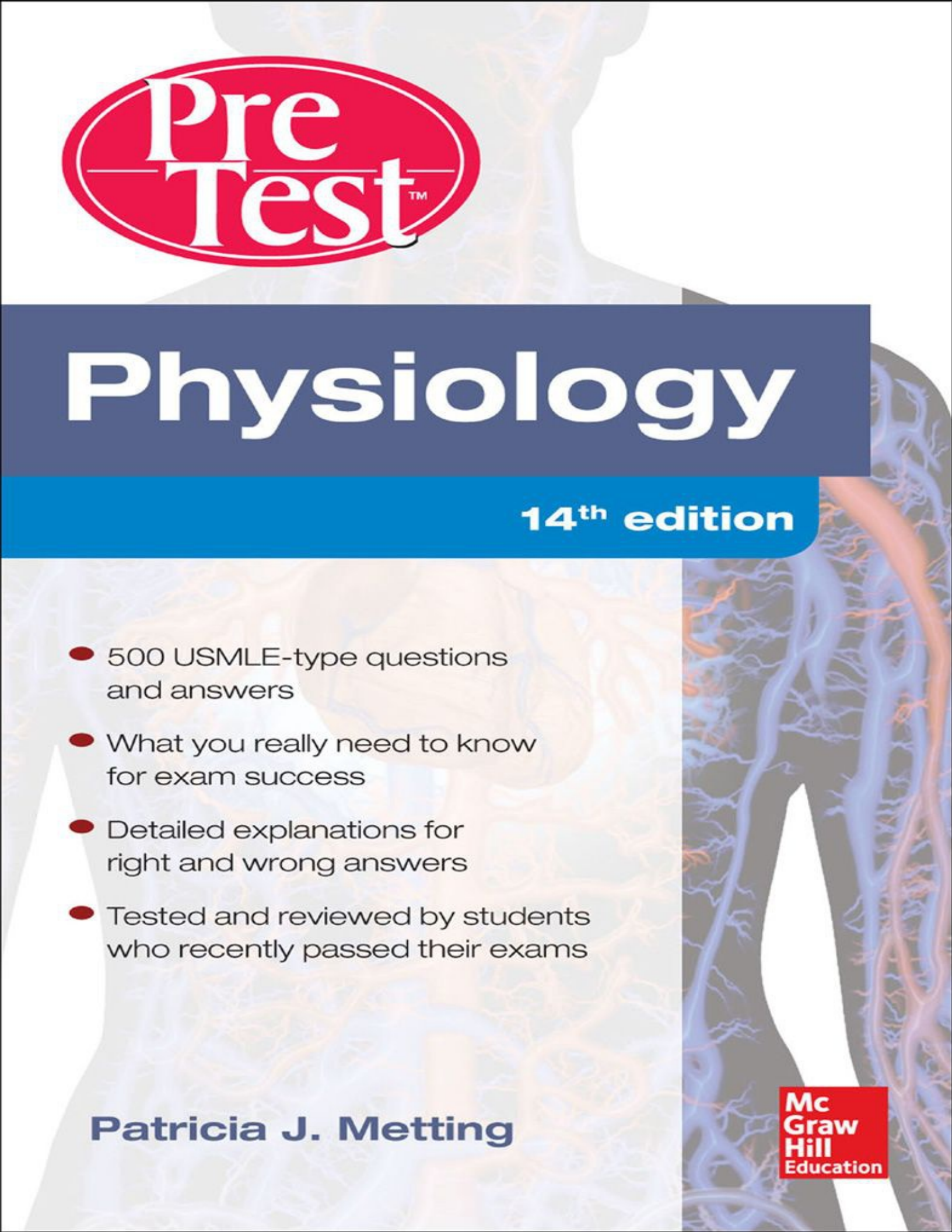


Physiology

14th edition

- 500 USMLE-type questions and answers
- What you really need to know for exam success
- Detailed explanations for right and wrong answers
- Tested and reviewed by students who recently passed their exams

Patricia J. Metting

Mc Graw Hill Education

Notice

Medicine is an ever-changing science. As new research and clinical experience broaden our knowledge, changes in treatment and drug therapy are required. The authors and the publisher of this work have checked with sources believed to be reliable in their efforts to provide information that is complete and generally in accord with the standards accepted at the time of publication. However, in view of the possibility of human error or changes in medical sciences, neither the authors nor the publisher nor any other party who has been involved in the preparation or publication of this work warrants that the information contained herein is in every respect accurate or complete, and they disclaim all responsibility for any errors or omissions or for the results obtained from use of the information contained in this work. Readers are encouraged to confirm the information contained herein with other sources. For example and in particular, readers are advised to check the product information sheet included in the package of each drug they plan to administer to be certain that the information contained in this work is accurate and that changes have not been made in the recommended dose or in the contraindications for administration. This recommendation is of particular importance in connection with new or infrequently used drugs.

Physiology

PreTest™ Self-Assessment and Review

14th Edition

Patricia J. Metting, PhD
Professor, Departments of Physiology & Pharmacology and Medicine
Vice Chancellor and Senior Associate Dean for Student Affairs
The University of Toledo College of Medicine and Life Sciences
Toledo, Ohio

New York Chicago San Francisco Athens London Madrid
Mexico City Milan New Delhi Singapore Sydney Toronto

ISBN: 978-0-07-179143-4
MHID: 0-07-179143-4

The material in this eBook also appears in the print version of this title: ISBN: 978-0-07-179142-7, MHID: 0-07-179142-6.

E-book conversion by codeMantra
Version 1.0

Student Reviewers

Maxx Gallegos
Medical Student
University of Kansas School of Medicine

Russel Kahmke
Medical Student
SUNY Upstate Medical University

Benjamin O. Lawson
Medical Student
Universidad Autónoma de Guadalajara
School of Medicine

Daniel Marcovici
Medical Student
Sackler School of Medicine
Tel Aviv University

Shama Patel
Medical Student
Ross University School of Medicine

Sheree Perron
Medical Student
Eastern Virginia Medical School

Kendall Smith
Medical Student
University of Kansas School of Medicine

Contents

Contributors
Introduction
Acknowledgments

High-Yield Facts

High-Yield Facts in Physiology

General Principles: Cellular Physiology

Questions
Answers

General Principles: Multisystem Processes

Questions
Answers

Physiology of the Hematopoietic and Lymphoreticular Systems

Questions
Answers

Neurophysiology

Questions
Answers

Musculoskeletal Physiology

Questions
Answers

Respiratory Physiology

Questions
Answers

Cardiovascular Physiology

Questions
Answers

Gastrointestinal Physiology

Questions
Answers

Renal and Urinary Physiology

Questions
Answers

Reproductive Physiology

Questions
Answers

Endocrine Physiology

Questions
Answers

Bibliography
Index

Contributors

Adam C. Calaway, MD

Resident, Urology

Indiana University School of Medicine

Indianapolis, Indiana

Chapter 1. Renal and Urinary Physiology Section of High-Yield Facts

Chapter 10. Renal and Urinary Physiology

Meredith L. Dorr, MD

Resident Physician

Department of Obstetrics and Gynecology

Indiana University School of Medicine

Indianapolis, Indiana

Chapter 1. Endocrine Physiology Section of High-Yield Facts

Chapter 12. Endocrine Physiology

Patricia J. Metting, PhD

Professor, Departments of Physiology & Pharmacology and Medicine

Vice Chancellor and Senior Associate Dean for Student Affairs

The University of Toledo College of Medicine and Life Sciences

Toledo, Ohio

Chapter 1. High-Yield Facts in Physiology

Chapter 2. General Principles: Cellular Physiology

Chapter 3. General Principles: Multisystem Processes

Chapter 4. Physiology of the Hematopoietic and Lymphoreticular Systems

Chapter 5. Neurophysiology

Chapter 6. Musculoskeletal Physiology

Chapter 7. Respiratory Physiology

Chapter 8. Cardiovascular Physiology

Chapter 9. Gastrointestinal Physiology

Chapter 10. Renal and Urinary Physiology

Chapter 11. Reproductive Physiology

Chapter 12. Endocrine Physiology

Vicki A. Ramsey-Williams, MD, PhD

Associate Professor

Department of Neurology

The University of Toledo

Toledo, Ohio

Chapter 1. Neurophysiology Section of High-Yield Facts

Chapter 5. Neurophysiology

Mark K. Tuttle, MD

Clinical Fellow

Harvard Medical School

Resident, Internal Medicine

Beth Israel Deaconess Medical Center

Boston, Massachusetts

Chapter 1. Cardiovascular Physiology Section of High-Yield Facts

Chapter 8. Cardiovascular Physiology

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/Examinations/step1/step1_content.html). 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 and electrolyte balance and high-altitude physiology are topics covered under General Principles: Multisystem Processes and oxygen and carbon dioxide transport are covered in the chapter on the Physiology of the Hematopoietic and Lymphoreticular Systems, rather than under Renal or Respiratory Physiology, respectively, where you likely learned them during your medical school education. In addition to guiding your preparation for Step 1, the value of organizing the questions according to the Step 1 Content Outline is that the National Board of Medical Examiners (NBME) score reports that are given to each examinee provide 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 been updated to include more two-step questions that require test-takers to not only make a diagnosis based on the clinical vignette presented, but also demonstrate their knowledge of the physiology/pathophysiology of the disorder. 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 multiple answer options. For each question, select the *one best* answer from the choices given. The Question section of each chapter is followed by an Answers section that provides the correct answer for each question, along with an explanation. The explanation provides the reason why the correct answer is correct and, in most cases, the reasons why the wrong answers are wrong. The explanations also provide additional information relevant to the clinical vignette and its underlying basic and clinical science. The references accompanying each question are from excellent physiology, pathophysiology, internal medicine, and Step 1 preparation 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.

