

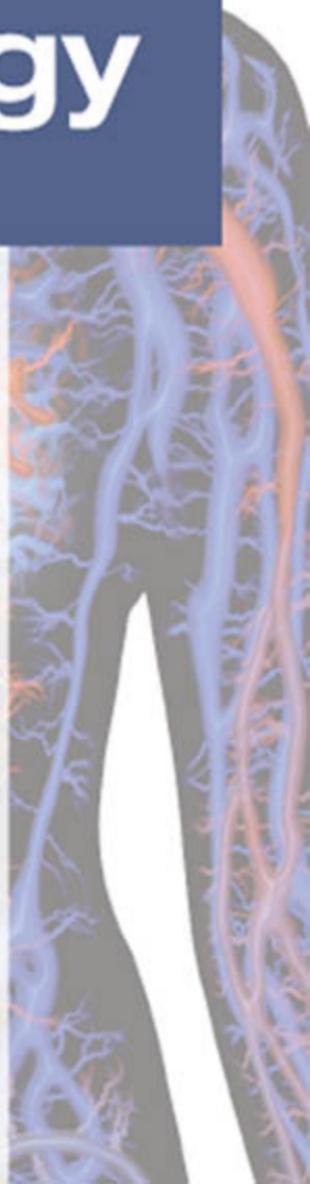


Physiology

twelfth edition

- 500 USMLE-type questions, answers, and explanations
- Explanations for right and wrong answers
- Targets what you really need to know
- Student tested and reviewed

Patricia Metting





Physiology

PreTestTM Self-Assessment and Review

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Physiology

PreTest™ Self-Assessment and Review
Twelfth Edition

Patricia J. Metting, PhD

Professor

Department of Physiology, Pharmacology, Metabolism, and Cardiovascular Science

Professor

Department of Medicine

Associate Dean for Student Affairs

College of Medicine

Vice Provost for Student Affairs

Health Science Campus

The University of Toledo

Toledo, Ohio



New York Chicago San Francisco Lisbon London Madrid Mexico City
Milan New Delhi San Juan Seoul Singapore Sydney Toronto

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To my husband, Mike, my children, Megan and Patrick, and in memory of my mother, Betty Jean Gongwer McDuffee, for your unconditional love and encouragement and the sacrifices you have made over the years in deference to my professional activities and responsibilities. I hope that somehow you know that there has never been anything more important in my life than all of you.

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Student Reviewers

Amy S. Arrington, PhD

Class of 2007

Baylor College of Medicine

Scott Feitell

Class of 2009

Philadelphia College of Osteopathic Medicine

Deborah L. Kem

Class of 2006

University of Louisville

Brad Miller

Class of 2006

Weill Medical College of Cornell University

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Introduction

Each *PreTest Self Assessment and Review* is designed to allow allopathic and osteopathic medical students, as well as international medical graduates, a comprehensive and convenient way to assess and review their knowledge of a particular medical science, in this instance, physiology. The 500 questions have been organized to parallel the Content Outline for the United States Medical Licensing Examination (USMLE™) Step 1 (<http://www.usmle.org/step1/s1princ.htm>). By familiarizing yourself with the Step 1 Content Outline, you will get a more accurate idea of the subject areas covered in each section. For example, acid-base balance and high altitude physiology are topics covered under General Principles: Multi-System Processes, rather than under Respiratory or Renal Physiology, where you likely learned them during your medical school education. Similarly, oxygen and carbon dioxide transport and capillary fluid balance are topics covered in the chapter on the Physiology of the Hematopoietic and Lymphoreticular Systems, rather than in the chapters on Respiratory or Cardiovascular Physiology. The value of organizing the questions this way is that the Step 1 Content Outline is used by the National Board of Medical Examiners (NBME) in the score reports that go to each examinee to provide them with their relative performance in each of the various areas tested by the USMLE Step 1. Thus, when you eventually find out how you performed in each category, you will have a more accurate understanding of your areas of strength and weakness.

Physiology PreTest has also been revised to incorporate a clinical vignette in the vast majority of the questions, in addition to questions that require interpretation of graphic information. In this way, the questions in *Physiology PreTest* more closely parallel the length and the degree of difficulty of the questions that you should expect to find on the USMLE Step 1.

Physiology PreTest will also be a valuable resource for osteopathic medical students studying for the Comprehensive Osteopathic Medical Licensing Examination (COMLEX)-USA. Similar to Step 1 of the USMLE, Level 1 of the COMLEX-USA, administered by the National Board of Osteopathic Medical Examiners, Inc., emphasizes an understanding of the basic science mechanisms underlying health and disease, and is constructed with clinical presentations in the context of medical problem solving (<http://www.nbome.org>).

Each question in *Physiology PreTest* is followed by four or more answer options. For each, select the *one best* answer from the choices given. Each question is also accompanied by the correct answer and its explanation.

The explanation provides the reason why the correct answer is correct and, in many cases, the reason why the wrong answers are wrong. The explanations also provide additional information relevant to the clinical vignette and the basic science topic the question is intended to test. The references accompanying each question are from popular and excellent physiology and internal medicine textbooks. Step 1 is the first of three exams required for medical licensure in the United States. Although it is a test that examines knowledge of the basic sciences, the expectation is that you can apply the basic knowledge in clinical problem-solving. By using clinical vignettes and clinical reference texts, our hope is that your preparation for the USMLE Step 1 (and/or COMLEX-USA Level 1) will also serve to enhance your ability to function competently in the clinical environment. The material in the referenced pages will provide a more expansive description of the subject matter covered by the question.

One effective way to use the *PreTest* is to use it as a review for each topic area. Start by reading the High Yield Facts on a selected topic found at the beginning of the book. The High Yield Facts are not meant to be a complete list of all of the important facts, concepts, and equations necessary for understanding physiology. Those that are included, however, offer a solid foundation and should be included in your review of physiology in preparation for a class test or for the USMLE Step 1. Once you've completed your reading on a topic, answer the questions for that chapter. As you check your answers, be sure to read the explanations, as they are designed to reinforce and expand on the material covered by the questions. If you are still unsure of why the correct answer is correct, you should also read the referenced text pages.

PreTest can also be used as a practice testing session. Set aside two and a half hours, and answer 150 of the questions, writing the answers on a separate sheet of paper. Once you have completed all 150, then you can go back and compare your answers to the ones provided in the book. This exercise will help you assess your level of competence and confidence prior to taking the USMLE Step 1. Whichever way you use *PreTest*, an important part of your review can be found in the explanations.

Good luck on your exam and best wishes for your clinical training. Keep in mind that there is a *PreTest* available for the other basic sciences, as well as in each of the required clinical disciplines, so we encourage you to make the *PreTest* series your review books of choice throughout the preclinical and clinical portions of the medical school curriculum, as well as during your preparation for Step 1 and Step 2 Clinical Knowledge (CK) of the USMLE or for the COMLEX-USA Level 1 and Level 2-Cognitive Evaluation (CE).

Acknowledgments

The contributions of the authors of all previous editions of this book are gratefully acknowledged, especially those of James P. Ryan, PhD and Michael B. Wang, PhD, the authors of the eleventh edition of *Physiology: PreTest™ Self Assessment and Review*. In addition, the input of the four medical student reviewers, Amy Arrington, PhD, Deborah Kem, Brad Miller, and Scott Feitel, was valuable for enhancing the quality of this latest revision. I would like to thank Robyn A. Gandy, PhD, Director of the Academic Enrichment Center at the University of Toledo Health Science Campus, for recommending me as a prospective author of this edition, and Catherine Johnson, Senior Editor, McGraw-Hill Medical Division, for providing me this opportunity. I would also like to thank Catherine Johnson and Marsha Loeb for their editorial assistance and guidance throughout the preparation of this text, and Madhu Bhardwaj, Project Manager, International Typesetting and Composition, for her assistance with the typesetting and revisions. I am indebted to all of the medical students at the University of Toledo (formerly the Medical College of Ohio) over the past thirty years for providing me with the incentive, challenge, and gratification to strive for excellence in the teaching of clinically relevant physiology, and to my colleagues on the faculty and in the administration for their support and encouragement throughout my career.

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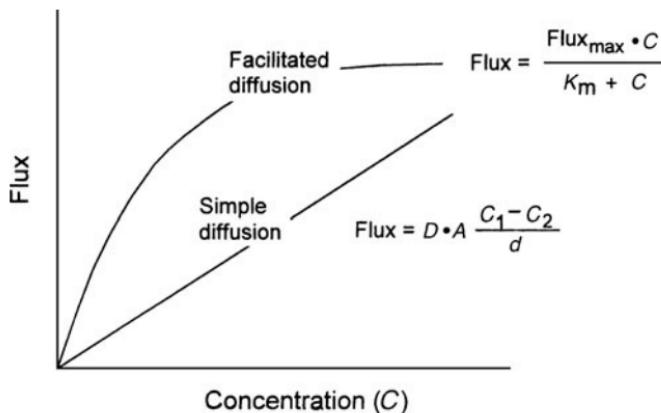
High-Yield Facts in Physiology

GENERAL PRINCIPLES: CELLULAR PHYSIOLOGY

(Ganong, pp 1–49. Ryan and Wang, pp 1–2, 7. Widmaier *et al.*, pp 47–61, 107–132, 133–150.)

Membrane Transport Mechanisms

The transport of ions, gases, nutrients, and waste products through biological membranes is essential for many cellular processes. *Diffusion* is defined as the net flux of a substance from an area of higher concentration to areas of lower concentration, which does not require energy input. Simple diffusion of a substance, as described by the Fick equation, is directly proportional to (1) the diffusion coefficient (D) of the substance, which is related to the size of the molecule, its solubility, and the viscosity of the medium, (2) the area available for diffusion, and (3) the concentration gradient of the substance. The rate of simple diffusion is inversely proportional to the distance for diffusion. *Facilitated diffusion*, in which carrier proteins move substances in the direction of their electrochemical gradients



2 Physiology

(e.g., glucose transport in adipose tissue and muscle), exhibits saturation kinetics described by the Michaelis-Menton equation, where $Flux_{max}$ is the maximal rate of transport, C is the concentration of the transported substance, and K_m is the concentration required for half-maximal transport of the substance.

Active transport is a carrier-mediated transport process that requires energy to transport substances against their electrochemical gradients. The energy for primary active transport, such as for the Na^+-K^+ pump, is derived from the hydrolysis of ATP. Secondary active transport processes, such as the glucose transporter, use the energy from the Na^+ electrochemical gradient.

Osmosis is defined as the flow of water across a semipermeable membrane from a compartment in which the solute concentration is lower to a compartment in which the solute concentration is higher.

The flow of water through membranes by osmosis is described by the osmotic flow equation,

$$\text{Flow} = \sigma \times L \times (\pi_1 - \pi_2)$$

Where σ = reflection coefficient

L = hydraulic conductivity

π = osmotic pressure

The reflection coefficient (σ) is an index of the membrane's permeability to the solute and varies between 0 and 1. Particles that are impermeable to the membrane have a reflection coefficient of 1. Particles that are freely permeable to the membrane have a reflection coefficient of 0.

The *osmotic pressure* (π) of a solution is the pressure necessary to prevent solute migration. The osmotic pressure (in units of mmHg) is calculated with the van't Hoff equation:

$$\pi = R T (\varphi i c)$$

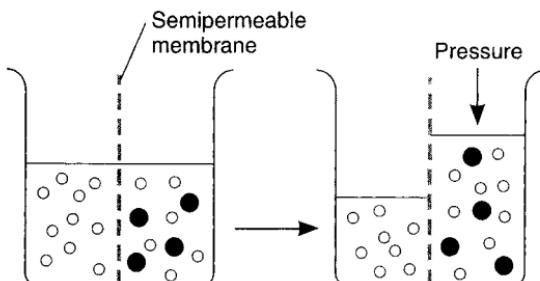
where R is the ideal gas constant, T is absolute temperature, φ is the osmotic coefficient, i is the number of ions formed by the dissociation of a molecule, c is the molar concentration of solute, and the term ($\varphi i c$) is thus the osmolarity of the solution.

The value of i is 1 for nonionic substances such as glucose and urea, 2 for substances such as HCl , NaCl , KCl , NH_4Cl , NaHCO_3 , and MgSO_4 , and 3 for compounds such as CaCl_2 and MgCl_2 . A value of 1 is often used as an approximate value of φ . Thus, the osmolarity and osmotic pressure of 1 M CaCl_2 > 1 M NaCl > 1 M glucose. Similarly, a 1 M solution of glucose

	Diffusion			Mediated Transport	
	Through Lipid Bilayer	Through Protein Channel	Facilitated Diffusion	Primary Active Transport	Secondary Active Transport
Direction of net flux	High to low concentration	High to low concentration	High to low concentration	Low to high concentration	Low to high concentration
Equilibrium or steady state	$C_0 = C_i$	$C_0 = C_i^*$	$C_0 = C_i$	$C_0 \neq C_i$	$C_0 \neq C_i$
Use of integral membrane protein	No	Yes	Yes	Yes	Yes
Maximal flux at high concentration (saturation)	No	No	Yes	Yes	Yes
Chemical specificity	No	Yes	Yes	Yes	Yes
Use of energy and source	No	NO	No	Yes: ATP	Yes: ion gradient (often Na^+)
Typical molecules using pathway	Nonpolar: $\text{O}_2, \text{CO}_2, \text{fatty acids}$	Ions: $\text{Na}^+, \text{K}^+, \text{Ca}^{2+}$	Polar: glucose	Ions: $\text{Na}^+, \text{K}^+, \text{Ca}^{2+}, \text{H}^+$	Polar: $\text{amino acids, glucose, some ions}$

*In the presence of a membrane potential, the intracellular and extracellular ion concentrations will not be equal at equilibrium.

Reproduced, with permission, from Widmaier EP et al. *Vander's Human Physiology: The Mechanisms of Body Function*, 10th ed. New York: McGraw-Hill, 2006:120.



(Reproduced, with permission, from Ganong, WF. Review of Medical Physiology, 22nd ed. New York: McGraw-Hill, 2005:5.)

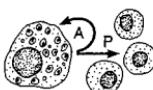
has approximately the same osmolarity and osmotic pressure as 0.5 M NaHCO₃ or 0.33 M MgCl₂.

One osmol is equal to 1 mol of solute particles. The osmolarity is the number of osmoles per liter of solution, for example, plasma, whereas the osmolality is the number of osmoles per kilogram of solvent. Therefore, the osmolarity of a solution is affected by the volume of the various solutes in a solution and the temperature but osmolality is not. Osmotically active substances in the body are dissolved in water, and the density of water is one, so osmolal concentrations can be expressed as osmoles per liter of water.

The plasma membranes of most cells are relatively impermeable to many of the solutes of the extracellular fluid but are highly permeable to water. Thus the movement of water by osmosis leads to swelling or shrinking of cells. The term tonicity is used to describe the osmolality of a solution relative to plasma. Solutions that have the same osmolality as plasma (~300 mOsm/L) are isotonic; those with greater osmolality are hypertonic; and those with lesser osmolality are hypotonic. Because of the predominant role of Na⁺, glucose, and urea (blood urea nitrogen, BUN), the plasma osmolality can be approximated as:

$$\text{Osmolality} = 2 [\text{Na}^+] + 0.055 [\text{Glucose}] = 0.36 [\text{BUN}] \\ (\text{mOsm/L}) \quad (\text{mEq/L}) \quad (\text{mg/dL}) \quad (\text{mg/dL})$$

Cells shrink when placed in hypertonic solutions and swell when placed in hypotonic solutions. Isotonic solutions are commonly used for intravenous fluid administration and as drug diluents because administration of an isotonic solution does not produce changes in cell volume. Isotonic saline has a concentration of 154 mM, containing 308 mM of

	GAP JUNCTIONS	SYNAPTIC	PARACRINE AND AUTOCRINE	ENDOCRINE
				
Message transmission	Directly from cell to cell	Across synaptic cleft	By diffusion in interstitial fluid	By circulating body fluids
Local or general	Local	Local	Locally diffuse	General
Specificity depends on	Anatomic location	Anatomic location and receptors	Receptors	Receptors

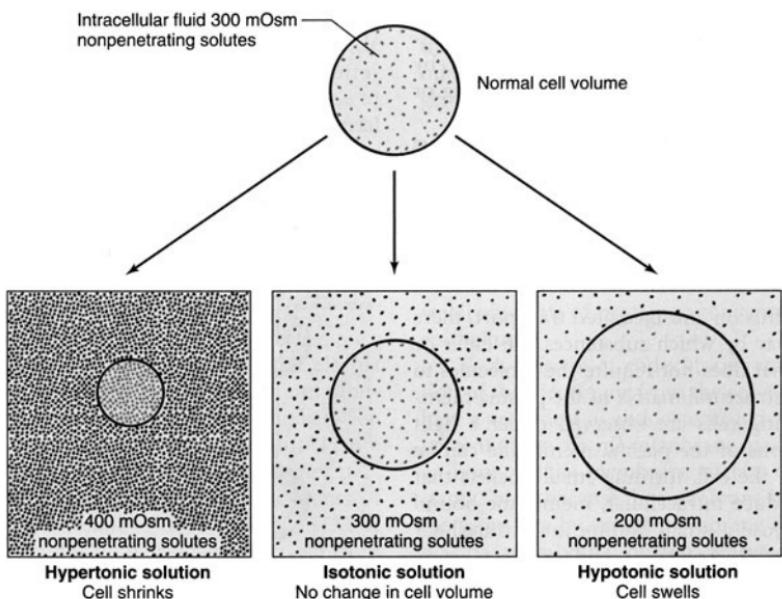
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OSMOLARITY AND TONICITY OF SOLUTIONS

Isotonic	A solution that does not cause a change in cell volume; one that contains 300 mOsmol/L of nonpenetrating solutes, regardless of the concentration of membrane-penetrating solutes present
Hypertonic	A solution that causes cells to shrink; one that contains greater than 300 mOsmol/L of nonpenetrating solutes, regardless of the concentration of membrane-penetrating solutes present
Hypotonic	A solution that causes cells to swell; one that contains less than 300 mOsm/L of nonpenetrating solutes, regardless of the concentration of membrane-penetrating solutes present
Isoosmotic	A solution containing 300 mOsm/L of solute, regardless of its composition of membrane-penetrating and nonpenetrating solutes
Hyperosmotic	A solution containing greater than 300 mOsm/L of solutes, regardless of its composition of membrane-penetrating and nonpenetrating solutes
Hypoosmotic	A solution containing less than 300 mOsm/L of solutes, regardless of its composition of membrane-penetrating and nonpenetrating solutes

*These terms are defined using an intracellular osmolarity of 300 mOsm, which is typical for human cells but not an absolute fixed number.

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osmotically active particles. An isotonic solution of glucose is a 5% dextrose solution. The following equation is used to calculate the steady state volume of the cell:

$$\pi_{\text{initial}} \times V_{\text{initial}} = \pi_{\text{final}} \times V_{\text{final}}$$

Intercellular Connections and Communication

Two types of connections form between the cells comprising a tissue. One type of junction serves to fasten the cells to one another and to surrounding tissues. Examples of fastening junctions that lend strength and stability to tissues include tight junctions or zona occludens, desmosomes, zona adherins, hemidesmosomes, and focal adhesions. The other type of connection between cells serves the purpose of transferring ions and other molecules from cell to cell. This type of junction is called a gap junction, though transport of ions across epithelial cells can occur via tight junctions.

In addition to the direct cell-to-cell communication via gap junctions, cells communicate with each other via chemical messengers in the extracellular

fluid, by a number of processes, including neural, endocrine, and paracrine communication.

In the case of intercellular communication mediated by chemical messengers in the extracellular fluid, there are generally “first messengers,” which constitute the extracellular ligands that bind to receptors in the cell membrane, and “second messengers,” which are the intracellular mediators that bring about the changes in cell function produced by binding of the “first messenger.” The principal mechanisms by which chemical messengers exert their intracellular effects are summarized in the table below.

Mechanism	Examples
Open or close ion channels in cell membrane	Acetylcholine on nicotinic cholinergic receptor; norepinephrine on K ⁺ channel in the heart
Act via cytoplasmic or nuclear receptors to increase transcription of selected mRNAs	Thyroid hormones, retinoic acid, steroid hormones
Activate phospholipase C with intracellular production of DAG, IP ₃ , and other inositol phosphates	Angiotensin II, norepinephrine via α ₁ -adrenergic receptor, vasopressin via V ₁ receptor
Activate or inhibit adenylyl cyclase, causing increased or decreased intracellular production of cAMP	Norepinephrine via β ₁ -adrenergic receptor (increased cAMP); norepinephrine via α ₂ -adrenergic receptor (decreased cAMP)
Increase cGMP in cell	ANP; NO (EDRF)
Increase tyrosine kinase activity of cytoplasmic portions of transmembrane receptors	Insulin, EGF, PDGF, M-CSF
Increase serine or threonine kinase activity	TGFβ, MAPKs

*For abbreviations, see Appendix.

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GENERAL PRINCIPLES: MULTISYSTEM PROCESSES

(Ganong, pp 1–4, 240–247, 713–720, 729–738. Levitzky, pp 163–187. Ryan and Wang, pp 24–26. Widmaier et al., pp 5–6, 119–124, 541–569, 633–649.)

Body Fluid Compartments

Sixty percent of the body mass is water. Of this water, one-third (20% of body mass) is *extracellular* and two-thirds (40% of body mass) is *intracellular*. The extracellular water is further divided into *interstitial* water (80% of extracellular fluid, or 15% of body mass) and *plasma* water (20% of extracellular fluid, or 5% of body mass). The percentage of water in the body is a function of body fat. The greater the percentage of body fat, the lower the percentage of body water. About three-fourths of the lean body mass (mass excluding fat) is water. The distribution of extracellular and intracellular water is a function of the extracellular osmolality. If the osmolality of the extracellular fluid is above normal, the proportion of water in the extracellular fluid, in comparison to that in the intracellular fluid, increases; hypotonicity of the extracellular fluid decreases the proportion of water in the extracellular fluid.

The composition of the extracellular and intracellular fluids is shown in the table below. The distribution of substances between the intracellular and extracellular fluid is unequal due to the membrane potential and the presence of various transporters and ion channels in the plasma membrane.

	Extracellular Concentration, mM	Intracellular Concentration,* mM
Na ⁺	150	15
K ⁺	5	150
Ca ²⁺	1	0.0001
Mg ²⁺	1.5	12
Cl ⁻	110	7
HCO ₃ ⁻	24	10
P _i	2	40
Amino acids	2	8
Glucose	5.6	1
ATP	0	4
Protein	0.2	4

*The intracellular concentrations differ slightly from one tissue to another, but the concentrations shown above are typical of most cells. For Ca²⁺, values represent free concentrations. Total calcium levels, including the portion sequestered by proteins or in organelles, approach 2.5 mM (extracellular) and 1.5 mM (intracellular).

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Fluid and Electrolyte Balance and Disorders

The extracellular volume is controlled by the NaCl content of the extracellular fluid. NaCl content is controlled by aldosterone and atrial natriuretic peptide (ANP). Extracellular volume is monitored by low-pressure baroreceptors within the thoracic venous vessels and the atria and by pressure receptors within the afferent arteriole of the kidneys. ANP release is controlled directly by stretch receptors within the right atrium.

Aldosterone secretion is controlled by the renin-angiotensin system. Renin is released from the juxtaglomerular cells (JG cells) of the kidney in response to (1) decreased perfusion pressure within the afferent arteriole, (2) sympathetic stimulation of the JG cells, and (3) decreased Cl⁻ concentration in fluid bathing the macula densa. Renin catalyzes the conversion of angiotensinogen to angiotensin I. Angiotensin I is converted to angiotensin II (AII) by angiotensin-converting enzyme (ACE) located within the lung. AII stimulates aldosterone secretion from the adrenal cortex gland. Extracellular K⁺ is controlled by aldosterone. Increases in extracellular K⁺ stimulate the secretion of aldosterone, causing K⁺ secretion to increase. K⁺ transport into cells is increased by epinephrine and insulin.

The extracellular osmolarity is controlled by antidiuretic hormone (ADH), also known as vasopressin. Increases in osmolarity stimulate the release of ADH from the posterior pituitary gland. ADH returns osmolarity toward normal by decreasing the amount of water excreted by the kidney. When osmolarity is decreased, ADH release is decreased and osmolarity is returned toward normal by increased water excretion. ADH is also secreted in response to low blood pressure. Under these conditions, reabsorption of water by the kidneys can make the extracellular fluid hypotonic.

Acid-Base Balance and Disorders

Each day, approximately 15,000 mmol of volatile acid (CO₂) and 50 to 100 mEq of fixed acid (hydrochloric acid, lactic acid, phosphoric acid, sulfuric acid, etc.) are produced by metabolism. The pH of the extracellular fluid is maintained by buffering the acid as it is formed and excreting the acid over time. The kidneys require approximately 24 h to excrete the fixed acids. CO₂ is rapidly excreted by the lungs.

When CO₂ is added to water, it forms carbonic acid (H₂CO₃), a reaction that is catalyzed by the enzyme carbonic anhydrase (CA). Once formed, carbonic acid rapidly dissociates into H⁺ and HCO₃⁻:



The *pH* of plasma is calculated with the Henderson-Hasselbalch equation:

$$\begin{aligned}\text{pH} &= 6.1 + \log [\text{HCO}_3^-]/[\text{Dissolved CO}_2] \\ &= 6.1 + \log [\text{HCO}_3^-]/(\text{PCO}_2 \text{ in mmHg} \times 0.03 \text{ mEq/L/mmHg})\end{aligned}$$

Arterial PCO_2 is normally maintained at 40 mmHg by the lungs and plasma HCO_3^- concentration is normally maintained at 24 mEq/L by the kidneys. Thus, normally,

$$\text{Arterial pH} = 6.1 + \log 24/(0.03 \times 40) = 6.1 + \log 20/1 = 7.40.$$

The normal ratio of $[\text{HCO}_3^-]/[\text{Dissolved CO}_2] = 20/1$. The four primary acid-base disorders result from abnormalities that alter the normal 20/1 ratio of $[\text{HCO}_3^-]/[\text{Dissolved CO}_2]$. Compensation for the acid-base disorders involves an attempt by the body to minimize the change in pH caused by the primary disorder by restoring the ratio of $[\text{HCO}_3^-]/[\text{Dissolved CO}_2]$ toward its normal value. In order to do so, if the primary disorder is a metabolic acid-base disturbance causing a change in the $[\text{HCO}_3^-]$, then the appropriate respiratory compensatory response will change the Paco_2 , and thus the $[\text{dissolved CO}_2]$ in the same direction. If the primary disorder is respiratory in origin, causing a change in the denominator of the ratio, then there will be renal compensation geared toward changing the $[\text{HCO}_3^-]$ in the same direction as the primary change in Paco_2 .

Characteristics of Primary Acid-Base Disorders

Disorder	pH	Primary Disturbance	Compensatory Response
Respiratory	↓	↑ Paco_2 (alveolar hypoventilation)	↑ $[\text{HCO}_3^-]$ (↑ renal H^+ excretion)
Acidosis			
Respiratory	↑	↓ Paco_2 (alveolar hyperventilation)	↓ $[\text{HCO}_3^-]$ (↓ renal H^+ excretion)
Alkalosis			
Metabolic	↑	↑ $[\text{HCO}_3^-]$	↑ Paco_2
Alkalosis			
Metabolic	↓	↓ $[\text{HCO}_3^-]$ (gain of HCO_3^- ; loss of H^+)	↓ Paco_2 (alveolar hypoventilation)
Acidosis			
		(gain of H^+ ; loss of HCO_3^-)	(alveolar hyperventilation)

Causes of Respiratory Acidosis (Alveolar Hypoventilation)

- I. Airway obstruction
 - A. Chronic obstructive lung disease
 - B. Upper airway obstruction

- II. Chest wall restriction
 - A. Kyphoscoliosis
 - B. Pickwickian syndrome
- III. Respiratory center depression
 - A. Anesthetics
 - B. Sedatives
 - C. Opiates
 - D. Brain injury or disease
 - E. Severe hypercapnia, hypoxia
- IV. Neuromuscular disorders
 - A. Spinal cord injury
 - B. Phrenic nerve injury
 - C. Poliomyelitis
 - D. Myasthenia Gravis
 - E. Guillain-Barré syndrome
 - F. Administration of curare-like drugs
 - G. Respiratory muscle diseases

Causes of Respiratory Alkalosis

- I. Respiratory center stimulation
 - A. CNS
 - 1. Anxiety
 - 2. Hyperventilation syndrome
 - 3. Inflammation (encephalitis, meningitis)
 - 4. Stroke
 - 5. Tumors
 - B. Drugs or hormones
 - 1. Salicylates
 - 2. Progesterone
 - 3. Hyperthyroidism
 - C. Reflex
 - 1. Hypoxemia
 - 2. High altitude
 - 3. Metabolic acidosis
 - 4. Sepsis, fever

Causes of Respiratory Alkalosis (Continued)

5. Pulmonary embolism
 6. Pulmonary edema
 7. Congestive heart failure
 8. Asthma
- II. Iatrogenic mechanical overventilation
- III. Liver failure

Causes of Metabolic Acidosis

- I. Loss of hydrogen ions
 - A. Vomiting
 - B. Nasogastric suction
 - C. Gastric fistulas
 - D. Diuretic therapy
 - E. Severe magnesium or potassium deficiency
 - F. Overproduction of mineralocorticoids
(Cushing's syndrome; Primary hyperaldosteronism; renal artery stenosis)
 - G. Ingestion of mineralocorticoids
(Licorice ingestion; chewing tobacco)
 - H. Inherited disorders
(Bartter's syndrome; Liddle's syndrome; Gitelman's syndrome)
- II. Ingestion or administration of excess bicarbonate or other bases
 - A. Intravenous bicarbonate
 - B. Ingestion of bicarbonate or other bases (e.g.; antacids)

Differential Diagnosis of Metabolic Acidosis

Normal anion gap (hyperchloremia)	Increased anion gap (normochloremic)
I. Gastrointestinal loss of HCO_3^-	I. Lactic Acidosis
<ol style="list-style-type: none">A. DiarrheaB. Small bowel or pancreatic drainage or fistulaC. Ureterosigmoidostomy, jejunal loop, ileal loop conduitD. Drugs	<ol style="list-style-type: none">II. Ketoacidosis<ol style="list-style-type: none">A. DiabeticB. StarvationC. AlcoholicIII. Ingestion of toxic substances<ol style="list-style-type: none">A. Salicylate overdose

- II. Renal Loss of HCO_3^-
 - A. Carbonic anhydrase inhibitors
 - B. Renal tubular acidosis (RTA)
- III. Miscellaneous
 - A. Dilutional acidosis
 - B. Hyperalimentation
- B. Paraldehyde poisoning
- C. Methyl alcohol ingestion
- D. Ethylene glycol ingestion
- IV. Failure of acid excretion
 - A. Acute renal failure
 - B. Chronic renal failure

PHYSIOLOGY OF THE HEMATOPOIETIC AND LYMPHORETICULAR SYSTEMS

(Ganong, pp 515–546, 666–670. Levitzky, pp 142–162. Widmaier *et al.*, pp 459–476, 500–507.)

Oxygen Transport in the Blood

O_2 is transported in the blood in two transport forms: (1) dissolved in plasma and (2) chemically combined with hemoglobin. The concentration of a gas dissolved in a liquid is proportional to its partial pressure and its solubility in the liquid. The solubility coefficient of oxygen in plasma at body temperature and pressure is 0.003 mL O_2 /100 mL blood/mm Hg. The concentration of O_2 combined with hemoglobin is determined by the equation:

$$\text{HbO}_2 \text{ (mL/dL blood)} = [\text{Hb}] \text{ (g/dL blood)} \times 1.34 \text{ mL O}_2/\text{gm Hb} \times \% \text{ O}_2 \text{ saturation}$$

The total O_2 content is the sum of the dissolved oxygen and the oxyhemoglobin content. Over 98% of the oxygen delivered to the blood is bound to hemoglobin (HbO_2), an amount 65 times greater than the amount dissolved in the arterial blood. Nonetheless, the dissolved oxygen is critical because it determines the amount of oxygen that combines with hemoglobin, as depicted by the oxyhemoglobin dissociation curve.

	Dissolved O_2	HbO₂	Total
Arterial blood (100 mmHg PO_2 ; 97% sat; 15 g/dL Hb)	0.3 mL O_2/dL	19.5 mL O_2/dL	19.8 mL O_2/dL
Venous blood (40 mmHg PO_2 ; 75% sat; 15 g/dL Hb)	0.12 mL O_2/dL	15.1 mL O_2/dL	15.2 mL O_2/dL

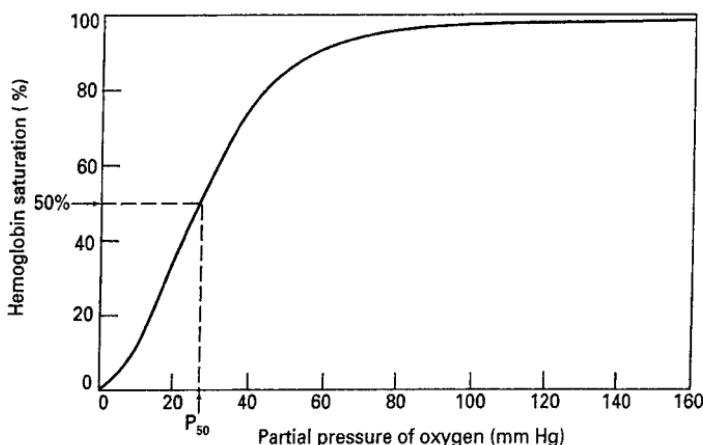
Oxygen delivery is the product of the cardiac output and the arterial oxygen content. Oxygen extraction is the difference between the arterial and venous oxygen contents ($a-v O_2$). According to the Fick equation, cardiac output (CO) can be calculated as the ratio of the oxygen consumption ($\dot{V}O_2$) and the oxygen extraction.

$$\text{Cardiac Output (CO)} = \dot{V}O_2 / a-v O_2$$

Reaction of Hemoglobin and Oxygen

Hemoglobin is a protein with four subunits, each of which has a heme moiety attached to a polypeptide chain (HbA: two α and two β chains). Heme is a complex consisting of a porphyrin and one atom of a ferrous iron. Each of the four iron atoms can bind reversibly one molecule of O_2 ($Hb_4 + O_2 = Hb_4O_2$).

The plot of the four reversible reactions of hemoglobin and oxygen is represented by the *oxyhemoglobin dissociation curve*, which shows the relationship between the P_{O_2} of the plasma and the percent of hemoglobin saturated with oxygen. The oxyhemoglobin dissociation curve has a characteristic sigmoidal shape reflecting the increased affinity of hemoglobin for oxygen as each additional molecule of oxygen binds to the four subunits of hemoglobin (cooperative binding). Conversely, dissociation of oxygen from hemoglobin facilitates additional dissociation. As a result, the slope of the curve decreases as one goes from low to high P_{O_2} values, with a plateau



(Reproduced, with permission, from Levitzky, MG. Pulmonary Physiology, 6th ed. New York: McGraw-Hill, 2003:146.)

reached when the PO_2 is above ~80 mmHg. This is important physiologically because the S-shape facilitates oxygen loading in the pulmonary capillaries, and oxygen unloading at the tissues. Also, there is an important physiological safety factor because a patient with a relatively low arterial PO_2 still has a relatively high O_2 saturation (e.g., 90% SO_2 at 60 mm Hg PO_2).

A rightward shift of the oxyhemoglobin dissociation curve is indicative of a decrease in HbO_2 affinity with less oxygen uptake at the pulmonary capillaries but greater release of oxygen to the tissues. The P_{50} , that is, the PO_2 at which hemoglobin is 50% saturated with oxygen, is increased above the normal value of ~27 mmHg. Factors that shift the oxyhemoglobin dissociation curve to the right include hyperthermia, increased PCO_2 or decreased pH (known as the Bohr effect), and increased [2,3-bisphosphoglycerate (2,3-BPG)] in erythrocytes.

A leftward shift of the oxyhemoglobin dissociation curve denotes a higher-than-normal HbO_2 affinity with greater oxygen uptake at the pulmonary capillaries delivery but less oxygen released at the tissue level. The P_{50} is lower than normal when affinity is increased. Factors that shift the oxyhemoglobin dissociation curve to the left include hypothermia, alkalosis or decreased PCO_2 (Bohr effect), and decreased erythrocyte 2,3-BPG (also known as DPG) concentration. The Hb-O_2 curve for fetal Hb (HbF) is shifted to the left of that for normal adult hemoglobin (HbA) because there is poor binding of 2,3-BPG to the γ chains in HbF compared to the β chains in HbA . The presence of carbon monoxide in the blood increases the affinity of hemoglobin for any oxygen that is already bound, thereby shifting the curve to the left.

There are hundreds of hemoglobin variants that have been described, most of which result from single point mutations. Hb variants are often classified as high affinity versus low affinity based on their P_{50} values.

CO₂ Transport in the Blood

Like oxygen, carbon dioxide can be physically dissolved in the plasma or chemically combined with hemoglobin (carbaminohemoglobin). Only ~5% of total CO_2 is dissolved, and, in contrast to oxygen combined to hemoglobin, carbaminohemoglobin only constitutes ~10% of total CO_2 in the blood. The majority of CO_2 in the blood (80–90%) is transported as bicarbonate, a product of the dissociation of carbonic acid from the CO_2 hydrolysis catalyzed by carbonic anhydrase, as discussed earlier.

There is no carbonic anhydrase in the plasma, so the CO_2 hydration equation proceeds very slowly in plasma. In contrast, the presence of carbonic anhydrase in red blood cells results in most HCO_3^- being formed within erythrocytes. However, the HCO_3^- then diffuses down its concentration

gradient from RBCs into the plasma in exchange for Cl^- , a process called the chloride shift, which is mediated by Band 3, a major membrane protein. Because of the chloride shift, the Cl^- content of the red cells in the venous blood is greater than that in the arterial RBCs.

The total CO_2 content in blood ($\sim 50 \text{ mL/dL}$) is much greater than total arterial O_2 content ($\sim 20 \text{ mL/dL}$).

NEUROPHYSIOLOGY

(*Ganong, pp 6–8, 51–64, 85–277. Ryan and Wang, pp 2–4. Widmaier et al., pp 151–277, 323–342.*)

Ionic Equilibria and Membrane Potentials

All cells have membrane potentials. The magnitude of the membrane potential is determined by the membrane permeability and the concentration gradient of the ions that are permeable to the membrane.

In the resting state, the membrane is primarily permeable to K^+ and, therefore, the resting membrane potential is close to the equilibrium potential for K^+ .

The equilibrium potential (E) is calculated with Nernst's equation:

$$E_{\text{ion}} = 61.5 \log C_{\text{out}}/C_{\text{in}}$$

The equilibrium potential for K^+ is -90 mv , for Na^+ is $+60 \text{ mv}$, and for Cl^- is -70 mv .

The resting membrane potential is calculated with the Goldman equation:

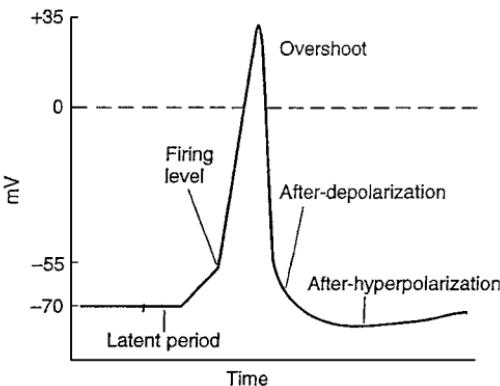
$$E_M = -61.5 \times \log [(P_{\text{Na}} \times [\text{Na}_{\text{in}}]) + (P_K \times [\text{K}_{\text{in}}]) / (P_{\text{Na}} \times [\text{Na}_{\text{out}}] + (P_K \times [\text{K}_{\text{out}}]))]$$

Because neither E_K nor E_{Na} is at the E_M of -70 mv , one would expect the cell to gradually gain Na^+ and lose K^+ if only passive electrical and chemical forces were acting on the membrane. In other words, there is more K^+ and less Na^+ in the neurons than can be accounted for by electrochemical gradients. This condition is maintained by the electrogenic $\text{Na}^+–\text{K}^+$ pump, that is, $\text{Na}^+–\text{K}^+$ -ATPase, which pumps three Na^+ out of the cell for every two K^+ it pumps into the cell for each molecule of ATP hydrolyzed.

Action Potential

If an axon is stimulated and the current has sufficient intensity, an action potential will be produced.

The *action potential* begins with an initial depolarization of about 15 mV. Once the impulse reaches threshold intensity at about -55 mV, a full action potential is produced as characterized by a rapid upstroke that overshoots the zero potential to approximately +35 mV. After the *overshoot*, the potential reverses and rapidly repolarizes toward the resting level. The sharp rise and fall constitute the *spike potential* of the neuron, which only lasts a millisecond or so. After repolarization is ~70% complete, the rate of repolarization decreases for about 4 ms (called *after-depolarization*) and is followed by an overshoot of the resting potential, called the *after-repolarization*, which is only 1-2 mV, but lasts about 40 ms. The action potential is said to be “*all or none*” because it will not occur if a stimulus is subthreshold, and if a stimulus is at or above threshold, the action potential occurs with a constant amplitude and forms regardless of the strength of the stimulus.



Action potentials are produced by ionic fluxes controlled by voltage-gated ion channels. Depolarization is produced by activation of voltage-gated Na^+ channels, which increases sodium conductance, that is, membrane permeability to Na^+ . The action potential moves toward the equilibrium potential for Na^+ (+60 mV), but does not reach it, primarily because the increase in sodium conductance is brief. Repolarization occurs because (1) the Na^+ channels enter a closed or inactivated state before returning to the resting state, and (2) voltage-gated K^+ channels open, which increases the membrane conductance to K^+ , resulting in K^+ efflux from the cell. The opening of the K^+ channels is slower and more prolonged than the opening of Na^+ channels, and the slow return of the K^+ channels to the closed state accounts for the after-hyperpolarization, as the membrane approaches the equilibrium potential of K^+ .

Functions of Nerves and the Nervous System

Neurons generally have four important functional areas: (1) a receptor or dendritic zone, where multiple local potentials generated by synaptic connections are integrated; (2) a site where propagated action potentials are generated, which is close to the receptor zone, and includes the initial segment in spinal motor neurons and the initial node of Ranvier in cutaneous sensory neurons; (3) an axonal process that transmits propagated impulses to nerve endings at various rates depending on whether the axons are myelinated or unmyelinated; and (4) the nerve endings, where action potentials cause the secretion of synaptic transmitters.

Synaptic transmission is used to transmit information from one cell to another. The synaptic transmitter, released from the presynaptic cell by exocytosis, diffuses across a synaptic cleft and binds to a receptor on the postsynaptic cell. The effect produced on the postsynaptic cell depends on both the synaptic transmitter and the receptor. Acetylcholine, which binds to the end plate of skeletal muscle cells, and glutamate and γ -amino butyric acid (GABA), which bind to the postsynaptic membranes of many central nervous system membranes, open ion selective channels. Norepinephrine and acetylcholine, which bind to the postsynaptic membranes of smooth muscle cells, produce their effect by activating a G protein which, in turn, activates an enzyme-mediated response.

Nerve fiber types are classified into A, B, and C groups based on their various speeds of conduction and fiber diameter (see table).

A numerical classification is often used for sensory neurons, as shown in the table.

- Sensory receptors (touch, pain, temperature, smell, taste, sound, and sight) are activated by environmental stimuli. The stimulus produces a receptor potential; the magnitude of the receptor potential is proportional to the stimulus. The receptor potential produces a train of action potentials. Tonic receptors fire as long as the stimulus is present and encode intensity. Phasic receptors slow down or stop firing during the presentation of the stimulus and encode velocity.
- The vestibular system provides information about the position and movement of the head, coordinates head and eye movements, and initiates reflexes that keep the head and body erect. Lesions to the vestibular system result in loss of balance and nystagmus.
- The cortex is responsible for cognition, language, emotions, and motivation.

Fiber Type	Function	Fiber Diameter (μm)	Conduction Velocity (m/s)	Spike Duration (ms)	Absolute Refractory Period (ms)
A α	Proprioception; somatic motor	12–20	70–120		
β	Touch, pressure, motor	5–12	30–70	0.4–0.5	0.4–1
γ	Motor to muscle spindles	3–6	15–30		
δ	Pain, cold, touch	2–5	12–30		
B	Preganglionic autonomic	<3	3–15	1.2	1.2
C					
Dorsal root	Pain, temperature, some mechano-reception, reflex responses	0.4–1.2	0.5–2	2	2
Sympathetic	Postganglionic sympathetics	0.3–1.3	0.7–2.3	2	2
A and B fibers are myelinated; C fibers are unmyelinated.					

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Number	Origin	Fiber Type
Ia	Muscle spindle, annulo-spiral ending	A α
Ib	Golgi tendon organ	A α
II	Muscle spindle, flower-spray ending; touch, pressure	A β
III	Pain and cold receptors; some touch receptors	A δ
IV	Pain, temperature, and other receptors	dorsal root C

Reproduced, with permission, from Ganong, WF. *Review of Medical Physiology*, 22nd ed. New York: McGraw-Hill, 2005:61.

- Movement is initiated by the motor cortex. Motor commands reach the spinal cord through the pyramidal system (corticospinal tract) and the nonpyramidal system (corticoreticular and corticovestibular pathways). Lesions to the nonpyramidal system cause spasticity.
- The basal ganglia and cerebellum assist in the control of movement. Lesions to the basal ganglia produce paucity of movement or uncontrolled movements.
- Lesions to the cerebellum produce uncoordinated movements (see table below).

Disease	Possible Cause	Clinical Manifestations
Tardive dyskinesia	Dopamine antagonists used to treat psychotic diseases	Rapid, irregular movements (chorea) or slow, writhing movements (athetosis) of the face, mouth, and limbs
Parkinson's disease	Degeneration of the substantia nigra dopaminergic neurons	Tremor at rest, bradykinesia, cogwheel rigidity
Huntington's disease	Degeneration of GABAergic neurons with the striatum	Chorea, ataxia, dementia
Hemiballism	Lesion of the contralateral subthalamic nucleus	Sudden flinging movements of the proximal limbs

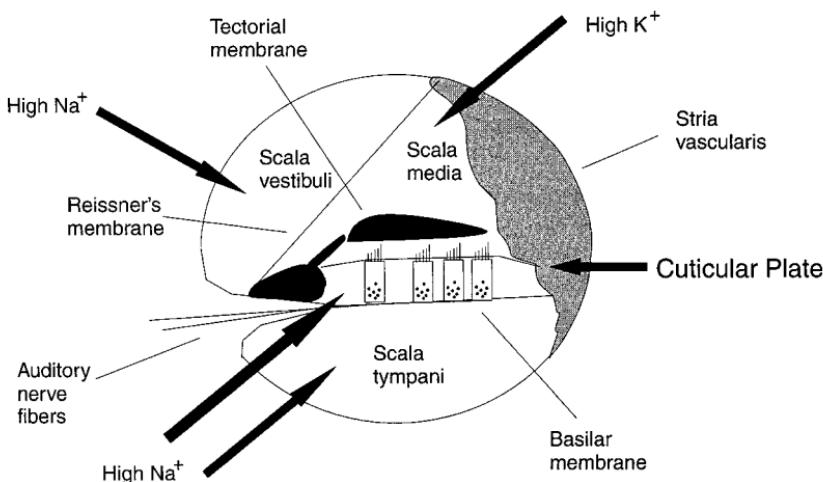
Special Senses

Hearing

Sounds are detected by the hair cells within the organ of Corti of the inner ear. The organ of Corti consists of the hair cells and an overlying membrane called the tectorial membrane to which the cilia of the hair cells are attached. Sounds entering the outer ear cause the tympanic membrane to vibrate. Vibration of the tympanic membrane causes the middle ear bones (malleus, incus, and stapes) to vibrate, which in turn causes the fluid within the inner ear to vibrate.

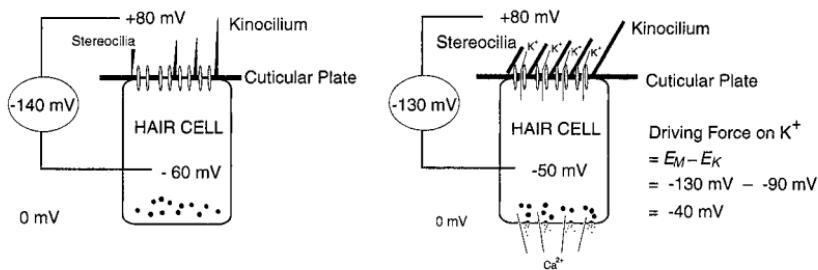
The inner ear is divided into three chambers (scala vestibuli, scala media, and scala tympani). The scala vestibuli is separated from the scala media by

Reissner's membrane; the scala media, and the scala tympani are separated by the basilar membrane. The stapes is attached to the membrane of the oval window, which separates the middle ear from the scala vestibuli. The scala tympani is separated from the middle ear by the round window. The organ of Corti sits on the basilar membrane. The fluid within the scala vestibuli and scala tympani (perilymph) is similar to interstitial fluid; the fluid within the scala media (endolymph) resembles intracellular fluid, in that it contains a high concentration of K^+ .



Vibration of the stapes causes the fluid within the scala tympani to vibrate, which in turn causes the basilar membrane to vibrate. Vibration of the basilar membrane causes the cilia to bend back and forth. Bending the stereocilia toward the kinocilium causes K^+ channels on the hair cells to open; bending the stereocilia away from kinocilium causes K^+ channels to close. Auditory hair cells are unusual because they are depolarized by the flow of K^+ into the cell. K^+ can flow into the hair cells because the endolymph surrounding the apical portions of the hair cells contains a high K^+ concentration.

The basilar membrane is most stiff at the base of the cochlea (near the middle ear) and most compliant at the apex of the cochlea. High-frequency sounds cause a greater vibration of the stiff portion of the cochlea, and, therefore, the hair cells located near the base of the cochlea transmit



information about high-frequency sounds to the auditory cortex. Similarly, low-frequency sounds are transmitted to the auditory cortex by the hair cells near the base of the cochlea, which are located on the more compliant portions of the basilar membrane.

Sight

Light is detected by the rods and cones contained in the retina of the eye. The retina contains five types of neurons: photoreceptors (rods and cones), bipolar cells, ganglion cells, horizontal cells, and amacrine cells. Light rays from distant objects are normally focused on the photoreceptors by the cornea and the relaxed lens. When objects are brought closer to the eye, they are kept focused on the retina by the accommodation reflex, which causes the refractive power of the lens to increase. The photoreceptors contain photopigments, which absorb light. There are four photopigments in the retina: rhodopsin, which is found in the rods, and one in each of the three cone types. Each photopigment contains two components: (1) opsin, a group of integral membrane proteins, which is different in each of the four photopigments and determines the wavelength of light absorbed, and (2) a chromophore molecule, retinal, which is a derivative of vitamin A, is the same in each photopigment, and is the actual light-sensitive part of the photopigment that undergoes isomerization by light.

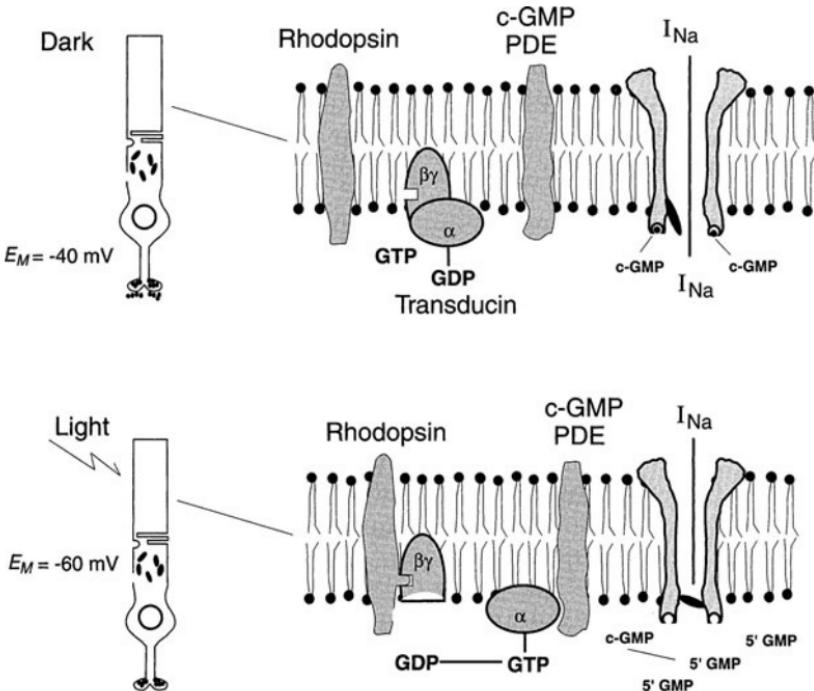
The photoreceptors are unusual because they hyperpolarize when they are stimulated by light. When the rods and cones are not stimulated, they are depolarized by the flow of Na^+ into the cell through Na^+ channels held in the open state by cGMP. The photoisomerization of retinal from its 11-cis form to its all-trans form activates rhodopsin and the other photopigments, which in turn activates a G protein called transducin. Activated transducin activates a cGMP phosphodiesterase (PDE). Hydrolysis of

cGMP causes Na^+ channels on the rod and cone outer segments to close, which produces the membrane hyperpolarization.

The neurotransmitter keeps the bipolar cells and, therefore, the ganglion cells, in a polarized and relatively quiescent state. Hyperpolarization of the photoreceptors stops the release of an inhibitory neurotransmitter, which in turn causes bipolar cells to depolarize. The bipolar cells stimulate ganglion cells, which in turn convey information about the light stimulus to the visual cortex. The ganglion cells are the only cells in the retina to produce an action potential. Their axons form the optic nerve.

MUSCULOSKELETAL PHYSIOLOGY

(*Ganong*, pp 65–84, 480–482, 547–549. *Ryan and Wang*, pp 2–8. *Widmaier et al.*, pp 279–321.)



	Slow-Oxidative Fibers	Fast-Oxidative Fibers*	Fast-Glycolytic Fibers
Primary source of ATP production	Oxidative phosphorylation	Oxidative phosphorylation	Glycolysis
Mitochondria	Many	Many	Few
Capillaries	Many	Many	Few
Myoglobin content	High (red muscle)	High (red muscle)	Low (white muscle)
Glycolytic enzyme activity	Low	Intermediate	High
Glycogen content	Low	Intermediate	High
Rate of fatigue	Slow	Intermediate	Fast
Myosin-ATPase activity	Low	High	High
Contraction velocity	Slow	Fast	Fast
Fiber diameter	Small	Intermediate	Large
Motor unit size	Small	Intermediate	Large
Size of motor neuron innervating fiber	Small	Intermediate	Large

*Because these fibers have significant glycolytic capacity, they are sometimes called “fast oxidative-glycolytic” (FOG) fibers.

Reproduced, with permission, from Widmaier EP et al. *Vander's Human Physiology: The Mechanisms of Body Function*, 10th ed. New York: McGraw-Hill, 2006:302.

Three types of muscle fibers have been identified based upon their maximal shortening velocities and the predominant pathway used to form ATP, as summarized in the table on the previous page.

Muscle cells, like neurons, can be excited to produce an action potential that is transmitted along their cell membranes. The electrical events and underlying ionic fluxes in skeletal muscle are similar to neurons. Unlike neurons, however, muscle action potentials initiate a contractile response. The process by which depolarization of the muscle fiber initiates contraction is called *excitation-contraction coupling*.

Muscle contraction is produced by repetitive cycling of the myosin cross-bridges on thick filaments. The cross-bridges attach to actin molecules on the thin filaments and cause the thin filaments to slide over the thick filaments toward the center of the sarcomere. In striated muscle, excitation-contraction coupling is initiated when Ca^{2+} binds to troponin. Troponin causes tropomyosin to move, thereby exposing the actin binding site to myosin.

In skeletal muscle, Ca^{2+} is released from the sarcoplasmic reticulum (SR) when the muscle fiber depolarizes. In cardiac muscle, Ca^{2+} is released from the SR by the Ca^{2+} that enters the cell during the cardiac action potential. In smooth muscle, excitation-contraction coupling is initiated when Ca^{2+} binds to calmodulin. The Ca^{2+} -calmodulin complex activates myosin light chain kinase (MLCK) which, in turn, phosphorylates the 20,000-Da myosin light chains (LC_{20}). Cross-bridge cycling begins when the myosin light chains are phosphorylated. When dephosphorylated, the cross-bridges stay attached (or cycle slowly). The attached, slowly cycling cross-bridges are called latch bridges. Latch bridges allow smooth muscle to maintain force while minimizing energy expenditure. A comparison of the properties of skeletal, cardiac, and smooth (single unit and multiunit) muscles is provided in the table on the next page.

RESPIRATORY PHYSIOLOGY

(Ganong, pp 647–697. Levitzky, pp 1–264. Ryan and Wang, pp 12–19. Widmaier et al., pp 477–523.)

Partial Pressures

The primary function of the lungs is O_2 and CO_2 exchange. When gas exchange is optimal, the arterial blood has normal values (range) of PO_2 , PCO_2 , and pH (at sea level) of 100 mmHg (80–100 mmHg), 40 mmHg (35–45 mmHg), and 7.40 (7.35–7.45), respectively.

Characteristic	Skeletal Muscle	Single Unit	Multiunit	Cardiac Muscle
Thick and thin filaments	Yes	Yes	Yes	Yes
Sarcomeres—banding pattern	Yes	No	No	Yes
Transverse tubules	Yes	No	No	Yes
Sarcoplasmic reticulum (SR)*	+++	+	+	++
Gap junctions between cells	No	Yes	Few	Yes
Source of activating calcium	SR	SR and extracellular	SR and extracellular	SR and extracellular
Site of calcium regulation	Troponin	Myosin	Myosin	Troponin
Speed of contraction	Fast-slow	Very slow	Very slow	Slow
Spontaneous production of action potentials by pacemakers	No	Yes	No	Yes in certain fibers, but most not spontaneously active
Tone (low levels of maintained tension in the absence of external stimuli)	No	Yes	No	No
Effect of nerve stimulation	Excitation	Excitation or inhibition	Excitation or inhibition	Excitation or inhibition
Physiological effects of hormones on excitability and contraction	No	Yes	Yes	Yes
Stretch of cell produces contraction	No	Yes	No	No

*Number of plus signs (+) indicates the relative amounts of sarcoplasmic reticulum present in a given muscle type.

Reproduced, with permission, from Widmaier EP et al. *Vander's Human Physiology: The Mechanisms of Body Function*, 10th ed. New York: McGraw-Hill, 2006:319.

Room air contains 21% O₂ and 0.04% CO₂; the major constituent of the atmosphere is N₂ (~79%). According to Dalton's Law, the total pressure of a gaseous mixture, such as the atmosphere, is equal to the sum of the partial pressures of the constituent gases. At standard temperature and pressure dry (STPD) (0°C, 760 mmHg, 0% H₂O vapor), the partial pressure of a gas (P_{gas}) is calculated as the product of the total pressure of the gas (i.e., atmospheric pressure) and the fractional concentration of the gas (F_i gas), that is, the percent concentration expressed as a decimal.

$$P_{\text{gas}} = (P_{\text{total}}) (F_{i\text{gas}}) = (P_{\text{total}}) (\%_{\text{gas}}/100)$$

Once air is inspired, it becomes warmed and humidified within the respiratory tract. Thus, when determining partial pressures of the gases anywhere in the body (BTPS, 37°C, 760 mmHg, 100% H₂O vapor), that is, in tracheal (conducting airways), alveolar, and exhaled air and in arterial and venous blood, the H₂O vapor tension (P_{H₂O} at 37°C is 47 mmHg) must be subtracted from the total pressure of 760 mmHg before multiplying by the fractional concentration of a gas, as follows:

$$P_{\text{gas}} = (P_{\text{total}} - P_{\text{H}_2\text{O}}) (F_{i\text{gas}}) = (P_{\text{total}} - 47 \text{ mmHg}) (\%_{\text{gas}}/100)$$

A summary of the partial pressures of the respiratory gases at sea level is presented in the table. The fractional concentration of the gases in the atmosphere does not change at high altitude, but as one ascends above sea level, the total barometric pressure decreases as the weight of the air above the atmosphere decreases. As a result, the partial pressure of oxygen and the other gases in the atmosphere decrease at high altitude.

The average partial pressure of oxygen in the alveoli is calculated using the alveolar gas equation:

$$P_{\text{AO}_2} = P_{\text{lO}_2} - (\text{PaCO}_2/\text{R})$$

R is the respiratory gas exchange ratio ($\dot{V}\text{CO}_2/\dot{V}\text{O}_2$). Under normal circumstances its value depends on metabolism and is equal to 0.8.

PARTIAL PRESSURES OF RESPIRATORY GASES AT SEA LEVEL (BP = 760 mmHg)

Gases	Dry Inspired Air (Atmospheric)	Humidified Inspired Air (Dead Space)	Alveolar Air	Mixed Expired Air	Arterial Blood	Mixed Venous Blood
PO ₂	159 (20.93)	149 (20.93)	104 (14.6)	120 (16.8)	100	40
PCO ₂	0.3 (0.04)	0.3 (0.04)	40 (5.6)	27 (3.8)	40	46
PN ₂	600 (79)	563 (79)	569 (79.8)	566 (79.4)	573	573
PH ₂ O	0.0 (0.0)	47	47	47	47	47
TOTAL	760	760	760	760	760	706

Note I: The partial pressures are given in mm Hg following in parenthesis by the percentage concentration.

Note II: H₂O vapor is not expressed as a % of the total because the PH₂O is temperature-dependent, not concentration-dependent. The PH₂O at 37°C is 47 mmHg. This value must be subtracted from the total pressure of 760 mmHg before multiplying by the fractional concentration of a gas when determining partial pressures of the gases anywhere in the body (BTPS), that is, in tracheal (conducting airways), alveolar, and exhaled air and in arterial and venous blood; only inspired atmospheric air is expressed under STPD.

Note III: In arterial and mixed venous blood, the respiratory gases are conventionally expressed in terms of their partial pressure. Therefore, the percentages are not indicated.

Ventilation

The air moving into the lung with each breath is called the *tidal volume* (V_T). The amount of air moving into the lung per minute is called the *minute ventilation* (\dot{V}_E), which is calculated as the product of the tidal volume and the respiratory rate:

$$\dot{V}_E \text{ (mL/min)} = V_T \text{ (mL)} \times \text{Respiratory rate (breaths/min)}$$

Functionally, the respiratory tract consists of the conducting airways, which extend from the nose down to the terminal bronchioles, and the

gas-exchanging airways, which extend from the respiratory bronchioles to the alveoli. The volume of the conducting airways is referred to as the *anatomical dead space* (V_D), which can be estimated as 1 mL/lb of body weight. The conducting airways do not participate in gas exchange because they are ventilated, but are perfused by systemic blood vessels, not by the pulmonary circulation. Sometimes, there are also alveoli that are ventilated but not perfused, which comprise areas of *alveolar deadspace*. The *physiological dead space* is the sum of the anatomical and alveolar dead spaces. The ratio of the physiological deadspace volume to the tidal volume (V_D/V_T) can be calculated using the Bohr equation, which takes advantage of the fact that any CO_2 present in the expired air ($P_{\text{E}}\text{CO}_2$) must have come from alveoli that are both ventilated and perfused.

$$V_D / V_T = \text{Paco}_2 - P_{\text{E}}\text{CO}_2 / \text{Paco}_2$$

The deadspace volume (V_D) must be subtracted from the tidal volume to determine the volume of gas that enters the gas-exchanging airways with each breath. The volume of gas going to the gas-exchanging airways each minute is called the *alveolar ventilation* (\dot{V}_A), and is calculated as:

$$\text{Alveolar ventilation} (\dot{V}_A) = (V_T - V_D) \times \text{Respiratory rate}$$

The average partial pressure of carbon dioxide in the alveoli is proportional to carbon dioxide production and inversely proportional to alveolar ventilation:

$$\text{Paco}_2 = (\dot{V}_{\text{CO}_2} / \dot{V}_A)$$

Thus, at a constant rate of CO_2 production,

Normal alveolar ventilation = Normal Paco_2 (35–45 mmHg)

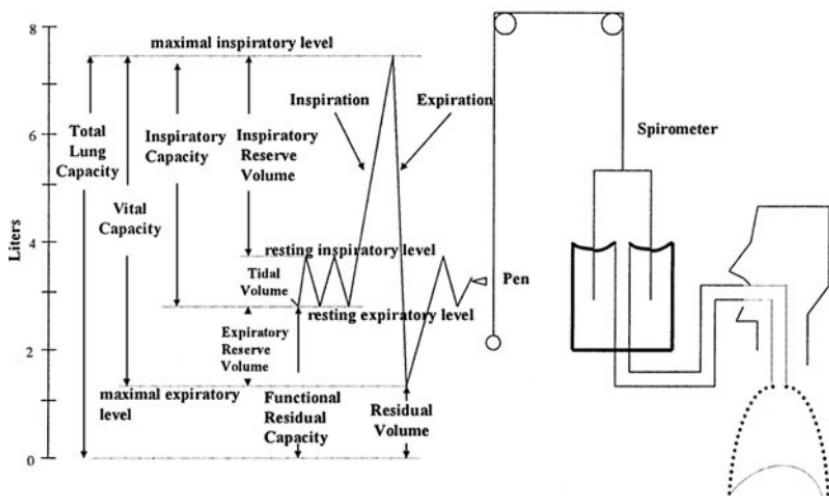
Hyperventilation = Decreased Paco_2 (<35 mmHg)

Hypoventilation = Increased Paco_2 (>45 mmHg)

Mechanics of Breathing

Air is moved in and out of the lungs by the movement of the diaphragm and chest. During inspiration, the diaphragm descends and the rib cage moves up and out. Because the lungs are connected to the chest wall via the pleura, expansion of the chest wall expands the lungs. In accordance with Boyle's law, expansion of the lungs creates a subatmospheric intraalveolar pressure, which draws air into the alveoli as air moves down its pressure gradient from an area of higher to lower pressure. Expiration is usually

Lung Volumes and Capacities



passive due to the elastic recoil of the lungs and chest wall when the inspiratory muscles cease contracting. Gas flow during expiration can be increased by actively contracting the expiratory muscles, but the maximum expiratory flow is limited by airway compression.

The gas moving in and out of the lungs is measured with spirometry. Tidal volume is the gas moving in and out of the lungs with each breath. The maximum amount of gas that can be expelled from the lungs after breathing in as far as possible is called the *vital capacity*. The maximum amount of gas that can be expelled from the lungs after a normal breath is called the *expiratory reserve volume*. The maximum amount of gas that can be inspired over and above the tidal volume is the *inspiratory reserve volume* and the maximum volume of gas that can be inspired from the resting expiratory level is the *inspiratory capacity*. The *total lung capacity* is the volume of gas present in the lungs after a maximum inspiration, and is equal to the sum of the four primary lung volumes. The gas remaining in the lung at the end of a quiet (tidal) expiration is the *functional residual capacity (FRC)* and the amount of gas remaining in the lung at the end of a maximum expiration is the *residual volume*. The residual volume cannot be measured by spirometry, and neither can the capacities that contain the residual volume, that is, the functional residual capacity and the total lung capacity.

The lungs and chest wall are elastic structures. The lungs tend to recoil inward from the chest wall at all lung volumes, creating a subatmospheric

intrapleural pressure, which becomes more negative with increases in lung volume. Intrapleural pressure is normally about $-5\text{ cm H}_2\text{O}$ at FRC, and decreases to about $-30\text{ cm H}_2\text{O}$ at TLC. The factors contributing to the lung's elastic recoil properties are elastic fibers and surfactant. The inverse of elastic recoil is compliance, which is defined as $\Delta V/\Delta P$, and represents the slope of a pressure-volume curve of the lung. Lung compliance is increased (elastic recoil is decreased) with alveolar septal departmenting and loss of elastic fibers that occur in emphysema and as part of the normal aging process. Lung compliance is decreased (increased elastic recoil, "stiff" lungs, restrictive lung disease) when normal elastic fibers are replaced by scar tissue (pulmonary interstitial fibrosis), in infiltrative diseases, when the lungs are filled with exudate or fluid, and when there is a deficiency of surfactant.

In addition to the elastic work of breathing, work is required to overcome the resistance to airflow offered by the airways. Airway resistance (R_{aw}) is defined as the driving pressure for airflow divided by the flow rate:

$$R_{aw} = \frac{\Delta P}{\dot{V}} = \frac{P_{atm} - P_{alv}, \text{ cmH}_2\text{O}}{\text{Flow Rate, L/sec}}$$

R_{aw} can also be defined by Poiseuille's Law:

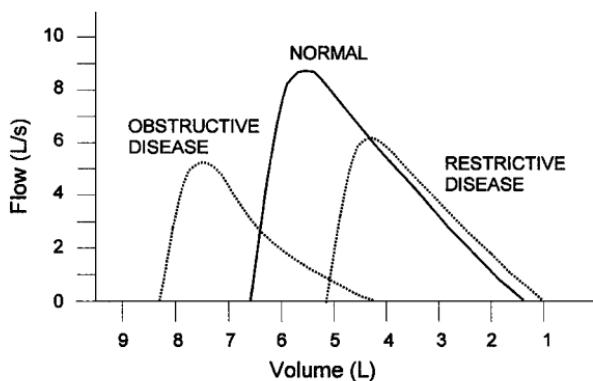
$$\frac{\Delta P}{\dot{V}} = \frac{8\eta l}{\pi r^4}$$

where l = length, η = viscosity, r = radius

Measurement of airway resistance requires a body plethysmograph to measure intrathoracic pressures. More frequently, airway resistance is assessed by changes in expiratory flow rates. An increase in airway resistance is the hallmark of obstructive lung disease. The effect of increased airway resistance (airway obstruction) is (1) to \downarrow expiratory flow rates (peak flow, forced vital capacity (FVC), forced expiratory volume in 1 second (FEV_{1.0}), and FEV_{1.0}/FVC) and (2) to increase residual volume, functional residual capacity, and total lung capacity. These effects also cause characteristic changes in the configuration of the maximal expiratory flow-volume curves of the lung.

Hypoxia and Hypoxemia

The causes of tissue hypoxia can be classified into four groups, hypoxic hypoxia (hypoxemia), anemic hypoxia, hypoperfusion or stagnant hypoxia,



and histotoxic hypoxia, as summarized in the table below. There are also four different categories of hypoxemia.

Classification	PAO_2	PAO_2	CaO_2	PvO_2	CvO_2	Increased Helpful?
Hypoxic hypoxia						
Low alveolar PO_2	Low	Low	Low	Low	Low	Yes
Diffusion impairment	N	Low	Low	Low	Low	Yes
Right-to-left shunts	N	Low	Low	Low	Low	No
\dot{V}/\dot{Q} mismatch	N	Low	Low	Low	Low	Yes
Anemic hypoxia	N	N	Low	Low	Low	No
CO poisoning	N	N	Low	Low	Low	Possibly
Hypoperfusion hypoxia	N	N	N	Low	Low	No
Histotoxic hypoxia	N	N	N	High	High	No

N = Normal.

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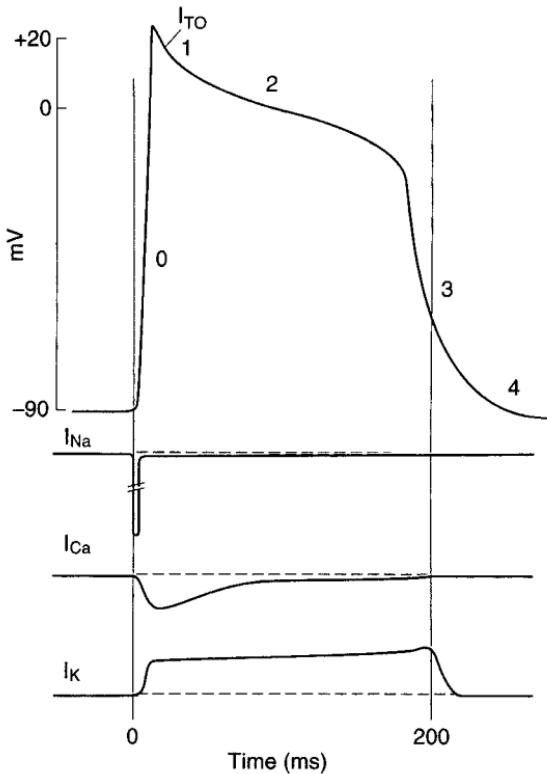
CARDIOVASCULAR PHYSIOLOGY

(Ganong, pp 547–644. Ryan and Wang, pp 8–12. Stead et al., pp 5–9. Widmaier et al., pp 387–476.)

Electrical Activity of the Heart

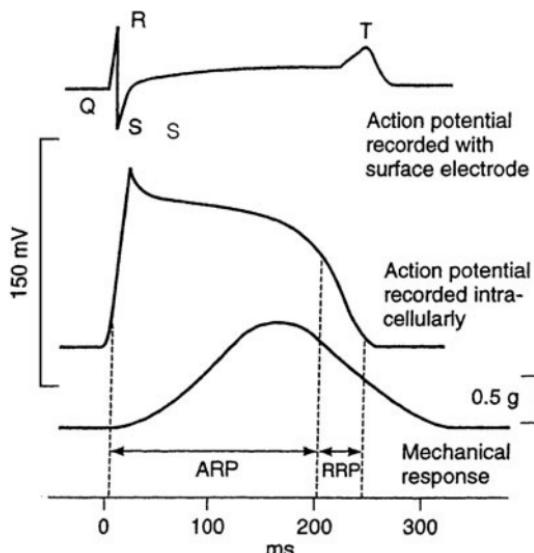
The contractile response of cardiac muscle begins just after the start of depolarization and lasts about 1.5 times as long as the action potential.

The initial rapid depolarization and overshoot (phase 0) are produced by the activation of Na^+ channels. The initial repolarization (phase 1) is produced by inactivation of Na^+ channels. The plateau (phase 2) is caused by the activation of Ca^{2+} channels and the closing of inward rectifying (anomalous) K^+ channels. The downstroke or final repolarization (phase 3) to the

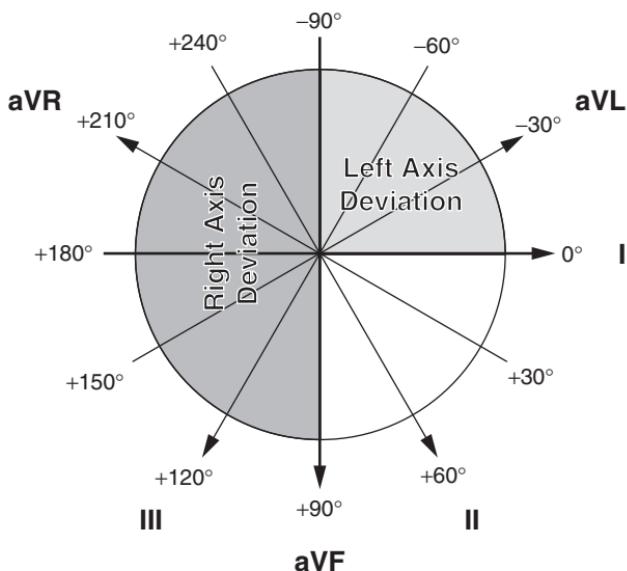


Top: Phases of the action potential of a cardiac muscle fiber. 0, depolarization; 1, initial rapid repolarization; 2, plateau phase; 3, late rapid repolarization; 4, baseline. Bottom: Diagrammatic summary of Na^+ , Ca^{2+} , and cumulative K^+ currents during the action potential. Inward current down, outward current up.

(Reproduced, with permission, from Gangong, WF. Review of Medical Physiology, 22nd ed. New York: McGraw-Hill, 2005:80.)



Action potentials and contractile response of mammalian cardiac muscle fiber plotted on the same time axis. ARP, absolute refractory period; RRP, relative refractory period. (Reproduced, with permission, from Ganong, WF. Review of Medical Physiology, 22nd ed. New York: McGraw-Hill, 2005:80.)



(Reproduced, with permission, from Stead, LG et al. First Aid for the Medicine Clerkship, 2nd ed. New York: McGraw-Hill, 2006:7.)

resting membrane potential (phase 4) is caused by closure (inactivation) of the Ca^{2+} channels and K^+ efflux through various types of K^+ channels.

Recording extracellularly, the electrocardiogram (ECG) represents the summed activity of all of the cardiac muscle cells. The P wave is produced by atrial depolarization, the QRS complex by ventricular depolarization, and the ST segment and T wave by ventricular repolarization. The PR interval is the time for atrial depolarization and conduction through the atrioventricular (AV) node. The mean electrical axis of depolarization (mean QRS vector) can be determined from the standard bipolar and the unipolar limb leads, as seen in the figure.

Mechanical Events of the Cardiac Cycle

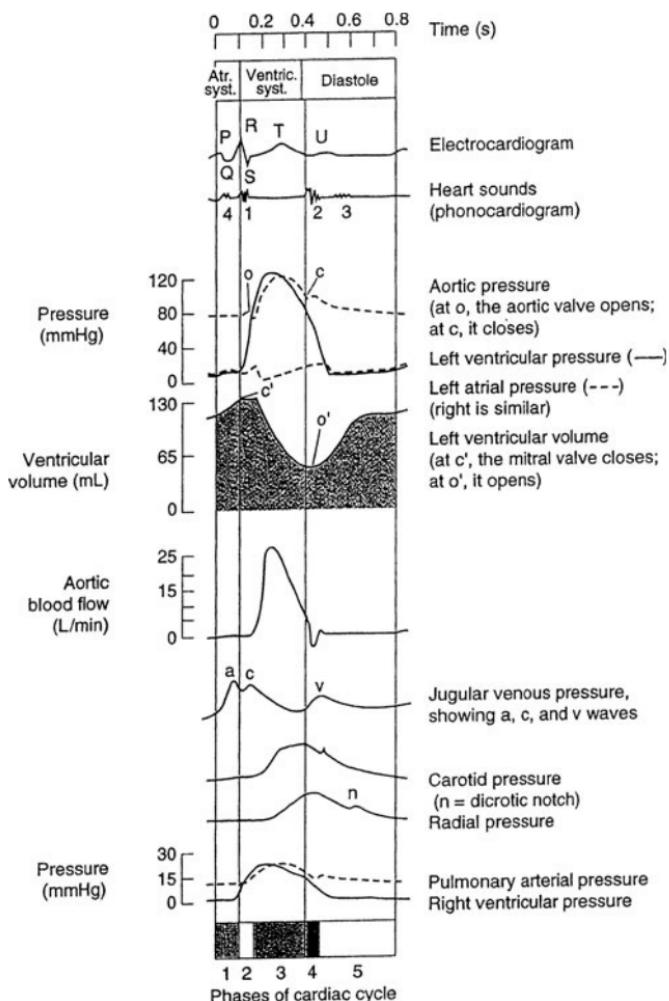
The cardiac action potential triggers a wave of contraction that spreads through the myocardium. The phases of the cardiac cycle include (1) atrial systole; (2) ventricular systole, which is comprised of isovolumetric contraction, rapid ejection, and reduced ejection; (3) and ventricular relaxation, which includes isovolumetric relaxation, rapid ventricular filling, and reduced ventricular filling.

Arterial Blood Pressure and Cardiac Output

The interaction of the factors controlling arterial blood pressure and cardiac output are summarized in the figure.

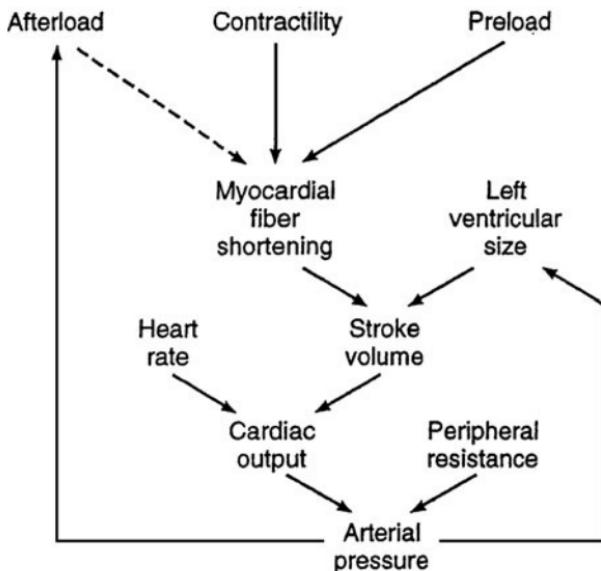
The heart rate is controlled primarily by the autonomic innervation of the heart, with sympathetic stimulation increasing heart rate by increasing the rate of phase 4 depolarization in the sinoatrial node, and vagal stimulation decreasing heart rate. Blood pressure is maintained by the baroreceptor reflex. Baroreceptors located in the carotid sinus and aortic arch respond to a decrease in blood pressure by reflexly stimulating sympathetic activity to the heart and blood vessels, which increases heart rate, contractility, and total peripheral resistance, and decreases venous compliance.

Stroke volume (and thus cardiac output) is dependent on preload, afterload, and contractility. The relationship between preload (end-diastolic fiber length) and stroke volume is known as the length-tension relationship, and is represented by a Starling curve. Increases in preload (as measured by such indices as ventricular end-diastolic volume, ventricular end-diastolic pressure, atrial pressure, or central venous pressure) cause increases in the tension developed by cardiac muscle, which increases the stroke volume and cardiac output. The Starling curve is shifted up and to

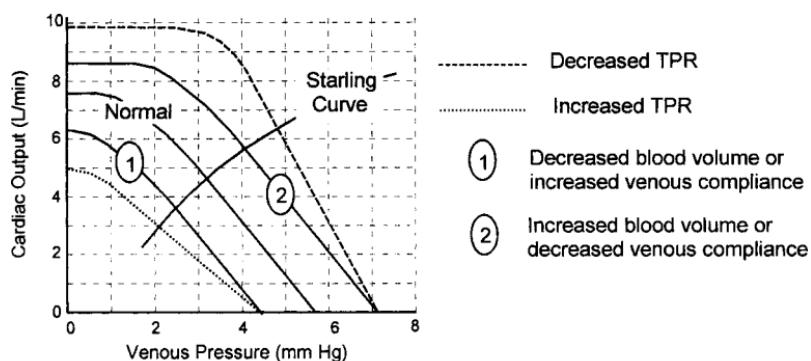
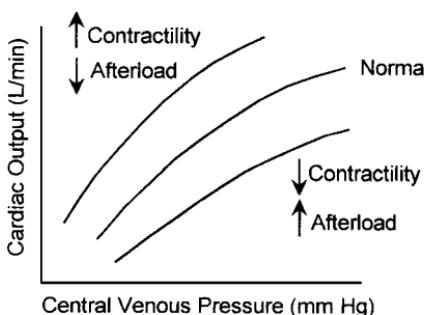


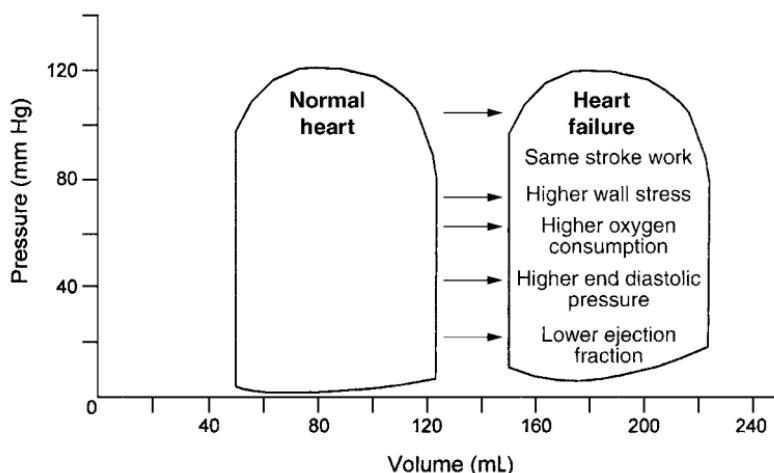
Events of the cardiac cycle at a heart of 75 beats/min. The phases of the cardiac cycle identified by the numbers at the bottom are as follows; 1, atrial systole; 2, isovolumetric ventricular contraction; 3, ventricular ejection; 4, isovolumetric ventricular relaxation; 5, ventricular filling. Note that late in systole, aortic pressure actually exceeds left ventricular pressure. However, the momentum of the blood keeps it flowing out of the ventricle for a short period. The pressure relationships in the right ventricle and pulmonary artery are similar; abbreviations; At. syst., atrial systole; Ventric. syst., ventricular systole.

