and 4) wet crackles (sounds created by airflow through fluid in small airways and alveoli). The clinical findings in this patient are most consistent with a right lower lobe consolidation secondary to a bacterial lobar pneumonia, most likely due to *Streptococcus pneumoniae*, the most common community-acquired typical pneumonia.

Asthmatic bronchitis (**choice A**) presents with cough and generalized wheezing, the latter due to inflammation of the terminal bronchioles with narrowing of the airways. Consolidation signs are absent.

In bullous emphysema (**choice B**) there is destruction of alveoli with formation of large air-filled bullae at the periphery of the respiratory unit (e.g., respiratory bronchiole, alveolar duct, and alveoli). Hyperresonance to percussion and dry crackles are commonly present rather than signs of consolidation.

Chronic bronchitis (**choice C**), like bullous emphysema, is most often secondary to smoking. The primary sites of inflammation are: (1) the segmental bronchi, inflammation of which leads to increased mucous production (productive cough) and sibilant rhonchi (whistling sounds that clear with coughing); and (2) the terminal bronchioles, in which inflammatory obstruction of airways leads to wheezing and trapping of air. Consolidation signs are absent.

Signs of consolidation may occur in congestive heart failure (**choice D**); however, unlike lobar pneumonia, the consolidation signs are bilateral, involving both lung bases.

A pleural effusion (**choice F**) refers to a collection of fluid in the pleural cavity. On physical examination, there is dullness to percussion. However, unlike lobar pneumonia, fluid in the pleural

cavity blocks transmission of sounds from the lung parenchyma. Therefore, tactile fremitus and crackles are absent. Signs of consolidation are absent.

Pleuritis (**choice G**) refers to inflammation of the pleura. The classic finding of pleuritis is a pleural friction rub. Patients experience severe, knife-like pain with inspiration from stretching of the inflamed pleura. Signs of consolidation are absent.

A pneumothorax (**choice H**) refers to collapse of the lung due to an open communication between the pleural cavity and the airways. It is usually secondary to rupture of a bleb (air-filled cavity) in or directly beneath the pleura. There is hyperresonance to percussion; breath sounds and tactile fremitus are absent. There are no consolidation signs.

A pulmonary embolism (**choice I**) produces sudden onset of tachypnea and dyspnea. Small emboli usually lodge in peripheral pulmonary arterial branches and produce a wedge-shaped area of hemorrhagic infarction extending to the pleural surface. Inflammation of the pleura produces pleuritic chest pain, a pleural friction rub, and a hemorrhagic pleural effusion.

**31. The correct answer is D.** Warfarin is a coumarin anticoagulant that works by blocking the vitamin K–dependent gamma-carboxylation of prothrombin, and factors VII, IX, and X as well as protein C. It is used in the prophylaxis and treatment of deep vein thrombosis and pulmonary embolism, and for the treatment of atrial fibrillation with embolism. It is also used as an adjunct in the treatment of coronary artery occlusion, in cerebral transient ischemic attacks, and as a prophylactic in patients with prosthetic cardiac valves. Inasmuch as the patient is going to receive trimethoprim-sulfamethoxazole (TMP-SMX) therapy for recurring urinary tract infections, the dosage of the warfarin will need to be decreased because the interaction between these two medications will increase the patient's prothrombin time (PT). The mechanism by which the PT will be elevated is probably related to one or more of the following factors: (1) TMP-SMX displaces warfarin from circulating plasma proteins, thus increasing warfarin levels; (2) because TMP-SMX and warfarin are both metabolized by the liver in a similar manner, the blood levels of both medications will increase due to a decreased rate of metabolism; and (3) because intestinal bacteria produce nearly one-half of our daily vitamin K requirements, TMP-SMX can also decrease production of this vitamin by eliminating these bacteria in the intestinal tract.

Initiating vitamin K therapy (**choice A**) would not be recommended because this would antagonize the effects of the warfarin.

Increasing the dose of the warfarin (**choice B**) would increase the patient's prothrombin time.

Making no alterations in warfarin (**choice C**) is incorrect because the dosage should be decreased.

Stopping the warfarin and beginning aspirin therapy (**choice E**) would not be recommended because aspirin therapy alone would not provide the level of anticoagulation therapy needed for a patient with a recent prosthetic heart valve replacement.

**32. The correct answer is C.** An abnormally increased amount of hepatic glycogen of normal structure indicates that glycogen is being synthesized normally. However, once made, it cannot be broken down and exported from the liver as glucose. After administration of oral fructose, there is no increase in serum glucose, indicating that fructose has not been converted into glucose and exported. The defect that could tie both of these clinical observations together is a deficiency of

the enzyme glucose-6-phosphatase. Glucose-6-phosphatase is the liver enzyme that removes the phosphate group from glucose, allowing it to leave the cell to supply the needs of the periphery. Both glycogen and fructose must first be transformed by the liver into glucose 6-phosphate and then to glucose in order to leave the cell.

A deficiency in fructokinase (**choice A**) would result in the inability of any cell to trap fructose by means of phosphorylation. After oral administration, blood and urine levels of fructose would rise.

A deficiency in glucokinase (**choice B**) would not allow the liver to remove excess glucose from the blood for storage.

A deficiency in phosphoglucomutase (**choice D**) would not allow the interconversion of fructose and glucose.

UDPG-glycogen transglucosylase (**choice E**) is another name for glycogen synthase.

**33. The correct answer is B.** The uterine tubes develop from the cranial portions of the müllerian (paramesonephric) system. Regression of the Müllerian ducts in the male normally occurs in response to secretion of müllerian inhibitory substance (MIS) by the Sertoli cells of the embryonic testes; failure to secrete MIS (or an abnormality in the receptor for MIS) can result in a genetic male with testes and normal male phenotypic development, but additionally, uterine tubes, a uterus, and an upper vagina.

The embryonic testes secrete testosterone rather than estrogen (**choice A**).

Production of testosterone by the embryonic testes (**choice C**) is necessary for the development of the Wolffian duct system derivatives (e.g., vas deferens) in the male.

An abnormal response to estrogen (**choice D**) is not likely to cause persistence of the Müllerian system. The predominant sex steroid in this genetic male would be testosterone.

Testosterone (**choice E**) does not cause regression of the Müllerian system, although it is essential for the development of Wolffian (mesonephric) structures in the male.

**34. The correct answer is C.** Very often, the doctor/patient relationship can be strengthened by being carefully attentive to the patient's needs, fears, and beliefs. Offering the patient analgesia addresses her stated reason for not having the mammograms.

Exaggerating the risk of breast cancer (**choice A**) is unethical and likely to be ineffective.

There is no indication that the patient has unresolved grief issues regarding the mother and grandmother. Insisting that she obtain counseling (**choice B**) would therefore be unproductive or even counterproductive.

Showing the woman photographs of untreated breast cancer (**choice D**) will probably shock her, but will leave a lasting negative impression regarding her physician and may damage the therapeutic relationship.

Telling the patient that the therapeutic relationship will be terminated unless she complies with medical advice (**choice E**) is an extreme move that should not be undertaken as long as open lines of communication exist between the doctor and patient.

**35. The correct answer is E.** Wernicke-Korsakoff syndrome, seen most often in this country in chronic alcoholics, is due to profound thiamine deficiency. Initially, confusion, ataxia, and ophthalmoplegia dominate the clinical picture, but if the thiamine deficiency is uncorrected, an amnesic syndrome called Korsakoff syndrome supervenes. Korsakoff syndrome is characterized by a striking loss of drives, and by dense anterograde amnesia with some retrograde amnesia with regard to recent events. Characteristic hemorrhagic lesions occur in the mammillary bodies, in the dorsomedial nucleus of the thalamus, and in the periventricular regions from the third to fourth ventricle.

The amygdala (**choice A**) is an almond-shaped collection of nuclei deep to the uncus of the parahippocampal gyrus. It is not damaged in Wernicke-Korsakoff syndrome.

The caudate nucleus (**choice B**) is a major component of the neostriatum that functions in the initiation of voluntary movements. It is not damaged in Wernicke-Korsakoff syndrome.

The hippocampus (**choice C**) is involved in processing new memories. Although hippocampal lesions produce amnesia, this structure is not damaged in Wernicke-Korsakoff syndrome.

The locus ceruleus (**choice D**) contains densely packed noradrenergic neurons that project to many areas of the brain. The locus ceruleus is involved in attention and arousal, and is not damaged in Wernicke-Korsakoff syndrome.

**36. The correct answer is C.** Both of these substances are potent secretagogues for gastric acid. Simultaneous administration results in potentiation of the effect. The key is that of the five answer choices, only this one includes two potent secretagogues that act synergistically.

**Choice A:** Acetylcholine increases acid secretion but secretin decreases it.

**Choice B:** Gastrin increases acid secretion but CCK does not.

**Choice D:** Histamine increases gastric acid secretion but VIP acts on intestinal and pancreatic secretion.

**Choice E:** Secretin inhibits gastric acid and CCK has no direct effect.

**37. The correct answer is E.** Sensitivity is defined as the ability of a test to detect the presence of a disease in those who truly have the disease. It is calculated as the number of people with a disease who test positive (true positive) divided by the total number of people who have the disease (true positive + false negative):

Test Result	Disease			
	Test Result	Present	Absent	Total Patients
Positive		60 (true +)	40 (false +)	100 (those with +)
Negative		20 (false -)	80 (true -)	100 (those with -)

$$\text{Sensitivity} = \frac{60 \text{ (true +)}}{60 \text{ (true +)} + 20 \text{ (false -)}} = \frac{60}{80} = 0.75$$

The positive predictive value is the probability that someone with a positive test actually has the illness:

$$\text{Positive predictive value} = \frac{60 \text{ (true +)}}{60 \text{ (true +)} + 40 \text{ (false +)}} = \frac{60}{100} = 0.60 \text{ (choice C)}$$

The specificity of a test is how well it identifies people who are truly well:

$$\text{Specificity} = \frac{80 \text{ (true -)}}{80 \text{ (true -)} + 40 \text{ (false +)}} = \frac{80}{120} = 0.67 \text{ (choice D)}$$

The negative predictive value is the probability that someone with a negative test is actually well:

$$\text{Negative predictive value} = \frac{80 \text{ (true -)}}{80 \text{ (true -)} + 20 \text{ (false -)}} = \frac{80}{100} = 0.80$$

**38. The correct answer is D.** The pulmonary artery carries mixed venous blood, which has an oxygen saturation typically ~75% (possibly as low as 60%); the upper limit of normal for pulmonary artery pressure is 30/15, so 26/14 is normal.

The ductus arteriosus (**choice A**) is closed in a healthy person but if open in an adult, it would carry highly oxygenated blood (probably >80% saturation) from the aorta (upper limit of normal pressure is 140/90 mm Hg) to the pulmonary artery and so would have a pressure somewhere between these values.

The foramen ovale (**choice B**) is also closed in a healthy adult but if open, would carry highly oxygenated blood (probably >80% saturation) from the left atrium (**choice C**) to the right atrium at atrial pressures; left atrial pressure ranges from a few mm Hg to the v wave peak of 20 mm Hg.

Right atrial blood (**choice E**) has low oxygen saturation (possibly 60%), but also low pressure (about 0 to 15 mm Hg).

**39. The correct answer is B.** The disease in question is irreversible and fatal, so clearly you don't want to miss a single case. Setting the cutoff at point B accomplishes this and keeps the number of false positives (healthy people who test positive on the screening test) minimal. In essence, the sensitivity (how well the test identifies people who have the disease) of the screening procedure is 100% at point B. The specificity of the test (how well it identifies people who do not have the disease) is acceptable at this point; the majority of healthy individuals will test negative.

The false-positive rate associated with a cutoff of **point A** is too high, as fully one-half of the healthy individuals will be told they have a fatal disease.

If **points C, D, or E** are used as cutoff points, too many individuals with the disease will escape detection and therefore cannot be treated (it should be assumed treatment does not involve great risk to the patient, as it would be otherwise be unacceptable to treat the false positives).

**40. The correct answer is B.** Recurrent pneumonias and poor pancreatic function clearly point to the diagnosis of cystic fibrosis. These patients have a defect in the chloride ion transporter gene on chromosome 17. Secretions are thick and hard to move. Secretions cannot leave the pancreatic duct, nor can cilia in the respiratory epithelium clear the mucus to help prevent infections.

Autoimmune disorders (**choice A**) may explain respiratory tract infections, such as IgA deficiency; this would not account for the lack of pancreatic function.

Trypsin (**choice C**) would not be absent in a patient with a disaccharidase deficiency (usually lactose intolerance).

Apolipoprotein B deficiency (**choice D**) would not predispose to respiratory tract infections.

Malabsorption syndromes (**choice E**) would lead to fatty stool but not a lack of trypsin.

**41. The correct answer is B.** Dextrocardia is a rightward positioning of the heart, the mirror image to how it is positioned normally. This may occur in isolation or in association with reversal of the orientation of the abdominal viscera (situs inversus totalis).

In a bifid heart (**choice A**), there is a cleft in the cardiac apex. It is a result of incomplete fusion of the separately developed right and left ventricles.

In a double-outlet right ventricle (**choice C**), both the aorta and pulmonary artery originate from the right ventricle. The ventricles, however, are in the normal position.

In embryonic development, the truncus arteriosus (**choice D**) separates to form the pulmonary artery and aorta. When this process fails, a single arterial trunk arises from the normally positioned ventricles.

Although the aorta and pulmonary artery are reversed in position in transposition of the great vessels (**choice E**), the ventricles and heart are in the normal position.

**42. The correct answer is E.** Enveloped viruses such as HIV are sensitive to organic solvents, alcohol, and ether because the envelope, which is derived from the cellular membrane, is easily destroyed by these agents. Once the envelope is destroyed, the virus cannot attach to a further generation of cells to infect them. Naked capsid viruses such as hepatitis A virus have a protein shell (capsid), which is resistant to these chemicals.