We wish you the very best on your examination, your clinical training, and your medical career. 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 you are encouraged 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 COMLEXUSA 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 F. Kleshinski, MD, co-editor of the 13th edition. The input of the medical student reviewers was valuable for enhancing the quality of this latest edition. Thanks to Catherine Johnson, Editor, Medical Publishing Division, McGraw-Hill Professional, for her expert editorial assistance and guidance, as well as her enthusiasm and commitment to providing medical students with the very best educational resources available in the market. In addition, the contributions of Ritu Joon, Thomson Digital, in the typesetting and revisions, as well as the involvement of Cindy Yoo, Project Development Editor, and Richard Ruzycka, Production Supervisor, McGraw-Hill Professional, are greatly appreciated.

GENERAL PRINCIPLES: CELLULAR PHYSIOLOGY

(*References: Barrett et al., pp 7-10, 35-66. Le et al., pp. 226, 230-231. Widmaier et al., pp 12-13, 45-56, 95-134.*)

Membrane Transport Mechanisms

The transport of ions, gases, nutrients, and waste products through biological membranes is essential for many cellular processes. Membrane transport mechanisms can be classified as *passive* (do not require energy input, as with simple diffusion or facilitated diffusion) and *active transport* (requires energy input). Membrane transport mechanisms can also be classified as either *simple diffusion* (does not require a membrane transporter, eg, diffusion through the lipid bilayer or diffusion through ion channels) or *mediated transport* (requiring an integral membrane protein transporter, as with facilitated diffusion or active transport).

Diffusion is defined as the net flux of a substance from an area of higher concentration to an area of lower concentration from movement solely by random thermal motion, which does not require energy input.

Facilitated diffusion is a type of mediated transport, but it is a passive process in which carrier proteins move substances in the direction of their electrochemical gradients (eg, glucose transport in adipose tissue and muscle).

Active transport is a carrier-mediated transport process that requires energy to transport substances against their electrochemical gradients. The most important primary active transporter in mammalian cells is the Na^+–K^+ pump, which generates energy from the hydrolysis of ATP. Secondary active transport processes derive their energy from ion gradients. One example is the glucose transporter, which uses energy derived from the Na^+ electrochemical gradient.

Table 1 summarizes the major characteristics of the various membrane transport processes. Note that nonpolar substances, such as oxygen, carbon dioxide, and fatty acids, are transported by simple diffusion through the lipid bilayer of biological membranes. Ions and hydrophilic solutes, which do not readily cross the lipid bilayer, utilize an integral membrane protein to cross the membrane either via diffusion through a protein channel or via a carrier-mediated transport process.

TABLE 1. MAJOR CHARACTERISTICS OF MEMBRANE TRANSPORT MECHANISMS

	Diffusion Through Lipid Bilayer	Diffusion Through Ion 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
Use of energy, energy source	No, passive	No, passive	No, passive	Yes, ATP	Yes, ion gradient
Equilibrium or steady state	$C_0 = C_i$	$C_0 = C_i$[a]	$C_0 = C_i$	$C_0 \neq C_i$	$C_0 \neq C_i$
Uses integral membrane protein	No	Yes	Yes	Yes	Yes
Exhibits saturation kinetics	No	No	Yes, mediated transport	Yes, mediated transport	Yes, mediated transport
Chemical specificity	No	Yes	Yes	Yes	Yes
Typical molecules using pathway	Nonpolar: O_2, CO_2, fatty acids	Ions: Na^+, K^+, Ca^{2+}	Polar: glucose	Ions: Na^+, K^+, Ca^{2+}, H^+	Polar: amino acids, glucose, some ions

[a]In the presence of a membrane potential, the intracellular and extracellular ion concentrations will not be equal at equilibrium.
(Modified, with permission, from Widmaier EP, Raff H, Strang KT. *Vander's Human Physiology: The Mechanisms of Body Function*. 11th ed. New York, NY: McGraw-Hill; 2008:108.)

The kinetics of diffusion versus carrier-mediated transport processes vary, as depicted in Figure 1.

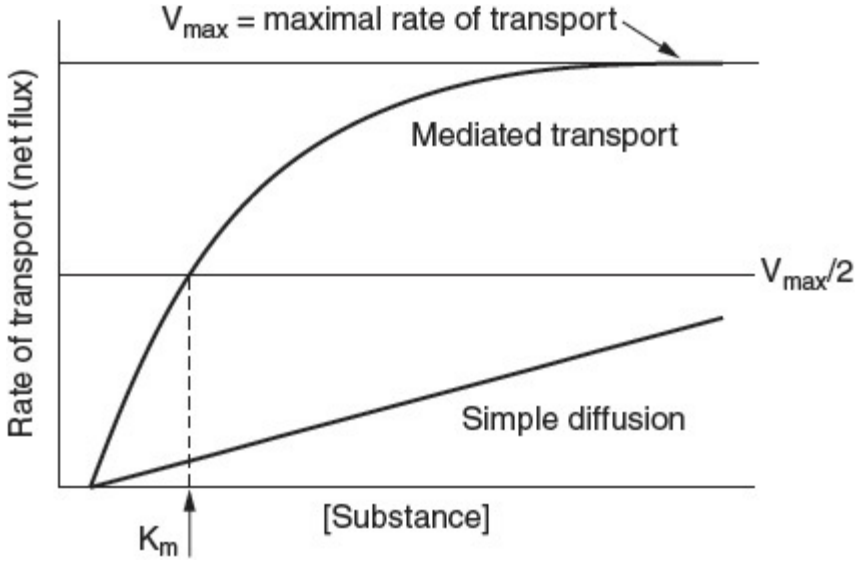


Figure 1

Simple diffusion of a substance is described by the Fick equation, as follows:

$$\text{Net flux} = A \times ([S_1] - [S_2]) \times D/d$$

where

A is the area available for diffusion,

$[S_1] - [S_2]$ is the concentration gradient of the substance across the membrane,

d is the distance for diffusion,

D is the diffusion coefficient of the substance,

$$= \text{solubility coefficient}/\sqrt{\text{gram molecular weight}} \text{ of the substance.}$$

According to the Fick equation, substances will diffuse more rapidly if the substance has a smaller mass, if the surface area for diffusion is increased, and if the concentration of the substance in one region greatly exceeds the concentration in the other region. For diffusion across membranes, the magnitude of the net flux is also directly proportional to the membrane permeability coefficient for the molecule.

*Mediated transpor*t exhibits saturation kinetics described by the Michaelis–Menten equation, as follows:

$$\text{Net flux} = V_{max} \times [S]/K_m + [S]$$

where V_{max} is the maximal rate of transport, $[S]$ is the concentration of the transported substance, and K_m is the concentration required for half-maximal transport of the substance.

Osmosis is a term given to the passive diffusion of water across a semipermeable membrane from a compartment in which the chemical potential of water is higher (solute concentration is lower) to a compartment in which the chemical potential of water is lower (solute concentration is higher), as depicted in Figure 2. A semipermeable membrane is permeable to water but impermeable to solutes.

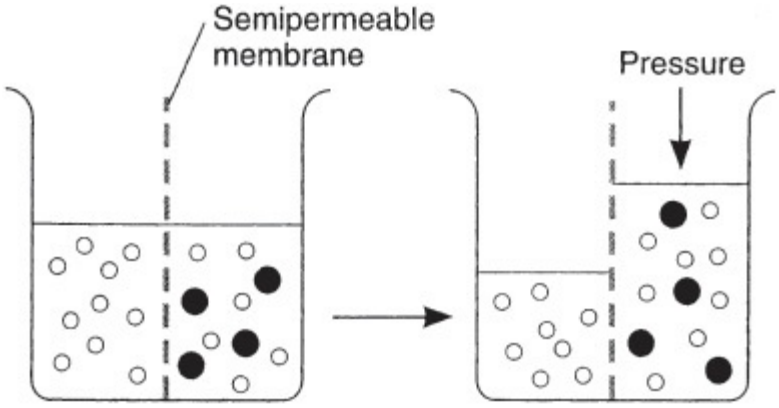


Figure 2

Diagrammatic representation of osmosis. Water molecules are the open circles, and solute molecules are the closed circles. Osmosis is the passive flow of water molecules across a semipermeable membrane from a compartment in which the chemical potential of water is higher (solute concentration is lower) to a compartment in which the chemical potential of water is lower (solute concentration is higher). (Reproduced, with permission, from Ganong WF. *Review of Medical Physiology.* 22nd ed. New York, NY: McGraw-Hill; 2005:5.)

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 is the reflection coefficient, L is the hydraulic conductivity, and $\pi_1 - \pi_2$ is the osmotic pressure difference across membrane.

The reflection coefficient (σ) is an index of the membrane's permeability to a 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 mm Hg) is calculated with the van't Hoff equation:

$$\pi = R\,T\,(\varphi ic)$$

where R is the ideal gas constant, T is the 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 (φic) is 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 has approximately the same osmolarity and osmotic pressure as 0.5 M $NaHCO_3$ or 0.33 M $MgCl_2$.

One osmol is equal to 1 mol of solute particles. The osmolarity is the number of osmoles per liter of solution, whereas the osmolality is the number of osmoles per kilogram of solvent. In the body, osmolal concentrations are expressed as osmoles per kilogram of water.

The plasma membranes of most cells are relatively impermeable to many of the solutes of the extracellular fluid (ECF) 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 osmolarity of a solution of nonpenetrating substances relative to plasma. Solutions of nonpenetrating solutes that have the same osmolarity as plasma (~300 mOsm/L) are isotonic; solutions containing greater than 300 mOsm of nonpenetrating solutes are hypertonic; and those containing less than 300 mOsm of non-penetrating solutes are hypotonic.