(Reproduced, with permission, from Ganong WF. Review of Medical Physiology, 22nd ed. New York: McGraw-Hill, 2005:567.)



(Reproduced, with permission, from Ganong WF. Review of Medical Physiology, 22nd ed. New York: McGraw-Hill, 2005:572.)





the left by an increase in contractility or a decrease in afterload. The Starling curve is shifted down and to the right by a decrease in contractility or an increase in afterload.

Preload is dependent on blood volume, venous compliance, and total peripheral resistance (TPR). The relationship between these variables is represented by a vascular function curve. Changes in vascular volume or venous compliance cause a parallel shift in the vascular function curves. Changes in TPR cause the slope of the vascular function curve to change.

The change in pressure and volume within the heart during one cardiac cycle can be represented by a pressure-volume curve. The work required to eject the blood is called the stroke work. The stroke work is the product of mean left ventricular systolic pressure and stroke volume, and is equal to the area within the pressure-volume curve. The energy required to eject the blood is dependent on the stroke work and the wall stress (tension). According to LaPlace's Law, wall stress (T) is proportional to the systolic pressure (P) and the radius of the ventricle (r) and inversely proportional to the thickness of the ventricular wall (w):

$$T = P \times r/w$$

Wall stress increases in heart failure because the preload increases to compensate for the decrease in contractility. The increased radius of the enlarged heart causes wall stress to increase, and, therefore, more energy is required to eject blood. If the coronary circulation cannot provide the necessary oxygen, ischemic pain (angina) results.

Blood pressure decreases as blood flows through the circulation. The magnitude of the decrease is proportional to the resistance of each segment of the circulation. The greatest decrease occurs as blood flows through the arterioles. The segments of the circulation are in series with each other. The quantity of blood flowing into each organ is inversely proportional to the relative resistance of each organ. For example, at rest approximately 20% of the cardiac output flows through the skeletal muscles. During exercise, when the resistance of the skeletal muscle vessels decreases, over 80% of the cardiac output can flow through the skeletal muscles. The organs in the body are in parallel with each other, with the exception of the lungs, whose blood flow is in series with the systemic circulation.

The velocity (v) of blood through a vessel is proportional to the flow of blood through the vessel (\dot{Q}) and inversely proportional to the area of the vessel (A):

$$v = \dot{Q}/A$$

Increasing the velocity of blood can change flow from laminar (streamline) to turbulent (rapid, disorderly), as predicted by a Reynold's number that exceeds 2000. Turbulent flow produces a sound called a murmur if it occurs in the heart, or a bruit if it occurs in a blood vessel. Flow through stenotic or incompetent heart valves produces cardiac murmurs. Occlusion of blood vessels by a sclerotic plaque, for example, will produce bruits.

Capillary Fluid Balance

Fluid exchange across capillaries is dependent on the balance between the hydrostatic (P) and the osmotic (π) pressures between the capillaries and interstitial space, and the permeability of the capillary wall (K_f), as predicted by Starling's law of capillary fluid balance:

$$\text{Filtration} = K_f [(P_{\text{cap}} + \pi_i) - (\pi_{\text{cap}} + P_i)]$$

Excess filtration out of the capillaries causes fluid accumulation in the interstitial space, called edema. Edema can result from an increase in capillary permeability (K_f), as during an inflammatory response, or a decrease in plasma proteins, as during malnutrition, which decreases π_{cap} , an increase in capillary hydrostatic pressure (P_{cap}), as in heart failure, or a decrease in interstitial hydrostatic pressure (P_i) as with rapid evacuation of a pneumothorax. Normally, the fluid filtered from the capillaries is

returned to the circulation by the lymphatic system, so blockage of the lymphatic circulation can also produce edema.

GASTROINTESTINAL PHYSIOLOGY

(*Ganong, pp 467–513. Ryan and Wang, pp 20–22. Widmaier et al., pp 575–614.*)

The first stage in the digestion and absorption of food is chewing and swallowing. Chewing and swallowing can be initiated voluntarily or involuntarily. Chewing breaks food into small pieces and mixes them with salivary secretions. Swallowing is coordinated by a swallowing center in the brainstem. During the oral phase of swallowing, the tongue pushes the food into the pharynx. During the pharyngeal phase, peristaltic contractions and relaxation of the upper esophageal sphincter (UES) allow the food to enter the esophagus. During the esophageal phase, the lower esophageal sphincter (LES) relaxes and the food is propelled into the stomach by primary peristalsis. A secondary peristaltic wave, initiated by the presence of food in the smooth muscle, clears the esophagus of any food not propelled into the stomach by primary peristalsis.

The stomach breaks food into small pieces and mixes the pieces with gastric secretions to produce a paste-like material called chyme. Liquids and chyme are forced through the pylorus by a rise in gastric pressure. Liquids empty from the stomach in one half-hour. Solids cannot pass through the pyloric sphincter until they are broken into small pieces (less than 1 mm³), and, therefore, emptying of solids takes from 1 to 3 hours.

Gastric emptying is slowed by the enterogastric reflex and the release of an inhibitory hormone called enterogastrone. The reflex and the secretion of enterogastrone are evoked by the presence of acid or fats in the duodenum. The secretion of gastric acid by the parietal cells is regulated by paracrine (histamine), neural (vagus nerve), and hormonal (gastrin) influences.

The intestine is responsible for the digestion and absorption of food and nutrients. During the digestive phase, food is slowly moved along the intestine by segmentation. During the interdigestive phase, the intestine is cleared of any nonabsorbed particles by the migrating motor complex.

Fats, proteins, and carbohydrates are digested by intestinal enzymes. Bile is necessary for the digestion and absorption of fats. However, the amount of bile acids emptied into the proximal small intestine from the gallbladder is insufficient for complete fat digestion and absorption. Receptor-mediated active transport of bile acids in the terminal ileum

GASTRIC FUNCTIONS		
Function	Oraad Stomach	Caudad Stomach
Motility	Tone Receptive relaxation Accommodation Emptying of liquids	Trituration Emptying of solids Reflux barrier
Secretion	HCl Intrinsic factor Mucus Pepsinogen	Gastrin

returns the bile acids via the portal blood to the liver for secretion into the small intestine (this circulation of bile is called the enterohepatic circulation). Approximately 95% of the bile acid pool is recirculated from the intestine and about 5% is lost in the stool.

Water absorption is caused by osmotic forces generated by active sodium absorption. The source of water is both exogenous (oral input) and endogenous (GI tract secretion) and averages 8 to 10 L/day. Generally, less than 0.2 L/day is eliminated in the stool. The majority of water absorption occurs in the duodenum and jejunum. The colon exhibits a limited capacity to absorb water (4–6 L/day).

INTESTINAL PHASE OF DIGESTION		
Stimulus	Mediator	Response
Partially digested nutrients	CCK	Pancreatic enzyme secretion Gallbladder emptying Decreased gastric emptying
Acid	Enterogastrone and enterogastric reflex Secretin	Decreased gastric emptying Decreased gastric acid secretion Pancreatic/hepatic HCO_3^- secretion Decreased gastric acid secretion
Osmoles or distension	Enterogastrone and enterogastric reflex	Decreased gastric emptying Decreased gastric acid secretion

SODIUM TRANSPORT MECHANISM IN THE INTESTINE

Nutrient-Coupled Intestine	Na ⁺ /H ⁺ Exchange Jejunum	Neutral Ileum and colon	Electrogenic Colon
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FUNCTIONS OF SMALL INTESTINE

Duodenum		Jejunum	Ileum
Motility		Segmentation (digestive period) Migrating Motor complex (interdigestive period)	
Secretion	CCK and secretin		HCO ₃ ⁻
Digestion		Intraluminal and brush border	
Absorption	Iron and folate	Folate	Bile acids and vitamin B ₁₂
←Nutrients, water, and electrolytes→			

RENAL AND URINARY PHYSIOLOGY

(Ganong, pp 505–551. Ryan and Wang, pp 22–25. Widmaier et al., pp 525–558.)

The kidney is responsible for maintaining the constancy and volume of the extracellular fluid. The functional unit of the kidney is the glomerulus and its associated nephron. The three basic components of renal function are glomerular filtration, tubular reabsorption, and tubular secretion, as depicted in the diagram below.

Each day, 160 to 180 L of fluid are filtered into the approximately one million nephrons in the human kidney. The glomerular filtration rate (GFR) is dependent on the Starling forces between the glomerular capillaries (cap) and Bowman's capsule (BC):

$$\text{GFR} = K_f [(P_{\text{cap}} + \pi_{\text{BC}}) - (\pi_{\text{cap}} + P_{\text{BC}})]$$

The amount of material filtered into the proximal tubule is called the filtered load. Approximately 20% of the plasma flowing through the glomerulus (renal plasma flow, RPF) is filtered into the proximal tubule:

$$\text{Filtration fraction} = \text{GFR}/\text{RPF}$$

The relative quantity of material excreted by the kidney (the renal clearance) is expressed as the volume of plasma that is completely cleared of the material by the kidney:

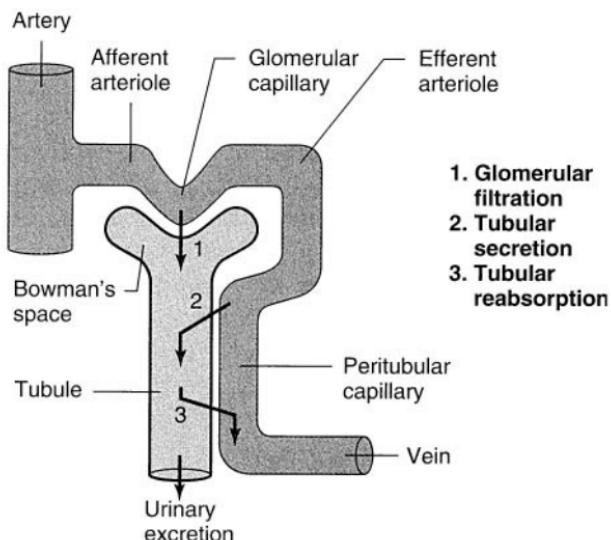
$$\text{Renal clearance} = (U_{\text{conc}} \times V)/P_{\text{conc}}$$

where U_{conc} = Urinary concentration of material

P_{conc} = Plasma concentration of material

V = Urinary flow rate

If a material is filtered but not reabsorbed or secreted, its renal clearance will be equal to the GFR. The clearances of creatinine or insulin are



The three basic components of renal function. This figure is to illustrate only the directions of reabsorption and secretion, not specific sites or order of occurrence. Depending on the particular substance, reabsorption and secretion can occur at various sites along the tubule.

(Reproduced with permission, from Widmaier EP et al. Vander's Human Physiology: The Mechanism of Body Function, 10th ed. New York: McGraw-Hill, 2006:531.)

used clinically to measure GFR. If a material is completely cleared from the plasma during its passage through the kidney by a combination of filtration and secretion, its renal clearance will be equal to the renal plasma flow (RPF). The clearance of the organic anion para-amino-hippurate(PAH) is used clinically to measure RPF:

$$\text{Renal blood flow (RBF)} = \text{RPF}/(1 - \text{hematocrit})$$

The proximal tubule is responsible for reabsorbing most of the material filtered from the glomerulus.

Material	% Reabsorbed	Mechanism
Na ⁺	60–70	Na/H exchange Na-nutrient cotransport Diffusion
K ⁺ , urea, Cl ⁻	60–70	Diffusion and solvng drag
Glucose, amino acids	100	Na-nutrient cotransport
Phosphate	90	Na-nutrient cotransport
Bicarbonate	85	Indirectly via Na/H exchange

The loop of Henle is responsible for producing a dilute filtrate. It reabsorbs approximately 25% of the salt and 15% of the water filtered from the glomerulus. The filtrate flowing from the loop of Henle to the distal convoluted tubule has a Na⁺ concentration of approximately 100 mEq/L.

The distal nephron is responsible for regulating salt and water balance. Na⁺ balance is regulated by aldosterone and atrial natriuretic peptide (ANP). Water balance is regulated by antidiuretic hormone (ADH), which is also called arginine vasopressin (AVP). K⁺ balance is regulated by aldosterone.

Aldosterone increases Na⁺ reabsorption and K⁺ secretion by the principal cells of the cortical and medullary collecting ducts. Aldosterone acts on the cell nucleus, increasing Na⁺ conductance of the apical membrane (which, by allowing more Na⁺ to enter the cell, increases Na⁺ reabsorption), the number of Na⁺,K⁺-ATPase pump sites (which, by increasing intracellular K⁺ concentration, increases K⁺ secretion), and the concentration of mitochondrial enzymes.

ANP decreases Na⁺ reabsorption by the renal epithelial cells of the medullary collecting ducts.

ADH increases water reabsorption by the principal cells of the cortical and medullary collecting ducts. ADH upregulates the number of water channels on the apical membrane of the epithelial cells by a cyclic adenosine monophosphate (cAMP)-dependent process.

Changes in renal hydrogen ion excretion are essential to the maintenance of acid-base balance in the body. The mechanisms of renal hydrogen ion excretion include (1) bicarbonate ion reabsorption, (2) titratable acid excretion, and (3) ammonium ion excretion (tubular secretion of H⁺, which combines with filtered phosphate).

Reproductive and Endocrine Physiology

(Ganong, pp 279–453. Ryan and Wang, pp 30–31. Widmaier et al., pp 343–386, 615–633, 651–699.)

Most of the hormones secreted by the endocrine glands are controlled by the endocrine hypothalamus and pituitary gland (hypophysis). The posterior pituitary gland is divided into a posterior and an anterior lobe. The pituitary gland contains the axons of neurons located within the paraventricular and supraoptic nuclei of the hypothalamus. These hypothalamic neurons synthesize oxytocin (responsible for milk ejection and uterine contraction) and ADH (increases water permeability of renal collecting ducts). The anterior hypothalamus secretes six major hormones as summarized in the table. The synthesis and release of these hormones are controlled by the hypothalamus. The hypothalamic releasing hormones are secreted into the median eminence from which they enter the capillary plexus that coalesces to form the anterior pituitary portal veins. These veins form another capillary plexus within the pituitary from which the releasing factors diffuse to the pituitary endocrine cells.

Thyroid hormone increases oxygen consumption and, therefore, the basal metabolic rate (BMR) by increasing the synthesis and activity of Na⁺, K⁺-ATPase. Thyroid hormone acts synergistically with growth hormone to promote bone growth. Thyroid hormone is essential for proper development of the nervous system in newborn infants and for normal cognitive function in adults.

Adrenocortical steroid hormones (glucocorticoids and adrenocorticoids) are synthesized from cholesterol. Glucocorticoids promote gluconeogenesis, inhibit the inflammatory immune responses, and are essential for the vasoconstrictive action of catecholamines.

Insulin and glucagon are secreted by the pancreas. Insulin affects carbohydrate, lipid, and protein metabolism in adipose, liver, and muscle

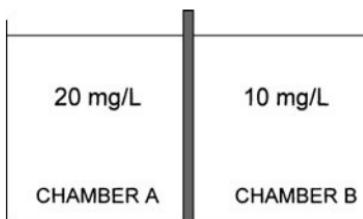
tissues. Insulin is secreted by the β cells of the islets of Langerhans. Insulin increases the entry of glucose, amino acids, and fatty acids into cells. It promotes the storage of these metabolites and inhibits their synthesis and mobilization. Glucagon is secreted by the α cells of the islets of Langerhans. Glucagon's effects oppose those of insulin.

Pituitary Hormone	Hypothalamic Hormone Attesting Pituitary Hormone	Major Action Pituitary Hormone
Thyroid-stimulating hormone (TSH)	Thyroid-releasing hormone (TRH)	Stimulates thyroid hormone synthesis and secretion
Adrenocorticotropic hormone (ACTH)	Corticotropin-releasing hormone (CRH)	Stimulates secretion of glucocorticoids, mineralocorticoids, and sex hormones from the adrenal cortex
Growth hormone	Growth hormone-releasing hormone Growth hormone inhibitory hormone (somatostatin)	Synthesis of somatomedins by liver, which, in turn stimulate protein synthesis, organ and bone growth
Follicle-stimulating hormone (FSH)	Gonadotropin-releasing hormone (GnRH)	Spermatogenesis (males) Estradiol synthesis (females)
Luteinizing hormone (LH)	Gonadotropin-releasing hormone (GnRH)	Testosterone synthesis (males) Ovulation (females)
Prolactin	Prolactin-inhibiting factor (dopamine) Thyroid-releasing hormone (TRH)	Breast development and milk production

General Principles: Cellular Physiology

Questions

1. The diagram below illustrates the concentration of a substance in two chambers. If the concentration of the substance in chamber A doubles, the diffusion of the substance will change from 10 mg/h to which of the following?

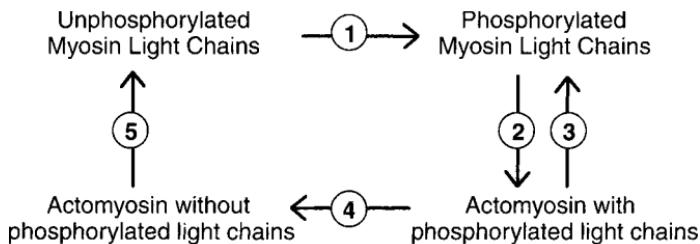


- a. 5 mg/h
 - b. 10 mg/h
 - c. 15 mg/h
 - d. 20 mg/h
 - e. 30 mg/h
2. A 49-year-old male in end-stage renal failure is able to perform peritoneal dialysis at home. The osmolality of the solution chosen for peritoneal dialysis will determine the rate of ultrafiltration. Which of the following statements best characterizes a molecule whose osmolality is zero?
- a. It will not permeate the membrane
 - b. It can only cross the membrane through the lipid bilayer
 - c. It causes water to flow across the membrane
 - d. It is as diffusible through the membrane as water
 - e. It is transported across the membrane by a carrier

- 3.** Which of the following characteristics of a water-insoluble substance is most important in governing its diffusibility through a cell membrane?
- Molecular weight
 - Electrical charge
 - Lipid solubility
 - Diameter
 - Three-dimensional shape
- 4.** Which of the following causes the rate of diffusion of a particle across a membrane to increase?
- The area of the membrane increases
 - The thickness of the membrane increases
 - The size of the particle increases
 - The concentration gradient of the particle decreases
 - The lipid solubility of the particle decreases
- 5.** The flow of calcium into the cell is an important component of the upstroke phase of action potentials in which of the following?
- Cardiac ventricular muscle
 - Intestinal smooth muscle
 - Skeletal muscle fibers
 - Nerve cell bodies
 - Presynaptic nerve terminals
- 6.** A patient with a family history of peripheral neuropathy is found to have a decrease in nerve conduction velocity and an X-linked mutation of connexin 32, consistent with Charcot-Marie-Tooth Disease. Connexin is an important component of which of the following?
- Gap junction
 - Sarcoplasmic reticulum
 - Microtubule
 - Synaptic vesicle
 - Sodium channel
- 7.** Which of the following would cause an immediate reduction in the amount of potassium leaking out of a cell?
- Increasing the permeability of the membrane to potassium
 - Hyperpolarizing the membrane potential
 - Decreasing the extracellular potassium concentration

- d. Reducing the activity of the sodium-potassium pump
 - e. Decreasing the extracellular sodium concentration
- 8.** Which of the following transport processes is a passive downhill process?
- a. Sodium out of brain cells
 - b. Calcium into the SR
 - c. Hydrogen into the lumen of canaliculi of the parietal cells of the stomach
 - d. Glucose into the fat cells of adipose tissue
 - e. Phosphate into epithelial cells lining the proximal tubule of the kidney
- 9.** A 61-year-old male with erectile dysfunction asks his physician to prescribe Viagra (sildenafil). Viagra produces its physiological effects by blocking the enzyme that hydrolyzes the second messenger by which nitric oxide produces its physiological effects. Which of the following is the second messenger?
- a. Bradykinin
 - b. Cyclic GMP
 - c. Protein kinase A
 - d. Endothelin
 - e. Inositol triphosphate
- 10.** A 43-year-old pregnant woman develops preeclampsia at 32 weeks gestation. Magnesium sulfate, which interacts with NMDA receptors in the central nervous system, is ordered for the prevention of eclamptic seizures until the fetus can be delivered. Which of the following activates the NMDA receptor?
- a. Glycine
 - b. Acetylcholine
 - c. Substance P
 - d. Histamine
 - e. Glutamate

11. Shown below is a diagram of the chemical reactions that occur during cross-bridge cycling in smooth muscle. Which of the following steps is responsible for the formation of latch bridges?



- a. Step 1
 - b. Step 2
 - c. Step 3
 - d. Step 4
 - e. Step 5
12. A 23-year-old man is brought to the Emergency Department after collapsing during basketball practice. On admission he is lethargic and appears confused. His coach reports that it was hot in the gym and he was drinking a lot of water during practice. An increase in which of the following is the most likely cause of his symptoms?
- a. Intracellular tonicity
 - b. Extracellular tonicity
 - c. Intracellular volume
 - d. Extracellular volume
 - e. Plasma volume
13. Which of the following is the approximate extracellular fluid volume of a normal individual?
- a. 5% of body mass
 - b. 10% of body mass
 - c. 20% of body mass
 - d. 40% of body mass
 - e. 60% of body mass

- 14.** A previously well 18-year-old girl is admitted to the ICU because of altered mental status. She does not respond to instructions and her arms are postured in a flexor position. Laboratory data reveal a serum sodium concentration of 125 mmol/L. Her friends indicate that the patient had taken ecstasy at a party the night before, and because she was extremely thirsty the next morning, she had consumed a lot of water in a short period of time. Assuming that the reduction in osmolarity is entirely due to water consumption, that her initial weight was 60 kg, and that her initial osmolarity was 300 mOsm/L, which of the following is approximately how much water she would have had to drink to produce the observed hyponatremia?
- a. 2.5 L
 - b. 3.5 L
 - c. 5 L
 - d. 6 L
 - e. 7 L
- 15.** A 42-year-old woman consults a dermatologist to evaluate and treat her glabellar lines (frown lines on the forehead just above the nose). After her treatment options are explained, the patient asks the dermatologist to administer Botox (botulinum type A). Botox injections smooth out glabellar lines by which of the following methods?
- a. Blocking the release of synaptic transmitter from α -motoneurons
 - b. Preventing the opening of sodium channels on muscle membranes
 - c. Decreasing the amount of calcium released from the sarcoplasmic reticulum
 - d. Increasing the flow of blood into the facial muscle
 - e. Enhancing the enzymatic hydrolysis of acetylcholine at the neuromuscular junction
- 16.** A 76-year-old woman with a history of uncontrolled hypertension presents in the Emergency Department with hypotension and shock-like symptoms. Her daughter reported systolic blood pressures near 200 mmHg earlier in the day, and suspects a dissecting aneurysm, which is confirmed with a CT of the chest. Biopsy of the repaired aorta shows giant cell arteritis, and the woman is placed on a regimen of high dose prednisone. The anti-inflammatory effect of exogenous glucocorticoids is thought to be due to which of the following?
- a. Increased capillary membrane permeability
 - b. Increased formation of leukotrienes
 - c. Increased release of interleukin-1 (pyrogen) from granulocytes
 - d. Activation of phospholipase A₂
 - e. Inhibition of the activation of NF- κ B

General Principles: Cellular Physiology

Answers

- 1. The answer is e.** (*Ganong, pp 4–5.*) Fick's law states that the net rate of diffusional flux (J) of a substance is proportional to its concentration difference (Δc). Doubling the concentration of the substance in chamber A from 20 to 40 mg/L, causes the concentration difference to increase by threefold from 10 to 30 mg/L. Therefore, the net rate of diffusion would increase from 10 to 30 mg/h.
- 2. The answer is d.** (*Ganong, pp 5–6.*) The osmolality of a substance is the number of osmoles per kg of solvent. One osmole (Osm) equals the gram molecular weight of a substance divided by the number of free moving particles that each molecule liberates in solution. Osmotically active substances in the body are dissolved in water, and the density of water is 1. Thus, osmolar concentrations can be expressed as osmoles (or milliosmoles) per liter of water. If the osmolality is zero, there are no free moving particles, and thus, the molecule is as diffusible as water through the membrane.
- 3. The answer is c.** (*Ganong, pp 4, 31.*) Materials that are not soluble in water can only diffuse across the membrane through the lipid bilayer. The most important factor determining how well a substance can diffuse across the lipid bilayer is the substance's lipid solubility. If two materials have the same lipid solubility, then the permeability of the smaller particle will be greater.
- 4. The answer is a.** (*Ganong, pp 4–5.*) The rate of diffusion is described by Fick's law, which states that the flux of material across a membrane is directly proportional to the area of a membrane, the concentration difference of the particles on either side of the membrane, and the lipid solubility of the particle. Net flux is inversely proportional to the thickness of the membrane and the size (specifically, the square root of the gram molecular weight) of the substance.

5. The answer is b. (*Ganong*, pp 58–59, 68, 78, 80, 481.) In intestinal smooth muscle, the upstroke of the action potential is caused by the flow of calcium into the cell. In cells of the cardiac ventricular muscle, the plateau phase of the action potential, but not the upstroke, is accompanied by the flow of calcium into the cells. Skeletal muscle fibers resemble nerve fibers. In both of these cells, the upstroke of the action potential is caused by the flow of sodium into the cell.

6. The answer is a. (*Ganong*, p 17. *Kasper et al.*, pp 2340, 2510–2512.) Connexin is a membrane-spanning protein that is used to create gap junction channels. The gap junction channel creates a cytoplasmic passage between two cells. Each cell membrane contains half of the channel. The channel, called a connexon, is constructed from six connexin molecules that form a cylinder with a pore at its center. Charcot-Marie-Tooth (CMT) disease comprises a heterogeneous group of inherited peripheral neuropathies. Approximately 1 in 2500 persons has some form of CMT, making it one of the most frequently occurring inherited neurological syndromes. Transmission is most frequently autosomal dominant but it may also be autosomal recessive or X-linked, like the mutation affecting the connexin 32 (Cx32), located in the folds of the Schwann cell cytoplasm around the nodes of Ranvier. This localization suggests a role for gap junctions composed of Cx32 in ion and nutrient transfer around and across the myelin sheath of peripheral nerves.

7. The answer is b. (*Ganong*, pp 7–8.) The amount of potassium leaking out of the cell depends on its membrane potential, its concentration gradient, and its membrane conductance. According to the Nernst equation, the electrical gradient for K^+ is inward and the concentration gradient is outward. Hyperpolarizing the membrane makes the inside of the cell more negative and therefore makes it more difficult for potassium to flow out of the cell. Decreasing the extracellular potassium concentration would increase the flow of potassium out of the cell, as would increasing the permeability of the membrane to potassium. Altering the activity of the sodium-potassium pump or the extracellular sodium concentration has no immediate effect on the flow of potassium across the membrane. Decreasing the activity of the sodium-potassium pump will ultimately depolarize the membrane, however, resulting in an increased flow of potassium out of the cell.

8. The answer is d. (*Ganong*, pp 31–35.) Glucose is transported into fat cells by facilitated diffusion and thus does not require the direct or indirect

use of energy. Insulin increases the rate of diffusion but is not necessary for the diffusion. All of the other transport systems require energy. Sodium is transported out of cells by Na^+/K^+ ATPase; calcium is transported into the SR by a Ca^{2+} -ATPase; and hydrogen is transported from the parietal cells of the stomach by a H^+/K^+ ATPase. All of these transporters use ATP directly in the transport process. The active transport of Na^+ is often coupled to the transport of other substances, a process called secondary active transport. In the proximal tubule, phosphate is transported into the luminal cells of the proximal tubule by a $\text{Na}^+/\text{HPO}_4^{2-}$ secondary active transport system. Secondary active transport usually involves the transepithelial movement of ions and other molecules in the gastrointestinal tract, pulmonary airways, renal tubules, and other structures.

9. The answer is b. (*Ganong*, pp 37–38, 43–44, 165, 427–428.) Erection is initiated by dilation of the arterioles of the penis, which increases blood flow into the erectile tissue of the organ. The increased turgor of the penis also results from compression of the veins, blocking the outflow of blood from the organ. Nitric oxide (NO) is a potent vasodilator that acts by activating guanylyl cyclase, resulting in increased production of the second messenger, cGMP. Viagra (sildenafil) is an effective and selective inhibitor of cGMP phosphodiesterase (PDE). By blocking the breakdown of cGMP, Viagra prolongs the action of NO and erections. Sildenafil is most active against PDE5, the type of PDE found in the corpora cavernosa. Erections are produced by the release of NO, which inhibits the smooth muscle of the corpora cavernosa, allowing blood to fill the penis. Sildenafil is also a potent inhibitor of PDE6 found in the retina, which accounts for the transient blue-green color weakness, one of the side effects of sildenafil.

10. The answer is e. (*Ganong*, pp 98, 108–110. *Kasper et al.*, p 33.) The NMDA receptor channel is a large channel permeable to Ca^{2+} , K^+ , and Na^+ . It is activated by glutamate, but unlike other glutamate receptor channels, the NMDA channel is blocked by Mg^{2+} in its resting state. Depolarization of the cell membrane to approximately -40 mV removes the Mg^{2+} blockade. Therefore, the NMDA channel is only opened when the cell is depolarized by other excitatory neurotransmitters. Preeclampsia is the development of high blood pressure during pregnancy. Other signs of preeclampsia include protein in the urine and severe edema (or swelling). The only treatment for preeclampsia is delivery of the baby, which may mean a premature birth. Magnesium sulfate is the treatment of choice for preventing and treating

eclamptic seizures, demonstrating superiority over phenytoin and diazepam in two large clinical trials.

11. The answer is d. (*Ganong*, pp 89–90.) Latch bridges are unphosphorylated myosin cross-bridges that are bound to actin. These cross-bridges cycle very slowly or not at all and are responsible for the ability of smooth muscle to maintain its tone for a long time without expending energy for cross-bridge cycling. The enzyme myosin light chain phosphatase is responsible for dephosphorylating cycling cross-bridges (Step 4). The smooth muscle relaxes when Ca^{2+} is removed from the myoplasm and the latch bridges detach from actin. Cross-bridge cycling in smooth muscle cannot begin until the myosin light chains are phosphorylated (Step 1). Phosphorylation is enzymatically stimulated by myosin light chain kinase (MLCK).

12. The answer is c. (*Ganong*, pp 6–7, 241–242, 729. *Kasper et al.*, pp 252–254. *Stead et al.*, p 226.) Drinking water after losing a significant volume of water as sweat decreases the osmolality of the extracellular fluid because the salt lost from the extracellular fluid in sweat is not replaced by the ingested water. When the extracellular osmolality is decreased, water flows from the extracellular to the intracellular body compartment, causing intracellular volume to increase. The patient's symptoms are caused by swelling of the brain.

13. The answer is c. (*Ganong*, pp 1–3, 6–7. *Stead et al.*, p 226.) Sixty percent of the body mass is water. Of this water, one-third (20% of body mass) is extracellular and two-thirds (40% of body mass) is intracellular. The extracellular water is further divided into interstitial water (80% of extracellular fluid, or 15% of body mass) and plasma water (20% of extracellular fluid, or 5% of body mass). The percentage of water in the body is a function of body fat. The greater the percentage of body fat, the lower the percentage of body water. About three-fourths of the lean body mass (mass excluding fat) is water. The distribution of extracellular and intracellular water is a function of the extracellular osmolality. If the osmolality of the extracellular fluid is above normal, the proportion of water in the extracellular fluid, in comparison to that in the intracellular water, increases; hypotonicity of the extracellular water decreases the proportion of water in the extracellular fluid.

14. The answer is e. (*Ganong*, pp 1, 5–6, 729. *Widmaier et al.*, pp 121–124.) When water is ingested from the intestine, it enters the plasma

and rapidly achieves osmotic equilibrium with the interstitial and intracellular compartments. Assuming that she had a normal osmolarity of 300 mOsmol/L initially, at her initial body weight of 60 kg, with 60% of body weight being water, her initial volume was 36 L. A sodium concentration of 125 mM is equivalent to an osmolarity of 250 mOsmol/L. Assuming that her normal osmolarity of 300 mOsm was reduced to 250 mOsm by the ingestion of water, she drank approximately 7 L.

$$\text{Osmolarity} = \text{mOsmol}/\text{Volume}$$

$$300 \text{ mOsm}/\text{L} = 60 \text{ kg} \times 60\% \times 300/\text{Initial Volume}$$

$$\text{Initial Volume} = 10,800 \text{ mOsmol}/300 \text{ mOsm}/\text{L} = 36 \text{ L}$$

$$250 \text{ mOsm}/\text{L} = 60 \text{ kg} \times 60\% \times 300/\text{New Volume}$$

$$\text{New Volume} = 10,800 \text{ mOsmol}/250 \text{ mOsmol}/\text{L} \cong 43 \text{ L}$$

$$\begin{aligned}\text{Volume Consumed} &= \text{New Volume} - \text{Initial Volume} \\ &= 43 \text{ L} - 36 \text{ L} = 7 \text{ L}\end{aligned}$$

The amount of water ingested by the patient was not likely this high because she probably lost significant amount of salt as sweat while under the influence of ecstasy. Her signs and symptoms are due to the brain swelling caused by hypotonicity.

15. The answer is a. (*Ganong, pp 87–88. Kasper et al., pp 842–844.*) Botulinum toxin inhibits the release of acetylcholine from α -motoneurons by blocking one of the proteins responsible for the fusion of the synaptic channel with the presynaptic membrane. Botulinum toxin also inhibits the release of acetylcholine from the neurons of the autonomic nervous system. Botulinum and tetanus toxin are released from the same class of bacteria (*Clostridium*). Tetanus toxin produces an increase in skeletal muscle contraction by blocking the release of inhibitory neurotransmitter from spinal interneurons.

16. The answer is e. (*Ganong, pp 371–372, 636.*) Evidence is accumulating that the transcription factor, nuclear factor- κ B (NF- κ B), plays a key role in the inflammatory response. NF- κ B is a heterodimer that normally exists in the cytoplasm of cells bound to I κ B α , which renders it inactive. Stimuli such as viruses, cytokines, and oxidants separate NF- κ B from I κ B α , and NF- κ B moves to the nucleus where it binds to DNA of the genes for numerous inflammatory mediators, resulting in their increased production and secretion. Glucocorticoids inhibit the activation of NF- κ B by increasing the

production of $I\kappa B\alpha$, and this is probably the main basis of their anti-inflammatory action. The anti-inflammatory effects of exogenous glucocorticoids are due to their ability to decrease capillary membrane permeability and probably also to its ability to stabilize lysosomal membranes and decrease the formation of bradykinin. Glucocorticoids inhibit the enzyme phospholipase A₂; this decreases the release of arachidonic acid and the variety of substances produced from it, such as leukotrienes, prostaglandins, thromboxanes, and prostacyclin. Cortisol owes its fever-reducing action to the hormone's ability to decrease the release of pyrogen (interleukin 1) from granulocytes. However, only in massive doses will the hormone achieve the effects described. Endogenous cortisol does not exert a significant anti-inflammatory action.

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General Principles: Multisystem Processes

Questions

17. A 62-year-old male presents to the emergency room with an acute onset of aphasia and hemiparesis. A computed tomography (CT) scan reveals an increase in intracranial fluid. Which of the following solutions will be most effective in reducing intracranial pressure following a large hemispheric stroke?

- a. 150 mmol sodium chloride
- b. 250 mmol glycerol
- c. 250 mmol glucose
- d. 350 mmol urea
- e. 350 mmol mannitol

18. An 82-year-old woman is brought to the emergency room complaining of nausea, vomiting, muscle cramps, and generalized weakness. Laboratory analysis reveals significant hyperkalemia. Elevations of extracellular potassium ion concentration will have which of the following effects on nerve membranes?

- a. The membrane potential will become more negative
- b. The sodium conductance will increase
- c. The potassium conductance will increase
- d. The membrane will become more excitable
- e. The $\text{Na}^+ \text{-K}^+$ pump will become inactivated

- 19.** A 65-year-old male on digoxin for atrial fibrillation is told by his physician to get a blood analysis for K^+ on a regular basis because hypokalemia will increase his risk of digitalis toxicity. In the presence of hypokalemia, the risk of digitalis toxicity is increased because of which of the following?
- The membranes of cardiac muscle cells are hypopolarized
 - The intracellular potassium concentration of red blood cells is increased
 - The excitability of nerve cells is increased
 - Inhibition of the Na^+-K^+ pump is increased
 - The amplitude of nerve cell action potentials is increased
- 20.** A 19-year-old man is admitted to the hospital after ingesting antifreeze containing ethylene glycol. His blood test reveals the following: $Na^+ = 135$ mEq/L, $K^+ = 5$ mEq/L, $Cl^- = 100$ mEq/L, $HCO_3^- = 5$ mEq/L, BUN = 25 mg/dL, Cr = 2.2 mg/dL. Which of the following is the size of his anion gap?
- 5 mEq/L
 - 10 mEq/L
 - 15 mEq/L
 - 25 mEq/L
 - 30 mEq/L
- 21.** Which of the following statements about the uptake of triglycerides into adipose tissue from plasma lipoproteins is correct?
- It is regulated by the activity of lipoprotein lipase
 - It is increased by catecholamines
 - It is decreased by glucose
 - It is decreased by insulin
 - It requires receptor-mediated endocytosis
- 22.** A medical student presents to the emergency room with a 2-day history of severe vomiting and orthostatic hypotension. Which of the following metabolic abnormalities are most likely present in this patient?
- Hypokalemia, hypochloremia, and metabolic acidosis
 - Hypokalemia, hypochloremia, and metabolic alkalosis
 - Hyperkalemia, hyperchloremia, and metabolic alkalosis
 - Normal serum electrolytes and metabolic acidosis
 - Normal serum electrolytes and metabolic alkalosis

23. A 58-year-old male is transported to the Emergency Department for impaired breathing. Arterial blood gases show a pH = 7.35, PaCO₂ = 60 mm Hg, and [HCO₃⁻] = 31 mEq/L. Which of the following is the most likely differential diagnosis of the patient?

- a. Narcotic overdose
- b. Chronic obstructive pulmonary disease (COPD)
- c. Cardiac and respiratory arrest
- d. Anxiety-induced hyperventilation
- e. Diabetic ketoacidosis

24. Which of the following is associated with an increased anion gap?

- a. Diarrhea
- b. Chronic obstructive pulmonary disease
- c. Diabetic coma
- d. Myasthenia gravis
- e. Nasogastric suctioning

25. A 10-month-old well-nourished, lethargic infant is brought to the Emergency Department with a history of vomiting and profuse watery diarrhea for 5 days. His mother reports that he has also had a marked decrease in urine output. Serum sodium is 190 mmol/L; urine sodium is 18 mmol/L. The infant is treated for gastroenteritis and a saline drip is started. After 3 days, he appears well and alert and his diarrhea and vomiting have subsided. However, he still has hypernatremia, polyuria, and low urine sodium. His persistent clinical signs are most likely due to which of the following?

- a. Hyperaldosteronism
- b. Diabetes insipidus
- c. Diabetes mellitus
- d. Renal failure
- e. Hypothyroidism

26. A 28-year-old man presents after 5 days of foul-smelling diarrhea and flatulence. He reports having been on a hiking and camping trip the previous week. Stool cultures confirm an infection with the protozoan *Giardia lamblia*. Which of the following arterial blood gases would be expected in this patient?

- a. pH = 7.22; $\text{Paco}_2 = 30 \text{ mmHg}$, $[\text{HCO}_3^-] = 15 \text{ mEq/L}$, Anion Gap = 12 mEq/L
- b. pH = 7.22; $\text{Paco}_2 = 30 \text{ mmHg}$, $[\text{HCO}_3^-] = 15 \text{ mEq/L}$, Anion Gap = 25 mEq/L
- c. pH = 7.22; $\text{Paco}_2 = 60 \text{ mmHg}$, $[\text{HCO}_3^-] = 26 \text{ mEq/L}$, Anion Gap = 12 mEq/L
- d. pH = 7.51; $\text{Paco}_2 = 49 \text{ mmHg}$, $[\text{HCO}_3^-] = 38 \text{ mEq/L}$, Anion Gap = 12 mEq/L
- e. pH = 7.51; $\text{Paco}_2 = 25 \text{ mmHg}$, $[\text{HCO}_3^-] = 22 \text{ mEq/L}$, Anion Gap = 22 mEq/L

27. A 48-year old woman suffering from a severe tension headache is brought to the Emergency Department after her husband discovered her unresponsive and barely breathing when he stopped at home from work during his lunch hour. A bottle of Vicodin was found next to the bathroom sink. Which of the following arterial blood gases are most consistent with her clinical presentation?

- a. pH = 7.27; $\text{Paco}_2 = 60 \text{ mmHg}$, $[\text{HCO}_3^-] = 26 \text{ mEq/L}$, Anion Gap = 12 mEq/L
- b. pH = 7.02; $\text{Paco}_2 = 60 \text{ mmHg}$, $[\text{HCO}_3^-] = 15 \text{ mEq/L}$, Anion Gap = 12 mEq/L
- c. pH = 7.10; $\text{Paco}_2 = 20 \text{ mmHg}$, $[\text{HCO}_3^-] = 6 \text{ mEq/L}$, Anion Gap = 30 mEq/L
- d. pH = 7.51; $\text{Paco}_2 = 49 \text{ mmHg}$, $[\text{HCO}_3^-] = 38 \text{ mEq/L}$, Anion Gap = 14 mEq/L
- e. pH = 7.40; $\text{Paco}_2 = 20 \text{ mmHg}$, $[\text{HCO}_3^-] = 10 \text{ mEq/L}$, Anion Gap = 26 mEq/L

28. A 22-year-old male is planning on running a marathon when he goes to visit his brother in Denver. Because of the high altitude, he decides to leave for Denver early to train for the event. While in Denver, he visits an urgent care center after experiencing extensive spasms and cramping in his calf muscles while running, symptoms that he seldom experienced at sea level. Laboratory analysis reveals hypocalcemia. Which of the following is the reason high altitude predisposes to tetany?

- a. Low oxygen tension causes a decrease in skeletal muscle blood flow
- b. Low oxygen tension causes an increase in skeletal muscle lactate
- c. Plasma protein concentration is reduced by hypoxia
- d. Stimulation of Na^+,K^+ -ATPase reduces the plasma concentration of free ionized Ca^{2+}
- e. Plasma proteins are more ionized in the presence of hyperventilation-induced alkalosis, providing more protein anion to bind with Ca^{2+}

29. A 40-year-old woman is admitted to the intensive care unit with hypotension and shortness of breath. Arterial blood gases reveal: PaCO_2 , 10 mmHg, and bicarbonate, 12 mEq/L. Which of the following is her acid-base status?

- a. Normal
- b. Respiratory acidosis
- c. Metabolic acidosis
- d. Respiratory alkalosis
- e. Metabolic alkalosis

30. A diabetic patient presents with a blood glucose concentration of 600 mEq/L. Which of the following values would likely be above normal in hyperglycemia?

- a. Arterial pH
- b. Alveolar PCO_2
- c. Urine flow
- d. Intracellular volume
- e. Plasma sodium concentration

31. A 72-year-old female presents to the Emergency Department with generalized weakness. An ECG reveals peaked T waves. Which of the following electrolyte disturbances should be corrected to return the ECG to normal?

- a. Hyperkalemia
- b. Hypokalemia
- c. Hypercalcemia
- d. Hypocalcemia
- e. Hypermagnesemia

32. A 49-year-old man is brought to the Emergency Department with severe gastric pain after ingesting a large quantity of unknown fluid. His blood pressure is 90/60 mmHg and his pulse rate is 106 beats/min. Laboratory results show the following:

$$\begin{aligned}\text{pH} &= 7.03 \\ \text{bicarbonate} &= 12 \text{ mEq/L} \\ \text{potassium} &= 6.3 \text{ mEq/L} \\ \text{anion gap} &= 32 \text{ mEq/L} \\ \text{ionized calcium} &= 1 \text{ mM}\end{aligned}$$

The high anion gap is most likely caused by an elevated plasma concentration of which of the following?

- a. Hydrogen ion
- b. Potassium
- c. Chloride
- d. Lactate
- e. Citrate

33. A 54-year-old man went out to shovel the snow so that he could drive his wife to her doctor's appointment. After getting some chest pain and feeling short of breath, he thought he better go in and rest a while before he finished shoveling. When his wife came downstairs, she found him sitting with his head down on the morning paper at the kitchen table. When the ambulance arrived, he was still responsive, but he had a cardiac and respiratory arrest en route to the hospital. Which of the following arterial blood gases would be expected given these findings?

- a. pH = 7.22; $\text{Paco}_2 = 60 \text{ mmHg}$, $[\text{HCO}_3^-] = 26 \text{ mEq/L}$, Anion Gap = 12 mEq/L
- b. pH = 7.05; $\text{Paco}_2 = 60 \text{ mmHg}$, $[\text{HCO}_3^-] = 15 \text{ mEq/L}$, Anion Gap = 25 mEq/L
- c. pH = 7.10; $\text{Paco}_2 = 20 \text{ mmHg}$, $[\text{HCO}_3^-] = 6 \text{ mEq/L}$, Anion Gap = 30 mEq/L
- d. pH = 7.51; $\text{Paco}_2 = 49 \text{ mmHg}$, $[\text{HCO}_3^-] = 38 \text{ mEq/L}$, Anion Gap = 14 mEq/L
- e. pH = 7.40; $\text{Paco}_2 = 20 \text{ mmHg}$, $[\text{HCO}_3^-] = 10 \text{ mEq/L}$, Anion Gap = 26 mEq/L

34. A 56-year-old man is admitted to the Emergency Department after ingesting a large dose of aspirin, most of which is still within the vascular system. The patient is diaphoretic and has the following blood gases: pH of 7.45, PCO_2 of 17 mmHg, and $[\text{HCO}_3^-]$ of 13 mmol/L. Aspirin has a pK of 3.5 and when it is in the unionized state will rapidly cross the blood-brain barrier. Which of the following treatment options would be most deleterious to this patient?

- a. Gastric lavage
- b. Intravenous glucose
- c. Decreasing alveolar ventilation
- d. Increasing fluid volume
- e. Administering activated charcoal

35. A child makes a blue slush drink using a container of windshield wiper fluid in the garage. The arterial blood gases shown below indicate that the child has which of the following?

$$\begin{aligned}\text{pH} &= 7.32 \\ \text{Paco}_2 &= 28 \text{ mmHg} \\ [\text{HCO}_3^-] &= 16 \text{ mEq/L} \\ \text{Anion gap} &= 28 \text{ mEq/L}\end{aligned}$$

- a. Respiratory alkalosis
- b. Respiratory acidosis
- c. Metabolic alkalosis
- d. Metabolic acidosis
- e. Respiratory and metabolic acidosis

36. A patient with Guillain-Barré syndrome develops paralysis of the respiratory muscles that increases Paco_2 from 40 to 60 mmHg and increases the concentration of hydrogen ion in arterial blood from 40 mEq/L (pH 7.4) to 50 mEq/L (pH 7.3). As a result, which of the following would happen?

- a. The plasma $[\text{HCO}_3^-]$ would decrease
- b. The pH of the urine would increase
- c. The amount of ammonium excreted in the urine would decrease
- d. The central chemoreceptors would be stimulated
- e. The peripheral chemoreceptors would be inhibited

37. A 65-year-old man is admitted to the hospital because of profound muscle weakness. His blood glucose is 485 mg/dL and his serum potassium is 8.2 mmol/L. He is diagnosed with diabetic ketoacidosis and hyperkalemia. In addition to the serum glucose and potassium, which of the following laboratory values would most likely be above normal?

- a. Serum $[\text{HCO}_3^-]$
- b. Anion gap
- c. Arterial PCO_2
- d. Plasma pH
- e. Blood volume

38. A patient presents with muscle weakness, cramping, irritability, and neuromuscular excitability. Electrolytes reveal hypokalemia and a higher-than-normal plasma bicarbonate concentration. Which of the following conditions is a cause of metabolic alkalosis?

- a. Hypoxemia
- b. Renal failure
- c. Diuretic therapy
- d. Hypoaldosteronism
- e. Diarrhea

39. A 23-year-old girl is admitted to the hospital with a 3-month history of malaise and generalized muscle cramps. Laboratory results reveal: serum sodium of 144 mmol/L, serum potassium of 2.0 mmol/L, serum bicarbonate of 40 mmol/L, and arterial pH of 7.5. Which of the following is the most likely cause of this patient's hypokalemic alkalemia?

- a. Hyperaldosteronism
- b. Hyperventilation
- c. Persistent diarrhea
- d. Renal failure
- e. Diabetes

40. A 20-year-old woman goes to the Emergency Department due to symptoms of palpitations, dizziness, sweating, and paresthesia that have not resolved over the past several days. Her history suggests an anxiety disorder, and blood gases and electrolytes are ordered. Her doctor prescribes a benzodiazepine after a positron emission tomography (PET) scan shows increased perfusion in the anterior end of each temporal lobe. Which of the following blood gases would be expected at the time of admission of this patient?

- a. pH = 7.51; $\text{Paco}_2 = 49 \text{ mmHg}$, $[\text{HCO}_3^-] = 38 \text{ mEq/L}$, Anion Gap = 12 mEq/L
- b. pH = 7.44; $\text{Paco}_2 = 25 \text{ mmHg}$, $[\text{HCO}_3^-] = 16 \text{ mEq/L}$, Anion Gap = 12 mEq/L
- c. pH = 7.28; $\text{Paco}_2 = 60 \text{ mmHg}$, $[\text{HCO}_3^-] = 26 \text{ mEq/L}$, Anion Gap = 12 mEq/L
- d. pH = 7.28; $\text{Paco}_2 = 20 \text{ mmHg}$, $[\text{HCO}_3^-] = 16 \text{ mEq/L}$, Anion Gap = 25 mEq/L
- e. pH = 7.51; $\text{Paco}_2 = 20 \text{ mmHg}$, $[\text{HCO}_3^-] = 24 \text{ mEq/L}$, Anion Gap = 12 mEq/L

- 41.** Most of the volatile acid entering the blood is buffered by which of the following?
- Bicarbonate
 - Plasma proteins
 - Hemoglobin
 - Phosphates
 - Lactate
- 42.** Metabolic acidosis is caused by which of the following?
- Hypoventilation
 - Hypovolemia
 - Hypokalemia
 - Hypocalcemia
 - Hypoaldosteronism
- 43.** An 18-year-old male presents with symptoms of vitamin B₁₂ deficiency. Further diagnostic tests reveal that he has pernicious anemia. The underlying problem in pernicious anemia is which of the following?
- Iron deficiency
 - Cobalt deficiency
 - Inadequate dietary intake of cyanocobalamin
 - Malabsorption of vitamin B₁₂ in gastrectomized patients due to removal of intrinsic-factor secreting tissue
 - Autoimmune destruction of parietal cells in the gastric mucosa
- 44.** A 65-year-old man with Type I diabetes presents to the Emergency Department with impaired mental status and generalized muscle weakness. Laboratory tests reveal a blood glucose of 500 mg/dL, a potassium concentration of 8.3 mmol/L, an anion gap of 22 mmol/L, a PCO₂ of 50 mmHg, and a bicarbonate of 14 mmol/L. The patient's blood values are atypical in which of the following ways?
- Hyperglycemia
 - Hyperkalemia
 - High anion gap
 - Hypercapnia
 - High creatinine

45. A patient is brought to the Emergency Department with weakness, confusion, and shortness of breath. The EKG reveals QRS widening and flattened P waves typical of serum potassium concentrations exceeding 7.5 mEq/L. Hyperkalemia may be observed in patients with which of the following?

- a. Volume depletion
- b. Diuretic therapy
- c. Administration of insulin
- d. Metabolic alkalosis
- e. Stimulation of adrenal medulla

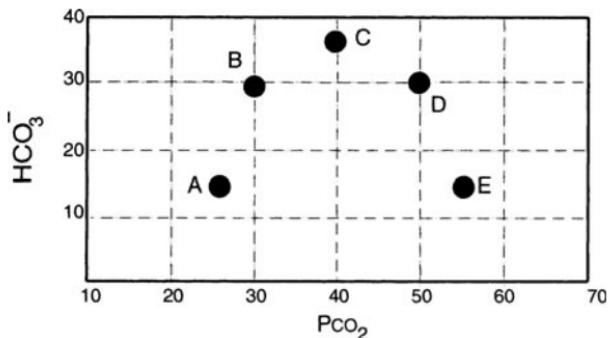
46. A patient comes into the Emergency Department exhibiting signs of hyperkalemia. The extracellular potassium of a hyperkalemic patient can be decreased by administering which of the following drugs?

- a. Atropine
- b. Epinephrine
- c. Glucagon
- d. Lactic acid
- e. Isotonic saline

47. Which of the following blood gas values is consistent with metabolic acidosis?

Paco ₂ (mm Hg)	[HCO ₃ ⁻] (mM)	pH
a. 25	30	7.7
b. 35	20	7.3
c. 40	25	7.4
d. 50	30	7.1
e. 60	20	7.1

48. Which of the following points on the graph below represents the blood gas values obtained from a patient who has ascended to high altitude?



- a. A
- b. B
- c. C
- d. D
- e. E

49. Hyponatremia will result from an excess secretion of which of the following?

- a. Vasopressin (AVP or ADH)
- b. Atrial natriuretic hormone
- c. Norepinephrine
- d. Insulin
- e. Aldosterone

50. A 39-year-old man presents to the emergency room complaining of tingling in his hands and muscle twitching. On admission, the patient is alert and stable, with an initial examination remarkable only for carpopedal spasm. Which of the following blood gas values will most likely be observed in this patient?

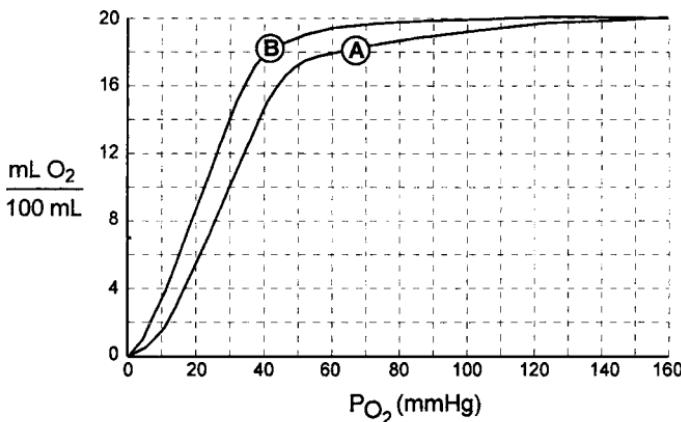
PaCO ₂ (mmHg)	[HCO ₃ ⁻] (mM)
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- a. 50 40
- b. 60 20
- c. 40 30
- d. 30 15
- e. 20 20

- 51.** The daily production of hydrogen ions from CO_2 is primarily buffered by which of the following?
- Extracellular bicarbonate
 - Red blood cell bicarbonate
 - Red blood cell hemoglobin
 - Plasma proteins
 - Plasma phosphate
- 52.** A 27-year-old male presents to the Emergency Department with asthmatic bronchitis that started 3 days ago. He is given an aerosolized bronchodilator treatment, which relieves his symptoms. An arterial blood gas analysis following bronchodilator therapy reveals a nonanion gap metabolic acidosis, which can be attributed to which of the following?
- A laboratory error
 - An increase in citrate from the vehicle used in the bronchodilator preparation
 - An increase in lactic acid secondary to the hypoxemia that existed prior to treatment
 - A decrease in plasma bicarbonate due to renal compensation for the respiratory alkalosis that existed prior to treatment
 - A decrease in plasma chloride concentration resulting from the chloride shift after the treatment restored alveolar ventilation
- 53.** A group of students in the Wilderness Medicine Club left for a Spring Break Rocky Mountain hiking trip right after their Organ Systems exam. They arrived at their lodge in Denver by 2 p.m. Mountain time, and then drove to the base camp (10,000 ft), where they camped for the night. The next day, several of the students were experiencing mental and muscle fatigue, and complained of headaches, nausea, and dyspnea, so the guide decided to acclimate at 10,000 ft. for another day. Three of the students grew impatient and announced that they were going to climb to Mt. Elbert, the highest mountain in Colorado (14,400 ft altitude, barometric pressure = 447 mmHg). About 3 hours later (less than 24 hours since they first arrived in Denver), one of the students returned in a panic to get medical help because his friends were disoriented, ataxic, short of breath, and vomiting. The guide called for the search and rescue helicopter, which located the hikers and took them to the nearest Emergency Department. A diagnostic work-up would likely show a decrease in which of the following values?
- pH
 - PaCO_2

- c. Pulmonary vascular resistance
- d. 2,3-Bisphosphoglycerate
- e. Erythropoietin

54. In the diagram below, which of the following conditions is most likely to shift the oxyhemoglobin curve from B to A?



- a. Hypothermia
- b. Hyperventilation
- c. Carbon monoxide poisoning
- d. Transfusion with banked blood
- e. Exercise

55. A pregnant woman develops placental insufficiency at 27-weeks gestation requiring a preterm caesarian section. To determine how soon the delivery can be done, a sample of amniotic fluid is aspirated. Measurement of the lecithin-sphingomyelin (L-S) ratio in amniotic fluid assesses which of the following?

- a. Fetal brain development
- b. Fetal kidney development
- c. Fetal adrenal function
- d. Fetal lung maturity
- e. The placenta's ability to oxygenate the fetus

56. A fourth year medical student from New Orleans enrolls in a month-long clinical elective in Denver, Colorado. Which of the following values will return toward normal after the student has acclimatized to high altitude?

- a. Arterial oxygen tension
- b. Plasma bicarbonate concentration
- c. Hemoglobin concentration
- d. Alveolar ventilation
- e. Cardiac output

57. A patient's arterial blood gas reveals a decrease in Paco_2 . Hyperventilation normally occurs during which of the following?

- a. Exercise
- b. Sleep
- c. Pregnancy
- d. Morphine administration
- e. Metabolic alkalosis

58. A patient waiting to see his doctor is sitting in a room in which the air temperature is 21°C (70°F), wearing only a thin gown that is open in the back. The majority of his body heat will be lost by which of the following?

- a. Radiation and conduction
- b. Vaporization of sweat
- c. Breathing
- d. Horripilation
- e. Cutaneous vasoconstriction

59. A 69-year-old alcoholic came into the Emergency Department after he blacked out and fell, hitting his head on the kitchen floor. Measurement of serum Na^+ , glucose, BUN, and osmolality indicate an osmolar gap between calculated and measured osmolarity. Which of the following changes in arterial blood gas values are consistent with a presentation of ethanol-induced coma?

	pH	Paco_2	PaO_2
A.	↑	↑	↑
B.	↓	↑	↑
C.	↑	↑	↓
D.	↓	↓	↑
E.	↑	↓	↓

- a. A
- b. B
- c. C
- d. D
- e. E

60. At concentrations present in the diet, which of the following vitamins is absorbed primarily by diffusion?

- a. Vitamin C
- b. Folate
- c. Vitamin D
- d. Niacin
- e. Vitamin B₁₂

61. A 27-year-old patient with insulin-dependent diabetes mellitus told his roommate that he could not afford to refill his insulin prescription until he got a paycheck. The roommate offered to get it for him, but the patient assured him he could wait until after the weekend. When the roommate returned from a weekend trip on Sunday evening, he found the man unresponsive on the couch, and called 9-1-1. Which of the following arterial blood gases taken in the Emergency Department would be expected in diabetic coma?

- a. pH = 7.22; PacO₂ = 60 mmHg, [HCO₃⁻] = 26 mEq/L, Anion Gap = 12 mEq/L
- b. pH = 7.02; PacO₂ = 60 mmHg, [HCO₃⁻] = 15 mEq/L, Anion Gap = 12 mEq/L
- c. pH = 7.10; PacO₂ = 20 mmHg, [HCO₃⁻] = 6 mEq/L, Anion Gap = 30 mEq/L
- d. pH = 7.51; PacO₂ = 49 mmHg, [HCO₃⁻] = 38 mEq/L, Anion Gap = 14 mEq/L
- e. pH = 7.40; PacO₂ = 20 mmHg, [HCO₃⁻] = 10 mEq/L, Anion Gap = 26 mEq/L

General Principles: Multisystem Processes

Answers

17. The answer is e. (*Ganong*, pp 6, 718–719. *Kasper et al.*, pp 255, 2374.) Rapid removal of fluid from the brain can be produced by the administration of a fluid that increases the osmotic pressure difference between the brain and the cerebral vessels. The appropriate solution must have a higher-than-normal osmolarity (that is, greater than 300 mOsm) and be composed of a solute that is impermeable to the blood-brain barrier. Of the solutions listed, only urea and mannitol are hyperosmotic and of these, only mannitol is impermeable to the blood-brain barrier.

18. The answer is c. (*Ganong*, p 81. *Kasper et al.*, pp 261–265, 1375. *Stead et al.*, pp 231–232.) An increase in extracellular K⁺ makes the membrane potential more positive. Depolarizing the membrane opens K⁺ channels causing an increase in membrane conductance. Prolonged depolarization, whether caused by an increase in extracellular K⁺ or by an action potential, inactivates Na⁺ channels, which decreases the excitability of the nerve membrane. The activity of the Na⁺-K⁺ pump is reduced in hypokalemia, not hyperkalemia.

19. The answer is d. (*Stead et al.*, p 230.) Digoxin is used to treat atrial fibrillation because it increases vagal tone and to treat congestive heart failure because it increases cardiac contractility. Digoxin produces its physiological effects by blocking the K⁺ binding site on the Na⁺-K⁺ pump. When the extracellular K⁺ concentration is low, digoxin produces a greater inhibition of the Na⁺-K⁺ pump. Hypokalemia results in hyperpolarization of the cardiac membrane.

20. The answer is e. (*Ganong*, pp 338, 563–564. *Kasper et al.*, pp 261–263. *Stead et al.*, pp 231–232.) The anion gap is equal to the difference between the plasma concentration of sodium, the major cation in the plasma, and the sum of the concentrations of plasma chloride and bicarbonate, the major measured anions in the plasma.

$$\begin{aligned}\text{Anion gap} &= [\text{Na}^+] - ([\text{Cl}^-] + [\text{HCO}_3^-]) \\ &= 135 \text{ mEq/L} - (100 \text{ mEq/L} + 5 \text{ mEq/L}) \\ &= 30 \text{ mEq/L}\end{aligned}$$

The normal anion gap is from 8 to 16 mEq/L. The anion gap is elevated when the concentration of unmeasured anions in the plasma increases. With antifreeze ingestion, the high anion gap metabolic acidosis is caused by the accumulation of the metabolic byproducts of ethylene glycol, namely, oxalic and glycolic acid.

21. The answer is a. (*Ganong*, pp 303–305, 342.) Triglyceride uptake into adipocytes is regulated by lipoprotein lipase. The uptake of triglycerides into adipose tissue and other tissues from plasma lipoproteins requires hydrolysis of triglyceride to fatty acids and glycerol by an enzyme bound to the endothelial surface, lipoprotein lipase. The activity of this enzyme varies in reciprocal fashion with that of cytoplasmic hormone-sensitive lipase; that is, its activity is enhanced by insulin and glucose and decreased by catecholamines. Lipoprotein lipase is present in nearly every tissue and acts at the capillary surface as it does in adipose tissue. Receptor-mediated endocytosis is important in the turnover of the protein portion of plasma lipoproteins.

22. The answer is b. (*Ganong*, pp 491–492, 723–724, 729–730, 734–736. *Stead et al.*, pp 221, 224–225, 230.) Analysis of serum electrolytes reveals low potassium (hypokalemia), low chloride (hypochloremia), and metabolic alkalosis. These abnormalities arise from two sources. First, gastric juice contains potassium and chloride in concentrations higher than found in the plasma. Loss of gastric juice through vomiting or drainage leads to depletion of these electrolytes from the plasma. Second, the metabolic abnormalities are exacerbated by the patient's dehydration. Contraction of the vascular volume leads to orthostatic hypotension and the activation of renal mechanisms important for conserving volume. As a result, water, sodium, and bicarbonate are reabsorbed at the expense of increased potassium and hydrogen excretion.

23. The answer is b. (*Ganong*, pp 734–738. *Levitzky*, pp 171–173, 176–179. *Stead et al.*, pp 221, 223–225, 262–263.) The interpretation of the arterial blood gas is compensated respiratory acidosis. The primary disturbance is an elevation in arterial PCO_2 due to alveolar hypoventilation from the impaired mechanics of breathing in COPD. The hypercapnia lowers the

ratio of HCO_3^- to dissolved CO_2 in the plasma, and thus lowers the pH according to the Henderson-Hasselbalch equation. To compensate for the acidosis, the kidneys increase the net excretion of H^+ , which increases the plasma $[\text{HCO}_3^-]$, returning the pH back into the normal range.

24. The answer is c. (*Ganong, pp 735–736. Levitzky, pp 179–180. Stead et al., p 222.*) The anion gap is equal to the difference between the plasma concentration of sodium, the major cation in the plasma, and the sum of the concentrations of plasma chloride and bicarbonate, the major measured anions in the plasma.

$$\text{Anion gap} = [\text{Na}^+] - ([\text{Cl}^-] + [\text{HCO}_3^-])$$

The normal plasma concentrations of Na^+ , Cl^- , and HCO_3^- are 142, 105, and 24 mEq/L, respectively. The normal anion gap is about 12 mEq/L, and is comprised of minor ions, such as lactate, phosphate, and sulfate. The anion gap is useful in differentiating the causes the metabolic acidosis. In normal anion gap metabolic acidosis, the decline in plasma bicarbonate ion is replaced by an increase in plasma chloride concentration with the concentration of unmeasured minor anions remaining normal, such as occurs with renal or gastrointestinal (GI) losses (e.g., diarrhea). High anion gap metabolic acidosis results from an increase in unmeasured organic anions, such as occurs in the lactic acidosis accompanying tissue hypoxia, the accumulation of ketoacids in diabetes and its resultant coma, or by an increase in organic anions or their metabolic byproducts produced from such ingested toxins as ethylene glycol, methanol, and salicylates. COPD and myasthenia gravis are causes of respiratory acidosis. Nasogastric suctioning causes metabolic alkalosis.

25. The answer is b. (*Ganong, pp 247, 713. Stead et al., pp 76–77.*) Diabetes insipidus (DI) is a disease caused by decreased release of ADH from the posterior pituitary or the inability of the kidney to response to ADH. It is characterized by high serum Na^+ , polyuria, and low urine osmolarity. The low urine osmolarity in the presence of the volume depletion points to diabetes insipidus. The diagnosis is confirmed by the persistent polyuria and low urine sodium after the baby's volume is returned to normal. DI is either central (idiopathic, traumatic, systemic) or nephrogenic in etiology. Nephrogenic DI can either be acquired (renal disease, drugs, hypokalemia, hypercalcemia) or familial.

26. The answer is a. (Stead *et al.*, pp 139–141, 221–222.) Diarrhea causes a loss of bicarbonate leading to metabolic acidosis, as evidenced by a reduction in plasma bicarbonate and a reduction in pH, with a normal anion gap. Respiratory compensation as a result of peripheral chemoreceptor stimulation by the increased arterial $[H^+]$ causes the arterial $Paco_2$ to be decreased.

27. The answer is a. (Ganong, pp 734–738. Stead *et al.*, pp 221, 223–225, 262–263, 321.) Narcotics used for the treatment of severe headache may depress the medullary respiratory center causing alveolar hypoventilation, as evidenced by an elevation in arterial Pco_2 . The hypercapnia lowers the ratio of HCO_3^- to dissolved CO_2 in the plasma, and thus lowers the pH according to the Henderson-Hasselbalch equation. Renal compensation for respiratory acidosis takes hours to start and days to be complete, and thus there has not been sufficient time for the body's compensatory mechanisms to take effect and for plasma $[HCO_3^-]$ to rise. Thus, the scenario is most consistent with an acute, uncompensated respiratory acidosis. The slight rise in plasma bicarbonate concentration can be attributed to extracellular buffering of the excess H^+ .

28. The answer is e. (Ganong, pp 35, 59, 382, 692, 736. Kasper *et al.*, pp 138, 270. Levitzky, pp 172–173. Stead *et al.*, pp 232–233.) A decrease in extracellular Ca^{2+} exerts a net excitatory effect on nerve and muscle cells, leading to hypocalcemic tetany, which is characterized by extensive spasms of skeletal muscle. Symptoms of tetany appear at much higher total calcium levels when pH is high, which occurs at high altitude due to hyperventilation. Plasma proteins are more ionized in an alkalotic environment, providing more protein anion to bind with Ca^{2+} . The extent of Ca^{2+} binding by plasma proteins is proportionate to the plasma protein level, so a decreased level of plasma proteins would decrease binding and increase the extracellular Ca^{2+} . Low oxygen tension leads to peripheral vasodilation and increased blood flow to skeletal muscle. An increase in lactate would lower pH. In heart but not skeletal muscle, Na^+-K^+ ATPase indirectly affects Ca^{2+} transport via an antiport in the cardiac muscle membranes which normally exchanges intracellular Ca^{2+} for extracellular Na^+ .

29. The answer is d. (Ganong, pp 732–734. Kasper *et al.*, pp 263–264, 270–271. Levitzky, pp 167–169, 172–173.) The arterial pH can be calculated using the Henderson-Hasselbalch equation.

$$\text{pH} = 6.1 + \log [\text{HCO}_3^-] / (\text{Paco}_2 \times 0.03 \text{ mmol/L/mmHg})$$

$$\text{pH} = 6.1 + \log 12 \text{ mmol/L} / (10 \text{ mmHg} \times 0.03 \text{ mmol/L/mmHg})$$

$$\text{pH} = 6.1 + \log 40 = 6.1 + 1.6 = 7.7$$

The patient has an alkalemia due to hyperventilation and therefore is suffering from a respiratory alkalosis. In an acute respiratory alkalosis, the bicarbonate typically decreases by 2 mM for each 10 mmHg decrease in PCO_2 ; in a chronic respiratory alkalosis, the bicarbonate typically decreases 4 mM for each 10 mmHg decrease in PCO_2 . In this case the PCO_2 has decreased by 30 mmHg. Because bicarbonate has decreased by 12 mM, the diagnosis is consistent with a chronic respiratory alkalosis.

30. The answer is c. (*Ganong, pp 340–343.*) The increase in blood glucose concentration will result in a filtered load of glucose in excess of what the proximal tubule is able to absorb. As a result, glucose will remain in the filtrate, where it will act as an osmotic diuretic increasing urinary flow. The excess blood glucose will cause water to shift from the intracellular compartment to the extracellular compartment, causing a decrease in intracellular volume and, by dilution, a decrease in plasma sodium concentration. The accompanying increase in ketoacid production will result in a metabolic acidosis (low pH) and a compensatory increase in alveolar ventilation, lowering alveolar PCO_2 .

31. The answer is a. (*Ganong, pp 563–564. Stead et al., pp 231–232.*) Hyperkalemia can be a life-threatening emergency. Normal plasma $[K^+]$ is 3.5 to 5 mEq/L. Mild hyperkalemia is 5 to 5.5 mEq/L. Severe hyperkalemia $[K^+]$ is 7 mEq/L. As the plasma K^+ level rises, the first change on the electrocardiogram is the appearance of tall, peaked T-waves. The peaked T waves are produced by an accelerated repolarization of ventricular muscle. Potentially fatal hyperkalemia can be treated by administering insulin (along with glucose), which helps K^+ transport into cells and therefore lowers extracellular K^+ , but the effect is temporary. Calcium administration produces cardiac membrane stabilization within minutes, but is contraindicated in patients on digoxin. Removal of potassium from the body can be accomplished with dialysis or with a cation exchange resin, such as Kayexalate, but takes hours to work.

32. The answer is e. (*Ganong, pp 735–736. Kasper et al., pp 263–266. Levitzky, pp 179–180. Stead et al., p 222.*) The anion gap is the difference

between the concentration of Na^+ and the concentration of the major plasma anions, Cl^- and HCO_3^- . The minor ions, lactate, phosphate, and sulfate, comprise the normal anion gap. Increases in lactate or citrate could have produced the increased anion gap. The low calcium favors citrate as the cause of the anion gap because citrate complexes with calcium. The low calcium inhibits contraction of vascular smooth muscle, accounting for the low blood pressure. The high serum potassium concentration results from the acidosis, which causes a shift of K^+ from the intracellular to the extracellular space.

33. The answer is b. (*Ganong, pp 637, 692, 731, 734. Kasper et al., pp 264–266, 269–270. Levitzky, pp 171–175, 180–183. Stead et al., pp 222–223.*) A cardiac and respiratory arrest generates a mixed acid-base disorder, with the coexistence of two primary acid-base disorders, namely respiratory and metabolic acidosis. The respiratory acidosis is due to the alveolar hypoventilation, which increases arterial PCO_2 and decreases pH. Cardiac arrest decreases cardiac output and thus oxygen delivery to the tissues, resulting in stagnant (hypoperfusion) hypoxia. The resultant increase in anaerobic glycolysis produces large amounts of lactic acid, which lowers plasma $[\text{HCO}_3^-]$ and decreases pH. The normal anion gap of about 12 mEq/L, calculated as the difference between the concentration of Na^+ and the concentration of the major plasma anions, $\text{Cl}^- + \text{HCO}_3^-$, increases due to the increase in the unmeasured organic anion, lactate. Because both independently existing disorders cause acidosis, mixed respiratory and metabolic acidosis may cause dangerously low pH levels and a poor outcome.

34. The answer is c. (*Ganong, pp 253, 614–615. Kasper et al., pp 266, 258.*) Although reducing alveolar ventilation would increase PCO_2 toward its normal value, it is an inappropriate therapy in this circumstance because the alkaline pH resulting from the hyperventilation is keeping most of the aspirin in an ionized form in which it cannot easily cross the blood-brain barrier. If the patient is placed on a ventilator to prevent muscle fatigue, it is important to maintain hypocapnic alkalosis or the aspirin will cross the blood-brain barrier and the situation may become far worse. Gastric lavage with isotonic saline followed by administration of activated charcoal is indicated. Excessive insensible water loss from vaporization of sweat may cause severe volume depletion, requiring fluid replacement. Glucose should be administered to prevent hypoglycemia.

35. The answer is d. (*Ganong*, pp 735–736. *Kasper et al.*, pp 266–267, 2590. *Stead et al.*, p 222.) The interpretation of the arterial blood gas is partially compensated metabolic acidosis. The primary disturbance is a decrease in the plasma $[HCO_3^-]$, which lowers the ratio of HCO_3^- to dissolved CO_2 in the plasma, and thus lowers the pH according to the Henderson-Hasselbalch equation. To compensate for the metabolic acidosis, the lungs increase the rate of alveolar ventilation, which decreases $PACO_2$ and thus dissolved CO_2 and returns the pH toward the normal range. The differential diagnosis of metabolic acidosis is divided into high anion gap and normal anion gap (hyperchloremic) acidosis. The increased anion gap of 28 mEq/L compared to a normal value of ~12 mEq/L is consistent with an increase in glycolic acid, a metabolite of ethylene glycol, which is a constituent of antifreeze.

36. The answer is d. (*Ganong*, pp 672–677, 734–735. *Kasper et al.*, pp 254, 269–270, 2513–2516. *Levitzky*, pp 171–177, 201–208.) Increasing arterial $PACO_2$ stimulates both the central and peripheral chemoreceptors. In respiratory acidosis, the increase in CO_2 drives the CO_2 hydrolysis equation to the right, with dissociation of carbonic acid into H^+ and HCO_3^- . The ratio of HCO_3^- to dissolved CO_2 decreases, causing a fall in pH, but the absolute concentration of plasma HCO_3^- increases slightly (1 mmol/L per 10 mmHg increase in $PACO_2$) because some of the hydrogen ions are buffered by non-bicarbonate buffers. In renal compensation for the respiratory acidosis, the increased arterial hydrogen ion concentration increases H^+ secretion by the distal tubule, lowering the pH of the urine and increasing NH_4^+ excretion. The excretion of H^+ is accompanied by the generation of new bicarbonate, causing the plasma bicarbonate ion concentration to increase to a greater extent (4 mmol/L per 10 mmHg increase in $PACO_2$), which helps to return the pH toward normal.

37. The answer is b. (*Stead et al.*, pp 63–68, 221–222.) In diabetic ketoacidosis, there is an increased production of acetoacetic and β -hydroxybutyric acids, which leads to an increase in plasma concentration of hydrogen ion. These fixed acids are buffered by all body buffers but mainly by bicarbonate. The concentration of plasma HCO_3^- is therefore below normal. The consumption of bicarbonate and the addition of the anions of the fixed acids to the plasma cause an elevation of the anion gap. The anion gap is equal to plasma $[Na^+] - (plasma [HCO_3^-] + plasma [Cl^-])$ and is normally about 12 mEq/L. The acidosis would stimulate the carotid body

chemoreceptors to cause an increase in ventilation, which decreases arterial PCO_2 . Although blood volume is not affected by metabolic acidosis, the osmotic diuresis that accompanies untreated diabetes may lead to a loss of blood volume.

38. The answer is c. (*Kasper et al.*, pp 267–269. *Levitzky*, pp 174–175.) Diuretic therapy can cause metabolic alkalosis by inducing volume depletion, which activates the renin-angiotensin-aldosterone system. Angiotensin II increases bicarbonate reabsorption in the proximal tubule by increasing Na/H exchange, and aldosterone increases distal bicarbonate reabsorption by promoting H^+ secretion. Diuretic therapy also tends to generate alkalosis and hypokalemia by increasing distal tubule salt delivery, which stimulates both K^+ and H^+ secretion. Renal failure, hypoxemia, and diarrhea all produce metabolic acidosis accompanied by a decreased plasma bicarbonate concentration.

39. The answer is a. (*Ganong*, pp 380–381. *Kasper et al.*, pp 267–269. *Stead et al.*, pp 93–94, 221–225, 230.) Aldosterone promotes the loss of both H^+ and K^+ , producing metabolic alkalosis and hypokalemia. Persistent diarrhea will cause the loss of bicarbonate from the body, resulting in metabolic acidosis. Renal failure is often accompanied by metabolic acidosis because of the inability to excrete H^+ . Diabetes also causes metabolic acidosis because of the accumulation of ketoacids. Hyperventilation results in a respiratory alkalosis, which is compensated for by a decreased bicarbonate concentration.

40. The answer is b. (*Ganong*, p 259. *Kasper et al.*, pp 1572–1573. *Levitzky*, pp 172–179. *Stead et al.*, pp 223–224.) Anxiety causes hyperventilation, which lowers Paco_2 and increases arterial pH, that is, respiratory alkalosis. In order to compensate for the increased pH, the kidneys decrease the secretion of hydrogen ions and decrease bicarbonate reabsorption. The resultant decrease in plasma bicarbonate concentration in compensated respiratory alkalosis helps to bring the pH back toward normal. The anion gap is normal in acute and compensated respiratory alkalosis.

41. The answer is c. (*Ganong*, pp 730–734.) A large amount of volatile acid (carbon dioxide) is produced by aerobic metabolism. The lungs excrete almost all of the CO_2 as it is formed. Nonbicarbonate buffers, primarily hemoglobin, buffer any CO_2 that accumulates in the blood. Phosphate,

lactate, and plasma proteins are also nonbicarbonate buffers, but they buffer only a small portion of the volatile acid dissolving in the blood.

42. The answer is e. (*Stead et al.*, pp 89–91, 230–233.) The principal function of aldosterone is to increase sodium reabsorption in the distal tubule and collecting ducts, which causes secretion of potassium and hydrogen ions. Hypoaldosteronism (e.g., in Addison's disease) therefore results in a decrease in H⁺ secretion, which leads to the production of metabolic acidosis (and hyperkalemia and hyponatremia). Hypoventilation produces respiratory acidosis. Hypokalemia causes an increase in K⁺ reabsorption and an increase in H⁺ secretion, resulting in a metabolic alkalosis. Hypovolemia results in an increase in aldosterone secretion, which can lead to an increase in H⁺ secretion and a metabolic alkalosis. Hypocalcemia does not directly affect acid-base balance.

43. The answer is d. (*Ganong*, pp 31, 315, 496. *Stead et al.*, pp 150–151.) Patients with pancreatic insufficiency, as well as patients with Crohn's disease, bacterial overgrowth, or who have undergone ileal resection, may exhibit vitamin B₁₂ deficiency. Cobalamin, also known as vitamin B₁₂, is an essential vitamin found in such foods as liver, fish, and dairy products. Absorption of cobalamin occurs exclusively from the ileum, where specific receptors on ileal enterocytes bind a complex of cobalamin and intrinsic factor. Although intrinsic factor is secreted by gastric parietal cells, binding of the vitamin to intrinsic factor occurs primarily in the proximal small intestine. The acidic environment of the gastric lumen favors the binding of cobalamin to R protein-type binding proteins that originate from salivary and gastric secretions. Pancreatic proteases in the small intestine degrade the R proteins, and the rise in pH favors rapid and complete transfer of the vitamin to intrinsic factor.

44. The answer is d. (*Ganong*, pp 340–343. *Stead et al.*, pp 63–65.) The normal compensation for metabolic acidosis is hyperventilation and decreased Pco₂. This patient exhibited hypoventilation. Hyperkalemia is frequently observed in patients with uncontrolled diabetic ketoacidosis. The hyperosmotic extracellular fluid draws water out of cells. K⁺ follows the water by solvent drag. Additionally, the lack of insulin decreases the ability of K⁺ to enter cells. The high anion gap is produced by the ketoacids. Bicarbonate levels are reduced by the metabolic acidosis.

45. The answer is a. (*Ganong, pp 723–724. Kasper et al, pp 258–263. Stead et al., pp 231–232.*) Hyperkalemia can result from an increased K⁺ load, decreased K⁺ excretion, or shift of K⁺ from the intra- to the extracellular fluid, such as occurs in acidosis. Volume depletion decreases distal tubular flow and NaCl delivery to the distal tubule, which decreases K⁺ excretion, leading to hyperkalemia. The most common cause of elevated potassium in lab results is a laboratory error called pseudohyperkalemia, a falsely elevated measurement due to hemolysis of the blood specimen with leakage of potassium from the lysed cells. The test should be repeated if you suspect pseudohyperkalemia.

46. The answer is b. (*Kasper et al, pp 258–263. Stead et al., pp 231–232.*) The movement of K⁺ into cells is facilitated by the presence of insulin and epinephrine. During exercise, epinephrine hastens the movement of K⁺ into muscle cells, preventing the accumulation of K⁺ in the extracellular space around active muscle cells. In cases of life-threatening hyperkalemia, insulin is often injected (along with glucose) to reduce the plasma K⁺ concentration.

47. The answer is b. (*Ganong, pp 734–736. Kasper et al., pp 263–267. Levitzky, pp 173–179. Stead et al., pp 221–223.*) Metabolic acidosis is characterized by a lower than normal pH (acidemia) due to a primary decrease in bicarbonate ion concentration (less than 24 mEq/L). There is also a lower than normal arterial PCO₂ (less than 35 mmHg) produced by respiratory compensation for the acidemia. Remember that the analysis of blood gases can suggest the presence of an acid-base disturbance, but a diagnosis requires knowledge of the complete clinical condition.

48. The answer is a. (*Ganong, pp 684–686. Levitzky, pp 234–239.*) As barometric pressure decreases with ascent to high altitude, the partial pressure of inspired oxygen decreases below normal (21% of lower barometric pressure). The resultant decrease in alveolar PO₂ leads to a decrease in arterial PO₂, a condition classified as hypoxic hypoxia or hypoxemia. Hypoxemia stimulates the peripheral chemoreceptors to increase ventilation, causing arterial PCO₂ to decrease and arterial pH to rise (respiratory alkalosis). Renal compensation for the respiratory alkalosis is a decrease in renal H⁺ excretion, which lowers plasma bicarbonate concentration.

49. The answer is a. (*Ganong*, pp 244–247, 716. *Stead et al.*, pp 77–78.)

Vasopressin (AVP or ADH) increases water reabsorption from the cortical and medullary collecting ducts in the kidney. ADH is normally released in response to a rise in plasma Na^+ concentration, and therefore the increased water reabsorption appropriately restores extracellular osmolarity toward normal. When excess ADH is excreted, the water reabsorption dilutes the extracellular fluid, producing a hypotonic hyponatremia accompanied by an increase in urinary sodium and urine osmolality. This condition is called the syndrome of inappropriate ADH secretion (SIADH) and can be life-threatening. The etiology of SIADH includes idiopathic overproduction associated with CNS disorders (head trauma, stroke, encephalitis) and pulmonary disease (tuberculosis, pneumonia), ectopic ADH production by malignant tumors, and drug-induced stimulation of the hypothalamic-pituitary axis (vincristine, carbamezine, chlorpropamide). Patients with SIADH usually improve with fluid restriction.