Icosahedral symmetry (**choice A**), or the lack thereof, does not play a role in resistance to chloroform or ether.

Reverse transcriptase (**choice B**) does not play a role in resistance to chloroform or ether.

Single-stranded RNA (**choice C**) does not play a role in resistance to these chemicals, and since both HIV and HAV are single-stranded RNA viruses, it is unlikely to account for this difference.

Spherical structure (**choice D**), or the lack thereof, does not play a role in resistance to chloroform or ether.

**43. The correct answer is C.** The described symptoms are characteristic of thyrotoxicosis: irritability, increased gastrointestinal motility, tachycardia, weight loss, and muscle wasting.

Congestive heart failure (**choice A**) may produce tachycardia but would not produce the constellation of symptoms in this patient; in particular, weight gain due to fluid accumulation is common with congestive failure.

The overwhelming majority (>90%) of patients with Cushing syndrome (**choice B**) present with obesity.

Mitral valve prolapse (**choice D**) classically presents with pulmonary edema, holosystolic murmur, and numerous other signs that were not noted in this case.

Pheochromocytoma (**choice E**) is likely to present with numerous symptoms that are absent in this patient, such as episodes of hypertension, hyperglycemia, and glycosuria. Also, pheochromocytoma is not strongly associated with gastrointestinal symptoms.

**44. The correct answer is C.** Gap junctions form hydrophilic channels between two cells, permitting the interchange of molecules with a molecular weight less than 1,500. Substances such as cAMP, cGMP, ions, and some hormones can pass between cells and spread information. This allows cells in a tissue to integrate their metabolic activities by sharing signals and metabolites.

The basal lamina (**choice A**) is the thin matrix of collagen and laminin upon which cells sit, tightly bound by specific receptor proteins.

Desmosomes (**choice B**) bind cells together to give tissues strength. There are three types of desmosomes: belt desmosomes, spot desmosomes, and hemidesmosomes. Belt desmosomes form a belt of cell-to-cell adhesion just under the tight junction. Spot desmosomes are button-like points of contact between cells. Hemidesmosomes anchor the plasma membrane to the extracellular matrix.

Glycosaminoglycans (**choice D**) are long, repeating, linear polymers of specific disaccharides. The backbone of peptidoglycan is an example.

Tight junctions (**choice E**) seal adjacent cells to prevent the passage of fluids between cell layers.

**45. The correct answer is A.** The pH is frankly acidotic. Acidosis with low bicarbonate is metabolic acidosis. Plasma anion gap is commonly calculated by  $\text{Na}^+ - (\text{Cl}^- + \text{HCO}_3^-)$ ; in this patient  $140 - (98 + 17) = 25$ . Using this formula, the normal value is  $12 \pm 2$ ; the value of 25 is grossly elevated. The best description of this condition is high anion gap metabolic acidosis.

High anion gap respiratory acidosis (**choice B**) and normal anion gap respiratory acidosis (**choice E**) are eliminated by the observation that  $\text{PCO}_2$  in this patient is on the low end of normal; respiratory acidosis is the result of increased arterial  $\text{PCO}_2$ .

As previously noted, the anion gap is grossly high; this eliminates low (**choice C**) and normal (**choice D**) anion gap metabolic acidosis.

**46. The correct answer is E.** The urachus is a thick, fibrous cord that remains upon obliteration of the allantois, the connection between the yolk sac and the presumptive bladder. The intraembryonic portion of the urachus extends from the apex of the bladder to the umbilicus. If the lumen of the allantois persists over a small region (i.e., is not obliterated during normal formation of the urachus), a cystic dilatation will form, which may become infected and enlarge. This is apparently the case in the patient described.

A hydrocele (**choice A**) results from a small opening at the abdominal end of the processus vaginalis that is too small to permit intestinal herniation but fills with peritoneal fluid. The processus vaginalis is the evagination of the peritoneum that forms the inguinal canal. Normally it obliterates, leaving an isolated tunica vaginalis (a peritoneal sac) related to the testis, but in hydrocele the closure is incomplete.

A Meckel cyst (**choice B**) is a variant of a Meckel diverticulum in which the proximal portion of the vitelline duct (yolk stalk), which in the early embryo is connected to the yolk sac, remains patent somewhere along its course. The yolk sac functions in transferring nutrients to the embryo before the uteroplacental circulation is established, so it must be connected to the developing midgut (by the vitelline duct). In this condition both ends of the vitelline duct are transformed into fibrous cords, but somewhere in the middle portion a lumen persists, forming a cyst hanging from the antimesenteric border of the ileum.

A Meckel diverticulum (**choice C**) is a small outpocketing of the antimesenteric border of the small intestine located 40 to 60 cm from the ileocecal junction. It represents the remnant of the proximal portion of the vitelline duct (yolk stalk), which in the early embryo is connected to the yolk sac. In normal development, the stalk is obliterated, forming a fibrous cord, but in approximately 2% of individuals the proximal portion (2 inches or so) persists.

An omphalocele (**choice D**) is a herniation of the abdominal viscera through an enlarged umbilical ring resulting from failure of the bowel to return to the peritoneal cavity after normal, physiologic herniation at 6 to 10 weeks of development.

**47. The correct answer is B.** Clozapine is an atypical antipsychotic that is used for severely ill schizophrenic patients who do not respond adequately to standard drug therapy. Clozapine has a significant risk of agranulocytosis, a potentially life-threatening side effect. Patients who are treated with clozapine should have a baseline white blood cell count and absolute neutrophil count before treatment, as well as regular testing during treatment and for at least 4 weeks after discontinuation of treatment.

Decreased erythrocyte count (**choice A**), decreased platelet count (**choice C**), increased eosinophil count (**choice D**), and increased hemolysis (**choice E**) are not associated with clozapine use.

**48. The correct answer is C.** The onset of focal neurologic symptoms attributable to a single dermatomal distribution strongly points to compression of the spinal sensory nerve. The posterior head and tragus are innervated by C2. The undersurface of the chin is also innervated by C2. It is important to remember that the C2 spinal nerves exit superiorly to the C2 vertebral body.

The patient would have both lower and upper extremity neurologic deficits if the cervical spinal cord (**choice A**) were compressed.

The superior portion of the face, above the eyes, is innervated by the first division of the trigeminal nerve (**choice B**).

The spinal accessory nerve (CN XI) (**choice D**) innervates the sternocleidomastoid and trapezius muscles.

Compression of the vertebral artery (**choice E**), depending on the integrity of the circle of Willis, would lead to central CNS defects.

**49. The correct answer is A.** Prostatic hypertrophy is a common cause of urinary outflow obstruction in aging men. One reason for this is an increase in smooth-muscle tone in the prostate and bladder neck, which is mediated by alpha-1 receptors. Nasal decongestants are generally alpha-1 agonists and can therefore increase urethral resistance, leading to difficulty in urination. In fact, alpha-1 antagonists such as prazosin, doxazosin, and terazosin are used in the treatment of benign prostatic hypertrophy.

Some cold medications, such as pseudoephedrine, may have some additional activity at beta-adrenergic receptors (**choice B**); this would not cause urinary dysfunction in patients with prostatic hypertrophy.

Cold medications are not active at ganglionic nicotinic receptors (**choice C**), nicotinic receptors at the neuromuscular junction (**choice D**), or serotonin receptors (**choice E**).

**50. The correct answer is A.** Oral ingestion of 1 L of water will decrease plasma osmolarity ( $P_{osm}$ ), which will decrease antidiuretic hormone (ADH), leading to a decrease in urine osmolarity ( $U_{osm}$ ) and an increase in urine flow rate ( $V$ ). This explains the change from X to Y, which indicates an increase in flow rate ( $V$ ) and a decrease in the ratio of urine osmolarity ( $U_{osm}$ ) to plasma osmolarity ( $P_{osm}$ ), or  $(U/P)_{osm}$ .  $U_{osm}$  normally ranges from ~1,200 mOsm/L to ~50 mOsm/L, while the normal  $P_{osm}$  range is 275–295 mOsm/L, so the decrease in  $(U/P)_{osm}$  is primarily due to a decrease in  $U_{osm}$ . ADH is the primary regulator of  $U_{osm}$  and  $V$ , and acts by

regulating the water permeability of the collecting duct (distal nephron). ADH is the primary regulator of  $U_{\text{osm}}$  and  $V$ , and acts by regulating the water permeability of the collecting duct (distal nephron).

Ingestion of 200 mL of isotonic fluid (**choice B**) will not change  $P_{\text{osm}}$  and is too small a change in plasma volume to affect ADH.

ADH secretion is primarily regulated by  $P_{\text{osm}}$ : increased  $P_{\text{osm}}$  (**choices C and D**) will increase ADH, thus increasing  $U_{\text{osm}}$  and decreasing  $V$ .

Increased ADH (**choice E**) will increase water permeability and water reabsorption, causing an increase in  $U_{\text{osm}}$  and a decrease in  $V$ .

## BLOCK 2

**51. The correct answer is B.** This question appears much more difficult than it really is. The  $x$  in this case represents any random unit, such as milligrams. As you know, drugs come in all sorts of dosages. Some drugs are in the 10 mg range, whereas other drugs such as Extra Strength Tylenol<sup>®</sup> are 500 mg per pill. Therefore, the column on the left, median effective dose, is merely a distraction from the real answer. The (toxic dose)/(effective dose) is also known as the therapeutic index. The lower the therapeutic index, the less amount of effective dose is required before the drug becomes toxic. A good example of this is warfarin. Therefore, in this case, the drug with the lowest therapeutic index, 2.1, is most likely to have the highest incidence of toxicity at the maximally effective therapeutic dose.

**52. The correct answer is B.** Increased amniotic fluid (polyhydramnios) occurs with duodenal atresia. The normal fetus will swallow amniotic fluid; however, this is prevented by the intestinal obstruction of duodenal atresia, and the amniotic fluid accumulates. Duodenal atresia presents in an infant with evidence of upper gastrointestinal obstruction, such as early vomiting and a “double bubble” sign on x-ray from the stomach and the dilated proximal duodenum.

Congenital heart disease (**choice A**) may present after birth with various features such as dyspnea, murmurs, tachycardia, failure to thrive, and cyanosis, among others.

Erythroblastosis fetalis (**choice C**) is a hemolytic disorder of the newborn. It most commonly occurs when an Rh-negative mother is sensitized to Rh factor from fetal blood (typically during delivery of a previous Rh-positive child). The mother will produce anti-Rh IgG, which crosses the placenta to cause fetal hemolysis, often causing anemia, hydrops (generalized edema), and hepatosplenomegaly. The disease can also occur with sensitization to non-Rh blood factors.

Horseshoe kidney (**choice D**) is quite common and is generally without consequence. The upper or lower poles of the kidneys are fused, essentially making one large kidney.

Neural tube defects (**choice E**) are associated with improper development and closure of the neural tube. They include anencephaly, spina bifida with meningocele or meningocele, and sacral agenesis. Open defects may result in elevated levels of alpha-fetoprotein (AFP) in the maternal serum (usually screened at 16 to 18 weeks of gestation).

**53. The correct answer is D.** The diastolic rumble with opening snap is the classic presentation of mitral stenosis. Rheumatic fever is the most common cause, with the stenosis becoming evident about 20 years later; this is also found in this patient’s history. Dyspnea caused by pulmonary edema is a frequent consequence of mitral stenosis because of increased left atrial pressure.

The murmur of aortic regurgitation (**choice A**) may occur in three forms: (1) high-pitched, early diastolic; (2) rumbling diastolic murmur at the apex; and (3) a crescendo-decrescendo systolic murmur at the left sternal border.

Aortic stenosis (**choice B**) causes systolic murmurs.

Mitral regurgitation (**choice C**) typically causes a pansystolic murmur loudest at the apex.

Pulmonic regurgitation (**choice E**) presents with a pansystolic murmur.

Pulmonic stenosis (**choice F**) presents with a systolic murmur.

Tricuspid regurgitation (**choice G**) causes a pansystolic murmur.

Tricuspid stenosis (**choice H**) rarely causes significant hemodynamic disturbance.

**54. The correct answer is B.** This boy is most likely affected by Lesch-Nyhan syndrome, a rare inherited disorder caused by a deficiency in hypoxanthine-guanine phosphoribosyltransferase (HGPRT). This X-linked recessive illness often presents at birth with severe mental and physical retardation, severe gout, spastic cerebral palsy, and a distinguishing feature of self-mutilation. The lack of HGPRT, which is involved in the pathway for purine salvage, causes accumulation of uric acid in all body fluids, producing sodium urate crystals in joints, kidneys, central nervous system, and other body tissues, which accounts for the symptoms.

A deficiency in adenine phosphoribosyltransferase (**choice A**) may result in kidney stones consisting of adenine and salts. Like HGPRT, the enzyme is also involved in the purine salvage pathway.

Increased cellular turnover of nucleic acids (**choice C**) may potentially increase the requirement for purine salvage but has not been associated with accumulation of uric acid crystals.

Increased conversion of hypoxanthine to inosine monophosphate (**choice D**) should reduce the production of uric acid because hypoxanthine is the precursor to xanthine, which is excreted as uric acid via the action of xanthine oxidase.

A deficiency in phosphoribosylpyrophosphate (PRPP) synthetase (**choice E**) would be beneficial to the patient in this setting because PRPP is a precursor to de novo purine synthesis. In fact, treatment of gout often includes allopurinol and 6-mercaptopurine, both of which act by inhibiting PRPP amidinotransferase, the next step following PRPP synthetase in the anabolic pathway for purine synthesis.

**55. The correct answer is C.** After the leg has been restrained by a cast for 6 weeks, one would expect atrophy of the gastrocnemius muscle. Atrophy is characterized by a loss of muscle cell mass due to a decrease in the number of myofibrils per cell, as in choice C, but not in the number of muscle cells (**choice B**).

Conversion of the muscle to fast fibers (**choice A**) would be expected to occur after denervation and reinnervation by a different nerve branch because the muscle fiber type (fast or slow fiber) is determined by the type of innervation. No evidence for denervation injury is given in the question.

