Appendix A ANSWERS TO TEST QUESTIONS

CHAPTER 1

Recall and Comprehend

1.1 b The four basic cell types are epithelial, muscle, nervous, and connective.

1.2 a Steady state requires energy input, but equilibrium does not.

1.3 c Muscles carry out the response (removing the hand from the stove).

1.4 c Circadian rhythms are typically entrained by the light–dark cycle, but in the absence of such cues, the rhythms "free-run" with their own endogenous cycle length.

1.5 b Intracellular fluid volume is greater than the sum of plasma and interstitial fluid.

1.6 epithelial (tissue)

1.7 extracellular (fluid), plasma, interstitial

1.8 feedforward

1.9 paracrine factor

1.10 negative

Apply, Analyze, and Evaluate

1.1 No. There may in fact be a genetic difference, but there is another possibility: The altered skin blood flow in the cold could represent an *acclimatization* undergone by each Inuit during his or her lifetime as a result of performing such work repeatedly.

1.2 This could occur in many ways. For example, suppose that an individual were to become dehydrated. What would happen to his or her plasma Na^+ *concentration*? Initially, the loss of fluid would result in an increased Na^+ concentration, even though the absolute amount of sodium may not have changed much. The increase in Na^+ concentration would trigger endocrine and renal responses that return the Na^+ concentration to normal. Another example occurs during mountain climbing. At high altitude, a person who is not acclimatized to low oxygen pressures will greatly increase the rate and depth of breathing to get more oxygen into his or her blood. One consequence of this, though, is that more of the carbon dioxide in the body is exhaled. Carbon dioxide tends to produce hydrogen ions in the blood (Chapters 13 and 14). Thus, ascent to high altitude leads to alkaline blood, which must then be compensated for by renal, endocrine, and other responses.

CHAPTER 2

Recall and Comprehend

2.1 e The continued creation of new free radicals is a chain reaction and contributes to the potentially damaging effects of a given free radical.

2.2 d

2.3 b This is a dehydration reaction. The reverse reaction would be hydrolysis.

2.4 b Uracil is found in RNA; thymine is found in DNA.

2.5 b

2.6 Sucrose (b); Glucose (a); Glycogen (c); Fructose (a); Starch (c)

2.7 c The other reactions in which larger molecules are formed occur via dehydration reactions.

2.8 alkaline, lower

2.9 amphipathic

2.10 primary

Apply, Analyze, and Evaluate

2.1 0.79 mol/L. The molecular weight of fructose can be calculated by adding up the weights of the individual atoms. However, since it is an isomer of glucose, you know that it must have the same molecular weight—180 daltons—as glucose. Thus, [100 g/0.7 L] × [1 mole/180 g] = 0.79 mol/L.

2.2 Using a calculator, simply enter −1.5 and select the inverse log function. The answer is approximately 0.03 mol/L or 3×10^{-2} M.

2.3 Recall that atomic mass is the sum of the protons and neutrons in a nucleus. Regardless of its ionization state, potassium has (39 − 19) or 20 neutrons. The number of electrons is equal to the number of protons in a nonionized atom; therefore, K has 19 electrons. When ionized, K^+ has a single positive charge; it still has 19 protons and 20 neutrons, but it now has only 18 electrons.

General Principles Assessment

2.1 The chemical and physical properties of atoms, such as the number of electrons in their outer shells or their solubility in water, determine their reactivity with other atoms and molecules. For example, proteins are made by the linkage of amino acids through peptide bonds, which depend on the reactivity between amino and carboxyl groups. Further chemical and physical interactions, such as electrostatic attraction or repulsion, and hydrophobicity of amino acid side groups, bend and twist the protein into its final three-dimensional shape. Some of these same forces may in certain cases create a larger protein from several subunits. Without the correct chemical and physical properties, proteins would not assume a proper shape; this is extremely important in physiology because the shape of a protein is critically linked with its function.

CHAPTER 3

Recall and Comprehend

3.1 a

3.2 b Transcription refers to the conversion of a gene's DNA into RNA; translation is the conversion of mRNA into protein.

3.3 a Allosteric modulation occurs at a site separate from the ligand-binding site. The resulting change in three-dimensional structure of the protein may enhance or reduce the ability of the protein to bind its ligand.

3.4 b

3.5 c

3.6 d Catabolism refers to the breakdown of fatty acids into usable forms for the production of ATP.

3.7 affinity

3.8 rate-limiting reaction

3.9 gap junctions

3.10 cytosol

Apply, Analyze, and Evaluate

3.1 Nucleotide bases in DNA pair A to T and G to C. Given the base sequence of one DNA strand as

A—G—T—G—C—A—A—G—T—C—T

a. The complementary strand of DNA would be

T—C—A—C—G—T—T—C—A—G—A

b. The sequence in RNA transcribed from the first strand would be

U—C—A—C—G—U—U—C—A—G—A

Recall that uracil (U) replaces thymine (T) in RNA.

3.2 The triplet code G—T—A in DNA will be transcribed into mRNA as C—A—U, and the anticodon in tRNA corresponding to C—A—U is G—U—A.

3.3 If the gene were only composed of the triplet exon code words, the gene would be 300 nucleotides in length because a triplet of three nucleotides codes for one amino acid. However, because of the presence of intron segments in most genes, which account for 75% to 90% of the nucleotides in a gene, the gene would be between 1200 and 3000 nucleotides long; moreover, it would also contain termination codons. Thus, the exact size of a gene cannot be determined by knowing the number of amino acids in the protein for which the gene codes.

3.4 A drug could decrease acid secretion by (a) binding to the membrane sites that normally inhibit acid secretion, which would produce the same effect as the body's natural messengers that inhibit acid secretion; (b) binding to a membrane protein that normally stimulates acid secretion but not itself triggering acid secretion, thereby preventing the body's natural messengers from binding (competition); or (c) having an allosteric effect on the binding sites, which would increase the affinity of the sites that normally bind inhibitor messengers or decrease the affinity of those sites that normally bind stimulatory messengers.

3.5 The reason for a lack of insulin effect could be either a decrease in the number of available binding sites insulin can bind to or a decrease in the affinity of the binding sites for insulin so that less insulin is bound. A third possibility, which does not involve insulin binding, would be a defect in the way the binding site triggers a cell response once it has bound insulin.

3.6 (a) Acid secretion could be increased to 40 mmol/h by (1) increasing the concentration of compound X from 2 pM to 8 pM, thereby increasing the number of binding sites occupied; or (2) increasing the affinity of the binding sites for compound X, thereby increasing the amount bound without changing the concentration of compound X. (b) Increasing the concentration of compound X from 20 pM to 28 pM will not increase acid secretion because, at 20 pM, all the binding sites are occupied (the system is saturated) and there are no further binding sites available.

3.7 The maximum rate at which the end product E can be formed is 5 molecules per second, the rate of the slowest (rate-limiting) reaction in the pathway.

3.8 During starvation, in the absence of ingested glucose, the body's stores of glycogen are rapidly depleted. Glucose, which is the major source of energy for the brain, must now be synthesized from other types of molecules. Most of this newly formed glucose comes from the breakdown of proteins to amino acids and their conversion to glucose. To a lesser extent, the glycerol portion of triglyceride is converted to glucose. The metabolites of the fatty acid portion of triglyceride cannot be converted to glucose.

3.9 Ammonia is formed in most cells during the oxidative deamination of amino acids and then travels to the liver via the blood. The liver detoxifies the ammonia by converting it to the nontoxic compound urea. Because the liver is the site in which ammonia is converted to urea, diseases that damage the liver can lead to an accumulation of ammonia in the blood, which is especially toxic to neurons. Note that it is not the liver that produces the ammonia.

General Principles Assessment

3.1 The extensive folding of the inner mitochondrial membrane increases the total surface area of the membrane. As shown in Figure 3.46, this is where the enzymes are located that are required for the generation of ATP. Thus, the structure of this membrane increases the ability of mitochondria to carry out their major function. The general principle that *structure is a determinant of—and has coevolved with—function* is also evident at the molecular (protein) level. In Figure 3.28, for example, it is clear that a protein's structure determines its function—in this case, its ability to bind particular ligands. Figure 3.32 shows how a protein's function is altered due to allosteric changes in its structure.

3.2 Proteins and ligands interact due to a variety of forces and molecular features, including complementary shapes. In addition, however, chemical or physical properties of molecules often strongly influence their ability to interact or bind with each other. In Figure 3.27, you can see how the structure of the protein results in an arrangement of certain charged amino acids. The fundamental property of physics that opposite charges attract one another means that a ligand with the correct electrical charges will be more likely to bind to this protein than another ligand without those charges.

3.3 Figure 3.54 summarizes how nutrients such as amino acids, glucose, and small lipids can be metabolized by a variety of mechanisms leading to the production of smaller molecules, which in turn can be used to eventually generate ATP. It is ATP that provides the energy required for the events that mediate all homeostatic processes, such as muscle contraction, neuron signaling, and so on. Recall from Chapter 1 (see Figure 1.6) that the generation of ATP is under negative feedback control, such that cells generate more ATP when required, and less when not required. Negative feedback is an essential component of homeostasis.

CHAPTER 4

Recall and Comprehend

4.1 c Channels are proteins that span the membrane and are opened by ligands, voltage, or mechanical stimuli.

4.2 d Facilitated diffusion does not require ATP. Recall that secondary active transport *indirectly* requires ATP because ion pumps were required to establish the electrochemical gradient for a particular ion (such as Na^+).

4.3 b After the initial movement of water out of the cells due to osmosis, the urea concentration quickly equilibrates across each cell's plasma membrane, removing any osmotic stimulus.

4.4 e Segregation of function on different surfaces of the cell, and the ability to secrete chemicals (e.g., from the pancreas), are two of the most important features of epithelial cells.

4.5 a Diffusion is slowed by the resistance of a membrane.

4.6 e Because ions are charged, both the chemical and the electrical gradients determine their rate and direction of diffusion.

4.7 net flux

4.8 exocytosis

4.9 aquaporins

4.10 facilitated diffusion

Apply, Analyze, and Evaluate

4.1 (a) During diffusion, the net flux always occurs from high to low concentration. Therefore, it will be from 2 to 1 in A and from 1 to 2 in B. (b) At equilibrium, the concentrations of solute in the two compartments will be equal: 4 mM in case A and 31 mM in case B.

(c) Both will reach diffusion equilibrium at the same rate because the absolute difference in concentration across the membrane is the same in each case, 2 mM [(3 − 5) = −2, and (32 − 30) = 2]. The two one-way fluxes will be much larger in B than in A, but the net flux has the same magnitude in both cases, although it is oriented in opposite directions.

4.2 The net transport will be out of the cell in the direction from the higher-affinity site on the intracellular surface to the lower-affinity site on the extracellular surface. More molecules will be bound to the transporter on the higher-affinity side of the membrane, and therefore more will move out of the cell than into it, until the concentration in the extracellular fluid becomes great enough that the number of molecules bound to transporters at the extracellular surface is equal to the number bound at the intracellular surface.

4.3 Although ATP is not used directly in secondary active transport, it is necessary for the primary active transport of Na^+ out of cells. Because it is the Na^+ concentration gradient across the plasma membrane that provides the energy for most secondary active transport systems, a decrease in ATP production will decrease primary active Na^+ transport, leading to a decrease in the sodium ion concentration gradient and therefore to a decrease in secondary active transport.

4.4 The solution with the greatest osmolarity will have the lowest water concentration. Recall that NaCl forms two ions in solution and $CaCl_2$ forms three. Thus, the osmolarities are

A. 20 + 30 + (2 × 150) + (3 × 10) = 380 mOsm

B. 10 + 100 + (2 × 20) + (3 × 50) = 300 mOsm

C. 100 + 200 + (2 × 10) + (3 × 20) = 380 mOsm

D. 30 + 10 + (2 × 60) + (3 × 100) = 460 mOsm

Solution D has the lowest water concentration. Solution B is isoosmotic because it has the same osmolarity as intracellular fluid. Solutions A and C have the same osmolarity.