50. The answer is e. (*Ganong*, pp 382, 392. *Stead et al.*, pp 223–224.)

The patient's condition is caused by a decrease in the serum concentration of ionized calcium (Ca^{2+}), which increases nerve and muscle excitability, leading to spontaneous axonal discharges and muscle contractions, called hypocalcemic tetany. Decreased serum ionized calcium and thus the symptoms of tetany can appear at higher total calcium levels when respiratory alkalosis is present because the H^+ that dissociates from plasma proteins in the presence of a high pH is replaced by Ca^{2+} . Although both a PaCO_2 of 30 mmHg and a PaCO_2 of 15 mmHg are consistent with respiratory alkalosis, only the combination of a PaCO_2 of 20 mmHg and a HCO_3^- of 20 mM, produces an alkaline pH (7.6). The combination of a PaCO_2 of 30 mmHg and a HCO_3^- of 15 mM is metabolic acidosis.

51. The answer is c. (*Ganong*, pp 730–733. *Kasper et al.*, pp 263–269. *Levitzky*, pp 165–171.)

Aerobic metabolism produces 13,000 to 24,000 mmol CO_2 per day. This yields close to that amount of H^+ ions produced per day via the reaction $\text{CO}_2 + \text{H}_2\text{O} \leftrightarrow \text{H}_2\text{CO}_3 \leftrightarrow \text{H}^+ + \text{HCO}_3^-$. At the tissues, CO_2 diffuses into the red blood cells, where the enzyme carbonic anhydrase accelerates the above reaction. The H^+ produced is buffered mainly by the large amount of hemoglobin in the red blood cells. Bicarbonate is not an effective buffer of volatile acid (from CO_2).

52. The answer is d. (*Levitzky, p 174. Stead et al., p 265.*) During the early stages of an asthmatic attack, patients often hyperventilate, producing a decrease in arterial CO₂ concentration (hypocapnia) and an increase in pH (respiratory alkalosis). Over 3 days, the kidneys compensate for the respiratory alkalosis by lowering bicarbonate. When the respiratory problem is resolved, the patient will be left with the decreased bicarbonate and a normal anion gap metabolic acidosis. Although hypoxemia may produce lactic acidosis, that would be accompanied by an increased anion gap.

53. The answer is b. (*Ganong, pp 684–686. Levitzky, pp 234–239.*) Hypoxemia at high altitude stimulates the peripheral chemoreceptors to increase ventilation, causing arterial Pco₂ to decrease and arterial pH to rise (respiratory alkalosis). Tissue hypoxia also stimulates erythropoietin production, which increases the number of red blood cells and the hemoglobin concentration, which increases arterial oxygen content, and thus tissue oxygen delivery. Hypoxia also increases the concentration of 2,3-bisphosphoglycerate, which decreases hemoglobin's affinity for oxygen, thereby increasing oxygen release to the tissues. Alveolar hypoxia constricts the pulmonary vessels at high altitude causing an increase in pulmonary vascular resistance and pulmonary artery pressure (pulmonary hypertension).

54. The answer is e. (*Ganong, pp 666–669. Levitzky, pp 145–155.*) During exercise, there is an increase in muscle temperature, carbon dioxide, and H⁺, all of which shift the oxyhemoglobin curve to the right and enhance oxygen release to the tissues. Hypothermia, hyperventilation (hypocapnic alkalosis), carbon monoxide, and transfusion with banked blood (decreased 2,3-bisphosphoglycerate) all shift the oxyhemoglobin dissociation to the left.

55. The answer is d. (*Ganong, pp 655–657. Levitzky, pp 26–28.*) The surface active component of the lung extract that is essential for stability of the lung during extrauterine respiration, is surfactant. Surfactant is a complex consisting of 10 to 15% proteins and 85 to 90% lipids, 85% of which is phospholipid (lecithin), and ~75% of which is dipalmitoyl phosphatidylcholine. The synthesis of lecithin increases as the fetus matures and thus the measurement of lecithin concentration in the amniotic fluid provides an index of fetal lung maturity. Sphingomyelin is another choline phospholipid found in a variety of tissues in the fetus. The lecithin-sphingomyelin (L/S) ratio has been reported to provide a more accurate assessment of fetal

lung maturity than lecithin concentration alone. An L/S ratio ≥ 2 is indicative of biochemical maturation of the lung. Infants born with L/S ratios < 2 have an increased incidence of respiratory distress syndrome (RDS) of the newborn, also known as hyaline membrane disease.

56. The answer is e. (*Levitzky, pp 237–239.*) Cardiac output, heart rate, and blood pressure initially increase upon ascent to high altitude, but return to normal after a few days. The arterial PO_2 remains low at high altitude due to the low inspired and alveolar PO_2 levels. The hypoxemia stimulates alveolar ventilation, which remains elevated at high altitude. To compensate for the respiratory alkalosis, plasma bicarbonate concentration decreases after several days at high altitude, and remains low. Hemoglobin concentration increases secondary to hypoxia-induced erythropoietin production.

57. The answer is c. (*Ganong, p 444. Levitzky, pp 172–177.*) The alveolar and arterial PCO_2 is determined as the rate of CO_2 production divided by the rate of alveolar ventilation. Thus, at any given metabolic rate (rate of CO_2 production = VCO_2), hyperventilation is by definition a decrease in Paco_2 . Pregnancy produces hyperventilation because progesterone stimulates the brainstem respiratory centers to increase alveolar ventilation. Sleep and morphine depress the respiratory centers and, therefore, produce hypoventilation. The compensatory response to metabolic alkalosis is a small decrease in alveolar ventilation. During exercise, alveolar ventilation increases in proportion to carbon dioxide production such that the arterial PCO_2 remains normal. Thus the increased rate of alveolar ventilation in exercise is not hyperventilation, but it has been given a special term, called exercise hyperpnea.

58. The answer is a. (*Ganong, pp 251–255, 760.*) Radiation and conduction account for 70% of heat lost when the environmental temperature is below body temperature. Insensible water loss from the vaporization of sweat accounts for another 27% of heat loss under these conditions. The remaining heat is normally lost by respiration (2%) and urination and defecation (1%). Cutaneous vasoconstriction would decrease heat loss.

59. The answer is d. (*Ganong, pp 734–736. Levitzky, p 178. Stead et al., pp 221–222.*) Alcoholic ketoacidosis is associated with a decrease in pH (high anion gap metabolic acidosis) and a compensatory rise in alveolar

ventilation, which lowers the arterial PCO_2 . Hyperventilation also causes a slight increase in PO_2 .

60. The answer is c. (*Ganong*, p 477.) Absorption of vitamin D increases linearly as the intraluminal concentration increases, suggesting absorption by a nonsaturable passive-diffusion mechanism. The term vitamin D refers to a family of essentially water-insoluble compounds involved primarily in the regulation of calcium homeostasis. Water-soluble vitamins, including vitamin C, folate, niacin, and vitamin B_{12} , are a diverse group of organic compounds that are essential for normal growth and development. At the low concentrations present in the diet (1 to 100 nM), transport of the vitamins across the brush border occurs by specialized mechanisms, such as membrane carriers, active transport systems, and membrane-binding proteins and receptors specific for a particular vitamin.

61. The answer is c. (*Ganong*, pp 735–736. *Kasper et al.*, pp 266–267, 2590. *Stead et al.*, p 222.) Diabetic ketoacidosis generates a partially compensated metabolic acidosis. The primary disturbance is a decrease in the plasma $[\text{HCO}_3^-]$, which lowers the ratio of HCO_3^- to dissolved CO_2 in the plasma, and thus lowers the pH according to the Henderson-Hasselbalch equation. To compensate for the metabolic acidosis, the lungs increase the rate of alveolar ventilation, which decreases Paco_2 and thus dissolved CO_2 and returns the pH toward the normal range. The differential diagnosis of metabolic acidosis is divided into high anion gap and normal anion gap (hyperchloremic) acidosis. The increased anion gap of 30 mEq/L compared to a normal value of ~12 mEq/L is consistent with an increase in ketoacids, that is, acetoacetic acid and β -hydroxybutyric acid, in the diabetic patient.

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Physiology of the Hematopoietic and Lymphoreticular Systems

Questions

62. A 52-year-old man is brought to the Emergency Department with severe chest pain. Angiography demonstrates a severe coronary occlusion. A thrombolytic agent is administered to reestablish perfusion. Which of the following does the thrombolytic agent activate?

- a. Heparin
- b. Plasminogen
- c. Thrombin
- d. Kininogen
- e. Prothrombin

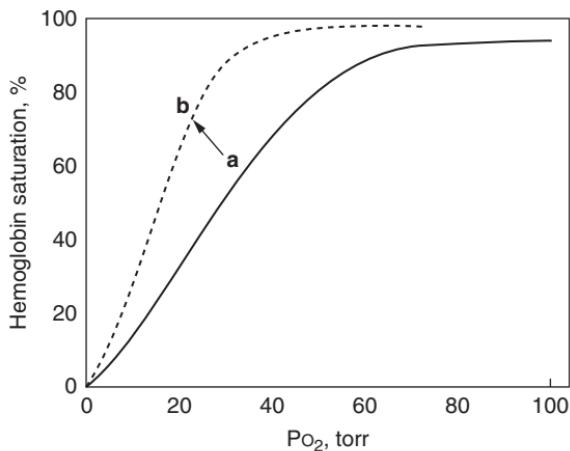
63. A 42-year-old patient with a rare blood type is scheduled for surgery that will likely require a transfusion. Because the patient has a rare blood type, an autologous blood transfusion is planned. Prior to surgery, 1500 mL of blood is collected. The collection tubes contain calcium citrate, which prevents coagulation by which of the following actions?

- a. Blocking thrombin
- b. Binding factor XII
- c. Binding vitamin K
- d. Chelating calcium
- e. Activating plasminogen

- 64.** Prior to having his first colonoscopy, a 50-year-old male undergoes a bleeding time test to rule out any clotting disorders. Bleeding time is determined by nicking the skin superficially with a scalpel blade and measuring the time required for hemostasis. It will be markedly abnormal (prolonged) in a person who has which of the following?
- Anemia
 - Vitamin K deficiency
 - Thrombocytopenia
 - Leukopenia
 - Hemophilia
- 65.** A 67-year-old woman with a history of venous thromboembolism is placed on warfarin (Coumadin) prophylactically. The blood concentration of Coumadin becomes too high and bleeding occurs. The bleeding can best be treated by the administration of which of the following?
- Fibrinogen
 - Thrombin
 - Platelets
 - Protein C
 - Vitamin K
- 66.** A 65-year-old smoker develops a squamous cell bronchogenic carcinoma, which metastasizes to the tracheobronchial and parasternal lymph nodes. Flow of fluid through the lymphatic vessels will be decreased if there is an increase in which of the following?
- Capillary pressure
 - Capillary permeability
 - Interstitial protein concentration
 - Capillary oncotic pressure
 - Central venous pressure
- 67.** A 44-year-old female with a history of excessive menstrual bleeding and menstrual cycles that generally last over 7 days, complains of increasing fatigue and cold extremities. Lab results reveal a hemoglobin (Hb) concentration of 6 g/dL. In this patient with anemia, which of the following would be reduced?
- Arterial PO_2
 - Total arterial oxygen content
 - Dissolved oxygen content

- d. Percent O₂ saturation in the arterial blood
- e. Oxygen extraction

68. During coronary artery bypass graft (CABG) surgery, a patient's oxygen saturation curve shown below shifts from **a** to **b**.



Which of the following conditions can account for this shift?

- a. A change in pH from 7.4 to 7.3
- b. A change in PCO_2 from 40 to 46 mmHg
- c. A decrease in core body temperature from 37° to 30°C.
- d. An increase in erythrocyte [2,3-bisphosphoglycerate]
- e. Transfusion of blood with a higher P_{50} than normal.

69. A patient with intractable hiccups is instructed to breathe into and out of a bag in order to rebreathe exhaled CO₂. In the blood, the majority of CO₂ is transported as which of the following?

- a. Dissolved CO₂
- b. Carbonic acid
- c. Carbaminohemoglobin
- d. Carboxyhemoglobin
- e. Bicarbonate

- 70.** A patient presents with a low exercise tolerance. Blood work shows a normal hematocrit and hemoglobin concentration, but a decreased P_{50} . Which would be true of his/her oxyhemoglobin transport and dissociation?
- Hemoglobin's affinity for oxygen is increased.
 - There is less loading of O_2 at the alveolar-capillary level than normal.
 - Oxygen unloading is increased at the tissue level.
 - Hemoglobin's saturation with oxygen is lower than normal at any PaO_2 .
 - The differential diagnosis includes a point mutation resulting in increased binding of 2,3-bisphosphoglycerate (BPG) to his/her hemoglobin chains.
- 71.** A 29-year-old male presents with recurring episodes of edema accompanied by chills and fever. A history reveals prolonged travel in the Far East and a diagnosis of parasites that block the lymph vessels. Which of the following characteristics of vessels is most different when comparing the vascular and lymphatic systems?
- Spontaneous vasomotor activity
 - Absorption of proteins from the interstitial fluid
 - Absorption of nutrients from the gastrointestinal (GI) tract
 - Backflow of fluid is prevented by valves
 - Endothelial cells form the vessel walls
- 72.** A 65-year-old slightly cyanotic male presents to his physician complaining of pruritis and nose bleeds. A blood test reveals a hematocrit of 62, leading to the diagnosis of polycythemia vera. Treatment includes aspirin to prevent thromboses and periodic phlebotomy to reduce the hematocrit. The reduction in hematocrit is beneficial because it does which of the following?
- Reduces blood viscosity
 - Increases arterial oxygen saturation
 - Reduces blood velocity
 - Increases cardiac output
 - Increases arterial oxygen content
- 73.** A chronic bronchitis patient is admitted to the Emergency Department with cyanosis and shortness of breath. The admitting physician orders partial pressure and saturation measurements of oxygen in both the arterial and venous blood. Results were:

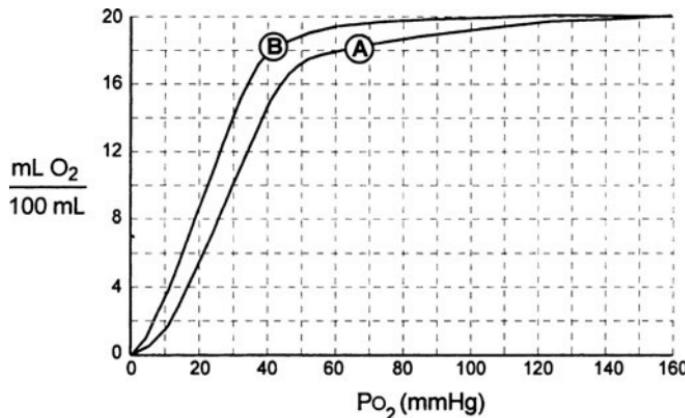
PaO_2	50 mmHg
$PaCO_2$	67 mmHg
PvO_2	30 mmHg
SaO_2	80%

Svo ₂	50%
[Hb]	20 g/dL

From these data, you can determine that the patient has which of the following?

- a. A higher than normal dissolved oxygen content in the venous blood
- b. A lower than normal oxyhemoglobin content in the arterial blood
- c. An increased oxygen extraction
- d. A decreased arteriovenous oxygen content difference
- e. A lower than normal dissolved CO₂ content in the arterial blood

74. What is the P₅₀ of the oxyhemoglobin curve labeled A in the diagram below?



- a. 80 mmHg
- b. 60 mmHg
- c. 40 mmHg
- d. 30 mmHg
- e. 20 mmHg

75. An increase in the P₅₀ of an oxyhemoglobin curve would result from a decrease in which of the following?

- a. Metabolism
- b. pH
- c. Temperature
- d. PCO₂
- e. 2,3-BPG

- 76.** A 61-year-old male presents to his family physician with the chief complaint of frequent diarrhea accompanied by weight loss. He reports a tendency to bruise easily and laboratory data reveal a prothrombin time of 19 seconds (normal = 11–14 seconds). The bruising and prolonged prothrombin time can be explained by a decrease in which of the following vitamins?
- Vitamin A
 - Vitamin C
 - Vitamin D
 - Vitamin E
 - Vitamin K
- 77.** A woman presents at the obstetrician's office for her second trimester evaluation. Which of the following values would normally be less in the fetus than in the mother?
- Hemoglobin concentration
 - Affinity of hemoglobin for oxygen
 - Erythrocyte binding of 2,3-BPG
 - Cardiac output/kg body weight
 - Cardiac glycogen content
- 78.** The percentage of hemoglobin saturated with oxygen will increase when which of the following occurs?
- The arterial PCO_2 is increased
 - The hemoglobin concentration is increased
 - The temperature is increased
 - The arterial PO_2 is increased
 - The arterial pH is decreased
- 79.** Which of the following best explains why oxygen delivery to the tissues may be adequate at rest in an acclimatized person at high altitudes?
- Arterial PO_2 returns to normal
 - Hemoglobin concentration increases
 - The blood flow to the lungs increases, improving the V/Q ratio
 - Nitric oxide release from endothelial cells is increased
 - There is a compensatory decrease in the number of mitochondria

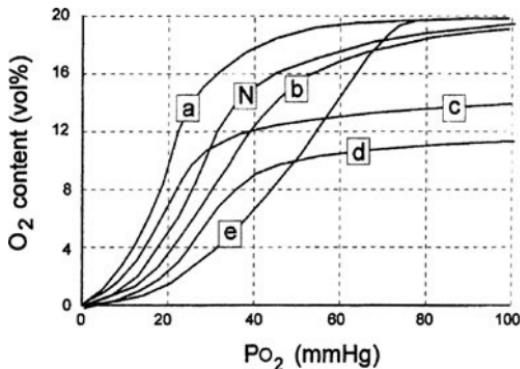
80. The affinity of hemoglobin for oxygen is increased by which of the following?

- a. Metabolic acidosis
- b. Exercise
- c. Hypoxemia
- d. Anemia
- e. Carbon monoxide poisoning

81. A 67-year-old male with chronic bronchitis is brought to the Emergency Department exhibiting labored breathing and cyanosis. The clinical sign of cyanosis is caused by which of the following?

- a. An increase in the affinity of hemoglobin for oxygen
- b. A decrease in the percent of red blood cells (hematocrit)
- c. An increase in the concentration of carbon monoxide in the venous blood
- d. A decrease in the concentration of iron in the red blood cells
- e. An increase in the concentration of deoxygenated hemoglobin

82. The normal oxyhemoglobin saturation curve for hemoglobin A is denoted by N in the diagram below. Which of the oxyhemoglobin saturation curves shown was obtained from fetal blood?



- a. a
- b. b
- c. c
- d. d
- e. e

Physiology of the Hematopoietic and Lymphoreticular Systems

Answers

62. The answer is b. (*Ganong, pp 540–545.*) Plasminogen is the inactive precursor of plasmin, the proteolytic enzyme involved in clot dissolution. An infusion of tissue plasminogen activator (tPA) soon after a heart attack (and possibly a thrombotic stroke) can lessen the chances of permanent damage. Thrombin, the enzyme ultimately responsible for the formation of fibrin monomers, is generated from prothrombin by activated factor X. Activation of factor X occurs via both extrinsic and intrinsic pathways. Kininogens are enzymes responsible for the production of peptides (kinins) associated with inflammation. Heparin is an anticoagulant found on endothelial cell surfaces.

63. The answer is d. (*Ganong, pp 542–544. Kasper et al., p 666. Stead et al., p 160.*) The citrate ion has three anionic carboxylate groups that avidly chelate calcium and reduce the concentration of free calcium in blood. Because free calcium (Ca^{2+}) is required for multiple steps in both coagulation pathways, citrate is a useful anticoagulant in vitro. The citrate ion is rapidly metabolized; thus, blood anticoagulated with citrate can be infused into the body without untoward effects. Oxalate, another calcium-chelating anticoagulant, is toxic to cells.

64. The answer is c. (*Stead et al., pp 161–163.*) An abnormally small number of platelets in the blood is called thrombocytopenia. Bleeding time is used to distinguish hemostatic abnormalities caused by a reduced number of platelets from those caused by coagulation defects. Hemostasis following blood vessel injury depends on (1) vascular spasm, (2) formation of

a platelet plug, and (3) clot formation. The time for a small cut to stop bleeding depends on the concentration of platelets.

65. The answer is e. (*Ganong*, p 544. *Kasper et al.*, pp 320, 409, 688–693, 1492. *Stead et al.*, pp 159–161.) Warfarin is often prescribed for patients at risk for thromboembolic episodes. Vitamin K is necessary for the conversion of prothrombin to thrombin. Thrombin is an important intermediate in the coagulation cascade. It converts fibrinogen to fibrin and is a powerful activator of platelets. Warfarin interferes with the activity of vitamin K and therefore reduces the likelihood of clot formation. Administering vitamin K can restore coagulation if warfarin therapy leads to excessive bleeding.

66. The answer is d. (*Ganong*, pp 592–594.) Lymph flow is proportional to the amount of fluid filtered out of the capillaries. The amount of fluid filtered out of the capillaries depends on the Starling forces and capillary permeability. Increasing capillary oncotic pressure directly decreases filtration by increasing the hydrostatic (osmotic) force drawing water into the capillary. Increasing capillary pressure, capillary permeability, and interstitial protein concentration (oncotic pressure) all directly increase lymph flow. When venous pressure is increased, the capillary hydrostatic pressure is increased and, again, capillary filtration is increased. Lymph flow is normally approximately 2 to 3 L per day.

67. The answer is b. (*Ganong*, pp 666–667, 683, 690. *Kasper et al.*, pp 329–335, 2203. *Levitsky*, pp 153–154.) A reduction in the concentration of hemoglobin reduces the oxyhemoglobin content, and thus the total arterial oxygen content. Oxygen extraction by the tissues increases to compensate for the reduced tissue oxygen delivery. Arterial PO_2 , dissolved oxygen, and the percent saturation of hemoglobin with oxygen are all normal in anemia.

68. The answer is c. (*Ganong*, pp 666–669. *Levitzky*, pp 146–152.) Hypothermia reduces hemoglobin's affinity for oxygen, causing the oxyhemoglobin dissociation curve to shift to the left. With a leftward shift, the saturation of hemoglobin with oxygen is greater than normal at any PO_2 , as denoted by a lower P_{50} value than normal. Acidosis, hypercapnia (increased PCO_2), and an increase in erythrocyte [2,3-BPG] all cause rightward shifts of the oxyhemoglobin dissociation curve.

69. The answer is e. (*Ganong*, pp 669–670.) CO_2 is transported in arterial blood in three forms: as physically dissolved CO_2 (about 5%), in combination with the amino groups of hemoglobin as carbaminohemoglobin (about 10%), and as bicarbonate ion HCO_3^- (about 85%). The amount of CO_2 actually carried as carbonic acid, H_2CO_3 , is negligible. Carboxyhemoglobin refers to the combination of carbon monoxide (CO) and hemoglobin.

70. The answer is a. (*Ganong*, pp 666–669.) A decreased P_{50} denotes a leftward shift of the oxyhemoglobin dissociation curve and an increase in hemoglobin's affinity for oxygen. A leftward shift indicates that more oxygen is loaded at the alveolar-capillary level, and that there is less oxygen unloading at the tissue level because hemoglobin binds the oxygen more tightly than normal. With a decreased P_{50} , oxygen saturation is higher than normal at any PO_2 . Increased 2,3-BPG shifts the oxyhemoglobin dissociation curve to the right.

71. The answer is b. (*Ganong*, pp 593–594. *Kasper et al.*, pp 1493–1494.) The primary function of the lymphatic vessels is to absorb the proteins that enter the interstitial fluid from the systemic capillaries. Vascular and lymphatic vessels share many characteristics: terminal arterials and lymphatics display vasomotor activity; both are involved in absorbing nutrients from the GI tract, both have valves, and the capillary vessels in both systems are composed of endothelial cells.

72. The answer is a. (*Kasper et al.*, pp 626–628. *Stead et al.*, pp 158–159.) Polycythemia vera is a disease in which an abnormally large number of red blood cells are produced. The large number of red blood cells causes an increase in blood viscosity by two or three times normal. Patients with polycythemia vera often have high blood pressure (because of increased blood volume) and cyanosis (because of increased oxygen extraction from blood flowing slowly through capillaries). In primary polycythemia vera, there is a primary bone marrow etiology. In secondary polycythemia vera, increased erythropoietin production occurs secondary to hypoxia (chronic obstructive pulmonary disease [COPD], high altitude), smoking (due to carboxyhemoglobin), or renal cell carcinoma.

73. The answer is c. (*Ganong*, pp 666–667. *Levitzky*, pp 146–147, 180–183.) The lower-than-normal levels of venous oxygen tension and saturation indicate that the tissues have extracted more oxygen than normal. O_2 extraction is the arteriovenous oxygen content difference, and could be calculated from the data given, though that would not be necessary to

answer this question. Total oxygen content is the sum of the dissolved oxygen (P_{O_2} in mmHg \times 0.003 mL O₂/100 mL blood/mmHg P_{O₂}) and the oxyhemoglobin content ([Hb] \times 1.34 mL O₂/g% Hb \times % O₂ saturation). Arterial oxygen content in this patient is therefore 21.6 mL O₂/100 mL blood and venous oxygen content is 13.5 mL O₂/100 mL blood, with the a-v O₂ = 8.1 mL O₂/100 mL blood, compared to a normal value of ~5 mL O₂/100 mL blood.

74. The answer is d. (Ganong, p 667. Levitzky, p 3.) The P₅₀ of the oxyhemoglobin curve is the oxygen tension at which half of the hemoglobin is saturated with oxygen. When fully saturated, the hemoglobin represented by curve A has an oxygen content of 20 mL/dL. Therefore, the P₅₀ is the P_{O₂} at which the hemoglobin contains one-half of 20 mL/dL (10 mL/dL), which is 30 mmHg.

75. The answer is b. (Ganong, pp 667–669. Levitzky, pp 148–152.) An increase in P₅₀ is associated with a rightward shift of the oxyhemoglobin dissociation curve. A decrease in pH shifts the curve to the right. Decreased temperature, 2,3-BPG, and metabolism (CO₂ production) all shift the oxyhemoglobin dissociation curve to the left.

76. The answer is e. (Ganong, pp 313, 509, 544–545. Stead et al., p 374.) Vitamin K is a fat-soluble vitamin produced by intestinal bacteria that is essential for maintaining normal clotting of blood. The vitamin is essential for hepatic synthesis of prothrombin and factors VII, IX, and X. Common causes of vitamin K deficiency include cholestasis, and factors that limit fat absorption.

77. The answer is c. (Ganong, p 669. Levitzky, pp 154–155.) Fetal hemoglobin (hemoglobin F) is chemically different from adult hemoglobin (hemoglobin A) in that it has two α and two γ chains instead of two α and two β chains. The γ chains of HbF do not bind 2,3-BPG, resulting in an increased affinity for oxygen, and a leftward shift of the oxygen dissociation curve of HbF. The greater affinity of hemoglobin for oxygen is advantageous in the placental exchange of O₂ from maternal blood (Pao₂ = 100 mmHg) to fetal blood (Pao₂ = 25 mmHg). Despite the low arterial P_{O₂}, the fetus is not hypoxic. Oxygen delivery in the fetus is enhanced by a higher hemoglobin concentration than in the adult and a cardiac output that is 2 to 4 \times higher than in the adult on a milliliter per kilogram basis. The fetal heart is protected by an increased cardiac glycogen content.

78. The answer is d. (*Ganong*, pp 666–669. *Levitzky*, pp 145–156.) The percentage of hemoglobin saturated with oxygen depends on the level of PO_2 in the blood and on other factors that affect the position of the oxyhemoglobin dissociation curve. Factors that shift the curve to the left, such as a decrease in PCO_2 , an increase in pH, or a decrease in temperature, would increase the percentage of hemoglobin saturated with oxygen as would an increase in PO_2 , provided that the percentage of saturation was not already at 100%. At a given PO_2 , increasing the concentration of hemoglobin would not affect the percentage of saturation but would increase the oxygen content of the blood.

79. The answer is b. (*Ganong*, pp 684–686. *Levitzky*, pp 234–239.) At high altitude, arterial PO_2 is low because of a low barometric pressure. Chronic hypoxia at high altitudes or in disease states stimulates the increased release of erythropoietin from the kidneys, which increases the hematocrit and thereby increases the hemoglobin concentration of the blood. Chronic hypoxia also stimulates increased capillary growth and mitochondria in tissues. Ventilation increases from stimulation of the carotid body chemoreceptors, and PaO_2 increases somewhat, although it does not return to a normal, sea-level value. Hypoxia leads to pulmonary vascular constriction and a decrease in blood flow to the lungs.

80. The answer is e. (*Ganong*, p 690. *Levitzky*, pp 153–154.) Hemoglobin's affinity for oxygen is increased by carbon monoxide. In carbon monoxide poisoning, carbon monoxide not only displaces O_2 from hemoglobin, it also makes it more difficult for the O_2 that is bound to Hb to dissociate from it in the tissues. Increasing H^+ ion concentration (decreasing pH) by metabolic acidosis or respiratory acidosis (decreased alveolar ventilation) decreases the affinity of hemoglobin for O_2 . Exercise decreases the affinity of Hb for O_2 by increasing the temperature of the exercising muscles. A decrease in arterial PO_2 (hypoxemia) decreases Hb's affinity for oxygen.

81. The answer is e. (*Ganong*, p 684. *Kasper et al.*, pp 210–211. *Levitzky*, p 156. *Stead et al.*, pp 262–263.) Cyanosis is the blue color of the skin produced by desaturated hemoglobin. Cyanosis appears when 5 g of hemoglobin per 100 mL of blood are desaturated. For a person with a normal hemoglobin concentration of 15 g/100 mL, cyanosis appears when one-third of the blood is desaturated. For a person with polycythemia (a higher-than-normal concentration of hemoglobin), cyanosis may appear when only one-fourth of the hemoglobin is desaturated (e.g., if hemoglobin concentration is

20 g/100 mL). This individual may not be hypoxic because of the high concentration of saturated hemoglobin. On the other hand, a person with anemia (a lower than normal concentration of hemoglobin) may have a significant portion of the hemoglobin desaturated without displaying cyanosis. This individual will not appear cyanotic but may be hypoxic.

82. The answer is a. (*Ganong, p 669. Levitzky, pp 154–155.*) The oxyhemoglobin (HbO_2) dissociation curve represents the relationship between the partial pressure of oxygen and the amount of oxygen bound to hemoglobin (Hb). Normal Hb is 50% saturated at a PO_2 of approximately 27 mmHg (the P_{50}), 75% saturated at a PO_2 of 40 mmHg (the normal PO_2 of mixed venous blood), and 97% saturated at a PO_2 of 100 mmHg (the normal arterial PO_2). Fetal blood has a higher-than-normal oxygen affinity and therefore is represented by the curve labeled a. Increasing the affinity of Hb for O_2 shifts the HbO_2 saturation curve to the left and decreases the P_{50} .

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Neurophysiology

Questions

83. A 10-year-old girl with Type I diabetes develops a neuropathy limited to sensory neurons with free nerve endings. Quantitative sensory testing will reveal higher-than-normal thresholds for the detection of which of the following?

- a. Fine touch
- b. Vibration
- c. Pressure
- d. Temperature
- e. Muscle length

84. A 16-year-old boy is brought to the emergency room by ambulance after suffering a concussion during a football game. When he awoke there was no difficulty with his speech and he was able to understand and follow commands, but he had difficulty understanding written language and pictures. His condition is most likely caused by damage to which of the following?

- a. The hippocampus
- b. Angular gyrus in the categorical hemisphere
- c. Broca's area in the frontal lobe
- d. Wernicke's area at the posterior end of the superior temporal gyrus
- e. The arcuate fasciculus connecting Broca's and Wernicke's areas.

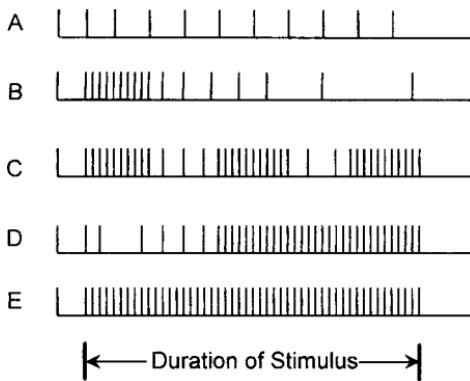
85. A 13-year-old boy has no movement in his legs after falling out of a tree. Neurological examination shows absence of both the myotatic (stretch) and reverse myotatic reflexes in the lower extremities. Which of the following is the most important role of the γ motoneurons?

- a. Stimulate skeletal muscle fibers to contract
- b. Maintain Ia afferent activity during contraction of muscle
- c. Generate activity in Ib afferent fibers
- d. Detect the length of resting skeletal muscle
- e. Prevent muscles from producing too much force

86. A 72-year-old man visits his physician because he finds it difficult to hold his hand steady when painting. Examination reveals a resting tremor and rigidity. The symptoms are relieved by single dose of levodopa, suggestive of Parkinson's disease. This patient's neurological signs are most likely related to a lesion within which of the following?

- a. The cerebellum
- b. The substantia nigra
- c. The premotor area
- d. The caudate nucleus and putamen
- e. The hippocampus

87. Each of the figures in the diagram below illustrates a train of action potentials in response to a sudden limb movement. The sensory neuron encoding the velocity of the limb movement is illustrated by which of the following figures?



- a. A
- b. B
- c. C
- d. D
- e. E

88. The precentral gyrus and corticospinal tract are essential for which of the following?

- a. Vision
- b. Olfaction

- c. Auditory identification
- d. Kinesthesia
- e. Voluntary movement

89. A 28-year-old woman hits her head on the windshield in an automobile accident. She becomes confused, and develops urinary incontinence and a gait disorder. An MRI of the brain reveals enlarged ventricles, suggestive of normal pressure hydrocephalus. Lumbar puncture confirms normal intracranial pressure, and her symptoms are found to improve after removal of a volume of her cerebrospinal fluid (CSF). Normally, which of the following is true regarding CSF?

- a. It is absorbed by the choroid plexus
- b. It circulates in the epidural space
- c. It has a higher protein concentration than plasma
- d. It has a lower glucose concentration than plasma
- e. Its absorption is independent of CSF pressure

90. A 72-year-old male is evaluated by a physiatrist after a stroke. The patient is observed to suffer from dysmetria, ataxia, and an intention tremor. These neurological signs are most likely related to a lesion within which of the following regions of the brain?

- a. Cerebellum
- b. Medulla
- c. Cortical motor strip
- d. Basal ganglia
- e. Eighth cranial nerve

91. A 41-year-old man is seen by his physician complaining of “always feeling tired” and having “vivid dreams when he is sleeping.” He is referred to the hospital’s sleep center for evaluation. He is diagnosed with narcolepsy based on his clinical history and the presence of rapid eye movements (REM) as soon as he falls asleep. Which of the following signs will be observed when the patient is exhibiting REM sleep?

- a. Hyperventilation
- b. Periods of loss of skeletal muscle tone
- c. Slow but steady heart rate
- d. High amplitude EEG wave
- e. Decreased brain metabolism

92. A 43-year-old woman has a chief complaint of muscle weakness. The distribution of muscle weakness and the presence of hyperactive tendon reflexes is consistent with pyramidal tract disease. Tapping the patella tendon elicits a reflex contraction of the quadriceps muscle. Which of the following occurs during the contraction of the quadriceps muscle?

- a. The Ib afferents from the Golgi tendon organ increase their rate of firing
- b. The Ia afferents from the muscle spindle increase their rate of firing
- c. The α motoneurons innervating the extrafusal muscle fibers decrease their rate of firing
- d. The γ motoneurons innervating the intrafusal muscle fibers increase their rate of firing
- e. The α motoneurons to the antagonistic muscles increase their rate of firing

93. A 64-year-old female patient is referred to a neurologist because her sister and brother both suffered recent strokes. She is diagnosed with an antiphospholipid antibody syndrome, a condition that causes hypercoagulation, and placed on warfarin. Despite the anticoagulation therapy she develops a thrombotic cerebral infarct, which leads to spasticity of her left wrist, elbow, and knee. The lesion most likely affected which of the following?

- a. The corticospinal fibers
- b. The vestibulospinal fibers
- c. The Ia afferent fibers
- d. The corticoreticular fibers
- e. The reticulospinal fibers

94. A 27-year-old patient with a chief complaint of mild vertigo of 3-months duration is seen by a neurologist. Examination reveals a positional (horizontal and vertical) nystagmus that is bidirectional. The patient reports the absence of tinnitus. Which of the following is the most likely etiology of the vertigo?

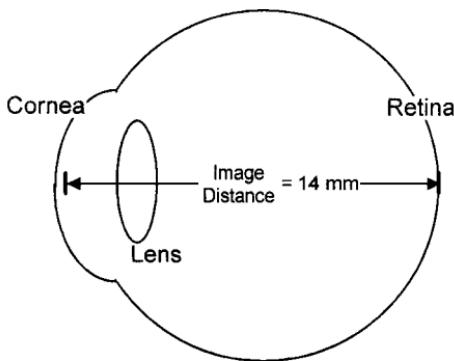
- a. Labyrinthitis
- b. Ménière's syndrome
- c. Lesion of the flocculonodular lobe of the cerebellum
- d. Lesion of the spinocerebellum
- e. Psychogenic

95. A 16-year-old girl with epilepsy has an electroencephalogram (EEG) recording done during a routine visit to her neurologist. The α -rhythm appearing on an EEG has which of the following characteristics?

- a. It produces 20 to 30 waves per second
- b. It disappears when a patient's eyes open

- c. It is replaced by slower, larger waves during REM sleep
- d. It represents activity that is most pronounced in the frontal region of the brain
- e. It is associated with deep sleep

96. The image distance of a normal relaxed eye is indicated in the diagram below. If an object is placed 25 cm away from the eye, the image will be focused on the retina if the refractive power of the eye is increased to which of the following?



- a. 40 diopters
- b. 44 diopters
- c. 56 diopters
- d. 71 diopters
- e. 75 diopters

97. A 59-year-old woman is admitted to the hospital because of agitation and aggression. Three years prior to admission her irregular, flinging movements had become so severe that she could not walk or assist in her own care. She is diagnosed with Huntington's chorea, which is a hereditary disease affecting neurons within which of the following?

- a. Anterior cerebellum
- b. Subthalamus
- c. Substantia nigra
- d. Striatum
- e. Limbic system

98. A 22-year-old female takes a diet supplement containing ephedrine. Activation of the sympathetic nervous system by ephedrine causes tachycardia, palpitations, and contraction of the smooth muscle in which of the following?

- a. Bronchioles
- b. Pupils
- c. Intestine
- d. Arterioles
- e. Ciliary body

99. A 22-year-old musician visits an otolaryngologist complaining of ringing in his ear. An audiometry test reveals a high-frequency hearing loss in which the threshold for hearing high-frequency sounds is raised by 1000 times. If a patient is unable to hear high-frequency sounds, the damage to the basilar membrane is closest to which of the following?

- a. Oval window
- b. Helicotrema
- c. Stria vascularis
- d. Modiolus
- e. Spiral ganglion

100. A 3-month-old baby is brought to her pediatrician for a check up. Stroking the plantar surface of the foot produces a reflex extension of the large toe rather than the expected flexion. The Babinski sign elicited by the physician indicates damage to which of the following?

- a. Spinal cord
- b. Brainstem
- c. Cerebellum
- d. Basal ganglia
- e. Pyramidal tracts

101. A 41-year-old man complains to his physician about jet lag whenever he flies long distances to meetings. Melatonin is prescribed as a way to reset his circadian rhythm. The circadian rhythm is controlled by which of the following?

- a. Paraventricular nucleus
- b. Ventromedial nucleus
- c. Arcuate nucleus
- d. Lateral nucleus
- e. Suprachiasmatic nucleus

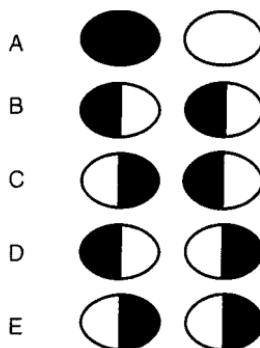
102. A 48-year-old woman with multiple sclerosis with increasing spasticity is treated with an intrathecal infusion of baclofen, a GABA_B agonist which mediates presynaptic inhibition. Presynaptic inhibition in the central nervous system affects the firing rate of α motoneurons by which of the following means?

- a. Increasing the chloride permeability of the presynaptic nerve ending
- b. Decreasing the potassium permeability of the α motoneuron
- c. Decreasing the frequency of action potentials by the presynaptic nerve ending
- d. Hyperpolarizing the membrane potential of the α motoneuron
- e. Increasing the amount of the neurotransmitter released by the presynaptic nerve ending

103. A 29-year-old woman who complains of slowly progressive loss of vision on her right side affecting both eyes is seen by her neurologist. A CT scan demonstrates a high-density space-occupying lesion. The lesion produces the visual field defect by compressing which of the following?

- a. The right lateral geniculate
- b. The left optic nerve
- c. The right visual cortex
- d. The optic chiasm
- e. The left optic tract

104. A 62-year-old woman is referred to a neurologist by her family physician because of a recent loss of initiative, lethargy, memory problems, and a loss of vision. She is diagnosed with primary hypothyroidism and referred to an endocrinologist for treatment of her thyroid problem and to a neuro-ophthalmologist for visual field evaluation. Which of the following visual field defects is most likely to be found?



- a. A
- b. B
- c. C
- d. D
- e. E

105. A 34-year-old woman, who has been immobilized with a sprained ankle for the past 4 days, develops a throbbing pain that has spread to her entire left leg. History reveals that she has been taking oral contraceptives for 15 years. Compared to localized pain, such as one might experience from a needle stick, which of the following is true of ischemic pain?

- a. Ischemic pain sensory fibers are classified as A delta ($A\delta$) sensory fibers.
- b. Ischemic pain is produced by overstimulating somatic touch receptors.
- c. Ischemic pain is transmitted to the brain through the neospinothalamic tract.
- d. Ischemic pain receptors quickly adapt to a painful stimulus.
- e. Ischemic pain sensory fibers terminate within the substantia gelatinosa of the spinal cord.

106. A 17-year-old boy is admitted to the hospital with a traumatic brain injury, sustained when he fell off his motorcycle. He develops a fever of 39°C, which is unrelated to an infection or inflammation. The fever is most likely due to a lesion of which of the following?

- a. The lateral hypothalamus
- b. The arcuate nucleus
- c. The posterior nucleus
- d. The paraventricular nucleus
- e. The anterior hypothalamus

107. A 29-year-old man is brought to the emergency room after a traffic accident causing a traumatic brain injury. Within several hours he begins eating objects such as paper, is unable to maintain attention, and displays increased sexual activity. He is diagnosed with Klüver-Bucy syndrome. A diagnostic MRI is ordered to confirm bilateral lesions of which of the following regions of the brain?

- a. Temporal lobe
- b. Hypothalamus
- c. Olfactory lobe
- d. Hippocampus
- e. Cingulate gyrus

108. In which one of the following sensory systems does stimulation cause the receptor cell to hyperpolarize?

- a. Vision
- b. Hearing
- c. Taste
- d. Touch
- e. Smell

109. A 22-year-old man sees his ophthalmologist because it is becoming increasingly difficult for him to read the newspaper. His vision problem most likely results from an inability to contract which of the following?

- a. The iris
- b. The ciliary body
- c. The suspensory ligaments
- d. The extraocular muscles
- e. The pupil

112 Physiology

110. At a first grade parent-teacher conference, the teacher of a 6-year-old boy indicates that the boy seems to have difficulty hearing. His parents take him to the pediatrician, who refers the boy to an otolaryngologist. The boy is found to have a significant hearing deficit accompanying a middle ear infection that also involves the middle ear bones. Which of the following is the primary function of the middle ear bones?

- a. To amplify sounds
- b. To filter high-frequency sounds
- c. To localize a sound
- d. To enhance frequency discrimination
- e. To protect the ear from loud sounds

111. The morning after a rock concert, a 20-year-old college student notices difficulty hearing his professor during lecture. The physician at the Student Health Center suspects possible damage to his hair cells by the loud music. Depolarization of the hair cells in the cochlea is caused primarily by the flow of which of the following?

- a. K^+ into the hair cell
- b. Na^+ into the hair cell
- c. Cl^- out of the hair cell
- d. Ca^{2+} into the hair cell
- e. K^+ out of the hair cell

112. A 62-year-old man with a history of hypertension and hyperlipidemia is admitted to the hospital for evaluation after demonstrating signs and symptoms of a stroke. Subsequent CT scans, perceptual tests, and a neurological examination provide evidence for impairment of the otolith pathways. The otolith organs (utricle and saccule) are responsible for which of the following?

- a. Producing the vestibular-ocular reflex
- b. Detecting the position of the head in space
- c. Producing rotary nystagmus
- d. Detecting angular acceleration
- e. Producing the stretch reflex

113. A 68-year-old man presents with a chief complaint of night blindness (nyctalopia). He is found to have avitaminosis A, which underlies the impairment of rod function. Which of the reactions in the retinal rods is caused directly by the absorption of light energy?

- a. Dissociation of scotopsin and metarhodopsin
- b. Decomposition of scotopsin
- c. Transformation of 11-cis retinal to all-trans retinal
- d. Transformation of metarhodopsin to lumirhodopsin
- e. Transformation of vitamin A to retinene

114. A 20-year-old boxer suffers from disequilibrium after several blows to the ears. Which of the following normally happens when a person slowly rotates toward the right?

- a. The stereocilia on the hair cells in the right horizontal semicircular canal bend away from the kinocilium
- b. Both the left and right eyes deviate toward the left
- c. The hair cells in the left horizontal semicircular canal become depolarized
- d. The visual image on the retina becomes unfocused
- e. The endolymph in the left and right horizontal semicircular canals moves in opposite directions

115. A 58-year-old woman goes to her physician because she is having difficulty threading needles. An eye examination leads to the diagnosis of presbyopia (old eyes). Her condition is most likely caused by which of the following?

- a. Clouding of the vitreous
- b. Retinal detachment
- c. Ciliary muscle paralysis
- d. Stiffening of the lens
- e. Degeneration of the macula

116. An eight-year-old boy is hit in the head by a baseline drive during a little league game. His father, a doctor, rushes out on the field to do a neurological assessment, including use of his penlight to check reactivity of the pupils. When light strikes the eye, which of the following normally increases?

- a. The activity of transducin
- b. The amount of transmitter released from the photoreceptors
- c. The concentration of all-trans retinal within the photoreceptors
- d. The concentration of calcium within the photoreceptors
- e. The activity of guanylyl cyclase

117. A 59-year-old woman with bilateral glaucoma is treated with drops of the parasympathetic agent pilocarpine. Cholinergic stimulation of the pupil causes which of the following?

- a. Pupillary dilation (mydriasis)
- b. Pupillary constriction (miosis)
- c. Inequality of pupil size
- d. Tonic pupil (slow redilation after exposure to light)
- e. Absence of the pupillary response to light

118. A 20-year-old female complains of altered taste following extraction of her wisdom teeth. Which of the following is the most likely cause of the dysgeusia?

- a. A disturbed salivary milieu
- b. Injury to the taste receptor cells
- c. Impaired transport of the tastant to the receptor cells in the taste bud
- d. Damage to the gustatory afferent nerves
- e. Damage to the central gustatory pathways

119. A 52-year-old male smoker complains of the inability to smell. Which of the following is the most likely cause of his anosmia?

- a. Interference with transport of odorants to the receptor cells
- b. Carbon monoxide-induced damage to the olfactory afferent nerves
- c. Metaplasia of the olfactory neuroepithelium
- d. Nicotine-induced damage to the central olfactory pathways
- e. A neoplasm of the inferior frontal region

120. What percentage of the human genome is involved in the formation and function of the nervous system?

- a. 20
- b. 40
- c. 60
- d. 80
- e. >90

121. A 24-year-old medical student develops apprehension, restlessness, tachycardia, and tachypnea as he enters the testing center for his initial licensure examination. Activation of which of the following receptors would be expected to decrease his anxiety?

- a. Neuropeptide Y
- b. Glutamate

- c. GABA_A
- d. Histamine
- e. Neurokinin 1 (NK-1, Substance P)

122. The daughter of an 85-year-old man brings him to his doctor's appointment. She reports that he has memory loss, is often confused, and has been having increasing difficulty with routine activities that he used to do on his own, such as paying bills and going grocery shopping. She wonders if this is just old age or a more serious problem. Which of the following would provide the definitive diagnosis of Alzheimer's Disease?

- a. Nonspecific slowing of the EEG
- b. Presence of an apolipoprotein $\epsilon 4$ (Apo $\epsilon 4$) allele on chromosome 19
- c. Improved symptoms with cholinesterase inhibitors
- d. Cerebral cortical atrophy on CT or MRI
- e. Microscopic pathological findings on autopsy, including neuritic plaques containing A-beta ($A\beta$) amyloid bodies and silver-staining neurofibrillary tangles in neuronal cytoplasm

123. A 26-year-old African-American female medical student goes to the Emergency Department when she sees flashes of light, moving spots, and has reduced visual acuity. An ophthalmology consult reveals that she is myopic, does not have eye pain, and has a scotoma in the peripheral vision field of her right eye. There is no cherry red spot on the fovea. Which of the following is the most likely cause for her acute vision loss?

- a. Central retinal artery embolism
- b. Retinal detachment
- c. Optic neuritis
- d. Glaucoma
- e. Macular degeneration

124. After sitting with one leg crossed under the other for several hours while working on a document at her computer terminal, a 52-year-old woman went to stand up, but could not walk on the crossed leg, and felt tingling and pain in it. Which of the following explains the loss of motor function without the loss of pain sensation in the peripheral nerves.

- a. $A\beta$ fibers are more sensitive to pressure than C fibers
- b. C fibers are more sensitive to pressure than $A\beta$ fibers
- c. C fibers are more susceptible to hypoxia than B fibers
- d. A fibers are more susceptible to local anesthetics than C fibers
- e. C fibers have higher conduction velocities than A fibers.

125. Three weeks following a GI infection with *Campylobacter jejuni*, a 60-year-old male develops weakness and tingling in his legs. Over the next few days, his legs and face become paralyzed, and he is hospitalized with Guillain-Barré Syndrome. Which of the following is the most likely underlying cause of motor paralysis?

- a. Demyelination of B fibers
- b. Demyelination of C fibers
- c. Demyelination of $A\beta$ fibers
- d. Antibodies against nerve growth factor
- e. Antibodies against oligodendroglialocytes

126. A 32-year-old woman presents with muscular weakness and fatigue, as well as ptosis and diplopia, with worsening of symptoms as the day progresses. An MRI of the chest shows enlargement of the thymus gland. The neuropathy of myasthenia gravis is caused by antibodies against which of the following?

- a. Acetylcholine
- b. Nicotine
- c. Acetylcholinesterase
- d. Acetylcholine receptors
- e. The thymus gland

127. Which of the following characteristics of an axon is most dependent on its diameter?

- a. The magnitude of its resting potential
- b. The duration of its refractory period
- c. The conduction velocity of its action potential
- d. The overshoot of its action potential
- e. The activity of its sodium-potassium pump

128. An 80-year-old farmer presented with complaints of weakness and fatigue, aching, orthostatic hypotension, constipation, and sleep disturbances. His family physician told him that he was just getting old, and would have to get used to it. His bradykinesia worsened and he couldn't pick up his feet when he walked. When he was no longer able to plow his own fields, he got depressed, and his wife said he would just sit at the table and rub his thumb along his fingers. She called her son-in-law, a neurologist, and asked him if he'd come out to the country to evaluate "Pops." The pathophysiology of Parkinson's disease can be attributed to a paucity of which of the following neurotransmitters?

- a. Acetylcholine
- b. Dopamine
- c. Glutamate
- d. Neuropeptide Y
- e. Serotonin

129. A 62-year-old male with COPD presents to the emergency room in respiratory distress. The attending physician uses succinylcholine to produce skeletal muscle relaxation prior to tracheal intubation. Soon after infusion of the succinylcholine, the patient develops a severe bradycardia. Which of the following drugs would counteract the bradycardia without affecting muscle relaxation?

- a. Curare
- b. Atropine
- c. Epinephrine
- d. Acetylcholine
- e. Dopamine

130. A fireman suffers extensive burns, resulting in a fluid and electrolyte imbalance. Which of the following conditions will produce a decrease in the magnitude of a nerve membrane action potential?

- a. Hyperkalemia
- b. Hypokalemia
- c. Hypernatremia
- d. Hyponatremia
- e. Hypocalcemia

131. An 18-year-old male, who became ill after eating mushrooms, is brought to the Emergency Department, where he is treated for muscarinic poisoning. Which of the following signs is consistent with muscarinic poisoning?

- a. Skeletal muscle contractures
- b. Bradycardia
- c. Dilation of the pupils
- d. Hypertension
- e. Diuresis

132. A 19-year-old woman with a history of diplopia and paresthesia is diagnosed with multiple sclerosis (MS). MS is a demyelinating disease characterized by a failure of nerve conduction. Immersion of an affected limb in a cold bath restores nerve conduction in many of these patients. The explanation often cited for this effect is that cold increases the duration of the action potential. Which of the following best explains why increasing the duration of the action potential can restore nerve conduction in patients with MS?

- a. The capacitance of the nerve fiber membrane is increased
- b. The duration of the refractory period is increased
- c. The potassium conductance of the membrane is increased
- d. The amount of sodium entering the nerve with each action potential increases
- e. The membrane potential becomes more positive

133. The membrane potential will depolarize by the greatest amount if the membrane permeability increases for which of the following?

- a. Potassium
- b. Sodium and potassium
- c. Chloride
- d. Potassium and chloride
- e. Sodium

134. Which of the following is less during the overshoot of an action potential than during the resting state?

- a. Membrane conductance for sodium
- b. Membrane conductance for potassium
- c. Transference for sodium
- d. Transference for potassium
- e. Total membrane conductance

135. A 52-year-old male was given a shot of procaine prior to oral surgery to extract an abscessed tooth. Preventing the inactivation of sodium channels by local anesthetics will decrease which of the following?

- a. The relative refractory period of nerve cells
- b. The upstroke velocity of nerve cell action potentials
- c. The downstroke velocity of nerve cell action potentials
- d. The magnitude of the overshoot in nerve cell action potentials
- e. The duration of nerve cell action potentials

136. A 13-year-old boy on the junior high wrestling team experiences attacks of proximal muscle weakness that last from 30 minutes to as long as 4 hours following exercise and fasting. The trainer attributed it to the symptoms of fatigue, but his mother recalled having similar symptoms when she was dieting. Genetic testing revealed an inherited channelopathy. Electrically excitable gates are normally involved in which of the following?

- a. The depolarization of the end-plate membrane by acetylcholine
- b. Hyperpolarization of rods by light
- c. Release of calcium from ventricular muscle sarcoplasmic reticulum
- d. Transport of glucose into cells by a sodium-dependent, secondary active transport system
- e. Increase in nerve cell potassium conductance caused by membrane depolarization

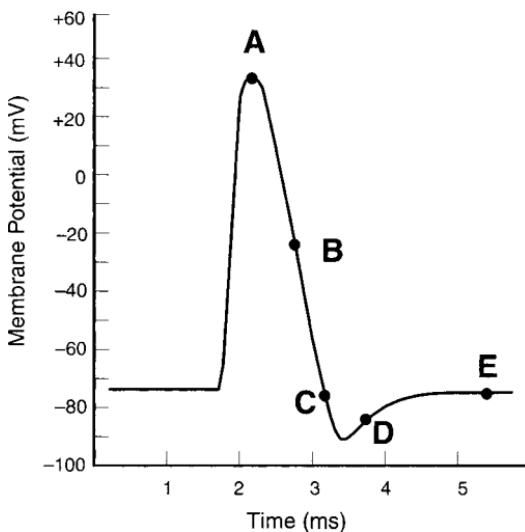
137. Which of the following is true regarding the sodium gradient across the nerve cell membrane?

- a. It is a result of the Donnan equilibrium
- b. It is significantly changed during an action potential
- c. It is used as a source of energy for the transport of other ions
- d. It is an important determinant of the resting membrane potential
- e. It is maintained by a $\text{Na}^+/\text{Ca}^{2+}$ exchanger

138. A 19-year-old sexually active female presents with lower abdominal pain for 1 week. Physical exam reveals a temperature of 101°F, tenderness on pelvic exam, and a mucopurulent vaginal discharge. Synaptic transmission between pain fibers from the pelvis and spinal cord neurons is mediated by which of the following?

- a. Acetylcholine
- b. Substance P
- c. Endorphins
- d. Somatostatin
- e. Serotonin

I39. At which point on the action potential shown in the diagram below is the membrane closest to the Na^+ equilibrium potential?



- a. Point A
- b. Point B
- c. Point C
- d. Point D
- e. Point E

I40. A 16-year-old, highly allergic girl who is stung by a bee gives herself a shot of epinephrine prescribed by her physician. Because epinephrine activates β -adrenergic receptors, it will relieve the effects of the bee sting by decreasing which of the following?

- a. The contraction of airway smooth muscle
- b. The strength of ventricular muscle contraction
- c. The rate of depolarization in the SA node
- d. The transport of calcium into skeletal muscle fibers
- e. The rate of glycogenolysis in the liver

141. An 86-year-old woman develops unilateral vesicular eruption on the trunk in a T₈ dermatomal pattern. Fluorescent staining of the skin scrapings confirms a diagnosis of herpes zoster. The woman complains of significant pain, as well as increased sensitivity to touch. Which of the following receptors is responsible for measuring the intensity of a steady pressure on the skin surface?

- a. Pacinian corpuscle
- b. Ruffini ending
- c. Merkel's disk
- d. Meissner's corpuscle
- e. Krause ending

142. A 24-year-old man complains of fatigue, increased daytime somnolence, and periodic sudden loss of muscle tone. Polysomnography confirms the diagnosis of narcolepsy. Narcolepsy is associated with which of the following?

- a. Increased discharge of noradrenergic neurons in the locus ceruleus
- b. Increased discharge of serotonergic neurons in the midbrain raphé
- c. Decreased adenosine levels in the reticular formation
- d. The presence of prions
- e. Hypothalamic dysfunction with decreased CSF levels of orexins

Neurophysiology

Answers

83. The answer is d. (*Ganong, pp 141–143.*) Free nerve endings contain receptors for temperature, pain, and crude touch. However, fine touch, pressure, and vibration are detected by nerve endings contained within specialized capsules that transmit the stimulus to the sensory receptors. Muscle length is encoded by the primary nerve endings of Ia fibers, which are located on intrafusal fibers within the muscle spindle.

84. The answer is b. (*Ganong, pp 272–275. Kasper et al., pp 145–148.*) Aphasias are language disorders in which a person is unable to properly express or understand certain aspects of written or spoken language. Aphasias are caused by lesions to the language centers, which are located in the categorical hemisphere of the neocortex. There are a number of different classifications of aphasias, but one divides them into fluent, nonfluent, and anomic aphasias. In this case, the boy developed an anomic aphasia, in which there was no difficulty with his speech and he was able to understand and follow commands, but he had difficulty understanding written language and pictures. Anomic aphasia is the single most common language disturbance seen in head trauma, metabolic encephalopathy, and Alzheimer's disease. Anomic aphasia can be caused by lesions anywhere within the language network, but often is caused by damage to the angular gyrus without damage to Broca's or Wernicke's areas. A lesion in Broca's area leads to nonfluent aphasia, such as seen in Pick's disease. Fluent aphasias are due to lesions to Wernicke's area or to lesions in and around the auditory cortex. Language disorders caused by memory loss, which could be the result of a hippocampal lesion, are not classified as aphasias, nor are language disorders caused by vision or hearing abnormalities or motor paralysis.

85. The answer is b. (*Ganong, pp 130–133.*) The γ motoneurons innervate the intrafusal fibers of the muscle spindles. When a skeletal muscle contracts, the intrafusal muscle fiber becomes slack and the Ia afferents stop firing. By stimulating the intrafusal muscle fibers during a contraction, the γ motoneurons prevent the intrafusal muscle fibers from becoming slack and thus maintain Ia firing during the contraction.

86. The answer is b. (*Ganong, pp 202–222. Kasper et al., pp 2406–2414. Stead et al., pp 325–326. Widmaier et al., pp 333–335.*) Parkinson's disease is characterized by resting tremor rigidity and akinesia. It is caused by destruction of the dopamine secreting neurons within the substantia nigra of the basal ganglia. Levo (L)-dopa is a precursor for dopamine. L-dopa, rather than dopamine, is administered because it can cross the blood-brain barrier, but dopamine cannot. In contrast to the resting tremor of Parkinson's disease, cerebellar disease is characterized by an intention tremor. In contrast to damage to the nigrostriatal dopaminergic system in Parkinson's disease, Huntington's disease results in a loss of the intrastriatal GABAergic and cholinergic neurons in the caudate nucleus and putamen of the basal ganglion.

87. The answer is b. (*Ganong, pp 129–132. Widmaier et al., pp 327–329.*) The Ia afferents, which innervate the muscle spindles, have a phasic and tonic component. **B** illustrates the response of Ia afferents to a sudden movement of a limb. The high-frequency burst of action potentials encodes the velocity of the initial movement, whereas the steady firing encodes the position of the limb when the movement is completed. **A** and **E** illustrate the behavior of a tonic receptor, which discharges at the same rate for as long as the stimulus is present.

88. The answer is e. (*Ganong, pp 202–205.*) The precentral gyrus is the motor area of the cortex that contains the cell bodies of the neurons that form the corticospinal tract (also referred to as the pyramidal tract). The corticospinal tract contains axons that cross to the contralateral side of the brain within the pyramids and end within the motor areas of the spinal cord. These structures are essential for the generation of fine voluntary movements. Kinesthesia, the sense of movement and position of the limbs, is handled primarily by the Ia and Ib afferents that innervate the muscle spindles and Golgi tendon organs, respectively, and by the parietal lobe.

89. The answer is d. (*Ganong, pp 612–614. Stead et al., pp 326–327.*) The concentrations of protein and glucose within the cerebrospinal fluid (CSF) are much lower than those of plasma. Changes in the CSF concentrations of these substances are helpful in detecting pathologic processes, such as tumor or infection, in which the blood-brain barrier is disrupted. Cerebrospinal fluid, which is in osmotic equilibrium with the extracellular fluid of the brain and spinal cord, is formed primarily in the choroid plexus by an active secretory process. It circulates through the subarachnoid space

between the dura mater and pia mater and is absorbed into the circulation by the arachnoid villi. The epidural space, which lies outside the dura mater, may be used clinically for instillation of anesthetics.

90. The answer is a. (*Ganong*, pp 221–222. *Kasper et al.*, pp 139, 2418–2424.) Ataxia, dysmetria, and an intention tremor all are classic findings in a patient with a lesion involving the cerebellum. Affected persons also exhibit adiadochokinesia, which is a loss of ability to accomplish a swift succession of oscillatory movements, such as moving a finger rapidly up and down. High-amplitude EEG waves occur in the late stages of slow-wave sleep.

91. The answer is b. (*Ganong*, pp 195–201. *Kasper et al.*, pp 153–162.) In a normal sleep cycle, a person passes through the four stages of slow-wave sleep before entering REM sleep. In narcolepsy, a person may pass directly from the waking state to REM sleep. REM sleep is characterized by irregular heart beats and respiration and by periods of atonia (loss of muscle tone). Hypoventilation is characteristic of both REM and non-REM sleep because sleep depresses the central chemoreceptors. Brain activity during REM sleep is higher than during wakefulness so there is an increase in brain metabolism. It is also the state of sleep in which dreaming occurs.

92. The answer is a. (*Ganong*, pp 129–133.) The Ib afferents innervating the quadriceps muscles are activated when the quadriceps contracted in response to tapping the patella tendon. Stretching the patella tendon stretches the intrafusal muscle fibers within the quadriceps muscle and causes an increase in Ia afferent activity. The increase in Ia afferent activity causes an increase in α motoneuron activity, which results in contraction of the quadriceps muscle. When the muscle contracts, the intrafusal muscle fibers are unloaded and the Ia afferent activity is reduced.

93. The answer is d. (*Kasper et al.*, pp 138–141.) Spasticity results from overactivity of the α motoneurons innervating the skeletal musculature. Under normal circumstances, these α motoneurons are tonically stimulated by reticulospinal and vestibulospinal fibers originating in the brainstem. These brainstem fibers are normally inhibited by fibers originating in the cortex. Cutting the cortical fibers releases the brainstem fibers from inhibition and results in spasticity. Cutting the fibers from the reticular formation, vestibular nuclei, or the Ia afferents will reduce the spasticity.

94. The answer is c. (*Ganong*, pp 184, 220–221. *Kasper et al.*, pp 130–133, 176.) Pathologic vertigo is generally classified as peripheral (labyrinthine) or central (brainstem or cerebellum). The clinical presentation in this case is most consistent with central vertigo. Positional (especially horizontal) nystagmus (to-and-fro oscillation of the eyes) is common in vertigo of central origin, but absent or uncommon in peripheral vertigo. The chronicity of the vertigo is characteristic of central vertigo, whereas the symptoms of peripheral vertigo generally have a finite duration and may be recurring. Tinnitus and/or deafness is often present in peripheral vertigo, but absent in central vertigo. The flocculonodular lobe, or vestibulocerebellum, is connected to the vestibular nuclei and participates in the control of balance and eye movements, particularly changes in the vestibuloocular reflex (VOR), which serves to maintain visual stability during head movement; a lesion of this area of the cerebellum may result in vertigo and nystagmus, whereas the spinocerebellum is involved in the coordination of limb movement. Labyrinthitis and Ménière's syndrome are examples of vertigo of peripheral origin. In psychogenic versus organic vertigo, nystagmus is absent during a vertiginous episode.

95. The answer is b. (*Ganong*, pp 194–196.) In a totally relaxed adult with eyes closed, the major component of the electroencephalogram (EEG) will be a regular pattern of 8 to 12 waves per second, called the α rhythm. The α rhythm disappears when the eyes are opened. It is most prominent in the parieto-occipital region. In deep sleep, the α rhythm is replaced by larger, slower waves called delta waves. In REM sleep, the EEG will show fast, irregular activity.

96. The answer is e. (*Ganong*, pp 153–156. *Kasper et al.*, pp 162–164.) The focal length of an ideal refractive surface is equal to the distance between the refractive surface and the image formed by a distant object. In a normal eye, the image of a distant object is formed on the retina. Therefore, the focal length is 14 mm. If the image is formed in front of the retina, the eye would be myopic (near-sighted); if the image formed behind the retina, the eye would be hyperopic (far-sighted). When an image is placed close to the eye (in ophthalmology, close means less than 20 ft or 6 m), the eye must accommodate (increase its refractive power) for near vision. The refractive power of a lens system in diopters is equal to the reciprocal of the focal length ($1/f$) in meters. The relationship between the refractive power P , or focal distance, the image distance i , and the object distance o is given by the lens formula

$$P = 1/f = 1/o + 1/i$$

where each of the distances is given in meters. If the object distance is 0.25 m and the image distance, the distance from the cornea to the retina, is 0.014 m, the refractive power of the eye is 75 diopters ($0.264/0.0035$). The initial refractive power was 71 diopters ($1/0.014$). Therefore, to form a clear image of the object on the retina, the accommodation reflex for near vision increased the refractive power of the eye by 4 diopters.

97. The answer is d. (*Ganong, pp 213–216. Kasper et al., pp 138–140, 2415–2416.*) Huntington's chorea is an inherited genetic defect leading to the degeneration of neurons with the striatum (the caudate nucleus and putamen). It is progressive disease characterized by uncontrolled movements, irritability, depression, and ultimately dementia and death. Lesions of the subthalamic nucleus produce wild flinging movements called ballism; those within the anterior cerebellum produce ataxia; those within the substantia nigra produce Parkinson's disease; and those within the limbic system yield emotional disorders.

98. The answer is d. (*Ganong, pp 226–230.*) The catecholamines, norepinephrine and epinephrine, will activate both α - and β -adrenergic receptors. When the α_1 -adrenergic receptors are stimulated, they activate a G protein, which in turn activates phospholipase C, which hydrolyzes PIP₂ and produces IP₃ and DAG. The IP₃ causes the release of Ca²⁺ from the sarcoplasmic reticulum, which in turn increases muscle contraction. α_1 -Adrenergic receptors predominate on arteriolar smooth muscle, so these muscles contract when stimulated with norepinephrine. The bronchiolar, pupillary, and ciliary smooth muscles all contain β receptors, which cause smooth muscle relaxation. The intestinal smooth muscle relaxation is initiated by an α_2 -adrenergic receptor.

99. The answer is a. (*Ganong, pp 182–183. Kasper et al., pp 181–184.*) The portion of the basilar membrane vibrated by a sound depends on the frequency of the sound. High-frequency sounds produce a vibration of the basilar membrane at the base of the cochlea (near the oval and round windows); low-frequency sounds produce a vibration of the basilar membrane at the apex of the cochlea (near the helicotrema). The modiolus is the bony center of the cochlea from which the basilar membrane emerges, the spiral ganglion contains the cell bodies of the auditory nerve fibers, and the stria vascularis is the vascular bed located on the outer wall of the scala media of the cochlea responsible for endolymph secretion.

100. The answer is e. (*Ganong, p 206. Kasper et al., pp 134, 2348.*) The Babinski reflex causes the toes to dorsiflex in response to stroking the plantar or lateral portion of the foot. It is an abnormal reflex caused by damage to the corticospinal (pyramidal) tract that travels from the cortical motor cortex through the pyramids to the spinal cord. Other signs of pyramidal tract lesions include loss of the hopping and placing reaction, the cremasteric reflex, and the abdominal scratch reflex. Damage confined to the pyramidal tract results in distal muscular weakness and loss of fine motor control. Damage to other areas of the cortical motor control system is referred to as upper motor neuron disease and produces spasticity. Damage to the basal ganglia produces a variety of signs including dystonia (striatum), ballism (subthalamic nucleus), and tremor at rest (substantia nigra). Damaging the cerebellum causes uncoordinated movements (dysmetria, ataxia, intention tremor).

101. The answer is e. (*Ganong, pp 234–235.*) A variety of physiological functions, such as alertness (the sleep-wake cycle), body temperature, and secretion of hormones, exhibits cyclic activity that varies over a 24-h period of time. These variations in activity are called circadian rhythms and are controlled by the suprachiasmatic nucleus of the hypothalamus. The paraventricular nucleus secretes oxytocin and vasopressin, the ventromedial and lateral nuclei control food intake, and the arcuate nucleus secretes gonadotropin-releasing hormone.

102. The answer is a. (*Ganong, pp 92–93. Kasper et al., pp 2461–2471.*) Presynaptic inhibition is caused by interneurons that secrete a transmitter that increases the Cl^- conductance of the presynaptic nerve ending. The increase in Cl^- conductance causes a partial depolarization of the presynaptic nerve ending and a decrease in the magnitude of the action potential in the presynaptic nerve ending. Because the number of synaptic vesicles released from the presynaptic neuron is proportional to the magnitude of the action potential, fewer vesicles are released and magnitude of the postsynaptic potential is reduced. Reducing the magnitude of the postsynaptic potential decreases the probability that an action potential will be generated by the postsynaptic cell. Presynaptic inhibition does not change the membrane potential of the α motoneuron.

103. The answer is e. (*Kasper et al., pp 164–165.*) The loss of vision on one side of the visual field is called hemianopia. If it affects the same half of

the visual field on both eyes, it is called a homonymous hemianopia. A right-sided homonymous hemianopia (E) is caused by a lesion affecting the left visual pathway distal to the optic chiasm, where the visual information from the nasal portion of the left retina (the right hemifield of the left eye's visual field) and the temporal portion of the right retina (the right hemifield of the right eye's visual field) are carried within the same nerve tract. Bitemporal hemianopia (D) results from more symmetric compression of the optic chiasm, as may occur with pituitary adenoma, meningioma, glioma, or aneurysm.

104. The answer is d. (*Kasper et al.*, pp 164–165.) The optical field defect is produced by an enlarged pituitary gland, which impinges on the optic chiasm. Compression of the optic chiasm by the pituitary gland damages the nasal portion of each optic nerve, which produces a loss of vision in the temporal visual field of both eyes. This defect is referred to as a bitemporal hemianopia.

105. The answer is e. (*Ganong*, pp 122, 142–147.) Activating nociceptors on the free nerve endings of C fibers produces ischemic pain. The C fibers synapse on interneurons located within the substantia gelatinosa (laminae II and III) of the dorsal horn of the spinal cord. The pathway conveying ischemic pain to the brain is called the paleospinothalamic system. In contrast, well-localized pain sensations are carried within the neospinothalamic tract. Ischemic pain does not adapt to prolonged stimulation. Pain is produced by specific nociceptors and not by intense stimulation of other mechanical, thermal, or chemical receptors.

106. The answer is e. (*Ganong*, pp 251–255.) The hypothalamus regulates body temperature. Core body temperature, the temperature of the deep tissues of the body, is detected by thermoreceptors located within the anterior hypothalamus. The anterior hypothalamus also contains neurons responsible for initiating reflexes, such as vasodilation and sweating, which are designed to reduce body temperature. Heat-producing reflexes, such as shivering, and heat-maintenance reflexes, such as vasoconstriction, are initiated by neurons located within the posterior hypothalamus.

107. The answer is a. (*Guyton*, pp 686–687.) The Klüver-Bucy syndrome is produced in animals by removal of the amygdala from both temporal lobes. The syndrome is characterized by excessive sexual behavior and a tendency to examine objects orally. The full syndrome is rarely encountered

in humans but many of its characteristics are observed in patients with bilateral temporal lobe lesions produced by encephalitis or traumatic injury.

108. The answer is a. (*Ganong, pp 156–160. Widmaier et al., pp 233–238.*) The visual receptor cells, the rods and cones, are depolarized when the eyes are in the dark. When exposed to light, they hyperpolarize. Light causes the rods and cones to hyperpolarize by activating a G protein called transducin, which leads to the closing of Na^+ channels. Auditory receptors are depolarized by the flow of K^+ into the hair cells. Touch receptors are activated by opening channels through which both Na^+ and K^+ can flow. Depolarization is caused by the inward flow of Na^+ . Smell and taste receptors are activated by G protein-mediated mechanisms, some of which cause the receptor cell to depolarize; other G proteins cause the release of synaptic transmitter without any change in membrane potential.

109. The answer is b. (*Ganong, pp 148–170. Widmaier et al., pp 230–233.*) Contracting the ciliary body increases the refractive power of the eye for near vision. When the ciliary muscle contracts, it pulls the suspensory ligaments toward the cornea, which causes the lens surface to bulge, increasing its refractive power. The muscles of the iris control the size of the pupils, and the extraocular muscles control the position of the eye in the socket.

110. The answer is a. (*Ganong, pp 171–183. Widmaier et al., pp 238–246.*) When sound waves pass from air to water, most of the energy contained in the sound stimulus is lost. Because the auditory receptors within the inner ear are bathed in liquid, most of the energy in the sound stimulus could be lost as the sound travels from air to water. The bones of the middle ear significantly reduce the amount of loss by amplifying the sound stimulus. Audiologists refer to this amplification phenomenon as impedance matching. Sound localization is carried out by the central nervous system (CNS), which integrates information from both ears. Frequency discrimination is a function of the basilar membrane. The stapedius and tensor tympani muscles protect the ear from loud sounds.

111. The answer is a. (*Ganong, pp 171–183. Widmaier et al., pp 243–246.*) When the hair cells are bent, K^+ selective channels open, K^+ flows into the cell, and the cell depolarizes. This unusual situation occurs because the apical surface of the hair cells, on which the stereocilia are located, is

bathed in endolymph, which contains a high concentration of K^+ . Moreover, the endolymph is positively charged with respect to the perilymph, which surrounds the basal lateral portion of the hair cell. Because the intracellular concentration of K^+ is similar to the extracellular concentration of K^+ , the electrical gradient determines the direction of K^+ flow. Because the endolymph is positively charged and the intracellular fluid is negatively charged, K^+ flows into the cell.

112. The answer is b. (*Ganong*, pp 171–172, 183–184. *Widmaier et al.*, p 246.) The otolith organs provide information about the position of the head with respect to gravity. When the head is bent away from its normal upright position, otoliths (small calcium carbonate crystals within the utricle and saccule) are pulled downward by gravity. The crystals bend the stereocilia on the hair cells, causing the hair cells to depolarize. Depolarization of the hair cells stimulates the vestibular nerve fibers. Bending the head in different directions causes different otoliths to move. Therefore, the particular group of vestibular nerve fibers that is stimulated signals the direction in which the head bends.

113. The answer is c. (*Ganong*, pp 158–159, 167.) The light-sensitive chemical in the retinal rods is called rhodopsin. It is a combination of 11-cis retinal and opsin. The photoisomerization of 11-cis retinal to all-trans retinal activates rhodopsin. The subsequent separation of opsin and retinal and the reformation of 11-cis rhodopsin are not necessary for the activation of the visual receptors. Rhodopsin cannot absorb another photon of light, however, until it is enzymatically isomerized back to its 11-cis conformation.

114. The answer is b. (*Ganong*, pp 173–184. *Widmaier et al.*, pp 244–247.) When the head rotates in one direction, the hair cells mounted on the cristae rotate along with the head. However, the flow of endolymph is delayed and as a result the cupula is moved in a direction opposite to the movement of the head. When the head moves to the right, the cupula moves toward the left; this bends the stereocilia on the hair cells in the right horizontal canal toward the kinocilium and bends the stereocilia on the hair cells in the left horizontal canal toward the kinocilium. As a result, the hair cells in the right horizontal canal depolarize and those in the left horizontal canal hyperpolarize. The depolarization of the hair cells in the right horizontal canal stimulates the right vestibular nerve, which in turn causes the eyes to deviate toward the left. The movement of the eyes toward the left as the head deviates toward the right keeps the image on the retina in focus.

115. The answer is d. (*Ganong, pp 153–156. Widmaier et al., pp 230–233.*) The increase in lens power that normally occurs when objects are placed close to the eye (the accommodation reflex) does not take place in presbyopia. The failure of the accommodation reflex occurs because the lens and lens capsule stiffen with age. There are some reports of ciliary muscle weakness accompanying presbyopia but there are none indicating the presbyopia is caused by ciliary muscle paralysis.

116. The answer is a. (*Ganong, pp 157–160.*) Transducin is the G protein activated by rhodopsin when light strikes the eye. Transducin activates a phosphodiesterase that hydrolyzes cGMP. When cGMP concentrations within the rods or cones decrease, sodium channels close, sodium conductance decreases, and the cell membrane potential becomes more negative (hyperpolarizes). Hyperpolarization of the cell causes a decrease in the release of neurotransmitter. Eventually the all-trans retinal dissociates from opsin and reduces the concentration of rhodopsin in the cell.

117. The answer is b. (*Ganong, p 227. Kasper et al., pp 163–164.*) Parasympathetic stimulation or cholinergic muscarinic agonists used to treat glaucoma produce miosis, that is, pupillary constriction caused by contraction of the sphincter muscle of the iris. Anticholinergic agents (e.g., atropine) or sympathetic stimulation produce mydriasis, that is, pupillary dilation, in which the increase in pupil size results from contraction of the radial muscle of the iris mediated by α_1 -adrenergic receptors.

118. The answer is d. (*Kasper et al., pp 178–179.*) Trauma to the chorda tympani branch of the facial nerve during third molar extractions or middle ear surgery is relatively common and can cause dysgeusia. Other mechanisms of disorders of the sense of taste besides damage to the gustatory afferent nerves include damage to central gustatory pathways (trauma, diabetes mellitus, hypothyroidism, stroke, CNS disorders), sensory losses (aging, Candidiasis, viral infections, many drugs, especially those that interfere with cell turnover such as antineoplastic and antithyroid agents), and transport gustatory losses (interference with access of tastant to receptor cells, such as with xerostomia, Sjögren's syndrome, heavy metal intoxication, oral radiation therapy). No effective therapies exist for the sensorineural disorders of taste. Altered taste due to surgical stretch of the chorda tympani nerve usually improves within 3 to 4 months.

119. The answer is c. (*Ganong*, pp 185–188, 250–251. *Kasper et al.*, pp 176–179.) Exposure to cigarette smoke and other airborne toxic chemicals can cause metaplasia of the olfactory neuroepithelium with resultant anosmia (absence of smell), hyposmia (decreased sense of smell), or dysosmia (distorted sense of smell). Spontaneous recovery can occur if the insult is discontinued. Vitamin A deficiency can also cause anosmia as a result of epithelial degeneration. The most common etiologies of olfactory disorders are head trauma in children and young adults (neural loss) and viral infections in older adults (sensory and transport loss). In addition, olfactory thresholds increase with age; more than 75% of people over the age of 80 have an impaired ability to identify smells. Other examples of transport losses include allergic or bacterial rhinitis, nasal polyps, nasal surgery, deviated nasal septum, and congenital abnormalities (e.g., Kallman syndrome (hypogonadotropic hypogonadism with hypoosmia or anosmia, albinism)). Other examples of sensory losses of smell due to injury to the receptor region include neoplasms, radiation therapy, and drugs. Currently, no clinical tests exist to differentiate these different types of olfactory losses.

120. The answer is b. (*Ganong*, pp 51, 742.) It has been calculated that 40% of the human genes participate to some extent in the formation of the 100 billion neurons that comprise the human central nervous system.

121. The answer is c. (*Ganong*, pp 107–112, 238, 259, 746.) γ -Aminobutyric acid (GABA) is the major inhibitory mediator in the brain. GABA_A receptors are pentameric Cl⁻ ion channels that are widely distributed in the CNS. The increase in Cl⁻ conductance produced by GABA_A receptors is potentiated by the anxiolytic drug, diazepam, and other benzodiazepines. Glutamate is the major excitatory transmitter in the brain. Neuropeptide Y is an excitatory neurotransmitter that has a stimulatory effect on food intake. Central nervous system actions of histamine have been implicated in arousal, sexual behavior, drinking, pain thresholds, and the sensation of itch. Antagonism of central NK-1 receptors has antidepressant activity in humans.

122. The answer is e. (*Kasper et al.* pp 2393–2400. *Stead et al.*, pp 324–325.) The presence of an apolipoprotein ε4 (Apo ε4) allele on chromosome 19, especially in the homozygous 4/4 state, is an important risk factor for Alzheimer's disease (AD) and cortical atrophy on CT or MRI is a diagnostic sign of AD. Also, cholinesterase inhibitors may be used to improve memory in AD by increasing available levels of acetylcholine. However, the

definitive diagnosis of AD is only obtained by tissue examination on autopsy, with the presence of amyloid plaques and neurofibrillary tangles in the neurons of the cerebral cortex, primarily in the temporal lobe, hippocampus, and nucleus basalis of Meynert (lateral septum). Short of autopsy, diagnosis is mainly clinical. Alzheimer's is the most common cause of dementia. It is a slowly progressive dementia, and a clinical diagnosis must rule out other causes of dementia, including other major common causes such as vascular disease, Parkinson's disease, alcohol dependence, alcoholism or other drug/medication intoxication.

123. The answer is b. (*Kasper et al.*, pp 167–172. *Stead et al.*, pp 322–323.) Among the causes of acute vision loss, detachment of the retina is painless, and accompanied by floaters, flashing lights, and a scotoma in the peripheral visual field corresponding to the detachment. The diagnosis is confirmed by ophthalmoscopic examination of the dilated eye. Patients with a history of myopia, trauma, or prior cataract extraction are at greatest risk for retinal detachment. Another cause of sudden painless vision loss is a transient ischemic attack of the retina, also called amourosis fugax. Amourosis fugax usually results from an embolus that lodges in a retinal arteriole. Complete occlusion of the central retinal artery produces arrest of blood flow and a milky retina with a cherry red spot on the fovea. Optic neuritis is a common inflammatory disease of the optic nerve that is accompanied by eye pain, especially with eye movements. It is caused by demyelination, and often progresses to multiple sclerosis. Glaucoma and macular degeneration cause chronic vision loss. Glaucoma is the leading cause of blindness in African-Americans; it is a slowly progressive, insidious optic neuropathy. Macular degeneration is the major cause of gradual, painless, bilateral central blindness in the elderly.