Considering that exercise, which requires aerobic metabolism, increases the mitochondrial content of muscle (**choice D**), immobility would be expected to decrease the mitochondrial content.

Satellite cells are normally quiescent cells in skeletal muscle that become active in regeneration and hypertrophy, and so would not be expected to increase in number with immobility (**choice E**).

**56. The correct answer is D.** The most likely diagnosis in this patient is multiple myeloma. This is an abnormal proliferation of plasma cells that secrete predominantly immunoglobulin light chains (Bence-Jones proteins). Serum protein electrophoresis reveals a monoclonal peak. These light chains are also secreted in the urine. The high amount of protein filtered by the kidneys and precipitation within the kidneys result in impaired renal function. Normal hematopoietic marrow is crowded out by the abnormally proliferating plasma cells. The anemia is therefore normocytic and normochromic. In multiple myeloma, there are lytic bone lesions that lead to high serum calcium.

Neither basophils (**choice A**) nor macrophages (**choice C**) proliferate abnormally in multiple myeloma.

Although plasma cells are derived from lymphocytes (**choice B**), so are other cells, and therefore this is not the best answer.

Reticulocytes (**choice E**) are immature red blood cells.

**57. The correct answer is E.** There are two muscles that separately control the diameter of the pupil. The radial dilator muscle, which contracts (producing mydriasis) with  $\alpha$ -adrenergic receptor stimulation, is under the control of the sympathetic nervous system. The pupillary sphincter muscle (sometimes called the pupillary constrictor muscle) produces pupillary constriction with muscarinic cholinergic receptor stimulation and is controlled by the parasympathetic nervous system. Without treatment, the left eye is slightly smaller than the right, which by itself could indicate either decreased sympathetic tone or increased parasympathetic tone in the left eye.

Tyramine is an indirect-acting sympathomimetic (it is taken up by sympathetic nerve terminals and displaces the norepinephrine [NE] into the synapse). For tyramine to work, sympathetic nerves must be intact. Tyramine had an effect on the right eye but failed to affect the left, which is consistent with sympathetic denervation (**choice E**). However, **choice A** cannot be ruled out yet because  $\alpha$ -adrenergic receptor blockade could have prevented NE's actions on the radial dilator muscle. The treatment with EPI can distinguish between **choices A and E**. If the answer was A, then EPI should have no effect. However, EPI produced an unusually large effect in the left eye, which is consistent with sympathetic denervation supersensitivity.

Blockade of  $\beta$ -adrenergic receptors (**choice B**) can be quickly eliminated because  $\beta$ -receptors do not play a role in controlling the diameter of the eye.

Blockade of muscarinic receptors (**choice C**) can be quickly eliminated because without treatment, the left eye would be dilated.

If the left eye had been previously treated with cholinesterase inhibitors (**choice D**), tyramine still could have produced some dilation.

**58. The correct answer is E.** The HMG CoA reductase inhibitors (“statins”) have shown tremendous potential to lower serum cholesterol, as well as having other anti-inflammatory properties. However, several side effects have been noted, including myositis and, less frequently, rhabdomyolysis. The appropriate treatment is the withdrawal of the statin, after which the problem usually resolves.

Bile-binding resins (**choice A**) do not lead to muscle pain.

Cholesterol absorption blockers (**choice B**) decrease LDL but only rarely increase liver enzymes. They are not associated with myositis.

There are variety of methods to reduce the production of LDL (**choice C**), some of which may affect the muscle and liver; this is, however, not the best answer.

Lipoprotein lipase (**choice D**) is expressed on the surface of endothelial cells, and its inhibition is not associated with muscle pain.

**59. The correct answer is D.** Various forms of familial dyslipidemias exist. In type IIa hypercholesterolemia, there is a defect in the LDL receptor. The mutation prevents receptor clustering into clathrin pits and subsequent endocytosis. Without endocytosis, LDL is not brought into the cell, is not broken down, and fails to downregulate the cholesterol synthetic pathway. Patients with this disorder have high circulating levels of LDL and triglycerides. They are predisposed to early atherosclerotic disease.

Apolipoprotein A2 (**choice A**) is a component of the HDL particle.

Apolipoprotein C2 (**choice B**) deficiency is characterized by high circulating triglycerides. The function of the protein is to activate lipoprotein lipase.

Apolipoprotein ε4 (**choice C**) is important for the chylomicron remnant uptake into the liver.

The VLDL receptor (**choice E**) is important in binding VLDL particles, which are high in triglycerides and cholesterol esters.

**60. The correct answer is E.** Paraneoplastic syndromes are syndromes associated with malignancies that are not due to distant or local spread of the tumor or release of normally produced materials. Several paraneoplastic syndromes are associated with bronchogenic malignancies secondary to factors released from them, such as antidiuretic hormone (ADH), adrenocorticotrophic hormone, and parathyroid-like hormone. The hyponatremia and lack of cushingoid features indicate that the product produced is almost certainly ADH.

Adenocarcinoma of the lung (**choice A**) is not associated with ADH production; it can be associated with a hypercoagulable state.

If a craniopharyngioma (**choice B**) is large enough, it can have compressive effects on the pituitary gland. This would lead to decreased ADH production.

Medullary carcinomas of the thyroid gland (**choice C**) are associated with excess calcitonin production.

Renal cell carcinoma (**choice D**) is associated with polycythemia.

**61. The correct answer is E.** Insertion of a uracil after the end of codon 135 changes the reading frame, and produces the following codons: UUU, AUG, UGU, and UAA (a stop codon). Thus, three amino acids are added after codon 135, before the stop codon UAA, and the total number of amino acids is 138.

**62. The correct answer is E.** Spontaneous pneumothoraces can occur in apparently healthy individuals. Typically resulting from subpleural blebs, patients with these pneumothoraces are classically tall and slender in appearance.

Bronchiectasis (**choice A**) occurs in the setting of chronic lung infections or scarring.

A patient with a lung abscess (**choice B**) would exhibit progressively worsening fever and chills.

Panacinar emphysema (**choice C**) is a common finding in patients with  $\alpha$ -1-antitrypsin deficiency.

Two forms of pulmonary sequestration occur (**choice E**): intralobar and extralobar. These are unlikely to result in a spontaneous pneumothorax.

**63. The correct answer is C.** Beta-hemolytic streptococci are subdivided into groups A through D, F, and G using antibodies against the heat- and acid-stable carbohydrate antigens in their cell walls. *Streptococcus agalactiae*, a group B beta-hemolytic *Streptococcus*, colonizes the vagina in some women. It is primarily a pathogen of newborns (acquired during delivery or from contact with the mother), pregnant women, and diabetics. Its main virulence factor is a capsule that prevents phagocytosis. Meningitis due to *Streptococcus agalactiae* is primarily caused by organisms with capsule type III, and occurs mostly in infants between the ages of approximately 7 and 30 days, although later-onset infection can occur up to about 3 months of age.

**64. The correct answer is E.** The finding of curved rods in biopsy material from a patient with epigastric pain and occult blood suggests infection with *Helicobacter pylori*. This is a urease-positive bacterium that invades the stomach and causes gastritis and ulcers.

Achlorhydria (**choice A**), or lack of gastric acid, is a result of gastric mucosal atrophy. It is not usually associated with *Helicobacter* infection.

Antiparietal cell antibodies (**choice B**) would cause megaloblastic anemia, which is not mentioned in the vignette.

Cholecystitis with antral seeding (**choice C**) is not known to be associated with *Helicobacter* infection.

**65. The correct answer is G.** Sulfonylurea drugs are oral hypoglycemic agents; the principal mechanism of action is stimulation of insulin secretion by beta cells of the pancreas via inhibition of potassium channels.

Decreased entry of glucose into the muscle cells (**choice A**) is incorrect because sulfonylureas increase plasma insulin levels, which promotes glucose uptake.

Hepatic production of glucose will decrease (**choice B**), but this is secondary to the action of the drug to increase secretion of insulin.

Decreased secretion of insulin from the pancreas (**choice C**) is incorrect because insulin secretion is increased.

Sulfonylurea drugs do not block (**choice D**) or stimulate (**choice H**) intestinal absorption of carbohydrates.

Increased entry of glucose into the muscle cells (**choice E**) occurs but is secondary to the increased secretion of insulin.

Increased production of glucose from the liver (**choice F**) is incorrect because increased plasma insulin inhibits gluconeogenesis.

**66. The correct answer is C.** This woman is exhibiting regression, an automatic retreat to a less mature level of behavior in times of stress. Regression is an ego defense mechanism in which there is a return to an earlier (often infantile) stage of development. It occurs in many mental illnesses and in normal individuals experiencing tragic or extremely stressful events.

Denial (**choice A**) is an extremely common defense mechanism, especially for individuals who receive devastating medical news. Elisabeth Kübler-Ross considered denial the first step toward eventual acceptance of one's own mortality.

Displacement (**choice B**) involves transferring feelings to an inappropriate person, situation, or object (e.g., a man who has been yelled at by his boss takes out his anger on his wife).

Repression (**choice D**) occurs when conflict-provoking thoughts or feelings are hidden from the person's awareness. Forgetting an emotionally charged event is an example of repression.

Sublimation (**choice E**) is a mature defense mechanism that involves consciously turning socially unacceptable impulses into acceptable or more benign forms in order to allow their expression; for example, a young college girl immerses herself in athletics rather than engage in premarital sex.

**67. The correct answer is A.** Based on the white blood cell counts shown, the patient's neutrophil counts were impressively increased after treatment with this hematopoietic growth factor. Relative lymphocyte counts were decreased, and eosinophil counts were unchanged. The cytokine most likely to cause this effect is granulocyte colony-stimulating factor.

Transforming growth factor- $\beta$  (**choice B**) is a product of macrophages, T lymphocytes, and endothelial cells that stimulates isotype switching in B lymphocytes.

Interleukin-6 (**choice C**) is a product of macrophages that causes the acute phase response.

Interleukin-8 (**choice D**) stimulates neutrophil chemotaxis but not neutrophil production from the bone marrow.

Macrophage colony-stimulating factor (**choice E**) is not correct because the number of blood monocytes is not listed as having been changed by the treatment.

**68. The correct answer is B.** First, notice that point Y represents a patient with a higher-than-normal  $\text{PCO}_2$ , but a nearly normal pH. These data indicate that the situation is chronic, because the pH has almost completely compensated. The only two conceivable ways to arrive at these values are: respiratory acidosis with renal compensation, or metabolic alkalosis with respiratory compensation. The fact that the pH is slightly below 7.4 points to the former option, because compensation brings the pH toward normal but does not shoot past it. In chronic obstructive pulmonary disease, respiratory acidosis can result from an inability to blow off enough  $\text{CO}_2$ ; if this persists, the kidneys will compensate by conserving  $\text{HCO}_3^-$  and secreting  $\text{H}^+$ , thus correcting the body's pH.

Because of the low oxygen availability at high altitudes (**choice A**), a person would hyperventilate to try to inspire adequate oxygen. This would lower the body's  $\text{PCO}_2$ , resulting in respiratory alkalosis. Renal compensation could occur; however, the  $\text{PCO}_2$  would remain below 40 mm Hg. Also, respiratory alkalosis with renal compensation would result in a low serum bicarbonate.

Both diarrhea (**choice C**) and ingestion of a strong acid (**choice D**) could produce a metabolic acidosis, but in order to compensate for this, one would hyperventilate, which would lower the  $\text{PCO}_2$  to below 40 mm Hg. In addition, metabolic acidosis with respiratory compensation results in a low serum bicarbonate.

Severe and prolonged vomiting (**choice E**) would result in a metabolic alkalosis because of the loss of acids. In theory, the patient could compensate by hypoventilating, thus raising  $\text{PCO}_2$ ; however, in reality, respiratory compensation of metabolic alkalosis is often small or absent.

**69. The correct answer is C.** Loss of a plasmid carrying a gene for ampicillin resistance accounts for the relatively abrupt loss of resistance seen here in strain Y.

Downregulation (**choice A**) would be expected to be reversed when antibiotics are reintroduced, so a delay in growth in the presence of the antibiotic might be seen rather than an outright loss of resistance.

Insertion of a transposon (**choice B**), point mutations (**choice D**), and recombination (**choice E**) would be expected to affect only a small number of the bacteria, with the rest retaining the antibiotic resistance.

**70. The correct answer is A.** The description of a painful genital ulcer producing gram-negative coccobacilli that grow on supplemented chocolate agar suggests a diagnosis of *Haemophilus ducreyi* chancroid.

Herpes simplex virus (**choice B**) causes painful vesicular genital ulcers but it is a virus, so bacteria would not be cultured from the lesion.

*Neisseria gonorrhoeae* (**choice C**) is an extracellular gram-negative diplococcus that grows on chocolate agar (or Thayer-Martin agar) but produces a white leukorrheic discharge from the urethral meatus of males; it does not produce chancres or chancroids.

*Treponema pallidum* (**choice D**) is a gram-negative spirillar bacterium that produces painless, indurated genital lesions.

*Trichomonas vaginalis* (**choice E**) is a protozoan parasite that produces vaginitis, not chancres or chancroids.

**71. The correct answer is E.** Selective constriction of efferent arterioles will increase glomerular capillary pressure, leading to increased GFR. At the same time, it will increase vascular resistance of the renal vessels. This will decrease renal blood flow, and hence renal plasma flow. Because filtration fraction is GFR divided by renal plasma flow, the filtration fraction will increase. All other choices contain at least one false prediction.

**72. The correct answer is D.** This woman is dehydrated from vomiting and diarrhea, and should be trying to retain sodium and water and excrete urine. The fact that her serum sodium is so low suggests that the drive to retain water is greater than the drive to retain salt. Of all the answer choices, only increased serum ADH is plausible under these circumstances. ADH conserves water by increasing the permeability of the collecting ducts to water, resulting in water reabsorption.

The patient will be trying to save sodium, so aldosterone will be increased, not decreased (**choice A**).