4.5 Initially, the osmolarity of compartment 1 is (2 × 200) + 100 = 500 mOsm and that of 2 is (2 × 100) + 300 = 500 mOsm. The two solutions therefore have the same osmolarity, and there is no difference in water concentration across the membrane. Because the membrane is permeable to urea, this substance will undergo net diffusion until it reaches the same concentration (200 mM) on the two sides of the membrane. In other words, in the steady state, it will not affect the volumes of the compartments. In contrast, the higher initial NaCl concentration in compartment 1 than in compartment 2 will cause, by osmosis, the movement of water from compartment 2 to compartment 1 until the concentration of NaCl in both is 150 mM. Note that the same volume change would have occurred if there were no urea present in either compartment. It is only the concentration of nonpenetrating solutes (NaCl in this case) that determines the volume change, regardless of the concentration of any penetrating solutes that are present.

4.6 The osmolarities and nonpenetrating solute concentrations are

Solution	Osmolarity (mOsm)	Nonpenetrating Solute Concentration (mOsm)
A	(2 × 150) + 100 = 400	2 × 150 = 300
B	(2 × 100) + 150 = 350	2 × 100 = 200
C	(2 × 200) + 100 = 500	2 × 200 = 400
D	(2 × 100) + 50 = 250	2 × 100 = 200

Only the concentration of nonpenetrating solutes (NaCl in this case) will determine the change in cell volume. The intracellular concentration of nonpenetrating solute is typically about 300 mOsm, so solution A will produce no change in cell volume. Solutions B and D will cause cells to swell because they have a lower concentration of nonpenetrating solute (higher water concentration) than the intracellular fluid. Solution C will cause cells to shrink because it has a higher concentration of nonpenetrating solute than the intracellular fluid.

4.7 Solution A is isotonic because it has the same concentration of nonpenetrating solutes as intracellular fluid (300 mOsm). Solution A is also hyperosmotic because its total osmolarity is greater than 300 mOsm, as is also true for solutions B and C. Solution B is hypotonic because its concentration of nonpenetrating solutes is less than 300 mOsm. Solution C is hypertonic because its concentration of nonpenetrating solutes is greater than 300 mOsm. Solution D is hypotonic (less than 300 mOsm of nonpenetrating solutes) and also hypoosmotic (having a total osmolarity of less than 300 mOsm).

4.8 Exocytosis is triggered by an increase in cytosolic Ca^{2+} concentration. Calcium ions are actively transported out of cells, in part by secondary countertransport coupled to the downhill entry of sodium ions on the same transporter (see Figure 4.15). If the intracellular concentration of sodium ions were increased, the sodium ion concentration gradient across the membrane would be decreased, and this would decrease the secondary active transport of Ca^{2+} out of the cell. This would lead to an increase in cytosolic Ca^{2+} concentration, which would trigger increased exocytosis.

General Principles Assessment

4.1 One example of the general principle that *homeostasis is essential for health and survival* illustrated in Figures 4.8–4.10 is mediated transport across plasma membranes. For example, the presence of glucose transporters (GLUTs) in plasma membranes helps maintain homeostatic concentrations of glucose in the extra- and intracellular fluids. This is important because glucose is the major source of energy for cells. Also, the regulated changes in aquaporin numbers in the epithelial cells of the kidneys help maintain water homeostasis by controlling the rate at which water is lost in the urine; this is particularly important in situations such as dehydration. A third example is osmosis, which regulates water flux across membranes (see Figure 4.17); this, in turn, helps maintain proper cell shape and size and the ability of cells to perform signaling functions.

4.2 The general principle that *controlled exchange of materials occurs between compartments and across cellular membranes* is apparent from the many diverse types of mechanisms by which solutes may cross plasma membranes. The control arises from such mechanisms as gates in ion channels that may open or close depending on cell requirements, and the just-mentioned glucose transporters and aquaporins, the concentrations of which can increase or decrease in plasma membranes under different conditions.

4.3 The general principle that *physiological processes are dictated by the laws of chemistry and physics* is evident from the relationship between the chemical nature (e.g., degree of hydrophobicity) of solutes and the ease with which they can diffuse through a lipid bilayer. The greater a molecule's hydrophobicity, the more likely it is to dissolve in the lipid bilayer of membranes and thus diffuse across cells. Electrochemical gradients aid in the diffusion of charged molecules (ions) through membrane channels because of the basic physical principle that like charges repel and opposite charges attract each other. Finally, molecular movement (and therefore potential interactions between molecules) is directly related to heat energy; solutes move through solution at faster rates at higher temperatures.

CHAPTER 5

Recall and Comprehend

5.1 b

5.2 a

5.3 e

5.4 a Calmodulin is a calcium-binding protein that is inactive in the absence of Ca^{2+}.

5.5 d Lipid-soluble messengers cross the plasma membrane and act primarily on cytosolic and nuclear receptors.

5.6 b

5.7 d

5.8 a Neurotransmitters and hormones are just two of many types of ligands that act as signaling molecules and first messengers, via their binding to a receptor.

5.9 e

5.10 b

Apply, Analyze, and Evaluate

5.1 Patient A's drug very likely acts to block phospholipase A_2, whereas patient B's drug blocks lipoxygenase (see Figure 5.12).

5.2 The chronic loss of exposure of the heart's receptors to norepinephrine causes an up-regulation of this receptor type (i.e., more receptors in the heart for norepinephrine). The drug, being an agonist of norepinephrine (i.e., able to bind to norepinephrine's receptors and activate them) is now more effective because there are more receptors for it to combine with.

5.3 None. You are told that all six responses are mediated by the cAMP system; consequently, blockage of any of the steps listed in the question would eliminate all six of the responses. This is because the cascade for all six responses is identical from the receptor through the formation of cAMP and activation of cAMP-dependent protein kinase. Therefore, the drug must be acting at a point beyond this kinase (e.g., at the level of the phosphorylated protein mediating this response).

5.4 Not in most cells, because there are other physiological mechanisms by which signals impinging on the cell can increase cytosolic Ca^{2+} concentration. These include (a) second-messenger-induced release of Ca^{2+} from the endoplasmic reticulum and (b) voltage-sensitive Ca^{2+} channels.

General Principles Assessment

5.1 Figures 5.5a and 5.9 illustrate ways in which movement of ions, for example, is controlled by first and second messengers. These messengers may open ion channels or activate or induce production of ion transporters in plasma membranes. In this way, ions may move between fluid compartments in the body—for example, from interstitial fluid to intracellular fluid.

5.2 Certain forms of cell signaling require a supply of ATP to form cAMP, a major second messenger, and to phosphorylate proteins. Without a homeostatic balance of cellular energy stored in the terminal bond of ATP molecules, most cell signaling pathways would be deficient or impossible.

CHAPTER 6

Recall and Comprehend

6.1 b Afferent neurons have peripheral axon terminals associated with sensory receptors, cell bodies in the dorsal root ganglion of the spinal cord, and central axon terminals that project into the spinal cord.

6.2 c Oligodendrocytes form myelin sheaths in the central nervous system.

6.3 d Insert the given chloride ion concentrations into the Nernst equation; remember to use -1 as the valence (Z).

6.4 d A, B, and C all are correct. Using the Nernst equation to calculate the Na^+ equilibrium potential gives values of +31, +36, and +40 mV for A, B, and C. If the membrane potential was +42 mV, the outward electrical force on Na^+ would be greater than the inward concentration gradient, so Na^+ would move out of the cell in each of these cases.

6.5 e Neither Na^+ nor K^+ is in equilibrium at the resting membrane potential, but the action of the Na^+/K^+-ATPase pump prevents the small but steady leak of both ions from dissipating the concentration gradients.

6.6 a Because Na^+ is farther away from its electrochemical equilibrium than is K^+, there would be more Na^+ entry than K^+ exit, causing local depolarization and local current flow that would decrease with distance from the site of the stimulus.

6.7 c Due to the persistent open state of the voltage-gated K^+ channels, for a brief time at the end of an action potential the membrane is hyperpolarized. When the voltage-gated K^+ channels eventually close, the K^+ leak channels once again determine the resting membrane potential.

6.8 d The IPSP caused by neuron B would summate with (subtract from) the amplitude of the EPSP caused by neuron A's firing.

6.9 a Dopamine, like norepinephrine and epinephrine, is a catecholamine neurotransmitter manufactured by enzymatic modification of the amino acid tyrosine.

6.10 b Norepinephrine is the neurotransmitter released by postganglionic neurons onto smooth muscle cells.

Apply, Analyze, and Evaluate

6.1 Little change in the resting membrane potential would occur when the pump first stops because the pump's *direct* contribution to charge separation is very small. With time, however, the membrane potential would depolarize progressively toward zero because the Na^+ and K^+ concentration gradients, which depend on the Na^+/K^+-ATPase pumps and which give rise to the membrane potential, run down.

6.2 The resting potential would decrease (i.e., become less negative) because the concentration gradient causing net diffusion of this positively charged ion out of the cell would be smaller. The action potential would fire more easily (i.e., with smaller stimuli) because the resting potential would be closer to threshold. It would repolarize more slowly because repolarization depends on net K^+ diffusion from the cell, and the concentration gradient driving this diffusion is lower. Also, the after hyperpolarization would be smaller.

6.3 The hypothalamus was probably damaged. It plays a critical role in appetite, thirst, and sexual capacity.

6.4 The drug probably blocks cholinergic muscarinic receptors. These receptors on effector cells mediate the actions of parasympathetic nerves. Therefore, the drug would remove the slowing effect of these nerves on the heart, allowing the heart to speed up. Blocking their effect on the salivary glands would cause the dry mouth. We know that the drug is not blocking cholinergic nicotinic receptors because the skeletal muscles are not affected.

6.5 Because the membrane potential of the cells in question depolarizes (i.e., becomes less negative) when Cl^- channels are blocked, we can assume there was net Cl^- diffusion into the cells through these channels prior to treatment with the drug. Therefore, we can also predict that this passive inward movement was being exactly balanced by active transport of Cl^- out of the cells.

6.6 Without acetylcholinesterase, more acetylcholine would remain bound to the receptors, and all the actions normally caused by acetylcholine would be accentuated. Consequently, there would be significant narrowing of the pupils, airway constriction, stomach cramping and diarrhea, sweating, salivation, slowing of the heart, and decrease in blood pressure. On the other hand, in skeletal muscles, which must repolarize after excitation in order to be excited again, there would be weakness, fatigue, and finally inability to contract. In fact, lethal poisoning by high doses of cholinesterase inhibitors occurs because of paralysis of the muscles involved in respiration. Low doses of these compounds are used therapeutically.

6.7 These K^+ channels, which open after a short delay following the initiation of an action potential, increase K^+ diffusion out of the

cell, hastening repolarization. They also account for the increased K^+ permeability that causes the after hyperpolarization. Therefore, the action potential would be broader (that is, longer in duration) and would return to resting level more slowly, and the after hyperpolarization would be absent.

6.8 If there are no Cl^- pumps, then the resting membrane potential determined by Na^+ and K^+ will move Cl^- out of the cell until the gradient is such that the equilibrium potential for Cl^- is equal to the resting membrane potential (−80 mV). Plugging the known values into the Nernst equation (and adjusting the sign of the constant to account for the negative charge of Cl^-), then solving for $[Cl^-]$ in yields the following:

$$-80 = -61 \log (100/[Cl^-]in)$$
$$-80/-61 = \log 100 - \log [Cl^-]in$$
$$1.31 - 2 = -\log [Cl^-]in$$
$$4.88 \text{ mM} = [Cl^-]in$$

General Principles Assessment

6.1 The autonomic nervous system controls many physiological functions through its sympathetic and parasympathetic subdivisions. The most common structural pattern is dual innervation—organs receive signals along neurons from both the sympathetic and parasympathetic division—and typically the effects of those signals are opposite. For example, action potentials along parasympathetic neurons increase secretions and contractions of the gastrointestinal tract, while action potentials along sympathetic pathways tend to decrease them. By having such dual regulatory control, more precise regulation of organ function is made possible. Other examples of dual sympathetic/parasympathetic regulatory control can be found in Figure 6.44.