124. The answer is a. (*Ganong*, pp 60–61, 742.) Mammalian nerve fibers are classified into A, B, and C groups, and A fibers are further subdivided into α , β , γ , and δ fibers, each of which has different histologic characteristics and functions. $A\beta$ fibers have touch, pressure, and motor functions. The dorsal root C fibers conduct some impulses generated by touch and other cutaneous receptors, as well as impulses generated by pain and temperature receptors. $A\beta$ fibers are most susceptible to pressure and C fibers are least susceptible to pressure, which explains why a limb with a transiently compressed nerve loses motor function, but not pain sensation. B fibers are preganglionic autonomic nerves; they are most susceptible to hypoxia, whereas C fibers are least susceptible to hypoxia. Local anesthetics

depress transmission in the group C fibers before they affect the touch fibers in the A group. C fibers are unmyelinated, whereas A and B fibers are myelinated. In addition, C fibers generally have smaller diameters than A or B fibers. For both reasons, C fibers have lower conduction velocities than A fibers.

125. The answer is c. (*Ganong*, pp 51–53, 60–63. *Kasper et al.*, pp 2513–2516. *Stead et al.*, pp 319–320.) Guillain-Barré Syndrome (GBS) is an acute, rapidly evolving demyelinating polyradiculopathy, that generally manifests as an areflexic ascending motor paralysis and is autoimmune in nature. The basis for the flaccid paralysis and sensory disturbance is conduction block in the $A\beta$ fibers; axonal conduction remains intact unless there is secondary axonal degeneration. Most cases are preceded by a viral upper respiratory infection or a GI infection. Twenty to thirty percent of all cases occurring in North America, Europe, and Australia are preceded by infection or reinfection with *Campylobacter jejuni*. A similar proportion are preceded by a herpes virus infection, often CMV or Epstein-Barr virus. The postulated immunopathogenesis of GBS associated with *C. jejuni* infection involves production of autoantibodies against gangliosides present on the surface of Schwann cells, causing widespread myelin damage. The widespread administration of the swine influenza vaccine in the United States in 1976 was associated with an increased occurrence of GBS, but influenza vaccines in use from 1992 to 1994 resulted in only one additional case of GBS per million persons vaccinated. Older type rabies vaccines prepared in nervous system tissue are still used in developing countries and are thought to be a trigger for GBS, presumably via immunization of neural antigens. Nerve growth factor is necessary for the growth and maintenance of sympathetic neurons and some sensory neurons, not motoneurons. Experimental injection of antiserum against nerve growth factor in newborn animals produces an immunosympathectomy. Oligodendroglialocytes are involved in myelin formation in the CNS, whereas Schwann cells are involved in myelin formation in peripheral nerves.

126. The answer is d. (*Ganong*, pp 216–217. *Kasper et al.*, pp 2518–2523. *Stead et al.*, pp 318–319.) Myasthenia gravis is an autoimmune disease in which circulating antibodies against the postsynaptic nicotinic acetylcholine receptor destroy the receptors and/or prevent acetylcholine from binding. As a result, the end-plate potential is decreased at the neuromuscular junction, causing weakness and fatigue of skeletal muscles. Approximately 75% of patients with myasthenia gravis have thymic hyperplasia,

and may benefit from thymectomy. Other treatments for myasthenia gravis include anticholinesterase medications, immunosuppressive agents, and plasmapheresis or intravenous immunoglobulin.

127. The answer is c. (*Ganong*, pp 51–64.) The conduction velocity of an action potential along an axon is proportional to the axon's diameter for both unmyelinated and myelinated axons. The resting membrane potential, the duration of the relative refractory period, and the magnitude of the action potential are dependent on the type and density of electrically excitable gates and the ability of the Na^+,K^+ -ATPase to establish and maintain the concentration gradients. These characteristics are not related in any systematic way to the axon diameter.

128. The answer is b. (*Ganong*, pp 118, 202–222. *Kasper et al.*, pp 2406–2414. *Stead et al.*, pp 325–326. *Widmaier et al.*, p 334.) Parkinson's disease results from a reduction of dopaminergic transmission within the basal ganglia, generally due to degeneration of nigrostriatal dopaminergic neurons. The fibers going to the putamen are most severely affected. Dopaminergic neurons and receptors are steadily lost with age in the basal ganglia, but an abnormal acceleration of that process results in Parkinson's disease. The diagnosis of Parkinson's disease can generally be made with at least two of the cardinal signs of parkinsonism, that is, resting tremor, paucity and slowness of movement (bradykinesia), rigidity, shuffling gait, and flexed posture.

129. The answer is b. (*Ganong*, pp 100, 603.) Succinylcholine is a rapidly acting neuromuscular blocking agent with a very short duration of action. Respiratory paralysis can be produced in less than 60 seconds and normal respiration typically returns within 15 minutes. Because succinylcholine can also stimulate autonomic postganglionic fibers, vagal fibers innervating the heart are stimulated. The vagal fibers release acetylcholine, which binds to muscarinic receptors on the SA node, slowing the heart. The bradycardia can be prevented by administering atropine, which blocks the muscarinic receptors on the SA node.

130. The answer is d. (*Ganong*, p 59. *Kasper et al.*, pp 252–263. *Stead et al.*, pp 226–234.) The upstroke of the action potential is caused by an inward flow of sodium ions, and therefore its magnitude depends on the extracellular sodium concentration. Decreasing the external Na^+ concentration decreases the size of the action potential, but has little effect on the

resting membrane potential because the permeability of the membrane to Na^+ at rest is low. Conversely, increasing the external K^+ concentration decreases the resting membrane potential. Changes in external Ca^{2+} concentration affect the excitability of nerve and muscle cells, but not the magnitude of the resting potential or the action potential.

131. The answer is b. (*Ganong*, pp 223–231.) Muscarine binds to acetylcholine muscarinic receptors on cardiac and smooth muscle. These are the same receptors activated by the release of acetylcholine by the vagus nerve. Cardiac muscarinic receptors decrease the rate of phase 4 depolarization and therefore, decrease the heart rate. A heart rate less than 60 beats per minute is called bradycardia. Acetylcholine receptors on the skeletal muscle end plate are nicotinic receptors and do not respond to muscarine. Dilation of the pupils and hypertension are signs of sympathetic, not parasympathetic activity.

132. The answer is d. (*Ganong*, pp 51–64.) In order for propagation of an action potential to occur, the depolarization produced by one action potential must depolarize the adjacent patch of excitable membrane to the threshold level. In demyelinating diseases, such as multiple sclerosis, too much charge leaks from the membrane and as a result, not enough charge is available to bring the next patch of membrane to threshold. Increasing the duration of the action potential increases the amount of charge entering the cell and therefore increases the probability that the next patch of excitable membrane will be depolarized to threshold. Increasing the duration of the refractory period will not affect the amount of charge entering the cell. Depolarizing the membrane and increasing potassium conductance will make it more difficult to produce an action potential. If membrane capacitance is increased, the amount of charge required to excite the next patch of membrane will be increased.

133. The answer is e. (*Ganong*, pp 51–64. *Widmaier et al.*, pp 159–165.) When the permeability of a particular ion is increased, the membrane potential moves toward the equilibrium potential for that ion. The equilibrium potentials for chloride (-80 mV) and potassium (-92 mV) are close to the resting membrane potential, so increases in their permeability have little effect on the resting membrane potential. The equilibrium potential for sodium ($+60\text{ mV}$) is very far from the resting membrane potential. Thus, increasing the permeability for sodium causes a large depolarization.

134. The answer is d. (*Ganong, pp 51–64.*) During an action potential, the conductances for sodium and for potassium are higher than at rest. However, the conductance for sodium is higher than the conductance for potassium during the overshoot; as a result, the transference for potassium is less. Recall that transference is a measure of an ion's relative conductance:

$$T_{\text{Na}} = g_{\text{Na}} / (g_{\text{Na}} + g_{\text{K}}) \text{ and } T_{\text{K}} = g_{\text{K}} / (g_{\text{Na}} + g_{\text{K}})$$

where T = transference and g = conductance.

135. The answer is c. (*Ganong, pp 51–64. Widmaier et al., pp 164–175.*) The repolarization phase of the action potential is produced by a decrease in Na^+ conductance caused by the inactivation of Na^+ channels, and the increase in K^+ conductance due to the activation of K^+ channels. Preventing the inactivation of Na^+ channels will decrease the downstroke velocity of the action potential. This will slow the normal repolarization phase of the action potential and thereby prolong the duration of the action potential. The relative refractory period is prolonged because of the prolonged duration of the action potential. The upstroke velocity and the magnitude depend on how rapidly and how long the sodium channels are opened. By preventing inactivation of the Na^+ channel, the rate of the upstroke and the magnitude of the overshoot may be increased.

136. The answer is e. (*Ganong, pp 30–34. Kasper et al., pp 2339, 2536–2537.*) Electrically excitable gates are those that respond to a change in membrane potential. The most notable electrically excitable gates are those on the sodium and potassium channels that produce the nerve action potential. The potassium channel gate is opened by depolarization. Ventricular muscle SR releases its calcium in response to an increase in intracellular calcium. The gates opened by ACh are chemically excitable gates. In rods, sodium channels are closed when cGMP is hydrolyzed. Electrically excitable gates do not regulate the active transport of glucose.

137. The answer is c. (*Ganong, pp 6–8, 30–35, 58–59. Widmaier et al., pp 116–119.*) The sodium-potassium pump uses the energy contained in ATP to maintain the sodium gradient across the membrane. The sodium gradient, in turn, is used to transport other substances across the membrane. For example, the Na/Ca exchanger uses the energy in the sodium gradient to help maintain the low intracellular calcium required for normal cell function. Although sodium enters the cell during an action potential,

the quantity of sodium is so small that no significant change in intracellular sodium concentration occurs. Because the sodium transference is so low, the sodium equilibrium potential is not an important determinant of the resting membrane potential.

138. The answer is b. (*Ganong*, pp 111–112, 142. *Kasper et al.*, pp 71–76, 764, 769–771. *Stead et al.*, pp 187–188.) Pain is the most common presenting symptom, and thus understanding pain is essential to the goals of relieving suffering, as well as preserving and restoring health. The function of the pain sensory system is to protect the body by detecting, localizing, and identifying tissue-damaging processes. Different diseases produce characteristic patterns of tissue damage; the resultant manifestations of pain and tenderness can provide important diagnostic clues and can also be used to evaluate treatment regimens. Pelvic Inflammatory Disease (PID) is an infection of the upper genital structures in women (uterus, ovaries, oviducts) often with involvement of neighboring organs, which is generally accompanied by lower abdominal pain with pelvic, adnexal, and cervical motion tenderness. Peripheral nerves consist of primary sensory afferent axons, motor neurons, and sympathetic postganglionic neurons. Primary sensory afferent nerves include those with large-diameter A-beta (A β), which normally are not involved in pain, as well as two populations of primary afferent nociceptors, the small-diameter myelinated A-delta (A δ) and unmyelinated (C fiber) axons, which are both present in nerves to the skin and to deep somatic and visceral structures. Many A δ and C fibers innervating viscera are completely insensitive in normal, uninjured, noninflamed tissue, but become sensitive to mechanical stimuli in the presence of inflammatory mediators. An important concept to emerge in recent years is that afferent nociceptors also have a neuroeffector function, in that they contain polypeptide mediators that are released from their nerve terminals when activated. Most notably, Substance P, an 11-amino acid polypeptide found in neurons within the hypothalamus and spinal cord, is released from small A δ and C fibers that relay information from nociceptors to neurons within the substantia gelatinosa of the spinal cord. The biologic actions of substance P include vasodilation, neurogenic edema and the accumulation of bradykinin, the release of histamine from mast cells and the release of serotonin from platelets. Endorphins and other opioid peptides such as the enkephalins may partially inhibit the perception of pain by presynaptically inhibiting the release of substance P from nociceptor afferent fibers.

139. The answer is a. (*Ganong*, pp 7–8. *Widmaier et al.*, pp 158–165.) The Na $^+$ equilibrium potential is approximately +60 mV and is based on the

ratio of the intracellular and extracellular Na^+ concentrations. During an action potential, the peak of the action potential (point A) is close, but not equal, to the Na^+ equilibrium potential. The membrane potential doesn't reach the Na^+ equilibrium potential because the Na^+ channels start to inactivate and the K^+ channels begin to activate during the upstroke of the action potential.

140. The answer is a. (*Ganong, pp 101–105, 227–229, 262–263, 289–290, 325–326, 344, 356–361, 641.*) Epinephrine (adrenalin) acts on both α - and β -adrenergic receptors, but has a greater affinity for β -adrenergic receptors. Activation of β_2 -adrenergic receptors leads to relaxation of smooth muscle in the bronchi, vasculature, intestine, uterus, and bladder, to increased pancreatic insulin and glucagon secretion, and an increase in liver glycogenolysis. The bronchodilator effects of epinephrine are key in the treatment of the life-threatening effects of anaphylactic shock. Activation of β_1 - and β_2 -adrenergic receptors in the heart leads to an increase in the rate of SA nodal phase 4 depolarization and thus heart rate (positive chronotropic response), an increase in contractility (positive inotropic response), an increase in conduction velocity (positive dromotropic response), and an increase in cardiac excitability/irritability. The transport of Ca^{2+} into skeletal muscle fibers is not affected by β receptors. The effects of epinephrine-induced β -adrenergic receptor activation are due to G-protein mediated activation of adenylate cyclase, which catalyzes the formation of cyclic adenosine monophosphate (cAMP) and activation of protein kinase A.

141. The answer is b. (*Ganong, pp 121–127, 746. Kasper et al., pp 142–144, 1042–1045. Stead et al., pp 353–355. Widmaier et al., p 225.*) The Ruffini ending is a tonic receptor that produces a train of action potentials proportional to the intensity of pressure applied to the skin. The Pacinian corpuscle is a very rapidly adapting receptor that fires once or twice in response to skin deformation, but can produce a continuous train of action potentials if the stimulus is repetitively applied and withdrawn. Therefore, the Pacinian corpuscle is used to encode vibration.

142. The answer is e. (*Ganong, pp 199–201, 755–756.*) Narcolepsy is associated with low CSF levels of the orexins and a defect in one of the receptors for orexins (hypocretins) in the hypothalamus. Adenosine induces sleep and serotonin agonists suppress sleep. Fatal familial insomnia is a progressive prion disease, characterized by worsening insomnia, impaired autonomic and motor functions, dementia, and death.

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Musculoskeletal Physiology

Questions

143. A patient with severe kyphoscoliosis presents with increasing dyspnea consistent with a decrease in chest wall compliance. With contraction of the external intercostal muscles during inspiration, the Golgi tendon organ (GTO) provides the central nervous system with information about which of the following?

- a. The length of the muscle being moved
- b. The velocity of muscle movement
- c. The blood flow to the muscle being moved
- d. The tension developed by the muscle being moved
- e. The change in joint angle produced by the movement

144. A 56-year-old woman presents with a flat red rash on the face and upper trunk and an erythematous rash on the knuckles and in the shape of a V on the neck and anterior chest. She also complains of muscle weakness with difficulty getting out of a chair and combing her hair. Lab findings include positive antinuclear antibody and anti-Mi2 dermatomyositis specific antibodies. In addition to oral prednisone, physical therapy is ordered with the goal of improving muscle strength, and thus ability to perform activities of daily living. Repetitive stimulation of a skeletal muscle fiber will cause an increase in contractile strength due to an increase in which of the following?

- a. The duration of cross-bridge cycling
- b. The concentration of calcium in the myoplasm
- c. The magnitude of the end-plate potential
- d. The number of muscle myofibrils generating tension
- e. The velocity of muscle contraction

145. A 34-year-old woman presents with a complaint of fatigue and generalized muscle weakness. As one way to evaluate a neural versus muscular basis for her symptoms, the woman is instructed to rapidly flex her arm. During this maneuver, which of the following occurs?

- a. Activity of Ia afferent fibers from the biceps (the agonist) increases
- b. Activity of Ib afferent fibers from the biceps (the agonist) decreases
- c. Activity of Ia afferent fibers from the triceps (the antagonist) increases
- d. Activity of Ib afferent fibers from the triceps (the antagonist) decreases
- e. Activity of alpha motoneurons to the triceps (the antagonist) increases

146. A 62-year-old male presents with a hypokinetic movement disorder characterized by bradykinesia (paucity and slowness of movement). During a normal voluntary movement, which of the following occurs?

- a. Large muscle fibers are recruited before small muscle fibers
- b. Fast muscle fibers are recruited before slow muscle fibers
- c. Weak muscle fibers are recruited before strong muscle fibers
- d. Poorly perfused muscle fibers are recruited before richly perfused muscle fibers
- e. Anaerobic fibers are recruited before aerobic fibers

147. A 35-year-old woman having an anxiety attack collapses. The EMT who arrives on the scene notes that she is hyperventilating and suspects that she is suffering from tetany, a continuous contraction of skeletal muscle fibers caused by an increase in the excitability of nerves and muscle membranes. The increased membrane excitability is caused by which of the following?

- a. Decreased release of inhibitory neurotransmitter from nerve terminals
- b. Depolarization of the nerve and muscle membranes
- c. Spontaneous release of calcium from the sarcoplasmic reticulum
- d. Activation of sodium channels at more negative membrane potentials
- e. Increased magnitude of the action potentials invading nerve terminals

148. A 32-year-old woman undergoing surgery for appendicitis develops malignant hyperthermia following halothene anesthesia. The life-threatening increase in metabolic rate and body temperature is attributed to a mutation of the ryanodine receptor in skeletal muscle, resulting in which of the following?

- a. Excess calcium release from the sarcoplasmic reticulum (SR) during muscle contraction
- b. Rapid repetitive firing of the presynaptic terminals of α motoneurons
- c. Inability of skeletal muscle cells to repolarize

- d. An increase in the refractory period of the α motoneurons
- e. Production of endogenous muscle pyrogens

149. Which of the following muscle proteins plays an important role in contraction of both smooth and striated muscle?

- a. Calmodulin
- b. Troponin
- c. Tropomyosin
- d. Actin
- e. Myosin light chains

150. A 47-year-old male presents with pain and swelling in the left big toe. He has been on a high protein diet and training extensively for an iron man competition, which includes weight lifting, running, swimming, and biking. An aspirate of joint fluid demonstrated negative birefringent urate crystals and 24-hour urinary uric acid levels were elevated. For maintenance therapy, which of the following agents would be best to treat the cause of his gout?

- a. Aspirin
- b. Allopurinol
- c. Colchicine
- d. Nonsteroidal antiinflammatory drugs (NSAIDs)
- e. Uricosurics

151. A 35-year-old woman is seen by a neurologist to evaluate her incapacitating muscle weakness. The neurologist suspects myasthenia gravis and decides to confirm his diagnosis by administering a drug that increases the force of muscle contraction in patients with myasthenia gravis. Caution is advised when administering the drug to patients with heart disease because bradycardia may develop. Which of the following most likely explains the ability of the drug to increase the force of muscle contraction in patients with myasthenia gravis?

- a. Increasing the amount of acetylcholine (ACh) released by α motoneurons
- b. Increasing the affinity of the skeletal muscle acetylcholine receptors to acetylcholine
- c. Increasing the α motoneuron discharge rate
- d. Decreasing the metabolic breakdown rate of acetylcholine
- e. Decreasing the concentration of calcium in the extracellular fluid

152. A 5-year-old boy presents with abnormal running, jumping, and hopping. His parents have observed that he uses his arms to climb up his legs when rising from the floor. The pediatrician suspects Duchenne muscular dystrophy, and electromyography confirms a myopathy. The amount of force produced by a skeletal muscle can be increased by which of the following?

- a. Increasing extracellular Mg^{2+}
- b. Decreasing extracellular Ca^{2+}
- c. Increasing the activity of acetylcholine esterase
- d. Decreasing the interval between contractions
- e. Increasing the preload beyond 2.2 mm

153. A 32-year-old man sees his physician after collapsing suddenly without any other physical distress. Laboratory results demonstrate an elevated serum concentration of potassium and he is diagnosed with periodic hyperkalemic paralysis, a clinical condition in which a sudden increase in extracellular potassium concentration results in muscle weakness. Which of the following is most likely to cause muscle weakness as a result of increased extracellular potassium concentration?

- a. Hyperpolarization of muscle cells
- b. Inactivation of sodium channels in muscle cells
- c. Increased release of neurotransmitters from α motoneurons
- d. Decreased potassium conductance in muscle cells
- e. Increased duration of action potentials produced by α motoneurons

154. An increase in sodium conductance is associated with which of the following?

- a. The plateau phase of the ventricular muscle action potential in heart
- b. The downstroke of the skeletal muscle action potential
- c. The upstroke of the smooth muscle action potential
- d. The refractory period of the nerve cell action potential
- e. The end-plate potential of the skeletal muscle fiber

155. A 16-year-old boy on the track team asks his pediatrician if he can take creatine on a regular basis in order to increase his muscle strength prior to a track meet. Which of the following most likely explains why he wants to take creatine?

- a. Creatine increases plasma glucose concentration
- b. Creatine prevents dehydration
- c. Creatine increases muscle glycogen concentrations

- d. Creatine is converted to phosphocreatine
- e. Creatine delays the metabolism of fatty acids

156. An 18-month-old boy presents with delayed dentation, short stature, difficulty and painful walking, and bowing of the legs. In vitamin D deficiency, which of the following is defective in bone?

- a. Bone formation by osteoblasts
- b. The composition of bone collagen
- c. Calcification of the bone matrix
- d. Bone resorption by osteoclasts
- e. The blood supply to the haversian canals

157. When comparing the contractile responses in smooth and skeletal muscle, which of the following is most different?

- a. The source of activator calcium
- b. The role of calcium in initiating contraction
- c. The mechanism of force generation
- d. The source of energy used during contraction
- e. The nature of the contractile proteins

158. A 12-year-old male with muscular dystrophy is found to have a mutation of the gene that encodes the protein dystrophin. Genetic alterations in dystrophin lead to progressive muscular weakness because dystrophin provides structural support to the sarcolemma by binding which of the following?

- a. β -Dystroglycan to laminin
- b. Actin to β -dystroglycan
- c. Actin to the Z lines
- d. Z lines to M lines
- e. Z lines to the sarcolemma

159. Which of the following is true regarding the action potential of skeletal muscle?

- a. It spreads inward to all parts of the muscle via the T-tubules
- b. It has a prolonged plateau phase
- c. It causes the immediate uptake of Ca^{2+} into the lateral sacs of the sarcoplasmic reticulum
- d. It is longer than the action potential of cardiac muscle
- e. It is not essential for contraction

160. Which of the following is true regarding the contractile response of skeletal muscle?

- a. It starts after the action potential is over
- b. It does not last as long as the action potential
- c. It produces more tension when the muscle contracts isometrically than isotonically
- d. It produces more tension when the muscle contracts isotonically than isometrically
- e. It decreases in magnitude with repeated stimulation

161. A patient presents with greatly reduced exercise tolerance, including muscle pain and stiffness on exertion. The differential diagnosis includes McArdle's syndrome, which results from a deficiency of which of the following enzymes?

- a. Myophosphorylase
- b. Hexokinase
- c. Glucose 6-phosphatase
- d. Galactose 1-phosphate uridyl transferase
- e. Glycogen synthase

162. A 20-year-old male presents with stiffness in the lower back that improves with exercise. A pelvic radiograph reveals sacroiliitis. Patients with ankylosing spondylitis (AS) show a dramatic response to all symptoms with therapeutic blockade of which of the following?

- a. Prostaglandin E
- b. Cyclooxygenase 2 (COX-2)
- c. Tumor necrosis factor α (TNF- α)
- d. $\text{Na}^+ \text{-K}^+$, ATPase
- e. *Tropheryma whippelii*

163. Which of the following characteristics is the most similar between the capillaries in the skeletal muscle and pulmonary circulations?

- a. The interstitial protein concentration
- b. The interstitial hydrostatic pressure
- c. The capillary oncotic pressure
- d. The capillary hydrostatic pressure
- e. The capillary permeability to proteins

Musculoskeletal Physiology

Answers

143. The answer is d. (*Ganong, pp 133–135. Widmaier et al., pp 327–331.*) The GTO is located in the tendon of skeletal muscles and therefore is in series with the muscle. Each time the muscle contracts, the GTO is stretched in proportion to the tension developed by the muscle. The Ib afferent fibers (which innervate the GTO) produce a train of action potentials with a frequency that is in proportion to the deformation of the GTO. The muscle length and speed of shortening are sent to the CNS by Ia afferents that innervate the intrafusal fibers within muscle spindles.

144. The answer is a. (*Ganong, pp 65–78. Kasper et al., pp 2540–2545. Stead et al., pp 292–293. Widmaier et al., pp 283–311.*) Each time a skeletal muscle fiber is stimulated by an α motoneuron, enough Ca^{2+} is released from its sarcoplasmic reticulum to fully activate all the troponin within the muscle. Therefore, every cross bridge can contribute to the generation of tension. However, the transmission of force from the cross bridges to the tendon does not occur until the series elastic component (SEC) of the muscle is stretched. Repetitive firing increases the amount of SEC stretch by maintaining cross-bridge cycling for a longer period of time. Repetitive firing increases neither the concentration of Ca^{2+} within the myoplasm, the number of myofibrils that are activated, nor the magnitude of the end-plate potential. Because all of the cross bridges are activated each time a skeletal muscle fiber is activated, an increase in Ca^{2+} concentration would have no effect on muscle strength. Limitation in rising from a seated position or combing hair is suggestive of proximal muscle weakness, characteristic of dermatomyositis.

145. The answer is c. (*Ganong, pp 131–134. Kasper et al., pp 134–138, 2506–2507, 2524–2527.*) The firing of the α motoneurons to the biceps muscle produces rapid flexion of the arm. Because the arm is rapidly flexed, the Ia afferent neurons innervating the muscle spindles in the biceps, which detect muscle length, will reduce their firing rate. The Ib afferents, innervating the Golgi tendon organs from the biceps, will detect

the contractile activity of the biceps and increase their firing rate. The triceps are stretched during arm flexion and so their Ia afferents will increase their firing rate. Ib afferents do not respond when muscles are passively stretched, so their firing rate will not change.

146. The answer is c. (*Ganong, pp 73–76. Kasper et al., pp 138–139.*) In general, small, weak, slow, fatigue-resistant muscle fibers are innervated by small spinal motoneurons, whereas, large spinal motoneurons innervate large, fast, strong, easily fatigable muscle fibers. During most normal reflex or voluntary movements, small spinal motoneurons are recruited before large motoneurons. The slow fatigue-resistant muscle fibers have a dense capillary network for perfusion and use mitochondrial oxidative metabolism to produce adenosine triphosphate (ATP).

147. The answer is b. (*Ganong, pp 59, 382, 692. Kasper et al., p 138. Widmaier et al., p 308.*) Membrane excitability is related to the ease with which depolarization opens Na^+ channels. The opening of the Na^+ channel in response to depolarization is, in part, related to the extracellular Ca^{2+} concentration; the lower the extracellular Ca^{2+} concentration, the easier it is for Na^+ channels to open when the membrane depolarizes. Hyperventilation (lowering arterial CO_2 tension) decreases extracellular Ca^{2+} concentration by increasing arterial pH. When pH rises, H^+ is released from plasma proteins in exchange for Ca^{2+} , and ionized Ca^{2+} concentration decreases.

148. The answer is a. (*Ganong, p 255. Kasper et al., pp 105, 2522–2523.*) The ryanodine receptor or calcium release channel on the sarcoplasmic reticulum (SR) is normally opened when skeletal muscle is activated. The flow of calcium through the open ryanodine receptor binds to troponin and initiates muscle contraction. The metabolic activity accompanying muscle contraction can warm the body. If a mutation in the ryanodine receptor causes uncontrolled release of calcium from the SR, the body temperature can rise to levels that cause brain damage.

149. The answer is d. (*Ganong, pp 69–70, 82–83.*) In both smooth and striated muscle, contraction is produced by the cross-bridge cycle in which the cross-bridge on the thick filament binds to the actin molecule on the thin filament. In excitation-contraction coupling in striated muscle, calcium initiates contraction by binding to troponin. The calcium-activated troponin then acts to remove the tropomyosin-mediated inhibition of the actin-myosin interaction. In excitation-contraction coupling in smooth

muscle, calcium initiates contraction by binding to calmodulin. The calcium-activated calmodulin then activates the myosin light chain protein kinase enzyme, which phosphorylates the myosin light chains. Actin-myosin interaction follows light-chain phosphorylation.

150. The answer is b. (*Ganong*, pp 297–298. *Stead et al.*, pp 298–299.) Strenuous exercise and a high protein diet can cause overproduction of uric acid. Allopurinol, which inhibits xanthine oxidase, decreases the primary cause of gout by decreasing uric acid production. Colchicine is given in acute gout to inhibit phagocytosis of uric acid crystals by leukocytes, a process that in some way produces the joint symptoms. Nonsteroidal anti-inflammatory agents, particularly indomethacin, are also used to relieve the acute arthritic symptoms of gout. Aspirin is contraindicated in acute gout because it decreases urate excretion. Uricosurics are effective in increasing the excretion of uric acid in patients whose gout is caused by decreased urate excretion, such as chronic renal disease, diabetes ketoacidosis, use of thiazide diuretics, and ethanol ingestion.

151. The answer is d. (*Ganong*, p 118. *Kasper et al.*, pp 137, 2518–2523. *Widmaier et al.*, p 308.) The drug used to test for myasthenia gravis is an acetylcholine esterase inhibitor such as neostigmine. The drug prevents the breakdown of acetylcholine, increasing the duration of time acetylcholine remains in the synaptic cleft. Because acetylcholine can bind to the end-plate receptors for a longer time, the magnitude of the end-plate potential increases, increasing the probability of it generating an action potential. The greater the action potential force rate, the greater the source of muscle contraction. Increasing the amount of acetylcholine released by the α motoneurons, by increasing the affinity of the skeletal muscle receptors for acetylcholine or increasing the discharge rate of α motoneurons could cause a similar effect. However, none of these changes would affect heart rate. The cautious use of this test in patients with heart failure results from the possibility that the decreased breakdown of acetylcholine released by the vagus nerve could decrease heart rate to dangerously low levels.

152. The answer is d. (*Ganong*, p 77. *Kasper et al.*, pp 2526–2529. *Widmaier et al.*, pp 308–310) When the interval between skeletal muscle contractions is small, the force produced by the two successive contractions will summate. The shorter the interval between the contractions, the greater the summation will be. Maximum summation is called tetanus. Decreasing extracellular Ca^{2+} will increase the excitability of skeletal muscle fibers but

does not have a direct effect on contractile force. Increasing the Mg²⁺ concentration will decrease skeletal muscle excitability. Increasing the preload beyond 2.2 mm decreases the overlap between thick and thin filaments and therefore decreases the force of contraction. Increasing the activity of acetylcholine esterase enhances the hydrolysis of ACh and therefore decreases the likelihood that muscle contraction will be initiated.

153. The answer is b. (*Kasper et al.*, pp 261–263, 2536–2537, 2543.) Periodic hyperkalemic paralysis results from inactivation of the skeletal muscle membranes produced by depolarization of the skeletal muscle membrane in the presence of an increased extracellular potassium concentration. Inactivation of the sodium channels on the skeletal muscle membrane prevents action potentials from being produced and therefore leads to muscle weakness or paralysis. Although the exact mechanism of periodic hyperkalemic paralysis is not known, it appears to be due to a mutation in the gene coding for the sodium inactivation gate.

154. The answer is e. (*Ganong*, pp 58–59, 68–69, 78–81, 82–83, 116–118.) The end-plate potential in skeletal muscle is produced by an influx of sodium into the cell, which results from the increase in sodium permeability that occurs with acetylcholine binding to the nicotinic receptors on the membrane of the motor end plate. Acetylcholine binding at the motor end plate also increases the potassium conductance of the membrane. The plateau phase of ventricular muscle action potentials and the upstroke of smooth muscle action potentials are produced by an increase in calcium conductance. An increase in potassium conductance is responsible for the down-stroke of the action potential. The refractory period is caused by an increase in potassium conductance and a decrease in the number of sodium channels available to produce an action potential (i.e., sodium channel inactivation).

155. The answer is d. (*Ganong*, pp 294–296.) Phosphocreatine is rapidly converted to ATP in muscle. When the metabolic demands exceed the rate at which ATP can be generated by aerobic metabolism or glycolysis, phosphocreatine can supply the necessary ATP for a brief period of time. An increase in the concentration of phosphocreatine in muscle may increase the amount of ATP that can be produced and therefore enhance performance.

156. The answer is c. (*Ganong*, pp 384–389. *Kasper et al.*, pp 1700–1701.) Vitamin D deficiency causes defective calcification of the bone matrix as a

result of inadequate delivery of Ca^{2+} and PO_4^{3-} to the sites of mineralization. The disease in children is called rickets, and is characterized by growth retardation, weakness and bowing of the weight-bearing bones, dental defects, and hypocalcemia, which increases parathyroid hormone and urinary phosphate losses. Several different types of inheritance lead to the vitamin D deficiency disorders, including X-linked dominant and autosomal dominant hypophosphatemic rickets, vitamin D-dependent rickets Type I, an autosomal recessive disorder caused by inactivating mutations in the gene encoding 1α -hydroxylase enzyme, and vitamin D-dependent rickets Type II, in which there is end-organ resistance to $1,25(\text{OH})_2\text{D}_3$, which is also usually inherited as an autosomal recessive disorder.

157. The answer is b. (*Ganong, pp 65–84.*) The greatest difference in excitation-contraction coupling between skeletal muscle and smooth muscle involves the role of calcium in initiating contraction. In smooth muscle, calcium binds to and activates calmodulin, which, by activating myosin light chain kinase, catalyzes the phosphorylation of the 20,000-Da myosin light chain (LC_{20}). Once the light chains are phosphorylated, myosin cross-bridges bind to actin on the thin filaments, which initiates contraction. In skeletal muscle, calcium binds to troponin, which removes the tropomyosin-mediated inhibition of the actin-myosin interactions. Once the inhibition is removed, cross-bridge cycling (and contraction) begins. In both smooth and skeletal muscle, the cycling of cross-bridges generates force. ATP provides the energy for the cycling of the cross-bridges in both muscles. In skeletal muscle, activator calcium comes exclusively from the SR, whereas in smooth muscle calcium can come from both the SR and the extracellular fluid.

158. The answer is b. (*Ganong, pp 65–68, 77. Kasper et al., pp 2532–2537.*) Dystrophin is a large protein that forms a rod, which connects the thin filaments of actin to the transmembrane protein β -dystroglycan in the sarcolemma. β -Dystroglycan is connected to laminin in the extracellular matrix by α -dystroglycan. The dystroglycans are also associated with a complex of four transmembrane glycoproteins, called sarcoglycans. The dystrophin-glycoprotein complex adds strength to the muscle by providing a scaffolding for the fibrils and connecting them to the extracellular environment. Muscular dystrophy is the term used for some 50 diseases that cause progressive skeletal muscle weakness. Duchenne's and Becker's muscular dystrophy are two types resulting from mutations in the dystrophin gene.

159. The answer is a. (*Ganong*, pp 65–73, 78–80, 743.) Depolarization of the muscle fiber is essential for initiating muscle contraction. The action potential of skeletal muscle is transmitted to all of the fibrils along T-tubules, triggering the release of Ca^{2+} from the lateral sacs of the sarcoplasmic reticulum next to the T-system. The electrical events in skeletal muscle and the ionic fluxes underlying them are similar to those in nerve. In contrast, the action potential in cardiac muscle is longer and has a prolonged plateau phase.

160. The answer is c. (*Ganong*, pp 58–71.) In isometric (same measure or length) contractions, muscle contraction increases the tension of the muscle. Isometric contraction is possible because muscles have elastic and viscous elements in series with the contractile elements, so contraction can occur without an appreciable decrease in length. In contrast, isotonic (same tension) contractions are contractions against a constant load, which decrease muscle length. Muscle fiber membrane depolarization during an action potential initiates muscle contraction via a process called excitation-contraction coupling. The duration of the contractile response of skeletal muscle (muscle twitch) exceeds the duration of the action potential, but varies with muscle fiber type. Because the muscle contractile mechanism does not have a refractory period, repeated stimulation before relaxation causes greater tension development than during a single muscle twitch, a process called summation of contractions.

161. The answer is a. (*Ganong*, pp 289–290.) In McArdle's syndrome, glycogen accumulates in skeletal muscles because of a deficiency of muscle phosphorylase. Without adequate myophosphorylase, patients cannot break down their muscle glycogen to provide the energy for muscle contraction, except for normal activity or mild exercise. Thus, they have a greatly reduced exercise tolerance.

162. The answer is e. (*Kasper et al.*, pp 1993–1996. *Stead et al.*, pp 293–294.) AS is a chronic systemic inflammatory disorder affecting primarily the axial skeleton, but may have multiple organ involvement. The pathogenesis of AS is incompletely understood, but the dramatic response of all aspects of the disease to blockade of $\text{TNF-}\alpha$ indicates that this cytokine almost certainly plays a major role in the immunopathogenesis. Prior to the 2000 report of the effectiveness of anti- $\text{TNF-}\alpha$ in the treatment of AS and other spondyloarthrides, NSAID therapy with indomethacin, and more recently COX-2 inhibitors, combined with

exercise programs constituted the primary management. *Tropheryma whippelii* is the organism causing the rare chronic bacterial infection, Whipple's disease, which initially presents with arthritic symptoms. Antibiotic therapy is curative, whereas the untreated disease is fatal.

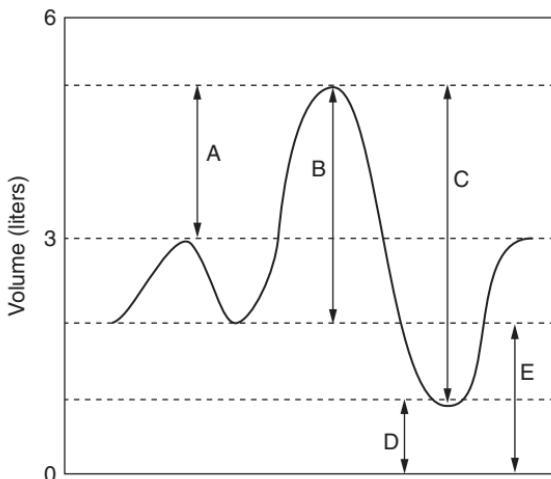
163. The answer is c. (*Ganong*, pp 632–633, 661–664. *Levitzky*, pp 86–92, 107–110.) Blood flows in series through the systemic and pulmonary circulations, and, therefore, blood perfusing the skeletal muscles has the same oncotic pressure as the blood flowing through the pulmonary circulation. However, the blood pressure is much lower in the pulmonary circulation than in the systemic circulation, and because the thoracic cavity has a negative pressure, the interstitial fluid pressure is more negative in the pulmonary circulation than in the systemic circulation. The pulmonary interstitium is contiguous with the pulmonary lymph vessels, and, therefore, there is a relatively high interstitial concentration of protein in the lungs. Skeletal muscle capillaries are not very permeable to proteins, resulting in low interstitial protein concentration in skeletal muscle.

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Respiratory Physiology

Questions

164. A healthy, 30-year-old woman is referred for a life insurance physical. She has never smoked, and her breath sounds are normal. Her expiratory reserve volume, as depicted in the spirometry tracing below, equals which of the following?



- a. C
- b. D
- c. E
- d. C + D
- e. E - D

165. A group of third year medical students accompanied a medical mission team to Peru. After arriving at the airport in Bolivia, they hiked to a remote mountain village in the Andes. At this elevation of 18,000 ft, the barometric pressure was 380 mmHg, resulting in a PO_2 of the dry inspired air of what?

- a. 160 mmHg
- b. 100 mmHg
- c. 80 mmHg
- d. 70 mmHg
- e. 38 mmHg

166. A 28-year-old man is admitted to the Emergency Department with multiple fractures suffered in a car accident. Arterial blood gases are ordered while the patient is breathing room air. After obtaining the arterial blood sample, the blood-gas technician draws room air into the syringe before measuring the blood-gas values. As a result, which of the following is true?

- a. The measured values of both PaO_2 and Paco_2 will be higher than the patient's actual values
- b. The measured values of both PaO_2 and Paco_2 will be lower than the patient's actual values
- c. The measured PaO_2 will be higher and the measured Paco_2 will be lower than the patient's actual blood gas values
- d. The measured PaO_2 will be lower and the measured Paco_2 will be higher than the patient's actual blood gas values
- e. The measured values of PaO_2 and Paco_2 will accurately reflect the actual values

167. A 68-year-old woman with pulmonary fibrosis, who presents with a complaint of increasing dyspnea while performing activities of daily living, is referred for pulmonary function testing. Which of the following laboratory values is consistent with her diagnosis?

- a. Decreased diffusing capacity of the lung
- b. Increased residual volume
- c. Decreased FEV_1/FVC
- d. Increased lung compliance
- e. Increased airway resistance corrected for lung volume

168. A 24-year-old woman collapsed in a New York City subway station. An autopsy showed that a blood clot had traveled to her lung and caused her death. The medical examiner ultimately ruled that the blood clot was caused by the use of a birth control patch. Which of the following occurs if the blood flow to an alveolus is totally obstructed by a pulmonary thromboembolism?

- a. The V/Q ratio of the alveolus equals zero
- b. The P_{O_2} of the alveolus will be equal to that in the inspired air
- c. The P_{O_2} of the alveolus will be equal to the mixed venous P_{O_2}
- d. There will be an increase in shunting (venous admixture) in the lung
- e. There will be a decrease in alveolar deadspace

169. A 150-lb patient scheduled for abdominal surgery is sent for pre-op evaluation and testing. His chest x-ray is normal, and pulmonary function results on room air show:

Tidal volume = 600 mL

Respiratory rate = 12/min

Vital capacity = 5000 mL

$P_{aO_2} = 90$ mmHg

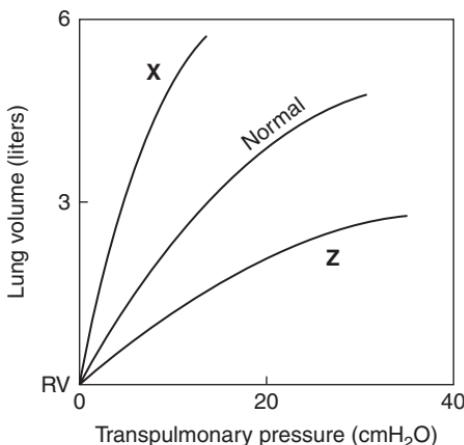
$P_{aCO_2} = 40$ mmHg

$P_{eCO_2} = 28$ mmHg

The volume of the patient's physiological dead space, determined by applying Bohr's equation, equals which of the following?

- a. 7200 mL
- b. 420 mL
- c. 180 mL
- d. 150 mL
- e. 0.3 mL

170. A hospitalized patient has tachypnea and significantly labored respirations requiring mechanical ventilation. Based on the pressure-volume curve of the lungs shown as Curve Z in the figure below, which of the following is the most likely diagnosis for the patient?

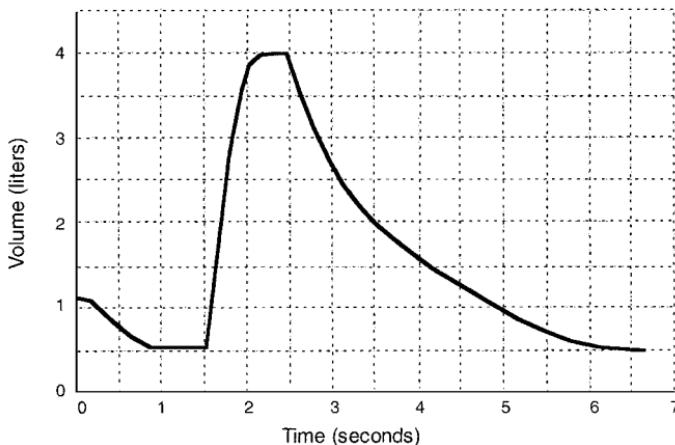


- a. Emphysema
- b. Asthma
- c. Dyspnea with aging
- d. Pulmonary edema
- e. Newborn with lecithin to sphingomyelin (L/S) ratio greater than 2

171. A 6 feet 3 inches tall, 140-lb, 20-year-old male was watching television when he felt pain in his shoulder blades, shortness of breath, and fatigue. His father noticed how pale he was and took him to the Emergency Department, where a chest X-ray revealed a 55% pneumothorax of the right lung due to rupture of a bleb on the surface of the lung. Which of the following is true?

- a. The intrapleural pressure in the affected area is equal to atmospheric pressure
- b. The chest wall on the affected side recoils inward
- c. There is hyperinflation of the affected lung
- d. The \dot{V}/\dot{Q} ratio on the affected side is higher than normal
- e. The mediastinum shifts further to the right with each inspiration

172. An 18-year-old girl with a 9-year history of wheezing on exertion is referred for pulmonary function tests. The diagram below represents the spirometry tracing of a forced vital capacity. Her total lung capacity was 110% of predicted. Which of the following values will most likely be above normal?



- a. Vital capacity
- b. Residual volume
- c. Expiratory reserve volume
- d. FEV_{1.0}/FVC
- e. Maximum voluntary ventilation

173. A 125-lb, 40-year-old woman with a history of nasal polyps and aspirin sensitivity since childhood presents to the Emergency Department with status asthmaticus and hypercapnic respiratory failure. She requires immediate intubation and is placed on a mechanical ventilator on an F_iO₂ of 40%, a control rate of 15 breaths/min, and a tidal volume of 500 mL. Which of the following is her approximate alveolar ventilation?

- a. 375 mL/min
- b. 3500 mL/min
- c. 5250 mL/min
- d. 5625 mL/min
- e. 7500 mL/min

174. A medical student waiting to do her first patient interview at the Clinical Skills Center becomes very anxious and increases her rate of alveolar ventilation. If her rate of CO₂ production remains constant, which of the following will decrease?

- a. pH
- b. PaO₂
- c. Paco₂
- d. V/Q
- e. Alveolar-arterial PO₂ difference

175. A 36-year-old man with a history of AIDS and *Pneumocystis* infection presents to the Emergency Department with severe respiratory distress. The patient is placed on a ventilator at a rate of 16, tidal volume of 600 mL, and F_iO₂ of 1.0. An arterial blood sample taken 20 minutes later reveals a PO₂ of 350 mmHg, a PCO₂ of 36 mmHg, and a pH of 7.32. At a barometric pressure of 757 mmHg, and assuming a normal respiratory exchange ratio (R) of 0.8, the patient's alveolar oxygen tension is approximately which of the following?

- a. 105 mmHg
- b. 355 mmHg
- c. 576 mmHg
- d. 665 mmHg
- e. 712 mmHg

176. A sedentary individual goes to her physician's office for a cardiopulmonary exercise stress test evaluation prior to starting a weight-loss exercise regimen. Physiological changes that occur during deep inspirations as lung volume approaches total lung capacity include which of the following?

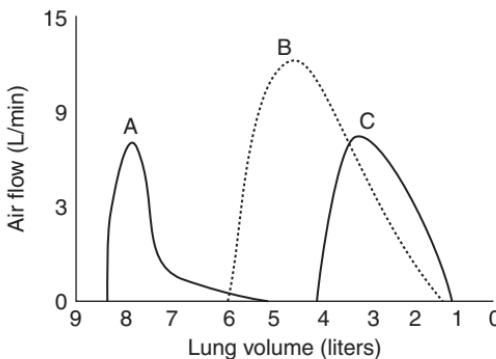
- a. Elastic recoil of the lungs decreases
- b. Lung compliance increases
- c. Intrapleural pressure becomes less subatmospheric
- d. Airway resistance increases
- e. Pulmonary vascular resistance increases

177. A 27-year-old man develops adult respiratory distress syndrome (ARDS) after near-drowning. Conventional mechanical ventilation on 100% O₂ together with inhaled nitric oxide do not provide sufficient oxygenation. Porcine surfactant is instilled via fiberoptic bronchoscope, and the Paco₂, fraction of inspired oxygen (F_iO₂), and shunting improve

impressively. The improvements in respiratory function occurred because surfactant increased which of the following?

- a. Bronchiolar smooth muscle tone
- b. The pressure gradient needed to inflate the alveoli
- c. Lung compliance
- d. Alveolar surface tension
- e. The work of breathing

178. In the maximal expiratory flow-volume curves below, Curve A would be typical of which of the following clinical presentations?



- a. A 75-year-old man who has smoked two packs of cigarettes per day for 60 years. His breath sounds are decreased bilaterally, and his chest x-ray shows flattening of the diaphragm
- b. A 68-year-old man presents with a dry cough that has persisted for 3 months. His chest x-ray shows opacities in the lower and middle lung fields. The man states he was exposed to asbestos for approximately 10 years when he worked in a factory in his thirties
- c. A 57-year-old woman with pulmonary fibrosis who presents to the emergency room with shortness of breath
- d. An 84-year-old woman with a history of myocardial infarction who reports shortness of breath that worsens in the recumbent position
- e. A healthy, 22-year-old man getting his Army enlistment physical. He has never smoked, but is tired that morning, and does not use much effort while exhaling

179. A 30-year-old female patient is admitted to the Emergency Department with dyspnea, tachycardia, confusion, and other signs of hypoxia. The following laboratory data were obtained while the patient was breathing room air.

$$\text{PaO}_2 = 67 \text{ mmHg}$$

$$\text{Paco}_2 = 60 \text{ mmHg}$$

$$\text{pH} = 7.27$$

$$[\text{HCO}_3^-] = 26 \text{ mEq/L}$$

$$[\text{Hb}] = 15 \text{ g\%}$$

$$\text{SaO}_2 = 90\%$$

$$\text{Pvo}_2 = 30 \text{ mmHg}$$

$$\text{Svo}_2 = 55\%$$

$$\dot{\text{V}}\text{O}_2 = 350 \text{ mL/min}$$

$$\text{CaO}_2 - \text{Cvo}_2 = 7 \text{ mL O}_2/100 \text{ mL}$$

Which of the following is the most appropriate classification of the patient's hypoxia?

- a. Hypoxic hypoxia (hypoxemia)
- b. Anemic hypoxia
- c. Stagnant (hypoperfusion) hypoxia
- d. Histotoxic hypoxia
- e. Carbon monoxide poisoning

180. A patient with parotid gland cancer has damage to the glossopharyngeal nerve. As a result, which of the following respiratory reflexes will be impaired?

- a. Hering-Breuer inflation reflex
- b. Juxta pulmonary capillary (J) receptor reflex
- c. Irritant airway reflex
- d. Aortic chemoreceptor reflex
- e. Carotid body chemoreceptor reflex

181. A 68-year-old woman convalescing from surgery developed a fever, hypoxemia, and shortness of breath. She was given 100% O₂ for 30 minutes, and the lab results were as follows:

$$\text{PaO}_2 = 95 \text{ mmHg}$$

$$\text{Paco}_2 = 33 \text{ mmHg}$$

$$\text{pH} = 7.46$$

$$[\text{HCO}_3^-] = 22 \text{ mEq/L}$$

$$[\text{Hb}] = 15 \text{ g\%}$$

$$\text{SaO}_2 = 95\%$$

The response to 100% O₂ reveals that the patient has which of the following?

- a. Alveolar hypoventilation
- b. Diffusion impairment
- c. \dot{V}/\dot{Q} inequality with low V/Q units
- d. Right-to-left shunting
- e. Carbon monoxide poisoning

182. A patient with right lower lobar pneumonia exhibits increasing respiratory distress. The patient is intubated, placed on a mechanical ventilator, and positioned on his left side. The dependent lung has a lower:

- a. Rate of alveolar ventilation per unit volume
- b. Pulmonary blood flow
- c. V/Q ratio
- d. PaCO₂
- e. Lung compliance

183. A subject training for a triathlon reaches a workload while running that exceeds his anaerobic threshold. As a result, which of the following is increased?

- a. PaCO₂
- b. Arterial pH
- c. [HCO₃⁻]
- d. Alveolar ventilation
- e. Firing of the central chemoreceptors

184. A candidate for cardiac transplantation undergoes cardiac catheterization. Hemodynamic findings include:

Pulmonary Artery Pressure = 35 mmHg

Cardiac Output = 4 L/min

Left Atrial Pressure = 15 mmHg

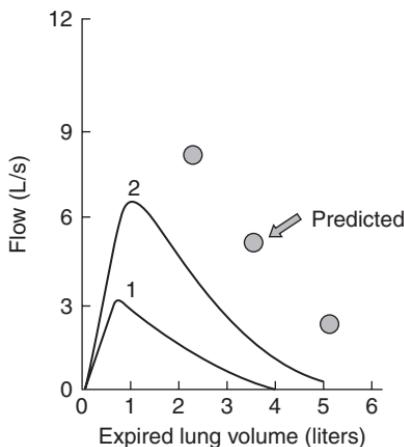
Which of the following is his pulmonary vascular resistance?

- a. 0.11 L/min/mmHg
- b. 0.2 L/min/mmHg
- c. 5 mmHg/L/min
- d. 8.75 mmHg/L/min
- e. 80 mmHg/L/min

185. A woman found comatose in her house is life-flighted to the nearest regional medical center. Blood gases reveal a normal PaO_2 but a lower than normal arterial O_2 saturation. Which of the following conditions is most consistent with the findings?

- a. Anemia
- b. Carbon monoxide poisoning
- c. Low V/Q ratio
- d. Hypoventilation
- e. Right-to-left shunt

186. During a pulmonary function test, a patient first generated Curve #1. Subsequent to administration of a bronchodilator, she generated Curve #2.



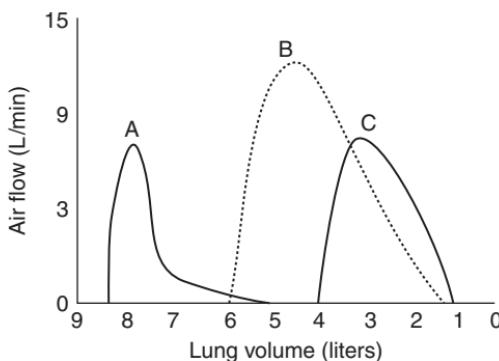
The increased flow in Curve #2 versus Curve #1 is a result of which of the following?

- a. Stimulation of β_2 -adrenergic receptors in bronchial smooth muscle
- b. Stimulation of α -adrenergic receptors in bronchial smooth muscle
- c. Stimulation of parasympathetic nerves to airway smooth muscle
- d. Stimulation of irritant airway receptors in airway epithelium
- e. Mast cell degranulation in the airways

187. An asthmatic patient experiences an acute exacerbation, which causes her breathing to become labored and faster. As a result, which of the following changes in airflow is expected?

- Turbulent flow will increase as Reynold's number decreases
- Flow is more likely to be turbulent in the peripheral airways than in the trachea
- The resistance to airflow will decrease
- The resistance to airflow will increase with increases in airway radius
- The pressure gradient required for airflow will increase

188. Diagnostic pulmonary function screening tests are ordered on a patient with a persistent cough. The patient is instructed to take in a maximal inspiration and then to exhale the breath as hard and fast as he can to generate a maximal expiratory flow-volume (MEFV) curve. As a result, the patient generates Curve C shown below.



The patient's MEFV curve is consistent with which of the following sets of values for the forced vital capacity (FVC) and the forced expiratory volume in one second (FEV₁)?

FVC (liters)	FVC (% predicted)	FEV ₁ (liters)	FEV ₁ (% predicted)
a. 4.2	85	3.4	90
b. 4.2	85	2.1	32
c. 3.1	48	2.8	50
d. 3.1	48	2.0	40
e. 1.5	25	1.0	20

189. Noninvasive color Doppler ultrasound studies are ordered on a term infant and a preterm infant of 28-weeks gestation. Which of the following is likely to have a lower value in the preterm infant?

- a. Pulmonary artery pressure
- b. Pulmonary blood flow
- c. Pulmonary vascular resistance
- d. Pulmonary capillary hydrostatic pressure
- e. Blood flow from the pulmonary artery through the ductus arteriosus

190. A 35-year-old woman with gestational diabetes develops hypertension and preeclampsia, requiring the preterm delivery of her fetus of 30-weeks gestation. The mother is given two doses of betamethasone, 12 mg, intramuscularly, 24 hours apart. Which of the following is the purpose of the antenatal steroid therapy?

- a. Increase fetal PO_2
- b. Increase blood flow to the fetal lungs
- c. Shift the fetal oxyhemoglobin dissociation curve to the right
- d. Increase blood flow from the right atrium into the left atrium across the foramen ovale
- e. Increase the lecithin/sphingomyelin ratio in the amniotic fluid

191. A patient with congestive heart failure (CHF) develops increasing shortness of breath in the recumbent position. A chest x-ray reveals cardiomegaly, horizontal lines perpendicular to the lateral lung surface indicative of increased opacity in the pulmonary septa, and lung consolidation. Pulmonary edema in CHF is promoted by which of the following?

- a. Decreased pulmonary interstitial oncotic pressure
- b. Increased pulmonary capillary hydrostatic pressure
- c. Increased pulmonary capillary oncotic pressure
- d. Increased pulmonary interstitial hydrostatic pressure
- e. Decreased pulmonary capillary permeability

192. A patient with emphysema is referred for his annual pulmonary function testing to assess the progression of his disease. As a result of alveolar-septal departmenting in emphysema, there is a decrease in which of the following?

- a. Lung compliance
- b. Airway resistance
- c. Alveolar dead space
- d. Diffusing capacity
- e. Total lung capacity

193. A Swan-Ganz catheter is placed in a post-myocardial infarction (MI) patient in the Medical Intensive Care Unit. The patient is found to have a pulmonary artery wedge pressure of 25 mmHg, which is indicative of which of the following?

- a. Decreased pulmonary capillary hydrostatic pressure
- b. Decreased left atrial pressure
- c. Decreased left ventricular end-diastolic pressure
- d. Decreased left ventricular preload
- e. Increased net fluid movement out of the pulmonary capillaries

194. A 68-year-old male with chronic obstructive pulmonary disease entered the Emergency Department complaining of shortness of breath. His respirations were 35 per minute and labored. He had a productive cough and rales were heard over all lung fields. The patient had a rather ashen complexion and his nail beds gave clear evidence of cyanosis. An arterial blood sample was obtained and a chest x-ray was ordered. The patient was then placed on an O₂ mask delivering 40% O₂. One-half hour later, the physician was called to the bedside by the nurse who found the patient unresponsive. The patient's complexion had changed to a flushed pink with no trace of cyanosis. His respirations were quiet at a rate of 6 per minute and a tidal volume of 300 mL. Repeat arterial blood gases showed that his arterial PCO₂ had increased from 55 to 70 mmHg, and his PaO₂ increased from 55 to 70 mmHg. Oxygen therapy most likely resulted in which of the following?

- a. Alveolar hypoventilation
- b. Hypoxic pulmonary vasoconstriction
- c. Increased firing of carotid body chemoreceptors
- d. Elimination of the hypercapnic drive
- e. Oxygen toxicity

195. A scientist doing experiments with sodium cyanide started experiencing headache, dizziness, clumsiness, decreased visual acuity, and nausea. The medical student doing research in the laboratory was not certain if this was unusual behavior for the professor, but thought it best to take him to the Emergency Department to be evaluated for possible hypoxia. Blood values obtained on the professor while he was breathing room air were as follows:

Hb: 16 g%	SaO ₂ : 97.5%
Pao ₂ : 102 mmHg	Pvo ₂ : 65 mmHg
Paco ₂ : 27 mmHg	Svo ₂ : 90%
pH: 7.57	Cardiac Output: 5.6 L/min
[HCO ₃ ⁻]: 23 mEq/L	

The professor's hypoxia is most likely the result of which of the following?

- a. Hypoxemia
- b. Impaired hemoglobin oxygen transport
- c. Impaired oxygen delivery
- d. Impaired oxygen utilization
- e. Impaired diffusion across the alveolar-capillary membrane

196. A 42-week gestation infant is delivered by cesarean section. Which of the following occurs with the baby's first diaphragmatic respiration?

- a. Pao₂ increases
- b. Pulmonary vascular resistance increases
- c. Pulmonary capillary hydrostatic pressure increases
- d. Systemic vascular resistance decreases
- e. All of the fetal vascular channels functionally close

197. A 29-year-old woman is admitted to the hospital because of increasing dyspnea and swelling of both feet. An examination of her chest shows a severe pectus excavatum with only 2 cm of space between the vertebral bodies and the sternum. Pulmonary function tests show FVC and FEV₁/FVC values that were 15 and 100%, respectively, of predicted. Which of the following laboratory measurements will most likely be below normal in this patient?

- a. Elastic recoil of the chest wall
- b. Arterial PCO₂
- c. Hemoglobin concentration
- d. Plasma bicarbonate concentration
- e. Arterial pH

198. An 18-year-old college student living in a dormitory contracts meningitis, which causes a centrally mediated increase in his respiratory rate. The basic respiratory rhythm is generated in which of the following regions of the brain?

- a. Cerebral cortex
- b. Hypothalamus
- c. Reticular activating system
- d. Medulla
- e. Nucleus parabrachialis

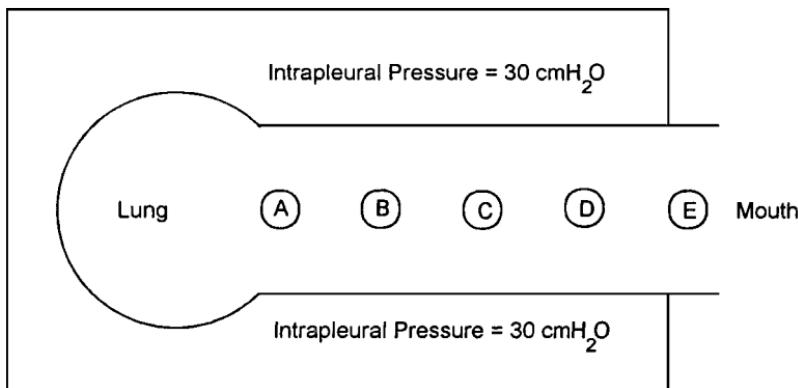
199. A 56-year-old man presents to the Emergency Department with severe abdominal pain and a temperature of 103°F. The patient is in severe respiratory distress. Moderate amounts of pulmonary edema fluid are aspirated during suctioning. The patient is placed on a ventilator with an F_iO_2 of 0.5 and an arterial blood gas sample reveals a Po_2 of 160 mmHg and a PCO_2 of 40 mmHg. His alveolar oxygen tension, at a barometric pressure of 747 mmHg and a respiratory exchange ratio (R) of 0.8, is approximately what?

- a. 100 mmHg
- b. 200 mmHg
- c. 300 mmHg
- d. 400 mmHg
- e. 500 mmHg

200. A 68-year-old man who has chronic obstructive pulmonary disease (COPD) presents to his pulmonologist with fatigue, dyspnea at rest, and peripheral edema. His blood gases on room air are $Pao_2 = 60$ mmHg, $Paco_2 = 60$ mmHg, and $pH = 7.36$. His alveolar-arterial (A-a) O_2 gradient, at a barometric pressure of 760 mmHg and a respiratory exchange ratio (R) of 0.8, is approximately what?

- a. 5 mmHg
- b. 10 mmHg
- c. 15 mmHg
- d. 20 mmHg
- e. 25 mmHg

201. The diagram below illustrates the intrapleural pressure generated by a patient during a forced expiration. The equal pressure point will move closer to the mouth and the forced expiratory volume will increase if there is an increase in which of the following?



- a. Inspired lung volume
- b. Lung compliance
- c. Airway resistance
- d. Expiratory effort
- e. Airway smooth muscle tone

202. A healthy, 24-year-old man is prescribed sustained-release bupropion (Zyban) for smoking cessation. Twenty-one days after therapy he presents to his family physician with intermittent fever and a generalized rash, at which point the bupropion therapy is discontinued. A month later he develops a dry, intermittent cough and dyspnea. Which of the following pulmonary function test results is consistent with a diagnosis of allergic bronchospasm?

- a. An increased forced vital capacity
- b. A decreased FEV₁/FVC
- c. An increased diffusing capacity
- d. A decreased residual volume
- e. An increased lung compliance

203. A 5-month-old boy is admitted to the hospital for evaluation because of repeated episodes of sleep apnea. During a ventilatory response test, his ventilation did not increase when Paco_2 was increased, but decreased during hyperoxia. Which of the following is the most likely cause of this infant's apnea?

- a. Bronchospasm
- b. Diaphragmatic fatigue
- c. Decreased irritant receptor sensitivity
- d. Peripheral chemoreceptor hypersensitivity
- e. Dysfunctional central chemoreceptors

204. A patient presents with a chief complaint of fatigue. He had an increase in heart rate and respiratory rate. The history also revealed symptoms of chills and spiking fever. The right lower lobe was dull to percussion. Vocal fremitus was increased over the right lower lobe and bronchovesicular breathing was present in the region, as well. Ventilation-perfusion (V/Q) abnormalities occurring in a patient with lobar pneumonia will generally cause a decrease in which of the following?

- a. Alveolar ventilation
- b. Arterial carbon dioxide tension
- c. Arterial pH
- d. Anion gap
- e. A-a gradient for oxygen

205. A patient with congestive heart failure, orthopnea, and paroxysmal nocturnal dyspnea is referred for pulmonary function testing in the supine and upright positions. Which of the following is higher at the apex of the lung than at the base when a person is upright?

- a. Ventilation
- b. Blood flow
- c. V/Q ratio
- d. $PACO_2$
- e. Lung compliance

206. A 58-year-old factory worker, who has worked in the insulation industry for over 30 years, develops progressive shortness of breath. His wife has tried to get him to go to the doctor, and he finally relents with the appearance of hemoptysis. A chest x-ray is consistent with an alveolitis from asbestos inhalation. Which of the following is the major route for removal of small particles from the alveoli?

- a. Bulk flow
- b. Diffusion
- c. Expectoration
- d. Phagocytosis
- e. Ciliary transport

207. A patient presents with signs of hypoxia. Arterial blood gases reveal that the PaO_2 is normal but the arterial O_2 saturation is reduced. Which of the following conditions is the most likely cause of the hypoxia?

- a. Anemia
- b. Carbon monoxide poisoning
- c. A low V/Q ratio
- d. Hypoventilation
- e. Right-to-left shunt

208. The wife of a recently married 24-year-old medical student reports that even though her husband doesn't snore, he stops breathing for periods of 1 to 2 minutes while he is sleeping. His physician refers him for a polysomnography study and pulmonary function testing, including ventilatory response curves. The tests confirm the apneic episodes during sleep and show depressed ventilatory responsiveness of both the peripheral and central chemoreceptors. Peripheral and central chemoreceptors both contribute to the increased ventilation that occurs as a result of which of the following?

- a. A decrease in arterial oxygen content
- b. A decrease in arterial blood pressure
- c. An increase in arterial carbon dioxide tension
- d. A decrease in arterial oxygen tension
- e. An increase in arterial pH

209. A 57-year-old female presents with dyspnea on exertion. Pulmonary function studies with plethysmography demonstrate an increase in the work of breathing, and the oxygen consumption is higher-than-normal at rest. Which of the following will decrease the oxygen consumption of the respiratory muscles?

- a. A decrease in lung compliance
- b. A decrease in airway resistance
- c. A decrease in the diffusing capacity of the lung
- d. An increase in the rate of respiration
- e. An increase in tidal volume

210. An 18-year-old male is thrown from his motorcycle and suffers a complete transection of the brainstem above the pons. As a result, which of the following will most likely occur?

- a. All breathing movements will cease
- b. The Hering-Breuer reflex will be abolished
- c. The central chemoreceptors will no longer be able to exert any control over ventilation
- d. The peripheral chemoreceptors will no longer be able to exert any control over ventilation
- e. The limbic system will no longer be able to exert any control over ventilation

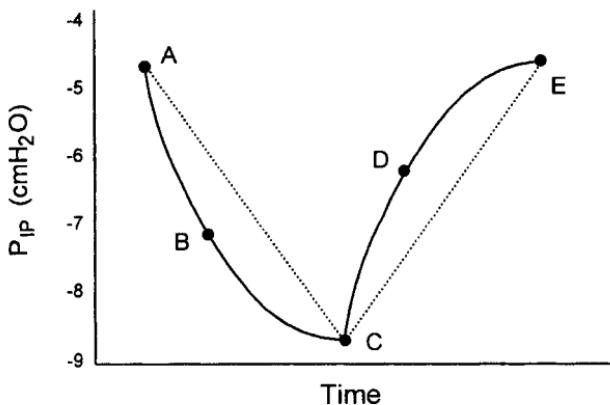
211. A 48-year-old coal miner complains of shortness of breath and a productive cough. The history reveals that he has smoked 1 to 2 packs of cigarettes per day since he was 16 years old. Pulmonary function studies are ordered including an esophageal balloon study to measure intrapleural pressures. Normally, intrapleural pressure is negative throughout a tidal inspiration and expiration because of which of the following?

- a. The lungs have the tendency to recoil outward throughout a tidal breath
- b. The chest wall has the tendency to recoil inward throughout a tidal breath
- c. The intact pleura causes the lungs and chest wall to recoil away from each other throughout a tidal breath
- d. The intact pleura causes the lungs and chest wall to recoil in the same direction throughout a tidal breath
- e. There is always a small leak in the visceral pleura causing some air to escape into the pleural space during a tidal breath

212. When the respiratory muscles are relaxed, the lungs are at which of the following?

- a. Functional residual capacity (FRC)
- b. Expiratory reserve volume (ERV)
- c. Residual volume (RV)
- d. Inspiratory reserve volume (IRV)
- e. Total lung capacity (TLC)

213. The diagram below illustrates the change in intrapleural pressure during a single tidal breath.



At which point on the diagram is inspiratory airflow the greatest?

- a. A
- b. B
- c. C
- d. D
- e. E

214. Which of the following is higher at total lung capacity than it is at residual volume?

- a. Airway resistance
- b. Lung compliance
- c. Alveolar pressure
- d. Anatomical dead space
- e. Intrapleural pressure

Questions 215–216

A 32-year-old male is hospitalized with severe respiratory disease following aspiration pneumonia. Inhaled nitric oxide is administered and he is placed in a prone position to improve oxygenation. Values obtained after the administration of nitric oxide are

Mean pulmonary capillary oxygen content = 19 mL/dL

Arterial oxygen content = 18 mL/dL

Mixed venous oxygen content = 14 mL/dL

Cardiac output = 6 L/min

215. Which of the following is the patient's shunt fraction (the ratio of shunted to total pulmonary blood flow)?

- a. 10%
- b. 20%
- c. 30%
- d. 40%
- e. 50%

216. The patient's oxygen consumption is what?

- a. 200 mL/min
- b. 210 mL/min
- c. 220 mL/min
- d. 230 mL/min
- e. 240 mL/min

217. A 37-year-old woman is admitted to the hospital with severe kyphoscoliosis. Over time, this anatomical distortion results in respiratory muscle weakness. Which of the following physiological variables will most likely be above normal in this patient?

- a. Total lung capacity
- b. Vital capacity
- c. Chest wall compliance
- d. Arterial carbon dioxide tension
- e. Arterial pH

218. A hospitalized patient is found semicomatose. Arterial blood gases reveal hypercapnia. Which of the following is the most likely cause of the high arterial PCO_2 ?

- a. Decreased metabolic activity
- b. Decreased alveolar dead space
- c. Profound hypoxia
- d. Alveolar capillary block
- e. Increased alveolar ventilation

219. Pulmonary vascular resistance decreases if which of the following occurs?

- a. The lungs are inflated to total lung capacity
- b. Sympathetic stimulation to the pulmonary vessels is increased
- c. Alveolar oxygen tension is decreased
- d. Plasma hydrogen ion concentration is decreased
- e. Cardiac output is increased

220. A healthy 32-year-old woman undergoes pulmonary exercise stress testing prior to starting a training regimen in preparation for her first marathon. Normally, during moderate aerobic exercise, which of the following occurs?

- a. PaO_2 increases
- b. PaCO_2 decreases
- c. Arterial pH decreases
- d. Alveolar ventilation increases
- e. Blood lactate level increases

221. A 72-year-old woman presents to her physician with dyspnea. Pulmonary function tests revealed an increase, rather than a decrease, in the diffusing capacity of the lung. Which of the following conditions best accounts for an increase in the diffusing capacity?

- a. Polycythemia
- b. Fibrotic lung disease
- c. Pulmonary embolism
- d. Congestive heart failure
- e. COPD

222. A 49-year-old farmer develops a headache and becomes dizzy after working on a tractor in his barn. His wife suspects carbon monoxide poisoning and brings him to the Emergency Department where he complains of dizziness, lightheadedness, headache, and nausea. The patient's skin is red, he does not appear to be in respiratory distress, and denies dyspnea. Blood levels of carboxyhemoglobin are elevated. Which of the following best explains the absence of respiratory signs and symptoms associated with carbon monoxide poisoning?

- a. Blood flow to the carotid body is decreased
- b. Arterial oxygen content is normal
- c. Cerebrospinal fluid pH is normal
- d. Central chemoreceptors are depressed
- e. Arterial oxygen tension is normal

223. A 68-year-old patient with shortness of breath is referred for pulmonary function testing, including lung volumes, flow-volume curves, and lung compliance. Which one of the following statements best characterizes pulmonary compliance?

- a. It is equivalent to $\Delta P/\Delta V$
- b. It is inversely related to the elastic recoil properties of the lung

- c. It decreases with advancing age
- d. It increases when there is a deficiency of surfactant
- e. It increases in patients with pulmonary edema

224. A 36-year-old man visits his doctor because his wife has long complained of his snoring, but recently observed that his breathing stops for a couple of minutes at a time while he is sleeping. He undergoes polysomnography and ventilatory response testing to ascertain the extent and cause of his sleep apnea. The activity of the central chemoreceptors is stimulated by which of the following?

- a. An increase in the PCO_2 of blood flowing through the brain
- b. A decrease in the PO_2 of blood flowing through the brain
- c. An increase in the pH of the CSF
- d. A decrease in the metabolic rate of the surrounding brain tissue
- e. Hypoxemia, hypercapnia, and metabolic acidosis

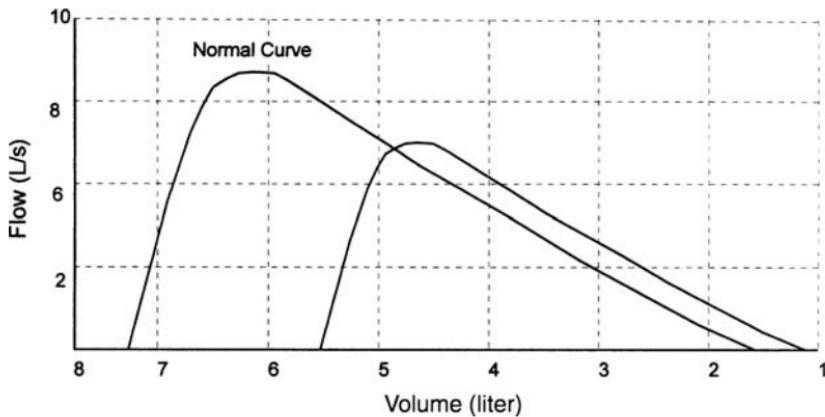
225. A patient complains of paroxysmal episodes of not being able to catch her breath. When no abnormalities are detected with conventional pulmonary function screening, the pulmonologist orders a methacholine challenge test. Which of the following will increase as a result of stimulating cholinergic receptors on the bronchial smooth muscle?

- a. Lung compliance
- b. Airway diameter
- c. Elastic work of breathing
- d. Resistive work of breathing
- e. Anatomic dead space

226. A 28-year-old on oral contraceptives develops tachypnea and reports dyspnea. A ventilation/perfusion scan is ordered to check for pulmonary thromboemboli. Which of the following best explains why, as she takes in a normal inspiration, more air goes to the alveoli at the base of the lung than to the alveoli at the apex of the lung?

- a. The alveoli at the base of the lung have more surfactant
- b. The alveoli at the base of the lung are more compliant
- c. The alveoli at the base of the lung have higher V/Q ratios
- d. There is a more negative intrapleural pressure at the base of the lung
- e. There is more blood flow to the base of the lung

227. Which of the following conditions is most likely to produce the change from the normal maximum flow-volume curve illustrated below?



- a. Sarcoidosis
- b. Emphysema
- c. Asthma
- d. Cystic fibrosis
- e. Fatigue

228. An increase in cardiac output and skeletal muscle blood flow during exercise causes which of the following?

- a. The blood flow to the lungs to decrease
- b. The overall V/Q ratio of the lung to decrease
- c. Diffusing capacity of the lungs to increase
- d. Pulmonary vascular resistance to increase
- e. Pulmonary artery pressure to decrease

229. Which of the changes in arterial blood gas values was obtained from a patient with an atelectatic left lung causing a large intrapulmonary shunt?

	pH	P _{CO₂}	P _{O₂}
A.	↑	↑	↑
B.	↓	↑	↑
C.	↑	↑	↓
D.	↓	↓	↑
E.	↑	↓	↓

- a. A
- b. B
- c. C
- d. D
- e. E

230. A 49-year-old coal miner presents with dyspnea, a nonproductive cough, and decreased exercise tolerance. Lung function tests reveal: total lung capacity = 3.34 L (56% of predicted), residual volume = 0.88 L (54% of predicted), and forced vital capacity = 1.38 L (30% of predicted). His arterial PO_2 is 68 mmHg. Which of the following values will be approximately normal?

- a. FEV_1/FVC ratio
- b. Tidal volume
- c. \dot{V}/\dot{Q} ratio
- d. Diffusing capacity
- e. Lung compliance

231. Airway resistance is lowest in which of the following?

- a. During a forced expiration
- b. At total lung capacity
- c. At residual volume
- d. During vagal stimulation
- e. In the total cross-section of the central airways compared to the peripheral airways.

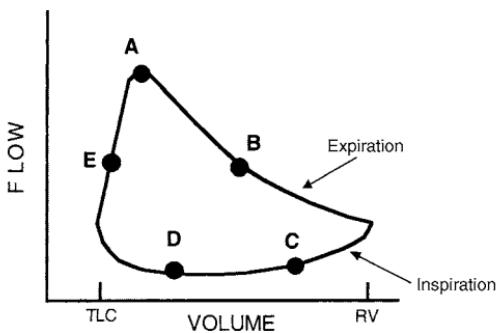
232. A spirometer can be used to measure directly which of the following?

- a. Total lung capacity
- b. Functional residual capacity
- c. Residual volume
- d. Inspiratory capacity
- e. Physiological dead space

233. A patient with Wegener's glomerulonephritis presents with sinusitis and hemoptysis. His chest radiograph shows several large cavitary pulmonary nodules, consistent with ventilation-perfusion imbalance with low \dot{V}/\dot{Q} units. Which of the following will be greater than normal in a patient with a low \dot{V}/\dot{Q} ratio?

- a. PaCO_2
- b. PaO_2
- c. A-a gradient
- d. Oxygen dissolved in blood
- e. Oxygen combined with hemoglobin

234. An 18-year-old girl presents to her primary care physician with an increased frequency of asthma exacerbations over the previous year. At the time of her visit, her physical examination and flow-volume loop are normal. At which point on the flow-volume loop pictured below will airflow remain constant despite an increased respiratory effort?



- a. A
- b. B
- c. C
- d. D
- e. E

Respiratory Physiology

Answers

164. The answer is e. (*Ganong, pp 651–652. Kasper et al., pp 1498–1499. Levitzky, pp 54–57.*) Expiratory reserve volume (ERV) is the maximal volume of gas that can be exhaled in excess of a passive, tidal expiration. The ERV is not labeled in the diagram, but can be calculated from the difference between the functional residual capacity (FRC) and the residual volume (RV), designated as E and D, respectively. The FRC is the volume of gas remaining in the lungs following a passive, tidal exhalation. The RV is the volume of gas remaining in the lungs following a maximal expiration. The inspiratory reserve volume (IRV) is designated by A, the inspiratory capacity (IC) as B, and the vital capacity (VC) by C in the diagram.

165. The answer is c. (*Ganong, pp 647–648, 684–685. Levitzky, pp 71–72, 234.*) According to Dalton's Law, the partial pressure of a gas is the product of the fractional composition of the gas and the total pressure of the gaseous mixture. Oxygen constitutes approximately 21% of dry atmospheric air. Therefore, the partial pressure of O₂ in dry atmospheric air equals the fractional concentration of oxygen (F_iO₂) times the atmospheric (barometric) pressure. At sea level, the barometric pressure is 760 mmHg, yielding a P_iO₂ of 160 mmHg. At high altitude, the barometric pressure decreases in proportion to the decreased weight of the air above it. At an elevation of 18,000 feet in the Peruvian Andes, the barometric pressure is 380 mmHg, yielding a P_iO₂ of 80 mmHg. Once inside the respiratory tract, the inspired air becomes warmed and humidified. The partial pressure of H₂O vapor is temperature-, rather than concentration-dependent, and at body temperature (37°C) is 47 mmHg. The presence of H₂O vapor reduces the partial pressure of the other gases in the atmosphere, and the P_{H2O} must be subtracted from the total barometric pressure before multiplying by the fractional concentration of a gas to yield the partial pressure of the gas. Thus, at sea level, the humidified P_iO₂ in the conducting airways is 0.21 (760–47) or 150 mmHg, whereas, at 18,000 feet, the humidified tracheal Po₂ would be 0.21 (380–47) or 70 mmHg.

166. The answer is c. (*Ganong, pp 647–648. Levitzky, pp 71–72.*) Room air contains 21% O₂ and 0.04% CO₂, yielding a P_iO₂ of 160 mmHg and a P_iCO₂

of 0.3 mmHg. Thus, if a sample of arterial blood is equilibrated with room air, the measured Pao_2 will have an inaccurately high reading and the $Paco_2$ will have an inaccurately low reading. For this reason, collecting an “anaerobic” blood sample is critical in blood gas analysis. Also, once the sample is obtained, the syringe should be placed in a container of crushed ice to prevent any metabolism by the red blood cells, which can also affect the accuracy of the readings. In addition to being certain that an air bubble is not left in the syringe, it is best to use a glass rather than a plastic syringe because the arterial pressure will pump the blood sample into a glass syringe without requiring aspiration, and glass is more impermeable to the diffusion of gases than plastic. A plastic syringe is permissible if one is drawing the blood sample from an arterial line rather than doing an arterial “stick” and if the sample is promptly analyzed.

167. The answer is a. (*Ganong, pp 660–661. Kasper et al., pp 1498–1505, 1556. Levitzky, pp 44–46, 58, 139–140, 263. Stead, pp 255–257.*) In pulmonary fibrosis, the diffusing capacity of the lung is decreased due to an increase in the thickness of the diffusional barrier, as predicted by Fick’s law of diffusion. Pulmonary fibrosis causes “stiff” lungs, and is characterized by a decrease in lung compliance and an increase in lung elastic recoil. This results in pulmonary function findings typical of a restrictive impairment, including a decrease in all lung volumes and capacities and a ratio of the forced expiratory volume exhaled in one second ($FEV_{1.0}$) to the total forced vital capacity (FVC) that is normal or increased. Although airway resistance is increased at lower lung volumes, the airway resistance in restrictive disorders is normal when corrected for lung volume. An increased airway resistance is the hallmark of an obstructive impairment.

168. The answer is b. (*Kasper et al., pp 282, 1561. Levitzky, pp 114–117. Stead, pp 272–273.*) A pulmonary thromboembolism results in areas of the lung that are ventilated, but not perfused, yielding \dot{V}/Q ratios of infinity and an increase in alveolar deadspace. When the \dot{V}/Q ratio equals ∞ , the P_{AO_2} of the affected alveoli will be the same as that in the humidified inspired air because atmospheric air enters the alveoli via the process of ventilation but no gas exchange takes place because the alveoli are not perfused. Areas of the lung that are perfused but not ventilated constitute areas of shunting (venous admixture), characterized as a \dot{V}/Q ratio equal to 0, and having P_{AO_2} values that equilibrate with the mixed venous blood.

169. The answer is c. (*Ganong*, pp 658–660. *Levitzky*, pp 67–71.) Physiological deadspace is the volume of the respiratory tract, that is ventilated but not perfused by the pulmonary circulation. Bohr's equation for determination of the ratio of the physiologic deadspace (V_D) to the tidal volume (V_T) is

$$V_D/V_T = \text{Paco}_2 - \text{P}_{\text{E}}\text{CO}_2/\text{Paco}_2$$

$$V_D/V_T = 40 - 28/40 = 0.3$$

$$V_D/V_T \times V_T = V_D$$

$$0.3 \times 600 \text{ mL} = 180 \text{ mL}$$

$$\text{Physiologic Deadspace Volume} = \text{Anatomic} + \text{Alveolar Deadspace}$$

Anatomic deadspace can be measured by Fowler's technique, but is often estimated as 1 mL per pound of body weight. Because there is normally no alveolar deadspace, physiologic deadspace volume approximates anatomic deadspace volume in persons with normal lung function.