The patient will be trying to save sodium, so atrial natriuretic peptide will decrease, not increase (**choice B**).

The circulating volume is decreased, not increased (**choice C**).

Both ADH and aldosterone should be high, but the drive to retain water is stronger than the drive to retain sodium, so urine osmolality is greater than, not less than, serum osmolality (**choice E**).

**73. The correct answer is C.** Thiamine is a coenzyme in the oxidative decarboxylation of alpha-ketoacids, as well as a cofactor for transketolase and maintains the integrity of nerve cells. The patient described here suffers from Wernicke encephalopathy, which is characterized by the clinical triad of ataxia, eye movement problems (ophthalmoplegia and nystagmus), and severe cognitive deficits, and is caused by protracted thiamine deficiency. In this patient's case, ingestion of a meal that presumably contained carbohydrate exhausted his limited stores of thiamine and actually worsened his condition. If untreated, Korsakoff psychosis, characterized by severe anterograde and some retrograde amnesia, can result.

Folate deficiency (**choice A**) is characterized by megaloblastic anemia.

Vitamin A deficiency (**choice B**) causes epithelial metaplasia and especially affects the eyes, causing dryness of the conjunctiva, eventual keratomalacia, or erosion of the cornea, which may lead to blindness.

Pyridoxine (**choice D**) deficiency causes seborrheic dermatitis, cheilosis, glossitis, peripheral neuropathy, or even seizures.

Deficiency of cyanocobalamin (vitamin B<sub>12</sub>; **choice E**) causes megaloblastic anemia, peripheral neuropathy, spinal cord lesions, and decreased fertility.

**74. The correct answer is C.** Cytomegalovirus infection is a feared and unfortunately fairly frequent complication of profound immunosuppression such as that seen in transplant patients and AIDS patients. Many individuals harbor quiescent CMV virus in their bodies that may become active, involving multiple organs in the immunosuppressed. The clinical scenario presented here is typical.

**75. The correct answer is E.** Stranger anxiety develops in most infants between 7 and 9 months of age. The infant will become very apprehensive in the presence of a stranger, and will respond by turning away, clinging to the primary caregiver, or crying. Stranger anxiety is thought to signify a major step in psychological development because it indicates that the infant is capable of distinguishing one person from another, and of recognizing the relative importance of different people.

Separation anxiety is also a normal developmental phase. It occurs later than stranger anxiety, and is precipitated by separation from a person to whom the infant is attached. Separation anxiety disorder (**choice D**) is characterized by extreme distress due to separation or anticipated separation from caregivers, the home, or familiar surroundings. It is the most common anxiety disorder of childhood, but is nonetheless rare before age 6 years.

The other choices are not supported by the patient's history.

**76. The correct answer is B.** Coccidioidomycosis is caused by the dimorphic, primary pathogenic fungus *Coccidioides immitis*, native to the deserts of the Southwestern United States. Arthroconidia, the infectious mycelial form of the fungus, are inhaled, and develop into endospore-containing spherules that eventually burst, releasing endospores into the surrounding tissue. Each endospore then develops into a new spherule. Most infections are subclinical, but the disease can present as an acute pneumonia that can be complicated by dissemination of the organism to other sites via the bloodstream. The clinical spectrum associated with disseminated disease is very wide, and includes osteomyelitis, arthritis, subcutaneous nodules, and an extremely virulent form of meningitis. Dissemination is most often seen in those with defects in cell-mediated immunity, although Blacks and Filipinos have a tenfold greater incidence of dissemination.

Blastomycosis (**choice A**) is caused by the dimorphic fungus *Blastomyces dermatitidis*, which is endemic to the Central United States from the Great Lakes to Arkansas. It usually affects the lungs, but may disseminate.

Histoplasmosis (**choice C**) is caused by the dimorphic fungus *Histoplasma capsulatum*, which is most common in soil contaminated with bird or bat droppings in the Mississippi and Ohio River Valleys. It usually affects the lungs, but may disseminate.

*Mycobacterium marinum* (**choice D**) is an atypical mycobacterium found in swimming pools and fish tanks. It is the cause of “fish fancier’s finger,” a chronic, localized granulomatous infection found among keepers of tropical fish.

*Mycoplasma pneumoniae* (**choice E**) is a common cause of atypical pneumonia.

**77. The correct answer is D.** A peak of 17- $\beta$ -estradiol (an estrogen) in the absence of progesterone will act through positive feedback to cause an LH surge, which will peak about 24 hours after the estradiol peak. Ovulation will follow the LH peak by about 12 hours.

Basal temperature rises slightly immediately after ovulation (compare with **choice B**). After ovulation, the corpus luteum will secrete both estradiol and progesterone; in this combination, the ability of estrogen to cause endometrial proliferation is inhibited and progesterone causes differentiation of the previously thickened endometrium into its secretory form, ready for implantation. Continued low plasma LH levels after the peak initiate luteolysis (death and regression of the corpus luteum) on about day 25 (**choice E**). This causes a drop in estrogen and progesterone levels; the drop in progesterone destabilizes the lysosomes of the endometrial cells, causing inflammation, and menstruation begins about 3 days later (day 1 of the next menstrual cycle; **choice C**). Menstruation lasts for about 4 to 7 days in most women (**choice A**).

**78. The correct answer is A.** The patient is described as having both upper motor neuron signs (hyperreflexia of lower limbs, extensor plantar responses, weakness) and lower motor neuron signs (atrophy of the forearm, fasciculations of the muscles of the chest, flaccid paralysis) with no impairment of sensation. Amyotrophic lateral sclerosis (ALS) is characterized by degeneration of both upper and motor neurons, while sparing sensation.

Dementia of the Alzheimer type (**choice B**) would not cause any motor problems.

Guillain-Barré syndrome (**choice C**) is a demyelinating disorder of peripheral nerves, and therefore would produce only lower motor neuron signs (ascending weakness/paralysis). Mild sensory loss can also occur.

Multiple cerebral infarcts (**choice D**) could produce upper motor neuron signs but would not lead to lower motor neuron symptoms.

Multiple sclerosis (**choice E**) is a demyelinating disorder of the central nervous system, and could therefore produce upper but not lower motor neuron symptoms.

**79. The correct answer is C.** After initial immunization, a booster injection is essentially a reexposure to the immunizing antigen (tetanus toxoid, in this case). The reaction described is sometimes called the Arthus reaction, a localized form of type III hypersensitivity, induced by fixation of complement by preformed circulating antibodies. In severe cases, the degree of complement fixation can be so substantial that it induces local tissue necrosis.

This reaction is mediated predominantly by vascular changes induced by the complement reaction rather than by accumulation of mononuclear cells (**choice A**).

This reaction consumes preformed (usually IgG) antibodies and does not require antigen capture by Langerhans cells in the epidermis (**choice B**).

This reaction does not involve the IgE/histamine pathway (**choice D**).

This reaction utilizes preformed (usually IgG) antibodies rather than requiring IgM synthesis (**choice E**).

**80. The correct answer is B.** Individuals with antisocial personality disorder have difficulty obeying the law and social norms. Poor social function is further compounded by bouts of violence and impulsivity. Multiple episodes of incarceration are common. This disorder has a strong male predominance and is seen more commonly in the lower socioeconomic groups. In order to meet the diagnostic criteria, the patient must be over age 18 and must have had a history of conduct disorder prior to the age of 15.

Adjustment disorder (**choice A**) is associated with a change of environment. It is not associated with criminal behavior.

A manic phase of bipolar disorder (**choice C**) is associated with increased energy and impulsivity. It is not specifically associated with repeated episodes of violence, although violence can occur.

Borderline patients (**choice D**) are also impulsive, with self-destructive behaviors.

In a narcissistic patient (**choice E**), the individual is self-important with a lack of concern for others.

This patient is not paranoid (**choice F**); his actions are deliberate and calculated. There is no history of a traumatic episode, and even if there were, this would not be associated with repeated criminal behavior.

The patient does not exhibit delusional activity characteristic of schizophrenia, paranoid type (**choice H**).

**81. The correct answer is A.** The dermis is attached to the underlying tissues via the suspensory ligaments (retinacula cutis). When the dermis swells considerably in association with lymphedema caused by blockage of the lymphatics, the sites of attachment become visibly dimpled. In the entity known as inflammatory breast carcinoma, widespread lymphatic involvement with corresponding lymphedema is especially likely to produce the dermatologic changes described in the question stem.

Scarring of subcutaneous tissue (**choice B**) causes a broad retraction of the skin.

Focal invasion of the dermis by neoplastic cells (**choice C**) contributes to lymphatic blocking with consequent swelling but does not directly cause the “orange-peel” appearance.

The dimples are not openings of sebaceous (**choice D**) or sweat glands (**choice E**).

**82. The correct answer is F.** Patients with sickle cell disease have, for reasons that are somewhat unclear, a marked and specific propensity for developing osteomyelitis due to *Salmonella* infection. Damage to the spleen also leaves these patients vulnerable to infections by encapsulated bacteria such as pneumococci. Patients with sickle cell disease do not have increased susceptibility to the organisms listed in the other answer choices.

**83. The correct answer is E.** The median nerve lies between flexor carpi radialis and flexor digitorum superficialis in the wrist. The recurrent branch of the median nerve supplies three of four thenar muscles: the abductor pollicis brevis, the flexor pollicis brevis, and the opponens pollicis, all of which participate in opposition of the thumb. Thus, damage to the median nerve would paralyze these muscles, preventing opposition of the thumb.

The muscles that adduct and abduct the fingers (**choice A**; palmar and dorsal interossei, respectively) are supplied by the ulnar nerve (deep branch), which runs more medially in the wrist through a passage formed by the pisiform bone, the hook of the hamate bone, and the flexor retinaculum.

The muscles that extend the index finger (**choice B**; extensor digitorum and extensor indicis) are supplied by the radial nerve (posterior interosseus branch), which runs deep in the posterior compartment of the forearm and likely would not be damaged by cutting the wrist.

Although damage to the median nerve might be expected to affect finger flexion due to loss of innervation of flexor digitorum superficialis, the wrist injury is likely to be distal to the branches that supply this muscle. In addition, two other muscles specifically involved in fourth (ring) and fifth (little) finger flexion (**choice C**)—the medial half of flexor digitorum profundus and the medial two lumbricals—are supplied by the ulnar nerve.

Sensation to skin at the base of the little finger (**choice D**) is supplied by the ulnar nerve (dorsal or cutaneous branch), which runs more medially between the ulna and flexor carpi ulnaris.

**84. The correct answer is D.** In “starvation” (after glycogen stores are depleted), the body eventually shifts to using fatty acids and other fat-derived substances. Muscle specifically uses serum fatty acids for nutrition in this setting.

Creatine phosphate (**choice A**) is a temporary energy storage form for muscle. Muscle glycogen (**choice B**) would be exhausted after 2 days.

Triglycerides are not stored in muscle (**choice C**) for energy, although they are present in muscle membranes.

Serum glucose (**choice E**) will be relatively low in this setting and is “reserved” primarily for the central nervous system.

**85. The correct answer is B.** The patient described suffers from a pheochromocytoma. In this disorder, a neoplasm of the adrenal medulla cells produces and secretes catecholamines (epinephrine and norepinephrine), giving rise to hypertension, tremor, anxiety, sweating, palpitations, and increased urinary excretion of catecholamines and their metabolites. Most occur sporadically, but a small percentage occurs in association with certain familial syndromes (e.g., multiple endocrine neoplasia types IIa and IIb, von Hippel-Lindau syndrome). Most pheochromocytomas are benign, although some are malignant (**choice D**) and may metastasize.

Adrenal cortical masses (**choices A and C**) are unlikely to be associated with catecholamine production; instead they may produce excess steroid hormones.

Diffuse hyperplasia of the adrenal cortex (**choice E**) is associated with adrenocortical hyperfunction rather than medullary hyperfunction.

Diffuse hypoplasia (**choice F**) of the adrenal medulla would lead to decreased catecholamine production and excretion.

**86. The correct answer is H.** Ulcerative colitis (UC) is an inflammatory bowel disease characterized histologically by a hyperemic, edematous mucosa with small hemorrhages that develop into crypt abscesses (small, focal collections of inflammatory cells and necrosis in the colonic crypts). Crypt abscesses may progress to small ulcers, which coalesce into larger ones. Ulcerative colitis typically affects only the mucosa, unlike Crohn disease (**choice C**), which affects the entire thickness of the bowel wall (transmural involvement). Both UC and Crohn can produce bloody diarrhea, but blood is usually more prominent in UC. UC characteristically begins at the rectum and works backwards; Crohn lesions can “skip” areas of bowel and tend to occur in the right colon. Crohn is also characterized by granuloma formation and the development of strictures or fissures; UC is much less likely to show these.

In amebiasis (**choice B**), which is caused by *Entamoeba histolytica*, characteristic flask-shaped ulcers are produced but these extend through the mucosa into the submucosa.

None of the other diseases listed in the question produce a histologic/clinical picture compatible with the stated case; most produce a nonspecific enterocolitis:

AIDS-associated gastroenteritis (**choice A**), or HIV enteropathy, is associated with diarrhea in some cases; however, the clinical picture here is strongly suggestive of UC and there is no suggestion that the patient is infected with HIV.

*Clostridium difficile* (**choice D**) is notable for producing pseudomembranous colitis, usually in response to prior or concurrent antibiotic therapy.

*Escherichia coli*-associated colitis (**choice E**) is unlikely, given the biopsy results and the pattern of involvement of the bowel.

Ischemic colitis (**choice F**) is often transmural, and could conceivably be limited to the mucosa. The presence of acute and chronic inflammation in addition to the areas of the bowel involved, however, suggest inflammatory bowel disease instead.

Salmonella gastroenteritis (**choice G**) typically involves the ileum (including Peyer patches) and the colon.

**87. The correct answer is D.** The unfortunate girl described here succumbed to congestive heart failure secondary to rheumatic heart disease. Rheumatic fever typically occurs 1 to 5 weeks after a bout of acute streptococcal pharyngitis.