As shown in Figure 3, cells shrink when placed in hypertonic solutions and swell when placed in hypotonic solutions.

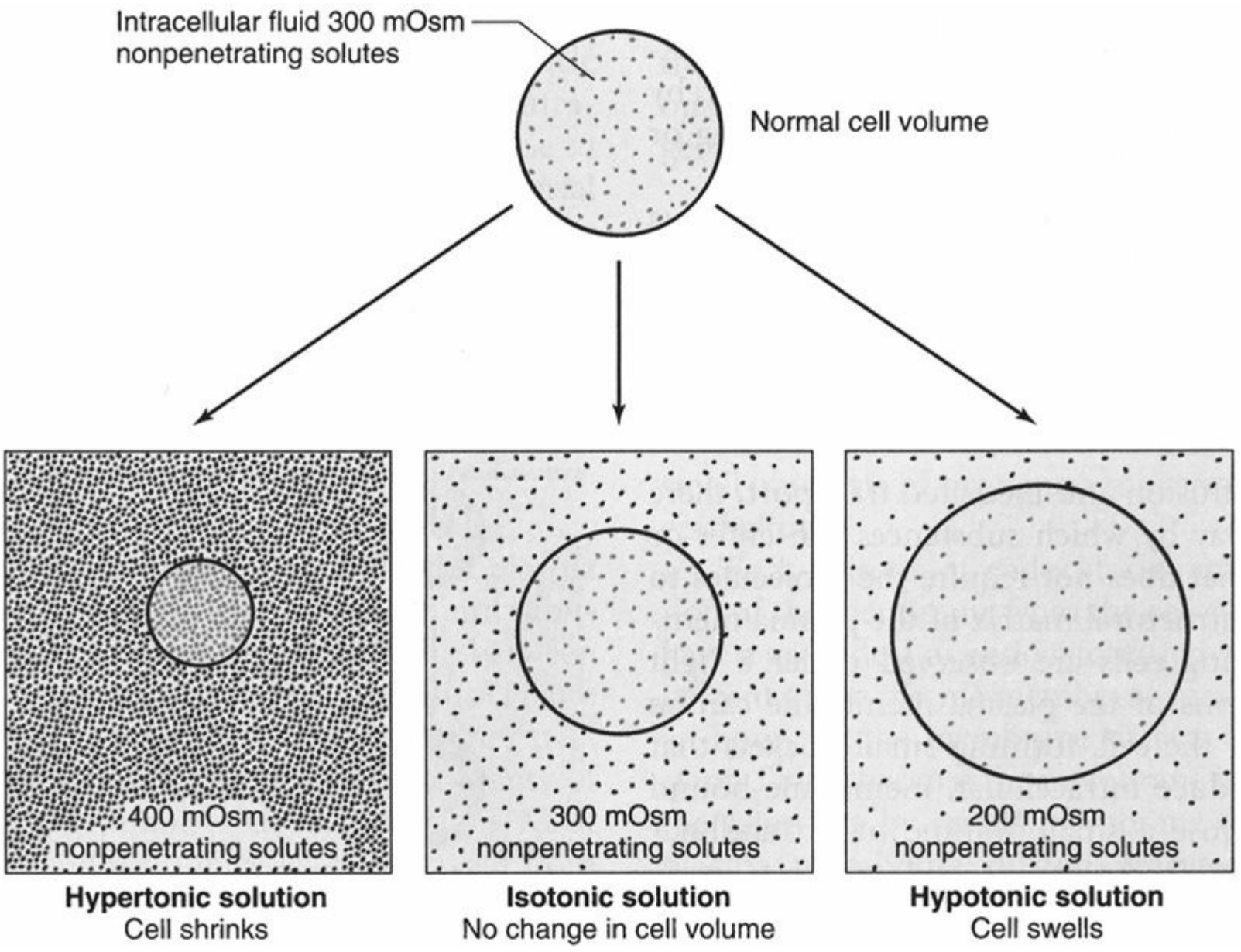


Figure 3

Cell volume changes with hypertonic, isotonic, and hypotonic solutions. (Reproduced, with permission, from Widmaier EP, Raff H, Strang KT. *Vander's Human Physiology*: *The Mechanisms of Body Function*. 11th ed. New York, NY: McGraw-Hill; 2008:111.)

The steady-state volume of a cell can be calculated as follows:

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

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, that is, no net water movement. Isotonic saline has a concentration of 154 mM NaCl, containing 154 × 2 or 308 mM of osmotically active particles. An isotonic solution of glucose is a 5% dextrose solution.

Another set of terms—isosmotic, hyperosmotic, and hypoosmotic— denotes the osmolarity of a solution relative to that of normal ECF independent of whether the solute is penetrating or nonpenetrating. For example, a solution containing 150 mOsm each of nonpenetrating Na^+ and Cl^- and 100 mOsm of the penetrating solute urea, which can readily cross cell membranes, would have a total osmolarity of 400 mOsm (hyperosmotic), but a tonicity of 300 mOsm (isotonic), and thus there would be no net change in the volume of a cell immersed in the solution.

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, and zona adherens, as well as hemidesmosomes and focal adhesions, which attach cells to their basal laminas.

The other type of connection between cells serves the purpose of transferring ions and other molecules from cell to cell, as well as the rapid propagation of electrical activity. This type of intercellular connection, called a gap junction, is a dodecameric structure formed by the alignment of units called connexons in the membranes of each cell. Each connexon is made up of six protein subunits called connexins, each of which has four membrane-spanning regions. Connexin mutations are now known to cause almost 20 different human diseases, including X-linked Charcot–Marie–Tooth disease (Cx32), skin disorders such as Clouston syndrome (Cx30) and erythrokeratoderma variabilis (Cx30.3 and Cx31), inherited deafness (Cx26, Cx30, and Cx31), cataracts (Cx46 and Cx50), and predisposition to myoclonic epilepsy (Cx36) and arteriosclerosis (Cx37).

In addition to the direct cell-to-cell communication via gap junctions, cells communicate with each other via chemical messengers in the ECF by a number of processes, including neural, endocrine, and paracrine communication.

In the case of intercellular communication mediated by chemical messengers in the ECF, 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 intra-cellular effects are summarized in Table 2.

TABLE 2. PRINCIPAL MECHANISMS FOR INTRACELLULAR EFFECTS OF CHEMICAL MESSENGERS

Mechanism	Examples
1. Open or close ion channels in cell membrane	• Acetylcholine on nicotinic cholinergic receptor • Norepinephrine on cardiac K^+ channel
2. Act via cytoplasmic or nuclear receptors to increase transcription of selected mRNAs	• Thyroid hormones • Steroid hormones • Retinoic acid • 1,25-dihydroxycholecalciferol
3. G_q-mediated activation of phospholipase C with intracellular production of diacylglycerol (DAG) (which activates protein kinase C) and inositol triphosphate (IP_3) (which increases intracellular $[Ca^{2+}]$ in smooth muscle)	• Acetylcholine acting on M_1 and M_3 receptors • Angiotensin II • Histamine via H_1 receptor • Norepinephrine via α_1-adrenergic receptor • Vasopressin via V_1 receptor
4. G_s-mediated activation of adenylyl cyclase, causing increased intracellular production of cyclic AMP with corresponding activation of protein kinase A, which increases intracellular $[Ca^{2+}]$ in heart and myosin light-chain kinase in smooth muscle	• Dopamine via D_1 receptor • Histamine via H_2 receptor • Norepinephrine via β_1 and β_2 adrenergic receptors • Vasopressin via V_2 receptor

5. G_i-mediated inhibition of adenylyl cyclase, causing decreased intracellular production of cyclic AMP with corresponding inactivation of protein kinase A, which decreases intracellular $[Ca^{2+}]$ in heart and myosin light-chain kinase in smooth muscle	• Acetylcholine acting on M_2 receptor • Dopamine via D_2 receptor • Norepinephrine via α_2-adrenergic receptor
6. Increase cyclic GMP in cell, which activates cGMP-dependent protein kinase	• Atrial natriuretic peptide • Nitric oxide
7. Increase tyrosine kinase activity of cytoplasmic portions of transmembrane receptors	• Insulin • Growth factors (EGF, PDGF) • Monocyte colony-stimulating factor
8. Increase serine or threonine kinase activity	• TGF-β • Activins and inhibins

(Modified, with permission, from Barrett et al. *Ganong's Review of Medical Physiology.* 24th ed. New York, NY: McGraw-Hill; 2012:56 and Le et al. *First Aid for the USMLE Step 1 2013.* New York, NY: McGraw-Hill; 2013:230–231.)

GENERAL PRINCIPLES: MULTISYSTEM PROCESSES

(*References: Barrett et al., pp 3-8, 316-320, 650-651, 697-719. Kaufman et al., pp 239-256. Levitzky, pp 163-188. Longo et al., pp 341-373. Widmaier et al., pp 5-19, 28-29, 417-433, 454-460, 490-515, 569-585.*)

Body Fluid Compartments

Water is the most abundant constituent in the body. *Total body water* (TBW) is approximately 60% of lean 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.

As shown in Figure 4, TBW is distributed between intracellular and extracellular fluid compartments.