6.2 The establishment of neuronal resting membrane potential clearly demonstrates at least two general principles of physiology: *Controlled exchange of materials occurs between compartments and across cellular membranes,* and *Physiological processes are dictated by the laws of chemistry and physics.* The concentration and movement of Na^+ and K^+ ions across the plasma membrane are carefully controlled as a result of the hydrophobic properties of the phospholipid bilayer, the action of Na^+/K^+-ATPase pumps, and the gating of ion-specific channels. Given the establishment of concentration gradients for these ions (and associated anions) across the membrane, Fick's first law of diffusion (Chapter 4) and the electrical repulsion and attraction between charged ions then enable the storage of energy (electrical potential) across the membrane. The potential energy stored in this gradient is the basis of a substantial amount of cellular activity in nerve, skeletal muscle, cardiac muscle, and many other tissues.

6.3 As discussed in Section 6.1, some neurons have a large number of dendrites—as many as 400,000—that vastly increase the surface area over which the cell can receive inputs from other neurons. Additionally, the human cerebral cortex is elaborately folded into sulci and gyri, which vastly increases the surface area. As Figure 6.39 shows, the majority of the cells of the cerebral hemispheres lie within a few millimeters of the surface. The tortuous folding of the cortex allows far more cells to fit within the confines of the cranium, and along with a greater number of cells comes a greater potential for neural processing power. This accounts in part for the advanced cognitive capabilities and complex behaviors of humans as compared to animals with less complex folding of the cerebral cortex.

CHAPTER 7

Recall and Comprehend

7.1 a For example, photons of light are the adequate stimulus for photoreceptors of the eye, and sound is the adequate stimulus for hair cells of the ear.

7.2 b Receptor potentials generate only local currents in the receptor membrane that transduces the stimulus, but when they reach the first node of Ranvier, they depolarize the membrane to threshold, and there the voltage-gated Na^+ channels first initiate action potentials. Beyond that point, the receptor potential decreases with distance, whereas action potentials propagate all the way to the central axon terminals.

7.3 d Lateral inhibition increases the contrast between the region at the center of a stimulus and regions at the edges of the stimulus, which increases the acuity of stimulus localization.

7.4 a The occipital lobe of the cortex is the initial site of visual processing. (Review Figure 7.13.)

7.5 e Somatic sensations include those from the skin, muscles, bones, tendons, and joints, but not encoding of sound by cochlear hair cells.

7.6 b A myopic (nearsighted) person has an eyeball that is too long. When the ciliary muscles are relaxed and the lens is as flat as possible, parallel light rays from distant objects focus in front of the retina, whereas diverging rays from near objects are able to focus on the retina. (Recall that with normal vision, it takes ciliary muscle contraction and a rounded lens to focus on near objects.)

7.7 d When the right optic tract is destroyed, perception of images formed on the right half of the retina in both eyes is lost, so nothing is visible at the left side of a person's field of view. (Review Figure 7.31.)

7.8 a Pressure waves traveling down the cochlea make the cochlear duct vibrate, moving the basilar membrane against the stationary tectorial membrane and bending the hair cells that bridge the gap between the two.

7.9 c With the sudden head rotation from left to right, inertia of the endolymph causes it to rotate from right to left with respect to the semicircular canal that lies in the horizontal plane. This fluid flow bends the cupula and embedded hair cells within the ampulla, which influences the firing of action potentials along the vestibular nerve.

7.10 d "Umami" is derived from the Japanese word meaning "delicious" or "savory"; the stimulation of these taste receptors by glutamate produces the perception of a rich, meaty flavor.

Apply, Analyze, and Evaluate

7.1 (a) Use drugs to block transmission in the pathways that convey information about pain to the brain. For example, if substance P is the neurotransmitter at the central endings of the nociceptor afferent fibers, give a drug that blocks the substance P receptors. (b) Cut the dorsal root at the level of entry of the nociceptor fibers to prevent transmission of their action potentials into the central nervous system. (c) Give a drug that activates receptors in the descending pathways that block transmission of the incoming or ascending pain information. (d) Stimulate the neurons in these same descending pathways to increase their blocking activity (stimulation-produced analgesia or, possibly, acupuncture). (e) Cut the ascending pathways that transmit information from the nociceptor afferents. (f) Deal with emotions, attitudes, memories, and so on to decrease sensitivity to the pain. (g) Stimulate nonpain, low-threshold afferent fibers to block transmission through the pain pathways (TENS). (h) Block transmission in the afferent nerve with a local anesthetic such as Novocaine or Lidocaine.

7.2 Information regarding temperature is carried via the anterolateral system to the brain. Fibers of this system cross to the opposite side of the body in the spinal cord at the level of entry of the afferent fibers (see Figure 7.20a). Damage to the left side of the spinal cord or any part of the left side of the brain that contains fibers of the pathways for temperature would interfere with awareness of a heat stimulus on the right. Thus, damage to the somatosensory cortex of the left cerebral hemisphere (i.e., opposite the stimulus) would interfere with awareness of the stimulus. Injury to the spinal cord

at the point at which fibers of the anterolateral system from the two halves of the spinal cord cross to the opposite side would interfere with the awareness of heat applied to either side of the body, as would the unlikely event that damage occurred to relevant areas of both sides of the brain.

7.3 Vision would be restricted to the rods; therefore, it would be normal at very low levels of illumination (when the cones would not be stimulated anyway). At higher levels of illumination, however, clear vision of fine details would be lost, and everything would appear in shades of gray, with no color vision. In very bright light, there would be no vision because of bleaching of the rods' rhodopsin.

7.4 (a) The individual lacks a functioning primary visual cortex. (b) The individual lacks a functioning visual association cortex.

7.5 Because it is common for somatic receptors in visceral organs to converge onto ascending pathways for receptors in the skin, muscles, and joints (see Figure 7.17), physicians must be aware that complaints about pain in superficial structures may indicate a deeper problem. For example, a person having a heart attack may complain of pain in the left arm, a patient with stomach cancer may experience pain in the middle of the back, and a patient with kidney stones may complain of an ache in the upper thigh or hip. Review Figure 7.18 for a map of surface regions of the body where referred pain from deeper organs can be perceived.

General Principles Assessment

7.1 Nociceptors detect stimuli indicating potential or actual damage to tissues, which could threaten homeostasis. By allowing us to perceive those stimuli, nociceptors not only help us to learn to avoid them but also let us respond quickly to minimize damage when they occur (like quickly removing your hand from a hot stove burner). In these ways, we can avoid injuries like burns or cuts that may threaten homeostasis by causing fluid loss from the body. As another example, pain stops us temporarily from overusing injured limbs, giving them time to heal so that our ability to move and obtain food or avoid life-threatening situations is not permanently impaired.

7.2 A good example of the importance of controlled exchange between extracellular compartments in the vestibular and auditory systems is the endolymph found within the cochlear duct and vestibular apparatus. The unusually high K^+ concentration allows current to flow into the cells when tip links are stretched, generating a receptor potential that leads to neurotransmitter release from the hair cells. This, in turn, generates action potentials in the afferent neuron (review Figure 7.41). In addition, like in all neurons and excitable cells, the maintenance of Na^+ and K^+ concentration gradients between the intracellular and extracellular fluid compartments by Na^+/K^+-ATPase pumps is essential for the transmission of action potentials in the auditory and vestibular afferent neurons (review Chapter 6, Section B).

7.3 An excellent example of a body structure that has maximized surface area to maximize function is a photoreceptor cell. Repeated foldings of the membranous discs in rods and cones greatly increases the surface area available for the retinal-containing photopigments, making the eye exquisitely sensitive to light.

CHAPTER 8

Recall and Comprehend

8.1 d

8.2 c

8.3 a

8.4 b

8.5 e See Figures 8.6 and 8.7.

8.6 b If by experience you discover that a persistent stimulus like the noise from a fan does not have relevance, there is a reduction in conscious attention directed toward that stimulus. This is an example of "habituation."

8.7 c The mesolimbic dopamine pathway mediates the perception of reward that is associated with adaptive behaviors, including goal-directed behaviors related to preserving homeostasis, like eating and drinking.

8.8 d Serotonin-specific reuptake inhibitors (SSRIs) are the most widely used antidepressant drugs, although other types of antidepressants additionally enhance signaling by norepinephrine.

8.9 a Short-term memories are transferred into new long-term memories in the process of consolidation, which requires a functional hippocampus. When the hippocampus is destroyed, previously formed long-term memories remain intact, but the ability to form new memories is lost.

8.10 c Broca's area is located near the region of the left frontal lobe motor cortex that controls the face; when it is damaged, individuals have "expressive aphasia." This means that they comprehend language but are unable to articulate their own thoughts into words.

Apply, Analyze, and Evaluate

8.1 Dopamine is depleted in the basal nuclei of people with Parkinson's disease, and they are therapeutically given dopamine agonists, usually L-dopa. This treatment raises dopamine concentrations in other parts of the brain, however, where the dopamine concentrations were previously normal. Schizophrenia is associated with increased brain dopamine concentrations, and symptoms of this disease appear when dopamine concentrations are high. The converse therapeutic problem can occur during the treatment of schizophrenics with dopamine-lowering drugs, which sometimes cause the symptoms of Parkinson's disease to appear.

8.2 Experiments on anesthetized animals often involve either stimulating a brain part to observe the effects of increased neuronal activity, or damaging ("lesioning") an area to observe resulting deficits. Such experiments on animals, which lack the complex language mechanisms humans have, cannot help with language studies. Diseases sometimes mimic these two experimental situations, and behavioral studies of the resulting language deficits in people with aphasia, coupled with study of their brains after death, have provided a wealth of information.

General Principles Assessment

8.1 A general principle of physiology demonstrated very well by Figure 8.7 states that *most physiological functions are controlled by multiple regulatory systems, often working in opposition.* The orexin and monoaminergic RAS neurons compete with the sleep center in regulating the state of consciousness. When the orexin/RAS neurons are active, not only do they arouse the cortex and cause wakefulness, but they also inhibit the sleep center. When the sleep center neurons become active, the exact opposite occurs.

8.2 There seems to be a homeostatic set point for the amount of sleep we need. In addition to a daily increase in activity of the SCN that wakes us up, inputs related to energy homeostasis also prevent sleep from being prolonged (see Figure 8.7). On the other hand, sleep deprivation impairs the immune system, causes cognitive and memory defects, can result in decreased growth hormone secretion and growth velocity in children, and if prolonged can lead to psychosis and even death. When sleep is disrupted or postponed for even one day, we respond with bouts of "make-up" sleep, as though some chemical or factor has gone too far from its homeostatic set point and needs to be restored toward normal. Adenosine has been proposed to be a homeostatic sleep regulator.

CHAPTER 9

Recall and Comprehend

9.1 a A single skeletal muscle fiber, or cell, is composed of many myofibrils.

9.2 e The dark stripe in a striated muscle that constitutes the A band results from the aligned thick filaments within myofibrils, so thick filament length is equal to A-band width.

9.3 b As filaments slide during a shortening contraction, the I band becomes narrower, so the distance between the Z line and the thick filaments (at the end of the A band) must decrease.

9.4 d DHP receptors act as voltage sensors in the T-tubule membrane and are physically linked to ryanodine receptors in the sarcoplasmic reticulum membrane. When an action potential depolarizes the T-tubule membrane, DHP receptors change conformation and trigger the opening of the ryanodine receptors. This allows Ca^{2+} to diffuse from the interior of the sarcoplasmic reticulum into the cytosol.

9.5 c In an isometric twitch, tension begins to rise as soon as excitation–contraction is complete and the first cross-bridges begin to attach. In an isotonic twitch, excitation–contraction coupling takes the same amount of time, but the fiber is delayed from shortening until after enough cross-bridges have attached to move the load.

9.6 b In the first few seconds of exercise, mass action favors transfer of the high-energy phosphate from creatine phosphate to ADP by the enzyme creatine kinase.

9.7 d Fast-oxidative-glycolytic fibers are an intermediate type that are designed to contract rapidly but to resist fatigue. They utilize both aerobic and anaerobic energy systems; thus, they are red fibers with high myoglobin (which facilitates production of ATP by oxidative phosphorylation), but they also have a moderate ability to generate ATP through glycolytic pathways. (Refer to Table 9.3.)