170. The answer is d. (*Ganong*, pp 654–658. *Levitzky*, pp 20–28.) Lung compliance is defined as the ease with which the lungs are expanded, and is calculated as the change in volume per change in pressure ($\Delta V/\Delta P$), which is the slope of the pressure-volume curve of the lung. Thus, Curve Z is the pressure-volume curve of an individual with a decrease in lung compliance. The abnormal accumulation of fluid in the lungs (pulmonary edema) causes a restrictive pulmonary impairment characterized by a decreased lung compliance. An L/S ratio ≥ 2 indicates normal biochemical maturation of the lung, with normal surfactant production and lung compliance (normal curve). If the L/S ratio is less than 2, there is an increased incidence of respiratory distress syndrome of the newborn, which would be represented by Curve Z. Aging and emphysema are characterized by an increase in lung compliance (Curve X), which increases airway resistance. The increase in airway resistance in asthma is not associated with an increase (or decrease) in lung compliance.

171. The answer is a. (*Ganong*, p 688. *Kasper et al.*, p 1568. *Levitzky*, pp 12, 116–117. *Stead et al.*, pp 273–274.) When air enters the pleural space due to interruption of the pleural surface through either the rupture of the lung or a hole in the chest wall, the pressure in the pleural space becomes atmospheric, the lung on the affected side collapses because of the lung's tendency to recoil inward, and the chest wall on the affected side recoils outward. Because the intrapleural pressure is atmospheric, the mediastinum shifts farther to the normal side with each inspiration. With collapse of the lung, the \dot{V}/\dot{Q} ratio on the affected side decreases.

172. The answer is b. (*Ganong*, pp 651–652, 688–689. *Kasper et al.*, p 1511. *Levitzky*, pp 41–42, 58–59, 263. *Stead et al.*, pp 255–256, 263–265.) During a forced vital capacity (FVC), the patient is asked to breathe in as much air as possible (up to the total lung capacity), and then exhale all of the gas in her lung as fast as possible, which, in this case is 3.5 liters. The FEV_{1.0} is the volume of gas expelled from the lung during the first second, which, in this case, is 2 L. The ratio of the FEV_{1.0} to the FVC in this patient is 2 L/3.5 L, which equals 0.57. Normally, FEV_{1.0}/FVC should be ≥ 0.8 . The decreased FEV_{1.0}/FVC is indicative of an obstructive impairment. Obstructive lung diseases, such as asthma, are characterized by a greater-than-normal total lung capacity (TLC), residual volume (RV), and functional residual capacity (FRC). The inspiratory and expiratory reserves (inspiratory capacity and expiratory volume) are decreased, as is the vital capacity and the maximum voluntary ventilation.

173. The answer is d. (*Ganong*, pp 658–660. *Kasper et al.*, pp 1508–1516. *Levitzky*, pp 67–71.) Alveolar ventilation (\dot{V}_A) equals the tidal volume (V_T) minus the deadspace volume (V_D) times the breathing frequency (f). The deadspace volume can be estimated as 1 mL/lb of body weight.

$$\begin{aligned}\dot{V}_A &= (V_T - V_D) \times f \\ \dot{V}_A &= (500 \text{ mL} - 125 \text{ mL}) \times 15 \text{ breaths/min} \\ \dot{V}_A &= 5625 \text{ mL/min}\end{aligned}$$

174. The answer is c. (*Levitzky*, pp 73–75.) Because the deadspace air does not participate in gas exchange, the entire output of CO₂ in the expired gas comes from the alveolar gas. Accordingly, CO₂ output (V_{CO_2}) can be expressed in terms of alveolar ventilation (\dot{V}_A) and alveolar PCO₂, according to the equation:

$$Paco_2 = \dot{V}_{CO_2}/\dot{V}_A$$

Because Paco₂ is essentially equal to PaCO₂, this equation can also be expressed as

$$Paco_2 = V_{CO_2}/V_A$$

Thus, an increase in alveolar ventilation at a constant rate of carbon dioxide production will lower the Paco₂ and PaCO₂. Hyperventilation increases PaO₂ and PaO₂, with no change in the alveolar-arterial PaO₂ difference. The V/Q would be normal or increased.

175. The answer is d. (Ganong, p 660. Kasper et al., pp 1194–1196, 1583, 1592–1595. Levitzky, p 75. Stead et al., pp 202–204.) The alveolar air equation is used to calculate the P_{AO_2} .

$$P_{AO_2} = P_{iO_2} - (PaCO_2/R)$$

Given the barometric pressure of 757 mmHg, $F_{iO_2} = 1.0$ (100% O₂), $PaCO_2 = 36$ mmHg, and $R = 0.8$, then

$$\begin{aligned} P_{AO_2} &= (1.0)(757 - 47) - (36/0.8) \\ &= 710 - 45 = 665 \text{ mmHg} \end{aligned}$$

Pneumocystis is an opportunistic fungal pulmonary pathogen that is an important cause of pneumonia (pneumocystosis) in immunocompromised hosts. HIV patients with a CD4+ cell count below 200/ μ L have an increased risk of developing *Pneumocystis* pneumonia. According to new, and still evolving nomenclature, *Pneumocystis carinii* is the name of the organism derived from rats, and *Pneumocystis jiroveci* is the name of the organism derived from humans.

176. The answer is e. (Ganong, pp 654–655, 658–659. Levitzky, pp 20–23, 36–37, 92–95.) Pulmonary vascular resistance (PVR) varies with lung volume. PVR is lowest at functional residual capacity, and increases at both high and low lung volumes. The increased pulmonary vascular resistance seen at total lung capacity (TLC) is due to an increase in the resistance of the alveolar vessels (pulmonary capillaries) caused by compression by the high alveolar volume. The increased pulmonary vascular resistance seen at residual volume is due to an increase in the resistance of the extra-alveolar vessels caused by compression by the positive intrapleural pressure generated during a forced expiration. As lung volume increases toward TLC, the compliance of the lungs (slope of pressure-volume curve) decreases and elastic recoil of the lung increases, that is, the lungs resist further expansion. Intrapleural pressure becomes more subatmospheric during inspiration, approaching –30 cm H₂O at TLC; as a result, the transmural pressure across the intrathoracic airways ($P_{in} - P_{out}$) increases, which increases airway radius, and decreases airway resistance according to Poiseuille's law.

177. The answer is c. (*Ganong, pp 654–6558. Kasper et al., pp 1583, 1592–1595. Levitzky, pp 26–28. Stead et al., p 270.*) Pulmonary surfactant increases lung compliance by lowering alveolar surface tension. As a result, the pressure gradient needed to inflate the alveoli decreases, as does the work of breathing.

178. The answer is a. (*Kasper et al., pp 1499–1450, 1547–1554. Levitzky, pp 44–46. Stead et al., pp 255–256.*) Cigarette smoking is the major cause of chronic obstructive pulmonary disease (COPD). In obstructive lung diseases, the increase in airway resistance causes a decrease in expiratory flow rates and “air-trapping,” which results in an increased residual volume, and thus total lung capacity. This hyperinflation pushes the diaphragm into a flattened position. Asbestosis and pulmonary fibrosis are restrictive lung diseases, in which Curve C would be the typical maximal expiratory flow-volume (MEFV) curve. Decreased effort would decrease flow rates during the effort-dependent portion of a MEFV curve, but not during the effort-independent portion.

179. The answer is a. (*Ganong, pp 683–691. Levitzky, pp 180–183.*) Alveolar hypoventilation (as evidenced by the higher than normal value of Paco_2) is a type of hypoxic hypoxia or hypoxemia (as evidenced by the decreased PaO_2). Anemic hypoxia is characterized by a decreased concentration of hemoglobin (anemia) or a reduction in the saturation of hemoglobin with oxygen (SaO_2) expected for a given PaO_2 , as would occur in carbon monoxide poisoning or methemoglobinemia. Stagnant hypoxia is characterized by a decreased cardiac output; in this patient, cardiac output, calculated as $(\dot{V}\text{O}_2/\text{CaO}_2 - \text{CvO}_2)$, is 5 L/min, which is normal. In histotoxic hypoxia, oxygen extraction is impaired, and thus $\text{CaO}_2 - \text{CvO}_2$ would be less than normal and SvO_2 would be greater than normal.

180. The answer is e. (*Ganong, pp 672–675, 678–679. Levitzky, pp 194–200.*) The afferent pathway from the carotid body chemoreceptors is Hering's nerve, a branch of cranial nerve IX, the glossopharyngeal nerve. The vagus nerve constitutes the afferent pathway from the aortic chemoreceptors, the J receptors, the irritant airway receptors, and the rapidly adapting stretch receptors mediating the Hering-Breuer inflation reflex.

181. The answer is d. (*Ganong, pp 683–691. Levitzky, pp 180–183.*) The classification of the causes of hypoxemia (low PaO_2) are (1) reduced P_{aO}_2 (alveolar hypoventilation or reduced P_{lO}_2 found at high altitude or with

breathing low concentrations of oxygen), (2) diffusion impairment, (3) ventilation/perfusion inequality, and (4) right-to-left shunting (venous admixture). Left-to-right shunting does not cause hypoxemia. Administration of 100% O₂ corrects the hypoxemia caused by alveolar hypoventilation, diffusion impairment, or ventilation/perfusion inequality, but not that due to right-to-left shunting (venous admixture). Alveolar hypoventilation would have an increased PacO₂. In carbon monoxide poisoning, the SaO₂ would be lower than normal. On 100% O₂, the PaO₂ should be ≥ 500 mmHg and the A-a PO₂ difference should be ≤ 100 mmHg. This patient's PaO₂ is only 95 mmHg on 100% O₂, indicating the presence of right-to-left shunting, that is, areas of the lung that are perfused but not ventilated (V/Q ratio = 0). Post-op complications such as pneumonia, pulmonary edema, and atelectasis are all causes of intrapulmonary right-to-left shunts.

182. The answer is c. (*Ganong, pp 662–663. Kasper et al., p 1537. Levitzky, pp 125–127.*) Even in normal individuals, the dependent lung has a greater ventilation per unit volume and a greater pulmonary blood flow, but because the effects of gravity (hydrostatic pressure) are greater for blood than air because blood is more dense, the increase in perfusion exceeds the increase in ventilation, and the V/Q ratio decreases. An area with a lower V/Q has less gas exchange, and thus PacO₂ increases and PaO₂ decreases. These changes are exacerbated in pneumonia, which causes an increase in the number of low V/Q areas in the lung. The greater hydrostatic pressure in the dependent lung causes an increased (less negative) intrapleural pressure, which decreases lung volume, and places the pressure-volume curve of the lung on a steeper slope (increased compliance). In patients with unilateral pneumonia, simply positioning the unaffected lung downward may result in improved ventilation-perfusion matching and an increase in PaO₂ of 10–15 mmHg.

183. The answer is d. (*Ganong, pp 681–683. Levitzky, pp 208–212.*) During exercise, minute ventilation and alveolar ventilation increase linearly with carbon dioxide production up to a level of about 60% of the maximal workload. Above that level, called the anaerobic threshold, muscle lactate spills into the circulation causing a metabolic acidosis, characterized by a decrease in pH and [HCO₃⁻]. The increased [H⁺] stimulates the peripheral (not central) chemoreceptors to increase alveolar ventilation, resulting in a decrease in PacO₂.

184. The answer is c. (*Ganong*, p 650. *Levitzky*, pp 90–91.) Pulmonary vascular resistance (PVR) is calculated as:

$$\text{PVR} = \Delta P/Q = \text{Mean PAP} - \text{Mean LAP} / \text{Pulmonary Blood Flow}$$
$$= 35 - 15 \text{ mmHg}/4 \text{ L/min} = 5 \text{ mmHg/L/min}$$

185. The answer is b. (*Ganong*, pp 683–691. *Levitzky*, pp 180–183.) Hemoglobin has 210× greater affinity for carbon monoxide than for oxygen. Thus, in carbon monoxide poisoning, the amount of dissolved oxygen, as reflected by the PaO_2 may be normal, but the saturation of hemoglobin with oxygen will be lower than expected for a given PaO_2 . V/Q mismatch with low V/Q units, hypoventilation, and right-to-left shunting are all causes of hypoxemia (decreased PaO_2). In anemia, hemoglobin concentration is reduced, but the saturation of hemoglobin O₂ is normal.

186. The answer is a. (*Ganong*, p 654. *Kasper et al.*, pp 1512–1514. *Levitzky*, pp 35–36.) Reversibility of airway obstruction is assessed by the change in expiratory flow rate before and after administration of a bronchodilator. Stimulation of β_2 -adrenergic receptors mediates dilation of bronchial smooth muscle. Mast cell degranulation or stimulation of α -adrenergic receptors, parasympathetic nerves to bronchial smooth muscle, or irritant airway receptors all cause bronchoconstriction, which would decrease expiratory flow rates.

187. The answer is e. (*Ganong*, pp 582–585. *Levitzky*, pp 32–35.) An increased velocity of airflow will increase turbulence, as predicted by Reynold's number. Resistance to turbulent airflow exceeds that for laminar airflow, and thus the pressure gradient required for airflow increases when flow is turbulent. Because the velocity of airflow is greatest in the trachea and large airways, the predisposition to turbulent airflow is greater in the central than in the peripheral airways. Airway resistance varies inversely with the fourth power of airway radius, according to Poiseuille's law.

188. The answer is c. (*Kasper et al.*, pp 1499–1450. *Levitzky*, pp 44–46. *Stead et al.*, pp 255–257.) Curve C is the maximal expiratory flow-volume (MEFV) curve typical of a restrictive impairment. In restrictive parenchymal diseases, lung compliance is decreased and lung elastic recoil is increased, causing all lung volumes and capacities to be lower than normal (which eliminates choices a and b) and the $\text{FEV}_{1.0}/\text{FVC}$ ratio to be normal or increased above the normal value of 0.8 (which eliminates choices d and e).

189. The answer is b. (*Ganong*, pp 627–629.) In the fetal circulation, pulmonary vascular resistance is increased compared to the term infant or the adult circulation because of (a) the increased muscular media of the pulmonary vessels and (b) the pulmonary vascular Po_2 of only ~25 mmHg, which causes hypoxic pulmonary vasoconstriction. As a result, pulmonary artery pressure (PAP), as well as the pulmonary capillary hydrostatic pressure, is greater and pulmonary blood flow is less in the preterm than in the term infant. The greater PAP increases the pressure gradient from the pulmonary artery to the aorta, which increases the flow through the ductus arteriosus in the preterm infant.

190. The answer is e. (*Ganong*, pp 656–657. *Kasper et al.*, p 1480.) Maturation of surfactant production in fetal lungs is accelerated by glucocorticoid hormones, which increases the lecithin to sphingomyelin (L/S) ratio of the amniotic fluid. Lecithin (phosphatidylcholine) and sphingomyelin are choline phospholipids found in a variety of tissues. Lecithin is a major component of surfactant and its synthesis increases as the fetus matures and the lungs are prepared for expansion. Surfactant, a lipoprotein mixture, prevents alveolar collapse by permitting the surface tension of the alveolar lining to vary during inspiration and expiration. Thus, measurement of the L/S ratio in amniotic fluid provides an index of fetal lung maturity.

191. The answer is b. (*Ganong*, pp 592–594, 662. *Kasper et al.*, p 204. *Levitzky*, pp 107–110. *Stead et al.*, pp 25–26.) In congestive heart failure, left ventricular dysfunction increases left ventricular end-diastolic pressure, which raises left atrial pressure, pulmonary venous pressure and pulmonary capillary pressure, which is the hydrostatic pressure tending to drive fluid movement out of the pulmonary capillaries, according to Starling's law. Thus, pulmonary edema, generally limited to the interstitium of the lungs, is a hallmark of congestive heart failure. All of the other responses would act to decrease fluid movement out of the capillary, in accordance with Starling's law.

192. The answer is d. (*Ganong*, pp 654–655, 660–661, 689. *Levitzky*, pp 22–23, 39–40, 58–59, 81, 140.) Destruction of the alveolar septa in emphysema causes a loss of pulmonary capillaries, which decreases the surface area available for diffusion, and therefore decreases the rate of diffusion in accordance with Fick's law. Alveolar septal departmention with destruction of pulmonary capillaries results in enlargement of the air spaces distal to the terminal bronchioles and an increase in alveolar deadspace, that is,

alveoli that are ventilated but not perfused. Elastic fibers are also found in the alveolar septa. In emphysema, the destruction of elastic fibers decreases lung elastic recoil, and increases lung compliance. The loss of elastic recoil increases intrapleural pressures, which decreases transmural pressure across the noncartilaginous airways (less radial traction), which decreases airway caliber and increases airway resistance in accordance with Poiseuille's law. In addition, the loss of elastic recoil impairs the ability to oppose dynamic compression of the airways. As a result, dynamic compression occurs closer to the alveoli during forced expirations, resulting in air trapping and an increase in residual volume and total lung capacity.

193. The answer is e. (*Ganong*, pp 592–594, 662. *Kasper et al.*, p 204. *Levitzky*, pp 107–110. *Stead et al.*, pp 25–26.) Pulmonary artery wedge pressure (PAWP) measured with a Swan-Ganz catheter is an index of the pulmonary capillary hydrostatic pressure. Normal PAWP is ≤ 12 mmHg. Thus, an elevated PAWP of 25 mmHg will drive fluid movement out of the pulmonary capillaries, according to Starling's law. Because of the paucity of smooth muscle in the pulmonary vasculature, pulmonary vascular resistance is distributed evenly across the arterioles, capillaries, and venules and there is a steady decline in pressures across the pulmonary circulation, with no large pressure drop across any element, such as seen in the systemic arterioles. As a result, PAWP is also an index of the pressures downstream in the left atrium and in the left ventricle at the end of diastole; that is, PAWP is an index of left ventricular preload.

194. The answer is a. (*Ganong*, pp 684, 691. *Kasper et al.*, p 204. *Levitzky*, pp 156, 180–181, 201–210. *Stead et al.*, pp 262–263.) The hypercapnic drive for breathing is attenuated in COPD patients with chronic hypercapnia because compensated respiratory acidosis in the cerebrospinal fluid eliminates the direct stimulus to the central chemoreceptors. Because alveolar ventilation also causes hypoxemia, the decrease in PaO_2 stimulating the peripheral chemoreceptors (hypoxic drive) becomes the primary drive to breathe in chronic hypercapnia. Administration of too much oxygen can raise PaO_2 above the threshold necessary for adequate firing of the peripheral chemoreceptors, which will "knock out" the hypoxic drive and cause an O_2 -induced hypoventilation, as evidenced by a further rise in Paco_2 . The potential for O_2 -induced hypoventilation should not be a deterrent to oxygen therapy when indicated in patients with COPD, as supplemental oxygen is the only therapy for COPD shown to extend life, in addition to improving IQ, exercise tolerance, and cor pulmonale.

195. The answer is d. (*Ganong*, pp 683–691. *Levitzky*, pp 180–183.) Cyanide impairs oxidative phosphorylation, which impairs the ability of the tissues to utilize oxygen causing hypoxia. In histotoxic hypoxia, oxygen extraction ($\text{CaO}_2-\text{CvO}_2$) is impaired, as evidenced by greater than normal values of PvO_2 (normal = 40 mmHg) and SvO_2 (normal = 75%). The patient is not hypoxemic and does not have a diffusion defect because PaO_2 is not lower than normal (80–100 mmHg). Hemoglobin oxygen transport is not impaired because both hemoglobin concentration and hemoglobin saturation with oxygen are normal. Oxygen delivery is not impaired because both cardiac output and arterial oxygen content are normal.

196. The answer is a. (*Ganong*, pp 628–629.) With the first diaphragmatic respiration in extrauterine life, the lungs replace the placenta as the organ of gas exchange and the infant's PaO_2 increases, which attenuates the hypoxic pulmonary vasoconstriction present in the fetus, causing pulmonary vascular resistance and pressures to decrease. The increased PaO_2 constricts the systemic vessels, and, coupled with elimination of the placental circulation, which contributes 40% of the cardiac output in the fetus, results in a rise in systemic vascular resistance. Five of the six vascular channels functionally close at birth, but the ductus arteriosus remains open normally for ~48 hours (though ductal flow is reversed from that in fetal life).

197. The answer is e. (*Kasper et al.*, pp 203, 1569. *Levitzky*, pp 20–23, 41–42. *Stead et al.*, pp 255–257.) The low FVC (forced vital capacity) with a normal FEV_1/FVC ratio is indicative of a severe restrictive impairment, consistent with the presentation of pectus excavatum, an abnormal formation of the rib cage where the breastbone caves in, resulting in a sunken chest appearance. As a result, hypoventilation (increased PaCO_2) and respiratory acidosis (decreased pH) would ensue. To compensate for the respiratory acidosis, arterial bicarbonate concentration would increase. The decreased chest wall compliance in pectus excavatum would increase the elastic recoil of the chest wall.

198. The answer is d. (*Ganong*, pp 192–193, 671–673. *Levitzky*, pp 188–194, 200.) The main components of the respiratory control pattern generator for the automatic control of breathing are located in the medulla. The basic respiratory rhythm is initiated by a small group of synaptically coupled pacemaker cells in the pre-Bötzinger complex on either side of the medulla between the nucleus ambiguus and the lateral reticular nucleus. This basic

rhythm can be modified by many factors, including higher centers in the cerebral cortex and hypothalamus and input from the reticular activating system and pontine respiratory centers, including the pneumotaxic center in the nucleus parabrachialis.

199. The answer is c. (*Levitzky*, pp 75, 262.) The alveolar oxygen tension is calculated using the modified alveolar gas equation:

$$P_{AO_2} = P_{I O_2} - PaCO_2/R$$

$$P_{AO_2} = [0.5 \times (747 - 47 \text{ mmHg})] - 40 \text{ mmHg}/0.8$$

$$P_{AO_2} = 350 \text{ mmHg} - 50 \text{ mmHg} = 300 \text{ mmHg}$$

200. The answer is c. (*Levitzky*, pp 75, 180–181, 262.) The A-a O₂ gradient is the partial pressure difference between the alveolar gas and arterial blood. The PaO₂ has been measured. The alveolar oxygen tension must be calculated using the modified alveolar gas equation

$$P_{AO_2} = P_{I O_2} - PaCO_2/R$$

$$P_{AO_2} = [0.21 \times (760 - 47 \text{ mmHg})] - 60 \text{ mmHg}/0.8$$

$$P_{AO_2} = 150 \text{ mmHg} - 75 \text{ mmHg} = 75 \text{ mmHg}$$

$$(A-a) O_2 \text{ gradient} = 75 \text{ mmHg} - 60 \text{ mmHg} = 15 \text{ mmHg}$$

The patient's low arterial oxygen tension (hypoxemia; hypoxic hypoxia) results from a low P_AO₂ due to hypoventilation (as evidenced by the elevated PaCO₂), and thus the (A-a) O₂ gradient is within the normal range.

201. The answer is a. (*Levitzky*, pp 37–40.) The equal pressure point is the point at which the pressure inside the airways equals the intrapleural pressure. The intra-airway pressure closest to the alveoli equals the sum of the recoil pressure (exerted by the alveoli) and the intrapleural pressure (produced by the muscles of expiration). The equal pressure point moves further away from the lungs if the recoil force is increased and moves closer to the lungs when the intrapleural pressure is increased. Increasing the lung volume expands the alveoli, making their recoil force greater and the intrapleural pressure less (more negative). This moves the equal pressure point toward the mouth. If airway resistance increases by increasing airway smooth muscle tone or increasing lung compliance, then a greater expiratory effort and consequently a greater intrapleural pressure will be necessary to expel the gas from the lungs. The higher intrapleural pressure when airway resistance is increased will cause the

equal pressure point to be reached closer to the alveoli, decreasing the volume of gas exhaled, and increasing residual volume due to air trapping behind the compressed airways.

202. The answer is b. (Levitzky, pp 34–36, 40–46.) Bronchospasm increases the resistance to airflow, which makes it more difficult to expel gas rapidly from the lung during expiration, so although both FEV₁ and vital capacity decrease, the percent of gas expelled in 1 second as a function of the total amount that can be expelled (the FEV₁/FVC ratio) also decreases dramatically. Obstructive disease also produces air trapping, which increases the residual volume, functional residual capacity, and total lung capacity.

203. The answer is e. (Ganong, pp 672–678, 693–694. Levitzky, pp 196–198, 201–210.) The central chemoreceptors respond to changes in [H⁺] in the cerebrospinal fluid (CSF), which are brought about by changes in arterial PCO₂. The failure of CO₂ to increase ventilation indicates that the central chemoreceptors are not functioning properly. The peripheral chemoreceptors are stimulated by hypoxia, hypercapnia, and acidemia, and thus are functioning appropriately because ventilation decreased when PO₂ was increased (hyperoxia). Obstructive sleep apnea is caused by upper airway obstruction due to hypotonic pharyngeal or genioglossus muscles or too much fat around the pharynx, but not because of obstruction of the tracheobronchial tree by bronchospasm. Diaphragmatic fatigue can cause hypoventilation, but is not associated with apneic episodes, perhaps because of the increased contribution of the accessory muscles of respiration. The reflex effect of stimulation of the irritant receptors by mechanical or chemical irritation of the airways is bronchoconstriction and cough.

204. The answer is b. (Ganong, pp 662, 672–677, 686–688. Levitzky, pp 114–116, 180–182, 201–210.) V/Q mismatches will cause arterial oxygen levels (PaO₂) to decrease. Decreased PaO₂ will stimulate the peripheral chemoreceptors, which, in turn, will increase alveolar ventilation and decrease Paco₂. The decreased Paco₂ will cause a respiratory alkalosis (increasing pH). Hypoxemia may also cause lactate levels to rise, increasing the anion gap (and blunting the rise in pH). The fall in PaO₂ causes the A-a gradient to rise.

205. The answer is c. (Ganong, pp 643–644, 662–663, 686–688. Levitzky, pp 123–128. Stead et al., pp 25–27.) The alveoli at the apex of the lung are

larger than those at the base so their compliance is less. Because the compliance is reduced, less inspired gas goes to the apex than to the base. Also, because the apex is above the heart, less blood flows through the apex than through the base. However, the reduction in airflow is less than the reduction in blood flow, so that the \dot{V}/\dot{Q} ratio at the top of the lung is greater than it is at the bottom. The increased \dot{V}/\dot{Q} ratio at the apex makes $P_{A}CO_2$ lower and P_{AO_2} higher at the apex than they are at the base.

206. The answer is d. (*Ganong, pp 664–665. Kasper et al., pp 1522–1523. Levitzky, pp 216–221. Stead et al., pp 276–277.*) The lung has a variety of mechanisms to remove particulate matter from the inspired gas. Large particles become deposited in the mucus layer that lies within the bronchi. The mucus is swept up and out of the bronchioles by the ciliated epithelial cells that line the bronchioles. Smaller particles remain suspended in the inspired gas and reach the alveoli. Alveolar macrophages remove these particles by phagocytosis. The macrophages are usually removed from the lung through the lymphatic or blood circulation.

207. The answer is b. (*Ganong, pp 690–692. Kasper et al., pp 147, 169, 209, 600, 1502, 1634–1635. Levitzky, pp 153–155, 180–183. Stead et al., p 253.*) Because carbon monoxide (CO) competes with O_2 on the hemoglobin molecule, CO poisoning causes a decrease in hemoglobin's saturation with oxygen, and thus in the amount of oxygen bound to hemoglobin, even when the PO_2 (and dissolved oxygen content) is normal. In anemia, the concentration of hemoglobin is less than normal, reducing the oxygen content, but the oxygen saturation is unchanged and the PO_2 (and dissolved oxygen content) may be normal. A low \dot{V}/\dot{Q} ratio, hypoventilation, or a right-to-left shunt all cause hypoxemia.

208. The answer is c. (*Ganong, pp 662, 672–677, 686–688. Levitzky, pp 114–116, 180–182, 201–210.*) Both the central chemoreceptors, located on or near the ventral surface of the medulla, and the peripheral chemoreceptors, in the carotid and aortic bodies, cause an increase in ventilation in response to an increase in $Paco_2$. The peripheral chemoreceptors also cause an increase in ventilation in response to a decrease in arterial pH and a decrease in PaO_2 , but the central chemoreceptors are unresponsive to hypoxemia and do not cause an increase in ventilation in response to a decrease in arterial pH because the blood-brain barrier is relatively impermeable to hydrogen ions. Neither the central chemoreceptors nor the carotid bodies are stimulated by a decrease in arterial blood pressure or O_2 content.

209. The answer is b. (*Ganong, pp 657–658. Levitzky, pp 49–51.*) Respiratory muscles consume oxygen in proportion to the work of breathing. The work of breathing is equal to the product of the change in volume for each breath and the change in pressure necessary to overcome the resistive work of breathing and the elastic work of breathing. Resistive work includes work to overcome tissue as well as airway resistance; thus a decreased airway resistance will decrease the work of breathing and the oxygen consumption of the respiratory muscles. A decreased lung compliance would increase the elastic work of breathing. An increase in respiratory rate or tidal volume increases the work of breathing.

210. The answer is e. (*Ganong, pp 671–679. Levitzky, pp 188–201.*) Transection of the brainstem above the pons would prevent any voluntary changes in ventilation by cutting the pathways from the higher centers. Breathing would continue because the pontine-medullary centers that control rhythmic ventilation would be intact. Inputs to the brainstem from the central and peripheral chemoreceptors that stimulate ventilation and from lung stretch receptors that inhibit inspiration (Hering-Breuer reflex) would also be intact and these reflexes would be maintained.

211. The answer is c. (*Ganong, pp 665–655. Levitzky, pp 17–23, 29–31.*) When the pleura, and hence the lung-chest wall system, are intact, the inward elastic recoil of the lung opposing the outward elastic recoil of the chest wall results in a subatmospheric (negative) pressure with the pleural space. When one reaches lung volumes in excess of ~70% of the total lung capacity, the chest wall recoil is also inward.

212. The answer is a. (*Ganong, pp 665–655. Levitzky, pp 29–31.*) The functional residual capacity (FRC) occurs at the lung volume at which the outward recoil of the chest wall is equal to the inward recoil of the lungs, which occurs when no respiratory muscles are actively contracting, that is, at the end of a tidal expiration. The FRC is therefore also referred to as the resting expiratory level, or simply, the resting level.

213. The answers is b. (*Ganong, pp 651–655. Levitzky, pp 17–20.*) During inspiration (curve ABC), the respiratory muscles pull the chest wall out and diaphragm down and intrapleural pressure (P_{IP}) becomes more negative (subatmospheric). The muscles must overcome the elastic recoil forces of the lungs and the resistance of the airways to airflow. The P_{IP} necessary to overcome the elastic forces of the lung is depicted by dashed line AC. The

P_{IP} necessary to overcome the airway resistance is the difference between dashed line AC and curve ABC. The maximum airflow occurs at point B, where the difference between the two is the greatest.

214. The answer is d. (*Levitzky*, pp 11–14, 18–22, 36–37.) Expanding the lungs expands the airways, which increases their volume and, therefore, the volume of the anatomical deadspace. Expanding the lungs lowers the intrathoracic pressure and the intrapleural pressure, which causes the airways to expand. Expanding the airways also causes a decrease in airway resistance. Lung compliance is decreased, that is, the lungs are more difficult to inflate (stiffer), at high lung volumes. Alveolar pressure is atmospheric at residual volume and at total lung capacity.

215 and 216. The answers are 215-b, 216-e. (*Ganong*, pp 570–571. *Levitzky*, pp 120–122, 263.) The fraction of the pulmonary blood flowing bypassing the lung (the shunt, \dot{Q}_S) compared to the total pulmonary blood flow (\dot{Q}_T) is calculated using the equation

$$\begin{aligned}\dot{Q}_S/\dot{Q}_T &= C_eO_2 - C_aO_2 / C_eO_2 - C_vO_2 \\ &= \frac{19 \text{ mL/dL} - 18 \text{ mL/dL}}{19 \text{ mL/dL} - 14 \text{ mL/dL}} \\ &= 0.2\end{aligned}$$

where C_e is the end pulmonary capillary blood oxygen content, C_aO_2 is the arterial oxygen content, and C_vO_2 is the mixed venous oxygen content. At a resting cardiac output, the normal amount of shunting is 3–5% of the cardiac output. In this case, there is a 20% shunt.

The oxygen consumption can be calculated if the cardiac output (CO) and the difference between the arterial and venous oxygen content are known using the Fick equation:

$$\begin{aligned}\dot{V}O_2 &= CO \times (C_aO_2 - C_vO_2) \\ \dot{V}O_2 &= 6 \text{ L/min} \times (18 \text{ mL/dL} - 14 \text{ mL/dL}) \\ \dot{V}O_2 &= 240 \text{ mL/min}\end{aligned}$$

217. The answer is d. (*Kasper et al.*, pp 203, 1556. *Levitzky*, pp 23, 171–173. *Stead et al.*, pp 255–257.) Kyphoscoliosis is a deformity of the spine involving both lateral displacement (scoliosis) and anteroposterior angulation (kyphosis). Muscle weakness can produce inadequate ventilation, which can lead to an accumulation of carbon dioxide and a decrease

in arterial pH (respiratory acidosis). Chest wall compliance is decreased, which manifests as a restrictive lung impairment characterized by a decrease in all lung volumes and capacities.

218. The answer is c. (*Kasper et al.* pp 209–210, 1624–1637. *Levitzky*, pp 66, 73–74, 136–138.) Profound hypoxia depresses the central nervous system, including the medullary respiratory centers. As a result, alveolar ventilation may decrease, resulting in an increased PaCO_2 . A decrease in metabolic activity would decrease the rate of production of carbon dioxide (VCO_2), which would decrease Paco_2 , assuming that alveolar ventilation does not change. If an alveolar capillary block is severe, retention of CO_2 could briefly occur, but the coexistent hypoxemia would cause reflex hyperventilation with a decrease in Paco_2 . At a constant tidal volume and respiratory rate, a decrease in the deadspace volume would increase alveolar ventilation, and thus lower the Paco_2 .

219. The answer is e. (*Ganong*, pp 661–664. *Levitzky*, pp 92–107.) Increasing cardiac output or pulmonary artery pressure causes pulmonary vascular resistance (PVR) to passively decrease due to two mechanisms—distention of the perfused vessels, and recruitment of more parallel vascular beds. At high lung volumes, the pulmonary capillaries (“alveolar” vessels) are stretched and compressed causing an increased PVR. At low lung volumes, the “extra-alveolar” blood vessels are compressed, increasing PVR. The lowest PVR occurs near FRC. Decreasing PO_2 or increasing PCO_2 or H^+ concentration causes PVR to rise. The sympathetic nervous system has little effect on PVR under physiologic conditions, but experimentally, stimulation of sympathetic nerves will constrict the pulmonary vessels, causing increased PVR.

220. The answer is d. (*Ganong*, pp 74–75, 681–683. *Levitzky*, pp 228–233). During moderate aerobic exercise, oxygen consumption and CO_2 production increase, but alveolar ventilation increases in proportion. Thus, Paco_2 (and PaO_2) do not change. Arterial pH and blood lactate concentration are also normal during moderate aerobic exercise, but during anaerobic exercise, which is reached at workloads that exceed ~60% of the maximal workload (called the anaerobic threshold), there is increased production of muscle lactic acid, which spills over into the circulation, causing an increase in the concentration of blood lactate and a decrease in the pH of the blood.

221. The answer is a. (*Ganong*, pp 660–661. *Kasper et al.*, pp 201–204. *Levitzky*, pp 130–140.) The diffusing capacity is the volume of gas transported

across the lung per minute per mmHg partial pressure difference. Diffusing capacity is measured by measuring the transfer of oxygen or carbon monoxide across the alveolar-capillary membrane. Because the partial pressure of oxygen and carbon monoxide is affected by their chemical reactions with hemoglobin, as well as their transfer through the membrane, the diffusing capacity of the lung is determined both by the diffusing capacity of the membrane itself, as well as by the reaction with hemoglobin. Increases in the diffusing capacity can be produced by increasing the concentration of hemoglobin within the blood (polycythemia). The diffusing capacity of the membrane can be calculated by rearranging Fick's law for diffusion, and is related to the ratio of the surface area available for diffusion and the thickness of the alveolar-capillary interface. The area available for diffusion is decreased by alveolar-septal departitioning in emphysema and by obstruction of the pulmonary vascular bed by pulmonary emboli. The thickness of the diffusional barrier is increased by interstitial fibrosis and by interstitial or alveolar edema found in congestive heart failure.

222. The answer is e. (*Ganong*, pp 690–691. *Kasper et al.*, pp 147, 169, 209, 600, 1502, 1634–1635, 2590. *Levitzky*, pp 153–154, 182. *Stead et al.*, p 253.) The decrease in arterial oxygen saturation caused by carbon monoxide poisoning reduces the oxyhemoglobin and thus total arterial oxygen contents but does not reduce the amount of oxygen dissolved in the plasma, which determines the arterial oxygen tension. Carbon monoxide is odorless and tasteless and dyspnea and respiratory distress are late signs, which is the reason that it is so important to install carbon monoxide detectors in homes and businesses. Respiratory distress becomes manifest with severe tissue hypoxia and anaerobic glycolysis, which leads to lactic acidosis. The decrease in arterial pH stimulates ventilation via the peripheral chemoreceptors. The resultant hyperventilation decreases arterial (and CSF) PCO_2 , causing CSF pH to rise. Carboxyhemoglobin has a cherry-red color.

223. The answer is b. (*Ganong*, pp 654–657. *Levitzky*, pp 20–28.) Lung compliance is an index of lung distensibility or the ease with which the lungs are expanded; thus, compliance is the inverse of elastic recoil. Compliance is defined as the ratio of change of lung volume to the change in pressure required to inflate the lung ($\Delta V/\Delta P$). Compliance decreases in patients with pulmonary edema or surfactant deficiency and increases when there is a loss of elastic fibers in the lungs, such as occurs in patients with emphysema and with aging.

224. The answer is a. (*Ganong, pp 675–678. Levitzky, pp 206–208.*) The central chemoreceptors, located at or near the ventral surface of the medulla, are stimulated to increase ventilation by a decrease in the pH of their extracellular fluid (ECF). The pH of this ECF is affected by the PCO_2 of the blood supply to the medullary chemoreceptor area, as well as by the CO_2 and lactic acid production of the surrounding brain tissue. The central chemoreceptors are not stimulated by decreases in PaO_2 or blood oxygen content but rather can be depressed by long-term or severe decreases in oxygen supply.

225. The answer is d. (*Ganong, pp 649–650, 654, 657–659. Levitzky, pp 34–36, 49–50.*) Methacholine is a cholinergic agonist, which causes constriction of bronchial smooth muscle. Bronchoconstriction reduces airway radius, which increases airway resistance, and thus the resistive work of breathing. Methacholine-induced bronchoconstriction decreases the anatomic deadspace but has no significant effect on the lung compliance, and thus does not affect the elastic work of breathing.

226. The answer is b. (*Ganong, pp 658. Levitzky, pp 125–127.*) During inspiration, when all alveoli are subjected to essentially the same alveolar pressure, more air will go to the more compliant alveoli in the base of the lung. Because the lungs are essentially “hanging” in the chest, the force of gravity on the lungs causes the intrapleural pressure to increase (become less negative) at the base of the lungs compared to the apex (more negative intrapleural pressure). This also causes the alveoli at the apex of the lung to be larger than those at the base of the lung. Larger alveoli are already more inflated and are less compliant than smaller alveoli. Because of the effect of gravity on blood, more blood flow will go to the base of the lung. Ventilation is about three times greater at the base of the lung, but flow is about 10 times greater at the base than at the apex of the lung; therefore, the V/Q ratio is lower at the base than at the apex in a normal lung.

227. The answer is a. (*Levitzky, pp 44–46. Stead, pp 255–257, 289–290.*) A restrictive impairment in which lung elastic recoil is increased and lung compliance is decreased, such as occurs in sarcoidosis, shifts the normal maximal expiratory flow-volume curve down and to the right. Maximum expiratory flows are also decreased in conditions that increase airway resistance, for example, asthma, emphysema, and cystic fibrosis, and when muscular effort is decreased, for example, fatigue, but lung volumes would be increased in the obstructive impairments and normal if fatigue was an isolated factor.

228. The answer is c. (*Levitzky, pp 95–98, 130–132, 230–232.*) The lungs and heart are in series, so the entire cardiac output flows through the lungs. The increased pulmonary blood flow during exercise increases the surface area for diffusion, and therefore increases the diffusing capacity in accordance with Fick's law of diffusion. The increased perfusion of the lungs is accompanied by an even greater increase in ventilation, so the V/Q ratio of the whole lung, as well as most areas of the lung, increases during exercise. The increase in blood flow through the pulmonary circulation during exercise increases the diameter of the pulmonary vessels and therefore decreases their resistance. Systolic, diastolic, and mean pulmonary artery pressure increase slightly during exercise because of the increased pulmonary blood flow and blood volume.

229. The answer is e. (*Levitzky, pp 180–182.*) A large intrapulmonary shunt will cause arterial oxygen tension to decrease. This will increase respiratory drive, causing a respiratory alkalosis.

230. The answer is a. (*Levitzky, pp 41–46. Stead, pp 255–257.*) The reduced lung volumes indicate a restrictive lung disease. Although the amount of gas that can be expelled from the lung in 1 second will be less than normal, the increased recoil force of the lung will produce an FEV₁/FVC ratio that is close to normal. Patients with restrictive lung disease have small tidal volumes. The diffusing capacity will be reduced because the small lung volumes reduce the surface area available for gas exchange, and the fibrotic changes in the lungs increase the thickness of the diffusion barrier. The presence of V/Q abnormalities is indicated by the need for supplemental oxygen.

231. The answer is b. (*Levitzky, pp 35–41.*) Airway resistance decreases as lung volume increases because the increasingly subatmospheric intrapleural pressure increases the radial traction on the airways, thereby increasing airway diameter and decreasing airway resistance. During a forced expiration or at the residual volume, the intrathoracic pressure is positive, compressing the airways and increasing their resistance. The vagus nerve constricts airway smooth muscle. Resistances in parallel add as reciprocals. Thus, the large number of small, peripheral airways increases the number of airways arranged in parallel, and lowers the total resistance of the peripheral airways compared to the total cross-section of the central airways.

232. The answer is d. (*Ganong, pp 651–652. Levitzky, p 59.*) A spirometer is an instrument that records the volume of air moved into and out of the

lungs during breathing, and therefore can only be used to measure lung volumes and capacities that can be exchanged with the environment. Spirometry can be used to measure the inspiratory capacity, which is the maximal amount of gas that can be inspired following a tidal expiration. Spirometry cannot be used to measure the volume of the gas that remains in the lungs following a maximal expiration, that is, the residual volume, and thus cannot directly measure the lung capacities that contain the residual volume, that is, the functional residual capacity and the total lung capacity. Every lung volume and capacity, including the residual volume, contains deadspace volume, and thus spirometry cannot be used to measure the physiological dead space.

233. The answer is c. (*Levitzky, pp 113–116, 122–123.*) Areas with low V/Q ratios produce hypoxemia or a decreased P_aO_2 , which leads to (a) a decrease in the dissolved oxygen content of the blood and (b) a decrease in P_aCO_2 , due to stimulation of the peripheral chemoreceptors. At lower P_aO_2 levels, arterial oxygen saturation is decreased, which decreases the oxyhemoglobin content. Because the mixed alveolar PO_2 is normal and the arterial PO_2 is less than normal, the A-a gradient is greater than normal.

234. The answer is b. (*Levitzky, pp 44–48.*) A maximal expiratory flow-volume curve is generated during a forced vital capacity maneuver. Only the initial expiratory flow is effort-dependent. That is, increasing expiratory effort will increase expiratory flow at points E and A (peak flow), but not at point B, which is referred to as the effort-independent portion of the maximal expiratory flow-volume curve. The inability to increase flow rates during the effort-independent portion is caused by compression of the noncartilaginous airways by the positive intrapleural pressures that are generated during a forced expiration when the expiratory muscles are actively contracted, a phenomenon called dynamic compression of the airways. No effort limitation occurs during inspiration (points C and D) because increased inspiratory efforts make the intrapleural pressure more negative, which expands the airways, lowering their resistance.

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Cardiovascular Physiology

Questions

235. A 42-year-old woman with mitral prolapse is admitted to the hospital for evaluation of her cardiac function. Which of the following values is the best index of the preload on her heart?

- a. Blood volume
- b. Central venous pressure
- c. Pulmonary capillary wedge pressure
- d. Left ventricular end-diastolic volume
- e. Left ventricular end-diastolic pressure

236. A patient presents to the Emergency Department with intermittent chest pain. The ECG and blood tests are negative for myocardial infarction, but the echocardiogram shows thickening of the left ventricular muscle and narrowing of the aortic valve. Medications to lower afterload are prescribed. Which of the following values would provide the best measure of the effectiveness of the medication in lowering left ventricular afterload in this patient?

- a. Left ventricular end-diastolic pressure
- b. Left ventricular mean systolic pressure
- c. Pulmonary capillary wedge pressure
- d. Total peripheral resistance
- e. Mean arterial blood pressure

237. A 55-year-old male reports several recent episodes of syncope. An electrocardiogram is performed. Which of the following arrhythmias is most commonly associated with syncope?

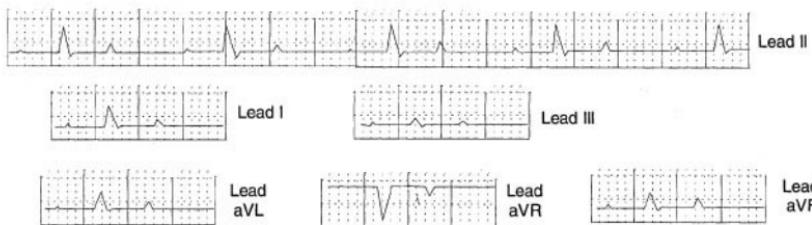
- a. Sinus arrhythmia
- b. First-degree heart block
- c. Second-degree heart block
- d. Third-degree heart block
- e. Tachycardia

238. During a routine physical examination, a 32-year-old female is found to have second-degree heart block. Which of the following ECG recordings was obtained from the patient during her physical examination?



- a. A
- b. B
- c. C
- d. D
- e. E

239. The following 6-lead frontal ECG was performed as part of an annual physical exam. What is the mean electrical axis of the patient?



- a. -10 degrees
- b. +10 degrees
- c. +20 degrees
- d. +40 degrees
- e. +70 degrees

240. The spouse of a 58-year-old man calls 9-1-1 because her husband complains of chest pain radiating down his left arm. He is transported to the Emergency Department, where an electrocardiogram and cardiac enzymes indicate a recent myocardial infarction. The man is sent for a cardiac catheterization, including coronary angiography and hemodynamic recordings throughout the cardiac cycle. No valvular defects were present. During ventricular ejection, the pressure difference smallest in magnitude is between which of the following?

- a. Pulmonary artery and left atrium
- b. Right ventricle and right atrium
- c. Left ventricle and aorta
- d. Left ventricle and left atrium
- e. Aorta and capillaries

241. An 82-year-old woman was admitted to the hospital with ascites, peripheral edema, and shortness of breath. Cardiac catheterization was ordered and the following values were obtained:

$$\text{Pulmonary artery O}_2 \text{ content} = 20 \text{ mL/100 mL}$$

$$\text{Pulmonary vein O}_2 \text{ content} = 12 \text{ mL/100 mL}$$

$$\text{Oxygen consumption} = 280 \text{ mL/min}$$

$$\text{Stroke volume} = 40 \text{ mL}$$

What is the woman's cardiac output?

- a. 2.86 L/min
- b. 3.5 L/min
- c. 7.0 L/min
- d. 8 mL/100 mL
- e. 4500 mL/min

242. A 66-year-old male is referred to a cardiologist for evaluation. Physical examination reveals a diastolic murmur prominent over the left sternal border, a decrease in diastolic pressure, and an increase in pulse pressure. Which of the following is the most likely diagnosis?

- a. Aortic regurgitation
- b. Pulmonic stenosis
- c. Mitral valve prolapse
- d. Pulmonary regurgitation
- e. Aortic stenosis

243. A patient undergoes cardiac transplantation for severe idiopathic cardiomyopathy. Upon release from the hospital, the patient is referred to a cardiac rehabilitation program. The exercise technologist starts the patient on a walking regimen. In transplant patients, stroke volume may increase during exercise by which of the following mechanisms?

- a. An increase in heart rate
- b. An increase in arterial blood pressure
- c. A decrease in venous compliance
- d. A decrease in myocardial contractility
- e. An increase in total peripheral resistance

244. A patient complaining of an irregular heart beat is referred for a cardiac electrophysiological (EP) study. Propagation of the action potential through the heart is fastest in which of the following?

- a. SA node
- b. Atrial muscle
- c. AV node
- d. Purkinje fibers
- e. Ventricular muscle

245. A 75-year-old woman presents with fatigue, edema, and shortness of breath. Her physician prescribes a diuretic and a positive inotropic agent. Which of the following changes is primarily responsible for the improvement in her condition?

- a. A reduction in heart rate
- b. A reduction in heart size
- c. An increase in ventricular end-diastolic pressure
- d. An increase in wall thickness
- e. An increase in cardiac excitability

246. A 37-year-old woman undergoes a CT scan of the abdomen, which reveals a large peritoneal mass. A subsequent magnetic resonance angiography study showed that the abdominal aorta was constricted to one-half of its resting diameter. As a result, resistance to blood flow through the vessel would be which of the following?

- a. Decreased in half
- b. Decreased 16-fold
- c. Increased by 50%
- d. Doubled
- e. Increased 16-fold

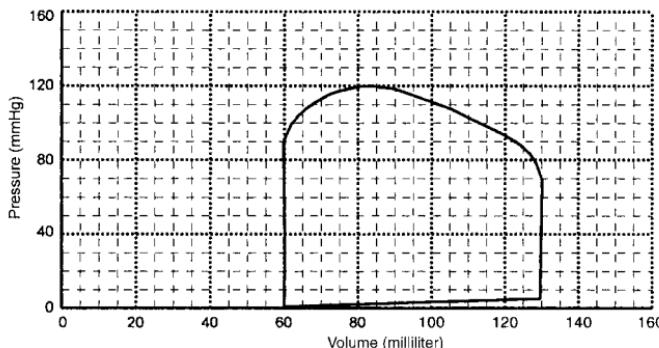
247. A 52-year-old man presents with tar-black stools. An endoscopy is ordered and reveals a bleeding ulcer in the antrum of the stomach. Baroreflex-induced compensation for the mild hemorrhage will cause which of the following values to be lower than it was before the hemorrhage?

- Venous capacitance
- Ventricular contractility
- Total peripheral resistance
- Heart rate
- Coronary blood flow

248. A 22-year-old woman is hospitalized with a history of respiratory distress, fever, and fatigue. ST segment and T wave abnormalities suggest myocarditis, which is attributed to an acute viral origin. Over the next several days, significant peripheral edema develops. The edema is most likely caused by which of the following?

- Decreased capillary permeability
- Decreased arterial pressure
- Increased plasma protein concentration
- Increased lymphatic flow
- Increased central venous pressure

249. A patient undergoes cardiac catheterization to assess his left ventricular function prior to thoracic surgery. What is his ejection fraction, as determined from the left ventricular pressure-volume curve illustrated below.



- 0.54
- 0.60
- 1.20
- 70 mL
- 120 mmHg

250. A 38-year-old man has a murmur that ceases with the onset of the second heart sound. The second heart sound occurs at the onset of which phase of the cardiac cycle?

- a. Isovolumetric contraction
- b. Rapid ejection
- c. Systole
- d. Isovolumetric relaxation
- e. Rapid ventricular filling

251. A 58-year-old woman with idiopathic pulmonary hypertension presents with right ventricular hypertrophy and cor pulmonale. Her electrocardiogram shows positive QRS complexes in leads V₁, III, and aVF, and equiphasic QRS complexes in lead aVR. Which of the following is her mean QRS vector?

- a. -120°
- b. -150°
- c. +120°
- d. +90°
- e. +60°

252. A 57-year-old male complains of an irregular heart beat that he notices is relieved by pressing on his eyeball. An electrocardiogram reveals atrial fibrillation. Which of the following is most likely to accompany this condition?

- a. An increased venous A wave
- b. An increased left atrial pressure
- c. A decreased heart rate
- d. An increased stroke volume
- e. An increased mean arterial blood pressure

253. A 24-year-old woman undergoes an annual physical examination for participation on the varsity track team at her college. While auscultating her heart sounds, the sports medicine physician instructs the woman to take in a deep inspiration. During this maneuver, he detects splitting of the second heart sound. Which of the following is the mechanism underlying this finding?

- a. A decrease in heart rate
- b. An increased left ventricular stroke volume
- c. Delayed closing of the aortic valve
- d. Delayed opening of the mitral valve
- e. Delayed closing of the pulmonic valve

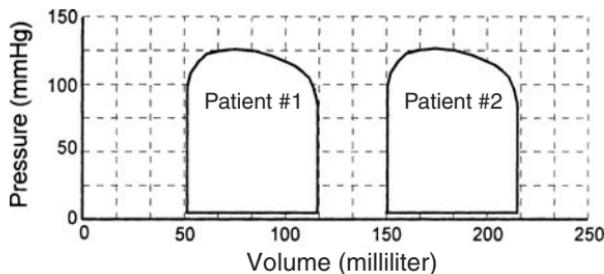
254. A 55-year-old female presents for her annual physical examination. Upon auscultation, a third heart sound is heard. The differential diagnosis of this finding includes which of the following?

- a. Anemia
- b. Tachycardia
- c. Mitral stenosis
- d. Aortic regurgitation
- e. Right bundle branch block

255. A 23-year-old female presents with fatigue and is found to have a systolic murmur and higher than normal cardiac output. The differential diagnosis based on these findings includes which of the following?

- a. Hypertension
- b. Mitral valve prolapse
- c. Anemia
- d. Aortic regurgitation
- e. Cardiac tamponade

256. Ventricular pressure-volume curves are determined in two different patients, as illustrated below. Which of the following is greater in Patient #1?



- a. Preload
- b. Afterload
- c. Stroke volume
- d. Cardiac work
- e. Cardiac efficiency

257. Physical examination of a 41-year-old narcotic abuser reveals an early systolic murmur. The physician also notes a 7-cm distance between the height of the blood in his right internal jugular vein and sternal angle (normal = 3 cm). Which of the following conditions is most likely responsible for the physical findings?

- a. Mitral stenosis
- b. Tricuspid regurgitation
- c. Atherosclerosis
- d. Aortic regurgitation
- e. Tachycardia

258. A 42-year-old woman with lightheadedness and recurrent syncope is taken to the emergency department where she is given atropine. Her symptoms are relieved by an increase in which of the following?

- a. Heart rate
- b. PR interval
- c. Ventricular contractility
- d. Ejection fraction
- e. Stroke volume

259. A 32-year-old female complains of intermittent chest discomfort that occurs most frequently when she drinks lots of coffee to stay up to meet deadlines at work. She is referred to cardiology for an exercise stress test to rule out cardiac ischemia as the cause for her angina. The test will be considered positive if which of the following occurs?

- a. Mean arterial blood pressure increases
- b. ST segment depression occurs
- c. Tachycardia develops
- d. A diastolic murmur is heard
- e. The QRS complex widens

260. A postlaminectomy patient suddenly stands up after being supine for 8 hours. As a result, which of the following hemodynamic variables will increase?

- a. End-diastolic volume
- b. Renal blood flow
- c. Venous return
- d. Pulse pressure
- e. Ejection fraction

261. A newborn baby is cyanotic upon delivery. The cyanosis is not relieved by breathing 100% oxygen. A diagnosis of persistent fetal circulation is made based on which of the following clinical signs?

- a. Mitral regurgitation
- b. Left ventricular hypertrophy
- c. Pulmonary vasoconstriction and hypertension
- d. Systemic hypertension
- e. Aortic coarctation

262. A 19-year-old male severs an artery in a motorcycle accident. A bystander applies a tourniquet to stop the bleeding. When the paramedics arrive, the blood pressure of the injured man was only slightly hypotensive and his pupils were reactive. The greatest percentage of the redistributed blood volume came from which of the following?

- a. Heart
- b. Aorta
- c. Arteries and arterioles
- d. Capillaries
- e. Venules and veins

263. An 84-year-old woman presents with paroxysmal dizziness, syncope, confusion, and fatigue. Her heart rate did not change when the patient was instructed to perform a Valsalva maneuver. 24-hour Holter monitoring revealed periodic episodes of sinus bradycardia. Phase-4 depolarization of SA nodal cells is caused by which of the following?

- a. An increase in the flow of sodium into the cell
- b. A decrease in the flow of potassium out of the cell
- c. An increase in the activity of the Na/Ca exchanger
- d. A decrease in the flow of chloride out of the cell
- e. A decrease in the activity of the Na-K pump

264. During auscultation of a patient with long-standing hypertension, the physician notes that the splitting of the second heart sound is reversed with P2 occurring before A2. Which of the following is a common electrocardiographic finding accompanying paradoxical splitting of the second heart sound?

- a. Sinus bradycardia
- b. Sinus tachycardia
- c. Sinus arrhythmia
- d. Left bundle branch block
- e. Right bundle branch block

265. An 83-year-old woman with long-standing hypertension presents after a near-syncopal episode upon standing. Her blood pressure is taken sitting and then standing. Systolic pressure decreased slightly and pulse pressure increased in the standing position. Which of the following can lead to an increased pulse pressure?

- a. An increased heart rate
- b. A decreased stroke volume
- c. An increase in total peripheral resistance
- d. A decrease in aortic compliance
- e. A decrease in venous capacitance

266. A 75-year-old woman makes an appointment to see her physician because she is having breathing difficulties when she lies down at night. An S_3 gallop is heard upon auscultation. Her signs and symptoms are most likely due to which of the following?

- a. Hypertension
- b. Mitral regurgitation
- c. Cor pulmonale
- d. Constrictive pericarditis
- e. Left heart failure

267. A cardiac catheterization is performed on a 39-year-old man who presents with angina. The left ventricular pressure-volume curve shows a decreased stroke volume and ejection fraction. Which of the following mechanisms may compromise stroke volume following myocardial infarction?

- a. An increase in central venous pressure
- b. An increase in heart rate
- c. A decrease in systemic blood pressure
- d. A decrease in total peripheral resistance
- e. A positive inotropic response

268. A 42-year-old athlete becomes alarmed when he notices a series of heart palpitations several hours after he exercises. After examining the patient's ECG, the physician notes a sinus rhythm with occasional PVCs (premature ventricular complexes). The physician tells his patient that the palpitations are due to interpolated beats and that they are not a cause for alarm. Benign PVCs may occur because the athlete has which of the following?

- a. A prolonged PR interval
- b. Bradycardia

- c. ST segment depression
- d. An alternative bundle of Kent
- e. Inverted atrial P waves

269. A 56-year-old male was admitted to the hospital with angina and diaphoresis. A myocardial infarction is suspected, and a 12-lead electrocardiogram (ECG) is ordered. The ECG is most effective in detecting a decrease in which of the following?

- a. Ventricular contractility
- b. Mean blood pressure
- c. Total peripheral resistance
- d. Ejection fraction
- e. Coronary blood flow

270. A 48-year-old sedentary, obese male with four-vessel coronary occlusive disease has a massive myocardial infarction while shoveling snow. In the blizzard conditions, it takes the ambulance over an hour to reach the man's home. When the paramedics arrive, the patient's radial pulse is rapid and thready, he has pink froth coming from his mouth, and he is nonresponsive. Increasing which of the following would lead to an increased stroke volume in cardiogenic shock?

- a. Heart rate
- b. Venous compliance
- c. Ventricular contractility
- d. Total peripheral resistance
- e. Pulmonary capillary wedge pressure

271. A patient comes to his physician complaining that he is no longer able to exercise as long as he used to. The physician auscultates crepitant rales and a third heart sound; blood pressure is normal. He sends the patient to cardiology to rule out heart failure. Which of the following is most consistent with a diagnosis of left heart failure?

- a. A decreased heart rate
- b. An increased left ventricular wall stress
- c. An increased left ventricular ejection fraction
- d. A decreased left ventricular energy consumption
- e. A decreased pulmonary arterial wedge pressure

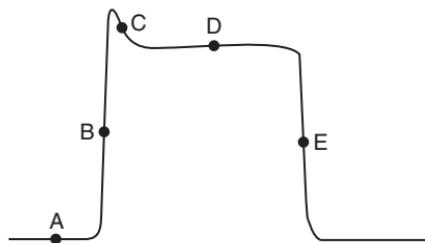
272. A pacemaker is inserted in a patient in order to shorten the PR interval detected on their ECG. Which of the following events normally occurs during the PR interval?

- a. The ventricle is contracting
- b. The cardiac action potential passes through the AV node
- c. There is no change in the voltage tracing on the ECG
- d. The mitral and aortic valves are both closed
- e. The second heart sound is heard

273. A 47-year-old female is brought to the Emergency Department because she fainted at the gym during her daily aerobic workout. A prominent systolic murmur is heard and a presumptive diagnosis of aortic stenosis is made. Which of the following is consistent with that diagnosis?

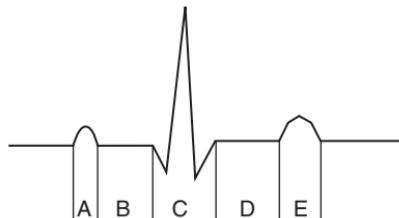
- a. A decreased pulse pressure
- b. An increased arterial pressure
- c. A decreased left ventricular diastolic pressure
- d. An increased ejection fraction
- e. A decreased cardiac oxygen consumption

274. The phases of the ventricular muscle action potential are represented by the lettered points on the diagram below. At which point on the ventricular action potential is membrane potential most dependent on calcium permeability?



- a. Point A
- b. Point B
- c. Point C
- d. Point D
- e. Point E

275. During which interval on the ECG below does the mitral valve close?

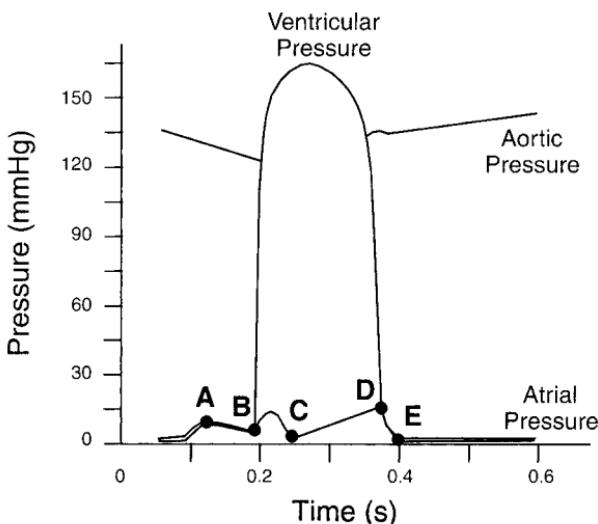


- a. A
- b. B
- c. C
- d. D
- e. E

276. A patient with an inferior MI develops a stable bradycardia of 50/min. The cardiologist orders an ECG to evaluate whether there is sinus node dysfunction or an atrioventricular conduction disturbance. The diagnosis of a first-degree heart block is made in which of the following cases?

- a. The PR interval of the ECG is increased
- b. The P wave of the ECG is never followed by a QRS complex
- c. The P wave of the ECG is sometimes followed by a QRS complex
- d. The T wave of the ECG is inverted
- e. The ST segment of the ECG is elevated

277. In the hemodynamic pressure tracings below, rapid ventricular filling begins at which point on the figure below?



- a. A
- b. B
- c. C
- d. D
- e. E

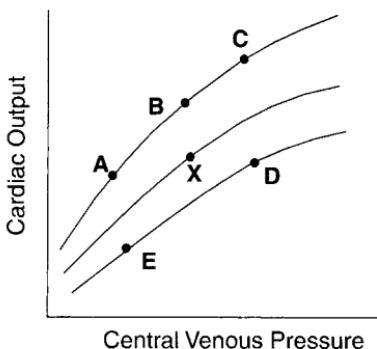
278. A 67-year-old man who has difficulty breathing when he exercises makes an appointment to see his physician. Auscultation reveals a holosystolic murmur leading to the diagnosis of mitral regurgitation. Which of the following laboratory findings is most likely to be present?

- a. A decreased arterial pressure
- b. An increased pulse pressure
- c. An increased a wave
- d. A decreased cardiac output
- e. A decreased left ventricular preload

279. A 43-year-old male comes to his physician complaining of exhaustion and shortness of breath. After completing the physical exam, the physician suspects the patient may be suffering from cardiac tamponade. Which of the following observations led to the physician's putative diagnosis?

- Hypertension
- Bradycardia
- Third heart sound
- Pulsus paradoxus
- Expiratory rales

280. Digitalis is administered to a patient in congestive heart failure. Which of the shifts in the Starling curves shown below are consistent with the changes in ventricular function before and after digitalis in a patient with heart failure?



- X → A
- D → X
- E → D
- C → B
- X → C

281. An EMT arrives at the scene of an automobile accident, and finds a hemorrhaging, unconscious young woman. Which of the following is a sign of hemorrhagic shock?

- Metabolic alkalosis
- Dry skin
- Polyuria
- Bradycardia
- Low hematocrit

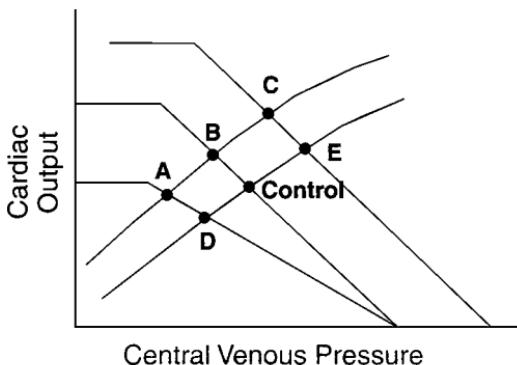
282. A 37-year-old patient is brought to the Emergency Department in shock. Which of the following is a reason to direct treatment toward anaphylactic shock rather than hypovolemic shock?

- a. Cardiac output is higher than normal
- b. Ventricular contractility is greater than normal
- c. Total peripheral resistance is greater than normal
- d. Serum creatinine is elevated
- e. Heart rate is greater than normal

283. During a routine physical examination, a 35-year-old male is found to have a blood pressure of 170/105 mmHg. History reveals episodes of headache accompanied by palpitations, diaphoresis, and anxiety. A tentative diagnosis of pheochromocytoma is confirmed when blood pressure falls in response to the administration of which of the following?

- a. An ACE inhibitor
- b. A β -adrenergic agonist
- c. An α -adrenergic blocker
- d. A loop diuretic
- e. An AII antagonist

284. Cardiac function and venous function curves were generated in a patient undergoing several maneuvers to evaluate his cardiac and cardiovascular reserves. Starting from the control point, to which point did the curves shift when the person was given a transfusion of saline?



- a. A
- b. B
- c. C
- d. D
- e. E

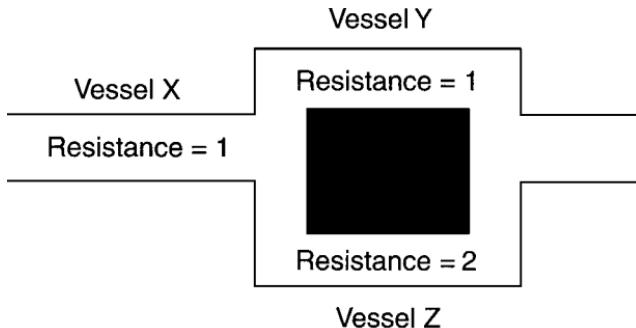
285. A woman with syndrome X is prescribed a low-calorie diet and 30-min of daily aerobic exercise. Sympathetic stimulation during exercise has which of the following cardiac effects?

- a. An increase in the duration of systole
- b. An increase in the duration of diastole
- c. An increase in the activity of the SR calcium pump
- d. A decrease in the affinity of troponin for calcium
- e. A decrease in the concentration of Ca^{2+} during systole

286. A 23-year-old collegiate dance squad member adopts a sedentary lifestyle once she starts medical school. After the Gross Anatomy course, she decides to restore her state of physical fitness by resuming a regular exercise routine. The cardiovascular responses to isotonic exercise include an increase in which of the following?

- a. Stroke volume
- b. Diastolic pressure
- c. Venous compliance
- d. Pulmonary arterial resistance
- e. Total peripheral resistance

287. The following diagram illustrates the relative resistance of three vessels. Which of the following is the ratio of the flow in vessel X to the flow in vessel Y?



- a. 1:1
- b. 3:2
- c. 2:1
- d. 3:1
- e. 4:3

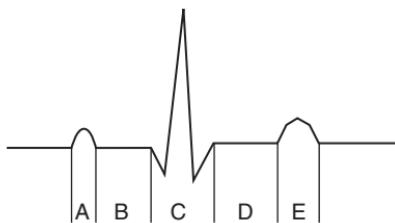
288. A 2-year-old boy is mauled by a black bear while hiking with his family in the Appalachian mountains. A claw puncture wound to the skull compressed the underlying brain tissue. Which of the following occurs in response to an increased intracranial pressure?

- a. Blood pressure and heart rate increase
- b. Blood pressure and heart rate decrease
- c. Blood pressure increases and heart rate decreases
- d. Blood pressure decreases and heart rate increases
- e. Blood pressure and heart rate remain constant

289. Left ventricular wall stress will be decreased by an increase in which of the following?

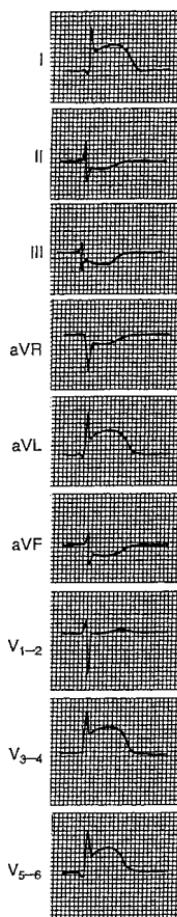
- a. Mean arterial pressure
- b. Total peripheral resistance
- c. Left ventricular end-diastolic volume
- d. Contractility of the left atrium
- e. The thickness of the free wall of the left ventricle

290. During which interval on the ECG below does the bundle of His depolarize?



- a. A
- b. B
- c. C
- d. D
- e. E

291. A 48-year-old man develops chest pain while running. His wife takes him to the Emergency Department, where the following ECG is obtained. The electrocardiographic changes are consistent with a diagnosis of which of the following?



- a. Hyperkalemia
- b. Hypokalemia
- c. Anterior infarction
- d. Posterior infarction
- e. Ventricular premature beat

292. A patient with Type II diabetes reports for his 6-month check-up. His doctor prescribes a daily 30-minute routine of walking at a brisk pace. During aerobic exercise, blood flow remains relatively constant within which of the following?

- a. Brain
- b. Heart
- c. Skin
- d. Skeletal muscles
- e. Kidneys

293. A 56-year-old man presents with complaints of fatigue and headaches. During the physical examination, he is found to have a wide pulse pressure. Which of the following conditions causes pulse pressure to increase?

- a. Tachycardia
- b. Hypertension
- c. Hemorrhage
- d. Aortic stenosis
- e. Heart failure

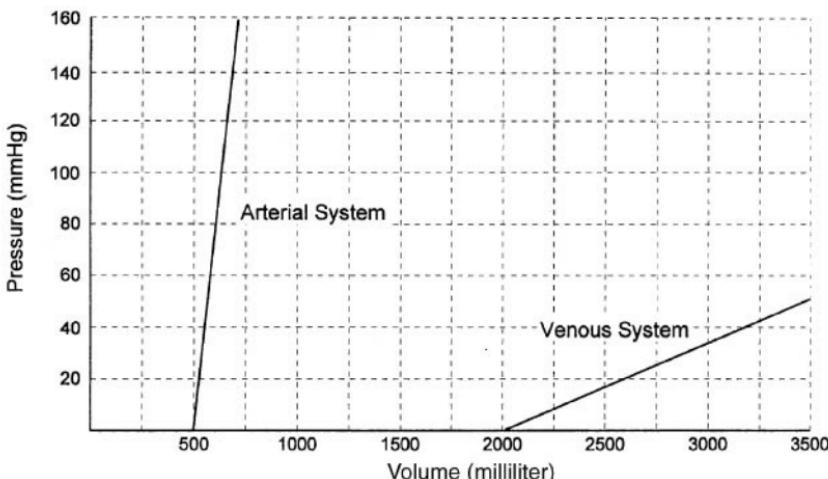
294. A 22-year-old male ruptures his spleen in a motorcycle accident. A reduction in blood pressure would cause a decrease in which of the following?

- a. Heart rate
- b. Myocardial contractility
- c. Total peripheral resistance
- d. Venous compliance
- e. Cardiac output

295. Which of the following organs has the highest arteriovenous O₂ difference under normal resting conditions?

- a. Brain
- b. Heart
- c. Skeletal muscle
- d. Kidney
- e. Liver

296. The graph below illustrates the pressure-volume curves for the arterial and venous systems. Which of the following is the approximate ratio of the arterial compliance to the venous compliance?



- a. 15:1
- b. 10:1
- c. 1:1
- d. 1:10
- e. 1:20

297. A 63-year-old woman with congestive heart failure is given digitalis. Positive inotropic drugs can reduce ischemic cardiac pain (angina) in a dilated failing heart by doing which of the following?

- a. Decreasing preload
- b. Increasing diastolic filling time
- c. Decreasing total peripheral resistance
- d. Increasing heart rate
- e. Increasing coronary blood flow

298. Which of the following characteristics is most similar in the systemic and pulmonary circulations?

- a. Preload
- b. Afterload
- c. Peak systolic pressure
- d. Blood volume
- e. Stroke work

299. A 6-year-old girl undergoes a routine physical examination for entry into the first grade. She is found to be tachycardic, and has a wide pulse pressure. A thrill and a continuous murmur with late systolic accentuation at the upper left sternal edge are detected upon auscultation. Echocardiography reveals a patent ductus arteriosus. Which of the following best describes the function of the ductus arteriosus in the fetal circulation?

- a. It delivers oxygenated blood from the placenta to the left ventricle
- b. It is located in the septum between the left and right atrium
- c. It diverts oxygenated blood away from the lungs to the aorta
- d. It allows blood to flow from the aorta to the pulmonary artery
- e. It is a high resistance conduit, which helps to maintain normal fetal blood pressure

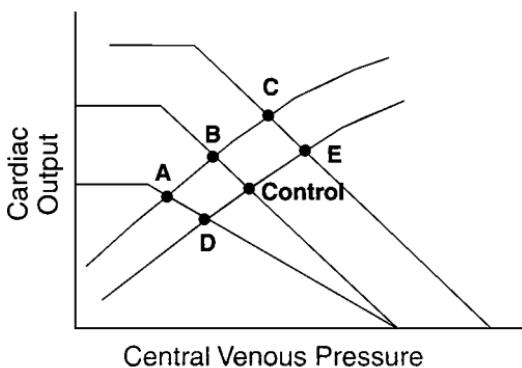
300. A 63-year-old woman presented with acute onset of right eye pain. Ophthalmic and neurologic examinations were normal except for a loud right carotid bruit. The eye pain ceased following carotid endarterectomy. The bruit was most likely caused by which of the following?

- a. A high velocity of blood within the carotid artery
- b. An increase in blood viscosity
- c. Widening of the carotid artery
- d. An increase in hematocrit
- e. Lengthening of the carotid artery

301. A 57-year-old woman is undergoing a femoral popliteal bypass for her peripheral vascular disease. The vascular surgeon wishes to induce a localized arteriolar constriction to help control hemostasis. An increase in the local concentration of which of the following agents will cause systemic vasoconstriction?

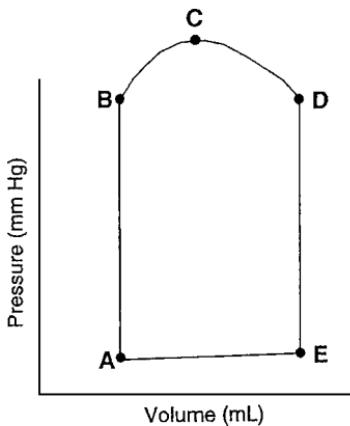
- a. Nitric oxide
- b. Angiotensin II
- c. Atrial natriuretic peptide
- d. A β_2 -adrenergic agonist
- e. Adenosine

302. A patient is referred to the Heart Station for exercise stress testing. Baseline and exercise levels of cardiac and venous function are measured and plotted on the graphs below. The point marked “Control” represents baseline cardiovascular function in the resting state in the supine position. During treadmill exercise, there will be a shift from the resting state to which of the following points?



- a. A
- b. B
- c. C
- d. D
- e. E

303. In the pressure-volume loop below, systole begins at which of the following points?



- a. A
- b. B
- c. C
- d. D
- e. E

304. Which of the following is true regarding the functional closure of the ductus arteriosus?

- a. It is independent of gestational age
- b. It occurs due to hypoxic pulmonary vasoconstriction
- c. It precedes closure of the foramen ovale
- d. It causes blood to flow from the aorta into the pulmonary artery
- e. It is the final event required for conversion of the transitional circulation in the newborn to the adult circulatory pattern

305. A 32-year-old male is diagnosed with primary hypertension. His physician recommends a new drug for hypertension that acts by decreasing vascular smooth muscle contractile activity without affecting ventricular contractility. Which of the following is the most likely site of action for the new drug?

- a. β -adrenergic receptors
- b. Calmodulin
- c. Troponin

- d. Tropomyosin
- e. Protein kinase A

306. A 64-year-old male was admitted to the hospital with edema and congestive heart failure. He was found to have diastolic dysfunction characterized by inadequate filling of the heart during diastole. The decrease in ventricular filling is due to a decrease in ventricular muscle compliance. Which of the following proteins determines the normal stiffness of ventricular muscle?

- a. Calmodulin
- b. Troponin
- c. Tropomyosin
- d. Titin
- e. Myosin light chain kinase

307. At which of the following sites in the cardiovascular system does the blood flow lose the greatest amount of energy?

- a. Mitral valve
- b. Large arteries
- c. Arterioles
- d. Capillaries
- e. Venules

308. During the cardiac cycle, when does the highest coronary blood flow per gram of left ventricular myocardium occur?

- a. When aortic pressure is highest
- b. When left ventricular pressure is highest
- c. At the beginning of isovolumic contraction
- d. When aortic blood flow is highest
- e. At the beginning of diastole

309. A 59-year-old male with an ejection fraction of 15%, who is being treated with medications for his heart failure, is asked whether he would like to participate in a trial for an experimental drug. The drug being tested is designed to decrease the expression of phospholamban on ventricular muscle cells. Which of the following would be increased by decreasing phospholamban?

- a. The activity of the sodium-potassium pump
- b. The diastolic stiffness of the ventricular muscle cells
- c. The activity of the L-type calcium channels
- d. The duration of the ventricular muscle action potential
- e. The concentration of calcium within the SR

310. A 29-year-old woman presents at the obstetrician/gynecologist's office with breast tenderness. She's concerned she may have a lump because her mother had breast cancer, and reports that she can't be pregnant because she just finished her menstrual period about 2 weeks ago. An assay for human chorionic gonadotropin (hCG) in her urine is positive, confirming pregnancy. In the developing fetus, which vessel has the greatest partial pressure of oxygen?

- a. Umbilical vein
- b. Umbilical arteries
- c. Aorta
- d. Ductus arteriosus
- e. Ductus venosus

Cardiovascular Physiology

Answers

235. The answer is d. (*Ganong, pp 571–574.*) Preload is the degree to which the myocardium is stretched before it contracts, i.e., the length of the sarcomere at the end of diastole. *In vivo*, the variable most directly related to sarcomere length during end-diastole is left ventricular end-diastolic volume. Although blood volume, central venous pressure, pulmonary capillary wedge pressure, and left ventricular end-diastolic pressure can all influence preload, they all exert their influence through changes in end-diastolic volume.

236. The answer is b. (*Ganong, pp 571–576.*) Afterload is the tension at which the load is lifted during the contraction of a sarcomere. According to the law of Laplace ($T = P \times r/w$), the tension (T) is proportional to the pressure (P) and radius (r) and inversely proportional to the thickness of the ventricle wall (w) during systole. The mean left ventricular systolic pressure would therefore be the best index of afterload *in vivo*. Mean arterial blood pressure (MAP) is normally the same as ventricular pressure and therefore a good index of afterload. However, in a patient with aortic stenosis, the ventricular pressure is higher than the aortic pressure. Although the total peripheral resistance (TPR) can influence afterload by causing changes in mean arterial blood pressure, changes in TPR do not always cause corresponding changes in afterload. For example, during aerobic exercise, afterload (MAP) is often increased, whereas TPR is reduced and following a hemorrhage, TPR is high, whereas afterload (MAP) is low. Pulmonary capillary wedge pressure and left ventricular end-diastolic pressure are estimates of the volume of blood in the ventricle during diastole and are indices of preload.

237. The answer is d. (*Ganong, pp 554–556, 640. Kasper et al., pp 126–130. Stead et al., pp 44–46.*) Syncope (fainting) is a transient loss of consciousness caused by an inadequate blood flow to the brain. Transient decreases in cerebral blood flow are usually due to one of three general mechanisms: disorders of vascular tone or blood volume, cardiovascular disorders, or cerebrovascular disease. Approximately one-fourth of syncopal episodes are of cardiac origin

and are due to either transient obstruction of blood flow through the heart or sudden decreases in cardiac output due to cardiac arrhythmias, such as bradycardia, heart block, or sinus arrest (neurocardiogenic syncope). Third-degree (complete) heart block results when conduction of the action potential from the atria to the ventricles is completely interrupted. Under these conditions, pacemaker cells within the His-Purkinje system or the ventricular muscle cause the ventricles to beat at a low rate (idioventricular rhythm) independently of the atria. Although the heart rate may be high enough to adequately perfuse the brain under resting conditions, Third-degree heart block is caused by conduction system disturbances, inferior wall MI, and digitalis toxicity. When the conduction disturbance is due to disease in the AV node, the idioventricular rhythm is normally about 45 beats/min. When the conduction disturbance is below the AV node (infranodal block) due to disease in the bundle of His, firing of more peripheral ventricular pacemakers can decrease heart rate to below 30 beats/min with periods of asystole that may last a minute or more. The resultant cerebral ischemia causes dizziness and fainting (Stokes-Adams syndrome). Sinus arrhythmia is a change of the heart rate produced by the normal variation in the rate of phase 4 depolarization of the SA nodal pacemaker cells between inspiration and expiration. First-degree heart block is defined as a higher-than-normal PR interval (greater than 0.2 seconds). Second-degree heart block occurs when the action potential fails to reach the ventricles some, but not all, of the time. Tachycardia is a heart rate above 100 beats per minute.

238. The answer is c. (*Ganong*, pp 554–556. *Stead et al.*, pp 6–8, 44–45.) Conduction abnormalities can produce first-degree, second-degree, or third-degree heart block. In a second-degree heart block, a P wave is not always followed by a QRS complex as in trace C, where the second P wave is not followed by a QRS complex. In a first-degree heart block, trace D, the interval between the beginning of the P wave and the beginning of the QRS complex (the PR interval) is longer than normal (greater than 0.2 seconds). In a third-degree heart block, conduction between the atria and ventricles is completely blocked so the atrial beats (represented by the P waves) and the ventricular beats (represented by the QRS complex) are completely dissociated.

239. The answer is d. (*Ganong*, p 553. *Stead et al.*, pp 6–7.) The mean electrical axis (MEA) represents the average direction traveled by the ventricular muscle action potentials as they propagate through the heart. The propagation path and the mass of tissue through which the action potentials travel influence the MEA. Normally the MEA ranges from -30° to $+100^\circ$. The MEA is approximately perpendicular to the axis of the limb lead with the smallest QRS wave

magnitude. In this case, the smallest deflection is in lead III. Therefore, the MEA lies along lead aVR. Because the QRS complex is negative in aVR, the MEA is approximately +30 degrees. Because the QRS complex is greater in lead II than in lead I, the MEA is between +60 degrees and +30 degrees.