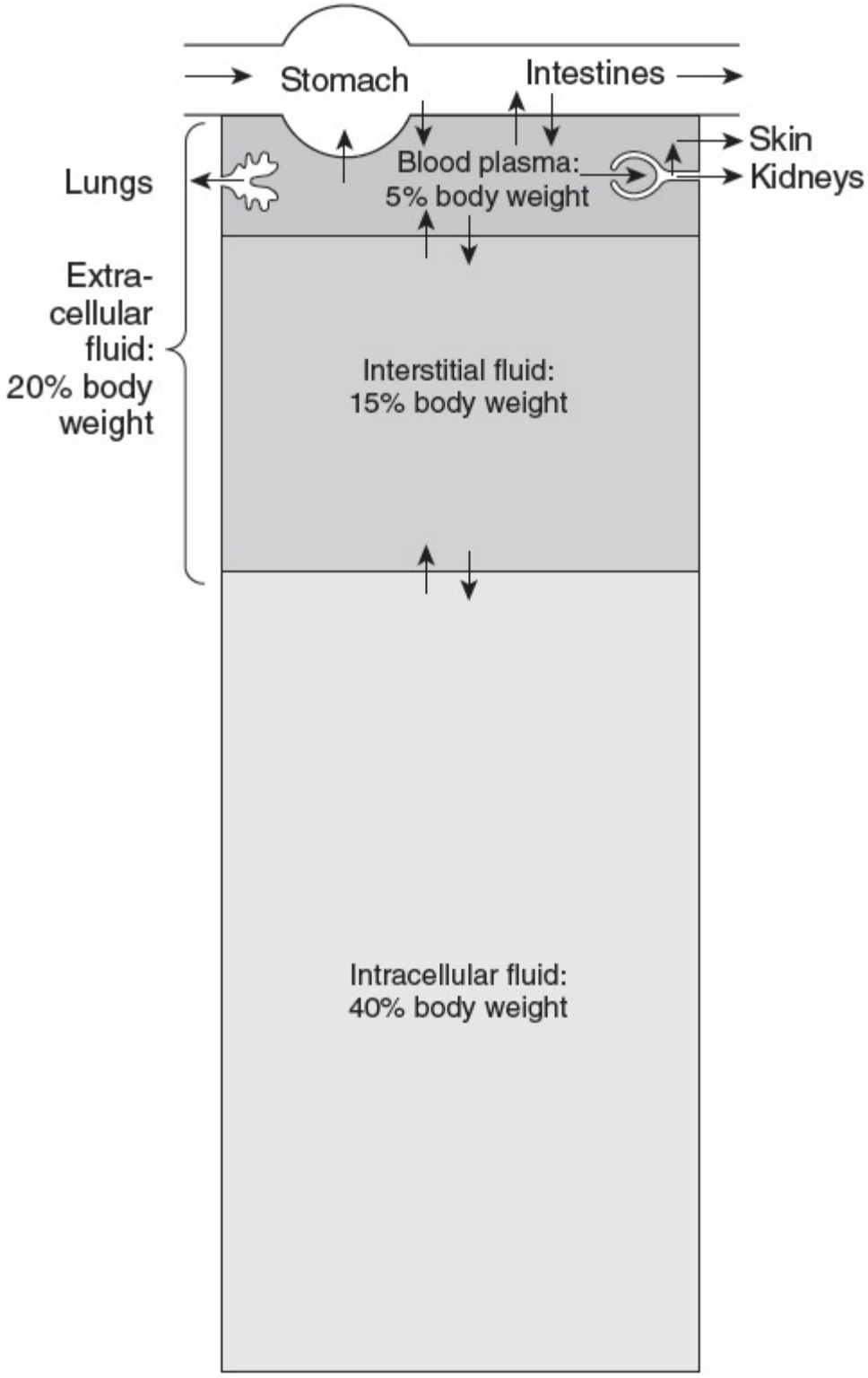


Figure 4

Body fluid compartments with approximate contribution to percentage body weight. *Arrows* represent fluid movement between compartments. (Reproduced, with permission, from Barrett et al. *Ganong's Review of Medical Physiology.* 24th ed. New York, NY: McGraw-Hill; 2012:5.)

- *Intracellular fluid* (ICF) comprises about two-thirds of TBW (40% of body mass).
- ECF is one-third of TBW (20% of body mass). The ECF water is further divided into:
  - *Plasma (intravascular) water*, which comprises approximately one-fourth of ECF or one-twelfth of TBW (5% of body mass), and
  - *Interstitial (extravascular) water*, which comprises approximately three-fourths of ECF or one-fourth of TBW (15% of body mass).

The composition of the extracellular and intracellular fluids is shown in Table 3. 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.

TABLE 3. ECF AND ICF COMPOSITION

Substance	Extracellular Concentration (mM)	Intracellular Concentration (mM)[a]
Na^+	150	15
K^+	5	150
Ca^{2+}	1	0.0001
Mg^{2+}	1.5	12
H^+	40×10^{-6}	100×10^{-6}
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

[a]The intracellular concentrations differ slightly from one tissue to another, but the concentrations shown above are typical of most cells. For Ca^{2+}, 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).
(Modified, with permission, from Widmaier EP, Raff H, Strang KT. *Vander's Human Physiology: The Mechanisms of Body Function*. 12th ed. New York, NY: McGraw-Hill; 2011:106.)

The solute or particle concentration of a fluid is its osmolality. Water shifts between the ECF and ICF in order to maintain osmotic equilibrium between the two compartments.

The normal range of plasma osmolality is 285 to 300 mOsm/kg, and the normal range of plasma osmolarity is 285 to 300 mOsm/L.

Because of the predominant role of the major solutes and the deviation of plasma from an ideal solution, plasma osmolarity can normally be estimated using the following formula:

$$\text{Osmolality (mOsm/L)} = 2\,[Na^+ \text{ in mEq/L}] + 0.055\,[\text{Glucose in mg/dL}] + 0.36\,[\text{Blood urea nitrogen in mg/dL}]$$

Fluid and Electrolyte Balance and Disorders

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 ECF hypotonic.

Plasma osmolality is elevated in:
- Dehydration
- Diabetes insipidus
- Hypernatremia
- Hyperglycemia
- Hypercalcemia
- Mannitol therapy
- Uremia
- Toxin ingestion (ethanol, methanol, ethylene glycol)

Plasma osmolality is decreased in:
- Addison disease
- Hyponatremia
- Hypothyroidism
- Syndrome of inappropriate antidiuretic hormone (SIADH)

• Overhydration

The extracellular volume is controlled by the NaCl content of the ECF. Hypovolemia, or volume depletion, generally refers to a state of combined salt and water loss exceeding intake, leading to ECF volume contraction. The loss of Na^+ may be renal or extrarenal (Table 4).

TABLE 4. CAUSES OF HYPOVOLEMIA

I. ECF volume contracted
- A. Extrarenal Na^+ loss
  - 1. Gastrointestinal (vomiting, nasogastric suction, drainage, fistula, diarrhea)
  - 2. Skin/respiratory (insensible losses, sweat, burns)
  - 3. Hemorrhage
- B. Renal Na^+ and water loss
  - 1. Diuretics
  - 2. Osmotic dieresis
  - 3. Hypoaldosteronism
  - 4. Salt-wasting nephropathies
- C. Renal water loss
  - 1. Diabetes insipidus (central or nephrogenic)

II. ECF volume normal or expanded
- A. Decreased cardiac output
  - 1. Myocardial, valvular, or pericardial disease
- B. Redistribution
  - 1. Hypoalbuminemia (hepatic cirrhosis, nephrotic syndrome)
  - 2. Capillary leak (acute pancreatitis, ischemic bowel, rhabdomyolysis)
- C. Increased venous capacitance
  - 1. Sepsis

(Reproduced, with permission, from Fauci AS, Braunwald E, Kasper DL, et al. *Harrison's Principles of Internal Medicine*. 17th ed. New York: McGraw-Hill; 2008:276.)

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 the following:

• Decreased perfusion pressure within the afferent arteriole

• Sympathetic stimulation of the JG cells

• Decreased Cl^- concentration in fluid bathing the macula densa

Renin catalyzes the conversion of angiotensinogen to angiotensin I. Angiotensin I is converted into angiotensin II by angiotensin-converting enzyme (ACE) located within the lung. Angiotensin II stimulates aldosterone secretion from the adrenal cortex gland.

Hyponatremia, defined as a plasma sodium concentration <135 mEq/L, is a very common disorder occurring in more than 20% of hospitalized patients. The disorder is almost always the result of an increase in circulating ADH and/or increased renal sensitivity to ADH. The underlying patho-physiology for the exaggerated or inappropriate ADH response differs in hyponatremic patients as a function of their ECF volume. Therefore, the causes of hyponatremia are subdivided into three categories based on coexisting urine sodium and osmolarity and volume status (Table 5).

TABLE 5. CAUSES OF HYPONATREMIA

		Urine Osmolality	Urine Sodium
Hypovolemic	Extrarenal: GI losses, skin losses, lung losses, third spacing (fistula, burns, vomiting, diarrhea, GI suction, edema, pancreatitis)	↑	↓
	Renal: Diuretics, intrinsic renal damage (including acute tubular necrosis), partial urinary tract obstruction, salt-wasting nephropathies	↑	↑
	Adrenal insufficiency (Addison)	↑	↑
Isovolemic	Water intoxication	↓	↓
	SIADH	↑	↑
Hypervolemic	Congestive heart failure, liver cirrhosis, and nephrotic syndrome	↑	↓

↓ = decreased; ↑ = increased.
(Reproduced, with permission, from Kaufman MS, Stead LG, Rusovici A. *First Aid for the Medicine Clerkship*. 3rd ed. New York, NY: McGraw-Hill; 2010:246.)

Hypernatremia is defined as a serum sodium concentration greater than 145 mEq/L. The causes of hypernatremia are subdivided into three categories based on the coexisting fluid status (Table 6).