9.8 c In smooth muscle cells, dense bodies serve the same functional role as Z lines do in striated muscle cells—they serve as the anchoring point for the *thin* filaments.

9.9 b When myosin-light-chain kinase transfers a phosphate group from ATP to the myosin light chains of the cross-bridges, binding and cycling of cross-bridges are activated.

9.10 d Stretching a sheet of single-unit smooth muscle cells opens mechanically gated ion channels, which causes a depolarization that propagates through gap junctions, followed by Ca^{2+} entry and contraction. This does not occur in multiunit smooth muscle.

9.11 e The amount of Ca^{2+} released during a typical resting heart beat exposes less than half of the thin filament cross-bridge binding sites. Autonomic neurotransmitters and hormones can increase or decrease the amount of Ca^{2+} released to the cytosol during EC coupling.

Apply, Analyze, and Evaluate

9.1 Under resting conditions, the myosin has already bound and hydrolyzed a molecule of ATP, resulting in an energized molecule of myosin ($M \cdot ADP \cdot P_i$). Because ATP is necessary to detach the myosin cross-bridge from actin at the end of cross-bridge movement, the absence of ATP will result in rigor mortis, in which case the cross-bridges become bound to actin but do not detach, leaving myosin bound to actin ($A \cdot M$).

9.2 The length–tension relationship states that the maximum tension developed by a muscle decreases at lengths below L_0. During normal shortening, as the sarcomere length becomes shorter than the optimal length, the maximum tension that can be generated decreases. With a light load, the muscle will continue to shorten until its maximal tension just equals the load. No further shortening is possible because at shorter sarcomere lengths the tension would be less than the load. The heavier the load, the less the distance shortened before reaching the isometric state.

9.3 Maximum tension is produced when the fiber is (a) stimulated by an action potential frequency that is high enough to produce a maximal tetanic tension and (b) at its optimum length L_0, where the thick and thin filaments have overlap sufficient to provide the greatest number of cross-bridges for tension production.

9.4 Moderate tension—for example, 50% of maximal tension—is accomplished by recruiting sufficient numbers of motor units to produce this degree of tension. If activity is maintained at this level for prolonged periods, some of the active fibers will begin to fatigue and their contribution to the total tension will decrease. The same level of total tension can be maintained, however, by recruiting new motor units as some of the original ones fatigue. At this point, for example, one may have 50% of the fibers active, 25% fatigued, and 25% still unrecruited. Eventually, when all the fibers have fatigued and there are no additional motor units to recruit, the whole muscle will fatigue.

9.5 The oxidative motor units, both fast and slow, will be affected first by a decrease in blood flow because they depend on blood flow to provide both the fuel—glucose and fatty acids—and the oxygen required to metabolize the fuel. The fast-glycolytic motor units will be affected more slowly because they rely predominantly on internal stores of glycogen, which is anaerobically metabolized by glycolysis.

9.6 Two factors lead to the recovery of muscle force. (a) Some new fibers can be formed by the fusion and development of undifferentiated satellite cells. This will replace some, but not all, of the fibers that were damaged. (b) Some of the restored force results from hypertrophy of the surviving fibers. Because of the loss of fibers in the accident, the remaining fibers must produce more force to move a given load. The remaining fibers undergo increased synthesis of actin and myosin, resulting in increases in fiber diameter and, consequently, their force of contraction.

9.7 In the absence of extracellular Ca^{2+}, skeletal muscle contracts normally in response to an action potential generated in its plasma membrane because the Ca^{2+} required to trigger contraction comes entirely from the sarcoplasmic reticulum within the muscle fibers. If the motor neuron to the muscle is stimulated in a Ca^{2+}-free medium, however, the muscle will not contract because the influx of Ca^{2+} from the extracellular fluid into the motor nerve terminal is necessary to trigger the release of acetylcholine that in turn triggers an action potential in the muscle.

In a Ca^{2+}-free solution, smooth muscles would not respond either to stimulation of the nerve or to the plasma membrane. Stimulating the nerve would have no effect because Ca^{2+} entry into presynaptic terminals is necessary for neurotransmitter release. Stimulating the smooth muscle cell membrane would also not cause a response in the absence of Ca^{2+} because in all of the various types of smooth muscle, Ca^{2+} must enter from outside the cell to trigger contraction. In some cases, the external Ca^{2+} directly initiates contraction, and in others it triggers the release of Ca^{2+} from the sarcoplasmic reticulum (Ca^{2+}-induced Ca^{2+} release).

9.8 Elevation of extracellular fluid Ca^{2+} concentration would increase the amount of Ca^{2+} entering the cytosol through L-type Ca^{2+} channels. This would result in a greater depolarization of cardiac muscle cell membranes during action potentials. The strength of cardiac muscle contractions would also be increased because this larger Ca^{2+} entry would trigger more Ca^{2+} release through ryanodine receptor channels, and consequently there would be a greater activation of cross-bridge cycling.

9.9 In order for unfused tetanus to occur, action potentials must occur more closely in time than the duration of a twitch cycle. Frequency is the inverse of cycle duration, so to produce unfused tetanus, action potentials must occur at a frequency greater than 1/0.04 seconds, or 25 action potentials per second.

General Principles Assessment

9.1 The control of cardiac muscle pacemaker cell activity by sympathetic and parasympathetic neurotransmitters is an excellent example of the general principle that *most physiological functions are controlled by multiple regulatory systems, often working in opposition*.

9.2 The forward motion of cross-bridges during the cross-bridge cycle (power stroke) is associated with a chemical reaction in which ADP and P_i are released as products (see step 2 in Figure 9.15). During high-frequency stimulation of muscles when cross-bridges cycle repeatedly, the concentrations of ADP and P_i build up in the muscle cytosol. Due to the law of mass action, the buildup of these products inhibits the rate of the chemical reaction and, thus, the power stroke of the cross-bridge cycle. This contributes to the reduction of contraction speed and force that occurs when muscles are fatigued.

9.3 The general principle that *controlled exchange of materials occurs between compartments and across cellular membranes* is demonstrated by the movements of Ca^{2+} and other ions involved in the skeletal muscle excitation–contraction coupling mechanism (see Figures 9.9 and 9.12). Controlled movement of Na^+, K^+ and Ca^{2+} across muscle cell plasma membranes maintains the resting membrane potential and allows the generation and propagation of action potentials. Sequestering Ca^{2+} in the sarcoplasmic reticulum allows the resting state of muscle to be maintained until controlled release of Ca^{2+} into the cytosol activates cross-bridge cycling and muscle contraction. The termination of muscle contraction requires the return of Ca^{2+} into the sarcoplasmic reticulum and extracellular fluid. This principle is also demonstrated by ion fluxes in cardiac muscle (see Figure 9.40).

CHAPTER 10

Recall and Comprehend

10.1 b The basal nuclei, sensorimotor cortex, thalamus, brainstem, and cerebellum are all middle-level structures that create a motor program based on the intention to carry out a voluntary movement.

10.2 c When a given muscle is stretched, muscle-spindle stretch receptors send action potentials along afferent fibers that synapse directly on alpha motor neurons to extrafusal fibers to that muscle, causing it to contract back toward the prestretched length.

10.3 a Afferent action potentials from pain receptors in the injured left foot would stimulate the withdrawal reflex of the left leg (activation of flexor muscles and inhibition of extensors) and the opposite pattern in the right leg (the crossed-extensor reflex).

10.4 d Activating the gamma motor neurons would cause contraction of the ends of intrafusal muscle fibers, stretching the muscle-spindle receptors, and the resulting action potentials would monosynaptically excite the alpha motor neurons innervating the extrafusal fibers of the stretch receptors.

10.5 c See Figure 10.10.

10.6 T Most descending corticospinal pathways cross the midline of the body in the medulla oblongata.

10.7 F Upper motor neuron disorders are typically characterized by hypertonia and spasticity.

10.8 F The reverse is actually true.

10.9 F In Parkinson's disease, a deficit of dopamine from neurons of the substantia nigra results in "resting tremors."

10.10 T *Clostridium tetani* toxin specifically blocks the release of neurotransmitter from neurons that normally inhibit motor neurons. The resulting imbalance of excitatory and inhibitory inputs causes spastic contractions of muscles.

Apply, Analyze, and Evaluate

10.1 None. The gamma motor neurons are important in preventing the muscle-spindle stretch receptors from going slack, but when this reflex is tested, the intrafusal fibers are not flaccid. The test is performed with a bent knee, which stretches the extensor muscles in the thigh (and the intrafusal fibers within the stretch receptors). The stretch receptors are therefore responsive.

10.2 The efferent pathway of the reflex arc (the alpha motor neurons) would not be activated, the effector cells (the extrafusal muscle fibers) would not be activated, and there would be no reflexive response.

10.3 The drawing must have excitatory synapses on the motor neurons of both ipsilateral extensor and ipsilateral flexor muscles.

10.4 A toxin that interferes with the inhibitory synapses on motor neurons would leave unbalanced the normal excitatory input to these neurons. Thus, the otherwise normal motor neurons would fire excessively, which would result in increased muscle contraction. This is exactly what happens in lockjaw as a result of the toxin produced by the tetanus bacillus.

10.5 In mild cases of tetanus, agonists (stimulators) of the inhibitory interneuron neurotransmitter gamma-aminobutyric acid (GABA) can shift the balance back toward the inhibition of alpha motor neurons. In more severe cases, paralysis can be induced by administering long-lasting drugs that block the nicotinic acetylcholine receptors at the neuromuscular junction.

General Principles Assessment

10.1 Unlike smooth and cardiac muscle cells, which are regulated directly by both excitatory and inhibitory inputs, skeletal muscle fibers only have excitatory inputs, so must be inhibited indirectly. They are inhibited from contracting when there are no action potentials arriving along their associated alpha motor neurons, so inhibition must occur at the level of the alpha motor neurons. The dendrites and cell bodies of alpha motor neurons found in the brainstem and spinal cord receive both excitatory and inhibitory inputs from interneurons, sensory neurons, and neurons in descending pathways. When the inhibitory inputs predominate, the alpha motor neuron does not generate action potentials and the muscle fibers it innervates remain relaxed.

10.2 One way that the withdrawal reflex contributes to homeostasis is by minimizing the extent of tissue injury that could potentially result from prolongation of a painful stimulus. Rapidly withdrawing a limb from a position where it is being cut, burned, or crushed helps to minimize the loss of blood, tissue fluid, and tissue function that could compromise homeostasis.

CHAPTER 11

Recall and Comprehend

11.1 c

11.2 a

11.3 e

11.4 b

11.5 d

11.6 a At any given concentration of hormone, more A is bound to receptor than B.

11.7 d Goiter results from dysfunction of the thyroid gland.

11.8 e Recall that thyroid hormone potentiates the effects of epinephrine and the sympathetic nervous system.

11.9 b

11.10 e Recall that there exists a large store of iodinated thyroglobulin in thyroid follicles and that the half-life of T_4 is very long (approximately 6 days).

11.11 c Low plasma Ca^{2+} decreases the filtered load of Ca^{2+}. It also stimulates parathyroid hormone, which increases Ca^{2+} reabsorption from the distal tubule. This helps to prevent the further loss of Ca^{2+} in the urine.

11.12 d Parathyroid hormone is a potent stimulator of Ca^{2+} resorption from bone.

11.13 T T_4 is the chief circulating form, but T_3 is more active.

11.14 F Acromegaly is associated with hyperglycemia and hypertension.

11.15 T

Apply, Analyze, and Evaluate

11.1 Epinephrine decreases to very low concentrations during rest and fails to increase during stress. The sympathetic preganglionics provide the only major control of the adrenal medulla.

11.2 The increased concentration of binding protein causes more T_3 and T_4 to be bound, thereby lowering the plasma concentration of *free* T_3 and T_4. This causes less negative feedback inhibition of

TSH secretion by the anterior pituitary gland, and the increased TSH causes the thyroid to secrete more T_3 and T_4 until the free concentration has returned to normal. The end result is an increased *total* plasma T_3 and T_4—most bound to the protein—but a normal free T_3 and T_4. There is no hyperthyroidism because it is only the free concentration that exerts effects on T_3 and T_4 target cells.