Migratory polyarthritis occurs commonly with rheumatic fever, typically affecting the large joints. An expanding erythematous rash with clearing in the center (erythema marginatum) is often seen, especially in children, and tends to occur in a “bathing-suit distribution” but may also affect the legs or face. Rheumatic fever is associated with pancarditis, an inflammation of all the layers of the heart. Inflammation of the endocardium may lead to valvular dysfunction, a serious consequence of the disease. The mitral valve is most commonly affected, followed by involvement of the mitral and aortic valves together; tricuspid and pulmonic involvement is relatively rare. Mitral stenosis, aortic regurgitation, and mitral regurgitation are frequent sequelae of rheumatic carditis. Myocarditis (i.e., inflammation of the myocardial layer) is the most serious

manifestation of acute rheumatic fever, and may lead to ventricular dilatation and acute decompensation.

Recent histories of cyanosis (**choice A**), jaundice (**choice B**), meningitis (**choice C**), or skin infection (**choice E**) are likely unrelated to the girl's clinical course.

**88. The correct answer is C.** An older descriptive, but rather insensitive, term for this condition was cri-du-chat ("cry of the cat"). There is deletion of a portion of the small arm of chromosome 5. The patients have a well-recognizable "meowing"-type cry. This has been attributed at least in part to development anomalies within the larynx. Other features are hypertelorism (widely-spaced eyes), a round face, low-set ears, micrognathia, and congenital heart defects. These patients are also mentally impaired, with marked cognitive and motor deficits.

Turner syndrome, 45,X (**choice A**) is characterized by a webbed neck and widely spaced nipples.

46,XX (**choice B**) is the normal female karyotype.

The 46,XX,t(14;21) translocation (**choice D**) is seen in Down syndrome.

46,XY (**choice E**) is the normal male karyotype.

Patients with trisomy 13, Patau syndrome, or 47,XX,+13 (**choice F**) have microcephaly, rocker-bottom feet, polydactyly, and cleft palates. A cat-like cry is not present.

Patients with Down syndrome, trisomy 21, or 47,XX,+13 (**choice G**) have protuberant tongues, simian creases, and increased incidence of heart defects. They have impaired intellectual function; the degree of impairment is variable.

69,XXY (**choice H**) is the karyotype seen in a partial hydatidiform mole.

**89. The correct answer is D.** Nephrotic syndrome is characterized by proteinuria, hypoalbuminemia, edema, and hyperlipidemia. Renal function is generally otherwise normal, and hypertension is uncommon. Nephrotic syndrome in children is usually due to minimal change disease (lipoid nephropathy). At the light microscopic level, glomeruli appear normal; however, podocyte foot-process fusion is observed with electron microscopy. In about 30% of cases, an upper respiratory tract infection precedes the onset of the renal disorder.

The absence of hypertension, azotemia, or hematuria makes focal glomerulosclerosis (**choice A**) unlikely.

Membranous glomerulopathy (**choice B**) is the most common cause of idiopathic nephrosis in adults, but it is uncommon in children.

In membranoproliferative glomerulonephritis (**choice C**), the nephrotic syndrome is typically accompanied by hypertension and hematuria as well as azotemia (increased BUN, creatinine).

In rapidly progressive glomerulonephritis (**choice E**), azotemia is common, and hematuria, proteinuria, and red cell casts are typical.

**90. The correct answer is A.** One receptor that norepinephrine activates is the alpha-1 adrenergic receptor, which is coupled to Gq. When Gq is activated, the membrane enzyme phospholipase C (PLC) is stimulated. PLC splits phosphoinositol-4,5-bisphosphate (PIP<sub>2</sub>) into two second messengers, inositol-1,4,5-triphosphate (IP<sub>3</sub>) and diacylglycerol. Diacylglycerol stays in the membrane and activates protein kinase C. IP<sub>3</sub> is water soluble and diffuses to internal storage sites, such as the endoplasmic reticulum, to trigger the release of calcium, thereby increasing intracellular calcium concentrations.

The Golgi complex (**choice B**) is a stack of membrane-bound vesicles where proteins and lipids made in the endoplasmic reticulum are modified and sorted.

Mitochondria (**choice C**) are membrane-bound organelles that carry out oxidative phosphorylation and produce most of the ATP in eukaryotic cells.

The nucleus (**choice D**) is a membrane-bound organelle containing DNA.

The plasma membrane (**choice E**) is a lipid bilayer with embedded proteins that surrounds a living cell.

**91. The correct answer is B.** The photograph shows a segment of bowel “telescoped” into the adjacent bowel. This is intussusception, which can cause abdominal pain and vomiting. The involved bowel may become infarcted and necrotic (a surgical emergency).

In appendicitis (**choice A**), the appendix would be inflamed and probably covered with pus. Involvement of the surrounding bowel would be unusual. Anorexia is common, and tenderness is invariably present eventually.

Meckel diverticulum (**choice C**) causes a fat outpouching of bowel coming off the small intestine.

Necrotizing enterocolitis (**choice D**) is usually a disease of neonates.

In strangulated hernia (**choice E**), the appearance would be similar to that in the photograph, but you would not see one loop of bowel telescoped into another.

**92. The correct answer is D.** Pyogenic (pus-forming) infections are almost always caused by bacteria (especially *Staphylococcus* or *Haemophilus*); recurrent bacterial infections with normal antibody production suggests a neutrophil defect. The history given is typical for children with congenital defects in neutrophil function. Normal cellular immunity (e.g., T cells, macrophages) is evidenced by successful immunizations and uneventful recovery from viral infections.

If the patient’s B lymphocytes (**choice A**) were defective, the child would not have normal antibody responses to immunizations.

Defective eosinophil production (**choice B**) does not seem to produce much clinical disease.

Defective macrophage function (**choice C**) is a possibility, but the specific vulnerability to pyogenic infections more strongly suggests neutrophil dysfunction.

Defective T lymphocytes (**choice E**) predisposes for problems with diseases that normally cause granuloma formation.

**93. The correct answer is C.** The woman in the question is experiencing a normal grief reaction 1 month after the traumatic loss of her daughter. Uncomplicated bereavement may last for up to 3 months (longer for close relations, and in some cultures), and is typically characterized by the type of symptoms described in the question stem.

Dysthymic disorder (**choice A**) is characterized by a depressed mood that lasts most of the day for the majority of time over a 2-year period, with the additional qualification that no major depressive episodes have occurred during that period.

Major depressive disorder (**choice B**) is characterized by the occurrence of at least one major depressive episode (depressed mood, loss of interest in everyday activities, anhedonia, feelings of worthlessness, etc.), and no manic or hypomanic episodes. Because the woman is experiencing depression secondary to the loss of a loved one, the diagnosis of major depressive episode does not apply and major depressive disorder is ruled out.

In obsessive-compulsive disorder (**choice D**), patients experience recurrent, intrusive thoughts (obsessions) that are relieved, to some extent, by engaging in repetitive, ritualistic behaviors (compulsions).

Schizoaffective disorder (**choice E**) is a psychotic disorder with prominent affective symptoms. There is no evidence to support a diagnosis of psychosis in this woman.

**94. The correct answer is A.** Presbycusis is the term for the progressive loss of sensitivity to high-frequency sounds that occurs with age. The cause may be degeneration or loss of elasticity of the basilar membrane in the first few millimeters of the basal end of the cochlea (the part that subserves high frequencies).

A loss of low-frequency tones (**choice B**) could occur with sensory–neural deafness (e.g., damage to the hair cell of the cochlea and/or vestibulocochlear nerve); however, a selective loss of sensitivity to higher frequency sounds is more typical.

Conduction deafness (e.g., wax in the external ear or impaired ossicular movement) typically produces a hearing loss across all frequencies (**choice C**).

Presbycusis would affect both air and bone conduction (compare with **choices D and E**).

**95. The correct answer is B.** There are four conditions that can lead to a right-shift of the oxygen dissociation curve, facilitating oxygen unloading. These are increased  $\text{PCO}_2$ , increased 2,3-bisphosphoglycerate, increased temperature, and decreased pH. Choice B is the only curve that is shifted to the right of the original curve.

**96. The correct answer is C.** Lovastatin is an HMG-CoA reductase inhibitor used to decrease cholesterol synthesis in patients with hypercholesterolemia. About 10% of patients taking reductase inhibitors intermittently show increases in creatine kinase (CK) activity, often in association with

heavy physical exercise. Patients may rarely present with striking elevations in creatine kinase activity accompanied by generalized pain in skeletal muscles. In such cases, if the drug is not discontinued, the ensuing rhabdomyolysis can cause myoglobinuria, which can produce renal failure.

Captopril (**choice A**) is an ACE inhibitor; toxic effects include hyperkalemia and cough.

Hydrochlorothiazide (**choice B**) is a thiazide diuretic; toxic effects include increased serum lipids, uric acid, and glucose, and potassium wasting.

Nicotinic acid (**choice D**), or niacin, is used to treat some hyperlipidemias. Toxic effects include flushing, pruritus, rashes, dry skin, acanthosis nigricans, hyperuricemia, and hypotension if the patient is receiving antihypertensive therapy.

Propranolol (**choice E**) is a nonselective beta-adrenergic antagonist. Toxic effects include bradycardia, atrioventricular blockade, congestive heart failure, and asthma attacks.

**97. The correct answer is D.** Parathion, an organophosphorus acetylcholinesterase inhibitor, increases synaptic acetylcholine (ACh) concentrations at parasympathetic effector sites, sympathetic at cholinergic effector sites, at neuromuscular junctions, and in the central nervous system. Increased parasympathetic cholinergic tone to the lungs can cause wheezing because of bronchial hypersecretion and bronchospasm. Increased parasympathetic tone to the gastrointestinal tract can cause diarrhea; nausea and vomiting also occur. Increased parasympathetic tone to salivary glands leads to excessive salivation. Sweating results from increased ACh at the sympathetic cholinergic synapses at sweat glands. CNS effects (depending on the degree of toxicity) include confusion, ataxia, slurred speech, loss of reflexes, convulsions, coma, and central respiratory paralysis. Generalized muscle weakness occurs because increased ACh at the neuromuscular junction produces a depolarizing blockade.

Glutethimide (**choice A**) is a sedative–hypnotic that can cause a variety of symptoms depending on the degree of toxicity. Symptoms include disinhibition, lethargy, stupor, coma, and nystagmus.

Heroin (**choice B**) is an opioid drug that can produce constipation, decreased blood pressure and heart rate, hypoventilation or apnea, pinpoint pupils, and sleepiness, lethargy, or coma.

Jimson weed (belladonna alkaloids; **choice C**) contains alkaloids that are muscarinic cholinergic antagonists. Predicted symptoms include constipation; urinary retention; dilated pupils; hyperthermia with hot, dry skin; tachycardia; and hypertension. Hallucinations, delirium, and coma can also occur. Phencyclidine (PCP; **choice E**) can cause tachycardia, hypertension, sweating, numbness, and nystagmus. Disorientation, distortion of body image, and loss of proprioception also occur.

**98. The correct answer is C.** Area C represents the location of the spinothalamic tract (spinal lemniscus) that carries pain and temperature information from the contralateral body. Pain and temperature information is initially carried by primary sensory neurons whose cell bodies reside in the dorsal root ganglia. Fibers of these neurons enter the dorsal spinal cord and synapse in the dorsal horn. The secondary neurons cross in the anterior white commissure, ascend as the spinothalamic tract in the ventrolateral cord, ascend in the brainstem as the spinal lemniscus, and synapse in the VPL nucleus of the thalamus.

**Choice A** is the hypoglossal nucleus, from which the hypoglossal nerve emanates. The hypoglossal nerve provides motor innervation to the intrinsic and extrinsic muscles of the tongue; a lesion of the hypoglossal nucleus would produce hemiparalysis of the ipsilateral tongue.

**Choice B** primarily depicts the descending tract of V (trigeminal nerve). This tract is composed of axons of primary sensory neurons that carry pain and temperature information from the ipsilateral face to synapse in the spinal nucleus of V (the structure just medial to B). A lesion in this area would cause ipsilateral loss of pain and temperature sensation of the face.

**Choice D** is a large lesion including the medullary pyramid, part of the medial lemniscus, and part of the inferior olivary nucleus. This lesion would produce left-sided paralysis of the body (pyramid), some left-sided loss of proprioception and discriminative touch (medial lemniscus), and possibly cerebellar signs (inferior olivary nucleus).

**Choice E** is a lesion of the medial lemniscus. This would produce a left-sided loss of proprioception and discriminative touch over the body.

**99. The correct answer is B.** The symptoms described (fever, malar rash, pericardial rub, arthritis) are suggestive of a lupus-like syndrome. Hydralazine can cause a lupus-like syndrome in a significant number of patients, especially if the dosage is high, and if therapy continues for more than 6 months. Females are more likely to suffer from this complication than are males, and so-called slow acetylators (acetylation is important in the metabolism of hydralazine) are more likely to develop this complication.

Captopril (**choice A**) is an ACE inhibitor and can cause hyperkalemia, cough, and acute renal failure in patients with preexisting renal disease.

Minoxidil (**choice C**) is a vasodilator and its toxic effects include salt and water retention, tachycardia, pericardial effusion, and hirsutism.

Nitroprusside (**choice D**) is a vasodilator. Toxic effects include hypotension, tachycardia, and accumulation of cyanide or thiocyanate in the blood.

Propranolol (**choice E**) is a nonselective beta antagonist, and its toxic effects include bradycardia, atrioventricular blockade, congestive heart failure, and asthmatic attacks in patients prone to airway disease.

**100. The correct answer is A.** Cimetidine is the most likely cause of the theophylline toxicity because it inhibits the cytochrome P450 oxidative drug metabolizing system. Theophylline's metabolism would be impaired, leading to toxic plasma levels.

Hydrochlorothiazide (**choice B**) and prazosin (**choice C**) should not alter levels of theophylline.