240. The answer is c. (*Ganong, pp 565–568.*) The pressure gradient between regions of the cardiovascular system is directly proportional to the resistance of the intervening structures. During ventricular ejection, the aortic valves are open and do not offer any significant resistance to blood flow. Therefore, there is very little, if any, pressure difference between the left ventricle and the aorta. Because the tricuspid valve is closed during ventricular ejection, there is an appreciable pressure difference between the right ventricle and the left atrium, although this pressure difference is opposite in direction to the flow of blood through the circulatory system. Although pulmonary vascular resistance is relatively small compared with systemic vascular resistance, it nonetheless produces a pressure drop between the right ventricle and the left atrium. Because most of the resistance in the systemic vasculature occurs at the level of the arterioles, there is a large pressure gradient between the aorta and the capillaries.

241. The answer is b. (*Ganong, pp 570–571.*) Cardiac output can be measured by using Fick's principle, which asserts that the rate of uptake of a substance by the body (e.g., O₂ consumption in milliliters per minute) is equal to the difference between its concentrations (milliliters per liter of blood) in arterial and venous blood multiplied by the rate of blood flow (cardiac output). This principle is restricted to situations in which arterial blood is the only source of the substance measured. If oxygen consumption by the body at steady state is measured over a period of time and the difference in arterial O₂ and venous O₂ measured by sampling arterial blood and pulmonary arterial blood (which is fully mixed venous blood), cardiac output is obtained from the expression

$$CO = \dot{V}O_2/a-vO_2$$

$$CO = \frac{280 \text{ mL/min}}{20 \text{ mL}/100 \text{ mL} - 12 \text{ mL}/100 \text{ mL}}$$

$$CO = \frac{280 \text{ mL/min}}{8 \text{ mL}/100 \text{ mL}}$$

$$\begin{aligned} CO &= 280 \text{ mL/min} \times 100 \text{ mL}/8 \text{ mL} \\ &= 3500 \text{ mL/min} \\ &= 3.5 \text{ L/min} \end{aligned}$$

242. The answer is a. (*Ganong*, pp 569–570.) Blood leaks from the aorta into the left ventricle during diastole in patients with regurgitant aortic valves producing a diastolic murmur. The rapid flow of blood into the left ventricle during diastole also causes an increase in end-diastolic volume (preload), which results in a larger stroke volume and therefore, a larger pulse pressure. Typically, mean blood pressure remains the same so the larger pulse pressure is accompanied by an increased systolic and decreased diastolic pressure. If too much of the stroke volume flows back into the heart during diastole, mean blood pressure will fall and the baroreceptor reflex will cause an increase in heart rate.

243. The answer is c. (*Ganong*, pp 571–579, 632–635.) Cardiac output increases during exercise primarily due to sympathetically mediated increases in heart rate. Patients with transplanted hearts are able to increase their cardiac output during exercise in the absence of cardiac innervation through increases in stroke volume brought about by operation of the Frank-Starling mechanism. Stroke volume increases with an increase in preload (Frank-Starling mechanism), a decrease in afterload, or an increase in contractility. Preload is the volume of blood within the ventricles at the end of diastole. Decreasing venous compliance forces more blood into the ventricle, resulting in an increased preload and an increased stroke volume. Increasing afterload (aortic pressure or total peripheral resistance) and decreasing contractility decrease stroke volume. An increase in heart rate may result in a decreased filling time and, therefore, a decrease in preload and stroke volume.

244. The answer is d. (*Ganong*, pp 549–550.) The most rapid conduction of the action potential occurs through the Purkinje fibers. The slowest conduction occurs in the AV node. Pacemaker cells located within the SA node initiate the cardiac action potential normally. The action potential propagates from the SA node into the atrial muscle fibers. It then passes through the AV node and the His-Purkinje network to the ventricular muscle fibers. The rapid conduction of the action potential through the His-Purkinje network ensures rapid and synchronous activation of the entire ventricular muscle. The slow conduction through the AV node produces a delay between atrial and ventricular systole, allowing the ventricle to receive the blood ejected by the atria before it contracts.

245. The answer is b. (*Ganong*, pp 643–644, 726. *Kasper et al.*, pp 1364–1377.) In heart failure, the inability to pump enough blood to

satisfy the energy requirements of the tissues leads to an increase in end-diastolic volume and end-diastolic pressure, which can lead to pulmonary edema, hence the term congestive heart failure. In addition, the large end-diastolic volume increases the wall stress that must be developed by the heart with each beat, and this increases the myocardial requirement for oxygen. Administration of a positive inotropic drug such as digoxin increases the stroke volume, which increases the cardiac output to the tissues. The greater ejection fraction lowers the end-diastolic volume, which decreases heart size and thus wall stress, according to LaPlace's Law. As a result, myocardial oxygen demand is lowered.

246. The answer is e. (*Ganong, pp 584–585.*) According to Poiseuille's law, resistance is inversely proportional to the fourth power of the radius [$R \propto (1/r^4)$]. Therefore, if the radius of a blood vessel is decreased by a factor of 2, the resistance to blood flow would increase by a factor of 2^4 , or by 16 times.

247. The answer is a. (*Ganong, pp 605–607, 636–639.*) The fall in blood volume and pressure produced by hemorrhage elicits the baroreceptor reflex. The reflex increases the activity of the sympathetic nervous system and decreases the activity of the parasympathetic nerves innervating the heart. Sympathetic stimulation of the smooth muscle surrounding the venous vessels decreases their compliance, causing end-diastolic volume (EDV) to increase. The EDV does not increase above the levels observed prior to the hemorrhage, however. Heart rate, ventricular contractility, and total peripheral resistance are all increased above their prehemorrhage levels by sympathetic stimulation. The coronary blood flow increases to meet the increased energy requirements of the heart beating at a higher rate with increased contractility.

248. The answer is e. (*Ganong, pp 592–594.*) Net filtration from systemic capillaries is dependent on the Starling forces and capillary permeability. The equation is

$$\text{Net filtration} = K_f [(P_{\text{capillary}} - P_{\text{tissue}}) - (\pi_{\text{capillary}} - \pi_{\text{tissue}})],$$

where K_f is the filtration coefficient of the membrane, and is directly proportional to capillary permeability, $P_{\text{capillary}}$ and P_{tissue} are the hydrostatic pressures in the capillary and tissue (interstitial space), respectively, and $\pi_{\text{capillary}}$ and π_{tissue} are the osmotic (colloid oncotic) pressures in the capillary and interstitial space, respectively. Increasing central venous pressure

increases the capillary hydrostatic pressure ($P_{\text{capillary}}$), which increases the filtration of fluid from the systemic capillaries, leading to edema. All of the other choices will cause a decrease in filtration.

249. The answer is a. (*Ganong*, pp 565, 643.) The ejection fraction (EF) is equal to the stroke volume (SV) divided by the end-diastolic volume (EDV) and the stroke volume (SV) is equal to the end-diastolic volume (EDV) minus the end-systolic volume (ESV).

$$\text{EF} = \text{SV}/\text{EDV} = \text{EDV} - \text{ESV}/\text{EDV}$$

In this case, the end-diastolic volume is 130 mL and the end-systolic volume is 60 mL. Therefore, the ejection fraction is 70 mL/130 mL or 0.54.

250. The answer is d. (*Ganong*, pp 99–103, 565–567.) Closure of the semilunar valves (aortic and pulmonic valves) marks the beginning of the isovolumetric relaxation phase of the cardiac cycle. During this brief period (approximately 0.06 seconds), the ventricles are closed and myocardial relaxation, which began during protodiastole, continues. Intraventricular pressure falls rapidly, although ventricular volume changes little. When intraventricular pressure falls below atrial pressure, the mitral and tricuspid valves open and rapid filling of the ventricles begins.

251. The answer is c. (*Ganong*, pp 551–553. *Kasper et al.*, pp 1312–1315.) The ECG leads are configured so that a positive (upright) deflection is recorded in a lead if the wave of depolarization spreads toward the positive pole of that lead, and a negative deflection if the wave spreads toward the negative pole. If the mean orientation of the depolarization vector is at right angles to a given lead axis, a biphasic (equally positive and negative) deflection will be recorded. Therefore, the equiphasic QRS complex in lead aVF indicates that the mean QRS vector is 90° away from -150° . If the QRS complex is positive in leads III and aVF, the mean electrical axis must move toward $+120^\circ$ and $+90^\circ$, respectively. Thus, the mean QRS vector must be $+120^\circ$. Right axis deviation (mean QRS vector to the right of 110°) is characteristic of the right ventricular strain or hypertrophy associated with pulmonary hypertension. The positive QRS complex in lead V₁ is also characteristic of right axis deviation.

252. The answer is b. (*Ganong*, pp 556–557, 569, 573.) Atrial fibrillation is an arrhythmia in which the electrical activity of the atrium becomes disorganized and therefore unable to produce a coordinated atrial contraction. The absence of an atrial pulse reduces the emptying of the atria during diastole and results in an enlarged left atrium and increased left atrial pressure. The venous A wave represents atrial contraction and disappears due to the absence of an atrial beat. Decreased filling of the heart results in a decrease in stroke volume. Heart rate increases because the continuous electrical activity of the atria initiates a high rate of ventricular activity. Systemic blood pressure typically falls because of inadequate filling of the ventricles and the resulting decrease in stroke volume.

253. The answer is e. (*Ganong*, pp 566–569.) The second heart sound (S_2) is associated with the closing of the aortic and pulmonic valves. The aortic valve normally closes slightly before the pulmonic valve, resulting in a splitting of the second heart sound into two components. During inspiration, the closing of the pulmonic valve is delayed, resulting in a prolongation of the interval between the two components of the second heart sound. During inspiration, the preload on the right heart is increased, resulting in a larger stroke volume, which causes the delay in the closing of the pulmonic valve. Closure of the mitral valve and tricuspid valves are associated with the first heart sound (S_1). Heart rate is higher during inspiration than during expiration.

254. The answer is a. (*Ganong*, pp 567–569. *Stead et al.*, pp 27–29.) The third heart sound (S_3) is associated with rapid ventricular filling of the left ventricle. S_3 is commonly heard in children and young adults and is also heard in conditions when rapid filling of the ventricle is abnormally high, for example, in anemia or mitral regurgitation. It can also occur in dilated cardiomyopathy, restrictive cardiomyopathy, or cardiac tamponade when the compliance of the left ventricle is reduced. An increased heart rate reduces the duration of diastole, and thus tends to decrease ventricular filling.

255. The answer is c. (*Ganong*, pp 569–570, 582–583.) The magnitude of the cardiac output is regulated to maintain an adequate blood pressure and to deliver an adequate supply of oxygen to the tissues. In anemia, a greater cardiac output is required to supply oxygen to the tissues because the oxygen-carrying capacity of the blood is reduced. The reduced blood viscosity increases the velocity and thus the turbulence of the blood flow, which makes systolic murmurs common in anemic patients. In aortic regurgitation,

the stroke volume will be increased, but a portion of the blood ejected by the heart will return to the heart during diastole. Thus, the output delivered to the tissues does not increase despite the fact that the blood ejected by the heart has increased. In hypertension, third-degree heart block, and cardiac tamponade (decreased filling of the heart due to accumulation of fluid within the pericardium), cardiac output will be normal or reduced.

256. The answer is e. (*Ganong, pp 570–576. Kasper et al., p 1365.*) Efficiency is defined as work divided by energy consumption. The heart represented by pressure-volume curve 1 in the diagram has a lower end-diastolic volume and, therefore, ejects blood at a lower wall stress than the heart represented by pressure-volume curve 2. Cardiac energy consumption is directly related to wall stress. Because both hearts eject the same amount of blood (stroke volume) at the same pressure, they perform the same amount of work.

257. The answer is b. (*Ganong, pp 569–570. Kasper et al., pp 1307–1311.*) Early systolic murmurs begin with the first heart sound and end in mid-systole. The higher-than-normal height of the jugular blood column reflects an increased right atrial pressure. The combination of an early systolic murmur and high right atrial pressure is indicative of tricuspid regurgitation. This lesion is common in narcotic abusers with infective endocarditis. Mitral stenosis and aortic regurgitation produce diastolic murmurs.

258. The answer is a. (*Ganong, p 100. Kasper et al., p 1339.*) Although the cause of her syncope is not given in the history, it is presumably produced by an abnormally slow heart rate due to increased release of acetylcholine by the vagus nerve or by acetylcholine agonists such as muscarine, which is found in certain mushrooms. Atropine blocks the acetylcholine receptors on the SA and AV node, leading to an increased heart rate.

259. The answer is b. (*Kasper et al., pp 1325–1326, 1436–1437.*) A stress test is conducted by asking a patient to increase his or her exercise intensity while monitoring blood pressure and the electrical activity of the heart. Ischemia occurs if the myocardial oxygen demand brought about by the increased exercise intensity is not matched by an increase in myocardial blood flow. An ischemic episode is indicated by ST segment depression. Mean arterial blood pressure and heart rate normally rise during exercise. The presence of a diastolic murmur or conduction abnormalities in the

ECG are not diagnostic of ischemic heart disease. The exercise test will also be terminated if dizziness, dyspnea, or ventricular tachycardia develop or if blood pressure falls.

260. The answer is e. (*Ganong, pp 630–631.*) When a person rises suddenly, blood pools in the dependent portions of the body, causing decreases in venous return, left ventricular end-diastolic volume, stroke volume, and pulse pressure. The reduced stroke volume leads to a drop in cardiac output and, therefore, a drop in blood pressure. Decreased blood pressure produces the baroreceptor reflex, leading to an increase in sympathetic activity, which increases total peripheral resistance, cardiac contractility, heart rate, and ejection fraction. These changes in the cardiovascular system return blood pressure toward normal.

261. The answer is c. (*Ganong, pp 627–629.*) Persistent fetal circulation (or persistent pulmonary hypertension) occurs when the normal reduction of pulmonary vascular resistance does not occur at birth. In utero, pulmonary artery pressure and pulmonary vascular resistance are high and pulmonary blood flow is low, constituting only ~5–10% of the cardiac output. Of the venous return to the right atrium, about one-third flows into the left atrium through the foramen ovale and the remaining two-thirds flows into the right ventricle and is pumped into the main pulmonary artery. Almost all of this blood (90%) flows from right-to-left into the aorta through the ductus arteriosus. At birth, initiation of extrauterine respiration raises alveolar PO_2 , causing a decrease in pulmonary vascular resistance accompanied by a decrease in pulmonary artery pressure and an increase in pulmonary blood flow. The increased pulmonary venous return to the left atrium raises left atrial pressure above right atrial pressure, causing functional closure of the foramen ovale. The ventilation-induced increase in arterial PO_2 constricts the systemic vessels, which, along with the elimination of the placental circulation that comprised 40% of the fetal cardiac output, increases systemic vascular resistance and aortic pressure rises above pulmonary artery pressure. As a consequence, blood flows across the ductus arteriosus from aorta to pulmonary artery (left-to-right). If the transition to extrauterine respiration is impaired, and the infant has arterial hypoxia despite administration of 100% O_2 , then pulmonary vascular resistance and pulmonary artery pressure remain high, causing the persistence of the right-to-left flow of blood across the ductus arteriosus, which exacerbates the hypoxemia, and causes cyanosis.

262. The answer is e. (*Ganong*, pp 577–580, 637–639.) The total circulating blood volume is approximately 70 mL/kg, about two-thirds of which is found in the systemic veins and venules. A significant volume of blood (15%) is found in the pulmonary circulation. The large volume of blood found on the venous side of the circulation is used to adjust circulating blood volume. For example during hemorrhage, contraction of the veins and venules of the skin increases the amount of blood available for perfusion of the heart and brain.

263. The answer is a. (*Ganong*, pp 78–81, 547–549.) Phase-4 depolarization is caused by the activation of a Na^+ channel. The channel is activated when the membrane hyperpolarizes in contrast to the Na channel responsible for the action potential, which is activated when the cell depolarizes. Potassium conductance decreases during phase-4 depolarization and thus the flow of potassium out of the cell is diminished. However, this change in potassium current is not responsible for phase-4 depolarization. Chloride conductance does not change during phase 4. The Na/Ca exchanger maintains low intracellular calcium at rest and may reverse its direction and pump calcium into the cell during phase 2 of the cardiac action potential. However, neither the Na/Ca exchanger nor the Na-K pump is involved in phase-4 depolarization.

264. The answer is d. (*Ganong*, pp 554–556, 566–570. *Kasper et al.*, pp 1307–1311.) Normal splitting of the second heart sound occurs because the aortic valve (A2) closes before the pulmonic valve (P2). The splitting will be reversed by any condition that delays the closing of the aortic valve. The most common cause of reversed splitting is left bundle branch block in which activation of the left ventricle is delayed. A right bundle branch block would prolong P2, thus causing increased physiological splitting. Similarly, during inspiration, there will be prolongation of the normal splitting of the second heart sound, not reversed splitting. Sinus arrhythmia refers to the increased heart rate during inspiration, which is accompanied by an increased venous return and thus an increased right ventricular preload, which prolongs the duration of right ventricular ejection, and thus delays closure of the pulmonic valve during inspiration. Increases or decreases in heart rate do not alter the normal pattern of valvular closure.

265. The answer is d. (*Ganong*, pp 587–592. *Widmaier et al.*, pp 414–417.) Pulse pressure is the difference between the systolic and diastolic pressure that occurs during the cardiac cycle. It is determined by the change in

volume in the aorta during systole and the compliance of the aorta. A decrease in aortic compliance (that is, an increase in the stiffness of the aorta) will increase pulse pressure. When mean arterial pressure increases, the average volume of blood in the aorta is higher than normal. The increased volume decreases aortic compliance. Assuming that the stroke volume remains normal, the decreased compliance will result in an increased pulse pressure. If heart rate increases, stroke volume and therefore pulse pressure will decrease. An increase in total peripheral resistance will prevent blood from flowing out of the aorta during systole and therefore decrease pulse pressure. In aortic stenosis, the rate at which blood is ejected from the ventricle is decreased. The decreased ejection rate provides time for blood to flow from the aorta to the periphery during systole. Therefore, the increase in aortic volume during systole and the pulse pressure are decreased.

266. The answer is e. (*Ganong, pp 643–644. Levitzky, pp 107–109. Stead et al., pp 25–27. Widmaier et al., pp 454–455.*) Orthopnea or dyspnea associated with lying down is caused by redistribution of blood from the periphery to the chest, leading to an increase in pulmonary capillary pressure. Pulmonary capillary pressure is elevated in patients with heart failure. When the patient lies down, the pulmonary capillary pressure is increased, causing the orthopnea. A third heart sound is often heard in heart failure and when associated with a high heart rate produces a gallop rhythm. The third heart sound can also be heard in patients with cor pulmonale (an enlargement of the right heart) and constrictive pericarditis. Neither, however, produces orthopnea. Mitral regurgitation can produce dyspnea but is not associated with a third heart sound.

267. The answer is b. (*Ganong, pp 571–576. Widmaier et al., pp 409–411.*) Stroke volume is determined by preload, afterload, and contractility. Increasing heart rate decreases the time for filling during diastole and may decrease preload and therefore stroke volume. Increasing preload by increasing central venous pressure will increase stroke volume. Similarly, decreasing afterload by decreasing total peripheral resistance or systemic blood pressure will cause an increase in stroke volume. Increasing contractility will also increase stroke volume.

268. The answer is b. (*Ganong, pp 556–559.*) A premature ventricular beat originates from ventricular pacemaker cells. Most often, these pacemaker cells are reset with each heart beat and therefore do not produce ventricular activation. However, when the sinus rhythm is very slow

(bradycardia), there is time for these pacemaker cells to reach threshold and produce a ventricular contraction. Because the patient is a well-trained athlete, his bradycardia is an index of his good aerobic conditioning and not a cause for alarm. If the ECG revealed a depressed ST segment, which is a sign of ventricular ischemia, the PVCs could have serious consequences. Although an inverted atrial wave can occur following a PVC (if the action potentials propagate into the atria) and a wide QRS complex, these are results, not causes of the premature contractions.

269. The answer is e. (*Ganong, pp 561–563. Kasper et al., pp 1316–1318.*) Abnormalities in coronary blood flow resulting in ischemia of the ventricular muscle will lead to a current of injury, which is reflected as an upward or downward shift in the ST segment of the ECG recording. The electrical activity of the heart does not reflect changes in ventricular contractility, blood pressure, ejection fraction, or total peripheral resistance, although all of these can be altered by changes in coronary blood flow.

270. The answer is c. (*Ganong, pp 571–576. Widmaier et al., pp 409–411.*) Stroke volume is influenced by ventricular preload, afterload, and contractility. Decreasing total peripheral resistance may result in a decrease in afterload and therefore an increase in stroke volume. Decreasing ventricular compliance (making the heart stiffer) or increasing venous compliance will decrease ventricular filling and, therefore, preload and stroke volume. Similarly, increasing heart rate will decrease filling and stroke volume.

271. The answer is b. (*Ganong, pp 575–576, 586.*) When the left ventricle fails, preload (left ventricular end-diastolic volume) is increased in an attempt to normalize stroke volume. The increase in radius of the dilated ventricle increases wall tension (stress) according to the Laplace relationship, $T = Pr/w$, where T = tension, P = systolic pressure, r = ventricular radius, and w = ventricular wall thickness. The increase in wall tension requires an increase in energy consumption. The increase in preload increases the left ventricular end-diastolic pressure. Because the pulmonary capillaries are supplying the blood to the left ventricle, an increase in left ventricular end-diastolic pressure must be accompanied by an increase in pulmonary capillary hydrostatic pressure. The decrease in left ventricular contractility associated with heart failure causes the ejection fraction to decrease. Heart rate will be increased by the increased sympathetic nerve activity that accompanies heart failure.

272. The answer is b. (*Ganong, pp 549–550, 565–569.*) The PR interval starts at the beginning of the P wave and ends at the beginning of the QRS complex. The physiologic events that occur during this time period include atrial depolarization, which is responsible for the P wave, AV nodal depolarization, and depolarization of the bundle of His and the Purkinje fibers. SA nodal depolarization precedes the P wave. Since the mass of the SA node is so small, this event cannot be detected on the standard ECG recording. The mitral and aortic valves are closed during isovolemic contraction, which occurs after the QRS complex has begun. The second heart sound occurs at the end of systole.

273. The answer is a. (*Ganong, pp 569–570. Stead et al., pp 37–38.*) In aortic stenosis, the resistance of the aortic valve increases, making it more difficult for blood to be ejected from the heart. Because a pressure drop occurs across the stenotic aortic valve, the ventricular pressure is much larger than the aortic pressure. Although stroke volume typically decreases leading to a decrease in pulse pressure, a normal cardiac output and arterial pressure can still be maintained by increasing heart rate. However, the increased afterload will lead to a decreased ejection fraction and increased cardiac oxygen consumption.

274. The answer is d. (*Ganong, pp 78–81, 548–549.*) The plateau phase (phase 2) is the result of the influx of calcium. Although calcium channels begin to open during the upstroke (phase 0), the greatest number of calcium channels is open during the plateau. The upstroke is primarily dependent on the opening of Na^+ channels. The initial repolarization (phase 1) is dependent on the inactivation of Na^+ channels and the opening of a transient K^+ channel. Repolarization (phase 3) is produced by the inactivation of Ca^{2+} channels and the activation of the delayed rectifier K^+ channels.

275. The answer is e. (*Ganong, pp 550–551, 565–569.*) The aortic valve closes when the pressure within the ventricle falls below the pressure within the aorta. This occurs when the ventricular muscle begins to relax. Relaxation begins at the end of the ventricular action potential, which is represented by the T wave (segment E) on the ECG recording.

276. The answer is a. (*Ganong, p 555. Stead et al., pp 6–8, 44–45.*) The PR interval represents the time it takes for the cardiac action potential to propagate from the SA node to the ventricular muscle. A delay in this interval, normally produced by a slowing in the conduction velocity

through the AV node, is called a first-degree heart block. A second-degree heart block occurs when the action potential does not always propagate through the SA node. This produces an uneven heart beat. A third-degree block occurs when the action potential never reaches the ventricle. Under these conditions, pacemakers within the ventricle produce ventricular contraction but the rate is very slow. Inversion of the T wave and elevation of the ECG are indicators of membrane potential defects within the ventricular muscle.

277. The answer is d. (*Ganong, pp 565–568.*) The graph illustrates the development of pressure in the aorta, the left atrium, and the left ventricle during a single cardiac cycle. At point D, the pressure within the left ventricle is less than the pressure in the left atrium, and, therefore, the mitral valve opens and ventricular filling begins. Although the volume in the left ventricle is increasing, the pressure is falling. During this time period, the recoil of the ventricle causes its pressure to decrease as it is filling. Later in diastole, the pressure of the blood returning from the lungs causes both volume and pressure in the ventricle to increase.

278. The answer is c. (*Ganong, pp 567, 569, 595–596.*) The a wave is the increase in central venous pressure that normally occurs during atrial contraction. Mitral regurgitation will produce a greater atrial preload and therefore a greater force of contraction. The increased atrial volume produces an increased ventricular preload. Blood pressure is typically normal in patients with mitral regurgitation. The greater left ventricular preload produces a greater-than-normal stroke volume. However, the forward stroke volume, the volume entering the aorta, does not increase, so there is no increase in pulse pressure or cardiac output.

279. The answer is d. (*Stead et al., pp 34–35.*) Cardiac tamponade is a disorder of the heart in which an increase in the volume of pericardial fluid compresses the heart and reduces ventricular filling during diastole. Pulsus paradoxus is a clinical sign in which there is an abnormally large decrease (greater than 10 mmHg) in systolic pressure during inspiration. The drop in systolic pressure normally occurs during inspiration because the decreased intrathoracic pressure reduces the flow of blood from the lungs to the left ventricle. The decrease in intrathoracic pressure also increases venous return to the right ventricle. The decrease in ventricular filling during inspiration is exacerbated in cardiac tamponade because the increased volume of blood in the right ventricle cannot push out the right

ventricular wall because of the increased fluid in the pericardial space. Instead, the blood pushes against the intraventricular septum, greatly reducing the volume of blood that can enter the left ventricle.

280. The answer is b. (*Ganong, pp 571–574.*) A normal Starling curve of the heart, showing stroke volume as a function of end-diastolic volume, is depicted by the curve on which an X is marked. The Starling curve below the normal one will result from a decrease in contractility (e.g., with heart failure) or an increase in afterload. The Starling curve above the normal curve will result from an increase in contractility or a decrease in afterload. Digitalis is a positive inotropic agent that will cause a point on the lower curve to shift to up and to the left, such that there is an increased stroke volume at a lower preload.

281. The answer is e. (*Ganong, pp 604–609. Widmaier et al., pp 446–447.*) Loss of blood causes blood pressure to fall. The baroreceptor reflex response to the fall in blood pressure causes a reflex increase in sympathetic outflow, causing an α -adrenergic receptor-mediated increase in arteriolar resistance, which further decreases capillary perfusing pressure. Because whole blood is lost, the concentration of circulating proteins remains normal and, therefore, the oncotic pressure remains the same. The decreased capillary pressure and normal oncotic pressure result in the transfer of fluid from the interstitium to the vascular bed, decreasing the hematocrit. The increased arteriolar constriction lowers blood flow to the kidney causing urine formation to decrease. Sympathetic stimulation causes peripheral constriction and produces sweating, resulting in the classic sign of hemorrhage: cold, damp skin. The baroreceptor reflex increases heart rate.

282. The answer is a. (*Ganong, pp 636–641.*) Anaphylactic shock is characterized by a decreased peripheral resistance and a high cardiac output. The decrease in peripheral resistance is so great that mean blood pressure falls below normal. Hypovolemic shock is caused by a decrease in circulating blood volume and pressure. In both types of shock, the baroreceptor reflex increases ventricular contractility and heart rate. Also, in both types of shock, blood is shunted away from the kidney, decreasing renal blood flow and glomerular filtration. As a result, plasma creatinine levels rise.

283. The answer is c. (*Ganong, pp 360, 642. Stead et al., pp 94–95.*) Pheochromocytoma is a tumor of the adrenal medulla characterized by an

excessive release of catecholamines. Severe hypertension can result from the increase in heart rate and contractility (β_1 -adrenergic activation by catecholamines) and vascular resistance (α -adrenergic activation). Blocking the α -adrenergic receptors will cause a decrease in TPR and a decrease in blood pressure.

284. The answer is e. (Ganong, pp 574–575, 633–634.) The diagram represents the cardiac (ventricular) function and venous function curves. Similar to the familiar Starling curves, cardiac output is graphed as a function of central venous pressure (preload). The cardiac function curves are shifted up and to the left by an increase in contractility and a decrease in afterload; they are shifted down and to the right by a decrease in contractility and an increase in afterload. The vascular function curves graph central venous pressure as a function of cardiac output. The independent variable, cardiac output, is represented on the y axis. An increase in cardiac output causes a fall in central venous pressure. A decrease in blood volume or venous tone shifts the vascular function curves to the left; an increase in blood volume or venous tone shifts the vascular function curves to the right. The point at which the two curves intersect represents the central venous pressure and cardiac output of the cardiovascular system. The shift from the resting state to point E represents an increase in vascular volume or venous tone without any change in TPR or ventricular contractility. This is consistent with an infusion of saline or a blood transfusion. An increase in total peripheral resistance (TPR) decreases the slope; a decrease in TPR increases the slope. An increase in TPR decreases the slope of the vascular function curve, and the increase in contractility shifts the cardiac function curve up and to the right. The new intersection of these curves is at point A. The shift from the resting state to point B represents an increase in contractility with no change in TPR. This is consistent with the administration of a positive inotropic drug. Upon sudden standing, contractility and TPR increase, whereas venous compliance decreases (i.e., venous tone increases). With exercise, there is an increase in contractility and a decrease in TPR and venous compliance.

285. The answer is c. (Ganong, pp 548–549, 565–568, 632–635. Kasper et al., pp 78, 1431–1432, 2158, 2296.) Sympathetic stimulation of the heart increases the activity of the SR Ca^{2+} pump. Sympathetic stimulation also increases the rate of SA nodal firing, which increases heart rate, and decreases the duration of the total cardiac cycle. Norepinephrine secreted by the sympathetic nerve endings binds to β_1 adrenergic

receptors, activating a G protein, which activates adenylyl cyclase and increases the intracellular concentration of cyclic AMP. Cyclic AMP activates protein kinase A, which leads to phosphorylation of the voltage-dependent Ca^{2+} channels, causing them to spend more time in the open state. Cyclic AMP also increases the active transport of Ca^{2+} to the sarcoplasmic reticulum, thus accelerating relaxation and shortening systole, which is important when heart rate is increased to permit adequate diastolic filling in the face of a decrease in the duration of diastole. It increases the amount of Ca^{2+} released from the SR during systole and decreases the affinity of troponin for Ca^{2+} . The increase in systolic Ca^{2+} concentration overcomes the decreased affinity of troponin for Ca^{2+} , resulting in an increased contractility.

286. The answer is a. (*Ganong, pp 80–81.*) During exercise, sympathetic stimulation of the heart increases contractility, and thus stroke volume. A decrease in venous compliance, caused by sympathetic stimulation, increases venous return to the heart, which also increases stroke volume by a Frank-Starling mechanism. The increased stroke volume, coupled with an increase in heart rate, cause an increase in cardiac output. Systemic arterial pressure also increases in response to the increase in cardiac output. However, the fall in total peripheral resistance, which is caused by dilation of the blood vessels within the exercising muscles, results in a decrease in diastolic pressure. The pulmonary vessels undergo passive dilation as more blood flows into the pulmonary circulation. As a result, pulmonary vascular resistance decreases.

287. The answer is b. (*Ganong, pp 581–585.*) The ratio of the blood flow through vessels Y and Z is inversely proportional to their resistance. Because vessel Y has half the resistance of vessel Z, it has twice the blood flow. The blood flowing through vessel X is the sum of the blood flowing through vessels Y and Z ($2 + 1 = 3$). Therefore, the ratio of the blood flowing through vessels X and Y is 3:2.

$$\begin{aligned}Q_{\text{Vessel Y}} &\propto 1/1; \quad Q_{\text{Vessel Z}} \propto 1/2 \\Q_{\text{Vessel Y}} / Q_{\text{Vessel Z}} &= \frac{1/1 \times 2/1}{1/2 \times 2/1} \\&= 2/1\end{aligned}$$

$$Q_{\text{Vessel X}} = Q_{\text{Vessel Y}} + Q_{\text{Vessel Z}} = 2 + 1 = 3$$

$$Q_{\text{Vessel X}} / Q_{\text{Vessel Y}} = 3/2$$

288. The answer is c. (*Ganong*, pp 604–608, 617. *Kasper et al.*, pp 1632–1634.) If intracranial pressure is rapidly elevated, cerebral blood flow is reduced. The increase in intracranial pressure stimulates the vasomotor center and produces an increase of systemic blood pressure that may lead to a restoration of cerebral blood flow. The increased blood pressure induces bradycardia mediated by the baroreceptor reflex.

289. The answer is e. (*Ganong*, pp 576, 586.) The factors that influence wall stress are given by the Laplace relationship—Tension (wall stress) = $[P \times r/w]$, where P equals the transmural pressure across the wall of the ventricle, r , the radius of the ventricle (determined by end-diastolic volume), and w , the thickness of the ventricular wall. Tension (wall stress) is reduced if the wall thickness increases. Increasing the systolic pressure developed by the heart (ventricular transmural pressure) or increasing the end-diastolic volume will increase wall stress. Wall stress will also be increased if total peripheral resistance is increased or mean arterial blood pressure is increased because, under both conditions, the heart will have to develop more pressure.

290. The answer is b. (*Ganong*, pp 547–554.) The bundle of His depolarizes during the PR segment (segment E), that is, during the interval between the end of atrial depolarization and the beginning of ventricular depolarization. Segment A, the P wave, represents atrial depolarization, segment C, the QRS complex, represents ventricular depolarization, and segment D, the ST segment, represents the time interval during which all of the ventricular muscle is depolarized.

291. The answer is c. (*Ganong*, pp 561–564. *Kasper et al.*, pp 1316–1318, 1448–1450.) Within hours after an acute myocardial infarction of the anterior ventricle, ST segment elevation appears in leads I, aVL, and the left precordial leads, V_{3–6}. Reciprocal ST depression occurs in leads II, III, and aVF. After some days or weeks, the ST segment abnormalities subside, the dead muscle and scar tissue become electrically silent. The infarcted area is therefore negative relative to the normal myocardium during systole, and it fails to contribute its share of positivity to the ECG complexes. Manifestations of this negativity include the appearance of Q waves and failure of progression of the R wave in the precordial leads.

292. The answer is a. (*Ganong*, pp 632–634.) Blood flow to the brain is kept relatively constant during both rest and exercise by local autoregulatory

mechanisms. During aerobic exercise, vasodilation of blood vessels in the working muscles increases skeletal muscle blood flow. Coronary blood flow increases to meet the increased metabolic needs of the heart. Blood flow to the gut, the kidneys, and the nonexercising muscles is reduced by sympathetic constriction of the arterioles leading to these organs. Blood flow to the skin is increased to prevent overheating.

293. The answer is b. (*Ganong, pp 586–590. Widmaier et al., pp 416–417.*) Pulse pressure is proportional to the amount of blood entering the aorta during systole and inversely proportional to aortic compliance. Pulse pressure increases with hypertension because hypertension causes aortic compliance to decrease. Whether the hypertension is a result of an increased cardiac output or an increased peripheral resistance, the higher arterial pressure is caused by an increase in arterial blood volume. The increased blood volume stretches the arterial wall, making it stiffer and decreasing its compliance. Stroke volume is decreased with tachycardia, hemorrhage, and heart failure, reducing pulse pressure in all three cases. In aortic stenosis, the ejection of blood from the ventricle is slowed and the increase in arterial blood volume during systole is less than normal.

294. The answer is d. (*Ganong, pp 605–607. Widmaier et al., pp 437–445.*) A reduction in carotid sinus pressure due to a decrease in mean blood pressure would elicit a baroreceptor reflex tending to restore blood pressure to normal. The reflex response includes an increase in sympathetic nervous system activity, which would cause an increase in heart rate and myocardial contractility, both of which would tend to increase cardiac output. Sympathetic stimulation would also cause constriction of both the arterioles and venous vessels. Arteriolar constriction would cause an increase in total peripheral resistance. Sympathetic stimulation of the venous vessels would cause a decrease in venous compliance.

295. The answer is b. (*Ganong, pp 612, 622, 632–634. Widmaier et al., p 424.*) The overall arteriovenous O₂ difference is determined by the oxygen consumption of a tissue and its blood flow. Because of the high rate of metabolism in the heart compared with its blood flow, it has the highest arteriovenous O₂ difference of any major organ of the body under normal conditions. The heart can extract a large amount of oxygen because of its high capillary density. Blood flow to the kidney and skin is far in excess of their metabolic needs, so little oxygen is removed from the blood as it passes through these organs; therefore, their arteriovenous O₂ differences

are rather small. Under normal conditions, the arteriovenous O₂ difference in skeletal muscle is quite low, but can increase substantially during vigorous exercise.

296. The answer is e. (Widmaier *et al.*, pp 415.) Compliance is defined as the change in volume divided by the change in pressure ($\Delta V/\Delta P$). The lower the compliance, the stiffer the vessel becomes. The venous system is much more compliant than the arterial system.

$$\text{Arterial compliance} = \Delta V/\Delta P = 250 \text{ mL}/160 \text{ mmHg} = 1.56 \text{ mL/mmHg}$$

$$\text{Venous compliance} = \Delta V/\Delta P = 1500 \text{ mL}/50 \text{ mmHg} = 30 \text{ mL/mmHg}$$

$$\begin{aligned}\text{Arterial compliance/Venous compliance} &= 1.56 \text{ mL/mmHg}/30 \text{ mL/mmHg} \\ &= 1:19.2\end{aligned}$$

297. The answer is a. (Ganong, pp 643–644. Kasper *et al.*, p 1375.) Ischemic cardiac pain is produced when oxygen demand is greater than the oxygen that can be delivered by the coronary arteries. Under normal circumstances an increase in contractility will increase oxygen demand, but in a dilated heart, an increase in contractility actually decreases oxygen demand. In heart failure, positive inotropic agents reduce oxygen demand by reducing end-diastolic volume (preload) and thus the wall stress that must be developed by the heart with each beat. Reducing volume decreases wall stress because, according to the law of Laplace, the wall stress is proportional to the product of force and radius (which is proportional to ventricular volume).

298. The answer is a. (Ganong, pp 565–569, 650, 660–662. Widmaier *et al.*, pp 403–409.) Although the left and right preloads are not identical, they are very similar (Right Atrial Pressure = 2 mmHg; Left atrial pressure = 5 mmHg). The right and left ventricles are in series with one another such that the right and left ventricular outputs are essentially equal. Because the two ventricles beat at the same rate, their stroke volumes are the same. The resistance of the pulmonary vasculature is much lower than that of the systemic circulation, however, yielding much lower pressures in the pulmonary artery than the aorta (mean Pulmonary Artery Pressure = 15 mmHg; mean Aortic Pressure = 90 mmHg). Thus, the afterload and stroke work are greater on the left side than on the right side. Because the same cardiac output is ejected into a higher resistance, peak systolic pressure is higher on the left side (120 mmHg) than on the right side (25 mmHg). Only about 10% of the blood volume is within the pulmonary circulation at any one

time, whereas approximately two-thirds of the blood volume is stored within the systemic veins and venules.

299. The answer is c. (*Ganong, pp 628–629. Kasper et al., p 1368.*) The ductus arteriosus is a low-resistance arterial vessel of the fetus through which highly oxygenated blood flows from the pulmonary artery to the aorta, bypassing the lungs. The ductus arteriosus empties into the aorta just distal to the left subclavian artery. Because blood is oxygenated in the placenta, pulmonary blood flow in the fetus serves only a nutritive, not a gas exchange, function for the developing lungs, and thus only about 5–10% of the cardiac output flows through the lungs. Soon after birth with the onset of extrauterine respiration, the pulmonary vascular resistance falls, allowing blood to flow from the pulmonary artery to the lungs. The high oxygen tension in the blood of the baby causes the resistance of the ductus arteriosus to increase, with functional closure occurring within several hours after birth. When the ductus arteriosus does not close, it is called a patent ductus arteriosus. If there is normal oxygenation with a normal regression of the pulmonary vasculature after birth, blood flow will reverse across the ductus arteriosus after birth, flowing from the aorta to the pulmonary artery. The left-to-right shunt persists throughout the cardiac cycle yielding the characteristic thrill and continuous murmur with late systolic accentuation at the upper left sternal edge. Cyanosis does not occur with a left-to-right shunt; however, the chronic increase in blood flow through the lungs may induce structural changes in the pulmonary vasculature leading to obstruction and pulmonary hypertension (Eisenmenger syndrome). The resultant right-to-left flow across the ductus causes the toes, but not the fingers, to become cyanotic and clubbed, a finding termed differential cyanosis.

300. The answer is a. (*Ganong, pp 582–585. Widmaier et al., pp 390–392.*) Turbulence, and consequently the bruit, was produced by the high velocity of blood within the stenotic area of the carotid artery, as predicted by Reynold's number. The widening of a vessel associated with aneurisms can also produce bruits but these are not relieved by endarterectomy. An increase in hematocrit or blood viscosity would decrease Reynold's number and decrease the tendency for turbulent flow.

301. The answer is b. (*Ganong, pp 454–457, 601–602. Widmaier et al., pp 422–424.*) Angiotensin II is a powerful vasoconstrictor that is formed when renin is released from the kidney in response to a fall in blood pressure or vascular volume. Renin converts angiotensinogen to angiotensin I.

Angiotensin II is formed from angiotensin I by angiotensin-converting enzyme localized within the vasculature of the lung. All the other listed substances cause vasodilation.

302. The answer is c. (*Ganong*, pp 574–575, 633–634.) This diagram depicts cardiac (ventricular) function and venous function curves. With the onset of exercise, there is an increase in contractility, which shifts the cardiac function curve up. Also accompanying the onset of exercise are decreases in total peripheral resistance and venous compliance, both of which shift the vascular function curve to the right and increase its slope. The point at which the cardiac function and venous function curves intersect (C) represents the central venous pressure and cardiac output of the cardiovascular system under these conditions.

303. The answer is e. (*Ganong*, pp 565–566, 573.) The left ventricular pressure-volume loop represents the changes in pressure and volume that occur during a cardiac cycle. Point E represents the end of the filling phase and the beginning of the isovolumic contraction phase. At this point, the pressure in the left ventricle increases above the pressure in the left atrium, causing the mitral valve to close. The retrograde flow of blood against the closed mitral valve produces the first heart sound. Systole is defined as the period between the first and second heart sounds and includes the isovolumic contraction and ejection phases. Aortic pressure continues to fall during the isovolumic contraction phase so that the rise in aortic blood pressure (which begins at point D) lags behind the beginning of systole. Point B represents the end of the ejection phase. At this point, the pressure in the left ventricle falls below the pressure in the aorta, and the aortic valve closes. The retrograde flow of blood against the closed aortic valve produces the second heart sound. Point A represents the end of the isovolumic relaxation phase and the beginning of the filling phase. At the point the pressure in the left ventricle falls below that in the left atrium, the mitral valve opens and blood begins to flow into the left ventricle.

304. The answer is e. (*Ganong*, pp 628–629.) At birth, with the onset of extrauterine respiration and elimination of the placental circulation, functional closure of the foramen ovale and the ductus venosus occur immediately, whereas functional closure of the ductus generally begins within a few hours after birth, and is not complete until about 48–72 hours. Immediately after birth, flow through the ductus switches, with blood flowing from the aorta to the pulmonary artery. The ductus arteriosus is a systemic blood vessel, and

thus it constricts in response to high oxygen tensions and dilates in response to hypoxemia (the opposite of the pulmonary vasculature). Ductal sensitivity to oxygen is age-dependent, however, and thus closure of the ductus arteriosus due to progressive constriction may be delayed in premature infants. Closure can be induced by infusion of cyclooxygenase inhibitors; drugs that inhibit both COX-1 and COX-2 have yielded the best results clinically.

305. The answer is b. (*Ganong, pp 78–84, 580–581. Kasper et al., pp 1470–1481.*) Smooth muscle contraction is regulated by a series of reactions that begins with the binding of calcium to calmodulin, in contrast to cardiac (and skeletal) muscle, where contraction is triggered by the binding of Ca^{2+} to troponin C, which by altering the position of tropomyosin on the thin filament, allows cross-bridge cycling to begin. The calcium-calmodulin complex in smooth muscle binds to and activates a protein kinase called myosin light chain kinase (MLCK), which catalyzes the phosphorylation of the myosin light chains (LC₂₀). Once these light chains are phosphorylated, myosin and actin interaction can occur and vascular smooth muscle shortens and develops tension. Although β -adrenergic receptor agonists may lower blood pressure by relaxing vascular smooth muscle, they also increase the rate and strength of the heart beat.

306. The answer is d. (*Ganong, pp 65–67. Kasper et al., p 1359.*) Titin is a large protein that connects the Z lines to the M lines, thereby providing a scaffold for the sarcomere. Titin contains two types of folded domains that provide muscle with its elasticity. The resistance to stretch increases throughout a contraction, which protects the structure of the sarcomere and prevents excess stretch.

307. The answer is c. (*Ganong, pp 577–582, 586–588.*) The energy imparted to the blood by ventricular systole is dissipated as the blood flows through the circulation. The greatest energy loss occurs where the resistance to blood flow is greatest. This would also be the site of the greatest pressure change. The arteriolar vessels produce the largest resistance to blood, and thus the greatest energy loss and pressure drop occur as the blood passes through them.

308. The answer is e. (*Ganong, pp 620–623.*) Blood flow through the coronary vessels of the left ventricle is determined by the ratio of perfusion pressure to vascular resistance. The perfusion pressure is directly related to the aortic pressure at the ostia of the coronaries. Myocardial

vascular resistance is significantly influenced by the contractile activity of the ventricle. During systole, when the ventricle is contracting, vascular resistance increases substantially. Flow is highest just at the beginning of diastole because, during this phase of the cardiac cycle, aortic pressure is still relatively high and vascular resistance is low due to the fact that the coronary vessels are no longer being squeezed by the contracting myocardium.

309. The answer is e. (*Kasper et al., p 1361.*) Phospholamban is a protein contained within the sarcoplasmic reticulum (SR) that inhibits the activity of the SR calcium pump. Inactivation of phospholamban results in an increase in calcium sequestration by the SR. Increasing the concentration of calcium within the SR increases the force of the ventricular contraction.

310. The answer is a. (*Ganong, pp 628–629. Kasper et al., p 2202.*) The fetus derives its oxygen from the maternal arterial blood supply by gas exchange across the placenta. The umbilical vein draining the placenta, therefore has the highest oxygenation in the fetus, with a PO₂ of ~30 mmHg and 80% oxygen saturation. The ductus venosus has only a slightly lower PO₂, and serves to direct much of the highly oxygenated blood from the umbilical vein to the inferior vena cava, bypassing the liver. From the right atrium, about two-thirds of the inferior venal caval flow (67% O₂ saturation) is diverted across the foramen ovale to the left atrium. The PO₂ in the left ventricular outflow tract going to the ascending aorta is ~25 mmHg. The PO₂ in the ductus arteriosus is ~18 mmHg, and blood in the descending aorta and umbilical arteries, is ~20 mmHg with an oxygen saturation of ~60%.

Gastrointestinal Physiology

Questions

311. A patient with diabetes mellitus presents with gastroesophageal reflux disease accompanying gastroparesis. Which of the following statements about gastric emptying is correct?

- a. Solids empty more rapidly than liquids
- b. Meals containing fat empty faster than carbohydrate-rich food
- c. Hyperosmolality of duodenal contents initiates a decrease in gastric emptying
- d. Acidification of the antrum increases gastric emptying
- e. Vagal stimulation decreases receptive relaxation in the upper portion of the stomach

312. A 27-year-old female medical student with irritable bowel syndrome (IBS) has an alteration in intestinal motility resulting in fluctuating constipation and diarrhea. Her condition has worsened in the past month as the date she has scheduled for her licensure examination approaches. Which of the following statements about small intestinal motility is correct?

- a. Contractile frequency is constant from duodenum to terminal ileum
- b. Peristalsis is the only contractile activity that occurs during feeding
- c. Migrating motor complexes occur during the digestive period
- d. Vagotomy abolishes contractile activity during the digestive period
- e. Contractile activity is initiated in response to bowel wall distention

313. An 18-year-old male with pernicious anemia lacks intrinsic factor, which is necessary for the absorption of cyanocobalamin. Vitamin B₁₂ is absorbed primarily in which portion of the GI tract?

- a. Stomach
- b. Duodenum
- c. Jejunum
- d. Ileum
- e. Colon

314. A 57-year-old man undergoes resection of the distal 100 cm of the terminal ileum as part of treatment for Crohn's disease. The patient likely will develop malabsorption of which of the following?

- a. Iron
- b. Folate
- c. Lactose
- d. Bile salts
- e. Protein

315. A 42-year-old salesman presents with the chief complaint of intermittent midepigastic pain that is relieved by antacids or eating. Gastric analysis reveals that basal and maximal acid output exceed normal values. The gastric acid hypersecretion can be explained by an increase in the plasma concentration of which of the following?

- a. Somatostatin
- b. Histamine
- c. Gastrin
- d. Secretin
- e. Enterogastrone

316. A 27-year-old female comes to the emergency room because of a 2-day bout of profuse watery diarrhea. Physical examination reveals dry lips and oropharynx. The patient is diagnosed with acute secretory diarrhea and dehydration, likely due to *Escherichia coli*. Which of the following sodium reabsorptive pathways is inhibited by the enterotoxin?

- a. Sodium-glucose-coupled cotransport
- b. Electroneutral NaCl transport
- c. Electrogenic sodium diffusion
- d. Sodium-hydrogen countertransport
- e. Sodium-bile salt cotransport

317. A 37-year-old male presents with dehydration and hypokalemic metabolic acidosis. This acid-base and electrolyte disorder can occur with excess fluid loss from which of the following organs?

- a. Stomach
- b. Ileum
- c. Colon
- d. Pancreas
- e. Liver

318. A 49-year-old man undergoes vagotomy for his peptic ulcer disease. As a result, which of the following gastrointestinal motor activities will be affected most?

- a. Secondary esophageal peristalsis
- b. Distention-induced intestinal segmentation
- c. Orad stomach accommodation
- d. Caudad stomach peristalsis
- e. Migrating motor complexes

319. A 35-year-old male smoker presents with burning epigastric pain that is most pronounced on an empty stomach. A paroxysmal rise in serum gastrin in response to intravenous secretin further supports a diagnosis of Zollinger-Ellison syndrome. Normally, basal acid output is increased by which of the following?

- a. Acidification of the antrum
- b. Administration of an H₂-receptor antagonist
- c. Vagotomy
- d. Alkalization of the antrum
- e. Acidification of the duodenum

320. A 42-year-old male develops a gastric carcinoma affecting the proximal third of his stomach. He is scheduled for a partial gastrectomy of the affected region, which will primarily affect which of the following processes?

- a. Accommodation
- b. Peristalsis
- c. Retropulsion
- d. Segmentation
- e. Trituration

321. A 68-year-old woman with rheumatoid arthritis, who has been taking nonsteroidal anti-inflammatory drugs (NSAIDS) for the past 10 years, complains of burning epigastric pain that is relieved by antacids, but worsened with food. Her doctor discontinues the NSAIDS and starts her on cimetidine. Which of the following is true regarding the pharmacological blockade of histamine H₂ receptors in the gastric mucosa?

- a. It inhibits both gastrin- and acetylcholine-mediated secretion of acid
- b. It inhibits gastrin-induced but not meal-stimulated secretion of acid
- c. It has no effect on either gastrin-induced or meal-stimulated secretion of acid
- d. It prevents activation of adenyl cyclase by gastrin
- e. It causes an increase in potassium transport by gastric parietal (oxyntic) cells

322. A 37-year-old male with AIDS presents with a fever, anorexia, weight loss, and GI bleeding. Physical examination reveals a palpable abdominal mass. Endoscopy and biopsy reveal a small-bowel malignancy, indicating surgical resection. Removal of proximal segments of the small intestine would most likely result in a decrease in which of the following?

- a. Basal acid output
- b. Maximal acid output
- c. Gastric emptying of liquids
- d. Gastric emptying of solids
- e. Pancreatic enzyme secretion

323. A 63-year-old female is diagnosed with an intractable duodenal ulcer. After consultation with a surgeon, it is recommended that she undergoes a parietal cell vagotomy. Subsequently the patient experiences nausea and vomiting after ingestion of a mixed meal. Which of the following best explains her symptoms?

- a. Increased gastric emptying of solids
- b. Decreased gastric emptying of solids
- c. Increased gastric emptying of liquids
- d. Decreased gastric emptying of liquids
- e. Increased emptying of liquids and solids

324. A 17-year-old male who is being treated with the macrolide antibiotic erythromycin complains of nausea, intestinal cramping, and diarrhea. The side effects are the result of the antibiotic binding to receptors on GI tract enteric nerves and smooth-muscle cells that recognize which gastrointestinal hormone?

- a. Gastrin
- b. Secretin
- c. Cholecystokinin
- d. Motilin
- e. Enterogastrone

325. A 23-year-old woman complains of abdominal cramps and bloating that are relieved by defecation. Subsequent clinical evaluation reveals an increased maximal acid output, decreased serum calcium and iron concentrations, and microcytic anemia. Inflammation in which area of the GI tract best explains these findings?

- a. Stomach
- b. Duodenum

- c. Jejunum
- d. Ileum
- e. Colon

326. Gastric emptying studies performed on a 49-year-old female reveal a time to one-half emptying of liquids of 18 min (normal <20 min) and a time to one-half emptying of solids to be 150 min (normal <120 min). Which of the following best explains the data?

- a. Increased amplitude of antral contractions
- b. Decreased orad stomach compliance
- c. Pyloric stenosis
- d. Sectioning of the vagus nerves to the stomach
- e. Inflammation of the proximal small intestine

327. A 57-year-old female undergoes resection of the terminal ileum as part of treatment for her chronic inflammatory bowel disease. Removal of the terminal ileum will most likely result in which of the following?

- a. Increased bile acid concentration in the enterohepatic circulation
- b. Decreased glucose absorption
- c. Increased water content of the feces
- d. Decreased fat absorption
- e. Increased fat absorption

328. A 67-year-old male with a history of alcohol abuse presents to the emergency room with severe epigastric pain, hypotension, abdominal distension, and diarrhea with steatorrhea. Serum amylase and lipase are found to be greater than normal, leading to a diagnosis of pancreatitis. The steatorrhea can be accounted for by a decrease in the intraluminal concentration of which of the following pancreatic enzymes?

- a. Amylase
- b. Trypsin
- c. Chymotrypsin
- d. Lipase
- e. Colipase

329. A 53-year-old male complains of a mild chronic cough and heartburn. Esophageal manometric and endoscopic evaluation reveal a hypotensive lower esophageal sphincter (LES) pressure and mild gastroesophageal reflux. Which of the following is the primary genesis of LES pressure in adults?

- a. Tonic excitatory sympathetic nerve input to the smooth muscle
- b. Tonic excitatory parasympathetic nerve input to the smooth muscle
- c. Circulating gastrin
- d. Myogenic properties of LES smooth muscle
- e. Local production of nitric oxide by enteric nerves

330. A patient presents with a chronic cough. The history and physical findings rule out postnasal drip, asthma, and other pulmonary disease. Upon questioning, the patient also reports substernal burning pain that is most pronounced after ingestion of coffee, chocolate, french fries, and alcohol. Which of the following is the most likely cause of gastroesophageal reflux disease (GERD) in this patient?

- a. Delayed gastric emptying
- b. Decreased esophageal motility
- c. Hiatal hernia
- d. Decreased lower esophageal sphincter tone
- e. Decreased upper esophageal sphincter tone

331. A 42-year-old male is referred to a gastroenterologist for evaluation of refractory peptic ulcer disease. Subsequent endoscopic and laboratory data are suggestive of Zollinger-Ellison syndrome. The increased basal acid output and maximal acid output of the patient is best explained by an increase in the plasma concentration of which of the following?

- a. Gastrin-releasing peptide
- b. Secretin
- c. Somatostatin
- d. Gastrin
- e. Histamine

332. A 63-year-old woman presents with diarrhea, abdominal pain, and flushing. The urinary excretion of the serotonin metabolite, 5-hydroxyindoleacetic acid (5-HIAA) is elevated. Abdominal CT reveals a tumor in the terminal ileum. Surgical resection of the terminal ileum will most likely result in which of the following?

- a. A decrease in absorption of amino acids
- b. An increase in the water content of the feces

- c. An increase in the concentration of bile acid in the enterohepatic circulation
- d. A decrease in the fat content of the feces
- e. An increase in the absorption of iron

333. Which of the following vitamins is both synthesized by intestinal bacteria and absorbed in significant quantities?

- a. Vitamin B₆
- b. Vitamin K
- c. Thiamine
- d. Riboflavin
- e. Folic acid

334. A 70-year old woman presents with abdominal pain, microcytic anemia, and weight loss. Colonoscopy with biopsy confirms colon cancer. Which of the following statements about the colon is correct?

- a. Absorption of Na⁺ in the colon is under hormonal (aldosterone) control
- b. Bile acids enhance absorption of water from the colon
- c. Net absorption of HCO₃⁻ occurs in the colon
- d. Net absorption of K⁺ occurs in the colon
- e. The luminal potential in the colon is positive

335. A patient's abdominal pain is subdued after eating. Which of the following is true regarding contraction of the gallbladder following a meal?

- a. It is inhibited by a fat-rich meal
- b. It is inhibited by the presence of amino acids in the duodenum
- c. It is stimulated by atropine
- d. It occurs in response to cholecystokinin
- e. It occurs simultaneously with the contraction of the sphincter of Oddi

336. A 42-year-old airline pilot presents to his family physician with a chief complaint of midepigastric pain that is relieved by antacids or eating. Endoscopic evaluation reveals the presence of a duodenal ulcer. Based on the diagnosis, which of the following also would be expected?

- a. Decreased basal acid output
- b. Increased maximal acid output
- c. Decreased gastric emptying of liquids
- d. Increased frequency of antral contractions
- e. Decreased orad stomach compliance

337. A 26-year-old male presents to the emergency room with a 48-hour bout of diarrhea with steatorrhea. Which of the following best accounts for the appearance of excess fat in the stool?

- a. Decreased bile salt pool size
- b. Delayed gastric emptying
- c. Decreased gastric acid secretion
- d. Decreased secretion of intrinsic factor
- e. Decreased gastric accommodation

338. A 43-year-old female presents with chief complaints of bulky and frequent diarrhea and weight loss. She experiences recurrent episodes of abdominal distension terminated by passage of stools. Laboratory data reveals a microcytic anemia, decreased serum calcium, and decreased serum albumin. After additional tests she is diagnosed with gluten-sensitive enteropathy. Her generalized decrease in intestinal absorption can be attributed to which of the following?

- a. Decreased intestinal motility
- b. Increased migrating motor complexes
- c. Decreased intestinal surface area
- d. Increased enterohepatic circulation of bile
- e. Decreased gastric emptying

339. A 32-year-old woman presents to the Emergency Department with abdominal pain and diarrhea accompanied by steatorrhea. Gastric analysis reveals a basal acid output (12 mmol/h) greater than normal (<5 mmol/h). The steatorrhea is most likely due to which of the following?

- a. Inactivation of pancreatic lipase due to low duodenal pH
- b. Delayed gastric emptying
- c. Decreased gastric acid secretion
- d. Decreased secretion of intrinsic factor
- e. Decreased pyloric sphincter tone

340. A patient presents with severe inflammation of the ileum. Clinical findings include which of the following?

- a. Increased vitamin B₁₂ absorption
- b. Decreased bile acid pool size
- c. Increased colon absorption of water
- d. Decreased release of secretin
- e. Increased absorption of dietary fats

341. A patient undergoes surgery for their GI symptoms. Which of the following procedures may result in nausea and a sense of early satiety?

- a. Surgical resection of the proximal small bowel
- b. A vagotomy of the distal stomach
- c. Surgical resection of the proximal stomach
- d. Surgical removal of the gastric antrum
- e. A vagotomy of the orad stomach

342. A patient with peptic ulcer disease is taken off their medication because of undesirable side effects. As a result, the patient has rebound gastric acid hypersecretion. Which of the following drugs best accounts for the observed result?

- a. An H₁-receptor antagonist
- b. A proton pump inhibitor
- c. A cholinergic receptor antagonist
- d. An antacid
- e. A CCKB receptor antagonist

343. A 49-year-old female is referred to surgery for removal of a tumor from the fundic region of the stomach. Resection of the fundus will likely result in which of the following outcomes?

- a. A decrease in the contractile frequency of the stomach
- b. An increase in the gastric emptying rate of liquids
- c. A decrease in the gastric emptying of solids
- d. An increase in maximal acid output
- e. A decreased gastrin release in response to ingestion of a meal

344. An 18-year-old college student reports that she experiences severe abdominal bloating and diarrhea within 1 hour of consuming dairy products. A subsequent H₂-breath test is abnormal. The diarrhea and bloating can best be explained by which of the following?

- a. A deficiency in the brush border enzyme lactase
- b. Carbohydrate-induced secretory diarrhea
- c. Decreased intestinal surface area
- d. Decreased carbohydrate absorption
- e. A decrease in exocrine pancreatic secretion

345. A 31-year-old male presents to the Emergency Department with the symptoms of heartburn and difficulty swallowing. Esophageal manometry reveals an inflamed esophageal mucosa and a hypotensive lower esophageal sphincter. A diagnosis of gastroesophageal reflux disease is made and the patient is subsequently treated with an H₂-receptor antagonist. Normally, which of the following is true regarding reflux of gastric acid into the esophagus?

- a. It initiates primary esophageal peristalsis
- b. It inhibits gastric acid secretion
- c. It initiates secondary esophageal peristalsis
- d. It inhibits esophageal bicarbonate secretion
- e. It inhibits gastric motility

346. A 42-year-old obese female presents to the Emergency Department with right upper quadrant pain, nausea, and vomiting. The pain is not related to food intake and lasts for several hours before resolving slowly. Ultrasound images are suggestive of gallstones with cystic duct obstruction. Which of the following is the primary physiological stimulus of gallbladder contraction in the digestive period?

- a. Acid-induced release of secretin from the small intestine
- b. Fat-induced release of cholecystokinin from the small intestine
- c. Calorie-induced release of enterogastrone from the small intestine
- d. Distension-induced release of glucagon from the small intestine
- e. Amino acid-induced release of motilin from the small intestine

347. A 20-year-old female presents with symptomatic hyperglycemia, and a diagnostic work-up confirms Type I diabetes mellitus. The patient is started on regular insulin. The metabolic effects of insulin include which of the following?

- a. Decreased glucose utilization
- b. Decreased lipolysis
- c. Increased proteolysis
- d. Increased gluconeogenesis
- e. Increased ketogenesis

348. A 56-year-old male presents with postprandial diarrhea persisting since an ileal resection. The gastric surgeon suspects bile acid malabsorption. Which of the following statements about bile acids is correct?

- a. They are essentially water-insoluble
- b. The majority of bile acids is absorbed by passive diffusion
- c. Glycine conjugates are more soluble than taurine conjugates

- d. The amount lost in the stool each day represents the daily loss of cholesterol
- e. The bile acid-dependent fraction of bile is stimulated by the hormone secretin

349. A 14-year-old female ballerina reports that she has chronic diarrhea. A detailed history reveals that she frequently drinks skim milk, that she does not use laxatives, and that she has noticed that her condition improves during times that she fasts for religious observances. In contrast to secretory diarrhea, which of the following is correct regarding osmotic diarrhea?

- a. It is characterized by an increase in the stool osmotic gap
- b. It is the result of increased crypt cell secretion
- c. It is the result of decreased electroneutral sodium absorption
- d. It is caused by bacterial toxins
- e. It occurs only in the colon

350. A newborn with severe diarrhea is found to have an inherited defect in a glucose transporter resulting in glucose/galactose malabsorption, necessitating a glucose- and galactose-free diet. Which of the following is the transport protein responsible for entry of glucose into the intestinal enterocyte?

- a. Glut-2
- b. Glut-5
- c. SGLT 1
- d. SGLT 2
- e. SGLT 5

351. An 83-year-old woman with constipation is prescribed a high-fiber diet, which leads to an increased production of short-chain fatty acids (SCFAs). SCFA absorption occurs almost exclusively from which of the following segments of the GI tract?

- a. Stomach
- b. Duodenum
- c. Jejunum
- d. Ileum
- e. Colon

352. Which of the following statements about medium-chain fatty acids is correct?

- a. They are more water-soluble than long-chain fatty acids.
- b. Within the enterocyte, they are used for triglyceride resynthesis
- c. They are packaged into chylomicrons
- d. They are transported in the lymph
- e. They require emulsification prior to enterocyte uptake

353. A 47-year-old woman with hypermenorrhea develops an iron-deficiency anemia requiring iron supplements. Which of the following statements is correct regarding iron digestion and absorption?

- a. About 100 mg of iron is absorbed per day
- b. Iron is absorbed rapidly from the small intestine
- c. Iron is transported in the blood bound to transferrin
- d. In general, iron must be oxidized from the ferrous to the ferric state for efficient absorption
- e. Iron is transported into enterocytes by a ferroportin transporter on the apical membrane

354. A patient with alcoholic cirrhosis comes in vomiting blood. After stabilizing him with IV fluids, the next step should be administration of an agonist/analog of which of the following agents to inhibit gastric acid secretion and visceral blood flow?

- a. Gastrin
- b. Somatostatin
- c. Histamine
- d. Pepsin
- e. Acetylcholine

355. A 56-year-old man presents with weight loss, cough, and diffuse chest pain. A chest x-ray reveals normal heart and lungs, but the radiologist detects a “bird’s beak” narrowing of the terminal esophagus, which is also seen with a barium swallow. Follow-up history indicates that the patient also has dysphagia and regurgitation. Manometry shows increased lower esophageal sphincter (LES) pressure with no relaxation upon swallowing, indicating a diagnosis of achalasia. Which of the following is the putative inhibitory neurotransmitter responsible for relaxation of gastrointestinal smooth muscle?

- a. Dopamine
- b. Vasoactive intestinal peptide
- c. Somatostatin
- d. Substance P
- e. Acetylcholine

356. A patient has vomiting and severe watery diarrhea after eating spoiled shellfish. Intravenous fluid and electrolyte replacement was started, and a stool specimen was taken, which came back positive for *Vibrio cholerae*. Which of the following statements best describes water and electrolyte absorption in the GI tract?

- a. Most water and electrolytes come from ingested fluids
- b. The small intestine and colon have similar absorptive capacities
- c. Osmotic equilibration of chyme occurs in the stomach
- d. The majority of absorption occurs in the jejunum
- e. Cholera toxin inhibits sodium-coupled nutrient transport

357. After secretion of trypsinogen into the duodenum, the enzyme is converted into its active form, trypsin, by which of the following?

- a. Enteropeptidase
- b. Procarboxypeptidase
- c. Pancreatic lipase
- d. Chymotrypsin
- e. An alkaline pH

358. A patient with cirrhosis undergoes a total colectomy. Removal of the entire colon would be expected to cause which of the following?

- a. Decreased urinary urobilinogen
- b. An increase in blood ammonia
- c. Megaloblastic anemia
- d. Severe malnutrition
- e. Death

359. An 18-year-old female decides to get a tattoo for her birthday. Two months later she presents with a fever, right upper quadrant pain, nausea, vomiting, and jaundice. Which of the following lab values would most likely be found in a patient with infectious hepatitis?

- a. An increase in plasma alkaline phosphatase
- b. An increase in plasma bile acids
- c. An increase in both direct and indirect plasma bilirubin
- d. An increase in direct bilirubin, and a decrease in indirect bilirubin in the plasma
- e. An decrease in both direct and indirect plasma bilirubin

360. A patient presents with a chief complaint of flatulence. Gas within the colon is primarily derived from which of the following sources?

- a. CO_2 liberated by the interaction of HCO_3^- and H^+
- b. Diffusion from the blood
- c. Fermentation of undigested oligosaccharides by bacteria
- d. Swallowed atmospheric air
- e. Air pockets within foodstuffs

361. Nearly all binding of cobalamin (vitamin B₁₂) to intrinsic factor occurs in which of the following organs?

- a. Stomach
- b. Duodenum
- c. Jejunum
- d. Ileum
- e. Colon

362. The rate of gastric emptying increases with an increase in which of the following?

- a. Intragastric volume
- b. Intraduodenal volume
- c. Fat content of duodenum
- d. Osmolality of duodenum
- e. Acidity of duodenum

363. Following an anastomosis of the jejunum to the stomach, a patient presents with discomfort after meals, including weakness, dizziness, and sweating. The symptoms of dumping syndrome are caused in part by which of the following?

- a. Increased blood pressure
- b. Increased secretion of glucagon
- c. Increased secretion of cholecystokinin
- d. Hypoglycemia
- e. Hyperglycemia

364. A 52-year-old woman who has been dieting for several weeks breaks down and eats half a pan of frosted brownies. Insulin secretion following a carbohydrate-rich meal is stimulated by which of the following?

- a. Gastrin
- b. Cholecystokinin (CCK)
- c. Serotonin
- d. VIP
- e. GLP-1 (7-36) amide

365. A new mother calls the pediatrician because she is concerned that her infant defecates after every meal. Which of the following is the cause of these normal bowel movements in newborns?

- a. The gastroileal reflex
- b. The gastrocolic reflex

- c. The intestino-intestinal reflex
- d. The defecation reflex
- e. Peristaltic rushes

366. A 10-year-old boy presents with below average body weight and height, signs of vitamin K deficiency, steatorrhea, and bloating. He is found to have the MHC class II antigen HLA-DQ2. Which of the following is the most appropriate dietary treatment for malabsorption in this condition?

- a. Fat-free diet
- b. Lactose-free diet
- c. Gluten-free diet
- d. High-fiber diet
- e. Low salt diet

367. A patient is found to have elevated levels of direct-acting plasma bilirubin. Which of the following is the most likely diagnosis?

- a. Tropical sprue
- b. Terminal ileal bypass
- c. Pancreatitis
- d. Obstruction of the common bile duct
- e. Bile reflux gastropathy

368. Which of the following is the major mechanism for absorption of sodium from the small intestine?

- a. $\text{Na}^+ - \text{H}^+$ exchange
- b. Cotransport with potassium
- c. Electrogenic transport
- d. Neutral NaCl absorption
- e. Solvent drag

369. A morbidly obese male presents with hypertension, hyperlipidemia, and Type II diabetes mellitus. Dietary fat, after being processed, is extruded from the mucosal cells of the gastrointestinal tract into the lymphatic ducts in the form of which of the following?

- a. Monoglycerides
- b. Diglycerides
- c. Triglycerides
- d. Chylomicrons
- e. Free fatty acids

370. Absorption of fat-soluble vitamins requires which of the following?

- a. Intrinsic factor
- b. Chymotrypsin
- c. Pancreatic lipase
- d. Pancreatic amylase
- e. Secretin

371. A 33-year-old female, who has been taking large doses of NSAIDs for her menstrual cramps, presents with burning epigastric pain. The pain improves after eating a meal, suggesting a duodenal versus a gastric ulcer. Which of the following is the major factor that protects the duodenal mucosa from damage by gastric acid?

- a. Pancreatic bicarbonate secretion
- b. The endogenous mucosal barrier of the duodenum
- c. Duodenal bicarbonate secretion
- d. Hepatic bicarbonate secretion
- e. Bicarbonate contained in bile

Gastrointestinal Physiology

Answers

311. The answer is c. (*Ganong, pp 480–482, 494–496. Kasper et al., pp 220–221, 1726, 2166. Stead et al., pp 109–110. Widmaier et al., pp 597–599.*) Gastroparesis is delayed emptying of food from the stomach, and is a common cause of gastroesophageal reflux disease (GERD). The rate of gastric emptying depends upon neural (enterogastric reflex) and hormonal inhibitory feedback from the proximal small bowel. Gastroparesis is common in diabetes mellitus because hyperosmolality of the duodenum initiates a decrease in gastric emptying, which is probably neural in origin and is sensed by duodenal osmoreceptors. Because solids must be liquefied prior to emptying from the stomach, the gastric emptying of liquids begins before the emptying of solids. Emptying is fastest with a carbohydrate meal, and slowest after a fatty meal. Acid in the antrum inhibits gastrin secretion, which may inhibit gastric motility. The vagus mediates receptive relaxation, the process in which the fundus and upper portion of the body of the stomach relax in response to movement in the pharynx and esophagus in order to accommodate food that enters the stomach.

312. The answer is e. (*Ganong, pp 480–482, 506–507.*) Contractile activity in the small intestine is initiated in response to distention of the bowel wall. Three types of smooth muscle contractions contribute to small intestinal motility—peristalsis, segmental contractions, and tonic contractions. A fourth type of contraction, peristaltic rushes, are very intense peristaltic waves that may occur in intestinal obstruction. The basal electrical rhythm (BER) are the spontaneous rhythmic fluctuations in membrane potential in the smooth muscle along the GI tract. The BER itself rarely causes muscle contraction, but contractions only occur during the depolarizing phase of BERs, which function to coordinate the various types of contractile activity. The BER is initiated by the interstitial cells of Cajal, which, in the small intestine, are located in the outer circular muscle layer near the myenteric plexus. There are an average of ~12 BER cycles/min in the duodenum and proximal jejunum and 8/min in the distal ileum. During

fasting between periods of digestion, cycles of motor activity, called migrating motor complexes (MMC), migrate from the stomach to the distal ileum. The MMCs immediately stop with ingestion of food. After vagotomy, contractile activity becomes irregular and chaotic.

313. The answer is d. (*Ganong, pp 313, 315, 477, 496. Kasper et al., pp 602–604. Stead et al., pp 150–151.*) Most vitamins are absorbed in the upper small intestine, but vitamin B₁₂ (cobalamin) is absorbed primarily in the terminal ileum. In the stomach, vitamin B₁₂ binds with intrinsic factor, a glycoprotein secreted by the parietal cells of the gastric mucosa. The vitamin B₁₂-intrinsic factor complex is emptied from the stomach and propelled along the small intestine to the terminal ileum, where specific active transporters located on the enterocyte microvilli bind the vitamin B₁₂-intrinsic factor complex and the complex is absorbed across the ileal mucosa. Pernicious anemia is a disease in which there is autoimmune destruction of the parietal cells. Vitamin B₁₂ can also be produced by gastrectomy with removal of the intrinsic factor-secreting tissue or by diseases of the terminal ileum. Binding of the Vitamin B₁₂-intrinsic factor complex requires Ca²⁺. Whereas vitamin B₁₂ and folate absorption are Na⁺-independent, all seven of the other water-soluble vitamins are absorbed by carriers that are Na⁺ cotransporters.

314. The answer is d. (*Ganong, pp 474–475, 507.*) The terminal ileum contains specialized cells responsible for the absorption of primary and secondary bile salts by active transport. Bile salts are necessary for adequate digestion and absorption of fat. Resection of the ileum prevents the absorption of bile acids, which leads to steatorhea. In addition, diarrhea results because the unabsorbed bile acids enter the colon where they increase adenylate cyclase activity, thus promoting the secretion of water into the lumen of the colon causing an increase in the water content of the feces. Distal small bowel resection causes a greater degree of malabsorption than removal of the same length of proximal bowel.

315. The answer is c. (*Ganong, pp 484–496.*) Increases in basal and maximal acid output are suggestive of inflammation or removal of the proximal small intestine. Intestinal receptors monitor the composition of chyme and elicit feedback mechanisms that regulate gastric acid secretion and gastric emptying. Absence of feedback leads to an increased presence of excitatory mediators of gastric function. Gastrin is the primary stimulus of meal-induced acid secretion by the parietal cells. Somatostatin (paracrine),

secretin (endocrine), and enterogastrone (endocrine) inhibit gastric acid secretion by the parietal cells. Histamine is an excitatory paracrine mediator of parietal cell acid secretion.

316. The answer is b. (*Ganong, p 512. Stead et al., pp 139–141.*) Diarrhea is the abnormal passage of fluid or semisolid stool with increased frequency. The general approach to the primary evaluation of patients with diarrhea is differentiating between an infectious versus noninfectious etiology. Although sodium is absorbed from the small intestine by several mechanisms, bacterial toxins specifically inhibit neutral NaCl absorption. In addition, the toxins augment diarrhea by increasing salt and water secretion by intestinal crypt cells. Oral rehydration involves utilizing the sodium-glucose-coupled cotransport pathway.

317. The answer is c. (*Ganong, pp 475–477, 491–492. Kasper et al., pp 263–268.*) Loss of gastric juice results in hypokalemic, metabolic alkalosis. Excessive loss of fluid from the gastrointestinal tract can lead to dehydration and, depending on the origin of the fluid loss, electrolyte and acid-base disturbances. The hydrogen ion and potassium ion concentration of gastric juice exceeds that of the plasma. As a result, excess fluid loss leads to metabolic alkalosis accompanied by hypokalemia. Because the pancreas, liver, ileum, and colon secrete bicarbonate, excessive loss leads to metabolic acidosis. In addition, the colon secretes potassium. Thus, the acidosis is accompanied by hypokalemia.

318. The answer is c. (*Ganong, pp 494–495.*) Orad stomach accommodation depends exclusively on an intact vago-vagal reflex. Vagal innervation of the gastrointestinal tract extends from the esophagus to the level of the transverse colon. Preganglionic fibers from cell bodies in the medulla synapse with ganglion cells located in the enteric nervous system. Distention-induced contraction of gastrointestinal smooth muscle develops as the result of long (vago-vagal) and local (enteric nerves) reflexes. The importance of long versus local reflex pathways varies along the gut. Secondary esophageal peristalsis, intestinal segmentation, and migrating motor complexes are unaffected by vagotomy, whereas caudad stomach peristalsis is decreased but not abolished by vagotomy.

319. The answer is d. (*Ganong, pp 484–488, 494–496.*) Alkalization of the antrum releases the gastrin-containing cells from the inhibitory influences of somatostatin and increases acid secretion. Acidification of the

antrum promotes the release of somatostatin from D cells in the gastrointestinal mucosa, which inhibits gastrin release and gastric acid secretion. Acidification of the duodenum elicits inhibitory neural and hormonal reflexes that also inhibit acid output. Administration of a histamine antagonist reduces acid secretion by decreasing the stimulatory effect of histamine.

320. The answer is a. (*Ganong*, pp 480, 494, 506.) Increases in intragastric volume normally are not associated with large increases in intragastric pressure because of distention-mediated activation of a vago-vagal inhibitory reflex, called receptive relaxation or the accommodation reflex. The reflex, which is abolished by vagotomy, is a property of the orad stomach only and counterbalances the stretch-induced myogenic contraction of the gastric smooth muscle. Peristalsis, trituration (grinding), and retropulsion (mixing) are terms referring to the contractile activity and functions of the caudad stomach. Segmental contractions are the primary contractile pattern of the small intestine during the digestive period.

321. The answer is a. (*Ganong*, pp 493–496.) Histamine (H_2) receptor antagonists inhibit both gastrin-induced and vagal-mediated secretion of acid. Secretion of acid by gastric parietal (oxyntic) cells involves stimulation of adenyl cyclase and cyclic AMP-mediated stimulation of the active transport of chloride and potassium-hydrogen ion exchange. Neither gastrin nor vagal stimulation activates adenyl cyclase directly; both depend on concomitant release of histamine and histamine-induced activation of adenyl cyclase.

322. The answer is e. (*Kasper et al.*, pp 531–532.) Inflammation or removal of the upper small intestine leads to a decrease in pancreatic and hepatobiliary function. The proximal small intestine contains a number of “receptors” that monitor the physical (volume) and chemical (pH, fat content, caloric density, osmolality) composition of the chyme emptied from the stomach. Stimulation of these receptors releases secretin, which acts on pancreatic ductal cells to increase HCO_3^- secretion, as well as cholecystokinin, which acts on pancreatic acinar cells to increase pancreatic enzyme secretion (lipases, amylases, and proteases). Stimulation of proximal small intestine receptors also activates neural reflexes, which initiate pancreatic enzyme and bicarbonate secretion, stimulate gallbladder emptying, and provide feedback for inhibitory regulation of gastric function (enterogastrone, enterogastric reflex). Removal of these reflexes decreases pancreatic

secretion and gallbladder emptying and increases gastric emptying and acid output.

323. The answer is b. (*Ganong*, p 494.) The vagus nerve is the primary neural mediator of gastric function. Activation of distension-mediated vago-vagal reflexes in response to the presence of food in the stomach will (1) increase gastric compliance (receptive relaxation or accommodation reflex) and promote gastric retention of food, (2) increase the strength of antral peristaltic contractions necessary for trituration of solids, and (3) increase gastric acid secretion. Sectioning of the vagus nerve fibers to the antral region of the stomach will decrease the strength of contractions thereby prolonging the emptying of solids. The emptying of liquids will be unaffected.

324. The answer is d. (*Ganong*, pp 96, 483–487.) Motilin is the gastrointestinal peptide hormone associated with the initiation of migrating motor complexes during the interdigestive period. The hormone stimulates increased contractions by a direct action on smooth muscle and by activation of excitatory enteric nerves. Erythromycin belongs to the group of macrolide antibiotics and also shows an ability to excite motilin-like receptors on enteric nerves and smooth muscle. As a result, a common side effect of the antibiotic is abdominal cramping and diarrhea.

325. The answer is b. (*Ganong*, pp 484, 496, 504–505. *Stead et al.*, pp 149–154.) Inflammation of the duodenum may lead to increased acid output, hypocalcemia, and microcytic anemia. Increased basal and maximal acid outputs may result from excessive stimulation of the parietal cell (e.g., hypergastrinemia) or reduced inhibitory feedback (i.e., reduced effect of enterogastrone and the enterogastric reflex). The latter may occur when the proximal small intestine is inflamed. Although calcium is absorbed along the entire length of the small intestine, it is absorbed primarily in the duodenum. Similarly, iron is absorbed primarily in the duodenum. Microcytic anemia is the result of reduced stores of iron, the most common anemia. Glucose-6-phosphatase deficiency is the most common metabolic disorder of red blood cells, and is also associated with a microcytic anemia, as is α -thalassemia.

326. The answer is c. (*Ganong*, pp 494–495.) The emptying of solids from the stomach is determined by the strength of antral peristaltic contractions and the resistance offered by the pyloric sphincter. Either a decrease in the

amplitude of the antral contractions or an increase in sphincter resistance will delay the emptying of solids from the stomach. Liquid emptying is regulated by the proximal stomach and is primarily a function of the difference between the intragastric pressure and the intraduodenal pressure.

327. The answer is c. (*Ganong*, pp 474–475, 507.) Removal of the terminal ileum can lead to diarrhea and steatorrhea. The terminal ileum contains specialized cells responsible for the absorption of primary and secondary bile salts by active transport. Bile salts are necessary for adequate digestion and absorption of fat. In the absence of the terminal ileum there will be an increase in the amounts of bile acids and fatty acids delivered to the colon. Fats and bile salts in the colon increase the water content of the feces by promoting the influx (secretion) of water into the lumen of the colon.

328. The answer is d. (*Ganong*, pp 473–475.) The process of fat digestion begins in the stomach and is completed in the proximal small intestine, predominately by enzymes synthesized and secreted by the pancreatic acinar cells. The major lipolytic pancreatic enzyme is the carboxylic esterase, known as lipase. Full activity requires the protein cofactor colipase, as well as an alkaline pH, bile salts, and fatty acids.

329. The answer is d. (*Stead et al.*, pp 109–110.) The lower esophageal sphincter is a high-pressure zone that exists between the esophageal body and the gastric fundus. The high pressure limits reflux of gastric contents into the esophageal body. Although excitatory vagal input contributes to the high-pressure zone, the principal determinant is intrinsic (myogenic) properties of the circular smooth muscle of the sphincter. Excess acid in the esophagus creates the pain sensation referred to as heartburn.

330. The answer is d. (*Ganong*, pp 232, 489–490. *Kasper et al.*, pp 205–207, 222–224, 1742–1743. *Stead et al.*, pp 109–110. *Widmaier et al.*, pp 593.) Delayed gastric emptying, hiatal hernia, and decreased esophageal motility are all causes of GERD, but the most likely cause of GERD in this patient is a relaxed or incompetent lower esophageal sphincter (LES), which allows the gastric contents to reflux into the esophagus. The hydrochloric acid from the stomach irritates the esophageal walls, producing the substernal pain of indigestion, called heartburn. Causes of decreased LES tone include alcohol, cigarettes, coffee (caffeine), and chocolate, as well as certain drugs (nitrates and calcium channel blockers) and hormones (estrogen and progesterone). The LES is comprised of smooth muscle at the junction of the

esophagus and the stomach. The upper esophageal sphincter is located between the pharynx and the esophagus and is comprised of skeletal muscle.