TABLE 6. CAUSES OF HYPERNATREMIA

		Urine Osm	Urine Sodium
Hypovolemic	Renal loss: Osmotic diuresis (glycosuria, urea), acute/chronic renal failure, partial obstruction	N/↓	↑
	Extrarenal loss: Hyperpnea, excessive sweating	↑	↑
	Extrarenal loss: Diarrhea, burns, moderate sweating	↑	↓
	Iatrogenic (bicarbonate, dialysis, salt tablets)	↑	↑
Isovolemic	Diabetes insipidus (from any cause)	↓	↓
Hypervolemic	Mineralocorticoid excess (eg, Conn syndrome)	N/↓	N/↓

↓ = decreased; ↑ = increased; N = normal.
(Reproduced, with permission, from Stead LG, Stead SM, Kaufman MS, et al. *First Aid for the Medicine Clerkship*. 2nd ed. New York, NY: McGraw-Hill; 2006:229.)

Potassium is the major intracellular cation with a normal concentration of approximately 150 mmol/L (Table 3). Homeostatic mechanisms maintain plasma K^+ concentration between 3.5 and 5 mmol/L despite marked variations in dietary K^+ intake. The ratio of intracellular to extracellular K^+ (normally 38:1) is the principal result of the resting membrane potential and is essential for normal neuromuscular function. Virtually all regulation of renal K^+ excretion and total body K^+ balance occurs in the distal nephron. Potassium secretion is regulated by aldosterone. Aldosterone is secreted by the zona glomerulosa cells of the adrenal cortex in response to increases in extracellular K^+ or angiotensin II, causing K^+ secretion to increase. K^+ transport into cells is increased by epinephrine and insulin.

The causes of *hypokalemia*, defined as a plasma K^+ concentration less than 3.5 mEq/L, are shown in Table 7. The causes of *hyperkalemia*, defined as a plasma K^+ concentration ≥ 5 mEq/L, are shown in Table 8. Hypokalemia occurs in up to 20% of hospitalized patients, and is associated with a tenfold increase in in-hospital mortality rates due to adverse effects on cardiac rhythm. Hyperkalemia occurs in up to 10% of hospitalized patients; severe hyperkalemia (>6 mEq/L) occurs in approximately 1% of patients and has a significantly increased risk of mortality.

TABLE 7. CAUSES OF HYPOKALEMIA

I. Decreased intake of K^+
   A. Starvation
   B. Clay ingestion
II. Redistribution of K^+ into cells
   A. Metabolic alkalosis
   B. Hormonal
      1. Insulin
      2. β_2-Adrenergic agonists (endogenous or exogenous)
      3. α-Adrenergic antagonists
   C. Anabolic state
      1. Vitamin B_{12} or folic acid administration (red blood cell production)
      2. Granulocyte-macrophage colony-stimulating factor (white blood cell production)
      3. Total parenteral nutrition
   D. Other
      1. Pseudohypokalemia
      2. Hypothermia
      3. Hypokalemic periodic paralysis
      4. Barium toxicity
III. Increased loss of K^+
   A. Nonrenal
      1. Gastrointestinal loss (diarrhea)
      2. Integumentary loss (sweat)
   B. Renal
      1. Increased distal flow: diuretics, osmotic diuresis, salt-wasting nephropathies

2. Increased secretion of potassium
   a. *Mineralocorticoid excess*
      i. Primary hyperaldosteronism (aldosterone-producing adenomas; primary or unilateral adrenal hyperplasia; idiopathic hyperaldosteronism due to bilateral adrenal hyperplasia, adrenal carcinoma)
      ii. Familial hyperaldosteronism (FH-I, FH-II, congenital adrenal hyperplasia)
      iii. Secondary hyperaldosteronism (malignant hypertension, renin-secreting tumors, renal artery stenosis, hypovolemia)
      iv. Cushing syndrome
      v. Bartter syndrome
      vi. Gitelman syndrome
   b. *Apparent mineralocorticoid excess*
      i. Genetic deficiency of 11β-dehydrogenase-2 (syndrome of apparent mineralocorticoid excess)
      ii. Inhibition of 11β-dehydrogenase-2 (carbenoxolone, glycyrrhetinic/glycyrrhizic acid—a natural sweetener found in licorice, chewing tobacco, and food products)
      iii. Liddle syndrome (genetic activation of epithelial Na^+ channels)
   c. *Distal delivery of non-reabsorbed anions*
      i. Vomiting, nasogastric suction
      ii. Proximal renal tubular acidosis (type 2)
      iii. Diabetic ketoacidosis
      iv. Glue-sniffing (toluene abuse)
      v. Penicillin derivatives
   d. *Magnesium deficiency*

(Reproduced, with permission, from Longo DL, Kasper DL, Jameson JL, et al. *Harrison's Principles of Internal Medicine*. 18th ed. New York, NY: McGraw-Hill; 2012:352.)

TABLE 8. CAUSES OF HYPERKALEMIA

I. Inadequate K^+ excretion
   A. Advanced renal insufficiency: chronic kidney disease, end-stage renal disease, acute oliguric kidney injury
   B. Decreased distal fluid delivery (ie, decreased effective circulating fluid volume)
      1. Congestive heart failure
      2. Volume depletion
   C. Hyporeninemic hypoaldosteronism
      1. Diabetes, diabetic nephropathy
      2. Tubulointerstitial diseases: SLE, sickle cell anemia, obstructive uropathy
      3. Drugs: NSAIDs, COX-2 inhibitors, beta-blockers, cyclosporine, taurine
      4. Pseudohypoaldosteronism type II: defects in WNK1 or WNK4 kinases
      5. Chronic kidney disease, advanced age
   D. Primary adrenal insufficiency
      1. Autoimmune: Addison disease, polyglandular endocrinopathy
      2. Hereditary: adrenal synthase deficiency, adrenal hypoplasia congenita, congenital lipoid adrenal hyperplasia
      3. Infectious: HIV, cytomegalovirus, TB, disseminated fungal infection
      4. Infiltrative: amyloidosis, malignancy, metastatic cancer
      5. Drug associated: heparin, low-molecular-weight heparin
      6. Adrenal hemorrhage or infarction, including in antiphospholipid syndrome

E. Renal resistance to mineralocorticoid
   1. Tubulointerstitial diseases: SLE, amyloidosis, sickle cell anemia, obstructive uropathy, post-acute tubular necrosis
   2. Hereditary: Pseudohypoaldosteronism type I: defects in mineralocorticoid receptor or ENaC
F. Inhibition of the renin–angiotensin–aldosterone axis: ↑ risk of hyperkalemia with:
   1. ACE inhibitors
   2. Renin inhibitors
   3. Angiotensin receptor blockers
   4. Mineralocorticoid receptor blockade: spironolactone, eplerenone, drospirenone
   5. Blockade of ENaC: amiloride, triamterene, trimethoprim, pentamidine

II. Intra- to extracellular shift of K^+
   A. Acidosis
   B. Hyperosmolality: radiocontrast, hypertonic dextrose, mannitol
   C. Digoxin and related glycosides (bufadienolide)
   D. Hyperkalemic periodic paralysis
   E. β-Adrenergic antagonists (noncardioselective agents)
   F. Succinylcholine, thermal trauma, neuromuscular injury, disuse atrophy, prolonged immobilization
   G. Rapid tumor lysis

III. "Pseudo" hyperkalemia
   A. Cellular efflux: thrombocytosis, erythrocytosis, leukocytosis, in vitro hemolysis
   B. Hereditary defects in red blood cell membrane transport

ACE, angiotensin-converting enzyme; HIV, human immunodeficiency virus; NSAIDs, nonsteroidal anti-inflammatory drugs.
(Modified, with permission, from Longo DL, Kasper DL, Jameson JL, et al. *Harrison's Principles of Internal Medicine*. 18th ed. New York, NY: McGraw-Hill; 2012:356.)

Acid–Base Balance and Disorders

Each day, approximately 15,000 mmol of volatile acid (CO_2) 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 ECF is maintained by buffering the acid as it is formed and excreting the acid over time. The kidneys require approximately 24 hours to excrete the fixed acids. CO_2 is rapidly excreted by the lungs.

When CO_2 is added to water, it forms carbonic acid (H_2CO_3), a reaction that is catalyzed by the enzyme carbonic anhydrase (CA). Once formed, carbonic acid rapidly dissociates into H^+ and HCO_3^-.

$$CO_2 + H_2O \xleftrightarrow{CA} H_2CO_3 \longleftrightarrow H^+ + HCO_3^-$$

The *pH of plasma* is calculated using the Henderson–Hasselbalch equation:

$$\text{pH} = 6.1 + \log [HCO_3^-]/[\text{dissolved } CO_2]$$
$$= 6.1 + \log [HCO_3^-]/(P_{CO_2} \text{ in mm Hg} \times 0.03 \text{ mEq/L/mm Hg}).$$

Arterial P_{CO_2} is normally maintained at 40 mm Hg by the lungs and arterial $[HCO_3^-]$ 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 $[HCO_3^-]$/[dissolved CO_2] = 20/1. The four primary acid–base disorders result from abnormalities that alter the normal 20/1 ratio of $[HCO_3^-]$/[dissolved CO_2], as summarized in Table 9.

TABLE 9. CHARACTERISTICS OF PRIMARY ACID–BASE DISORDERS

Disorder	pH	Primary Disturbance	Compensatory Response
Respiratory acidosis	↓	↑P_{aCO_2} (alveolar hypoventilation)	↑ $[HCO_3^-]$ (↑renal H^+ excretion)
Respiratory alkalosis	↑	↓P_{aCO_2} (alveolar hyperventilation)	↓$[HCO_3^-]$ (↓renal H^+ excretion)
Metabolic alkalosis	↑	↑ $[HCO_3^-]$ (gain of HCO_3^-; loss of H^+)	↑ P_{aCO_2} (alveolar hypoventilation)
Metabolic acidosis	↓	↓ $[HCO_3^-]$ (gain of H^+; loss of HCO_3^-)	↓ P_{aCO_2} (alveolar hyperventilation)

↓ = decreased; ↑ = increased.
Normal ranges: pH: 7.35–7.45; P_{aCO_2}: 35–45 mm Hg; $[HCO_3^-]$: 22–26 mEq/L.