Rifampin (**choice D**) would actually lower plasma levels of theophylline by inducing the cytochrome P450, thus hastening theophylline's metabolism.

## BLOCK 3

**101. The correct answer is A.** Following menopause and in the absence of hormonal stimulation, the follicles in the ovary undergo programmed cell death, otherwise known as apoptosis. This is a normal physiologic process.

The patient is not a frog; ovaries do not undergo metamorphosis (**choice B**).

Metaplasia (**choice C**), the transformation from one cell type to another (within the same germ cell layer), is an adaptive response to a variety of stimuli.

Necrosis (**choice D**) can be thought of as uncontrolled cell death, and is often associated with an inflammatory reaction.

Transformation (**choice E**) from one cell type to another does not fully describe the observed findings.

**102. The correct answer is D.** The lesion described is a pleomorphic adenoma (mixed tumor), which typically involves the parotid gland. This benign lesion tends to have poorly defined “fingers” extending into the parotid gland that may cause the tumor to recur if they are not completely excised (complete excision can be difficult because the surgeon must try to spare all of the branches of the facial nerve, which runs in the substance of the parotid gland).

Contralateral immune-mediated parotitis (**choice A**) would be seen in Sjögren syndrome.

Hematogenous metastases (**choice B**) would not be seen with pleomorphic adenoma because this is a benign tumor.

Pleomorphic adenomas do not usually involve the submaxillary gland (**choice C**).

Regional lymph node metastases (**choice E**) would not be seen because this is a benign tumor.

**103. The correct answer is A.** Breast abscess is caused by bacterial infection (usually *Staphylococcus aureus*) of the breast, which generally occurs if the normal barrier to infection provided by the skin of the nipple is compromised (usually by trauma due to nursing). The condition will usually respond to antibiotic therapy, but the resulting scar may mar the shape of the breast.

A fibroadenoma (**choice B**) usually causes a round, firm breast mass that would not resolve with antibiotic administration.

Fibrocystic change (**choice C**) can cause round, fluid-filled masses (cysts) or areas of thickened breast tissue (fibrosis) that would not resolve with antibiotics.

Infiltrating mammary carcinoma (**choice D**) can produce skin retraction, but would be very unusual in a 24-year-old and would not have responded to antibiotics.

Traumatic fat necrosis (**choice E**) follows trauma to the breast and would not be expected to respond to antibiotics.

**104. The correct answer is B.** Elderly individuals are particularly prone to delirium during hospitalizations. Sometimes termed “ICU psychosis,” delirium occurs in the setting of stressful situations. Appropriate treatment is to provide the patient with familiar surroundings, family members, etc. The delirium is not a permanent state. Delirium can also be secondary to medications with anticholinergic activity.

Emotional, not cognitive, impairment is more commonly associated with adjustment disorder (**choice A**).

The patient has no history of paranoid behavior prior to admission (**choice C**).

To warrant the diagnosis of schizophrenia (**choice D**), the periods of psychosis should be present for longer than 6 months.

Senile dementia, whether of the Alzheimer (**choice E**) or multi-infarct type, is progressive, not acute.

**105. The correct answer is B.** The patient is likely to have contracted malaria, so a Giemsa-stained blood film is the best means of finding the intra-erythrocytic parasites.

Acid-fast stain (**choice A**) is the stain of choice for mycobacteria. *Nocardia* is a genus that is partially acid-fast.

Gram stain (**choice C**) is the diagnostic of choice for the majority of bacteria. The agent of malaria, *Plasmodium*, is a protozoan parasite.

India ink wet mount (**choice D**) is a diagnostic for *Cryptococcus neoformans*, an encapsulated yeast that causes meningitis in the immunocompromised person.

KOH stain (**choice E**) is the diagnostic of choice for many fungal infections.

Methylene blue (**choice F**) is a stain that may be used to identify leukocytes, but it would not be the diagnostic stain of choice for an intraerythrocytic parasite.

**106. The correct answer is A.** Anemia and granulocytopenia are the most significant adverse effects encountered with the nucleoside polymerase inhibitors, such as zidovudine (AZT). Anemia is also caused by the protease inhibitors. The associated anemia typically occurs 4 to 6 weeks after the onset of therapy, and is caused by a decreased formation of erythrocytes by the marrow. Erythropoietin is the agent of choice to treat anemia in patients taking nucleoside polymerase inhibitors.

This type of anemia is not related to increased formation of erythrocyte antibodies (**choice C**) or increased fragility of erythrocytes (**choice D**).

Since there is no indication that the anemia is macrocytic or microcytic in nature, it is unlikely that the anemia is caused by folate (**choice B**) or iron (**choice E**) deficiency, respectively.

**107. The correct answer is F.**  $\beta$ -thalassemia major is a disease caused by reduced production of the  $\beta$ -globin protein. The three nucleotides indicated in the question are all located upstream of

the transcription start site, where the promoter is located. This means that the nucleotides are not transcribed and will not be present in the mRNA. Therefore, they cannot be involved in binding elongation factors involved in protein translation (**choices A and B**). Histone acetylase and deacetylase (**choices C and D**) are involved in regulating transcriptional control by changing chromatin structure and packing. However, they act on histones across the entire gene region, and would not necessarily be localized to the area upstream of the transcription start site. Therefore, the mutations are located in the promoter region, which transcription factors bind and act upon. Mutations most likely cause function loss, so interfering with positive-acting transcription factors will lead to reduced transcription of the  $\beta$ -globin mRNA, resulting in lower levels of  $\beta$ -globin protein. Defects in negative-acting transcription factor binding sites (**choice E**) would lead to increased production of the gene product, which does not occur in  $\beta$ -thalassemia major.

**108. The correct answer is B.** Adenosine deaminase deficiency is a genetic defect in which adenosine builds up and becomes toxic in developing lymphocytes. This enzyme has highest activity in lymphocytes, so it causes a severe combined immunodeficiency disease (SCID) because this toxic metabolite kills both B and T lymphocytes.

Adenine phosphoribosyltransferase (**choice A**) is an enzyme involved in purine salvage. Its deficiency would manifest with nephrolithiasis, acute renal failure, and permanent kidney damage because of the accumulation of the insoluble purine 2,8-dihydroxyadenine.

Adenosine kinase (**choice C**) is the enzyme responsible for the conversion of two ADPs to AMP plus one ATP, and vice versa. A deficiency of this enzyme would be likely to manifest symptoms in liver and muscle, where turnover of energy from ATP is high.

Adenylosuccinate synthetase (**choice D**) is an enzyme that catalyzes the substitution of succinate for the carbonyl oxygen of inosine monophosphate, a step in the biosynthesis of adenosine monophosphate. A deficiency of this enzyme would cause defects in energy production in cells, but would not be likely to have immunologic consequences such as those described here.

Hypoxanthine-guanine phosphoribosyltransferase (**choice E**) deficiency also causes problems with purine salvage but would be manifested by spastic cerebral palsy, self-mutilation, hyperuricemia, and early death.

Ribonucleotide reductase (**choice F**), or ribonucleoside diphosphate reductase, is the enzyme that is used to provide a balanced supply of deoxyribonucleotides for DNA synthesis. Its deficiency would cause defects of cell division that would mimic those of ADA deficiency but not be restricted to lymphocytes.

**109. The correct answer is E.** Obstruction of lymph vessels causes interstitial fluid accumulation and increased interstitial protein concentration. Increased tissue oncotic pressure increases filtration. Metastases of the ovarian cancer, an adenocarcinoma, are likely to block lymphatic vessels because they invade the lymphatics.

Decreased capillary hydrostatic pressure (**choice A**) and increased capillary oncotic pressure (**choice C**) are incorrect because they will cause decreased filtration, not edema.

Edema will cause increased interstitial hydrostatic pressure, so **choice B** is incorrect, because decreased pressure cannot exist in the same place at the same time as increased pressure.

Increased capillary permeability (**choice D**) may cause edema but is less likely in this case because the ovarian cancer is unlikely to cause increased permeability in a restricted region.

**110. The correct answer is E.** Strenuous exercise often results in the release of myoglobin from muscle cells with passage into the urine. The myoglobin results in a false-positive result in the urine blood test, which evaluates for heme-like compounds. Prolonged immobility of a joint, or the patient's passing out and remaining in a fixed position, can lead to the same findings.

Acute glomerulonephritis (**choice A**) with no preceding infection or other event and the lack of blood cells in the urine make this an unlikely diagnosis.

Hypovolemia (**choice B**) would not lead to blood in the urine.

Renal infarcts (**choice C**) or renal vein thrombosis (**choice D**) would present with pain and possible renal failure. In the absence of predisposing factors, these diagnoses are unlikely.

**111. The correct answer is A.** Irreversible dilated cardiomyopathy is a complication of doxorubicin therapy. The heart becomes dilated with impaired systolic function, reduced ejection fraction, and increased end systolic volume. Alcohol, in contrast, will initially cause a reversible dilated cardiomyopathy. These patients have progressive heart failure, exercise intolerance, and dyspnea. On gross evaluation, the heart is enlarged and boggy. Histologic analysis does not usually help in identifying an etiologic agent.

Obstructive pulmonary disease (**choice B**) represents a progressive chronic disease that may present with similar clinical findings. There is, however, no history to support this diagnosis.

Idiopathic pulmonary hypertension (**choice C**) is most common in young adult females (20 to 40 years of age).

Doxorubicin is not associated with a restrictive cardiomyopathy (**choice D**).

Restrictive pulmonary disease (**choice E**) may give a similar clinical picture, but with the history provided, this is a less likely diagnosis.

**112. The correct answer is E.** A threefold increase of angiotensin II (AII) represents a moderate rise. Exogenous administration of AII decreases secretion of renin via negative feedback systems. At moderate concentrations, AII has more vasoconstrictive effect on the efferent arteriole than on the afferent arteriole. The infusion will cause moderate efferent arteriolar constriction, which will increase both efferent resistance and glomerular capillary pressure. This will decrease renal blood flow, and hence renal plasma flow. Increased glomerular capillary pressure increases GFR. Because filtration fraction is GFR divided by renal plasma flow, the filtration fraction will increase. All other choices contain at least one false prediction.

**113. The correct answer is D.** The complete blood count shows normal amounts of red blood cells and white blood cells. There is, however, a markedly decreased number of platelets clinically presenting as petechiae. Immune (idiopathic) thrombocytopenic disorder is an autoimmune-mediated destruction of platelets. It is often preceded by a viral infection. There is

no splenomegaly. Bone-marrow smears show an increased number of megakaryocytes. The disorder is one of destruction, not production.

The increased number of megakaryocytes is compensatory, not leukemic (**choice A**).

Acute megakaryocytic leukemia (**choice B**) is the M7 class of AML.

Aplastic anemia (**choice C**) would present with a decrease in all blood cells.

EBV infections (**choice E**) are associated with mononucleosis, nasopharyngeal carcinoma, and some B-cell lymphomas.

Papovavirus infection (**choice F**) is not associated with decreased platelets.

Thrombotic thrombocytopenic purpura (**choice G**) is associated with neurologic abnormalities, fever, and renal dysfunction. Also, the blood smear would show anemia with schistocytes.

**114. The correct answer is B.** Cortisol inhibits the responses of muscle, adipose tissue, and liver to insulin. Cortisol is a principal stress hormone so plasma levels are expected to increase substantially during an infection or other stress. In such circumstances, its effects on response to insulin frequently induce hyperglycemia and ketoacidosis in patients with previously well-controlled diabetes mellitus.

Androstenedione (**choice A**) is incorrect because although high levels of androgens may be associated with insulin resistance, the clinical situation in this patient does not support elevated androgen levels.

Glucagon (**choice C**) is incorrect because glucagon does not act significantly on skeletal muscle.

Leptin (**choice D**) has predominately central nervous actions.

Thyroxine (**choice E**), in high concentrations typical of hyperthyroidism, causes loss of glycemic control; the clinical description of this case does not support hyperthyroidism.

**115. The correct answer is D.** During an immunization, CD4+ lymphocytes (helper T cells) that can respond to the particular antigens proliferate and simultaneously enhance proliferation of B cells that can respond to the same antigen. These helper lymphocytes are found in quadrant D on the chart (i.e., the cells exhibiting maximal CD4+ fluorescence and minimal CD8+ fluorescence).

Quadrant A (**choice A**) contains CD8+ lymphocytes, which have suppressor function.

Quadrant B (**choice B**) contains small numbers of CD4+/CD8+ lymphocytes, whose function remains unclear.

Quadrant C (**choice C**) does not contain any lymphocytes. If present, these would be “null” cells.

**116. The correct answer is E.** Gap junctions are a type of intercellular connection formed by connexon channel proteins, which allow the direct passage of small particles and ions between

cells. The “channel” portion of the connexon protein refers to the tubelike tunnel that traverses the plasma membrane and corresponds to the transmembrane region of the protein.

The amino terminus of a transmembrane protein (**choice A**) usually encodes the signal peptide, which is involved in targeting the protein but not in the protein’s actual function as a channel.

The carboxyl terminus of a protein (**choice B**) functions most often in signals for attachment of a poly-A tail, which maintains mRNA stability. It is not commonly associated with channel function.

The cytoplasmic (**choice C**) and extracellular (**choice D**) loops are most likely involved in anchoring with the cytoskeleton and neighboring cells, respectively. In particular, the extracellular portion of the connexin protein is likely required to recognize the extracellular domain of neighboring connexin proteins to form a functional channel.

**117. The correct answer is H.** Furosemide is the prototype “loop diuretic.” Its mechanism of action is the inhibition of the  $\text{Na}^+/\text{K}^+/\text{Cl}^-$  secondary active cotransporter in the thick ascending loop of Henle. Thus, transport in this segment decreases with administration of the drug. The rate of transport in this segment is a major contributor to the maintenance of the hyperosmotic condition of the interstitium of the medulla; therefore, with administration, the osmolarity of the interstitium decreases. Water absorption from the descending loop of Henle depends on the osmotic gradient between the tubular fluid as it enters the loop and the hyperosmotic interstitium of the medulla. The action of the drug to decrease osmolarity of the interstitium reduces the gradient; therefore, less water is reabsorbed from this segment. All of the other choices contain at least one incorrect prediction.