331. The answer is d. (*Kasper et al.*, pp 222, 1758–1760, 2222–2233. *Stead et al.*, pp 111–113, 233.) Zollinger-Ellison (ZE) has a triad of peptic ulcer disease, gastric acid hypersecretion, and an elevated gastrin level. In ZE, a pancreatic acinar cell adenoma (gastrinoma) is the site for the synthesis and secretion of large amounts of gastrin. Unlike gastrin released from the antrum in response to normal physiological stimuli, the pancreatic release of gastrin from the pancreas is not under physiological control, that is, intestinal feedback and gastric pH. ZE can be part of a multiple endocrine tumor (MEN I). Proton pump inhibitors (omeprazole, lansoprazole) are the treatment of choice for peptic ulcer disease in ZE, and have decreased the need for total gastrectomy.

332. The answer is b. (*Ganong*, pp 505–506. *Kasper et al.*, pp 2220–2226.) Removal of the terminal ileum can lead to diarrhea and steatorrhea. The terminal ileum contains specialized cells responsible for the absorption of primary and secondary bile salts by active transport. Bile salts are necessary for adequate digestion and absorption of fat. In the absence of the terminal ileum there will be an increase in the amounts of bile acids and fatty acids delivered to the colon. Fats and bile salts in the colon increase the water content of the feces by promoting the influx (secretion) of water into the lumen of the colon. Amino acids are absorbed in the jejunum. Iron is primarily absorbed in the duodenum. Gastrointestinal neuroendocrine tumors are derived from the diffuse neuroendocrine system of the GI tract, which is composed of amine- and acid-producing cells with different hormonal profiles, depending on the site of origin. The tumors they produce are generally divided into carcinoid tumors (ectodermal stem cells) and pancreatic endocrine tumors. One third of all primary gut tumors are carcinoid. Carcinoid tumors are frequently classified according to their anatomic area of origin (foregut, midgut, hindgut). Small intestinal (midgut) carcinoid tumors arise from the argentafin cells of the crypts of Lieberkühn in the terminal ileum, and have a high serotonin content. Small intestinal carcinoids are the most common cause of the carcinoid syndrome (classic triad: cutaneous flushing, diarrhea, bronchospasm, right heart valvular lesions), which is manifest when they metastasize, but only occurs in 5 to 10% of carcinoid tumors.

333. The answer is e. (*Ganong*, pp 477–478.) Folic acid is both produced in the intestine and absorbed from the intestine. In humans, several vitamins,

including vitamin K, several of the B complex, and folic acid, are synthesized by intestinal bacteria. However, only folic acid is absorbed by the host. Dietary intake of the other vitamins is necessary.

334. The answer is a. (*Ganong, pp 475–477.*) Both the absorption of Na^+ and secretion of K^+ from the colon are affected by changes in circulating levels of aldosterone. The major route of absorption of sodium in the colon is electrogenic transport. Because of the “tight” nature of the tight junctions that connect cells in the colon, a relatively large potential difference exists between the mucosal (negative) and serosal (positive) surfaces of the absorptive cells. This electrical difference favors the net secretion of K^+ into the lumen. Secretion of HCO_3^- occurs in exchange for absorption of Cl^- . No counterbalancing cation exchange pumps are present in the colon.

335. The answer is d. (*Ganong, pp 483–487, 500–503.*) Cholecystokinin is released from the upper small intestine in response to partially hydrolyzed dietary lipids and proteins and promotes gallbladder emptying. Gallbladder contraction and sphincter of Oddi relaxation are necessary for delivery of bile into the duodenum. These muscular actions are under both hormonal and neural control. Cholecystokinin contracts gallbladder smooth muscle by a direct action on the muscle and through activation of vagal afferent fibers leading to a vago-vagal reflex. Relaxation of sphincter of Oddi smooth muscle occurs via activation of inhibitory enteric nerves. Gallbladder contraction is also promoted by vagal stimulation, which is cholinergically mediated and blocked by the muscarinic receptor antagonist, atropine.

336. The answer is b. (*Ganong, pp 504–508.*) Inflammation of the proximal small intestine results in a decrease in the feedback regulation of gastric function by reducing the input of the enterogastric reflex and enterogastrone to gastric emptying and gastric acid secretion. Absent inhibitory input, basal and maximal acid output are increased, and the gastric emptying of liquids and solids is increased.

337. The answer is a. (*Ganong, pp 474–475, 507.*) Steatorrhea is defined as excess loss of fat in the stool. Numerous pathophysiological situations can cause the loss of excess fat in the stool including a decrease in bile acid pool size, inactivation or decreased intraluminal concentration of pancreatic lipase in the small intestine, and decreased intestinal absorptive surface area. A decrease in bile acid pool size results in an increased delivery of fats into the colon, which in turn inhibits fat absorption and promotes water secretion.

338. The answer is c. (*Ganong, p 507. Kasper et al., pp 229, 1770–1172. Stead, pp 142–143.*) Gluten-sensitivity enteropathy is characterized by an autoimmune-induced decrease in the absorptive surface area of the small intestine. In addition to a decrease in the area available for absorption of nutrients, minerals, electrolytes and water, the membrane transporters of the remaining villous tip cells are impaired or absent.

339. The answer is a. (*Ganong, pp 473–475.*) The process of fat digestion begins in the stomach and is completed in the proximal small intestine, predominately by enzymes synthesized and secreted by the pancreatic acinar cells. The major lipolytic pancreatic enzyme is the carboxylic esterase, known as lipase. Full activity requires the protein cofactor colipase, bile salts, fatty acids, as well as an alkaline pH. Excess delivery of acid into the proximal small intestine leads to reduced lipolytic activity.

340. The answer is b. (*Stead et al., pp 131–134.*) Individuals with inflammatory disease of the ileum have decreased bile acid pool size due to decreased bile acid reabsorption. This results in reduced absorption of dietary triglycerides and fat-soluble vitamins, including vitamin K. The efficient absorption of dietary fats requires the presence of critical concentrations of primary and secondary bile salts (1 to 5 mmol/L). Because the absolute amount of bile acids available for fat digestion during a meal (the bile acid pool size) is generally less than the amounts required for complete digestion and absorption, bile acids must be recirculated via the enterohepatic circulation. Conservation of bile acids during a meal is highly efficient and occurs primarily from the distal ileum via sodium-dependent, secondary active transport. The increased delivery of dietary fat and bile acids into the colon decreases colonic absorption of water. The loss of bile salts in the stool cannot be fully compensated for by increased hepatic synthesis, and, thus, there is a resultant decrease in bile acid pool size.

341. The answer is b. (*Kasper et al., pp 1756–1757.*) Patients often experience a sense of fullness (early satiety), abdominal bloating, and nausea following a vagotomy of the antrum. The stomach has three important motor functions: storage, trituration, and emptying. The ability of the stomach to serve as a reservoir is characteristic of the orad stomach (gastric fundus and corpus). Upon ingestion of a mixed meal (liquids and solids) a vago-vagal-mediated reflex, receptive relaxation, limits the rise in intragastric pressure in response to an increase in intragastric volume. Sectioning of the vagus nerve or gastric resection of the orad stomach

abolishes the reflex and leads to an increased intragastric pressure with a resultant increase in the gastric emptying of liquids. Trituration, the mechanical breakdown of large, solid food particles into smaller particles, is essential for the gastric emptying of solids. Trituration is the result of rhythmical contractions characteristic of the gastric antrum. Normally, solids do not empty until they are smaller than 1 to 2 mm in diameter. Distension of the antrum initiates both local, enteric neural reflexes and long, vago-vagal reflexes that increase the strength of antral contractions and promote the gastric emptying of solids. The loss of vagal input to the antrum markedly impairs the emptying of solids and often leads to an early sense of fullness.

342. The answer is b. (*Kasper et al.*, pp 1748–1759.) Withdrawal from long-term use of proton pump inhibitors prescribed for peptic ulcer disease may be associated with rebound gastric hypersecretion. Pharmacological suppression of gastric acid secretion can occur when the administered drug binds to a receptor present on the parietal cell or when it antagonizes the hydrogen-potassium-ATPase pump responsible for the active secretion of hydrogen ion into the gastric lumen. At the present time, the most effective antisecretory compounds work by blocking the histamine type-2 (H_2) receptor present on the parietal cell or by inhibition of the hydrogen pumps. The latter are the most potent and long-acting, thus increasing the probability of increasing serum gastrin.

343. The answer is b. (*Ganong*, pp 494–496.) The orad (proximal) region of the stomach is responsible for the regulation of the liquid component of a meal. Delivery of food into the orad stomach activates an inhibitory vago-vagal reflex that promotes the reservoir function of the stomach (accommodation reflex). Resection of the orad stomach lessens the vagal input to the orad stomach and leads to an enhanced increase in intragastric pressure in response to an increase in intragastric volume. Intragastric pressure is the primary determinant of the rate of liquid emptying from the stomach.

344. The answer is a. (*Ganong*, pp 469–470.) Lactase is a brush border enzyme that hydrolyzes milk sugar (lactose) into glucose and galactose. Patients with a lactase deficiency may experience diarrhea, cramps, and intestinal gas. The diarrhea and cramping reflect the osmotic effect of the sugar on water flux across the intestine. Colonic bacteria metabolize lactose to fatty acids, CO_2 , and H_2 .

345. The answer is c. (*Ganong*, pp 489–491.) Reflux of gastric contents into the smooth-muscle region of the esophagus leads to the development of secondary esophageal peristalsis, characterized by enteric nerve-initiated peristalsis, beginning at the site of irritation and LES relaxation. Primary peristalsis is initiated by the medullary swallowing center and is preceded by an oral-pharyngeal phase.

346. The answer is b. (*Ganong*, pp 482–488.) The delivery of food into the small intestine is characterized by prompt emptying of the gallbladder, resulting from fat-induced release of cholecystokinin. Secretin stimulates pancreatic bicarbonate secretion. Enterogastrone is inhibitory to gastric function; glucagon is involved in nutrient metabolism; motilin is an interdigestive hormone responsible for migrating motor complex activity.

347. The answer is b. (*Stead et al.*, pp 63–65.) Insulin, a pancreatic hormone, decreases tissue lipolysis. The main function of insulin is to stimulate anabolic reactions involving carbohydrates, fats, proteins, and nucleic acids. Therefore, insulin increases glucose utilization while also stimulating lipogenesis and proteogenesis. By promoting glucose utilization by cells, insulin decreases the need for gluconeogenesis and ketogenesis.

348. The answer is d. (*Kasper et al.*, p 230.) Although only small amounts of bile acids are lost in the stool each day, the loss represents the only route of elimination of cholesterol from the body. The predominant organic component of bile is the bile salts, which make up about 67% of the total solutes. Bile salts are amphiphilic molecules, that is, they exhibit both water and lipid solubility. Primary bile acids, cholic acid and chenodeoxycholic acid, are synthesized from cholesterol. Secondary bile acids, deoxycholic acid and lithocholic acid, are produced by biotransformation of primary bile acids by intestinal bacteria. Prior to secretion, the bile acids are conjugated with either glycine or taurine, which greatly enhances their water solubility. In general, taurine conjugates are more water-soluble than glycine conjugates.

349. The answer is a. (*Ganong*, p 512. *Kasper et al.*, pp 224–231, 1763–1767. *Stead et al.*, pp 139–141.) Osmotic diarrhea occurs when ingested, poorly absorbable, osmotically active solutes draw fluid into the lumen of the small intestine or colon leading to osmotic water loss in the stool. In osmotic diarrhea, the stool osmotic gap ($290 - 2[\text{Na}^+ + \text{K}^+]$) exceeds 50 mOsm, consistent with an unmeasured solute contributing to

the fecal electrolyte content. Osmotic diarrhea generally ceases with fasting or discontinued ingestion of the solute. The most common causes of osmotic diarrhea are (1) lactase (and other disaccharide) deficiency with resultant lactose intolerance and carbohydrate malabsorption, (2) ingestion of magnesium-containing antacids or laxatives, and (3) ingestion of nonabsorbable sugars, such as sorbitol. Secretory diarrhea, on the other hand, is caused by the overproduction of water by the small and large bowel. Crypt cell secretion of an isosmotic chloride solution increases combined with inhibition of electroneutral NaCl absorption from the small intestine. In contrast to osmotic diarrhea, secretory diarrhea has a normal stool osmotic gap and is not remedied with fasting. The other major pathophysiological mechanisms of chronic diarrhea include steatorrheal, inflammatory, infectious, dysmotile, radiation injury, and factitious causes.

350. The answer is c. (*Ganong*, pp 336–338, 470–472.) The transport protein responsible for the sodium-dependent glucose transport in the small intestine is termed the SGLT1 (Na⁺-glucose transporter). The absorption of glucose occurs through the coordinated action of transport proteins located in the brush border and basolateral membranes of the enterocyte. Glucose uptake into the enterocyte from the lumen of the GI tract occurs primarily via the sodium-dependent SGLT1 secondary active transport mechanism. Glucose exit from the enterocyte into the extracellular fluid occurs by facilitated diffusion and is mediated by the membrane transporter, Glut-2. The Na⁺-glucose cotransporter also transports galactose. Thus, when the cotransporter is congenitally defective, the resulting glucose and galactose malabsorption causes severe diarrhea that can be fatal if glucose and galactose are not removed from the diet. A similar secondary active transport process (Na⁺-glucose cotransport) occurs in the renal tubules via SGLT1 and SGLT2. Glut-5 is the membrane transporter located on the apical portion of the enterocyte responsible for the facilitated entry of fructose into the cell.

351. The answer is e. (*Ganong*, pp 474–475. *Kasper et al.*, p 231.) The colon is the major site for the generation and absorption of short-chain fatty acids. They are products of bacterial metabolism of undigested complex carbohydrates derived from fruits and vegetables. In addition to exhibiting trophic effects on the colonic mucosa, they are believed to promote sodium absorption from the colon. The mechanism of action remains controversial.

352. The answer is a. (*Ganong, pp 474–475.*) Medium-chain triglycerides are hydrolyzed by lipases more rapidly than long-chain fatty acids and are much more water-soluble than long-chain triglycerides. Medium-chain triglycerides (MCTs) are fatty acids of 6 to 12 carbon chain lengths that are present in small amounts in the normal diet. MCTs are not utilized for resynthesis of triglycerides and therefore are not packaged into chylomicrons. Instead, they are released directly into the portal blood. Because they are readily absorbed, MCTs can be used in patients with a wide variety of GI diseases resulting in malabsorption.

353. The answer is c. (*Ganong, pp 477–478.*) Iron is transported in the blood bound to the β globulin, transferrin. Excess iron is stored in all cells, but especially in hepatocytes where it combines with apoferritin. The stored form is called ferritin. The rate of iron absorption is extremely slow, with a maximum of only a few milligrams per day. Iron is absorbed primarily in the ferrous form. Therefore, ferrous iron compounds, rather than ferric compounds, are effective in treating iron deficiency.

354. The answer is b. (*Ganong, pp 487–495. Stead et al., pp 121–123.*) Somatostatin, located within the gastric antral mucosa, is the principal paracrine secretion involved in the inhibitory feedback of gastric acid secretion by parietal cells. Somatostatin has a short half-life of several minutes, which limits its clinical use, but the analog octreotide (Sandostatin) should be administered subcutaneously to inhibit the secretion of gastrin and gastric acid and visceral blood flow in patients with bleeding esophageal varices secondary to portal hypertension, after stabilizing with IV fluids, as acute variceal bleeds have a 50% mortality. Acid secretion is stimulated by acetylcholine (via M_3 muscarinic receptors), histamine (via H_2 receptors) and gastrin (directly via gastrin receptors and principally via stimulation of histamine secretion by enterochromaffin-like [ECL] cells). Gastrin secretion is stimulated by the amino acids and peptides produced by pepsin's action in protein digestion.

355. The answer is b. (*Ganong, p 490. Kasper et al., pp 1741–1742. Stead et al., pp 106–107.*) Important inhibitory neurotransmitters in the gastrointestinal tract include vasoactive intestinal peptide and nitric oxide. Relaxation of gastrointestinal smooth muscle occurs following activation of nonadrenergic, noncholinergic (NANC) enteric nerve fibers. Acetylcholine, substance P, and dopamine are excitatory neurotransmitters. Somatostatin is a paracrine secretory product with multiple effects on gastrointestinal function.

356. The answer is d. (*Ganong, pp 475–477. Stead et al., pp 139–140.*)

Most water and electrolyte absorption occurs in the jejunum, with the duodenum serving primarily as the site of osmotic equilibration of chyme. Water absorption is passive and occurs as the direct result of active sodium absorption. The small intestine and colon absorb approximately 9 to 12 L of fluid per 24-hour period, most of which comes from gastrointestinal secretions. In contrast to the small intestine, the colon has a limited capacity to absorb water (approximately 3 to 6 L per day); most water absorption in the colon occurs in the proximal colon.

357. The answer is a. (*Ganong, pp 468, 497–498.*) Liberation of the enzyme enteropeptidase (enterokinase) from the duodenal mucosal cells causes the inactive trypsinogen to be converted to the active form, trypsin. Enteropeptidase contains 41% polysaccharide. It is this high level of polysaccharide that protects enteropeptidase from digestion. Trypsin is responsible for the conversion of chymotrypsinogens and other proenzymes into their active forms.**358. The answer is b.** (*Ganong, pp 293–296, 470–478, 501–502, 509–511, 620, 782. Kasper et al., p 1867. Stead et al., pp 121, 123.*) One of the actions of colonic bacteria is to convert NH_3 to NH_4^+ . Thus, a total colectomy would increase blood ammonia levels, which would be exacerbated in a person with cirrhosis. NH_3 is in equilibrium with NH_4^+ . Most of the NH_4^+ formed by oxidative deamination of amino acids in the liver is converted to urea, and the urea is excreted in the urine. The NH_4^+ forms carbamoyl phosphate, and in the mitochondria it is transferred to ornithine by ornithine carbamoyl-transferase forming citrulline. Citrulline is converted to arginine, after which urea is split off and ornithine is regenerated (urea cycle). Most of the urea is formed in the liver, and in severe liver disease the blood urea nitrogen falls and blood NH_3 rises. Normally, about 5 to 10% of bile salts enter the colon. In the colon, bacteria convert the two primary bile acids, cholic acid and chenodeoxycholic acid to the secondary bile acids, deoxycholic acid and lithocholic acid, respectively. Lithocholate is relatively insoluble and is mostly excreted in the stool, but deoxycholate is reabsorbed from the colon, where it is transported back to the liver in the portal vein and reexcreted in the bile (enterohepatic circulation). Humans can survive after total removal of the colon if fluid and electrolyte balance is maintained. When total colectomy is performed, the ileum is brought out through the abdominal wall (ileostomy). Advances in surgical techniques make ileostomies relatively trouble-free and patients with them can lead essentially normal lives.

359. The answer is c. (*Ganong, pp 500–503, 782–783. Kasper et al., pp 238–243, 1764–1765, 1831–1833. Stead et al., pp 124–127.*) Infectious hepatitis is a systemic infection predominantly affecting the liver. When jaundice appears, serum bilirubin rises, and, in most instances, total bilirubin is equally divided between the conjugated (direct) and unconjugated (indirect) fractions. The bilirubin in serum represents a balance between input from production of bilirubin and hepatic/biliary removal of the pigment. Hyperbilirubinemia may result from (1) overproduction of bilirubin; (2) impaired uptake, conjugation, or removal of bilirubin; or (3) regurgitation of unconjugated or conjugated bilirubin from damaged hepatocytes or bile ducts. Alkaline phosphatase, which is excreted in bile, increases in patients with jaundice due to bile duct obstruction, but generally not when the jaundice is due to hepatocellular disease. Bile acids are synthesized in the liver by a series of enzymatic steps that also involve cholesterol catabolism. Liver disease decreases bile acid synthesis.

360. The answer is c. (*Ganong, p 491.*) Gas within the colon is derived primarily from fermentation of undigested material by intestinal bacteria to produce CO₂, H₂, and methane. The digestive tract normally contains about 150 to 200 mL of gas, most of which is in the colon (100 to 150 mL). Most of the gas in the stomach is derived from air swallowed during eating or in periods of anxiety. Gas is produced in the small intestine by interaction of gastric acid and bicarbonate in the intestinal and pancreatic secretions but does not accumulate because it is either reabsorbed or quickly passed into the colon. The amount of gas varies markedly from one person to another and is influenced by diet; for example, ingestion of large amounts of beans, which contain indigestible carbohydrates in their hulls, will increase gas formation by intestinal bacteria. Diffusion of gas from the blood to the intestinal lumen is responsible for the N₂ present in intestinal gas and is influenced by the atmospheric pressure.

361. The answer is b. (*Ganong, pp 313, 315, 496. Stead et al., pp 95–96.*) Although intrinsic factor is secreted by the oxyntic cells of the gastric mucosa, binding to cobalamin occurs in the duodenum. Cobalamin, also known as vitamin B₁₂, is synthesized only by microorganisms and, in the human diet, is provided almost entirely from animal products. Gastric digestion of food liberates cobalamin where, at low pH, it binds primarily to the R protein-type binder, haptocorrin, derived primarily from salivary secretions. In the duodenum, pancreatic proteases release cobalamin from the haptocorrin but have no effect on intrinsic factor derived from parietal

cells. Cobalamin rapidly complexes with intrinsic factor and is transported along the gut to the distal 60 cm of the ileum, where specific receptors located on the villus tip cells bind the cobalamin-intrinsic factor complex.

362. The answer is a. (*Ganong, pp 494–496.*) The initial rate of emptying varies directly with the volume of the meal ingested. Increasing the volume, fat content, acidity, or osmolarity of the lumen of the small intestine inhibits gastric emptying via neural, hormonal, and paracrine feedback mechanisms.

363. The answer is d. (*Ganong, pp 496–497, 783.*) Weakness, dizziness, and sweating, due in part to hypoglycemia, underlie the presentation of “dumping syndrome,” which may develop in patients in whom part of the stomach has been removed or the jejunum has been anastomosed to the stomach. Another cause of the symptoms is rapid entry of a hypertonic meal into the intestine, which promotes the movement of an abundance of water into the gut, producing significant hypovolemia and hypotension.

364. The answer is e. (*Ganong, pp 347–348, 486–487, 783.*) Glucagon-like polypeptide 1 (GLP-1) is a product of glucagon metabolism in the L cells of the lower intestinal tract. GLP-1 has no definite biological activity by itself but is processed further by removal of its amino-terminal amino acid residues, and the product, GLP-1 (7–36), is a potent stimulator of insulin secretion that also increases glucose utilization. Like GIP, it may be a physiologic B cell-stimulating hormone in the GI tract.

365. The answer is b. (*Ganong, pp 506–511, 783. Widmaier et al., pp 603–605.*) Distention of the stomach by food initiates contraction of the rectum and often, a desire to defecate. This response is called the gastrocolic reflex, but it may be mediated by the action of gastrin on the colon rather than being neurally mediated. This response leads to defecation after meals in infants and children. In adults, defecation may be inhibited by behavioral modification. The gastroileal reflex refers to the relaxation of the cecum and passage of chyme through the ileocecal valve when food leaves the stomach. Peristaltic rushes are very intense peristaltic waves that may occur with intestinal obstruction. The intestino-intestinal reflex refers to a complete cessation of intestinal motility that may be caused by large distensions of the intestine, injury to the intestinal wall, or various intestinal

bacterial infections. The defecation reflex refers to the sudden distention of the walls of the rectum produced by mass movement of fecal material into the rectum.

366. The answer is c. (*Ganong, p 507. Kasper et al., pp 1770–1773. Stead et al., p 142.*) Malabsorption syndrome refers to the inability to adequately absorb nutrients and vitamins from the intestinal tract. One example of a malabsorption syndrome is the autoimmune disease, celiac sprue, which is also called gluten enteropathy. The disease is characterized by a deficiency in MHC class II antigen HLA-DQ2, which causes an allergic response to ingestion of gluten and related proteins. Elimination of these proteins, which are found in wheat, rye, barley, and oats, can restore normal bowel function in these patients.

367. The answer is d. (*Ganong, pp 503, 783–784.*) When plasma bilirubin is increased due to bile duct obstruction, it is generally the conjugated form of bilirubin that increases due to reabsorption of bilirubin glucuronide into the blood.

368. The answer is d. (*Ganong, pp 475–477.*) Although multiple pathways exist for the absorption of Na^+ , neutral absorption is the major mechanism. Absorption of sodium is the primary absorptive event in the small intestine. Absorption of Na^+ is necessary for absorption of water and other electrolytes. Neutral absorption may occur in two ways: Na^+ cotransported with Cl^- or in exchange for H^+ ions.

369. The answer is d. (*Ganong, pp 473–475.*) Long-chain fatty acids are extruded from enterocytes in the form of chylomicrons into the lymphatic system. Triglycerides are hydrolyzed to monoglycerides and taken into mucosal cells. If the fatty acids are short chains (less than 10 to 12 carbon atoms), they are extruded in the form of free fatty acids into the portal blood. Chylomicrons represent triglycerides and esters of cholesterol that have been invested in the intestinal mucosa with a coating of phospholipid, protein, and cholesterol.

370. The answer is c. (*Ganong, p 477.*) Absorption of the fat-soluble vitamins (A, D, E, and K) is diminished if there is a lack of pancreatic lipase. Lipase is required to produce monoglycerides that, in combination with bile salts, make it possible to bring the fat-soluble vitamins close to the mucosal cell surface for absorption. With the exception of vitamin B_{12} ,

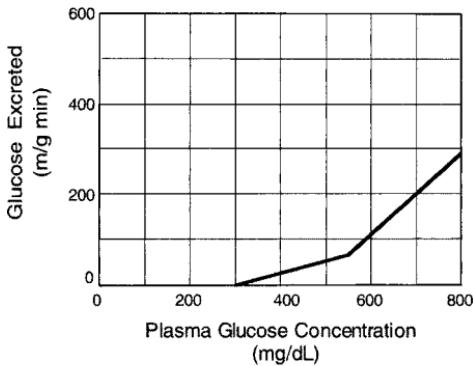
which is absorbed bound to intrinsic factor in the ileum, vitamins are absorbed chiefly in the upper small intestine.

371. The answer is a. (*Stead et al., pp 111–113.*) Pancreatic bicarbonate secretion into the small intestine is essential for neutralization of gastric acid emptied into the small intestine. Unlike the gastric mucosal lining, the mucosal surface of the small intestine does not provide a significant endogenous defense mechanism against the insult of HCl. Upon delivery into the proximal small intestine, hydrogen ions stimulate the release of the hormone secretin from the intestinal wall, which in turn stimulates pancreatic bicarbonate secretion. In fact, the acid output of the stomach during a meal is matched equally by the pancreatic output of bicarbonate. Although the liver secretes bicarbonate and bile contains bicarbonate, the amounts are not sufficient for acid neutralization.

Renal and Urinary Physiology

Questions

372. A 65-year-old man with uncontrolled Type II diabetes and sustained hyperglycemia (serum glucose = 550 mg/dL) and polyuria (5 L/day) is evaluated in the hospital's clinical laboratory because his urine glucose concentration (<100 mM) was much lower than expected. The graph below illustrates the relationship between plasma glucose concentration and renal glucose reabsorption for this patient. The glomerular filtration rate (GFR) is 100 mL/min. Which of the following is the T_{\max} for glucose?



- a. 100 mg/min
- b. 200 mg/min
- c. 300 mg/min
- d. 400 mg/min
- e. 500 mg/min

373. A 16-year-old girl with Liddle's syndrome presents with hypertension, hypervolemia, and hypokalemia, but low levels of renin and aldosterone. Her clinical condition is reversed by administration of a diuretic, which acts by blocking epithelial sodium channels. Which of the following is the major defect in Liddle's syndrome?

- a. Increased sodium reabsorption by the proximal tubules
- b. Increased sodium reabsorption by the distal nephron
- c. An inability of the distal nephron to secrete potassium ion
- d. An inability of the distal nephron to secrete hydrogen
- e. An inability of the distal nephron to concentrate urine

374. A previously well 12-year-old boy is brought to the Emergency Department with vomiting and severe abdominal cramps after a prolonged period of exercise. Elevated levels of serum creatinine and blood urea nitrogen suggest acute renal failure. Following treatment and recovery, his serum uric acid concentration (0.6 mg/dL) remains consistently below normal. To determine if his low serum uric acid level is related to renal dysfunction, uric acid clearance studies are conducted and the following data are obtained:

$$\text{Urine volume} = 1 \text{ mL/min}$$

$$\text{Urine uric acid} = 36 \text{ mg/dL}$$

Which of the following is the patient's uric acid clearance?

- a. 6 mL/min
- b. 12 mL/min
- c. 24 mL/min
- d. 48 mL/min
- e. 60 mL/min

375. A 69-year-old male presents with symptoms of thirst and dizziness, and physical evidence of orthostatic hypotension and tachycardia, decreased skin turgor, dry mucous membranes, reduced axillary sweating, and reduced jugular venous pressure. He was recently placed on an angiotensin-converting enzyme inhibitor for his hypertension. Urinalysis reveals a reduction in the fractional excretion of sodium and the presence of acellular hyaline casts. The internist suspects acute renal failure of pre-renal origin, which has increased renin secretion by the kidney. A stimulus for increasing renal renin secretion is an increase in which of the following?

- a. Mean blood pressure
- b. Glomerular filtration rate

- c. Sympathetic nerve activity
- d. Circulating angiotensin II
- e. Atrial natriuretic peptide secretion

376. A patient with uncontrolled hypertension is placed on a new diuretic targeted to the Na^+ reabsorption site from the basolateral surface of the renal epithelial cells. Which of the following transport processes is the new drug affecting?

- a. Na^+/H^+ exchange
- b. Na^+ -glucose cotransport
- c. Na^+/K^+ pump
- d. Facilitated diffusion
- e. Solvent drag

377. Which of the following is most likely to cause an increase in the glomerular filtration rate?

- a. Contraction of mesangial cells
- b. Blockage of the ureter
- c. Release of renin from the juxtaglomerular apparatus
- d. Dilation of the afferent arterioles
- e. Volume depletion

378. A 32-year-old man complaining of fatigue and muscle weakness is seen by his physician. Blood tests reveal a serum glucose level of 325 mg/dL and serum creatinine of 0.8 mg/dL. Results of a 24-hour urine analysis are as follows:

Total volume = 5 L

Total glucose = 375 g

Total creatinine = 2.4 g

The patient's glomerular filtration rate is approximately which of the following?

- a. 75 mL/min
- b. 100 mL/min
- c. 125 mL/min
- d. 200 mL/min
- e. 275 mL/min

379. A 38-year-old woman is admitted to the hospital by her physician because of decreased urine output. Prior to admission, she was rehearsing for a dance performance and had been taking Motrin for pain. Laboratory data reveal: blood urea nitrogen, 49 mg/dL; serum sodium, 135 mmol/L; serum creatinine, 7.5 mg/dL; urine sodium, 33 mmol/L, and urine creatinine, 90 mg/dL. Her fractional sodium excretion is approximately which of the following?

- a. 0.5%
- b. 1.0%
- c. 1.5%
- d. 2.0%
- e. 3.0%

380. An 85-year-old woman presents with a fever and hypovolemic hypotension. To assess her renal function, the filtration fraction is determined using a freely filterable substance that is neither reabsorbed nor secreted. The infusate yields a renal artery concentration of 12 mg/mL and a renal vein concentration of 9 mg/mL. Which of the following is the filtration fraction?

- a. 0.05
- b. 0.15
- c. 0.25
- d. 0.35
- e. 0.45

381. A 17-year-old girl went on a starvation diet for 3 days before prom so that she would look thin in her new dress. Her mother found her lethargic and hyperventilating, and took her to the Emergency Department for evaluation. Based on the following laboratory values, which of the following is her net acid excretion?

Plasma pH = 7.26

Urine flow = 1.2 L/day

Urine bicarbonate = 2 mEq/L

Urine titratable acids = 24 mEq/L

Urine ammonium = 38 mEq/L

Urine pH = 5.4

- a. 60 mEq/L
- b. 64 mEq/L
- c. 68 mEq/L
- d. 72 mEq/L
- e. 76 mEq/L

382. A 68-year-old woman presents with hypertension and oliguria. A CT of the abdomen reveals a hypoplastic left kidney. Based on the following laboratory data, which of the following is her estimated renal plasma flow?

Renal artery PAH = 6 mg/dL

Renal vein PAH = 0.6 mg/dL

Urinary PAH = 25 mg/mL

Urine flow = 1.5 mL/min

Hematocrit = 40%

- a. 475 mL/min
- b. 550 mL/min
- c. 625 mL/min
- d. 700 mL/min
- e. 775 mL/min

383. If a substance appears in the renal artery but not in the renal vein, which of the following is true?

- a. It must be filtered by the kidney
- b. It must be reabsorbed by the kidney
- c. Its clearance is equal to the glomerular filtration rate
- d. Its clearance is equal to the renal plasma flow
- e. Its urinary concentration must be higher than its plasma concentration

384. A 46-year-old man presents to his physician with a 12-week history of frontal headaches. A computed tomography (CT) of the brain shows a mass in the posterior pituitary, and the posterior pituitary "bright spot" is absent on MRI. The patient also complains of increased thirst and waking up frequently during the night. Which of the following best describes his urine?

- a. A higher-than-normal flow of hypotonic urine
- b. A higher-than-normal flow of hypertonic urine
- c. A normal flow of hypertonic urine
- d. A lower-than-normal flow of hypotonic urine
- e. A lower-than-normal flow of hypertonic urine

385. A 63-year-old woman is brought to the Emergency Department complaining of fatigue and headaches. She appears confused and apathetic. She has been taking diuretics to treat her hypertension and paroxetine for her depression. Laboratory results are as follows:

urine flow = 2 L/day
serum sodium = 125 mmol/L
serum potassium = 4 mmol/L
urine osmolality = 385 mOsm/L
urine sodium = 125 mmol/L
urine potassium = 25 mmol/L

Which of the following is this patient's approximate free water clearance?

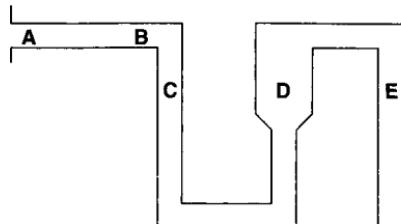
- a. -0.20 L/day
- b. -0.50 L/day
- c. -0.75 L/day
- d. +0.2 L/day
- e. +0.50 L/day

386. A 28-year-old woman with systemic lupus erythematosus (SLE) is brought to the Emergency Department after developing hypokalemic paralysis. Arterial blood-gas analysis shows a PaCO_2 of 102 mmHg and a pH of 7.1. She is diagnosed with Type I renal tubular acidosis caused by an autoimmune response that damages the H^+ -ATPase on the distal nephron. Which of the following laboratory measurements will most likely be normal in this patient?

- a. Net acid excretion
- b. Aldosterone secretion
- c. Serum bicarbonate
- d. Urine ammonium
- e. Anion gap

Questions 387–389.

Use the following diagram of a nephron to answer the next three questions.



387. In the absence of ADH, the luminal Na^+ concentration is lowest at which of the following points?

- a. A
- b. B
- c. C
- d. D
- e. E

388. Parathyroid hormone increases Ca^{2+} reabsorption at which of the following points?

- a. A
- b. B
- c. C
- d. D
- e. E

389. Aldosterone increases Na^+ reabsorption at which of the following points?

- a. A
- b. B
- c. C
- d. D
- e. E

390. A 92-year-old man presents with dehydration following four days of persistent diarrhea. Under these circumstances, hypotonic fluid would be expected in which of the following?

- a. Glomerular filtrate
- b. Proximal tubule
- c. Loop of Henle
- d. Cortical collecting tubule
- e. Distal collecting duct

391. A hospitalized patient becomes oliguric with increasing BUN and creatinine. Urine specific gravity is low and the urine sediment has red cell casts with hematuria and proteinuria. Which of the following statements concerning the normal renal handling of proteins is correct?

- a. Proteins are more likely to be filtered if they are negatively charged than if they are uncharged
- b. Proteins can be filtered and secreted but not reabsorbed by the kidney
- c. Most of the protein excreted each day is derived from tubular secretion
- d. Protein excretion is directly related to plasma protein concentration
- e. Protein excretion is increased by sympathetic stimulation of the kidney

392. Which of the following best explains why the pH of the tubular fluid in the distal nephron can be lower than that in the proximal tubule?

- a. A greater sodium gradient can be established across the wall of the distal nephron than across the wall of the proximal tubule
- b. More buffer is present in the tubular fluid of the distal nephron than in the proximal tubule
- c. More hydrogen ion is secreted into the distal nephron than into the proximal tubule
- d. The brush border of the distal nephron contains more carbonic anhydrase than that of the proximal tubule
- e. The tight junctions of the distal nephron are less leaky to solute than those of the proximal tubule

393. An 18-year-old male presents with muscle weakness, cramps, and tetany. Blood pressure is normal and no edema is present. Laboratory analysis reveals hypokalemic alkalosis, hyperaldosteronism, and high plasma renin activity, diagnostic of Bartter's syndrome. Which of the following statements about renin is true?

- a. It is secreted by cells of the proximal tubule
- b. Its secretion leads to loss of sodium and water from plasma
- c. Its secretion is stimulated by increased mean renal arterial pressure
- d. It converts angiotensinogen to angiotensin I
- e. It converts angiotensin I to angiotensin II

394. The effective renal plasma flow, determined from the clearance of *p*-aminohippuric acid (PAH), is less than the true renal plasma flow because of which of the following?

- a. The fraction of PAH filtered is less than the filtration fraction
- b. The plasma entering the renal vein contains a small amount of PAH
- c. The cortical and medullary collecting ducts are able to reabsorb some PAH

- d. The calculated clearance of PAH depends on the urinary flow rate
- e. The measured value of the plasma PAH concentration is less than the actual PAH concentration

395. A 63-year-old hospitalized woman becomes oliguric and confused. Her blood glucose is found to be only 35 mg/dL. An IV access is obtained and an ampule of 50% dextrose is given followed by a continuous infusion of 10% dextrose. Most of the glucose that is filtered through the glomerulus undergoes reabsorption in which of the following?

- a. Proximal tubule
- b. Descending limb of the loop of Henle
- c. Ascending limb of the loop of Henle
- d. Distal tubule
- e. Collecting duct

396. A patient with multiple myeloma develops a defect in renal bicarbonate reabsorption, which involves the proximal tubule, that is, Type 2 renal tubular acidosis (RTA). Which of the following structural features distinguishes the epithelial cells of the proximal tubule from those of the distal tubule?

- a. The distal tubule has a thicker basement membrane
- b. The proximal tubule has a thicker basement membrane
- c. The proximal tubule has a more extensive brush border
- d. The proximal tubule forms the juxtaglomerular apparatus
- e. The distal tubule has fewer tight intercellular junctions

397. A 35-year-old male with polycystic kidney disease has a decrease in both glomerular filtration rate (GFR) and renal blood flow (RBF). The nephrologist wants to administer a drug that will increase both GFR and RBF. GFR and RBF would both increase if which of the following occurred?

- a. The efferent and afferent arterioles are both dilated
- b. The efferent and afferent arterioles are both constricted
- c. Only the afferent arteriole is constricted
- d. Only the efferent arteriole is constricted
- e. The afferent arteriole is constricted and the efferent arteriole is dilated

398. A patient with Type IV renal tubular acidosis (RTA) has a defect in aldosterone secretion and ammonium excretion. Which of the following statements about ammonia (NH_3) is correct?

- a. It is impermeable to the epithelial cells of the proximal tubule
- b. It is classified as a titratable acid
- c. It is produced by epithelial cells in the distal nephron
- d. It reduces the concentration of bicarbonate in the plasma
- e. Its synthesis is increased in respiratory acidosis

399. A patient with hypertension is given a K^+ -sparing diuretic. The amount of potassium excreted by the kidney will decrease if which of the following occurs?

- a. Distal tubular flow increases
- b. Circulating aldosterone levels increase
- c. Dietary intake of potassium increases
- d. Na^+ reabsorption by the distal nephron decreases
- e. The excretion of organic ions decreases

400. Which of the following substances will be more concentrated at the end of the proximal tubule than at the beginning of the proximal tubule?

- a. Glucose
- b. Creatinine
- c. Sodium
- d. Bicarbonate
- e. Phosphate

401. Decreasing the resistance of the afferent arteriole in the glomerulus of the kidney will decrease which of the following?

- a. Glomerular filtration rate
- b. Renal plasma flow
- c. Filtration fraction
- d. The oncotic pressure of the peritubular capillary blood
- e. Renin release from juxtaglomerular cells

402. Electrically neutral active transport of sodium and chloride from the lumen of the kidney occurs in which of the following?

- a. Proximal tubule
- b. Descending limb of the loop of Henle
- c. Thin ascending limb of the loop of Henle
- d. Cortical collecting duct
- e. Medullary collecting duct

403. A postoperative patient develops a thready pulse, tachycardia, and hypotension. A decision is made to take the patient back to surgery to check for bleeding. Laboratory analysis shows an increase in plasma angiotensin II accompanied by an increase in glomerular filtration rate (GFR). When GFR increases, proximal tubular reabsorption of salt and water increases by a process called glomerulotubular balance. Contributions to this process include which of the following?

- a. An increase in peritubular capillary hydrostatic pressure
- b. A decrease in peritubular sodium concentration
- c. An increase in peritubular oncotic pressure
- d. An increase in proximal tubular flow
- e. An increase in peritubular capillary flow

404. A 24-year-old man with a history of renal insufficiency is admitted to the hospital after taking a large amount of ibuprofen. His BUN is 150 mg/dL. This patient's high serum urea nitrogen was most likely caused by which of the following?

- a. An increased synthesis of urea by the liver
- b. An increased reabsorption of urea by the proximal tubules
- c. A decreased secretion of urea by the distal tubules
- d. A decreased glomerular filtration rate
- e. An increased renal blood flow

405. A 36-year-old African-American male presents with low renin essential hypertension. Renin release from the juxtaglomerular apparatus is normally inhibited by which of the following?

- a. β -adrenergic agonists
- b. Prostaglandins
- c. Aldosterone
- d. Stimulation of the macula densa
- e. Increased pressure within the afferent arterioles

406. A patient undergoing surgery develops an increase in the secretion and plasma levels of ACTH, cortisol, and aldosterone. Which of the following statements about aldosterone is correct?

- a. It produces its effect by activating cAMP.
- b. It produces its effect by increasing distal tubular permeability to sodium.
- c. It causes an increased reabsorption of hydrogen ion.
- d. It has its main effect on the proximal tubule.
- e. It is secreted in response to an increase in blood pressure.

407. A trauma patient with multiple rib fractures requires intubation and mechanical ventilation. Mechanical ventilation causes an increase in the patient's vasopressin secretion and plasma levels. Which of the following is the effect of vasopressin on the kidney?

- a. Increased diameter of the renal artery
- b. Increased glomerular filtration rate
- c. Increased excretion of Na^+
- d. Increased excretion of water
- e. Increased permeability of the distal nephron to water

408. The ability of the kidney to excrete concentrated urine will increase if which of the following occurs?

- a. The reabsorption of Na^+ by the proximal tubule decreases
- b. The glomerular capillary pressure increases
- c. The flow of filtrate through the loop of Henle increases
- d. The activity of the Na^+-K^+ pump in the loop of Henle increases
- e. The permeability of the collecting duct to water decreases

409. A 16-year-old pregnant girl is admitted to the hospital in labor. Her blood pressure is 130/85 mmHg and her plasma creatinine is 2.7 mg/dL (normal 0.6 to 1.2 mg/dL). Renal ultrasonography demonstrates severe bilateral hydronephrosis (enlarged kidney). Which of the following is the most likely cause of this patient's high creatinine levels?

- a. Increased sympathetic nerve activity
- b. Coarctation of the renal artery
- c. Hyperproteinemia
- d. Ureteral obstruction
- e. Hypovolemia

410. A 54-year-old man with small cell lung cancer presents with lethargy, confusion, and muscle cramps. Blood work shows an increase in plasma levels of antidiuretic hormone (ADH), possibly from the ectopic production of ADH. In patients with the syndrome of inappropriate antidiuretic hormone (SIADH), which of the following will increase?

- a. The concentration of plasma sodium
- b. Intracellular volume
- c. Urinary flow
- d. Plasma oncotic pressure
- e. Plasma osmolarity

411. A patient with congestive heart failure is given the loop diuretic, furosemide, along with the potassium sparing diuretic, spironolactone. Which of the following comparisons between the distal nephron and the proximal tubule is correct?

- a. The distal nephron is more permeable to hydrogen ion than the proximal tubule.
- b. The distal nephron is less responsive to aldosterone than the proximal tubule.
- c. The distal nephron has a more negative intraluminal potential than the proximal tubule.
- d. The distal nephron secretes less potassium than the proximal tubule does.
- e. The distal nephron secretes more hydrogen ion than the proximal tubule does.

412. An elderly woman presents with spiking fever, shaking chills, nausea, and costovertebral angle tenderness. Urine cultures are positive and she is hospitalized for pyelonephritis. Her glomerular filtration rate (GFR) decreases with a resultant increase in the concentration of NaCl delivered in the intraluminal fluid to the thick ascending limb of the loop of Henle. Under these conditions, the macula densa will increase the formation and release of which of the following substances?

- a. ADH
- b. Aldosterone
- c. Adenosine
- d. Renin
- e. Angiotensinogen

413. Aldosterone secretion is increased when there is a decrease in the plasma concentration of which of the following?

- a. Renin
- b. Angiotensin II
- c. ACTH
- d. Sodium
- e. Potassium

414. A patient's 24-hour urine output is lower-than-normal. Which of the following situations would reduce urinary flow?

- a. Diabetes insipidus
- b. Diabetes mellitus
- c. Sympathetic stimulation
- d. Increased renal arterial pressure
- e. Infusion of mannitol

415. A 55-year-old hypertensive patient is placed on a potassium-sparing diuretic. Potassium-sparing diuretics inhibit Na^+ reabsorption in which of the following?

- a. Proximal tubule
- b. Distal tubule
- c. Thin descending limb of Henle's loop
- d. Thick descending limb of Henle's loop
- e. Thick ascending limb of Henle's loop

416. A patient has suffered from persistent diarrhea lasting for the past seven days. Which of the following would be increased in this patient?

- a. The filtered load of HCO_3^-
- b. The production of ammonia by the proximal tubule
- c. H^+ secretion by the distal nephron
- d. The anion gap
- e. The production of new bicarbonate by the distal nephron

417. In addition to increasing the permeability of the collecting duct to water, ADH increases the permeability of the collecting duct to which of the following?

- a. Hydrogen
- b. Ammonium
- c. Potassium
- d. Sodium
- e. Urea

418. The filtration fraction is increased by which of the following?

- a. Increasing renal blood flow
- b. Increasing afferent arteriolar resistance
- c. Increasing efferent arteriolar resistance
- d. Increasing plasma oncotic pressure
- e. Increasing the pressure within Bowman's capsule

419. A 23-year-old male is given acetazolamide to take for two days prior and throughout his four-day skiing trip to Breckenridge, Colorado (elevation = 10,000 ft) for the prophylactic treatment of high altitude sickness.

- a. The proximal tubule
- b. The thick ascending limb of Henle's loop
- c. The distal convoluted tubule
- d. The cortical collecting duct
- e. The outer medullary collecting duct

420. A patient with atherosclerosis shows signs of chronic renal failure attributed to poor renal perfusion and ischemic necrosis of the nephrons. Which of the following endogenous substances causes renal blood flow to decrease?

- a. Nitric oxide
- b. Atrial natriuretic peptide
- c. Acetylcholine
- d. Angiotensin II
- e. Dopamine

421. Which of the following substances is less concentrated at the end of the proximal tubule than at the beginning of the proximal tubule?

- a. Creatinine
- b. Hydrogen
- c. Chloride
- d. Phosphate
- e. Sodium

422. A patient develops acute renal failure due to an autoimmune disorder affecting the proximal tubules. What percentage of the filtered load of sodium is reabsorbed by the proximal tubule?

- a. 15%
- b. 25%
- c. 45%
- d. 65%
- e. 95%

423. A patient with congestive heart failure presents with jugular venous distention, ascites, and peripheral edema. Blood work shows elevated levels of plasma atrial natriuretic peptide (ANP). ANP decreases Na^+ reabsorption within which of the following?

- a. The proximal tubule
- b. The thick ascending limb of Henle's loop
- c. The distal convoluted tubule
- d. The cortical collecting duct
- e. The inner medullary collecting duct

424. Free water clearance by the kidney is increased by which of the following?

- a. Heart failure
- b. Renal failure
- c. Diuretic therapy
- d. Diabetes mellitus
- e. Diabetes insipidus

425. A 39-year-old man presents with severe writhing back pain, hematuria, and nausea. An intravenous pyelogram (IVP) confirms a diagnosis of renal calculi. The presence of strongly opaque stones on the plain film is suggestive of calcium oxalate stones, which have an increased incidence with hypophosphatemia. The renal clearance of phosphate is increased by which of the following hormones?

- a. Aldosterone
- b. Parathyroid hormone
- c. Norepinephrine
- d. Vasopressin
- e. Angiotensin

426. Which of the following will produce the greatest increase in potassium secretion?

- a. A decrease in urinary flow rates
- b. An increase in distal nephron sodium concentration
- c. A decrease in circulating blood volume
- d. An increase in sympathetic nerve activity
- e. A decrease in renal blood flow

427. A decrease in the concentration of NaCl in the intraluminal fluid causes the juxtaglomerular apparatus to release which of the following hormones?

- a. ADH
- b. Aldosterone
- c. Adenosine
- d. Renin
- e. Angiotensinogen

428. A hypertensive patient develops chronic renal failure from progressive nephrosclerosis. Which of the following should you expect to occur as a result?

- a. A decrease in the fractional excretion of sodium
- b. An increase in the free water clearance

- c. A decrease in net acid excretion
- d. A decrease in the excretion of creatinine
- e. No change in the anion gap

429. A patient with renal failure develops symptoms caused by the loss of a hormone produced by the kidney. Which of the following is the most likely diagnosis?

- a. Edema
- b. Hypertension
- c. Anemia
- d. Uremia
- e. Acidosis

430. In adults, the pulmonary circulation compared to the renal circulation has a greater what?

- a. Arterial pressure
- b. Vascular resistance
- c. Blood flow
- d. Capillary hydrostatic pressure
- e. Capillary oncotic pressure

431. Which of the following is correct regarding the consumption of oxygen by the kidney?

- a. It decreases as blood flow increases
- b. It is regulated by erythropoietin
- c. It remains constant as blood flow increases
- d. It directly reflects the level of sodium transport
- e. It is greatest in the medulla

432. In the presence of antidiuretic hormone (ADH), the filtrate will be isotonic to plasma in which of the following parts of the kidney?

- a. Descending limb of the loop of Henle
- b. Ascending limb of the loop of Henle
- c. Cortical collecting tubule
- d. Medullary collecting tubule
- e. Renal pelvis

433. The secretion of H⁺ in the proximal tubule is primarily associated with which of the following?

- a. Excretion of potassium ion
- b. Excretion of hydrogen ion
- c. Reabsorption of calcium ion
- d. Reabsorption of bicarbonate ion
- e. Reabsorption of phosphate ion

434. A 58-year-old male presents with hematuria, abdominal pain, and fatigue. Physical examination reveals a flank mass and an abdominal CT reveals a large solid mass on the left kidney. Laboratory studies show anemia and increased creatinine and BUN suggestive of advanced disease. A decrease in glomerular filtration rate would result from which of the following?

- a. Constriction of the efferent arteriole
- b. An increase in afferent arteriolar pressure
- c. Compression of the renal capsule
- d. A decrease in the concentration of plasma protein
- e. An increase in renal blood flow

Renal and Urinary Physiology

Answers

372. The answer is e. (*Ganong, pp 709–712. Widmaier et al., pp 536.*) The renal threshold for glucose is the plasma concentration at which glucose first appears in the urine. The graph shows that glucose is excreted at a plasma concentration of 300 mg/dL. (This is higher than the typical value of 200 mg/dL.) Glucose appears in the urine at a filtered load less than the T_{max} for glucose because of the differences in the reabsorptive capacity of the nephrons. Some nephrons can only reabsorb a small amount of glucose. When their reabsorptive capacity is exceeded, glucose is excreted. Other nephrons can absorb much more glucose. The T_{max} represents the average reabsorptive capacity of all the renal nephrons. The T_{max} for glucose is the maximum rate of glucose reabsorption from the kidney. Typically, the T_{max} is 375 mg/min. However, the T_{max} in this patient is 500 mg/min. The higher-than-normal reabsorptive capacity accounts for the lower-than-expected urinary concentration. The T_{max} is calculated by subtracting the amount of glucose excreted from the filtered load at any plasma concentration at which the amount of glucose excreted increases linearly as plasma glucose concentration increases. For example, when the plasma glucose concentration is 600 mg/dL, the filtered load of glucose is 600 mg/min, the amount of glucose excreted is 100 mg/min, and the amount of glucose reabsorbed (the T_{max}) is 500 mg/min.

373. The answer is b. (*Ganong, pp 642–643, 723.*) Sodium reabsorption in the distal nephron is normally under the control of aldosterone. In patients with Liddle's syndrome, the distal nephron reabsorbs excess Na^+ despite low levels of aldosterone and renin in the plasma, because a mutation in the genes for the renal epithelial sodium channels (ENaC) increases ENaC activity and sodium retention. Metabolic alkalosis, hypokalemia, and hypertension are also present secondary to the increased sodium (and water) reabsorption.

374. The answer is e. (*Ganong, pp 706–708. Kasper et al., pp 246–249, 1701, 2312, 2336.*) Clearance is a measure of how much plasma is totally cleared of a substance. It is calculated using the formula

$$\text{Clearance} = U_{\text{uric acid}} \times V/P_{\text{uric acid}} = 36 \text{ mg/dL} \times 1 \text{ mL/min} / 0.6 \text{ mg/dL}$$
$$= 60 \text{ mL/min}$$

The boy's hypouricemia is an inherited defect in the ability to reabsorb uric acid by the anion/urate exchangers on proximal tubule cells rather than an increased secretion of uric acid. Patients with hypouricemia sometimes develop exercise-induced acute renal failure. Although the mechanism is not known, some investigators suggest that uric acid has an important antioxidant role in the kidney and that the oxygen radicals produced during prolonged exercise are responsible for the acute renal failure in patients with low uric acid levels.

375. The answer is c. (*Ganong*, pp 454–459. *Kasper et al.*, pp 1647–1648.) Renin secretion is stimulated by the sympathetic nerves innervating the juxtaglomerular apparatus. Increasing mean blood pressure decreases sympathetic activity. Changes in GFR are detected by the macula densa. Decreases in GFR lead to an increase in renin release, whereas increases in GFR lead to the secretion of a mediator, perhaps adenosine or ATP, which contracts the afferent arteriole (tubuloglomerular feedback). ANP and angiotensin II decrease renin release.

376. The answer is c. (*Ganong*, pp 709–710, 715, 724–725.) The intracellular Na⁺ concentration of renal epithelial cells is pumped out of renal epithelial cells by Na⁺-K⁺ pumps located on the basolateral surface of the epithelial cells. The Na⁺/H⁺ exchanger and the Na⁺-glucose cotransporter are located on the apical surface of the epithelial cells. Na⁺ is transported from the peritubular spaces to the capillaries by solvent drag.

377. The answer is d. (*Ganong*, pp 705–708. *Widmaier et al.*, pp 532–534.) The GFR is proportional to the glomerular capillary hydrostatic pressure, the renal plasma flow, and the surface area and hydraulic conductivity of the diffusion barrier between the glomerular capillary and Bowman's space. Dilating the afferent arteriole causes an increase in glomerular capillary pressure and, therefore, an increase in GFR. Volume depletion causes a release of renin from the juxtaglomerular cells, leading to an increase in angiotensin II (AII) that causes constriction of the glomerular capillaries and contraction of the mesangial cells. Contraction of the mesangial cells causes a decrease in the surface area of the diffusion barrier between the glomerular capillary and Bowman's space. Blockage of the ureter causes an increase in tubular pressure that retards the filtration of water from the capillary to the nephron.

378. The answer is d. (*Ganong, pp 705–708. Widmaier et al., pp 537–538.*) Glomerular filtration rate is approximately equal to the clearance of creatinine, which in this case is

$$\text{Creatinine Clearance} = \text{Creatine Excreted}/\text{Plasma Creatinine Concentration}$$

$$\text{Creatinine Clearance} = 2.4 \text{ g/day}/0.8 \text{ mg/dL} = 300 \text{ L/day} = 208 \text{ mL/min}$$

379. The answer is d. (*Stead et al., pp 237–238.*) The fractional excretion (FE) is the fraction of the filtered load that is excreted. It is calculated using the formula

$$\text{FE} = \text{Amount Excreted}/\text{Amount Filtered} = (U_{\text{Na}} \times \dot{V})/(P_{\text{Na}} \times \text{GFR})$$

$$\text{Because GFR} = (U_{\text{creatinine}} \times \dot{V}/P_{\text{creatinine}}),$$

$$\text{FE} = (U_{\text{Na}} \times \dot{V})/[P_{\text{Na}} \times (U_{\text{creatinine}} \times \dot{V}/P_{\text{creatinine}})]$$

$$= (U_{\text{Na}} \times P_{\text{creatinine}})/(P_{\text{Na}} \times U_{\text{creatinine}})$$

$$= 33 \text{ mM} \times 7.5 \text{ mg/dL}/135 \text{ mM} \times 90 \text{ mg/dL} = 0.02$$

Fractional excretion is used to distinguish between a prerenal state, such as volume depletion, and intrinsic renal failure, such as acute tubular necrosis. A fractional excretion of less than 1% is consistent with volume depletion, whereas a fractional excretion of 2% or greater is consistent with acute renal failure. This patient, with a fraction excretion of 2%, was diagnosed with acute renal failure caused by excessive intake of Motrin.

380. The answer is c. (*Ganong, pp 705–708.*) Because the amount of fluid excreted by the kidney is only a small fraction of the renal plasma flow, the volume of fluid in the vein is essentially equal to that in the artery. Thus, the difference between the arterial and venous concentrations is due to the loss of solute. Because the material is neither reabsorbed nor secreted, its removal from the plasma must have been by glomerular filtration. Therefore the filtered solute equals (12 mg/mL – 9 mg/mL), and the percent of the arterial concentration that is filtered (and therefore, the fraction of plasma filtered) is

$$3 \text{ mg/mL}/12 \text{ mg/mL} = 0.25$$

381. The answer is d. (*Ganong, pp 720–722. Widmaier et al., pp 565–567.*) Net acid excretion is the amount of acid excreted each day. It is calculated using the formula

$$\text{Net Acid Excretion (NAE)} = (\text{TA} - \text{NH}_4^+ - \text{HCO}_3^-) \times \dot{V}$$

$$\text{NAE} = (24 \text{ mEq/L} + 38 \text{ mEq/L} - 2 \text{ mEq/L}) \times 1.2 \text{ L/day} = 72 \text{ mEq/L}$$

Almost all of the acid excreted is buffered by either phosphate, called titratable acid, and ammonia. The titratable acid is equal to the mM of NaOH that must be added to the urine to raise its pH back to that of plasma. Bicarbonate must be subtracted from the sum of acid excreted because each milliequivalent of excreted bicarbonate represents the addition of 1 mEq of acid to the plasma.

382. The answer is c. (*Ganong, pp 702–704.*) The clearance of PAH is a good estimate of renal plasma flow (RPF) because, under normal circumstances, almost all (more than 90%) of the PAH passing through the kidney is excreted.

$$\begin{aligned} C_{\text{PAH}} &= U_{\text{PAH}} \times \dot{V}/P_{\text{PAH}} = (25 \text{ mg/mL} \times 1.5 \text{ mL/min})/6 \text{ mg/100 mL} \\ &= 625 \text{ mL/min} \end{aligned}$$

If the clearance of PAH is 90% of the actual renal blood flow, then the true renal blood flow is approximately 695 mL/min.

383. The answer is d. (*Ganong, p 309.*) If a substance disappears from the circulation during its passage through the kidney, it usually indicates that it has been totally secreted into the nephron. In this case, its clearance will be equal to the RPF. If the substance is bound to plasma proteins, it can be secreted without being filtered. Even if it is entirely secreted by the kidney, its urinary concentration may be less than its plasma concentration if the urinary flow rate is very high.

384. The answer is a. (*Kasper et al., pp 2097–2100. Stead et al., pp 76–77.*) The presence of a mass in the posterior pituitary, coupled with the presentation of thirst and nocturia, suggest that the patient has a central diabetes insipidus with inadequate pituitary secretion of antidiuretic hormone (ADH). As a result of decreased ADH, the urine will have a low tonicity. On MRI, the absence of the normal bright spot in the region of the posterior pituitary further supports the diagnosis.

385. The answer is d. (*Ganong, pp 719–720.*) Free water clearance is the amount of water excreted in excess of that required to excrete urine that is

isoosmotic to plasma. A negative free water clearance indicates that the amount of water is less than that required to excrete urine that is isoosmotic to plasma. It is calculated using the formula:

$$\text{Free Water Clearance} (C_{H_2O}) = \dot{V} - C_{\text{osmolar}}$$

$$C_{\text{osmolar}} = U_{\text{osm}} \times \dot{V}/P_{\text{osm}}, \text{ where } U_{\text{osm}} = 2 \times (U_{Na^+} + U_{K^+})$$

$$C_{H_2O} = \dot{V} - [2 (U_{Na^+} + U_{K^+}) \times \dot{V}/P_{\text{osm}}]$$

$$C_{H_2O} = 1 \text{ L/day} - [2 (125 \text{ mM} + 25 \text{ mM}) \times 1 \text{ L/day}] / 2 \times 125 \text{ mM}$$

$$C_{H_2O} = -0.2 \text{ L/day}$$

This patient has a negative free water clearance, which means she is diluting her plasma despite her low serum sodium. The urine osmolarity is estimated from the concentration of sodium and potassium because these electrolytes determine the shift of water between intracellular and extracellular compartments. The measured osmolarity is not used because it includes urea, which has no effect on body fluid distribution. The serum hypotonicity (250 mOsm/L) causes brain swelling, accounting for her signs and symptoms. The negative free water clearance is probably caused by the combination of diuretics and antidepressants, which stimulate the release of ADH.

386. The answer is e. (*Stead et al.*, p 246.) The rise in H⁺ and fall in HCO₃⁻ that occurs in type I (distal) renal tubular acidosis (RTA) does not increase the anion gap because the decrease in HCO₃⁻ is accompanied by an increase in Cl⁻. The failure of the distal nephron H⁺ ATPase causes a reduction in net acid excretion and a reduced H⁺ secretion, which causes less ammonium to be excreted in the urine. The low HCO₃⁻ in the glomerular filtrate reduces Na⁺ reabsorption by the Na-H exchanger and therefore more Na⁺ is delivered to the distal nephron. The increased Na⁺ delivery results in salt wasting and a secondary hyperaldosteronism which, in turn, causes K⁺ concentration to fall.

387–389. The answers are 387-e, 388-d, 389-e. (*Ganong*, pp 391, 709–710, 716–718.) The ascending limb of Henle's loop dilutes the fluid within the nephron by reabsorbing Na⁺ without water. In the absence of ADH, the reabsorption of Na⁺ without water continues along the collecting duct, making the Na⁺ concentration lower and lower. In the presence of

ADH, water is reabsorbed from the collecting duct making the luminal fluid isotonic in the cortical collecting duct and hypertonic in the medullary collecting duct.

Parathyroid hormone (PTH) increases Ca^{2+} reabsorption from the thick ascending limb and the distal convoluted tubule. Although most of the filtered Ca^{2+} is reabsorbed in the proximal tubule, the regulation of Ca^{2+} excretion occurs in the thick ascending limb and the distal convoluted tubule. PTH regulates the reabsorption of HPO_4^{2-} in the proximal tubule.

Aldosterone increases the reabsorption of Na^+ from the principal cells within the cortical and medullary collecting ducts. Aldosterone increases Na^+ reabsorption by increasing the luminal permeability to Na^+ on the apical surface and the activity of the Na-K pump on the basal lateral surface of the principal cells. Aldosterone also increases the secretion of K^+ and H^+ from the collecting ducts.

390. The answer is c. (*Ganong*, pp 716–719, 240–246.) When a person is dehydrated, ADH secretion increases. In the presence of ADH, the cortical and medullary collecting tubules become permeable to water, and the filtrate within these portions of the nephron reaches osmotic equilibrium with the interstitial fluid surrounding them. The ascending limb of the loop of Henle is not affected by ADH and so remains impermeable to water. As sodium and other electrolytes are reabsorbed from the ascending limb, its filtrate becomes hypotonic. The glomerular filtrate and proximal tubular fluid remain isotonic to plasma, which in the case of dehydration is higher than normal.

391. The answer is e. (*Stead et al.*, pp 248–249.) Approximately two-thirds of the 40 to 150 mg of protein excreted per day by the kidney is derived from plasma proteins. The remainder is derived from the tubular secretion of a mucoprotein, the Tamm-Horsfall protein, that is present in tubular casts appearing in urinary sediment. Not all plasma proteins are filtered equally because glomerular permeability is related to molecular size and charge. The larger and negatively charged proteins are poorly filtered. Most of the filtered protein is reabsorbed in the proximal tubule unless the filtered load exceeds the tubular capacity. Such overload would occur following damage to the glomerular basement membrane and breakdown of normal barriers, or following an increase in the plasma concentration of a small protein, such as myoglobin. Protein excretion is also increased by sympathetic stimulation, such as that occurring during exercise. In this

situation, renal vasoconstriction reduces the glomerular filtration rate, which, by increasing the transit time of glomerular filtrate, favors diffusion of proteins across the basement membrane. The presence of protein in the urine indicates glomerular dysfunction. RBC casts are indicative of glomerulonephritis. A red color indicates the presence of hemoglobin, myoglobin, or red food.

392. The answer is e. (*Ganong, pp 714–715.*) The pH of the tubular fluid in the distal nephron can be lower than that in the proximal tubule because the tight junctions between the cells in the distal nephron are “tighter” than those in the proximal tubule. An H⁺ ion gradient of only 10 to 1 (i.e., a minimum luminal pH of about 6.4) can be established in the proximal tubule, whereas an H⁺ ion gradient of 1000 to 1 (i.e., a minimum luminal pH of 4.4) can be established in the distal nephron. Because of the tighter junctions, the distal nephron can also establish a greater sodium gradient. Even though the distal nephron can maintain a lower luminal pH, a lesser volume of H⁺ ions is actually secreted than in the proximal tubule. The distal nephron, unlike the proximal tubule, does not have a true brush border, and there is no carbonic anhydrase on the luminal surface of the cells as in the proximal tubule.

393. The answer is d. (*Ganong, pp 454–459, 715. Kasper et al., p 2146. Stead et al., p 230.*) Renin is secreted by the juxtaglomerular cells (near the afferent arterioles) in response to decreased renal arterial pressure. It acts on angiotensinogen to form angiotensin I. Angiotensin I is then converted to angiotensin II, a highly potent pressor agent that, despite a short half-life in humans, has numerous regulatory functions, including the control of aldosterone secretion and sodium and water conservation.

394. The answer is b. (*Ganong, pp 702–704.*) The clearance of PAH equals the true renal plasma flow only if the kidney reabsorbs all of the filtered PAH, that is, no PAH appears in the renal vein. Because the kidney is only able to reabsorb approximately 85 to 90% of the filtered PAH, some PAH appears in the renal vein, and the PAH clearance is less than the true renal plasma flow.

395. The answer is a. (*Stead et al., pp 69–70.*) Glucose reabsorption employs an active transport mechanism located in the proximal tubule. The same mechanism also transports fructose, galactose, and xylose. Essentially all filtered glucose is reabsorbed, inasmuch as the transport

maximum (T_{\max}) for glucose (320 mg/min) is not exceeded in normal persons. In diabetes mellitus, hyperglycemia results in a tubular filtration load that exceeds the T_{\max} , and glycosuria ensues.

396. The answer is c. (*Ganong*, pp 714–715. *Stead et al.*, p 246.) The major structural differences between epithelial cells of the proximal and distal tubules account for the fact that 65% of glomerular filtrate is reabsorbed in the proximal tubule and that the proximal tubule is more permeable to water. The proximal tubule has an extensive brush border composed of numerous microvilli, which markedly increase the surface area for reabsorption, and the tubule also has an extensive network of intracellular channels. The distal tubule has many more tight junctions between cells, which makes it less permeable to water. No significant difference in basement membrane thickness is observed between the proximal and distal tubules. Cells of the distal tubule lying adjacent to the afferent arteriole form the juxtaglomerular apparatus.

397. The answer is a. (*Ganong*, pp 702–705. *Stead et al.*, p 245.) The renal artery pressure and the resistance of the renal vascular bed determine renal blood flow. Decreasing the resistance of either the afferent or efferent arterioles could increase RBF. Alternatively, if the resistance of one of these vessels decreased more than the resistance of the other one increased, RBF would also increase. Glomerular filtration rate will increase if glomerular capillary pressure increases. This can occur if the afferent arteriolar resistance decreases or if the efferent arteriolar resistance increases.

398. The answer is e. (*Ganong*, pp 293–294, 721–722. *Stead et al.*, p 246. *Widmaier et al.*, pp 567–569.) Ammonia (NH_3) is produced from amino acids in the cells of the renal tubules (mainly the proximal tubules), and its rate of production increases during acidosis. This is important in acidosis because it increases the total amount of H^+ ion that can be excreted in a given volume of urine. The NH_3 freely diffuses into the tubular lumen, and because of the high pK_a (9.2) of the reaction, essentially all of it combines with H^+ to form NH_4^+ . This maintains the driving force for more NH_3 to passively diffuse into the lumen. The NH_4^+ that is formed gets “trapped” in the tubules and excreted because the tubules are impermeable to this cation.

399. The answer is d. (*Ganong*, pp 710–712, 724.) The amount of potassium excreted is controlled by the amount of potassium secreted by the

distal tubule. Potassium secretion is a passive process that depends on the electrochemical gradient between the distal tubular cells and the tubular lumen and the permeability of the luminal cells to potassium. By inhibiting Na^+ reabsorption, the intraluminal potential becomes less negative and K^+ secretion is reduced. K^+ -sparing diuretics such as amiloride act in this fashion. Aldosterone increases the intracellular potassium concentration by augmenting the activity of the Na-K pump and increasing the potassium permeability of the luminal membrane. Increasing dietary intake increases the plasma potassium concentration, which in turn stimulates aldosterone production. Increasing the rate of distal tubular flow increases the rate of K^+ secretion. The high flow maintains a low tubular K^+ concentration and therefore increases the electrochemical gradient for K^+ secretion.

400. The answer is b. (*Ganong, pp 709–714.*) Sodium is isosmotically reabsorbed from the proximal tubule; that is, when sodium is reabsorbed, water flows out of the proximal tubule to maintain a constant osmolarity. Thus, the concentration of sodium does not normally change as the filtrate flows through the proximal tubule. Because creatinine cannot be reabsorbed from the tubule, its concentration rises as water is reabsorbed. The concentration of glucose, bicarbonate, and phosphate are all less at the end of the proximal tubule than at the beginning.

401. The answer is e. (*Ganong, pp 702–728.*) Renal plasma flow, filtration fraction, the oncotic pressure, and the filtration rate all increase when the afferent arteriolar resistance is decreased. The renal blood flow increases because total renal resistance is less. Decreasing renal resistance also increases the glomerular capillary pressure, which results in an increase in filtration fraction. Because more fluid is filtered out of the glomerular capillaries and no plasma protein is removed, the oncotic pressure rises. The glomerular filtration rate (GFR) is proportional to the glomerular capillary pressure and the renal plasma flow (RPF). Because both of these increase, so does the GFR.

402. The answer is a. (*Ganong, pp 710–711, 715.*) Sodium and Cl^- are reabsorbed from the distal convoluted tubule by an electrically neutral carrier. The thick ascending limb of Henle's loop employs a carrier that binds one sodium, one potassium, and two chloride ions. It is also electrically neutral. Diffusion of Na^+ through channels on the apical surface of principal cells of the cortical and medullary collecting ducts is electrogenic.

403. The answer is c. (*Ganong*, pp 706–708.) When water is filtered across the glomerulus, the protein concentration (and thus the oncotic pressure) within the capillaries increases, which in turn increases the efficiency by which water reabsorbed from the proximal tubule is returned to the circulatory system. If GFR increases, it results in a larger increase in oncotic pressure. This in turn increases the amount of water reabsorbed from the proximal tubule.

404. The answer is d. (*Ganong*, pp 294–296, 710, 718. *Kasper et al.*, pp 246–249.) Urea is synthesized primarily in the liver. Its excretion is dependent on its concentration in plasma and the glomerular filtration rate (GFR) in the kidney. Approximately 50 to 60% of filtered plasma urea is passively reabsorbed in the proximal tubule at normal GFR. In renal insufficiency, in which GFR is decreased, less urea is filtered and therefore less urea is excreted. The decreased excretion of urea results in an increase in its plasma concentration.

405. The answer is e. (*Ganong*, pp 378–380, 454–459. *Kasper et al.*, pp 1463–1481.) Juxtaglomerular (JG) cells are sensitive to changes in afferent arterial intraluminal pressure. Increased pressure within the afferent arteriole leads to a decrease in renin release, whereas decreased pressure tends to increase renin release. Angiotensin appears to inhibit renin release by initiating the flow of calcium into the JG cells. Renin release is increased in response to increased activity in the sympathetic neurons innervating the kidney. Prostaglandins, particularly PGI₂ and PGE₂, stimulate renin release. Stimulation of the macula densa leads to an increase in renin release, and although the mechanism is not fully understood, it appears that increased delivery of NaCl to the distal nephron is responsible for stimulating the macula densa. Aldosterone does not appear to have any direct effect on renin release.

406. The answer is b. (*Ganong*, pp 367, 375–381. *Widmaier et al.*, pp 548–550, 554–557.) Aldosterone binds to an intracellular receptor that causes an increased synthesis of a variety of proteins, including K⁺ and Na⁺ ion channels and Na⁺-K⁺-ATPase, which together act to increase Na⁺ reabsorption and K⁺ secretion by the tubular cells of the distal nephron. The secretion of H⁺ is also enhanced by aldosterone. Aldosterone secretion is stimulated by a decrease in blood volume (through the renin-angiotensin system) and by increased plasma K⁺ concentrations.

407. The answer is e. (*Ganong*, pp 95, 113, 242–247, 456, 604, 713–716, 729–730. *Widmaier et al.*, pp 550–552.) The principal physiologic action of

antidiuretic hormone (ADH) is to increase water retention by the kidney. Antidiuretic hormone acts on the distal nephron to increase its permeability so that water more readily enters the hypertonic interstitium of the renal pyramids. Thus, the concentration of solutes in the urine is increased. Antidiuretic hormone increases Na^+ reabsorption so that the actual amount of Na^+ excreted is decreased. It also acts as a vasoconstrictor; hence, it is called arginine vasopressin (AVP). ADH has no effect on glomerular filtration rate, and because it increases water reabsorption, it would decrease urine formation.

408. The answer is d. (*Widmaier et al.*, pp 543–546.) Concentrated urine is produced by the reabsorption of water from the medullary collecting ducts down an osmotic gradient that is created by the reabsorption of sodium from the loop of Henle. If the Na^+-K^+ pump activity in the loop of Henle is increased, the osmotic gradient, and the ability to excrete concentrated urine, is increased. Water reabsorption will be reduced if the permeability of the collecting duct principal cells is reduced. Also, concentrated urine will be more difficult to produce if an increase in glomerular capillary increases the filtered load of Na^+ or if the reabsorption of Na^+ is decreased in the proximal tubule.

409. The answer is d. (*Kasper et al.*, 1722–1724.) The most likely cause of acute renal failure in this patient is ureteral obstruction, as evidenced by the swelling of the kidneys. The ureteral obstruction raises the hydrostatic pressure within Bowman's space, which reduces glomerular filtration. The decrease in GFR (postrenal renal failure) increases creatinine. The normal blood pressure rules out sympathetic discharge, coarctation of the renal artery, and hypovolemia as causes of her renal failure. Hyperproteinemia, although possibly a cause of renal failure, would not produce an enlarged kidney.

410. The answer is b. (*Stead et al.*, pp 77–78, 227, 277.) The increased secretion of antidiuretic hormone (ADH) increases the permeability of the distal nephron to water and therefore increases the reabsorption of water from the kidney. The excessive reabsorption of water dilutes the extracellular fluid, producing a decrease in plasma sodium, osmolarity, and oncotic pressure. The decreased extracellular osmolarity causes water to flow from the extracellular fluid compartment into the intracellular fluid compartment, increasing intracellular volume. Because more water is being reabsorbed, less is excreted and urinary flow is decreased.

411. The answer is c. (*Ganong, pp 724–725. Kasper et al., pp 1373–1374.*) The distal nephron has a negative luminal potential because it is poorly permeable to negatively charged ions. Therefore, when Na^+ is reabsorbed, negatively charged ions, primarily Cl^- , lag behind, producing a negative intraluminal potential. Although a similar situation occurs in the proximal tubule, the proximal tubule has a higher permeability to Cl^- and, therefore, does not develop as large a negative intraluminal potential. The distal nephron is less permeable to hydrogen than the proximal tubule. Aldosterone increases Na^+ reabsorption from the distal nephron but has no effect on the proximal tubule. K^+ is reabsorbed from the proximal tubule and secreted by the distal nephron. Although the amount of H^+ excreted each day is determined by the amount of H^+ secreted into the distal nephron, the proximal tubule secretes much more H^+ than the distal nephron. However, almost all of the H^+ secreted in the proximal tubule is reabsorbed in association with the reabsorption of HCO_3^- .

412. The answer is c. (*Ganong, pp 712–713. Stead et al., pp 181–183.*) The macula densa senses the chloride concentration of the fluid flowing from the ascending limb of Henle's loop into the distal convoluted tubule. An increase in NaCl concentration occurs when the amount of fluid flowing through the ascending limb increases because there is less time available for the reabsorption of NaCl . The resulting increase in Cl^- concentration results in the release of adenosine (and/or ATP) from the macula densa. Adenosine constricts the afferent arteriole, resulting in a decrease in filtration and a return of the flow rate within the nephron toward normal. This response is referred to as tubuloglomerular feedback. If the NaCl concentration decreases (e.g., when circulating blood volume decreases), the decreased Cl^- concentration results in the release of renin from granular cells of the juxtaglomerular apparatus. Spironolactone acts by competitive inhibition of aldosterone, thereby blocking Na^+ reabsorption in the distal tubules and collecting ducts. Potassium-sparing diuretics are relatively weak and therefore are most effective when administered in combination with loop and/or thiazide diuretics.

413. The answer is d. (*Ganong, pp 362–365, 377–381.*) A decrease in plasma sodium increases aldosterone secretion. Aldosterone secretion increases in response to an increase in all of the other answer choices. The effects of sodium on aldosterone secretion are mediated via the renin-angiotensin system. Hyponatremia, as may occur with a low-sodium diet, is associated with a decrease in extracellular volume, which increases renin

secretion, probably due to a reflex increase in renal sympathetic nerve activity. Increased renin leads to increased production of angiotensin II, which binds to AT₁ receptors in the zona glomerulosa, which act via a G protein to activate phospholipase C. The resultant increase in protein kinase C fosters the conversion of cholesterol to pregnenolone and facilitates the action of aldosterone synthase, resulting in the conversion of deoxycorticosterone to aldosterone. Increased potassium concentration directly stimulates aldosterone secretion. Like angiotensin II, K⁺ stimulates the conversion of cholesterol to pregnenolone and the conversion of deoxycorticosterone to aldosterone by aldosterone synthase. Potassium exerts effect on aldosterone secretion by depolarizing the the zona glomerulosa cells, which opens voltage-gated Ca²⁺ channels, increasing intracellular Ca²⁺. Adrenocorticotrophic hormone (ACTH) stimulates aldosterone synthesis and secretion via increases in cyclic AMP and protein kinase A. The stimulatory effect of ACTH on aldosterone secretion is usually transient, declining in 1–2 days, but persists in patients with glucocorticoid-remediable aldosteronism, an autosomal dominant disorder in which the 5' regulatory region of the 11β-hydroxylase gene is fused to the coding region of aldosterone synthase gene, producing an ACTH-sensitive aldosterone synthase.

414. The answer is c. (*Ganong, pp 340, 707–708, 718–719. Stead et al., pp 63–64, 76–77.*) The rate of fluid volume excretion is influenced by the glomerular filtration rate (GFR) and the rate of tubular reabsorption. Sympathetic stimulation, by causing vasoconstriction, decreases both GFR and urinary volume. Increased renal arterial pressure, on the other hand, increases urinary volume by increasing GFR. Infusion of the nonmetabolized carbohydrate mannitol or excess glucose in the urine in diabetes mellitus both cause osmotic diuresis. In diabetes insipidus, ADH secretion is markedly reduced or absent, and water passes through the relatively impermeable collecting ducts without being reabsorbed, causing an increase in urine volume.

415. The answer is b. (*Ganong, pp 724–725.*) Diuretics produce an increase in water excretion primarily by blocking Na⁺ reabsorption. If Na⁺ reabsorption is blocked in the proximal portions of the nephron, then the amount of Na⁺ in the filtrate flowing through the distal nephron increases. The increased Na⁺ load in the distal nephron results in an increased Na⁺ reabsorption and, as a result, an increased K⁺ secretion. If Na⁺ reabsorption in the distal nephron is blocked, then a diuresis can be produced without an excess loss of K⁺. These diuretics, some of which block the

aldosterone receptor, others of which block the Na⁺ channels on the apical surface of the distal nephron tubular cells, are called potassium-sparing diuretics.

416. The answer is c. (*Ganong*, pp 734–735.) Persistent diarrhea will result in a metabolic acidosis, due to the loss of the bicarbonate-rich secretions from the pancreas and gallbladder. The ensuing metabolic acidosis will decrease the plasma concentration of HCO₃⁻, decreasing the amount of bicarbonate that is filtered into the proximal tubule. At the same time, the metabolic acidosis will increase ammonia production by the proximal tubule as well as H⁺ secretion and production of new bicarbonate by the distal nephron. Because the metabolic acidosis is produced by the loss of bicarbonate, the anion gap will remain within normal limits.

417. The answer is e. (*Ganong*, pp 713–718.) ADH increases the permeability of the distal nephron to urea as well as to water. The increased urea permeability increases the urea concentration and osmolarity of the interstitial fluid surrounding the loop of Henle and the distal nephron. The high interstitial urea concentration helps to increase the osmolarity of the fluid within the descending limb of the loop of Henle, the reabsorption of Na⁺ from the ascending limb of the loop of Henle, and the reabsorption of water from the distal nephron.

418. The answer is c. (*Ganong*, pp 702–708. *Vander et al.*, pp 512–513.) The filtration fraction is directly proportional to the glomerular capillary pressure. Increasing the resistance of the efferent arteriole increases the glomerular capillary pressure and, therefore, the filtration fraction. Increasing renal blood flow will not have any direct effect on the filtration fraction but may cause the filtration fraction to decrease if the excess flow rate through the glomerulus limits the amount of filtration that can occur. Increasing the afferent arteriolar resistance will decrease glomerular capillary pressure and, therefore, the filtration fraction. Increasing the plasma oncotic pressure or the hydrostatic pressure within Bowman's capsule will decrease the filtration fraction because both of these Starling forces oppose filtration.

419. The answer is a. (*Ganong*, pp 720–725.) Carbonic anhydrase is the enzyme that catalyzes the formation of CO₂ and H₂O from HCO₃⁻ and H⁺. In the proximal tubule, the efficient reabsorption of bicarbonate requires the presence of carbonic anhydrase. Carbonic anhydrase inhibitors prevent the formation of CO₂ and therefore block the reabsorption of bicarbonate (and

Na^+), resulting in a diuresis. Because almost all of the filtered bicarbonate is reabsorbed in the proximal tubule, inhibiting carbonic anhydrase has little effect on bicarbonate reabsorption from other segments of the nephron.