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 $[HCO_3^-]$/[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 $[HCO_3^-]$, then the appropriate respiratory compensatory response will change the P_{aCO_2}, and thus the [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 $[HCO_3^-]$ in the same direction as the primary change in P_{aCO_2}.

The causes of the four primary acid–base disorders are listed in Tables 10 to 13.

TABLE 10. CAUSES OF METABOLIC ALKALOSIS

I. GI or renal loss of H^+/retention of HCO_3^-
   A. Vomiting, nasogastric suction, gastric fistulas
   B. Diuretic therapy
   C. Severe magnesium or potassium deficiency
   D. Excess mineralocorticoids
      1. High renin: renal artery stenosis, accelerated hypertension, renin-secreting tumor, estrogen therapy
      2. Low renin: primary aldosteronism, Cushing syndrome or disease, adrenal enzyme defects, ingestion of mineralocorticoids (licorice; chewing tobacco)
   E. Bartter syndrome (loss of function mutation of any of the five ion transport proteins in the thick ascending limb of the Loop of Henle)
   F. Gitelman syndrome (loss of function mutation in Na^+–Cl^- cotransporter in distal convoluted tubule)
   G. Liddle syndrome (gain-of-function mutation of renal epithelial sodium channel with ECFV expansion, hypertension, K^+ deficiency, and hyporeninemic hypoaldosteronism)
II. Ingestion or administration of excess bicarbonate or other bases
   A. Intravenous bicarbonate
   B. Ingestion of bicarbonate or other bases (eg, antacids)

(Modified, with permission, from Longo DL, Kasper DL, Jameson JL, et al. *Harrison's Principles of Internal Medicine*. 18th ed. New York, NY: McGraw-Hill; 2012:369.)

TABLE 11. CAUSES OF METABOLIC ACIDOSIS

Normal Anion Gap (Hyperchloremic)	Increased Anion Gap (Normochloremic)
I. Gastrointestinal loss of HCO_3^- A. Diarrhea B. Ileal loop conduit, jejunal loop, ureterosigmoidostomy C. External pancreatic or small bowel drainage D. Drugs 1. Calcium chloride 2. Magnesium sulfate 3. Cholestyramine II. Renal inability to reabsorb HCO_3^- (GFR: 20–50 mL/min) A. RTA (types 1, 2, and 4) B. Carbonic anhydrase inhibitors III. Drug-induced hyperkalemia (with renal insufficiency) A. ACE inhibitors and angiotensin-receptor blockers B. Potassium-sparing diuretics (amiloride, triamterene, spironolactone) C. Trimethoprin D. Pentamidine E. NSAIDs F. Cyclosporine and tacrolimus IV. Miscellaneous A. Expansion acidosis (rapid saline administration) B. Acid loads (ammonium chloride, hyperalimentation)	I. Increase in endogenous acid production A. Lactic acidosis 1. Type A: Poor tissue oxygenation (circulatory insufficiency, severe anemia, CO or CN^- poisoning) 2. Type B: Aerobic disorders (malignancies, nucleoside analogue reverse transcriptase inhibitors in HIV, cholera, malaria, seizures, renal or hepatic failure, thiamine deficiency, drugs/toxins B. Ketoacidosis (diabetic, starvation, and alcoholic) II. Uremia (GFR < 20 mL/min) A. Acute renal failure B. Chronic renal failure III. Drug/toxin-induced increases in organic/inorganic acids A. Ethylene glycol (metabolites: oxalic acid and glycolic acid) B. Salicylate (acetylsalicylic acid) C. Methanol (metabolites: formic acid and formaldehyde) D. Paraldehyde E. Isoniazid (causes lactic acidosis)

GFR, glomerular filtration rate; NSAIDs, nonsteroidal anti-inflammatory drugs.
(Modified, with permission, from Longo DL, Kasper DL, Jameson JL, et al. *Harrison's Principles of Internal Medicine*. 18th ed. New York, NY: McGraw-Hill; 2012:365, 368.)

TABLE 12. CAUSES OF RESPIRATORY ACIDOSIS (ALVEOLAR HYPOVENTILATION)

I. Airway obstruction
   A. Chronic obstructive lung disease (emphysema and chronic bronchitis)
   B. Severe asthma
   C. Upper airway obstruction
   D. Generalized bronchoconstriction (anaphylaxis, inhalational burn, toxin injury)
II. Restrictive parenchymal impairment
   A. Pulmonary fibrosis
   B. Sarcoidosis
   C. Pneumoconiosis
   D. Acute respiratory distress syndrome
   E. Pneumothorax, pleural effusion
   F. Pneumonia
   G. Pulmonary edema
III. Chest wall restriction
   A. Kyphoscoliosis
   B. Extreme obesity
IV. Respiratory center depression
   A. Drugs (general anesthetics, morphine, sedatives)
   B. Brain injury or disease (intracranial tumors [chronic], stroke)
   C. Sleep-disordered breathing, including the primary alveolar and obesity-hypoventilation syndromes
   D. Severe hypercapnia, hypoxia
V. 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. Muscular dystrophies and other respiratory muscle diseases
VI. Miscellaneous
   A. Iatrogenic mechanical hypoventilation
   B. Large increases in dead space (mechanical dead space, PEEP)

PEEP, positive end-expiratory pressure.
(Modified, with permission, from Levitzky MG. *Pulmonary Physiology.* 7th ed. New York, NY: McGraw-Hill; 2007:173 and Longo DL, Kasper DL, Jameson JL, et al. *Harrison's Principles of Internal Medicine.* 18th ed. New York, NY: McGraw-Hill; 2012:371.)

TABLE 13. CAUSES OF RESPIRATORY ALKALOSIS (ALVEOLAR HYPERVENTILATION)

I. Respiratory center stimulation
  A. Central nervous system
    1. Hyperventilation syndrome
    2. Anxiety, psychosis
    3. Fever
    4. Stroke
    5. Meningitis, encephalitis
    6. Tumors
    7. Trauma
    8. Drugs
      a. Salicylates (direct stimulation of medullary chemoreceptors)
      b. Pregnancy, progesterone
      c. Methylxanthines (theophylline and aminophylline)
  B. Reflex hyperventilation
    1. High altitude
    2. Hypoxemia
    3. Pulmonary embolism
    4. Asthma
    5. Fever
    6. Flail chest
    7. Congestive heart failure/interstitial pulmonary edema
II. Miscellaneous
  A. Gram-negative septicemia (before fever, hypoxemia, or hypotension develop)
  B. Hepatic failure
  C. Iatrogenic mechanical hyperventilation

(Modified, with permission, from Levitzky MG. *Pulmonary Physiology.* 7th ed. New York, NY: McGraw-Hill; 2007:174 and Longo DL, Kasper DL, Jameson JL, et al. *Harrison's Principles of Internal Medicine.* 18th ed. New York, NY: McGraw-Hill; 2012:371.)

PHYSIOLOGY OF THE HEMATOPOIETIC AND LYMPHORETICULAR SYSTEMS

(*References: Barrett et al., pp 555-570, 641-648. Levitzky, pp 142-162. Widmaier et al., pp 417-427, 454-459.*)

Oxygen Transport in the Blood

Oxygen is transported in the blood in two 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 following equation:

$$HbO_2\ (mL/dL\ blood) = [Hb]\ (g/dL\ blood) \times 1.34\ mL\ O_2/g\ Hb \times \%O_2\ saturation/100$$

As shown in Table 14, the total oxygen content is the sum of the dissolved oxygen and the oxyhemoglobin content. More than 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 (Figure 5).

TABLE 14. TOTAL O_2 CONTENT IN ARTERIAL AND VENOUS BLOOD

	Dissolved O_2	HbO_2	Total
Arterial blood (100 mm Hg PO_2; 97% O_2 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 mm Hg PO_2; 75% O_2 sat; 15 g/dL Hb)	0.12 mL O_2/dL	15.1 mL O_2/dL	15.2 mL O_2/dL