11.3 Destruction of the anterior pituitary gland or interference with hypophysiotrophic hormones reaching the anterior pituitary gland from the hypothalamus. These symptoms reflect the absence of, in order, growth hormone, the gonadotropins, and ACTH (the symptom is due to the resulting decrease in cortisol secretion). The problem is hyposecretion of anterior pituitary gland hormones due to a pituitary abnormality or because hypophysiotropic hormones are not reaching the anterior pituitary.

11.4 Vasopressin and oxytocin (the posterior pituitary hormones) secretion would decrease. The anterior pituitary gland hormones would not be affected because the influence of the hypothalamus on these hormones is exerted not by connecting nerves but via the hypophysiotropic hormones in the portal vascular system.

11.5 The secretion of GH increases. Somatostatin, coming from the hypothalamus, normally exerts an inhibitory effect on the secretion of this hormone.

11.6 The absorption of Ca^{2+} in the intestines would be decreased because of the loss of absorptive surface. The subsequent decrease in blood Ca^{2+} will result in an increase in PTH secretion. This is called secondary hyperparathyroidism because the increase in PTH secretion is secondary to the decrease in blood Ca^{2+}.

11.7 The high dose of the cortisol-like substance inhibits the secretion of ACTH by feedback inhibition of (1) hypothalamic corticotropin releasing hormone and (2) the response of the anterior pituitary gland to this hypophysiotropic hormone. The decrease in plasma ACTH causes the adrenal to atrophy and decrease its secretion of cortisol.

11.8 The hypothalamus. The low basal TSH indicates either that the pituitary gland is defective or that it is receiving inadequate stimulation (TRH) from the hypothalamus. If the thyroid itself were defective, basal TSH would be increased because of less negative feedback inhibition by T_3 and T_4. The TSH increase in response to TRH shows that the pituitary gland is capable of responding to a stimulus and so is unlikely to be defective. Therefore, the problem is that the hypothalamus is secreting too little TRH (in reality, this is very rare).

11.9 In utero malnutrition. Neither growth hormone nor thyroid hormone has a major effect on in utero growth, particularly in the last 2 trimesters of pregnancy.

11.10 Androgens stimulate growth by increasing growth hormone secretion, but also cause the ultimate cessation of growth by closing the epiphyseal plates. Therefore, there might be a rapid growth spurt in response to the androgens but a subsequent premature cessation of growth. Estrogens exert similar effects.

General Principles Assessment

11.1 Despite having many different actions, epinephrine, cortisol, and growth hormone all act on adipocytes and the liver to regulate energy balance. They do this by stimulating the production and/or release of glucose from liver cells, and the breakdown in adipocytes of triglycerides into usable substrates for energy that can enter the bloodstream. It should not be surprising that a function as critical as energy homeostasis would be regulated by multiple factors; indeed, these three hormones are only one part of a larger control mechanism that regulates energy balance (see Chapter 16).

11.2 The structure of the thyroid gland differs from other endocrine glands in that it consists of colloid-filled follicles that contain hormone precursors. These precursors can be metabolized to produce thyroid hormone as required. This structure most likely evolved as an adaptation to the relative rarity of iodine in animal diets, including our own. Because iodine is required for the synthesis of thyroid hormone, having a large store of extracellular iodinated precursors available in the thyroid gland ensures that even with prolonged deficiency of dietary iodine, thyroid hormone can still be produced.

11.3 Parathyroid hormone is a key part of the mechanism that regulates calcium ion homeostasis. The absence of PTH would have devastating health consequences, because it would result in decreased Ca^{2+} concentrations in the blood; Ca^{2+} is vitally important for proper functioning of all types of muscle tissue, including the heart, and also regulates neuronal function, among other actions. Antidiuretic hormone (vasopressin) contributes to the control of blood pressure and to water balance, because of its actions on kidney tubules. In its absence, blood pressure would be difficult to maintain, and the body would lose considerable volumes of water in the urine. That, in turn, would further compromise blood pressure and would also alter solute concentrations in the extracellular fluid. T_3 (thyroid hormone), through its calorigenic actions, is a major part of the mechanism by which body temperature homeostasis is maintained. In the absence of T_3, most people generally develop cold intolerance.

CHAPTER 12

Recall and Comprehend

12.1 b Reduced oxygen delivery to the kidneys increases the secretion of erythropoietin, which stimulates bone marrow to increase production of erythrocytes.

12.2 c

12.3 c Blood in the right ventricle is relatively deoxygenated after returning from the tissues.

12.4 e Resistance decreases as the fourth power of an increase in radius, and in direct proportion to a decrease in vessel length.

12.5 d See Figure 12.22.

12.6 d The large total cross-sectional area of capillaries results in very slow blood velocity.

12.7 a Increasing colloid osmotic pressure would decrease filtration of fluid from capillaries into the tissues.

12.8 d Pressures are higher in the systemic circuit, but because the cardiovascular system is a closed loop, the flow must be the same in both.

12.9 b The AV node is the only conduction point between atria and ventricles, and the slow propagation through it delays the beginning of ventricular contraction.

12.10 c The diastolic pressure in this example is 85; adding 1/3 of the pulse pressure gives a *MAP* of 101.7 mmHg.

12.11 d Reduced firing to arterioles would reduce total peripheral resistance and thereby reduce mean arterial pressure toward normal.

12.12 e Ventricular muscle cells do not have a pacemaker potential, and the L-type Ca^{2+} channel is not open during this phase of the action potential even in autorhythmic cells.

12.13 c

12.14 a Increased sympathetic nerve firing and norepinephrine release during exercise constrict vascular beds in the kidneys, GI tract, and other tissues to compensate for the large dilation of muscle vascular beds.

12.15 e t-PA is part of the fibrinolytic system that dissolves clots.

Apply, Analyze, and Evaluate

12.1 No. Decreased erythrocyte volume is certainly one possible explanation, but there is a second: The person may have a normal erythrocyte volume but an increased plasma volume. Convince yourself of this by writing the hematocrit equation as

$$\text{Erythrocyte volume}/(\text{Erythrocyte volume} + \text{Plasma volume})$$

12.2 A halving of tube radius. Resistance is directly proportional to blood viscosity but inversely proportional to the *fourth power* of tube radius.

12.3 The plateau of the action potential and the contraction would be absent. You may think that contraction would persist because most Ca^{2+} in excitation–contraction coupling in the heart comes from the sarcoplasmic reticulum. However, the signal for the release of this Ca^{2+} is the Ca^{2+} entering across the plasma membrane.

12.4 The SA node is not functioning, and the ventricles are being driven by a pacemaker in the AV node or the bundle of His.

12.5 The person has a narrowed aortic valve. Normally, the resistance across the aortic valve is so small that there is only a tiny pressure difference between the left ventricle and the aorta during ventricular ejection. In the example given here, the large pressure difference indicates that resistance across the valve must be very high.

12.6 This question is analogous to question 12.5 in that the large pressure difference across a valve while the valve is open indicates an abnormally narrowed valve—in this case, the left AV valve.

12.7 Decreased heart rate and contractility. These are effects mediated by the sympathetic nerves on beta-adrenergic receptors in the heart.

12.8 120 mmHg. $MAP = DP + 1/3\ (SP - DP)$.

12.9 The drug must have caused the arterioles in the kidneys to dilate enough to reduce their resistance by 50%. Blood flow to an organ is determined by mean arterial pressure and the organ's resistance to flow. Another important point can be deduced here: If mean arterial pressure has not changed even though renal resistance has dropped 50%, then either the resistance of some other organ or actual cardiac output has increased.

12.10 The experiment suggests that acetylcholine causes vasodilation by releasing nitric oxide or some other vasodilator from endothelial cells.

12.11 A low plasma protein concentration. Capillary pressure is, if anything, lower than normal and so cannot be causing the edema. Another possibility is that capillary permeability to plasma proteins has increased, as occurs in burns.

12.12 20 mmHg/L per minute. $TPR = MAP/CO$.

12.13 Nothing. Cardiac output and *TPR* have remained unchanged, so their product, *MAP,* also remains unchanged. This question emphasizes that *MAP* depends on cardiac output but not on the combination of heart rate and stroke volume that produces the cardiac output.

12.14 It increases. There are a certain number of impulses traveling up the nerves from the arterial baroreceptors. When these nerves are cut, the number of impulses reaching the medullary cardiovascular center goes to zero, just as it would physiologically if the mean arterial pressure were to decrease markedly. Accordingly, the medullary cardiovascular center responds to the absent impulses by reflexively increasing arterial pressure.

12.15 It decreases. The hemorrhage causes no immediate change in hematocrit because erythrocytes and plasma are lost in the same proportion. As interstitial fluid starts entering the capillaries, however, it expands the plasma volume and decreases hematocrit. (This is too soon for any new erythrocytes to be synthesized.)

12.16 Using the following equation, $MAP = DP + 1/3(SP - DP)$, inserting 85 for *MAP* and 105 for *SP,* solving for *DP* gives a value of 75 mmHg. Pulse pressure = $SP - DP$, or in this case, $105 - 75 = 30$ mmHg.

12.17 Transplant recipients can increase cardiac output during exercise in two ways. When exercise begins, epinephrine is released from the adrenal medulla and stimulates β-adrenergic receptors on the heart. This increases heart rate and contractility just like would happen in response to norepinephrine released directly from sympathetic neurons; only the response will be delayed in onset. Also, when the individual starts to exercise and venous return to the heart is increased, end-diastolic volume is increased. This initiates the Frank–Starling mechanism, increasing stroke volume and contributing to an increased cardiac output.

12.18 In lead aVR, the electrical poles of the leads are oriented nearly the opposite of lead 1: Lead 1 is a vector oriented from the right side of the body toward a positive pole on the left arm, while lead aVR is a vector oriented from the left side of the body toward a positive pole on the right arm. Thus, if the sweep of depolarization toward the positive pole in lead 1 generates an upright P wave, you can expect that same sweep of depolarization away from the positive pole in lead aVR to produce a downward P wave.

12.19 The stroke volume can be determined by inserting cardiac output and heart rate into the equation $CO = HR \times SV$: 5400 mL/min = 75 beats/min × *SV;* so *SV* = 72 mL. Next, the end-diastolic volume (*EDV*) can be determined using the equation $SV = EDV - ESV$: 72 mL = *EDV* − 60; so *EDV* = 132 mL. Finally, the ejection fraction (*EF*) is $EF = SV/EDV$, so *EF* = 72 mL/132 mL = 54.5%.

General Principles Assessment

12.1 Hormones of the endocrine system represent vital information that integrates the function of cells and organs that are widely distributed in the body. The circulatory system delivers blood and any hormones it may contain rapidly and efficiently to all cells throughout the body. Without this information-delivery system, the endocrine system could not function properly in the regulation of homeostasis.

12.2 Although it is possible that the difference in valve leaflet number is simply a random quirk of how the heart develops, a clear difference in the functional demands on the two AV valves is the amount of pressure they must withstand. At the peak of systole, the typical pressure gradient across the right AV valve is approximately 25 mmHg (pulmonary systolic pressure), while across the left AV valve it is approximately 120 mmHg (systemic systolic pressure). Having one less valve leaflet, the left AV valve has a smaller area where the edges of valve leaflets must seal. It seems likely that this structure makes it less susceptible to failure despite the greater pressure it encounters.

12.3 The liver produces plasma proteins at a rate that keeps their concentration in the plasma within a narrow range. Plasma proteins do not freely exchange across capillary walls, and their concentration determines the value of π_C, the main force that opposes bulk flow of fluid from the plasma to the interstitial fluid (see Figure 12.45). Maintaining balance in the bulk flow forces is essential for controlling the movement of fluid between the interstitial and plasma compartments. The failure of the liver to maintain plasma protein concentration in individuals who are protein starved (kwashiorkor) or who have hepatic damage results in excessive filtration of fluid from the plasma and tissue edema.