420. The answer is d. (*Ganong*, pp 703–705. *Stead et al.*, pp 242–243. *Vander et al.*, pp 414–416.) Blood flow through the kidney is controlled by numerous humoral agents. Angiotensin II decreases renal blood flow. It vasoconstricts efferent arterioles more than afferent arterioles, which helps to maintain glomerular filtration rate in the face of decreases in renal perfusion pressure. This may account for the renal failure that sometimes develops in patients with decreased renal perfusion who are taking angiotensin-converting enzyme inhibitors. Nitric oxide dilates the afferent arteriole and constricts the efferent arteriole, producing a rise in glomerular capillary pressure (and glomerular filtration) without having much of an effect on renal blood flow. Dopamine synthesized in the kidney increases renal blood flow and sodium excretion. Acetylcholine and atrial natriuretic peptide also produce renal vasodilation and an increase in renal blood flow.

421. The answer is d. (*Ganong*, pp 705–712.) The proximal tubule reabsorbs approximately two-thirds of the filtered water and two-thirds of the filtered Na^+ , Cl^- , and K^+ . Therefore, the concentration of these substances is the same at the beginning and end of the proximal tubule. Because creatinine is not reabsorbed, its concentration increases from the proximal to distal ends of the proximal tubule. Phosphate, however, is almost completely reabsorbed in the proximal tubule, so its concentration decreases along the length of the tubule.

422. The answer is d. (*Ganong et al.*, pp 709–713.) About two-thirds of the filtered load of sodium is reabsorbed by the proximal tubule. This percentage is maintained when there are spontaneous changes in the filtered load by a process called glomerular tubular balance. However, the percentage of reabsorption can be changed when necessary to maintain homeostasis. For example, the production of angiotensin II during volume depletion can result in the reabsorption of as much as 75% of the filtered load of Na^+ .

423. The answer is e. (*Ganong*, pp 460–462, 706–707, 723–724.) Atrial natriuretic peptide (ANP) increases Na^+ excretion by decreasing the amount of Na^+ reabsorbed from the inner medullary collecting duct via a decrease in the permeability of the apical membrane of the collecting duct epithelial cells. Less Na^+ is able to enter the epithelial cells and therefore, less Na^+ is reabsorbed. ANP also increases Na^+ excretion by increasing the filtered load of Na^+ .

424. The answer is e. (*Ganong, pp 719–720.*) Free water clearance is the amount of water excreted in excess of that required to make the urine isotonic to plasma. It is calculated using the formula: $C_{H_2O} = V - C_{osm}$. Free water clearance is positive when the urine is dilute (more than a sufficient amount of water is excreted), and free water clearance is negative when the urine is concentrated (not enough water is excreted to make the urine isotonic to plasma). An increase in free water clearance can lead to hypernatremia; a decrease in free water clearance can lead to hyponatremia. In diabetes insipidus, very little water is reabsorbed in the distal nephron, and, therefore, the free water clearance is very high. In heart failure or renal failure, very little free water can be generated even if the urine is dilute because the glomerular filtration rate is decreased. With diuretic therapy, Na^+ excretion is increased. Therefore, the increased water excretion is accompanied by an increased Na^+ excretion and the amount of free water generated is limited. Although the water loss is proportionally greater than the solute loss in diabetes mellitus, the amount of water excreted is much less and the solute concentration significantly higher than in diabetes insipidus, so the free water clearance is much less in diabetes mellitus than in diabetes insipidus.

425. The answer is b. (*Ganong, pp 391–393, 710. Stead et al., pp 246–249.*) Between 85 and 90% of the filtered phosphate is reabsorbed in the proximal tubule by a sodium-dependent secondary active transport system. The transporter is electrically neutral, requiring two Na^+ molecules for every HPO_4^{2-} molecule that it transports. The transporter is inhibited by parathyroid hormone (PTH). The decreased reabsorption of phosphate results in an increased clearance from the plasma. PTH is released from the parathyroid gland in response to lowered plasma Ca^{2+} concentrations. In addition to inhibiting the reabsorption of phosphate from the proximal tubule, PTH increases the reabsorption of Ca^{2+} from the loop of Henle.

426. The answer is b. (*Ganong, pp 710, 724.*) Potassium is secreted from the principal cells lining the cortical and medullary collecting ducts. Secretion is passive and is increased by increasing the electrochemical gradient driving the diffusion through the potassium channels on the apical surface of the principal cells. Increasing Na^+ concentration within the distal nephron increases Na^+ reabsorption, which, in turn, increases the negativity of the luminal electrical potential. The increased negativity drives K^+ into the lumen at a greater rate. Decreasing the distal flow rate, which occurs when circulating blood volume or renal blood flow decreases or when sympathetic nerve activity to the renal vessels increases, will allow the K^+ concentration within the distal nephron to

increase. The increase in K^+ concentration decreases the driving force for K^+ diffusion and, therefore, decreases K^+ secretion.

427. The answer is d. (*Ganong, pp 454–459. Widmaier et al., pp 548–550, 528–529.*) The juxtaglomerular apparatus (JGA) is responsible for releasing renin when the effective circulating blood volume is decreased. The JGA releases renin when the Cl^- concentration in the luminal fluid bathing the macula densa is decreased. The decrease in Cl^- (and Na^+) concentration occurs when the flow rate within the nephron decreases and ample time is available for the loop of Henle to remove NaCl from the lumen. Adenosine is released from the macula densa cells when the luminal Cl^- concentration increases in response to an increase in luminal flow rate. Adenosine decreases renal blood flow by constricting the afferent arteriole and, therefore, the blood flow through the glomerular capillary.

428. The answer is d. (*Ganong, pp 705–708, 725–726. Stead et al., pp 242–243.*) The excretion of creatinine, which is neither reabsorbed nor secreted in any significant amount, is dependent on filtration, which is in turn dependent on renal plasma flow. The decrease in renal plasma flow that accompanies chronic renal failure results in a decrease in creatinine excretion and an increase in plasma creatinine concentration. The increase in plasma creatinine concentration is used to assess the percentage of non functioning nephrons in renal failure. Interestingly, the remaining nephrons adapt to renal failure. To maintain Na^+ balance, less Na^+ is reabsorbed, so the fractional excretion (the fraction of filtered Na^+ that is excreted) goes up. Although the remaining nephrons are able to excrete a larger than normal amount of H^+ , secretion cannot fully compensate for the reduced number of nephrons because there is a limit to the amount of NH_4^+ that can be synthesized by the proximal tubules. Therefore, despite the overall increase in net acid excretion, H^+ accumulation leads to a metabolic acidosis. Even creatinine secretion can be increased so the plasma creatinine concentration does not increase proportionally to the amount of renal damage. The anion gap increases because of the reduced excretion of phosphate and other anions that are included in the anion gap. Free water clearance decreases because there is decreased filtration. Therefore, to prevent overhydration in patients with renal failure, water intake must be limited.

429. The answer is c. (*Ganong, pp 459–460.*) The kidney produces a number of important hormones, including erythropoietin. Erythropoietin is necessary for the normal production of red blood cells. The anemia

associated with renal failure results from the decrease in the synthesis of erythropoietin. Often, the first clinical sign of renal failure is the fatigue produced by anemia.

430. The answer is c. (*Ganong*, pp 650, 661–662, 702–705. *Levitzky*, pp 86–92.) Because the lungs are in series with the heart, pulmonary blood flow constitutes 100% of the cardiac output, whereas the kidneys receive ~25% of the cardiac output. As part of the systemic circulation, the renal circulation has higher vascular pressures, including both arterial pressure and capillary hydrostatic pressure. The capillary oncotic pressures in the renal and pulmonary circulations are essentially equal.

431. The answer is d. (*Ganong*, pp 612, 705.) Oxygen consumption by the kidney is directly proportional to the amount of sodium reabsorbed and is greatest in the cortex, where most tubular reabsorption of sodium occurs. An increase in renal blood flow will raise the glomerular filtration rate and increase the quantity of solute to be transported, so that oxygen consumption increases as blood flow increases and the arteriovenous oxygen difference remains constant. This is in contrast to the situation in other organs where increases in blood flow are accompanied by a decrease in arteriovenous oxygen difference. Erythropoietin is released in response to renal hypoxia and acts to increase erythrocyte production.

432. The answer is c. (*Ganong*, pp 240–246, 716–719.) In the absence of antidiuretic hormone (ADH, vasopressin), the cortical and medullary collecting tubules and ducts are impermeable to water. ADH increases the water permeability of these nephron segments and allows the filtrate to reach osmotic equilibrium with the interstitial fluid surrounding the nephron. The interstitial fluid in the cortex of the kidney is isotonic to plasma, and, therefore, the filtrate can become isotonic to plasma in the cortical collecting tubule. The interstitial fluid is hypertonic to plasma in the medullary collecting tubule, and so the filtrate becomes hypertonic to plasma in this region of the nephron and remains hypertonic as it passes through the renal pelvis. ADH has no effect on the water permeability of the loop of Henle. The filtrate is hypertonic to plasma in the descending limb and becomes hypotonic to plasma by the time it reaches the end of the ascending limb of the loop of Henle.

433. The answer is d. (*Ganong*, pp 709–710, 722.) In the proximal tubule, a large amount of H⁺ ion is secreted into the tubule lumen via an Na⁺-H⁺

antiporter (exchanger). Most of this H^+ combines with bicarbonate ion in the tubular fluid to form CO_2 and water. The CO_2 diffuses into the proximal tubular cells, where the opposite reaction takes place to form H^+ and HCO_3^- . The HCO_3^- exits the cells on the basolateral side and enters the blood as reabsorbed bicarbonate. Carbonic anhydrase is located on the luminal surface of the cells as well as inside the cells to facilitate the above reactions.

434. The answer is c. (*Ganong, pp 706–708. Kasper et al., pp 541–542.*) Glomerular filtration rate (GFR) will decrease if there is a decrease in the net glomerular capillary pressure or the flow of fluid through the glomerulus. The net glomerular capillary pressure (for Starling forces) is equal to the glomerular capillary pressure minus the sum of the plasma oncotic pressure and intrarenal pressure. Compression of the renal capsule increases the intrarenal pressure and therefore decreases the net capillary filtration pressure. Constriction of the efferent arteriole increases glomerular capillary pressure. Decreasing the concentration of plasma protein will decrease the plasma oncotic pressure and lead to an increase in GFR. In clinical practice, any solid renal masses should be considered malignant until proven otherwise. Renal cell carcinomas account for 90–95% of malignant neoplasms arising from the kidney.

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Reproductive Physiology

Questions

435. A 15-year-old boy presents for his annual athletic physical. A thorough examination reveals unilateral cryptorchidism. The physician schedules a follow-up visit with the boy and his parents to discuss his recommendation for surgery to correct the defect because of his concerns of possible infertility in the future. Which of the following statements about spermatogenesis is correct?

- a. Mature spermatozoa are present at birth, but cannot be released until puberty is reached.
- b. Spermatogenesis requires a temperature lower than internal body temperature.
- c. Spermatogenesis requires continuous release of gonadotropin-releasing hormone (GRH).
- d. Leydig cell secretion of testosterone requires follicle-stimulating hormone (FSH).
- e. Luteinizing hormone (LH) acts directly on Sertoli cells to promote cell division.

436. A 32-year-old male taking chlorpromazine for his schizophrenia presents with diminished libido and decreased beard growth. His blood prolactin level of 75 $\mu\text{g}/\text{L}$ confirms the presence of hyperprolactinemia. Which of the following statements about prolactin is correct?

- a. Normal adult serum levels of prolactin are much higher in women than men.
- b. Prolactin causes milk ejection during suckling.
- c. Prolactin inhibits the growth of breast tissue.
- d. Prolactin inhibits gonadotropin releasing hormone secretion by the hypothalamus.
- e. Prolactin inhibits gonadotropin secretion by the pituitary gland.

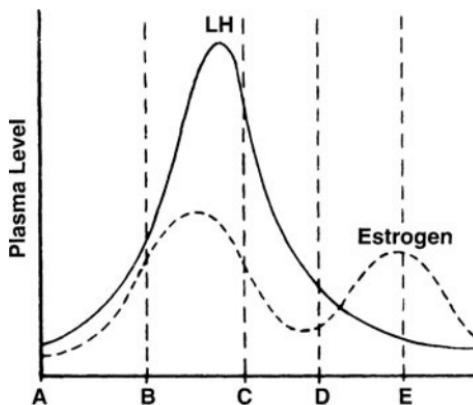
437. Which of the following is the source of estrogen and progesterone during the first two months of pregnancy?

- a. Ovary
- b. Placenta
- c. Corpus luteum
- d. Anterior pituitary
- e. Posterior pituitary

438. Which of the following is the source of estrogen and progesterone during the last 7 months of pregnancy?

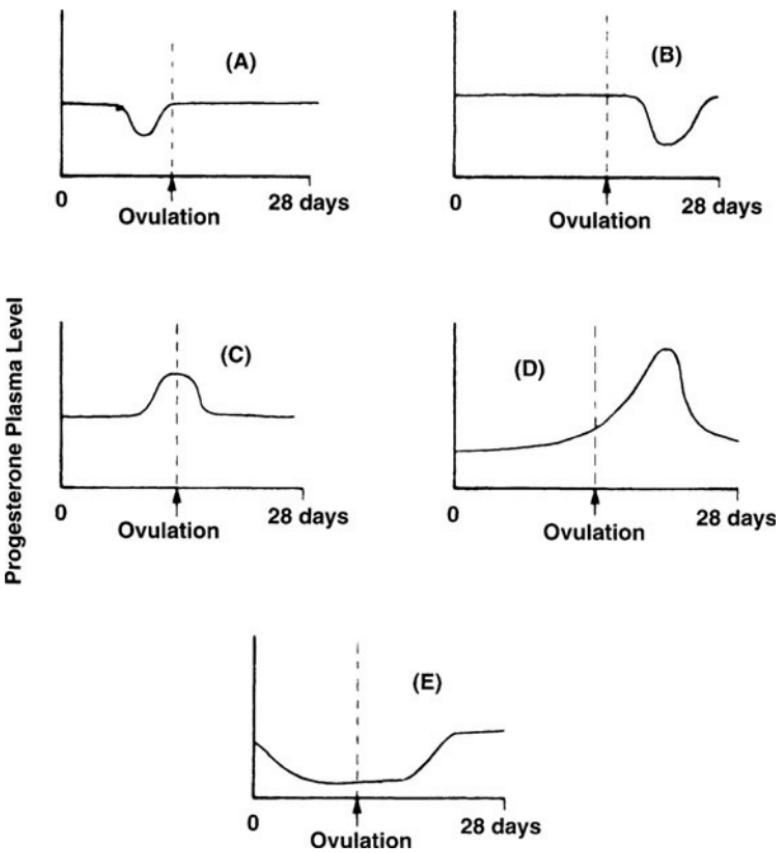
- a. Ovary
- b. Placenta
- c. Corpus luteum
- d. Anterior pituitary
- e. Posterior pituitary

439. In the graph below showing plasma hormone levels as a function of time, ovulation takes place at which of the lettered points on the time axis?



- a. A
- b. B
- c. C
- d. D
- e. E

440. The normal pattern of progesterone secretion during the menstrual cycle is exhibited by which of the following curves?

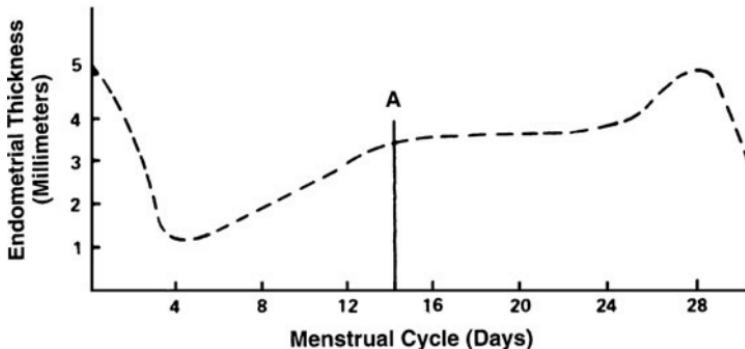


- a. A
- b. B
- c. C
- d. D
- e. E

441. An 18-year-old emaciated female who has been on a strict diet regimen and training for a marathon presents with amenorrhea. Exogenous pulsatile administration of gonadotropin-releasing hormone (GnRH) restores ovulation and menses. Ovulation is caused by a sudden increase in the secretion of which of the following hormones?

- a. LH
- b. FSH
- c. GnRH
- d. Estrogen
- e. Progesterone

442. In the following graph of changes in endometrial thickness during a normal 28-day menstrual cycle, the event designated A corresponds most closely to which of the following phases?



- a. The menstrual phase
- b. The maturation of the corpus luteum
- c. The early proliferative phase
- d. The secretory phase
- e. Ovulation

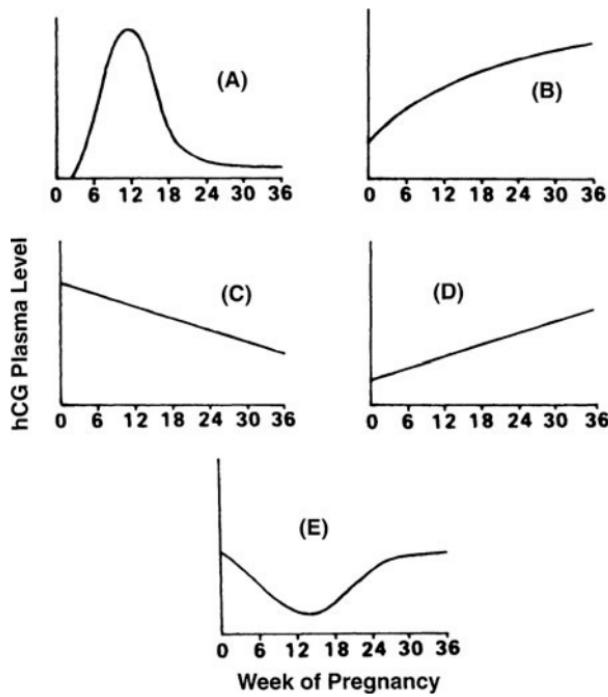
443. A couple presents at the Fertility Center concerned that they have not been able to conceive a child. The reproductive endocrinologist evaluates the wife to be certain that she is ovulating. Which of the following is an indication that ovulation has taken place?

- a. An increase in serum FSH levels
- b. A drop in body temperature
- c. An increase in serum LH levels
- d. An increase in serum progesterone levels
- e. An increase in serum estrogen levels

444. A 26-year-old male with Klinefelter's syndrome has seminiferous tubule dysgenesis. Which of the following is a function of Sertoli cells in the seminiferous tubules?

- a. Secretion of FSH into the tubular lumen
- b. Secretion of testosterone into the tubular lumen
- c. Maintenance of the blood-testis barrier
- d. Synthesis of estrogen after puberty
- e. Expression of surface LH receptors

445. In a normal pregnancy, human chorionic gonadotropin (hCG) prevents the involution of the corpus luteum that normally occurs at the end of the menstrual cycle. Which of the curves shown below approximates the level of this hormone during pregnancy?



- a. A
- b. B
- c. C
- d. D
- e. E

446. A woman presents to her obstetrician with concerns that she has had trouble breast feeding. She reports that her mother-in-law told her that alcohol would relax her and allow her milk to flow more readily, but it has not helped, even with drinking up to a bottle of wine a day. Which of the following hormones is involved in the ejection of milk from a lactating mammary gland?

- a. Growth hormone
- b. FSH
- c. LH
- d. Prolactin
- e. Oxytocin

447. Assuming a regular menstrual cycle of 28 to 30 days, ovulation would be expected to occur between which of the following days?

- a. Days 6 and 8
- b. Days 10 and 12
- c. Days 14 and 16
- d. Days 18 and 20
- e. Days 22 and 24

448. An 18-year-old college woman is brought to the Emergency Department by her roommate after she was raped walking back to the dorm from the library at night. She requests the “morning after pill” she has heard about to prevent pregnancy from the violation. She is given a postcoital contraceptive to prevent implantation and induce regression of the corpus luteum. Which of the following is correct regarding implantation of the zygote in the uterine wall?

- a. Precedes formation of the zona pellucida
- b. Involves infiltration of the endometrium by the syncytiotrophoblast
- c. Occurs 3 to 5 days after fertilization
- d. Occurs when the embryo consists of approximately 128 cells
- e. Is inhibited by secretion of progesterone from the corpus luteum

449. A 22-year-old woman presents at the obstetrician/gynecologist’s office with complaints of painful menstruation accompanied by profuse menstrual flow. The doctor prescribes a low-dose oral contraceptive for the menorrhagia and ibuprofen for the dysmenorrhea. Biological actions of estrogens include a decrease in which of the following?

- a. Ovarian follicular growth
- b. Duct growth in the breasts

- c. Uterine smooth muscle motility
- d. Serum cholesterol levels
- e. Libido

450. Which of the following hormones is primarily responsible for development of ovarian follicles prior to ovulation?

- a. Chorionic gonadotropin
- b. Estradiol
- c. Follicle-stimulating hormone
- d. Luteinizing hormone
- e. Progesterone

451. Which of the following statements about progesterone is true?

- a. Progesterone is secreted by the corpus luteum.
- b. Progesterone secretion by the placenta increases at week 6 of gestation.
- c. Plasma levels of progesterone increase during menses.
- d. Plasma levels of progesterone remain constant after implantation.
- e. Plasma levels of progesterone decrease after ovulation.

452. Administration of estrogens in women will do which of the following?

- a. Limit the growth of ovarian follicles
- b. Produce cyclic changes in the vagina and endometrium
- c. Cause cervical mucus to become thicker and more acidic
- d. Retard ductal proliferation in the breast
- e. Decrease bone density

453. A young couple presents with concerns that they have not been able to conceive a child. Physical examination of the 22-year-old husband reveals mild obesity, gynecomastia, and decreased facial and axillary hair. He has male genitalia, but penile length is decreased and the testes are small. Chromosomal analysis reveals the XXY pattern of Klinefelter's syndrome. Which of the following is the principal androgen responsible for transforming undifferentiated external genitalia in the fetus into male external genitalia?

- a. Testosterone
- b. Androstenedione
- c. Androsterone
- d. Dihydrotestosterone
- e. Müllerian-inhibiting substance

454. The action of which of the following hormones is prevented by inhibitors of microtubules?

- a. Oxytocin
- b. Progesterone
- c. Estradiol
- d. Insulin
- e. Prolactin

455. A 55-year-old woman is experiencing the signs and symptoms of menopause. Her gynecologist discusses with her the possibility of hormone replacement therapy, which has which of the following effects?

- a. Returns the menstrual cycle pattern to normal
- b. Reduces the incidence of hot flashes
- c. Reduces the risk of coronary artery disease and stroke
- d. Reduces the risk of breast cancer
- e. Increases the risk of osteoporosis

456. Which one of the following statements about semen is correct?

- a. The bulk of semen volume is contributed by the prostate gland
- b. Semen prevents sperm capacitation
- c. Semen is propelled out of the urethra by contraction of the smooth muscle comprising the bulbocavernosus muscle.
- d. Semen activates sperm motility in the male reproductive tract
- e. In the population, sperm counts in semen have increased over the last 20 years

457. Prolactin secretion is tonically suppressed in nonpregnant women by which of the following hormones?

- a. Estrogen
- b. Progesterone
- c. Dopamine
- d. FSH
- e. LH

458. A young couple has been trying to conceive a baby. The Medical Director of the Fertility Center has advised the woman to take her basal temperature readings on a daily basis and for them to have intercourse at the time the woman appears to be ovulating. Once conception takes place, which of the following must occur in order for the pregnancy to proceed uneventfully?

- a. The corpus luteum must secrete progesterone to sustain the endometrium.
- b. The pituitary must secrete hCG to maintain the corpus luteum.
- c. The pituitary must secrete prolactin to sustain the placenta.
- d. The placenta must secrete FSH to maintain ovarian function.
- e. The placenta must secrete LH to maintain ovarian function.

459. A 32-year-old woman presents at her physician's office complaining of nausea and vomiting. The history reveals that her symptoms have been present for over a month and that they seem to be worse in the morning. A urine sample is taken and shows that the woman is pregnant. Physiological changes that occur during pregnancy include which of the following?

- a. Decreased production of cortisol and corticosterone
- b. Increased conversion of glucose to glycogen
- c. Hypercapnia
- d. Increased hematocrit
- e. Reduced circulating gonadotropin levels

460. A 35-year-old woman presents at her obstetrician/gynecologist's office for her annual well-woman examination. She reports that she may have "a touch of the flu" because she has been tired and nauseated the past week and also has had fleeting episodes of lower abdominal pain. She wasn't sure when her last menstrual period started but after looking at a calendar, realized that it had been 38 days. A right adnexal mass was palpated on routine pelvic examination and subsequently observed on ultrasound. Urinalysis confirmed that the woman was pregnant and serum levels of the tumor marker CA-125 were elevated. The gynecologist informed the woman that she may have to have her ovary removed, but that they need to wait another week or two to do the laparotomy in order to protect her fetus. Ovariectomy before the sixth week of pregnancy leads to abortion, but thereafter has no effect on pregnancy because the placenta secretes adequate amounts of which of the following hormones?

- a. Estrogens and progesterone
- b. Estrogen and relaxin
- c. Progesterone and human chorionic gonadotropin (hCG)
- d. Human chorionic somatomammotropin (hCS) and hCG
- e. Growth hormone releasing hormone (GnRH) and corticotropin releasing hormone (CRH)

Reproductive Physiology

Answers

435. The answer is b. (*Ganong*, pp 425–427, 433. *Kasper et al.*, pp 280, 550, 2191, 2219.) The temperature of the testes must be considerably below that of the internal body temperature for spermatogenesis to occur. The testes are normally maintained at a temperature of about 32°C, and are kept cool by a countercurrent heat exchange between the spermatic arteries and veins and by air circulating around the scrotum. The testes develop in the abdomen but normally descend into the scrotum during fetal development. In ~10% of newborn males, one or, less commonly, both testes remain in the abdominal cavity or inguinal canal. Although most (98%) of undescended testes (cryptorchidism) spontaneously descend by 1 year, and all but 0.3% spontaneously descend by puberty, early surgical treatment is recommended because abdominal temperatures can cause irreversible damage to the spermatogenic epithelium and the incidence of malignant tumors is higher in undescended than in scrotal testes. Maturation of spermatogonia, the primitive germ cells, into primary spermatoocytes does not begin until adolescence. Throughout the reproductive life of the human male, 100 to 200 million sperm are produced daily. Of critical importance to the hormonal regulation of spermatogenesis are the pulsatile release of GRH and the subsequent involvement of FSH and LH at their target cells. FSH acts directly on the Sertoli cells of the seminiferous tubules to initiate mitotic and meiotic activity of germ cells. LH effects are thought to be mediated via stimulation of testosterone secretion by the Leydig cells.

436. The answer is d. (*Ganong*, pp 236, 248–249, 421–424, 450–452. *Kasper et al.*, pp 271–275, 2084–2087.) Prolactin is a single-chain protein structurally homologous to growth hormone, which is secreted by the anterior pituitary and has the principal physiologic effects of lactation (i.e., milk production), decreased reproductive function, and suppressed sexual drive. Normal adult serum levels of prolactin are about the same or only slightly higher in females compared to males. Consistent with its role in lactogenesis, prolactin secretion increases during pregnancy. Suckling increases prolactin secretion, but milk ejection during suckling is due to oxytocin release. Prolactin inhibits reproductive function by inhibiting

hypothalamic GnRH release and pituitary gonadotropin secretion. Hyperprolactinemia is the most common pituitary hormone hypersecretion syndrome in both males and females. Pregnancy and lactation are the most important physiological causes of hyperprolactinemia. Prolactin-secreting pituitary adenomas, hypothyroidism, and drug-induced inhibition or disruption of dopaminergic receptor function are other common causes of hyperprolactinemia.

437–438. The answers are c and b. (*Ganong, pp 448–451.*) During the first 2 months of pregnancy, estrogen and progesterone production is primarily the responsibility of the corpus luteum. The placenta serves as the source of the hormones during the remainder of pregnancy. Progesterone is essential to maintain placental implantation, inhibit uterine contractions, and suppress the maternal immune system response to fetal antigens. Estrogens serve to increase the size of the uterus, induce progesterone and oxytocin receptors, stimulate maternal hepatic protein secretion, and promote breast development. Estriol is the major estrogen produced during pregnancy. The production of estrogen and progesterone during gestation requires cooperation between the maternal, placental, and fetal compartments—the fetoplacental unit.

439. The answer is c. (*Ganong, pp 438–439.*) Ovulation takes place just after the peak of the luteinizing hormone (LH) and estrogen curves, which occurs on approximately the fourteenth day of the menstrual cycle. Although FSH is primarily responsible for follicular maturation within the ovary, LH is necessary for final follicular maturation; without it, ovulation cannot take place. Both estrogen, following a sharp preovulatory rise in plasma concentration, and progesterone are secreted in abundance by the postovulatory corpus luteum.

440. The answer is d. (*Ganong, pp 438–439.*) There is a marked increase in progesterone secretion following ovulation. Almost all the progesterone secreted in nonpregnant women is secreted by the corpus luteum. Secretion of both progesterone and estrogen is controlled by luteinizing hormone (LH) released by the adenohypophysis, and LH release itself is under the direction of a hypothalamic releasing factor.

441. The answer is a. (*Ganong, pp 433–442. Kasper et al., pp 431–432, 2198–2207.*) Ovulation is caused by a sudden increase in LH secretion. Both LH and FSH blood levels increase during the follicular phase of the

menstrual cycle and reach peak blood levels prior to ovulation. Estrogen levels follow a similar pattern during the follicular phase. The physiologic signal for ovulation is a surge in LH blood levels. Under the influence of LH, thecal and granulosa cells become the luteal cells of the corpus luteum. Progesterone production by the corpus luteum increases significantly. Estrogen levels also increase, but do not reach the levels achieved during the follicular phase. In anorexia nervosa, the regulation of virtually every endocrine system is altered, but the most striking changes occur in the reproductive system. Amenorrhea in anorexia nervosa is hypothalamic in origin and reflects decreased production of gonadotropin-releasing hormone (with low levels of LH and FSH) that may be due to a marked reduction in leptin associated with the decreased mass of adipose tissue. In up to 25% of patients, however, amenorrhea precedes significant weight loss.

442. The answer is e. (*Ganong, pp 434–440. Kasper et al., pp 2198–2202.*) Ovulation occurs at point A on the graph. In response to estrogen secretion by the ovary, the endometrial lining of the uterus undergoes proliferation of both glandular epithelium and supporting stroma during the first 10 to 14 days of the menstrual cycle. Following ovulation, the glands begin to secrete mucus and the stroma undergoes pseudodecidual reaction in preparation for potential pregnancy. When ovulation is not followed by implantation of a fertilized ovum, progesterone secretion declines as the corpus luteum involutes, and the endometrial lining is almost completely shed during menses.

443. The answer is d. (*Ganong, pp 438–440. Kasper et al., pp 279–283, 2199–2202.*) Progesterone production by the corpus luteum increases significantly at the time of ovulation. Progesterone affects the set point for thermoregulation and increases body temperature approximately 0.58°F. Both LH and FSH blood levels increase during the follicular phase of the menstrual cycle and reach peak blood levels prior to ovulation. Estrogen levels follow a similar pattern during the follicular phase. The physiologic signal for ovulation is a surge in LH blood levels. Under the influence of LH, thecal and granulosa cells become the luteal cells of the corpus luteum. Estrogen levels also increase, but do not reach the levels achieved during the follicular phase.

444. The answer is c. (*Ganong, pp 424–427.*) The Sertoli cells rest on a basal lamina and form a layer around the periphery of the seminiferous tubules. They are attached to each other by specialized junctional complexes

that limit the movement of fluid and solute molecules from the interstitial space and blood to the tubular lumen, and thus form a blood-testis barrier that provides an immunologically privileged environment for sperm maturation. Sertoli cells are intimately associated with developing spermatozoa and play a major role in germ-cell maturation. They secrete a variety of serum proteins and an androgen-binding protein into the tubular fluid in response to FSH and testosterone stimulation. Testosterone is synthesized and secreted by the interstitial Leydig cells. Estrogen is produced in small amounts by the Sertoli cells before puberty.

445. The answer is a. (*Ganong*, p 449.) Human chorionic gonadotropin (hCG) begins to appear in the maternal blood approximately 6 to 8 days following ovulation, upon implantation of the fertilized ovum in the endometrium. The secretion of hCG is essential to prevent involution of the corpus luteum and to stimulate secretion of progesterone and estrogens, which continues until the placenta becomes large enough to secrete sufficient quantities of those hormones. Following a peak at 7 to 9 weeks, hCG secretion gradually declines to a low level by 20 weeks gestation.

446. The answer is e. (*Ganong*, pp 236, 247–248, 451–452. *Kasper et al.*, pp 2097–2098.) A combined neurogenic and hormonal reflex involving oxytocin, a posterior pituitary hormone, causes the actual ejection (“let-down”) of milk from breast tissue. Although estrogen and progesterone are essential for the physical development of breast tissue during pregnancy, both hormones inhibit milk secretion. Milk secretion is regulated by prolactin, a pituitary hormone secreted throughout pregnancy and after parturition. Adequate amounts of growth hormone are required to provide the nutrients that are essential for milk production by breast tissue. Suckling on breast tissue is the stimulus that leads to milk secretion. The secretion of oxytocin is increased by stressful stimuli, and inhibited by alcohol. Furthermore, alcohol is transferred from the mother’s bloodstream into her breast milk and to the nursing infant, where it can have many deleterious effects.

447. The answer is c. (*Ganong*, pp 433–438. *Kasper et al.*, pp 2199–2202.) In a woman with a menstrual cycle of 28 to 30 days, ovulation generally occurs between days 14 and 16. The menstrual cycle is divided physiologically into three phases. The follicular phase begins with the onset of menses and lasts 9 to 13 days. The ovulatory phase lasts 1 to 3 days and culminates in ovulation. The luteal phase, the most constant phase of the cycle, lasts about 14 days and ends with the onset of menstrual bleeding.

448. The answer is b. (*Kasper et al., p 282. Ganong, pp 441, 446–449.*) Implantation of a zygote into the uterine wall involves infiltration of the endometrium by the syncytiotrophoblast. Fertilization and early cleavage of the zygote occur in the fallopian tube in the human female. After approximately 3 days, the zygote enters the uterine cavity, where it undergoes additional divisions over a period of 3 to 4 days to form a morula of approximately 60 cells that is transformed into a blastocyst consisting of the yolk sac and embryo. Enzymatic digestion of the zona pellucida and infiltration of the endometrium by the syncytiotrophoblast, which forms the outer layer of the blastocyst, result in implantation of the blastocyst within the endometrium, where it erodes into maternal vessels. During these early stages of embryogenesis, the endometrium is primed by progesterone secreted by the corpus luteum in the ovary in response to pituitary gonadotropin secretion. After 10 to 15 days, placental gonadotropins maintain the corpus luteum until placental synthesis of progesterone is established at 6 to 8 weeks of gestation. Large dose estrogens, diethylstilbestrol, and mifepristone (RU486) are examples of postcoital contraceptives.

449. The answer is d. (*Ganong, pp 306, 441–443.*) Estrogens have a significant plasma cholesterol-lowering action. Estrogens stimulate the growth and development of the female reproductive tract, including the ovarian follicles, duct growth and enlargement of the breasts, and uterine smooth muscle and its motility, as well as its blood flow. Estrogen increases libido in humans.

450. The answer is c. (*Ganong, pp 248, 422, 444–450.*) Preparation of primordial ovarian follicles for ovulation is the primary function of FSH. FSH stimulates development of the theca and granulose cells of the follicles and promotes the synthesis of estrogens, including estradiol. LH promotes luteinization of the postovulatory follicle and stimulates progesterone secretion by the corpus luteum. During pregnancy, hCG is secreted by the placenta and continues progesterone production.

451. The answer is a. (*Ganong, pp 443–451.*) Progesterone is secreted by the corpus luteum. The plasma level of progesterone is low during the menses and remains low until just prior to ovulation. It rises substantially after ovulation, owing to secretion by the corpus luteum. If fertilization occurs, the corpus luteum continues to secrete progesterone until the placenta develops and begins to produce large amounts of the hormone. The

plasma level of progesterone rises steadily throughout pregnancy after the placenta takes over production at about 12 weeks of gestation.

452. The answer is b. (*Ganong*, pp 438–443.) Estrogens cause the mucus secreted by the cervix to become thinner and more alkaline and to exhibit a fernlike pattern upon drying. The epithelium of the vagina is so sensitive to estrogen action that vaginal smear examination is used for a bioassay of the hormone. Estrogens can stimulate growth of ovarian follicles even in hypophysectomized women and also stimulate growth of the glandular epithelium of the endometrium, the smooth muscle of the uterus, and the uterine vascular system. Growth of the glandular elements of the breast is stimulated by progesterone; growth of the ductal elements is stimulated by estrogen.

453. The answer is d. (*Kasper et al.*, pp 2214–2216. *Ganong*, pp 413–417, 433.) The testosterone metabolite dihydrotestosterone (DHT) induces the formation of the male external genitalia and male secondary sex characteristics. The fetus develops with bipotential internal and external genitalia that can develop (at about 40 days gestation) into either a testis or ovary, depending upon which genes are expressed. When the embryo has functional testes, male internal and external genitalia develop. The Leydig cells of the fetal testis secrete testosterone and the Sertoli cells secrete müllerian-inhibiting substance (MIS), also known as antimüllerian hormone (AMH), a member of the TGF- β growth factor family. The development of male internal genitalia depends upon testosterone, which stimulates growth and development of the Wolffian ducts and MIS, which stimulates Müllerian duct regression. Individuals with Klinefelter's syndrome have an XXY chromosomal pattern, which is the most common sex chromosome disorder. These individuals have internal and external male genitalia, and testosterone secretion at puberty is often great enough for the development of male characteristics. However, the testes are small and the seminiferous tubules are abnormal, leading to infertility, eunuchoid proportions, gynecomastia, and poor virilization in phenotypic males. Mental retardation, developmental delay, or learning disabilities may be present. Patients with mosaic forms of Klinefelter's syndrome have less severe clinical features, larger testes, and may achieve fertility.

454. The answer is e. (*Ganong*, pp 242–244, 247–248, 421–424, 451–452.) Prolactin causes milk secretion from the breast after estrogen and progesterone priming. Its effect on the breast involves increased action of mRNA

and increased production of casein and lactalbumin, but the hormone action is not exerted on the cell nucleus. The actions of progesterone are prevented by inhibitors of microtubules. Oxytocin is a posterior pituitary peptide that promotes contraction of the myoepithelial cells surrounding breast ducts and causes expulsion of milk from lobular alveoli. Secretion of oxytocin is promoted by tactile stimulation of the breast by the nursing infant. It can also be elicited by psychic factors alone, such as the anticipation of nursing brought on by hearing the cry of the hungry infant. This anticipatory secretion of oxytocin may be experienced by the mother as a sensation of milk letdown in which milk appears at the nipple and may be forcibly ejected.

455. The answer is b. (*Kasper et al.*, pp 2210–2213.) Because of the challenge of weighing the benefits versus risks for each individual, whether or not to use postmenopausal hormone therapy is one of the most complex health-care decisions facing women. In both observational studies and randomized trials, hormone therapy (either estrogen alone or estrogen/progestin) shows definite improvement in vasomotor symptoms (i.e., hot flashes and night sweats) and vaginal dryness, and in increasing bone density and reducing the risk of fractures. However, observational studies promoting the use of hormone therapy as a strategy to delay the postmenopausal onset of cardiovascular disease have recently been refuted by randomized trials showing an increased risk of coronary artery disease in stroke with hormone replacement therapy. Hormone therapy also increases the risk of endometrial cancer, breast cancer (with long-term use), venous thromboembolism, and gallbladder disease. Estrogen therapy does not restore a woman's ability to have children.

456. The answer is b. (*Ganong*, pp 424–428.) Semen contains chemicals that prevent sperm capacitation, thereby prolonging the viability of the sperm. In addition, the high potassium content of the secretion inhibits sperm motility, further adding to the viability. Semen is secreted primarily by the seminiferous tubules and the alkaline nature of the secretion buffers the acidity of the vagina. In recent years, the average sperm count has decreased from approximately 100 million/mL of semen to 60 to 70 million/mL of semen. The bulbocavernosus muscle is a skeletal muscle.

457. The answer is c. (*Ganong*, *Kasper et al.*, pp 2084–2087.) In non-pregnant women, the secretion of prolactin is kept tonically suppressed by secretion of dopamine from the hypothalamus. Prolactin is the main

hormone of lactation. Hormone levels increase early in pregnancy due to the influence of estrogens. However, lactation does not occur early in pregnancy because estrogens and progesterone inhibit the interaction of prolactin with receptors located on the alveolar cell membranes. At term, estrogen and progesterone levels decrease and milk production begins usually within 3 days of delivery.

458. The answer is a. (*Ganong, pp 448–451. Kasper et al., pp 553–556.*) The corpus luteum in the ovary at the time of fertilization fails to regress and instead enlarges in response to stimulation by human chorionic gonadotropin (hCG) secreted by the placenta. During the first trimester, placental production of hCG sustains the corpus luteum and ensures continued progesterone secretion by the corpus luteum, which is essential for development of the fetus.

459. The answer is e. (*Ganong, pp 448–451.*) During pregnancy, the maternal hypothalamic-pituitary axis is suppressed due to high circulating levels of sex hormones. This leads to reduced gonadotropin levels, and, thus, ovulation does not occur. Additionally, hyperventilation leads to decreased arterial carbon dioxide levels. Increased water retention leads to decreased hematocrit. Maternal use of glucose declines and, as a result, gluconeogenesis increases. Plasma cortisol levels increase as the result of progesterone-mediated displacement from transcortin and its subsequent binding to globulin.

460. The answer is a. (*Ganong, pp 448–451. Kasper et al., pp 553–556.*) The placenta produces all of the hormones listed in the five answers at various times during pregnancy but it is the production of progesterone and estrogens (estradiol and estriol) from maternal and fetal precursors, which take over the function of the corpus luteum after the sixth week of pregnancy.

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Endocrine Physiology

Questions

461. A 43-year-old male develops a brain tumor that impinges on the supraoptic nucleus in the hypothalamus. As a result, the secretion of which of the following hormones is affected?

- a. Adrenocorticotrophic hormone (ACTH)
- b. Antidiuretic hormone (ADH)
- c. Follicle-stimulating hormone (FSH)
- d. Growth hormone (GH)
- e. Prolactin

462. Following neck surgery, a patient develops circumoral paresthesia and a long QT interval on the electrocardiogram consistent with hypocalcemia resulting from injury to the parathyroid glands. Which of the following is true regarding parathyroid hormone (PTH)?

- a. It is synthesized and secreted from the oxyphil cells in the parathyroid glands
- b. Secretion is increased in response to an increase in plasma-free Ca^{2+} concentration
- c. It acts directly on bone cells to increase Ca^{2+} resorption and mobilize Ca^{2+}
- d. It acts directly on intestinal cells to increase Ca^{2+} absorption
- e. It increases phosphate reabsorption in the renal proximal tubular cells

463. A 39-year-old man with an enlarged head, hands, and feet, osteoarthritic vertebral changes and hirsutism presents with a complaint of gynecomastia and lactation. The patient is most likely suffering from a tumor in which of the following locations?

- a. Hypothalamus
- b. Anterior pituitary
- c. Posterior pituitary
- d. Adrenal cortex
- e. Breast

464. A major league baseball player takes human growth hormone to increase his performance. Which of the following is true regarding human growth hormone?

- a. Secretion is stimulated by somatostatin and inhibited by ghrelin
- b. It has a long half-life
- c. It inhibits protein synthesis
- d. It decreases lipolysis
- e. It stimulates production of somatomedins (insulin-like growth factors I and II) by the liver, cartilage, and other tissues

465. A 28-year-old woman develops a posterior pituitary tumor. Which of the following hormones is secreted by the posterior pituitary gland?

- a. α -Melanocyte-stimulating hormone (α -MSH)
- b. β -Lipotropin (β -LPH)
- c. Leutinizing hormone (LH)
- d. Oxytocin
- e. Thyroid-stimulating hormone (TSH)

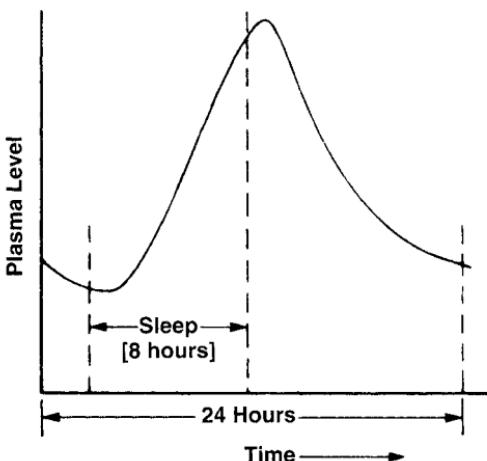
466. A 36-week pregnant mother has a decrease in urinary estriol excretion, indicating a decline in fetal adrenal cortical activity. Which of the following is the principal steroid secreted by the fetal adrenal cortex?

- a. Cortisol
- b. Corticosterone
- c. Dehydroepiandrosterone
- d. Progesterone
- e. Pregnenolone

467. A 22-year-old woman presents with a recurrent vaginal candidiasis that is refractory to nystatin treatment. Diabetes screening shows elevated fasting blood glucose, and the patient is started on 25 units of insulin per day. Which aspect of glucose transport is enhanced by insulin?

- a. Transport into adipocytes
- b. Transport across the tubular epithelium of the kidney
- c. Transport into the brain
- d. Transport through the intestinal mucosa
- e. Transport against a concentration gradient

468. A 52-year-old woman with a chief complaint of snoring is referred for a sleep study. As shown in the graph below, the concentration of a hormone varied over the 24-hour period of study. This diurnal variation in plasma level results from the secretion of which of the following hormones?



- a. Thyroxine
- b. Insulin
- c. Parathyroid hormone
- d. Cortisol
- e. Estrogen

469. A 24-year-old pregnant woman and her 3-year-old child are seen in a medical mission clinic in Sudan. The child is short in stature, has a pot-belly and enlarged protruding tongue, and is developmentally delayed. Iodine is prescribed for mother and child, with the hope of preventing mental retardation in the developing fetus. Iodides are stored in the thyroid follicles mainly in the form of which of the following?

- a. Thyroxine
- b. Triiodothyronine
- c. Thyroglobulin
- d. Monoiodotyrosine
- e. Thyroid peroxidase

470. A 15-year-old girl presents with loss of the outer one-third of her eyebrows. Physical examination demonstrates slight enlargement of the thyroid gland and delayed relaxation phase of deep tendon reflexes. Blood work shows an elevation in creatine phosphokinase (CPK) and thyroid-stimulating hormone (TSH). Thyroid hormone therapy is ordered. Physiologically active thyroxine exists in which of the following forms?

- a. Bound to albumin
- b. Bound to prealbumin
- c. Bound to globulin
- d. As a glucuronide
- e. Unbound

471. A patient with uncontrolled diabetes has an increase in the plasma concentration of free fatty acids that parallels his increase in plasma glucose. Which of the following is correct regarding activation of hormone-sensitive lipase in adipocytes?

- a. It causes increased hydrolysis of cholesterol esters.
- b. It is mediated by a cyclic AMP-dependent protein kinase.
- c. It is prevented by cortisol.
- d. It is stimulated by insulin.
- e. It results in accumulation of monoglycerides and diglycerides in adipocytes.

472. A patient with DiGeorge's congenital thymic aplasia presents with a seizure. An elevated serum phosphorus and low serum calcium confirm a hypoparathyroid state. Plasma levels of calcium can be increased most rapidly by the direct action of PTH on which of the following?

- a. Kidney
- b. Intestine
- c. Thyroid gland
- d. Bones
- e. Skeletal musculature

473. A 20-year-old male medical student presents with increasing daytime somnolence. A 24-hour sleep study showing a sudden onset of REM sleep without previous slow-wave sleep, confirms a diagnosis of narcolepsy. REM sleep decreases the secretion of growth hormone. The physiological secretion of growth hormone is increased by which of the following?

- a. Hypoglycemia
- b. Hyperglycemia
- c. Free fatty acids

- d. Somatostatin
- e. Growth hormone

474. A 50-year-old male alcoholic presents with cirrhotic liver disease and chronic pancreatitis. He has been nauseated for the past several days, and not eating. Blood glucagon levels are elevated with which of the following results?

- a. Stimulation of glycogenolysis in muscle
- b. Inhibition of insulin secretion
- c. Stimulation of gluconeogenesis in the liver
- d. Inhibition of adenylate cyclase
- e. Inhibition of phospholipase C

475. A patient in hyperkalemic renal failure is given an infusion of glucose and insulin. The actions of insulin include which of the following?

- a. Converting glycogen to glucose
- b. Stimulating gluconeogenesis
- c. Increasing plasma amino acid concentration
- d. Enhancing potassium entry into cells
- e. Reducing urine formation

476. A 47-year-old woman with an anterior pituitary tumor presents with poor wound healing and hypertension. The endogenous secretion of ACTH is correctly described in which of the following statements?

- a. It shows a circadian rhythm in humans.
- b. It is decreased during periods of stress.
- c. It is inhibited by aldosterone.
- d. It is stimulated by glucocorticoids.
- e. It is stimulated by epinephrine.

477. A patient with tuberculosis becomes confused and complains of muscle cramps and nausea. Lab results show a plasma sodium concentration of 125 mEq/L, serum osmolarity of 200 mOsm/kg, urine osmolarity of 1500 mOsm/kg, urine sodium of 400 mEq/day, and a normal blood volume. These clinical findings are consistent with which of the following?

- a. Increased secretion of atrial natriuretic peptide
- b. Decreased secretion of aldosterone
- c. Increased secretion of aldosterone
- d. Decreased secretion of antidiuretic hormone
- e. Increased secretion of antidiuretic hormone

478. A 29-year-old male recovering from a viral upper respiratory tract infection develops a tender, enlarged thyroid gland and subacute thyroiditis, requiring hormone therapy. Injection of thyroid hormone into a human subject will result in which of the following?

- a. Decrease the rate of oxygen consumption
- b. Increase muscle protein synthesis
- c. Decrease the need for vitamins
- d. Increase the plasma concentration of cholesterol
- e. Decrease the rate of lipolysis

479. An abdominal computed tomography (CT) in a patient with Conn's syndrome (primary hyperaldosteronism) shows multiple small adrenocortical masses. Which of the following clinical findings are most likely present?

- a. Hypertension
- b. Hyperkalemia
- c. Decreased extracellular fluid volume
- d. Increased concentrating ability of the kidney
- e. Increased hematocrit

480. A 75-year-old female with primary hyperparathyroidism presents at her physician's office with dehydration and malaise. Which of the following plasma levels are most likely to be decreased?

- a. Phosphate
- b. Sodium
- c. Calcium
- d. Potassium
- e. Calcitonin

481. A patient undergoes adrenalectomy to remove a tumor. Adrenalectomy is associated with which of the following?

- a. Euphoria
- b. Increased mobilization and utilization of fatty acids
- c. Hyperglycemia with decreased insulin sensitivity
- d. Improved resistance to infection or shock
- e. Augmented water excretion by the kidneys and sodium loss in the urine

482. A 37-year-old female presents with exophthalmus and an enlarged thyroid gland. The levels of free thyroxine and triiodothyronine in her blood are elevated. Other clinical findings of Graves' disease include which of the following?

- a. Anorexia
- b. Increased basal metabolic rate
- c. Bradycardia
- d. Increased weight gain
- e. Decreased sweating

483. A 20-year-old diabetic male forgets to take his insulin prior to the start of the National Collegiate Athletic Association (NCAA) swimming championships. Insulin-independent glucose uptake occurs in which of the following sites?

- a. Adipose tissue
- b. Cardiac muscle
- c. Skeletal muscle
- d. The brain
- e. The uterus

484. A 46-year-old woman on lithium therapy for her bipolar disorder, presents with complaints of weakness, arthralgia, and constipation. Blood work reveals hypercholesterolemia, increased levels of thyroid-stimulating hormone (TSH), and decreased T_4 and T_3 levels. Which of the following is also likely to be associated with her hypothyroid state?

- a. Tachycardia
- b. Increased metabolic rate
- c. Heat intolerance
- d. Sleepiness
- e. Decreased body mass index

485. A multisystem trauma patient develops hyperpyrexia, severe tachycardia, and high-output congestive heart failure with volume depletion, consistent with thyroid storm. Which of the following is the most appropriate treatment for the exaggerated hyperthyroidism?

- a. T_3 administration to induce negative feedback inhibition of T_4
- b. Aspirin to treat the fever
- c. Propylthiouracil to block synthesis of new thyroid hormone
- d. β_2 -adrenergic agents to mediate vasodilation and bronchodilation
- e. Iodine followed by propylthiouracil to block release and synthesis of thyroid hormone

486. A 5-year-old boy presents with sexual precocity. Twenty-four hour melatonin concentrations are found to be lower than normal. Which of the following is true regarding melatonin?

- a. It is synthesized in the anterior pituitary gland.
- b. It regulates skin pigmentation in humans.
- c. Its secretion is increased by darkness.
- d. Its secretion is inhibited by norepinephrine from the sympathetic nervous system.
- e. It is synthesized from the amino acid L-arginine.

487. A patient presents with Whipple's triad, including plasma glucose <60 mg/dL, symptomatic hypoglycemia, and improvement of symptoms with administration of glucose. CT of the abdomen shows enlargement of the islet cells suggestive of islet cell carcinoma. Which of the following is true regarding the islets of Langerhans?

- a. They are found primarily in the head of the pancreas.
- b. They constitute approximately 30% of the pancreatic weight.
- c. They contain six distinct endocrine cell types.
- d. They have a meager blood supply.
- e. They secrete insulin and glucagon.

488. A 59-year-old man is brought to his physician's office by his wife. She reports that he has been weak, nauseated, and urinates frequently. She has also noticed a fruity odor on her husband's breath. A urine sample is strongly positive for ketones and the finger-stick glucose is high, leading to a presumptive bedside diagnosis of diabetes. As a result of insulin deficiency, which of the following will most likely occur?

- a. Increased cellular uptake of glucose
- b. Decreased intracellular α -glycerophosphate in liver and fat cells
- c. Enhanced glucose uptake and use except by brain tissue
- d. Decreased fatty acid release from adipose tissue
- e. Indirect depression of glucose utilization due to excess fatty acids in the blood

489. A 24-year-old woman presents with a slightly elevated blood pressure. She has high plasma levels of T_3 , cortisol, and renin activity, but no symptoms or signs of thyrotoxicosis or Cushing's syndrome. Which of the following is the most likely explanation?

- a. She has been treated with ACTH and TSH.
- b. She has been treated with T_3 and cortisol.
- c. She has an adrenocortical tumor.
- d. She is in the third trimester of pregnancy.
- e. She has been subjected to chronic stress.

490. Which of the following hormones initiates its biological effects by activation of cell membrane receptors?

- a. Progesterone
- b. Estrogens
- c. Cortisol
- d. Thyroxine
- e. Epinephrine

491. A 13-year-old female presents for her annual sports physical. Her height is measured at 50 inches (>3 SD below the mean for her age), and the history suggests that the girl may be suffering from anorexia nervosa. Which of the following statements about growth and development is correct?

- a. Growth hormone activates the JAK2-STAT pathway
- b. Linear growth ceases earlier in boys than in girls
- c. Serum IGF-I levels decrease throughout childhood
- d. Growth hormone is essential for prenatal linear growth
- e. Normal growth during puberty is independent of thyroid function

492. Which of the following hormones interacts with a cytoplasmic receptor and then localizes in the nucleus and directs protein and nucleotide synthesis?

- a. Thyrotropin-releasing hormone
- b. Epinephrine
- c. Luteinizing hormone
- d. Cortisol
- e. Insulin

493. A patient with chronic asthma is started on glucocorticoid therapy. The treatment may result in bone loss because glucocorticoids do which of the following?

- a. Inhibit bone formation
- b. Increase calcium absorption from the GI tract
- c. Increase osteoblast growth
- d. Inhibit bone resorption
- e. Suppress vitamin D activation

494. A 29-year-old woman presents with paroxysmal episodes of headaches, anxiety, and palpitations. The physician suspects an anxiety disorder, but orders laboratory studies to rule out underlying disease. The lab findings of hypercalcemia and elevated urinary catecholamines suggest the possibility of Type II multiple endocrine neoplasia (MEN II). Which of the following is the hallmark of pheochromocytoma?

- a. Hypoglycemia
- b. Weight gain
- c. Dry skin
- d. Lethargy
- e. Hypertension

495. A 36-year-old male computer programmer works for a company that has just been acquired in a corporate take-over. He experiences symptoms of tachycardia, palpitations, and an irregular heart beat, particularly at night. His plasma catecholamine levels are found to be increased, which may result from which of the following?

- a. An increase in blood pressure
- b. An increase in blood volume
- c. An increase in plasma cortisol
- d. An increase in blood glucose
- e. Changing from the standing to the supine position

496. An 18-year-old man with hemophilia A suffered multiple internal injuries from a motorcycle accident. He is now presenting with dizziness, abdominal pain, dark patches on his elbows and knees, and cravings for chips and french fries. He is referred to an endocrinologist who makes the diagnosis of Addison's disease, and prescribes cortisol. Cortisol administration to a patient with adrenal insufficiency will result in which of the following?

- a. Increased insulin sensitivity in muscle
- b. Enhanced wound healing
- c. Increased corticotropin-releasing hormone secretion
- d. Increased ACTH secretion
- e. Increased gluconeogenesis

497. An 80-year-old man reports increasing dyspnea, which worsens with exertion. Echocardiography indicates that the ejection fraction is within normal limits, but the cardiologist orders blood levels of brain natriuretic peptide and atrial natriuretic peptide to evaluate possible congestive heart

failure. Which of the following statements about atrial natriuretic peptide (ANP) are correct?

- a. ANP enhances antidiuretic hormone (ADH) secretion.
- b. ANP constricts afferent renal arterioles.
- c. ANP acts only on the distal nephron to increase urine flow.
- d. ANP secretion increases when central venous pressure increases.
- e. ANP secretion is stimulated by hyponatremia.

498. A patient with multiple endocrine neoplasia Type I (MEN I) and acromegaly is found to have a deletion of the 11q13 region of chromosome 11, a suppressor gene for growth hormone. Growth hormone excess results in which of the following?

- a. Decreased gluconeogenesis
- b. Hypoglycemia
- c. Insulin resistance
- d. Decreased protein synthesis
- e. Decreased lipolysis

499. Sulfonylurea treatment in a diabetic patient causes a fall in the patient's plasma glucose concentration to 45 mg/dL. Which of the following is a sign and symptom of hypoglycemia?

- a. Dry skin
- b. Bradycardia
- c. Insomnia
- d. Loss of fine motor skills
- e. Satiety

500. Radiation treatment for a pituitary tumor in an 8-year-old boy results in the complete loss of pituitary function. As a result, the child is likely to experience which of the following symptoms?

- a. Hypothyroidism and goiter
- b. Absent sexual maturation
- c. Accelerated growth spurts
- d. Increased ACTH
- e. Increased TSH levels

501. A 49-year-old male patient with AIDS and declining CD4 counts has an increased frequency of systemic infections and develops sick euthyroid syndrome with a decline in T_4 and T_3 levels. With normal thyroid function, which of the following is correct?

- a. TSH initiates thyroid hormone secretion via activation of nuclear receptors in thyroid gland cells.
- b. Secretion of TSH is regulated primarily by the pituitary level of T_3
- c. TSH is secreted from the posterior pituitary
- d. T_4 is the physiologically active hormone
- e. T_4 is formed from T_3 by the process of monodeiodination.

502. The second year medical students started a hunger strike to protest the reduction in library hours. After 3 days of fasting, the students will most likely manifest which of the following?

- a. Decreased lipolysis
- b. Increased urinary excretion of nitrogen
- c. Decreased gluconeogenesis
- d. Increased glucose utilization by the brain
- e. Increased secretion of insulin

Endocrine Physiology

Answers

461. The answer is b. (*Ganong, pp 234–236, 242–250.*) Antidiuretic hormone (ADH), also called arginine vasopressin (AVP), is secreted from the posterior lobe of the pituitary gland (neurohypophysis) into the general circulation from the endings of supraoptic neurons in the hypothalamus. ACTH, FSH, GH, and prolactin are all secreted by the anterior pituitary gland (adenohypophysis) into the portal hypophysial circulation from the endings of arcuate and other hypothalamic neurons.

462. The answer is c. (*Ganong, pp 390–392. Stead et al., pp 88–89, 232–233.*) PTH, secreted by the chief cells of the parathyroid gland, is essential for life. PTH has a direct effect on bone to increase bone resorption and mobilize Ca^{2+} ; this effect is mediated by increasing intracellular cAMP levels in osteoblasts. PTH also increases calcium absorption from the gut, although that effect is the result of PTH-mediated increases in renal 1,2,5-dihydroxy-cholecalciferol. PTH has a phosphaturic action due to a decrease in phosphate reabsorption in the proximal tubules. The secretion of PTH is inversely related to the circulating levels of ionized calcium.

463. The answer is b. (*Ganong, pp 399–402, 409. Stead et al., pp 74–75, 233.*) Tumors of the somatotropes of the anterior pituitary gland secrete large amounts of growth hormone, leading to acromegaly in adults. When the epiphyses have not yet fused to the long bones, growth is stimulated by excess growth hormone leading to gigantism in children. Once the epiphyses have closed, linear growth is no longer possible, and growth hormone produces the pattern of bone and soft tissue abnormalities typical of acromegaly. Hypersecretion of growth hormone is accompanied by hypersecretion of prolactin in up to 40% of patients with acromegaly. Human growth hormone also has intrinsic lactogenic activity. Acromegaly can be caused by hypothalamic tumors that secrete growth hormone-releasing hormone (GRH), but these are rare.

464. The answer is e. (*Ganong, pp 248, 305, 352, 398–406.*) Growth hormone (GH) exerts many of its effects on growth and metabolism by stimulating the

production and release of polypeptide growth factors called somatomedins from the liver, cartilage, and other tissues. In humans, the principal circulating somatomedins are insulin-like growth factor I (IGF-I, somatomedin C) and IGF-II. GH release is stimulated by growth hormone-releasing hormone (GHRH) and ghrelin and inhibited by somatostatin. All of these peptides are synthesized and released by the hypothalamus, though the main site of ghrelin synthesis and secretion is the stomach. GH increases lipolysis; the resultant increase in free fatty acids, which takes several hours to develop, provides a ready source of energy for the tissues during hypoglycemia, fasting, and stressful stimuli. GH also has a protein anabolic effect. GH is metabolized rapidly; the half-life of circulating GH in humans is 6 to 20 minutes.

465. The answer is d. (*Ganong*, pp 396–397.) Oxytocin is secreted from the posterior lobe of the pituitary gland (neurohypophysis) into the general circulation from the endings of paraventricular neurons in the hypothalamus. LH, TSH, and β -lipotropin are all secreted by the anterior pituitary gland (adenohypophysis). α -MSH is released from the intermediate lobe of the pituitary.

466. The answer is c. (*Ganong*, pp 356, 361–366, 450.) Because it lacks 3β -hydroxysteroid dehydrogenase, the enzyme that converts pregnenolone to progesterone (the initial step in both glucocorticoid and mineralocorticoid synthesis), the fetal cortex synthesizes primarily dehydroepiandrosterone. This steroid is released as its sulfate and is metabolized further to estrogen and androgen by the placenta. During fetal life, the adrenal cortex consists of a thin subcapsular rim, which eventually gives rise to the adult cortex, and a thick inner fetal cortex, which constitutes 80% of the gland. This zone undergoes rapid involution after birth.

467. The answer is a. (*Ganong*, pp 336–338. *Stead et al.*, pp 63–65.) Insulin increases glucose uptake by adipocytes. Transport of glucose into cells is by facilitated diffusion. Insulin increases the number of transporters available for glucose uptake in many cells, including adipocytes, skeletal, and cardiac muscle, and some smooth muscle. Insulin does not enhance glucose transport into brain cells, intestinal mucosal cells, or renal tubular epithelial cells. Diabetics have increased susceptibility to infections due to decreased efficacy of granulocytes despite a normal number. Type 1 diabetes mellitus patients must use insulin. They cannot use oral hypoglycemic agents because they do not have any functional pancreatic β cells.

468. The answer is d. (*Ganong*, pp 373–374, 317–395, 411–453.) Cortisol is the only hormone that has a diurnal variation, as shown in the graph accompanying the question. Plasma cortisol levels rise sharply during sleep, peaking soon after awakening, and sinking to a low level approximately 12 hours later. This pattern is intimately related to the secretory rhythm of ACTH, which governs, and in turn is partly governed by, plasma concentration of cortisol.

469. The answer is b. (*Ganong*, pp 317–322, 328–329. *Kasper et al.*, pp 194, 2105.) The thyroid gland stores iodide primarily as thyroglobulin. The thyroid gland has a specialized active transport system that very efficiently traps iodide from circulating blood and can accumulate iodide against a large concentration gradient. Within the thyroid, the iodide rapidly undergoes organification by which it is oxidized and covalently linked to tyrosine residues in thyroglobulin. The iodinated tyrosine residues gradually become coupled to form thyroxine, the major secretion product of the thyroid. Children who are hypothyroid from birth or before are called cretins. Worldwide, congenital hypothyroidism is one of the most common causes of preventable mental retardation. Outside of the United States and most other developed countries, maternal iodine deficiency is a major cause of congenital hypothyroidism.

470. The answer is e. (*Ganong*, pp 321–323. *Stead et al.*, pp 81–83.) Only the free unbound form of thyroxine is physiologically active. Circulating thyroxine can be bound to albumin, thyroxine-binding prealbumin (TBPA), or thyroxine-binding globulin (TBG). Most thyroxine is bound, and, despite the large available pool of albumin, most of it is bound to TBG. This reflects the relatively greater affinity of TBG for thyroxine.

471. The answer is b. (*Ganong*, pp 305, 342.) Hormone-sensitive lipase is a cytoplasmic enzyme in adipocytes that catalyzes the complete hydrolysis of triglyceride to fatty acids and glycerol. It is activated by a cyclic AMP-dependent protein kinase that phosphorylates the enzyme, converting it to its active form. Because no accumulation of monoglycerides or diglycerides is detected in adipocytes following the action of hormone-sensitive lipase, it is the initial hydrolysis of triglyceride to fatty acid and diglyceride that is the rate-limiting step. Hormone-sensitive lipase is sensitive to several hormones in vitro, but it appears to be regulated in vivo primarily by epinephrine and glucagon, which activate it by increasing cyclic AMP, and insulin, which inhibits it by preventing cyclic AMP-dependent phosphorylation. Cortisol enhances lipolysis indirectly by promoting increased enzyme synthesis.

472. The answer is d. (*Ganong, pp 390–392. Kasper et al., pp 1942, 2264, 1382. Stead et al., pp 88–89.*) PTH increases plasma calcium levels primarily by mobilizing bone calcium. The main function of the parathyroid gland is to maintain a constant ionized calcium level in the extracellular fluid. To do this, PTH stimulates increased plasma calcium levels, chiefly by mobilizing calcium from bones. Although PTH can also increase renal tubular reabsorption of calcium and intestinal absorption of calcium, these effects depend on adequate dietary ingestion of calcium and thus occur more slowly.

473. The answer is a. (*Ganong, pp 201, 400–406. Stead et al., p 71.*) Synthesis and secretion of growth hormone (GH) by the anterior pituitary is regulated by a variety of metabolic factors, many of which act to alter the balance between release of growth hormone-releasing hormone (GRH) and somatostatin (SS) from the hypothalamus. Among the stimuli that increase GH secretion are: (1) conditions in which there is a deficiency of energy substrate (e.g., hypoglycemia, exercise, and fasting); (2) stressful stimuli (e.g., fever, various psychological stresses); (3) an increase in arginine and some other amino acids (e.g., protein meal, infusion of arginine); (4) glucagon; (5) L-Dopa and dopamine receptor agonists; (6) estrogens and androgens; and (7) going to sleep. Stimuli that decrease GH secretion include somatostatin, REM sleep, glucose, cortisol, free fatty acids, and GH itself.

474. The answer is c. (*Ganong, pp 348–350. Kasper et al., pp 1855–1859. Stead et al., pp 114–117.*) The primary action of glucagon is to increase blood glucose concentration, which it accomplishes by promoting gluconeogenesis and glycogenolysis in the liver but not in muscle. These effects are mediated by cyclic AMP, which is produced by hepatic adenylate cyclase following interaction of glucagon with its plasma membrane receptor. Interaction of glucagon with different hepatic plasma membrane receptors activates phospholipase C, which results in a rise in concentration of intracellular Ca^{2+} , which further stimulates glycogenolysis. Although glucagon opposes the action of insulin, it does not directly affect insulin secretion.

475. The answer is d. (*Ganong, pp 336–338.*) One of insulin's major effects is the stimulation of the Na^+-K^+ pump, which increases potassium entry into cells, with a resultant lowering of the extracellular K^+ concentration. Insulin given along with glucose, to prevent hypoglycemia, is often used as a treatment for hyperkalemia. Insulin's major effect on metabolism

is the synthesis of proteins and lipids and the storage of glucose as glycogen. Insulin stimulates the uptake of amino acids and glucose by most cells of the body and decreases the rate of gluconeogenesis. Insulin has no effect on urine formation, but in diabetes, when glucose levels increase to a level at which the kidney can no longer reabsorb the filtered glucose, glucose acts as an osmotic diuretic and increases the formation of urine.

476. The answer is a. (*Ganong, pp 372–375. Kasper et al., pp 2092–2094.*) The secretion of ACTH occurs in several irregular bursts during the day; the peak occurs early in the morning prior to awakening and thus is not due to the stress of arising. This circadian rhythm, maximum secretion in early morning and minimum secretion in the evening, is regulated by the hypothalamus through the secretion of corticotropin-releasing hormone (CRH) into the hypothalamic-hypophyseal portal capillary system. In addition to the basal rhythm, physical or mental stress will lead to increased ACTH secretion within minutes. ACTH is also regulated as a result of feedback inhibition by the hormones whose synthesis it stimulates, such as glucocorticoids. Aldosterone is a mineralocorticoid and is not controlled by ACTH. Epinephrine does not appear to have any effect on ACTH secretion.

477. The answer is e. (*Ganong, pp 246–247, 378–379, 729–730. Kasper et al., pp 213–214. Stead et al., pp 77–78, 226–228.*) An increase in antidiuretic hormone is associated with isovolemic, hypotonic hyponatremia, and an increase in both urine osmolarity and urine sodium. The etiology of syndrome of inappropriate antidiuretic hormone secretion (SIADH) includes idiopathic overproduction of ADH that is often associated with disorders of the CNS (encephalitis, stroke, head trauma) and pulmonary disease (TB, pneumonia). Hyperaldosteronism leads to decreased sodium (and water) excretion and thus hypernatremia and an increase in extracellular fluid volume. A decrease in aldosterone would be associated with hypovolemic hyponatremia. A decrease in ANP would lead to decreased sodium and water excretion.

478. The answer is b. (*Ganong, pp 323–326. Stead et al., pp 85–86.*) Thyroid hormone affects all aspects of metabolism; it increases calorigenesis in every tissue in the body. The hormone stimulates protein synthesis, which may be directly responsible for a portion of its calorigenic effect. Thyroid hormone affects both synthesis and degradation of lipids; the net effect is a decrease in lipid stores. By increasing the mechanisms by which cholesterol is eliminated from the body, thyroid hormone decreases plasma

cholesterol levels. Because of its stimulatory effect on metabolic processes, thyroid hormone increases the demand for coenzymes and vitamins.

479. The answer is a. (*Ganong*, pp 376–381. *Stead et al.*, pp 93–94.) The symptoms of primary hyperaldosteronism (Conn's syndrome) develop from chronic excess secretion of aldosterone from the zona glomerulosa of the adrenal cortex. Patients are hypertensive and have an expanded blood volume with a decreased hematocrit. They are not markedly hypernatremic because of a renal escape phenomenon. Patients are severely depleted of potassium and, as a consequence, suffer kidney damage, with a resulting loss in concentrating ability.

480. The answer is a. (*Ganong*, pp 392–393. *Stead et al.*, pp 87–88, 233–234.) Parathyroid hormone (PTH) is essential for maintaining plasma calcium and phosphate levels. It is released in response to decreased plasma calcium and acts to increase calcium reabsorption and phosphate excretion. Thus, hyperparathyroidism is characterized by hypophosphatemia and hypercalcemia.

481. The answer is c. (*Ganong*, p 381. *Stead et al.*, pp 89–91, 233–234.) Removal of the adrenal glands produces the clinical picture known as Addison's disease, a disorder associated with deprivation of adrenocortical hormones. A lack of glucocorticoids diminishes the body's ability to synthesize glucose by gluconeogenesis. Mineralocorticoid deprivation produces diuresis, natriuresis, and decreased potassium secretion leading to excessive potassium plasma levels and acidosis.

482. The answer is b. (*Ganong*, pp 329–330. *Stead et al.*, pp 78–81.) Hyperthyroidism can increase the basal metabolic rate 60 to 100% above normal. Thyroid hormone causes nuclear transcription of large numbers of genes in virtually all cells of the body. The result is a generalized increase in functional cell activity and metabolism. The increased metabolic activity of patients with hyperthyroidism is accompanied by increased food intake. Nevertheless, their body weight decreases. The generalized increase in cellular activity results in increased sweat production and increased heart rate. The latter sign is often used by physicians to determine whether a patient has increased thyroid hormone production.

483. The answer is d. (*Ganong*, pp 336–338.) Insulin does not promote glucose uptake by most brain cells. Insulin does increase glucose uptake in

skeletal muscle, cardiac muscle, smooth muscle, adipose tissue, leukocytes, and the liver. In most insulin-sensitive tissues, insulin acts to promote glucose transport by enhancing facilitated diffusion of glucose down a concentration gradient. In the liver, where glucose freely permeates the cell membrane, glucose uptake is increased as a result of its phosphorylation by glucokinase. Formation of glucose-6-phosphate reduces the intracellular concentration of free glucose and maintains the concentration gradient favoring movement of glucose into the cell.

484. The answer is d. (*Ganong, pp 323–326. Stead et al., pp 81–83.*) Sleepiness is common in patients with hypothyroidism. Hypothyroidism is a condition usually characterized by low levels of T_3 and T_4 , owing to atrophy of the thyroid gland. In very rare cases there is resistance to the effects of thyroid hormones. A deficiency of thyroid hormones or their effects results in bradycardia, which is due to decreased sympathetic activity, and a decreased metabolic rate with its associated sleepiness, weight gain, and cold intolerance. Excess thyroid hormone increases metabolic rate, which increases heat production, stimulates the appetite, and causes weight loss even in the face of increased intake of food. Heat intolerance is characteristic of hyperthyroidism.

485. The answer is c. (*Ganong, pp 321–326. Stead et al., pp 79–80.*) Thyroid storm is an exaggerated manifestation of hyperthyroidism. Thyroid storm is a medical emergency and mortality is high (20–50%) even with the correct treatment. After primary stabilization of the airway, breathing and oxygenation, circulation, and fluid balance, treatment includes propylthiouracil (PTU) or methimazole to block the synthesis of new thyroid hormone and β -blockers to block adrenergic effects. Iodine should not be given until after PTU has taken effect (~1.5) or more thyroid hormone will be produced. Aspirin displaces T_4 from thyroid binding protein, and therefore should not be used to treat fever. T_3 and T_4 inhibit the release of thyrotropin-releasing hormone (TRH) from the hypothalamus, which regulates thyroid-stimulating hormone (TSH) secretion from the anterior pituitary gland.

486. The answer is c. (*Ganong, pp 420, 462–465.*) Synthesis and secretion of melatonin are increased in the dark via input from norepinephrine secreted by postganglionic sympathetic neurons. Melatonin is synthesized in the pineal gland from the amino acid tryptophan. Pinealomas (tumors of the pineal gland) that destroy the pineal gland and reduce secretion of

melatonin and cause hypothalamic damage may cause precocious puberty by removing the inhibitory effect of melatonin on the pituitary response to gonadotropin-releasing hormone. Melatonin causes amphibian skin to become lighter in color but has no role in the regulation of skin color in humans.

487. The answer is e. (*Ganong, pp 333–334. Stead et al., pp 69–70.*) The islets of Langerhans, which constitute 1 to 2% of the pancreatic weight, secrete insulin, glucagon, somatostatin, and pancreatic polypeptide. Each is secreted from a distinct cell type, A, B, D, and F, respectively. The islets are scattered throughout the pancreas, but are more plentiful in the tail than in the body or head.

488. The answer is b. (*Ganong, pp 340–343. Stead et al., pp 63–68.*) α -Glycerophosphate is produced in the course of normal use of glucose. In the absence of adequate quantities of α -glycerophosphate, a normal acceptor of free fatty acids in triglyceride synthesis, lipolysis will be the predominant process in adipose tissue. As a result, fatty acids will be released into the blood. The prevailing insulin level is decisive in the selection of substrate by a tissue for the production of energy. Insulin promotes use of carbohydrate, and a lack of the hormone causes use of fat mainly to the exclusion of uptake and use of glucose, except by brain tissue. Indirect depression of glucose utilization due to excess fatty acids is a result, and not a contributing cause, of increased use of fat.

489. The answer is d. (*Ganong, pp 322, 449–450, 456, 777.*) Thyroxine-binding globulin (TBG) is increased in estrogen-treated patients and during pregnancy, increasing the total plasma levels of T_3 and T_4 , but with a normal level of the free thyroid hormones, such that the clinical state is euthyroid. Cortisol levels also increase during pregnancy and parturition due to increased production of corticotropin-releasing hormone (CRH) by the placenta (as well as the fetal hypothalamus). Although tissue renin contributes little to the circulating renin pool, pregnancy is associated with increased renin levels that may arise from components of the tissue renin-angiotensin system found in the uterus, the placenta, and the fetal membranes. Amniotic fluid contains large amounts of prorenin.

490. The answer is e. (*Ganong, pp 37–49.*) Due to their relatively low solubility within the lipid portions of the cell membrane, peptide hormones and catecholamines (epinephrine) must interact with receptors located on

the cell membrane. Activation of the receptor is followed by the generation of intracellular second messengers that ultimately mediate the biological response to the hormone. Steroid hormones and thyroid hormones readily pass through the cell surface membrane and interact with intracellular receptors to produce their effects by regulating gene expression within the nucleus.

491. The answer is a. (*Ganong*, pp 44–47, 326, 400–407.) Growth hormone activates many different intracellular enzyme cascades, including the JAK2-STAT pathway, which also mediates the effects of various growth factors and prolactin. Secretion of insulin-like growth factor I (IGF-I) increases throughout childhood and stimulate cell proliferation and growth in many different cell types, including chondrocytes within growth plates. Linear growth ends earlier in girls than in boys. IGF-II is largely independent of growth hormone and plays a role in the growth of the fetus before birth. Thyroid hormones are essential for normal linear growth and skeletal development. The growth-promoting effects of thyroid hormones occur via a synergistic effect with growth hormone.

492. The answer is d. (*Ganong*, pp 36–39, 375–376.) Cortisol, like other steroid hormones, diffuses into target cells and interacts with intracellular receptors. The steroid-receptor complex has a high affinity for the steroid-responsive element of DNA. Once bound to DNA, the hormone-receptor complex acts as a transcription factor to regulate gene expression and formation of specific messenger RNAs.

493. The answer is a. (*Ganong*, p 395.) Glucocorticoids lower plasma Ca^{2+} levels by inhibiting osteoclast formation and activity. Over long periods of time, glucocorticoids cause osteoporosis by decreasing bone formation and increasing bone resorption. They decrease bone formation by inhibiting protein synthesis in osteoblasts. Glucocorticoids also decrease the absorption of Ca^{2+} and PO_4^{3-} from the intestine and increase the renal excretion of these ions. Vitamin D formation is facilitated when plasma Ca^{2+} levels are low.

494. The answer is e. (*Ganong*, pp 360, 642. *Kasper et al.*, pp 234, 1424, 1467–1470, 2148–2152, 2234–2236. *Stead et al.*, pp 94–95.) The hallmark of pheochromocytoma is either sustained or paroxysmal hypertension. Pheochromocytoma is a rare catecholamine-secreting tumor of the adrenal chromaffin cells. Patients with the disease often have associated episodes of sweating, anxiety or nervousness, palpitations, headache, diaphoresis, and

hyperglycemia. In adults, approximately 80% of pheochromocytomas are unilateral and solitary. The 10% rule applies to pheochromocytomas, as follows: 10% in adults are bilateral, 10% are extraadrenal, 10% are malignant, and 10% are familial, inherited as an autosomal dominant trait either alone or in combination with MEN 2 (though recent evidence suggests that 25% of patients with pheochromocytoma may have an inherited form of the disease).

495. The answer is c. (*Ganong, pp 358–359.*) Phenylethanolamine-*N*-methyltransferase (PNMT), the enzyme that catalyzes the formation of epinephrine from norepinephrine, is found in appreciable quantities only in the brain and the adrenal medulla. Adrenal medullary PNMT is induced by glucocorticoids and glucocorticoids are necessary for the normal development of the adrenal medulla. Circumstances that increase sympathetic nerve input to the adrenal medulla increase catecholamine secretion. Major stressors include decreased intravascular volume or pressure, fear or rage, a change in posture from supine to standing, and hypoglycemia.

496. The answer is e. (*Ganong, pp 366–372. Stead et al., pp 89–91.*) Cortisol is defined as a glucocorticoid because it promotes the conversion of amino acids to glucose (gluconeogenesis). It also decreases glucose uptake by muscle and adipocytes by decreasing the sensitivity of the cells to insulin. The net result is to provide more glucose to non-insulin-requiring cells. Cortisol retards wound healing. It also decreases CRH and ACTH secretion by feedback inhibition.

497. The answer is d. (*Ganong, pp 460–462, 723.*) Atrial natriuretic peptide (ANP) is synthesized, stored, and secreted by cardiac atrial muscle, the latter in response to increased central venous pressure or increased plasma sodium concentrations. ANP increases glomerular filtration by simultaneous dilation of afferent and constriction of efferent renal arterioles. It decreases salt and water reabsorption along the entire length of the kidney. The excretion of water is enhanced by inhibition of ADH.

498. The answer is c. (*Ganong, pp 400–404. Stead et al., pp 74–75, 233.*) Patients with acromegaly have insulin resistance. In addition, they manifest increased lipolysis and increased gluconeogenesis due to their high growth hormone levels. The combination of enhanced glucose production and insulin resistance can produce hyperglycemia and diabetes mellitus. Protein synthesis increases to support tissue growth and proliferation.

499. The answer is d. (*Ganong, pp 353–354, 344–346. Stead et al., pp 69–70.*) Hypoglycemia can lead to loss of fine motor skills. Hypoglycemia refers to abnormally low blood glucose levels and is dangerous because glucose is the primary energy source for brain cells. Dysfunction of the nervous system can lead to dizziness, headache, mental confusion, convolution, and loss of consciousness. Increased sympathetic activity can produce sweating, tachycardia, hunger, and anxiety.

500. The answer is b. (*Ganong, pp 398, 406, 408–409. Stead et al., pp 72–74, 75–76.*) Radiation treatment likely produced panhypopituitarism in the young child. Sexual maturation and growth during development will not occur because of low levels of GH, FSH, LH, ILGF1, TSH and thyroid hormones, and gonadal hormones. The cortisol response to stress is decreased due to low ACTH levels. A goiter cannot develop in the absence of TH.

501. The answer is b. (*Ganong, pp 317–332. Kasper et al., pp 2107–2109.*) Secretion of TSH is regulated primarily by the pituitary levels of T_3 . As plasma thyroid hormone levels increase, pituitary T_3 levels rise and lead to inhibition of TSH synthesis and secretion. TSH stimulates thyroid gland function by binding to specific cell membrane receptors and increasing the intracellular levels of cAMP. The thyroid gland secretes thyroxine (T_4) and triiodothyronine (T_3); the latter is the physiologically active hormone. The majority of T_3 is formed in the peripheral tissues by deiodination of T_4 .

502. The answer is c. (*Ganong, pp 290–291, 298.*) With prolonged fasting of 3 days or more, gluconeogenesis is decreased partly due to increased ketogenesis and lipolysis. The increased availability of ketones and fatty acids as a source of fuel for brain cells decreases the demand by the brain for glucose. The decreased gluconeogenesis is reflected in a nitrogen excretion level at or below normal values. Insulin levels decrease beginning as early as 24 hour after a meal.

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