**118. The correct answer is B.** Although the presence of an intracranial bleed should raise the concern of child abuse, the other data indicating impairment of the coagulation cascade point away from the diagnosis. Synthesis of coagulation factors 2, 7, 9, and 10 require gamma carboxylation. Vitamin K, which is lacking in the patient’s diet, is a necessary cofactor for this process. Profuse bleeding can result. Depending on the location and extent of bleeding, treatment may include administration of plasma or vitamin K.

GABA (**choice A**) is a neurotransmitter and is not involved in producing intracranial hemorrhage.

There is no evidence to suggest that the patient is anemic (**choice C**).

Neither thymidine synthesis (**choice D**) nor xanthine oxidation (**choice E**) is required for the formation of coagulation factors.

**119. The correct answer is E.** Gestational onset of hypertension (usually after week 20), proteinuria, and edema are classic symptoms of preeclampsia, a multisystem disorder. Preeclampsia is associated with arteriolar spasm, possibly due to an unusually high ratio of thromboxane to prostacyclin. Renal vasospasm results in decreased glomerular filtration with increased blood urea nitrogen (BUN), increased creatinine, and proteinuria. Uterine vasospasm can cause placental ischemia and poor fetal growth; cerebral vasospasm can cause headaches. High levels of thromboxane can also cause aggregation of platelets, contributing to thrombosis and

thrombocytopenia. Evidence of intravascular hemolysis and liver damage indicate that the condition is severe.

Acute glomerulonephritis (**choice A**) is unlikely because there was no hematuria and red cell casts were absent.

The peripheral edema observed would require severe right-sided as well as left-sided heart failure, which is unlikely. Congestive heart failure (**choice B**) in the context of peripartum cardiomyopathy is typically left-sided and does not involve hypertension.

Seizures indicate eclampsia (**choice C**), a severe complication of preeclampsia.

Nephrotic syndrome (**choice D**) is characterized by proteinuria, hypoalbuminemia, and edema, but is not associated with hypertension.

**120. The correct answer is B.** The patient has a microcytic, hypochromic anemia. In the postmenopausal female and the middle-aged and older male, the primary concern must be chronic blood loss from a colonic neoplasm. These patients must be worked up.

In acute hemolytic anemia (**choice A**), because of the induced reticulocytosis, the MCV may be normal or elevated. (Reticulocytes are larger than red blood cells.)

Folate (**choice C**) or vitamin B<sub>12</sub> (**choice E**) deficiency would lead to a macrocytic anemia.

The patient is not going to present with thalassemia (**choice D**) at age 75.

**121. The correct answer is A.** The number-one etiologic agent that far outweighs the other factors listed is smoking. Reduction or elimination of smoking would have the biggest impact.

Radon exposure (**choice B**) is an important risk factor for lung cancer, but not the highest.

Aerobic exercise (**choice C**) would help, but is only a minor factor.

Flu (**choice D**) and pneumococcal (**choice E**) vaccinations reduce mortality in persons with chronic lung disease.

Removal of asbestos (**choice F**) from buildings and lead from gasoline and other fuels (**choice G**) would not have as great an effect as decreasing smoking.

**122. The correct answer is C.** Drug W diminishes the effect of Drug V in a noncompetitive manner. A noncompetitive antagonist results in inhibition that cannot be reversed by addition of an agonist. Because Drug W works at a site downstream of the receptor, addition of the agonist, Drug V, would not overcome the effects of Drug W.

A competitive antagonist (**choice A**) binds to a receptor without activating the receptor's effector system. The effects of a competitive antagonist can be reversed by addition of an agonist that competes for the same binding site. Drug W is not a competitive antagonist because it does not bind the receptor.

A full agonist (**choice B**) is an agent that can fully activate its effector system by binding to its receptor. A partial agonist (**choice D**) binds to its receptor but produces less than a full effect. Drug W is clearly neither a full or partial agonist because it prevents the effects of Drug V. Drug V, however, may be either a full or partial agonist.

A reverse agonist (**choice E**) binds to the receptor and results in the opposite of the normal effect of the natural agonist. Because Drug W does not bind the receptor, it cannot be a reverse agonist.

**123. The correct answer is B.** To facilitate rapid availability of enzymes, trypsinogen is stored in granules within the pancreas. Following stimulation, this is released into the pancreatic duct and subsequently converted to trypsin by enterokinase.

Trypsin (**choice A**) is formed from trypsinogen, not vice versa.

Trypsinogen is activated (**choice C**) in the duodenum, not the pancreas.

The protein is preformed; transcription (**choice D**) and translation (**choice E**) are not stimulated directly by the vagus nerve.

**124. The correct answer is C.** The direct actions of thyroid peroxidase include oxidation of iodide and iodination of tyrosine. The most direct effects of the deficiency state in this animal will be reduction of these two processes. The result is hypothyroidism due to decreased synthesis.

Ultimately, all other processes involved in the production, the storage in the follicular lumen, and the reuptake, cleavage, and release of  $T_4$  and  $T_3$  would be affected (**choices A, B, D, and E**). They are not the best choice because they are indirect consequences of the deficiency, whereas the effects on oxidation and iodination of tyrosine are direct. If binding of iodide to tyrosine were reduced, clearly its cleavage from tyrosine would also be reduced; however, the direct effect of the deficiency would be to impair synthesis. Similarly, the other listed processes may be impaired, but these are consequences of the main, direct effects as described in choice C.

**125. The correct answer is B.** Panic disorders are characterized by episodes of intense fear and discomfort and possibly palpitations, abdominal distress, sweating, and chest pain. This can be a crippling disorder for the patient. Patients are often worked up for heart attacks. Cognitive behavioral therapy is aimed finding, addressing, and resolving potential triggers.

The patient's problem is not one of assertiveness (**choice A**), but anxiety.

Dynamic psychotherapy (**choice C**) explores patient relationships with oneself and others.

Psychoanalysis (**choice D**) is an involved analysis into the psyche. It is not designed for panic attacks.

Psychodrama (**choice E**) is a group therapy modality.

**126. The correct answer is E.** Although neonatal screening varies a little by state, several diseases are screened for in every state. In phenylketonuria, there is decreased functioning of

either phenylalanine hydroxylase or the tetrahydrobiopterin cofactor, leading to accumulation of phenylacetic acid. Patients show both mental and growth retardation. These are obviously nonspecific findings. The telltale finding is a musty odor of the body and urine.

Patients with elevated homocysteine levels (**choice A**) have mental retardation and lens subluxation.

Urine from patients with alkaptonuria has elevated homogentisic acid (**choice B**) and turns black on standing.

Maple syrup urine disease is characterized by an inability to break down branched amino acids (including isoleucine, **choice C**). The urine has a maple syrup smell.

Isovaleric acid accumulation (**choice D**) results in CNS toxicity.

**127. The correct answer is H.** This girl is showing signs of completely normal motor (sitting and crawling) and language (babbling) development. The separation anxiety evidenced when the mother leaves the room is also normal. Separation anxiety can appear as early as 6 to 7 months of age, after object permanence is established; it is often worse from about 10 to 18 months of age, then fades as the second birthday approaches.

**128. The correct answer is A.** Nystatins and the imidazoles, the treatments for dermatophytic infections such as this one, target ergosterol, a unique constituent of the cellular membrane of the fungi.

Inhibition of DNA synthesis (**choice B**) is the mechanism of action of flucytosine, which would be the drug of choice for chromoblastomycosis and for combination use in candidiasis and cryptococcosis.

Inhibition of ribosomal protein synthesis (**choice C**) is the mechanism of action of several antibacterial drugs such as the aminoglycosides, macrolides, and tetracyclines, but these are not used in the treatment of dermatophytic infections.

Interference with mycolic acid synthesis (**choice D**) is the goal of isoniazid, which is used against the acid-fast prokaryotes.

Irreversible binding to DNA-dependent RNA-polymerase (**choice E**) is not a mechanism of action of any of the drugs used in treatment of fungal pathogens.

**129. The correct answer is E.** The described features of tetralogy of Fallot are ventricular septal defect, subpulmonic stenosis, overriding aorta, and right ventricular hypertrophy. With the impaired right ventricular outflow tract stenosis, there is right-to-left shunt. This disorder, therefore, presents with early cyanosis. Auscultation of the pulmonic valve reveals a mid-systolic murmur.

Atrial septal defects (**choice A**) do not present with early cyanosis.

A bicuspid aortic valve (**choice B**) is the most common cardiac anomaly. It presents with aortic valve calcification in later years.

Coarctation of the aorta (**choice C**) can present with differential blood pressures in the upper and lower extremities. If there is preductal coarctation, there may be early cyanosis. It would not, however, produce the described murmur.

A patent ductus arteriosus (**choice D**) presents with a machine-like (continuous) murmur.

**130. The correct answer is D.** Accommodation is the response to looking at something moving toward the eye. Contraction of the ciliary muscle, which is under parasympathetic control, causes the suspensory ligaments surrounding the lens to relax, producing a rounder, more convex lens shape. This increases the refractive power of the lens, allowing close objects to be brought into focus. Drugs with antimuscarinic properties prevent accommodation, and many antidepressant drugs have antimuscarinic side effects.

$\alpha$ -adrenergic drugs (**choice A**) would not prevent accommodation. Drugs that stimulate these receptors are sometimes used in glaucoma to produce vasoconstriction, causing greater aqueous humor outflow.

$\beta$ -adrenergic drugs (**choice B**) might affect aqueous humor production. For example, timolol, a beta blocker, decreases aqueous humor production.

Histaminergic drugs (**choice C**) would not prevent accommodation. However, many antihistaminergic drugs have antimuscarinic properties, and these types of drugs might affect accommodation.

Serotonergic drugs (**choice E**) do not prevent accommodation.

**131. The correct answer is C.** Isoniazid is indicated for prevention of active tuberculosis in a person known to be infected with the tubercle bacillus. Isoniazid causes drug-induced hepatitis in about 1% of patients receiving the drug. Once hepatitis occurs, the drug must be discontinued to prevent an increase in the severity of the damage. Age is the most important factor in determining the risk of isoniazid-induced hepatitis. In patients under the age of 20, the risk of hepatitis is less than 0.3%, but in a patient older than 50 years, the risk is approximately 2.3%.

Hepatic tuberculosis (**choice A**) is a rare condition that presents with fever and abnormalities of liver function tests. It can produce extrahepatic obstruction with ascending cholangitis.

Infection with hepatitis B virus (**choice B**) could produce the symptoms described here; however, there is no evidence in the history that this individual has an acute hepatitis B infection, and chronic carriers of hepatitis B virus tolerate isoniazid very well.

Pyridoxine (**choice D**) is given with isoniazid to minimize the incidence of peripheral neuritis. Such administration has not been associated with cholecystitis.

Tubercular pancreatitis (**choice E**) is very rare and resembles other infections or neoplastic changes of the pancreas.

**132. The correct answer is B.** This patient is suffering from an acute episode of gout. Colchicine, in most instances, can be effectively used to treat gout without adverse effects on the coexisting peptic ulcer.

Allopurinol (**choice A**) is used to treat chronic gout.

Morphine (**choice C**) may address the pain but will not affect the underlying cause.

Probenecid (**choice D**) is also used to treat chronic gout.

Sulfinpyrazone (**choice E**) is inappropriate in a patient with peptic ulcer disease.

**133. The correct answer is E.** Tissue plasminogen activator (tPA), which is secreted by endothelial cells, is optimized by binding to fibrin. This has the advantage of restricting the activity of tPA to the site of the clot. Plasmin degrades fibrin. It also degrades fibrinogen, but this is less frequent because of restriction of activity to the clot secondary to tPA localization.

Heparin (**choice A**) prevents clot formation; it is not involved in degradation.

Aspirin (**choice B**) inhibits platelet activity.

Factor II (**choice C**) is necessary to convert fibrinogen to fibrin.

Fibrinogen concentration (**choice D**) does not influence the activity of tPA.

**134. The correct answer is D.** The relationship between flow and pressure is described by the equation: pressure gradient  $DP = \text{flow (Q)} \times \text{resistance (R)}$ . If resistance is constant, as in a rigid tube, flow increases linearly with upstream perfusion pressure (P1, or arterial pressure in a vascular bed) as shown in **choice A**.

Autoregulation refers to the ability of the arterioles in a vascular bed to regulate their resistance in order to maintain a relatively constant flow in the face of a changing perfusion pressure gradient, for example, when mean arterial pressure (MAP) changes due to increased cardiac output, as shown in **choice D**. At very low MAP, the arterioles are maximally dilated, but as the MAP reaches the autoregulation range, the arterioles begin to constrict to compensate for the increased pressure (myogenic response). At very high MAP, arterioles reach maximum constriction, and further MAP increases will again raise flow (as seen on the far right-hand side of the curve). Many vascular beds show some degree of autoregulation, with the cerebral, renal, and coronary circulations exhibiting the strongest effects.

**135. The correct answer is C.** Eukaryotes are cells that have membrane-bound nuclei and organelles. Introns are noncoding regions of DNA that are transcribed into RNA. Subsequent translation into messenger RNA removes the introns, leaving only the coding regions. This requires trafficking in and out of the membrane nucleus. Prokaryotes do not have introns.

Both prokaryotes and eukaryotes have cell membranes (**choice A**), although they may differ somewhat in structure.

DNA (**choice B**) is not specific to eukaryotes.

Messenger RNA (**choice D**) and ribosomes (**choice E**) are used for protein synthesis and are not seen exclusively in eukaryotes.