CHAPTER 13

Recall and Comprehend

13.1 e If alveolar pressure (P_{alv}) is negative with respect to atmospheric pressure (P_{atm}), the driving force for airflow is inward (from the atmosphere into the lung).

13.2 a For the same change in transpulmonary pressure, a less compliant (i.e., stiffer) lung will have a smaller change in lung volume.

13.3 a Total minute ventilation is comprised of dead space plus alveolar ventilation. Minute ventilation is respiratory frequency (12 breaths per minute) multiplied by tidal volume (500 mL/breath) = 6000 mL/min. Subtract from that alveolar ventilation (4200 mL/min) and one gets 1800 mL/min.

13.4 d An increase in alveolar P_{O_2} results from an increase in alveolar ventilation (supply of oxygen) relative to metabolic rate (consumption of oxygen).

13.5 c The relationship between arterial P_{O_2} and arterial oxygen saturation is described by the oxygen–hemoglobin dissociation curve. The greatest increase in oxygen saturation for the same change in P_{O_2} occurs at the steepest part of the curve—a P_{O_2} of between 40 and 60 mmHg.

13.6 b Increases in blood temperature, decreases in blood pH, and increases in DPG shift the oxygen–hemoglobin curve downward, leading to a lower oxygen saturation at the same P_{O_2}

13.7 b There are forms of asthma that are not primarily due to the presence of allergens. Examples are exercise-induced or cold-air-induced asthma.

13.8 e Respiratory acidosis (increase in blood P_{CO_2} and decrease in pH) is a major stimulus to ventilation—this is mediated both by afferents from the peripheral chemoreceptors and by an increase in central chemoreceptor activity.

13.9 c Because of the shape of the oxygen–hemoglobin dissociation curve, small increases in P_{O_2} due to increases in ventilation cannot fully saturate hemoglobin. When the desaturated blood mixes with saturated blood, the average is still hypoxemic.

13.10 c Remember that a lung capacity is the sum of at least two volumes. Inspiratory capacity is the sum of tidal volume and inspiratory reserve volume.

Apply, Analyze, and Evaluate

13.1 200 mL/mmHg.

$$\begin{aligned}\text{Lung compliance} &= \Delta \text{ lung volume}/\Delta\,(P_{alv} - P_{ip})\\ &= 800 \text{ mL}/[0 - (-8)] \text{ mmHg} \\ &\qquad - [0 - (-4)] \text{ mmHg}\\ &= 800 \text{ mL}/4 \text{ mmHg} = 200 \text{ mL/mmHg}\end{aligned}$$

13.2 More subatmospheric than normal. A decreased surfactant level causes the lungs to be less compliant (i.e., more difficult to expand). Therefore, a greater transpulmonary pressure ($P_{alv} - P_{ip}$) is required to expand them a given amount.

13.3 No.

$$\begin{aligned}\text{Alveolar ventilation} &= (\text{Tidal volume} - \text{Dead space}) \times \text{Breathing rate}\\ &= (250 \text{ mL} - 150 \text{ mL})/\text{breath} \times 20 \text{ breaths/min}\\ &= 2000 \text{ mL/min}\end{aligned}$$

Normal alveolar ventilation is approximately 4000 mL/min in a 70 kg adult.

13.4 The volume of the snorkel constitutes an additional dead space, so total pulmonary ventilation must be increased if alveolar ventilation is to remain constant. The most efficient way to do this is to increase tidal volume.

13.5 The alveolar P_{O_2} will be higher than normal, and the alveolar P_{CO_2} will be lower. To better understand why, review the factors that determine the alveolar gas pressures (see Table 13.5).

13.6 No. Hypoventilation reduces arterial P_{O_2} but only because it reduces alveolar P_{O_2} That is, in hypoventilation, *both* alveolar and arterial P_{O_2} are decreased to essentially the same degree. In this problem, alveolar P_{O_2} is normal, and so the person is not hypoventilating. The low arterial P_{O_2} must therefore represent a defect that causes a discrepancy between alveolar P_{O_2} and arterial P_{O_2} Possibilities include impaired diffusion, a shunting of blood from the right side of the heart to the left through a hole in the heart wall, and a mismatch between airflow and blood flow in the alveoli.

13.7 Not at rest, if the defect is not too severe. Recall that equilibration of alveolar air and pulmonary capillary blood is normally so rapid that it occurs well before the end of the capillaries. Therefore, even though diffusion may be slowed as in this problem, there may still be enough time for equilibration to be reached. In contrast, the time for equilibration is decreased during exercise (because of an increase in the rate of blood flow through the pulmonary circulation), and failure to equilibrate is much more likely to occur, resulting in a lowered arterial P_{O_2}.

13.8 Only a few percent (specifically, from approximately 200 mL O_2/L blood to approximately 215 mL O_2/L blood). The reason the increase is so small is that almost all the oxygen in blood is carried bound to hemoglobin, and hemoglobin is almost 100% saturated at the arterial P_{O_2} achieved by breathing room air. The high arterial P_{O_2} achieved by breathing 100% oxygen does cause a directly proportional increase in the amount of oxygen *dissolved* in the blood (the additional 15 mL), but this still remains a small fraction of the total oxygen in the blood. Review the numbers given in the chapter.

13.9 All. Venous blood contains products of metabolism released by cells, such as carbon dioxide.

13.10 It would cease. Respiration depends on descending input from the medulla to the nerves supplying the diaphragm and the inspiratory intercostal muscles.

13.11 a The combination of hypercapnia (increased P_{CO_2} due to increased inspired CO_2) and hypoxia (due to decreased inspired O_2) greatly augments ventilation by stimulating central and peripheral chemoreceptors. Although CO decreases O_2 content, chemoreceptors are not stimulated and ventilation does not increase.

13.12 These patients have profound hyperventilation, with large increases in both the depth and rate of ventilation. The stimulus, mainly via the peripheral chemoreceptors, is the large increase in their arterial hydrogen ion concentration due to the acids produced. The hyperventilation causes an increase in their arterial P_{O_2} and a decrease in their arterial P_{CO_2}

13.13 In pure anatomical shunt, blood passes through the lung without exposure to any alveolar air. Therefore, increases in alveolar P_{O2} caused by increased inspired O_2 will not affect the P_{O2} of the shunt blood. By contrast, there is still some blood flowing through a region of the lung with a ventilation–perfusion mismatch. Therefore, an increase in P_{O2} in the alveoli can increase the P_{O2} in this blood, which, when mixing with blood leaving other areas of the lung, can increase the blood in the pulmonary vein and hence the arterial circulation.

General Principles Assessment

13.1 Boyle's law (see Figure 13.8) explains that the pressure exerted by a constant number of gas molecules (at constant temperature) is inversely proportional to the volume of a container. Therefore, when the volume of the lung increases during negative pressure breathing, the resultant decrease in pressure draws air into the lungs (inspiration). Conversely, when the lung deflates, the pressure in it increases pushing air out of the lung (expiration). The Law of Laplace (Figure 13.17) demonstrates that the larger the radius of a sphere (e.g., an alveolus), the lower the surface tension. This explains the need for pulmonary surfactant, which decreases the surface tension of smaller alveoli, thereby preventing smaller alveoli from collapsing. Dalton's law states that, in a mixture of gases, the pressure each gas exerts is independent of the pressure the others exert and is proportional to the percentage of that gas in the mixture. This explains, therefore, why the partial pressure of oxygen in air at sea level is equal to 0.21×760 mmHg, or 160 mmHg. Henry's law states that the amount of gas dissolved in a liquid will be directly proportional to the partial pressure of the gas with which the liquid is in equilibrium. This is extremely important in understanding the transfer of oxygen from the alveolar gas to the blood. Finally, the unique allosteric properties of hemoglobin shown in Figures 13.26 and 13.29 allow the appropriate delivery of oxygen from the lungs to the tissues. As the CO_2 diffuses out of the pulmonary capillaries, the decrease in CO_2 in the blood shifts the oxygen dissociation curve to the left allowing more oxygen uptake. Conversely, as the blood enters the tissue, CO_2 diffuses into the blood and shifts the oxygen dissociation curve to the right allowing a greater unloading of oxygen to the tissues.

13.2 The thinness of the alveolar wall minimizes the barrier for oxygen and carbon dioxide diffusion allowing an efficient

transfer of gases to and from the blood (Figure 13.4). The multiple branching of the airways into respiratory bronchioles and alveoli and the branching of the pulmonary artery into the pulmonary arterioles and capillaries greatly increase the surface area for gas exchange (Figure 13.3).

13.3 Some of the factors that influence alveolar ventilation are summarized in Figure 13.40. The three major stimulatory factors in the blood are a decrease in P_{O_2} an increase in nonvolatile acids, and an increase in P_{CO_2} Conversely, a decrease in acids and P_{CO_2} in the blood inhibit ventilation. These factors often work in opposition during the adaptation to hypoxia due, for example, to high altitude. In this case, P_{O_2} decreases due to a decrease in barometric pressure. The resulting increase in alveolar ventilation (Figure 13.35) leads to a decrease in P_{CO_2} (hyperventilation). This respiratory alkalosis attenuates the increase in alveolar ventilation that would have otherwise occurred with arterial hypoxia.

CHAPTER 14

Recall and Comprehend

14.1 c The main driving force favoring fluid filtration from the glomerular capillary to Bowman's space is glomerular capillary blood pressure (P_{GC}).

14.2 c In order for a substance to appear in the urine at a faster rate than its filtration rate, it must also be actively secreted into the tubular fluid.

14.3 a Excessive sweating will decrease blood volume. This will lead to compensatory mechanisms to preserve total-body water, including a decrease in urine production (antidiuresis).

14.4 e Urea is trapped in the medullary interstitium and is an osmotically active solute. The resultant increase in tonicity helps to maintain the gradient for medullary passive water reabsorption.

14.5 a A decrease in sodium intake stimulates renin because of the decrease in Na^+ delivery to the macula densa. This is detected and results in an increase in renin release from the juxtaglomerular cells.

14.6 c Parathyroid hormone stimulates Ca^{2+} reabsorption in the distal tubules of the nephron, thereby decreasing Ca^{2+} excretion. Because parathyroid hormone is increased in hypocalcemic states, the resulting decrease in Ca^{2+} excretion helps to restore blood Ca^{2+} to normal.

14.7 c Secretion of ammonium into the renal tubule is one way to rid the body of excess hydrogen ion (metabolic acidosis).

14.8 b Increases in ventilation greater than metabolic rate "blow off" CO_2 and result in a decrease in arterial P_{CO_2} Because of the buffering of bicarbonate ions, this increases arterial pH (respiratory alkalosis).

14.9 e Cortical nephrons either have short or absent loops of Henle. Only juxtamedullary nephrons have long loops of Henle, which plunge into the renal medulla and create a hyperosmotic interstitium via countercurrent multiplication and the trapping of urea.

14.10 a When the renal corpuscles become diseased, they greatly increase their permeability to protein. Furthermore, diseased proximal tubules cannot remove the filtered protein from the tubular lumen. This results in increased protein in the urine (proteinuria).

Apply, Analyze, and Evaluate

14.1 No. This is a possible answer, but there is another. Substance T may be secreted by the tubules.

14.2 No. It is a possibility, but there is another. Substance V may be filtered and/or secreted, but the substance V entering the lumen via these routes may be completely reabsorbed.

14.3 125 mg/min. The amount of any substance filtered per unit time is given by the product of the *GFR* and the filterable plasma concentration of the substance—in this case, 125 mL/min × 100 mg/100 mL = 125 mg/min.

14.4 The plasma concentration may be so high that the T_m for the amino acid is exceeded, so all the filtered amino acid is not reabsorbed. A second possibility is that there is a specific defect in the tubular transport for this amino acid. A third possibility is that some other amino acid is present in the plasma in high concentration and is competing for reabsorption.

14.5 No. Urea is filtered and then partially reabsorbed. The reason its concentration in the tubule is higher than in the plasma is that relatively more water is reabsorbed than urea. Therefore, the urea in the tubule becomes concentrated. Despite the fact that urea *concentration* in the urine is greater than in the plasma, the *amount excreted* is less than the filtered load (that is, net reabsorption has occurred).