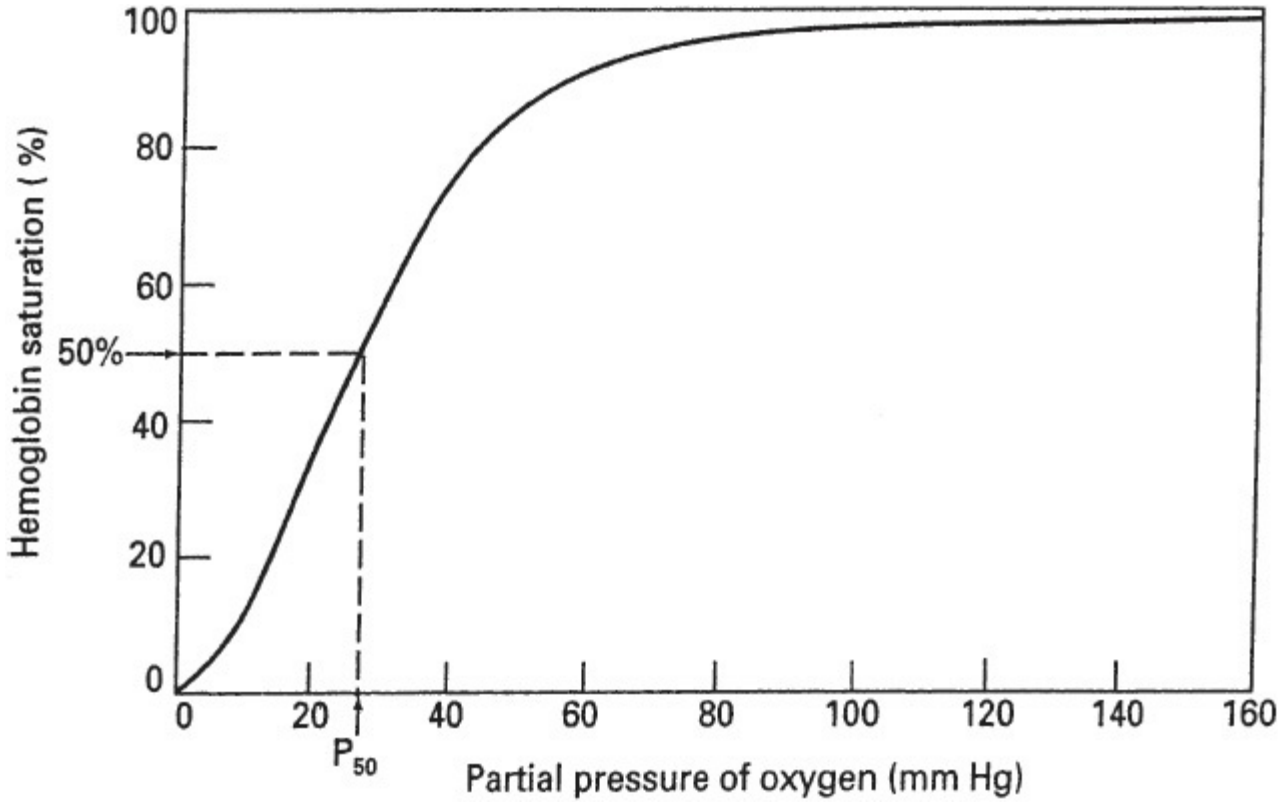


Figure 5

Oxyhemoglobin dissociation curve. (Reproduced, with permission, from Levitzky MG. *Pulmonary Physiology*. 7th ed. New York, NY: McGraw-Hill; 2007:146.)

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.

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

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 chains and two β chains). Heme is a complex consisting of a porphyrin and one atom of a ferrous (Fe^{2+}) 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 PO_2 of the plasma and the percent of hemoglobin saturated with oxygen (Figure 5).

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 reached when the P_{O_2} is above approximately 80 mm Hg.

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 P_{O_2} still has a relatively high O_2 saturation (eg, 90% SO_2 at 60 mm Hg P_{O_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 approximately 27 mm Hg. Factors that shift the oxyhemoglobin dissociation curve to the right include the following:

- Hyperthermia
- Increased P_{CO_2} or decreased pH (known as the Bohr effect)
- Increased erythrocyte [2,3-bisphosphoglycerate] (BPG, DPG, 2,3-BPG, 2,3-DPG)

A *leftward shift* of the oxyhemoglobin dissociation curve denotes a higher-than-normal HbO_2 affinity with greater oxygen uptake at the pulmonary capillaries 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 the following:

- Hypothermia
- Alkalosis or decreased P_{CO_2} (Bohr effect)
- Decreased erythrocyte 2,3-BPG concentration
- Carbon monoxide

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 with the β-chains in HbA.

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.

CO_2 Transport in the Blood

The total CO_2 content in blood (~50 mL/dL) is much greater than total arterial O_2 content (~20 mL/dL). Like oxygen, carbon dioxide can be physically dissolved in the plasma or chemically combined with hemoglobin (carbaminohemoglobin). Approximately 5% of total CO_2 is dissolved. Carbaminohemoglobin constitutes approximately 10% of total CO_2 in the blood, in contrast to oxygen combined to hemoglobin. 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.

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.

NEUROPHYSIOLOGY

(*References: Barrett et al., pp 8-10, 83-96, 119-296. McPhee and Hammer, pp 141-181. Widmaier et al., pp 135-249, 292-310.*)

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 equation:

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

The equilibrium potential for K^+ is −90 mV, for Na^+ is +60 mV, and for Cl^- is −70 mV.

The resting membrane potential is calculated with the Goldman equation:

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

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 Na^+–K^+ pump, that is, Na^+, 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 (Figure 6).

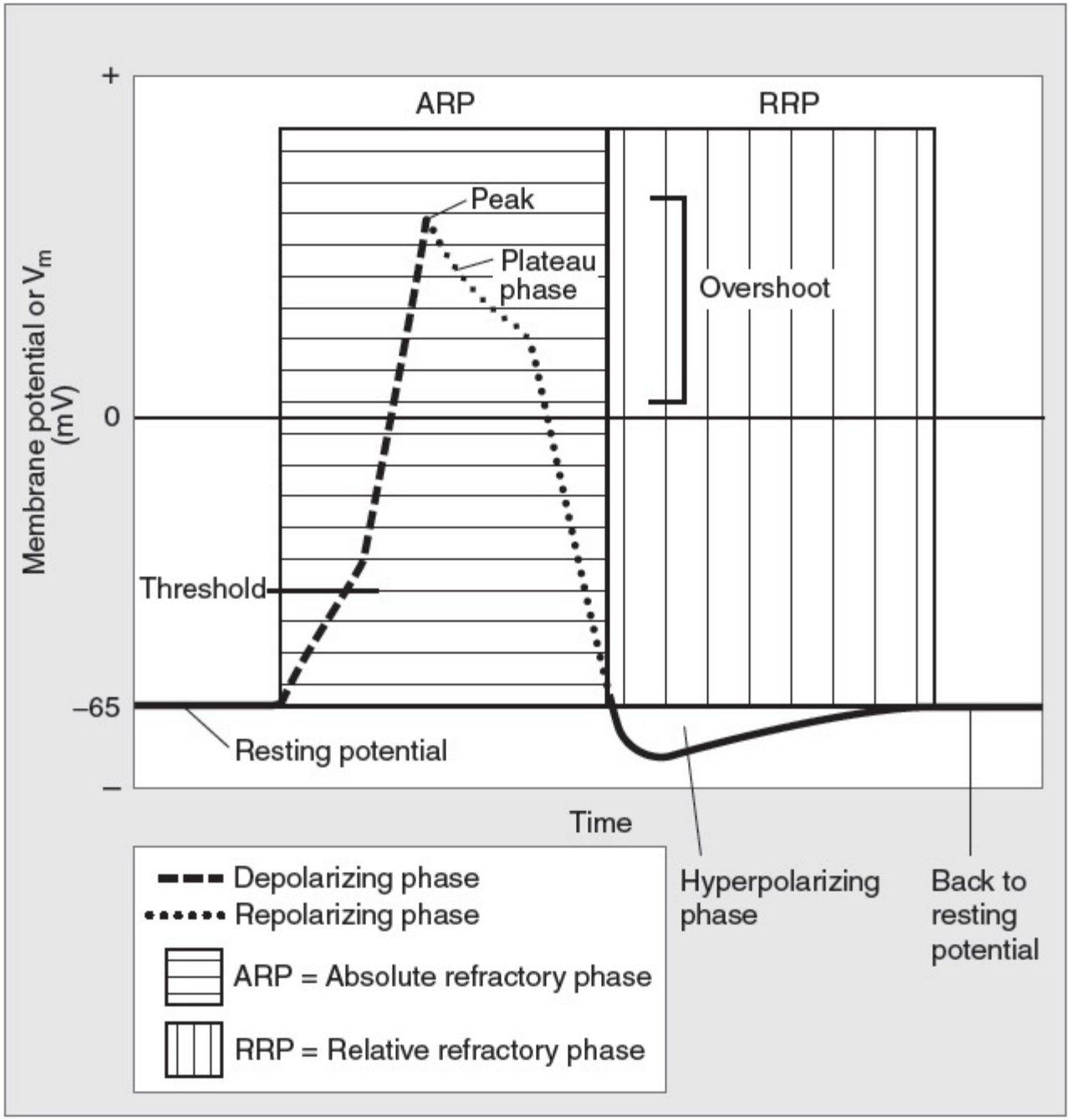


Figure 6

Components of an action potential. (Reproduced with permission from Toy et al. *Case Files™: Neuroscience.* www.accessmedicine.com. McGraw-Hill.)

The action potential is said to be "*all or none*" because it will not occur if a stimulus is sub-threshold, 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.

1. The *action potential* begins with an initial depolarization of about 10 to −15 mV from the resting potential.
2. Once the impulse reaches *threshold* intensity at about −55 mV, an action potential is produced as characterized by a *rapid upstroke* that *overshoots* the zero potential to approximately +35 mV.
3. 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.
4. After repolarization is approximately 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-hyperpolarization*, which is only 1 to 2 mV, but lasts about 40 ms.

Action potentials are produced by ionic fluxes controlled by voltage-gated ion channels.

During an action potential, 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. 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^+ and

2. Na^+ channels enter a closed or inactivated state before returning to the resting state.

Functions of Nerves

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.
4. The nerve endings, where action potentials cause the secretion of synaptic transmitters.

Nerve fiber types are classified into A, B, and C groups based on the speed of conduction and fiber diameter (Table 15). A numerical classification is often used for sensory neurons, as shown in Table 16.

TABLE 15. NERVE FIBER TYPES

Fiber Type	Function	Fiber Diameter (μm)	Conduction Velocity (m/s)	Spike Duration (ms)	Absolute Refractory Period (ms)
A (myelinated)					
Aα	Proprioception; somatic motor	12–20	70–120		
Aβ	Touch, pressure, motor	5–12	30–70	0.4–0.5	0.4–1
Aγ	Motor to muscle spindles	3–6	15–30		
Aδ	Pain, cold, touch	2–5	12–30		
B (myelinated)	Preganglionic autonomic	<3	3–15	1.2	1.2
C (unmyelinated)					
Dorsal root	Pain, temperature, mechanoreception reflex responses	0.4–1.2	0.5–2	2	2
Sympathetic	Postganglionic sympathetic	0.3–1.3	0.7–2.3	2	2

(Reproduced, with permission, from Barrett et al. *Ganong's Review of Medical Physiology*. 24th ed. New York, NY: McGraw-Hill; 2012:92.)