**136. The correct answer is E.** Sudden cardiac death secondary to ventricular fibrillation is a common cause of death in the United States. The fibrillating heart is unable to circulate blood effectively. The hypoperfusion of the brain results in collapse, followed rapidly by death. In the present case, by 10 minutes (when the paramedics arrived) the complete failure to circulate blood has resulted in death. The patient's history of diabetes, atherosclerotic coronary artery disease, and angina are strong predisposing factors.

In cardiac tamponade (**choice A**), there is impaired diastolic filling. Although the clinical presentation and EKG findings will vary by cause (wet versus dry) the event is not as acute as the one presented here, and there is usually a preceding event.

A stroke (**choice B**) is less likely to be so rapidly fatal, unless the stroke is massive. Focal neurologic impairment prior to the collapse is also likely.

Necrosis of the myocardium (**choice C**) would not occur so quickly.

Rupture of the papillary muscle (**choice D**) is usually a late complication.

**137. The correct answer is E.** Sarcoidosis is an idiopathic inflammatory disease affecting most commonly (but certainly not exclusively) young to middle-aged adult African American females. Although any organ can be involved, the lungs are most commonly affected. The usual presentation is respiratory difficulty or coughing. Radiographic evaluation reveals prominent interstitial markings and hilar adenopathy. Biopsy reveals the presence of noncaseating granulomas.

Pulmonary hemorrhage (**choice A**) could give bilateral opacities but not hilar adenopathy.

Liquefaction necrosis (**choice B**) in the lung occurs in the setting of abscess-forming infections. The patient would have a more acute presentation and would be more likely have a productive cough.

Dilation of the respiratory bronchioles (**choice C**) may be seen in pulmonary fibrosis (including end-stage sarcoidosis) and chronic infections. Given the present history, this is not a likely finding at this stage.

If this patient had microabscesses (**choice D**), she would be sicker. Bilateral microabscesses can be seen in the setting of infective endocarditis of the tricuspid valve.

**138. The correct answer is B.** This patient has *Streptococcus pneumoniae* meningitis. Neutrophils are called into the CSF by the production of C5a, which is strongly chemotactic for neutrophils.

Bradykinin (**choice A**) is a nonapeptide produced by activation of the kinin system in a number of inflammatory conditions. It is a potent vasodilator, increases vascular permeability, stimulates

pain receptors, and causes contraction of a variety of types of extravascular smooth muscle. It is not known to be chemotactic for neutrophils.

Factor XII (Hageman factor; **choice C**) is involved only indirectly in the chemotaxis of neutrophils. Because activation of Hageman factor starts the clotting cascade, and fibrinopeptides involved in the clotting cascade stimulate neutrophil diapedesis, this would be a secondary stimulus to neutrophilic infiltration.

Histamine (**choice D**) is not chemotactic for neutrophils.

Leukotriene E<sub>4</sub> (**choice E**) is not chemotactic for neutrophils; it is leukotriene B<sub>4</sub> that is chemotactic for these cells.

**139. The correct answer is B.** The autopsy findings of the adrenal glands are characteristic of atrophy caused by deficient circulating ACTH. The zona glomerulosa is prominent because this region produces aldosterone and is not dependent on ACTH. The atrophy of the zona fasciculata and zona reticularis is due to their dependence on control by ACTH. The adrenal crisis is the effect of inadequate secretion of cortisol. The likely sequence of events is compression of the pituitary stalk by the tumor, blocking hypothalamic control of the anterior pituitary. This causes a chronic decrease of ACTH, leading to adrenal atrophy.

Autoimmune destruction (**choice A**) is usually associated with specific histologic features of degeneration, which were not noted in this case.

Decreased cortisol concentration (**choice C**) causes increased secretion of ACTH due to loss of negative feedback; this causes hyperplasia rather than atrophy.

The adrenal medulla, not the cortex, would be impaired by denervation (**choice D**).

Granulomatous disease (**choice E**) presents with skin lesions, infections, and abscesses; abscesses of viscera can occur. The description of the present case includes none of the features of this disorder.

**140. The correct answer is D.** Normal laboratory findings in a patient with alternating episodes of diarrhea, constipation, and pain are highly suggestive of irritable bowel syndrome. These patients often have an urge to defecate after they eat. They should, however, be fully evaluated to eliminate other potential pathologies. Psychiatric intervention and counseling has proved helpful in treating this disorder.

Gastroenteritis (**choice A**) is unlikely to last a year and would have atypical lab findings.

Although there may be a comorbid anxiety disorder (**choice B**), it is not the root of the gastrointestinal problems.

With such specific, prolonged, and focused complaints, hypochondriasis (**choice C**) would not be at the top of a differential diagnosis.

This patient does not meet the criteria for either a major depressive (**choice E**) or somatization (**choice F**) disorder.

**141. The correct answer is D.** Because the patient has a fixed intake of NaCl of 200 mmol/day, after 4 days the total intake of NaCl will be 800 mmol. The total amount of NaCl excreted in the urine over the 4 days is 500 mmol; therefore, the patient has retained 300 mmol of NaCl. The patient will retain water to maintain a normal serum sodium concentration. If 1 L of normal saline containing 150 mmol of NaCl weighs 1 kg, then the 300 mmol of NaCl in the patient will increase the patient's weight by 2 kg. Hence, instead of 70 kg, the patient will weigh 72 kg after 4 days.

The most common cause of increasing weight in a hospitalized patient is sodium retention (any time a patient retains sodium, the body weight increases). Therefore, **choice A** (66 kg), **choice B** (68 kg), and **choice C** (70 kg) are incorrect because they do not demonstrate weight gain. **Choice E** (74 kg) is also incorrect, because the patient did not retain 600 mmol of NaCl after 4 days.

**142. The correct answer is A.** Sildenafil (Viagra™) is a drug used for erectile dysfunction. Erection occurs because of the release of nitric oxide (NO) in the corpus cavernosum during sexual stimulation. NO subsequently activates guanylate cyclase, leading to increased levels of cyclic guanosine monophosphate (cGMP), which produces smooth-muscle relaxation in the corpus cavernosum and permits the inflow of blood. Sildenafil inhibits phosphodiesterase-5 (PDE-5), which degrades cGMP, thus leading to increased levels of cGMP. In addition to being found in corpus cavernosum smooth muscle, PDE5 is also found in vascular smooth muscle, visceral smooth muscle, skeletal muscle, and platelets. Inhibition of PDE5 in vascular smooth muscle can lead to a decrease in basal vascular smooth muscle tone, which can contribute to the orthostatic hypotension seen in this patient.

Sildenafil does not directly affect autonomic nervous system activity (**choices B, C, E, and F**).

Sildenafil decreases, rather than increases (**choice D**), basal vascular smooth-muscle tone.

**143. The correct answer is E.** An ulcerated, red lesion in a sun-exposed area in an elderly individual is almost certainly squamous cell carcinoma. It is the most common tumor seen in sun-exposed areas in the elderly population. This is confirmed with the histologic findings.

Actinic keratoses (**choice A**) are red or skin-colored, with a rough consistency. They may be premalignant lesions.

In discoid lupus erythematosus (**choice B**), the lesions may be poorly defined and erythematous, or sharply defined and scaly.

Melanoma lesions (**choice C**) are classically seen in sun-exposed areas in younger individuals. They are dark in color with irregular borders. There is no ulceration.

Mycosis fungoides (**choice D**) is a T-cell proliferative disorder that affects the skin. It presents early as red-brown raised patches.

**144. The correct answer is A.** Assumptions that the doctor (or nurse) knows best, or the making of decisions on behalf of patients without involving them, is known as paternalism and is relatively common in modern health care systems. Although it may be well intentioned, it can produce an unhealthy dependency. The patient should always be as involved, if possible, in health

care decisions. If the patient is unable to participate, then the physician should attempt to ascertain—through advance directives (if present) or discussions with family members—what the patient’s wishes would be if he or she were able to decide.

Preserving fairness in resource use (**choice B**), protecting patient autonomy (**choice C**), and telling the truth (**choice E**) are all important ethical/legal considerations in modern health care delivery.

Rationing care (**choice D**) is considered inappropriate, except in extreme cases where resources are limited.

**145. The correct answer is D.** Particles have to be very small to reach the alveoli. Typically, only particles that are less than 0.1 micron (some authors say no larger than 2 microns) can reach the alveoli. Therefore, 20-micron particles could not reach the alveoli and would therefore be ineffective in measuring alveolar ventilation.

Nonuniform ingestion by alveolar macrophages (**choice A**) is not applicable because particles of this size would not reach the alveoli.

**Choice B**, that the majority of particles this size do not adhere to airway or alveolar walls, is incorrect. The hairs in the nostrils may filter out many particles larger than 10 microns, so most of these particles would not travel beyond this point. Some particles might settle in the mucous membranes of the nose and pharynx.

**Choice C**, that many particles are rapidly absorbed into the pulmonary capillary blood, is incorrect. In order to enter the pulmonary capillary system, the particles would need to be able to get into the alveoli, which would not occur with particles of this size.

**Choice E**, that removal of particles by the mucociliary system is too fast to allow scanning, is incorrect. Particles that are 2 to 10 microns in diameter may fall on bronchial walls and may be moved up by the mucociliary elevator. However, 20-micron particles would not make it this far.

**146. The correct answer is C.** The question refers to the lymphatic drainage of the extremities. Lymph nodes in the popliteal fossa drain the knee and receive drainage from the deep lymphatic vessels coming from the distal extremity. These popliteal nodes subsequently drain into the deep inguinal nodes.

The lateral surface of the thigh (**choice A**) drains into the inguinal nodes.

The posterior aspect of the medial ankle (**choice B**) would contain lymph nodes that drain the medial superficial aspect of the foot.

The drainage of lymph is toward the heart, not away from it toward the sole of the foot (**choice D**).

The superficial inguinal nodes (**choice E**) predominantly drain the superficial portions of the leg.

**147. The correct answer is E.** Ecchymosis, perifollicular petechiae, and swelling of the gums all point to a diagnosis of scurvy, caused by a deficiency of vitamin C. Vitamin C (ascorbic acid), a water-soluble antioxidant, is necessary for hydroxylation of proline in collagen synthesis, degradation of tyrosine, epinephrine synthesis, and bile acid formation. Defective collagen in vessel walls leads to bleeding, producing ecchymoses and petechiae. This man's diet of processed foods lacks a significant source of vitamin C (e.g., citrus fruits, strawberries, green vegetables, potato skins, and tomatoes).

The incorrect answers are conditions caused by other dietary deficiencies:

Beriberi (**choice A**) is caused by a deficiency of vitamin B<sub>1</sub> (thiamine). It is characterized by peripheral neuropathy and exhaustion. Beriberi can progress to cardiovascular, neurologic, and muscular degeneration.

Kwashiorkor (**choice B**) is a severe protein deficiency characterized by weight loss and edema.

Pellagra (**choice C**) is caused by a niacin deficiency, and is characterized by weight loss, dermatitis, digestive problems, depression, and dementia.

Rickets (**choice D**) is a disease in young children caused by a deficiency of vitamin D, leading to defective mineralization of bone matrix. In adults who are not exposed to sunlight and are deficient in vitamin D, it presents as osteomalacia, a softening of the bones.

**148. The correct answer is E.** The purpose of conjugating the capsular polysaccharide of *Haemophilus influenzae* with an unrelated protein is to stimulate T lymphocytes to provide help to B lymphocytes. Without T-cell help, B lymphocytes can only produce IgM antibodies, and since *H. influenzae* is a mucosal-surface pathogen, IgA would be the best isotype of antibody for protection.

B lymphocytes (**choice A**) present peptides in the context of class II MHC but are not stimulated in this way.

Macrophages (**choice B**) ingest, process, and present peptides in the context of MHC class II molecules but are not stimulated in this way.

Natural killer cells (**choice C**) are involved in the cell-mediated immune response against viruses and some tumors. They are not important in the immune responses to mucosal surface pathogens that are extracellular.

Plasma cells (**choice D**) are the antibody-producing factories of the body. They produce as much antibody as they can of a given isotype and idio type for a 2-week period, and then they die. They do not respond to stimulation; they are the products of stimulated B lymphocytes.

**149. The correct answer is D.** The patient described cannot adduct his right eye during conjugate gaze, but is able to adduct it during visual convergence. This patient has internuclear ophthalmoplegia (INO), which is caused by a lesion of the medial longitudinal fasciculus (MLF). The MLF connects the three brainstem nuclei that supply the extraocular muscles (oculomotor, trochlear, and abducens nuclei), enabling the nuclei to coordinate together for conjugate eye movements. Therefore, lesions of the MLF disrupt conjugate eye movements. The only other

plausible answer might have been a lesion of the medial rectus muscle (**choice B**), the muscle that adducts the eye. However, this clearly cannot be the answer because the patient was able to adduct his eye during visual convergence. In fact, INO can look very similar to a medial rectus lesion or to an oculomotor nerve or nucleus lesion, except for the fact that patients have the ability to converge their eyes.

The lateral rectus muscle, which is supplied by CN VI, abducts the eye.

A lesion of the medial rectus muscle (**choice B**) would result in the inability of the patient to adduct his eye during conjugate gaze and visual convergence.

The medial forebrain bundle (**choice C**) is a tract that originates in the olfactory region and septal nuclei, travels through the lateral hypothalamus, and continues caudally into the midbrain tegmentum. It is not involved in eye movement controls.

The oculomotor nucleus (**choice E**) supplies the medial rectus muscle. A lesion in this nucleus would result in the patient's inability to adduct his eye during conjugate gaze and visual convergence.

**150. The correct answer is E.** Norepinephrine and dopamine are the neurotransmitters most likely involved in the development of dependence in the patient. Increased dopamine in the nucleus accumbens has been most closely implicated in reward. Activation of the locus coeruleus, which contains noradrenergic cell bodies, has also been implicated in drug withdrawal. This has some treatment implications, such as the use of clonidine for opioid withdrawal.

Acetylcholine and serotonin (**choice A**), GABA and epinephrine (**choice B**), histamine and glycine (**choice C**), and nitric oxide and neurotensin (**choice D**) are not implicated in the development of dependence.