14.6 They would all be decreased. The transport of all these substances is coupled, in one way or another, to that of Na^+.

14.7 GFR would not decrease as much, and renin secretion would not increase as much as in a person not receiving the drug. The sympathetic nerves are a major pathway for both responses during hemorrhage.

14.8 There would be little if any increase in aldosterone secretion. The major stimulus for increased aldosterone secretion is angiotensin II, but this substance is formed from angiotensin I by the action of angiotensin-converting enzyme, and so blockade of this enzyme would block the pathway.

14.9 b Urinary excretion in the steady state must be less than ingested sodium chloride by an amount equal to that lost in the sweat and feces. This is normally quite small, less than 1 g/day, so that urine excretion in this case equals approximately 11 g/day.

14.10 If the hypothalamus had been damaged, there may be inadequate secretion of ADH. This would cause loss of a large volume of urine, which would tend to dehydrate the person and make her thirsty. Of course, the area of the brain involved in thirst might have suffered damage.

14.11 This is primary hyperaldosteronism or Conn's syndrome. Because aldosterone stimulates Na^+ reabsorption and K^+ secretion, there will be total-body retention of Na^+ and loss of K^+. Interestingly, the person in this situation actually retains very little Na^+ because urinary Na^+ excretion returns to normal after a few days despite the continued presence of the high aldosterone. One explanation for this is that GFR and atrial natriuretic factor both increase as a result of the initial Na^+ retention.

14.12 Sodium and water balance would become negative because of increased excretion of these substances in the urine. The person would also develop a decreased plasma bicarbonate ion concentration and metabolic acidosis because of increased bicarbonate ion excretion. The effects on acid–base status are explained by the fact that hydrogen ion secretion—blocked by the drug—is required both for HCO_3^- reabsorption and for the excretion of hydrogen ion (contribution of new HCO_3^- to the blood). The increased Na^+ excretion reflects the fact that much Na^+ reabsorption by the proximal tubule is achieved by Na^+/H^+ countertransport. By blocking hydrogen ion secretion, therefore, the drug also partially blocks Na^+ reabsorption. The increased water excretion occurs because the failure to reabsorb Na^+ and HCO_3^- decreases water reabsorption (remember that water reabsorption is secondary to solute reabsorption), resulting in an osmotic diuresis.

14.13 The overuse of diuretics can lead to significant hypovolemia, which leads to an increase in the release of renin from the kidney (see Figure 14.24). The resultant increase in angiotensin II and therefore aldosterone increases the distal tubular secretion of hydrogen ions (mostly in the form of NH_4^+), because of its exchange with sodium (see Figure 14.35). As you learned in Section 14.15, most diuretics not only increase sodium excretion (the desired effect) but increase potassium excretion. The resultant potassium depletion can weakly stimulate tubular hydrogen ion secretion. These two factors—increased aldosterone and potassium depletion—lead to an increase in the reabsorption of all the filtered bicarbonate as well as the generation of new

bicarbonate from glutamine (see Figure 14.35). This can generate a marked metabolic alkalosis that can have profound effects on multiple organ systems.

General Principles Assessment

14.1 The anatomy of the renal corpuscle is ideally suited to filter the plasma. As you learned in Figure 14.4, the fenestrated capillaries of the glomerulus allow the filtration of plasma but prevent the loss of larger molecules (like albumin). The juxtaglomerular apparatus is ideally located to sense the amount of sodium in the distal tubule such that renin secretion can be appropriately regulated. The anatomical placement of the afferent and efferent arterioles allows the precise regulation of the blood pressure within the glomerulus, thus regulating glomerular filtration rate.

14.2 The appreciation of the physical forces—such as hydrostatic pressure—that determine net movement of plasma out of capillaries (Starling's forces; Figure 14.8) is vital to understand the ultimate glomerular filtration rate. The expression of the enzyme carbonic anhydrase in the tubular epithelial cells catalyzes the conversion of H_2O and CO_2 to H_2CO_3, which then breaks down to provide H^+ for secretion into the tubular lumen and HCO_3^- for reabsorption into the interstitial fluid. The equilibrium of this reaction obeys the chemical law known as mass action (see Chapter 3).

14.3 There are a variety of stimulatory and inhibitory inputs involved in the control of vasopressin (Figures 14.26, 14.27, and 14.28). For example, an increase in the osmolarity of the blood increases vasopressin by stimulation of the central osmoreceptor, whereas an increase in plasma volume decreases vasopressin by stimulation of the low-pressure baroreceptors in the heart. So, a person with an increased plasma osmolarity and plasma volume due to, for example, an extremely high salt intake, would demonstrate a smaller increase in vasopressin than a person with increased osmolarity but decreased plasma volume that may occur during dehydration.

CHAPTER 15

Recall and Comprehend

15.1 c When the stomach contents, which are very acidic, move into the small intestine, it stimulates the release of secretin, which circulates to the pancreas and stimulates the release of HCO_3^- into the small intestine. This neutralizes the acid and protects the small intestine.

15.2 d GIP release is a feedforward mechanism to signal the islet cells in the pancreas that the products of food digestion are on their way to the blood. This results in an augmented insulin response to a meal.

15.3 a Gastrin is a major controller of acid secretion by the stomach. When the stomach becomes very acidic, gastrin release is inhibited, preventing continued acid production.

15.4 b Cholecystokinin is the primary signal from the small intestine to the pancreas to increase digestive enzyme release into the small intestine.

15.5 d The enzyme pepsin is produced from pepsinogen in the presence of acid. This zymogen accelerates protein digestion.

15.6 b Because fat is insoluble in an aqueous environment, micelles keep fat droplets from re-aggregating and small enough to be absorbed.

15.7 c Distention of the duodenum signals the stomach that the meal has moved on and continued acid secretion in the stomach is not necessary until the next meal.

15.8 a HCO_3^- in the bile is secreted by the epithelial cells lining the bile ducts.

15.9 e Although the primary movement of chyme in segmentation is back and forth, the overall, net movement of chyme is from the small intestine to the large intestine.

15.10 a The active transport of Na^+ in the large intestine is the driving force for the osmotic absorption of water.

Apply, Analyze, and Evaluate

15.1 If the salivary glands fail to secrete amylase, the undigested starch that reaches the small intestine will still be digested by the amylase the pancreas secretes. Thus, starch digestion is not significantly affected by the absence of salivary amylase.

15.2 Alcohol can be absorbed across the stomach wall, but absorption is much more rapid from the small intestine with its larger surface area. Ingestion of foods containing fat releases enterogastrones from the small intestine, and these hormones inhibit gastric emptying and thereby prolong the time alcohol spends in the stomach before reaching the small intestine. Milk, contrary to popular belief, does not "protect" the lining of the stomach from alcohol by coating it with a fatty layer. Rather, the fat content of milk decreases the rate of absorption of alcohol by decreasing the rate of gastric emptying.

15.3 Fat can be digested and absorbed in the absence of bile salts, but in greatly decreased amounts. Without adequate emulsification of fat by bile salts and phospholipids, only the fat at the surface of large lipid droplets is available to pancreatic lipase, and the rate of fat digestion is very slow. Without the formation of micelles with the aid of bile salts, the products of fat digestion become dissolved in the large lipid droplets, where they are not readily available for diffusion into the epithelial cells. In the absence of bile salts, only about 50% of the ingested fat is digested and absorbed. The undigested fat is passed on to the large intestine, where bacteria produce compounds that increase colonic motility and promote the secretion of fluid into the lumen of the large intestine, leading to diarrhea.

15.4 Damage to the lower portion of the spinal cord produces a loss of voluntary control over defecation due to disruption of the somatic nerves to the skeletal muscle of the external anal sphincter. Damage to the somatic nerves leaves the external sphincter in a continuously relaxed state. Under these conditions, defecation occurs whenever the rectum becomes distended and the defecation reflex is initiated.

15.5 Vagotomy decreases the secretion of acid by the stomach. Impulses in the parasympathetic nerves directly stimulate acid secretion by the parietal cells via release of acetylcholine, and also cause the release of gastrin, which in turn stimulates acid secretion. Impulses in the vagus nerves are increased during both the cephalic and gastric phases of digestion. Vagotomy, by decreasing the amount of acid secreted, decreases irritation of existing ulcers, which promotes healing and decreases the probability of acid contributing to the production of new ulcers.

General Principles Assessment

15.1 The liver is ideally situated to process materials absorbed from the lumen of the small intestine that end up in the hepatic portal vein (Figure 15.32). One very important example of this is the detoxification of harmful substances that are ingested and absorbed. Notice in Figure 15.31 that the hepatocytes (liver cells) form sheets, thereby maximizing their contact with blood in the hepatic sinusoids. This ensures that most, if not all, of the toxic substances absorbed in the small intestine can be taken up from the blood in the branches of the portal vein and rendered harmless in the hepatocytes. Furthermore, contact with the bile canaliculi ensures the ability of the hepatocytes to rid the body of toxic metabolites by secretion into the bile.

15.2 (1) Figures 15.10, 15.11, 15.12, and 15.13 demonstrate the chemical property of polarity. That is, steroids are nonpolar rendering them relatively insoluble in water. Chemical additions to the basic structure of the steroid molecule (for example, hydroxyl groups) result in polar portions exposed on the surface of the molecule that are water soluble. This results in a molecule that is amphipathic enabling it to bind to lipids on the nonpolar regions and also to dissolve in water on the polar region, thereby

emulsifying lipids for absorption. Interestingly, chemical emulsifiers are often added to salad dressing to allow the oil and the water portions to stay mixed after shaking. (2) Figure 15.19 demonstrates the ability of an enzyme—carbonic anhydrase—to catalyze the conversion of CO_2 and H_2O to H_2CO_3 which then breaks down to HCO_3^- and H^+; the secretion of the latter in the lumen of the stomach results in a very acidic environment ideal for the initial digestion of proteins as well as a way to kill most ingested bacteria. (3) Another interesting example of chemistry is shown in Figure 15.22 in which an inactive enzyme precursor (pepsinogen) is activated in the acidic environment of the gastric lumen to the active enzyme pepsin that catalyzes the breakdown of proteins to peptides. (Figure 15.28 gives another example of this concept for pancreatic enzymes.) In both cases, the secretion of an inactive form of the enzyme prevents self-destruction of the cells responsible for producing the enzyme.

15.3 Figure 15.14 illustrates in several ways the general principle that *information flow between cells, tissues, and organs is an essential feature of homeostasis and allows for integration of physiological processes.* How do you perceive the sensation of "fullness" when you have ingested a large meal? Afferent nerves from the upper GI tract "tell" the brain that you are full. How do emotions influence gastrointestinal motility? Efferent autonomic input to the GI tract can alter the activity of the enteric nervous system, thus altering smooth muscle activity in the GI tract.

CHAPTER 16

Recall and Comprehend

16.1 a Glucose can be metabolized to synthesize fatty acids, but fatty acids cannot be converted to glucose.

16.2 b HSL is an intracellular enzyme that acts on triglycerides.

16.3 a Glucagon acts to prevent hypoglycemia from occurring.

16.4 c If untreated, type 1 DM causes an osmotic diuresis when the transport maximum for glucose is exceeded in the kidneys.

16.5 d Insulin stimulates lipogenesis, not lipolysis.

16.6 e Recall that vitamin deficiencies can occur even with normal dietary intake of vitamins, because the metabolic rate is increased in hyperthyroidism.

16.7 b

16.8 T

16.9 F Core temperature is generally kept fairly constant, but skin temperature can vary.

16.10 T

16.11 F As muscles begin contracting during exercise, they become partially insulin-independent.

16.12 F BMI equals body mass in kg divided by (height in meters)^2.

16.13 T

16.14 F Skin vessels dilate in such conditions in order to help dissipate heat by bringing warm blood close to the skin surface.

16.15 T

Apply, Analyze, and Evaluate

16.1 The concentration in plasma would increase, and the amount stored in adipose tissue would decrease. Lipoprotein lipase cleaves plasma triglycerides, so its blockade would decrease the rate at which these molecules were cleared from plasma and would decrease the availability of the fatty acids in them for the synthesis of intracellular triglycerides. However, this would only reduce but not eliminate such synthesis, because the adipose-tissue cells could still synthesize their own fatty acids from glucose.

16.2 It will lower plasma cholesterol concentration. Bile salts are formed from cholesterol, and losses of these bile salts in the feces will be replaced by the synthesis of new ones from cholesterol. Chapter 15 describes how bile salts are normally absorbed from the small intestine so that very few of those secreted into the bile are normally lost from the body.

16.3 Plasma concentrations of HDL and LDL. It is the ratio of LDL cholesterol to HDL cholesterol that best correlates with the development of atherosclerosis (HDL cholesterol is "good" cholesterol). The answer to this question would have been the same regardless of whether the person was an athlete, but the question was phrased this way to emphasize that people who exercise generally have increased HDL cholesterol.

16.4 The person may have type 1 diabetes mellitus and require insulin, or may be a healthy fasting person; plasma glucose would be increased in the first case but decreased in the second. Plasma insulin concentration would be useful because it would be decreased in both cases. The fact that the person was resting and unstressed was specified because severe stress or strenuous exercise could also produce the plasma changes mentioned. Plasma glucose would increase during stress and decrease during strenuous exercise.

16.5 Glucagon, epinephrine, cortisol, and growth hormone. The insulin will produce hypoglycemia, which then induces reflexive increases in the secretion of all these hormones.

16.6 It may reduce it but not eliminate it. The sympathetic effects on organic metabolism during exercise are mediated not only by circulating epinephrine but also by sympathetic nerves to the liver (glycogenolysis and gluconeogenesis), to adipose tissue (lipolysis), and to the pancreatic islets (inhibition of insulin secretion and stimulation of glucagon secretion).

16.7 Heat loss from the head, mainly via convection and sweating, is the major route for loss under these conditions. The rest of the body is *gaining* heat by conduction, and sweating is of no value in the rest of the body because the water cannot evaporate. Heat is also lost via the expired air (insensible loss), and some people actually begin to pant under such conditions. The rapid, shallow breathing increases airflow and heat loss without causing hyperventilation.

General Principles Assessment

16.1 Insulin and glucagon are both secreted by the endocrine pancreas; they have opposite effects on plasma concentrations of glucose. They achieve these effects in part through opposite actions on key metabolic organs such as the liver. In the liver, insulin stimulates glycogen synthesis and inhibits gluconeogenesis, whereas glucagon stimulates glycogen breakdown and gluconeogenesis. Insulin and glucagon are always present in plasma; it is the ratio of the two hormones that determines the net effect that will be to either decrease (insulin) or increase (glucagon) the concentration of plasma glucose.

16.2 The factors that control hunger (appetite) are summarized in Figure 16.15. Neural and endocrine signals arising from the gastrointestinal tract and adipocytes appear to be very important regulators of appetite. Other factors, such as plasma glucose and insulin concentrations, body temperature, and behavioral mechanisms also play a role.

16.3 As described in the chapter, the first law of thermodynamics states that energy can neither be created nor destroyed but can be transformed from one type to another. This is demonstrated by the production of heat within cells during the breakdown of organic molecules such as glucose. Some of the energy from the chemical bonds in organic molecules is transferred to ATP, and some is released as heat. This heat contributes to body temperature. Maintaining body temperature in a homeostatic range also depends upon the properties of heat; for example, heat flows from a region of higher temperature to one of lower temperature. In Figure 16.17, for example, heat is shown entering the body by radiation from the sun and conduction from the hot water.

CHAPTER 17

Recall and Comprehend

17.1 e Without the presence of the Y chromosome in the testes and the local production of SRY protein, the undifferentiated gonads are programmed to differentiate into ovaries.

17.2 c Only females exhibit gonadal steroid (estrogen) positive feedback on GnRH release.

17.3 d The luteal phase of the ovary, when progesterone production is maximal, occurs after ovulation but before the end of the menstrual cycle.

17.4 c Estrogen stimulates LH release (positive feedback) just before the LH surge and ovulation (usually on day 14).

17.5 b One follicle becomes dominant early in the menstrual cycle.

17.6 e The death of the corpus luteum (in the absence of pregnancy and hCG) results in a dramatic decrease in ovarian progesterone and estrogen production.

17.7 a The loss of ovarian steroid production with the death of the corpus luteum releases the pituitary gland from negative feedback and allows FSH to increase. This stimulates the maturation of a small number of follicles for the next menstrual cycle.

17.8 c The primary function of the Leydig cell is the production of testosterone in response to stimulation with LH.

17.9 b Prolactin is produced by the maternal pituitary gland. It is homologous to but not the same peptide as human placental lactogen, which is produced by the placenta.

17.10 a The primary event in menopause is the loss of ovarian function. The decrease in estrogen leads to an increase in pituitary gland gonadotropin release (loss of negative feedback).

Apply, Analyze, and Evaluate

17.1 Sterility due to lack of spermatogenesis would be the common finding. The Sertoli cells are essential for spermatogenesis, and so is testosterone produced by the Leydig cells. The person with Leydig cell destruction, but not the person with Sertoli cell destruction, would also have other symptoms of testosterone deficiency.

17.2 The androgens act on the hypothalamus and anterior pituitary gland to inhibit the secretion of the gonadotropins. Therefore, spermatogenesis is inhibited. Importantly, even if this man were given FSH, the sterility would probably remain because the lack of LH would cause deficient testosterone secretion, and *locally* produced testosterone is required for spermatogenesis (i.e., the exogenous androgen cannot do this job).

17.3 Impaired function of the seminiferous tubules, notably of the Sertoli cells. The increased plasma FSH concentration is due to the lack of negative feedback inhibition of FSH secretion by inhibin, itself secreted by the Sertoli cells. The Leydig cells seem to be functioning normally in this person because the lack of demasculinization and the normal plasma LH indicate normal testosterone secretion.

17.4 FSH secretion. FSH acts on the Sertoli cells and LH acts on the Leydig cells, so sterility would result in either case, but the loss of LH would also cause undesirable elimination of testosterone and its effects.

17.5 These findings are all due to testosterone deficiency. You would also expect to find that the testes and penis were small if the deficiency occurred before puberty.

17.6 They will be eliminated or become very irregular. The androgens act on the hypothalamus to inhibit the secretion of GnRH and on the pituitary gland to inhibit the response to GnRH. The result is inadequate secretion of gonadotropins and therefore inadequate stimulation of the ovaries. In addition to the loss of regular menstrual cycles, the woman may suffer some degree of masculinization of the secondary sex characteristics because of the combined effects of androgen excess and estrogen deficiency.

17.7 Such treatment may cause so much secretion of FSH that multiple follicles become dominant and have their eggs ovulated during the LH surge.

17.8 An increased plasma LH. The other two are due to increased plasma progesterone and so do not occur until *after* ovulation and formation of the corpus luteum.

17.9 The absence of sperm capacitation. When test-tube fertilization is performed, special techniques are used to induce capacitation.

17.10 The fetus is in difficulty. The placenta produces progesterone entirely on its own, whereas estriol secretion requires participation of the fetus, specifically, the fetal adrenal cortex.

17.11 Prostaglandin antagonists, oxytocin antagonists, and drugs that lower cytosolic Ca^{2+} concentration. You might not have thought of the last category because Ca^{2+} is not mentioned in this context in the chapter, but as in all muscle, Ca^{2+} is the immediate cause of contraction in the myometrium.

17.12 This person would have normal male external genitals and testes, although the testes might not have descended fully, but would also have some degree of development of uterine tubes, a uterus, and a vagina. These internal female structures would tend to develop because no MIS was present to cause degeneration of the Müllerian duct system.

17.13 No. These two hormones are already increased in menopause, and the problem is that the ovaries are unable to respond to them with estrogen secretion. Thus, the treatment must be with estrogen itself.

General Principles Assessment

17.1 Although several answers are possible, differentiation of the internal and external genitalia is a wonderful example of the general principle that *structure is a determinant of—and has coevolved with—function*. The male and female genitalia arise from the same primordial cluster of cells in the embryo. The reproductive structures diverge in early embryonic development to form organs suited for their function. For the male, it is the production of sperm and the development of a penis that evolved to fit into the vagina of the female. In the female, it is to produce ova and to receive sperm to allow fertilization of the ova. So even though they started the same, through differentiation, the male and female tracts develop into complementary structures suited for their functions.

17.2 The amount of FSH and LH secreted from the gonadotrophs of the anterior pituitary at any one time in the male is determined by two opposing inputs. Stimulatory input is from GnRH released from hypophysiotropic nerves into the hypophyseal portal blood, and inhibitory negative feedback input is from the two different hormones released by the testes—inhibin and testosterone—that reach the anterior pituitary from the systemic circulation. The effect of inhibin at the anterior pituitary primarily reduces the release of FSH, whereas testosterone primarily reduces the release of LH.

17.3 The adaptation to pregnancy is one of the best examples of integration of multiple organ systems. Here are some examples that are listed in Table 17.9:

- Increase in maternal bone turnover to supply calcium and phosphorus to the placenta necessary for normal fetal bone development.
- Increase in maternal blood volume and red blood cell production. This allows the increase in cardiac output and perfusion of the rapidly growing placenta as well as increase in blood flow to, for example, the maternal kidneys to enable the excretion of the additional waste products produced by the fetus.
- Increase in maternal alveolar ventilation enables the mother to rid the body of the extra carbon dioxide produced by the fetus.
- Mobilization of maternal glucose meets the metabolic needs of the developing fetus.

As a test of your knowledge, you should be able to explain the mechanism of these and other adaptations to pregnancy listed in Table 17.9.

CHAPTER 18

Recall and Comprehend

18.1 c

18.2 a

18.3 b This is known as active immunity.

18.4 c IgA antibodies act in this way.

18.5 F Antibiotics are bactericidal. They are sometimes given in viral diseases to eliminate or prevent secondary infections caused by bacteria, however.

18.6 T For example, rheumatoid arthritis and inflammatory bowel disease are not associated with infection.

18.7 T Some lymphocytes are B cells.

18.8 F Edema is a consequence of inflammation and has no known adaptive value.

18.9 F These are the primary lymphoid organs. An example of a secondary organ is a lymph node.

18.10 F Toll-like receptors are an important part of the innate immune system and recognize conserved molecular features on pathogens.

Apply, Analyze, and Evaluate

18.1 Both would be impaired because T cells would not differentiate. The absence of cytotoxic T cells would eliminate responses mediated by these cells. The absence of helper T cells would impair antibody-mediated responses because most B cells require cytokines from helper T cells to become activated.

18.2 Neutrophil deficiency would impair nonspecific (innate) inflammatory responses to bacteria. Monocyte deficiency, by causing macrophage deficiency, would impair both innate inflammation and adaptive immune responses.

18.3 The drug may reduce but would not eliminate the action of complement, because this system destroys cells directly (via the membrane attack complex) as well as by facilitating phagocytosis.

18.4 Antibodies would bind normally to antigen but may not be able to activate complement, act as opsonins, or recruit NK cells in ADCC. The reason for these defects is that the sites to which complement C1, phagocytes, and NK cells bind are all located in the Fc portion of antibodies.

18.5 They do develop fever, although often not to the same degree as normal. They can do so because IL-1 and other cytokines secreted by macrophages cause fever, whereas the defect in AIDS is failure of helper T-cell function.

General Principles Assessment

18.1 As shown in Figure 18.22, a wide range of changes occur in physiological variables following infection, including changes in plasma concentrations of minerals (iron, zinc), energy sources (fatty acids, amino acids), and hormones (cortisol). In each case, the respective variable is decreased or increased beyond its usual homeostatic range. Although these changes are adaptive to fight infection, they may come with a cost, as does any challenge to homeostasis. For example, elevated concentrations of cortisol may temporarily result in hyperglycemia, water retention, and potentiated actions of catecholamines on cardiovascular function. Other responses to infection, such as fever, accelerate the rate of chemical reactions in all cells (increase metabolism) and, if fever is sufficiently high, may damage neuronal function.