TABLE 16. CLASSIFICATION OF SENSORY NEURONS

Number	Origin	Fiber Type
Ia	Muscle spindle, annulospiral ending	Aα
Ib	Golgi tendon organ	Aα
II	Muscle spindle, flower-spray ending; touch, pressure	Aβ
III	Pain and cold receptors; some touch receptors	Aδ
IV	Pain, temperature, and other receptors	Dorsal root C

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

Synaptic transmission is one mechanism 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. After a neurotransmitter binds to its postsynaptic

receptor, it will activate a reaction, known as the second messenger. Acetylcholine, which binds to the end plate of skeletal muscle cells, and glutamate and γ-amino butyric acid (GABA), which bind to the post-synaptic 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 that, in turn, activates an enzyme-mediated response.

Central and Peripheral Neurophysiology

A summary of the functions of the major parts of the brain is provided in Table 17.

TABLE 17. SUMMARY OF FUNCTIONS OF THE MAJOR PARTS OF THE BRAIN

I. Forebrain (cerebrum and diencephalon)
  A. Cerebral hemispheres (major part of cerebrum)
    1. Cerebral cortex
      a. Perception
      b. Generation of skilled movements
      c. Reasoning, learning, and memory
    2. Subcortical nuclei, including basal ganglia
      a. Coordination of skeletal muscle activity, movement, and posture
    3. Interconnecting fiber pathways
  B. Thalamus (part of diencephalon)
    1. Acts as a synaptic relay for sensory pathways on their way to the cerebral cortex
    2. Participates in control of skeletal muscle coordination
    3. Plays key role in awareness
  C. Hypothalamus (part of diencephalon)
    1. Regulates anterior pituitary gland function
    2. Participates in regulation of autonomic nervous system
    3. Regulates eating and drinking behavior
    4. Regulates water balance
    5. Regulates reproductive system
    6. Generates and regulates circadian rhythms
    7. Regulates body temperature
    8. Participates in generation of emotional behavior
  D. Limbic system
    1. Participates in generation of emotions and emotional behavior
    2. Plays essential role in most kinds of learning
II. Cerebellum
  A. Coordinates movements, including those for posture and balance
  B. Participates in some forms of learning
III. Brainstem (midbrain, pons, medulla oblongata)
  A. Contains all fibers passing between spinal cord, forebrain, and cerebellum
  B. Contains the reticular formation and its various integrating centers, including those for cardiovascular and respiratory activity
  C. Contains nuclei for cranial nerves III through XII

(Modified, with permission, from Widmaier EP, Raff H, Strang KT. *Vander's Human Physiology: The Mechanisms of Body Function*. 12th ed. New York, NY: McGraw-Hill; 2011:171.)

Control of Movement

• 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 either paucity of movement (hypokinetic) or excessive, uncontrolled movements (hyperkinetic). Some basal ganglia movement disorders are highlighted in Table 18.

TABLE 18. EXAMPLES OF BASAL GANGLIA DISEASES

Disease	Possible Cause	Clinical Manifestations
Parkinson disease	Degeneration of neurons in the substantia nigra with loss of dopaminergic inhibition and relative excess of cholinergic activity. Associated with Lewy bodies (intracellular inclusions of α-synuclein and barkin)	Tremor at rest, rigidity, akinesia (or bradykinesia), postural instability (TRAP), shuffling gait with loss of arm swing, masklike, unemotional appearance
Huntington disease	Autosomal-dominant trinucleotide (CAG) repeat disorder with degeneration of GABAergic neurons within the striatum	Rapid, jerky, purposeless movements (chorea), slow, writhing movements (athetosis) of proximal limbs and trunk, slurred speech, aggression, progressive dementia followed by death in 10–15 years after onset of symptoms
Wilson disease (hepatolenticular degeneration)	Rare disorder of copper metabolism in which there is degeneration of the putamen, a part of the lenticular nucleus	Asterixis (wing-beating tremor), dysartria, unsteady gait, rigidity
Ballismus	Lesion of the contralateral subthalamic nucleus (eg, lacunar stroke in hypertension)	Sudden, wild flailing of 1 arm +/– leg
Tardive dyskinesia	Iatrogenic basal ganglia disease resulting from administration of dopamine antagonists (phenothiazides, haloperidol) in psychosis	Rapid, jerky movements (chorea), slow, writhing movements (athetosis) of the face, tongue, and limbs

• Lesions to the cerebellum produce uncoordinated movements, characterized by intention tremor; inability to start or stop movements quickly or easily; inability to

combine the movements of several joints into a single, smooth, coordinated movement; unstable posture; awkward gait; and difficulty in learning new motor skills.

Special Senses

Sight

Light is detected by the rods and cones contained in the retina of the eye. The retina contains five types of neurons:

1. Photoreceptors (rods and cones)
2. Bipolar cells
3. Ganglion cells
4. Horizontal cells
5. Amacrine cells

Light rays from distant objects are normally focused on the photo-receptors 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.
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. Hydrolysis of cGMP causes Na^+ channels on the rod and cone outer segments to close, which produces the membrane hyperpolarization (Figure 7).

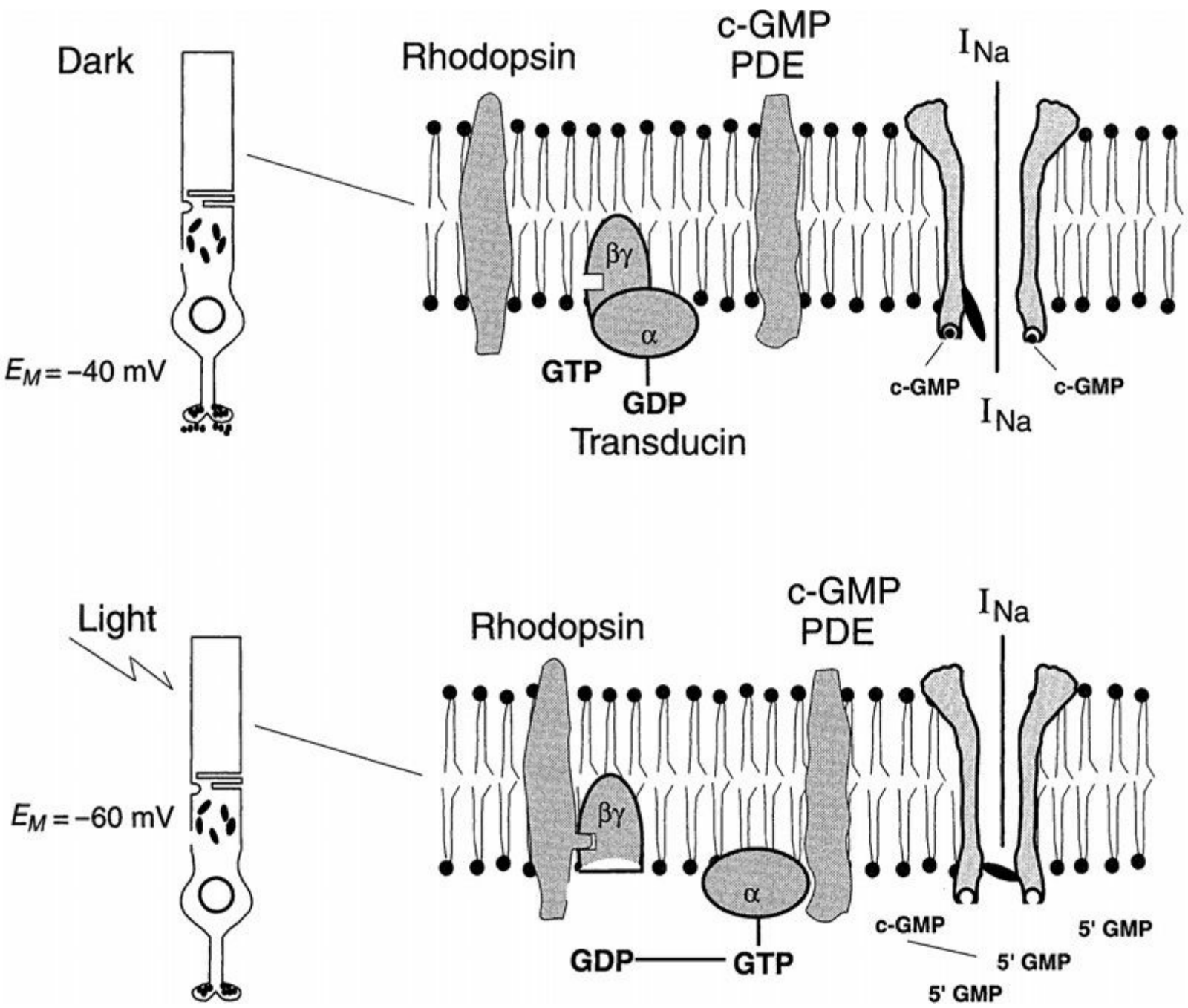


Figure 7
The photoreceptors. (See text for explanation.)

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.

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 membrane; the scala media and the scala tympani are separated by the basilar membrane. 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, with a high concentration of Na^+. The fluid within the scala media (endolymph) resembles ICF, 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^+ flows into the hair cells because the endolymph surrounding the apical portions of the hair cells contains a high K^+ concentration (Figure 8).

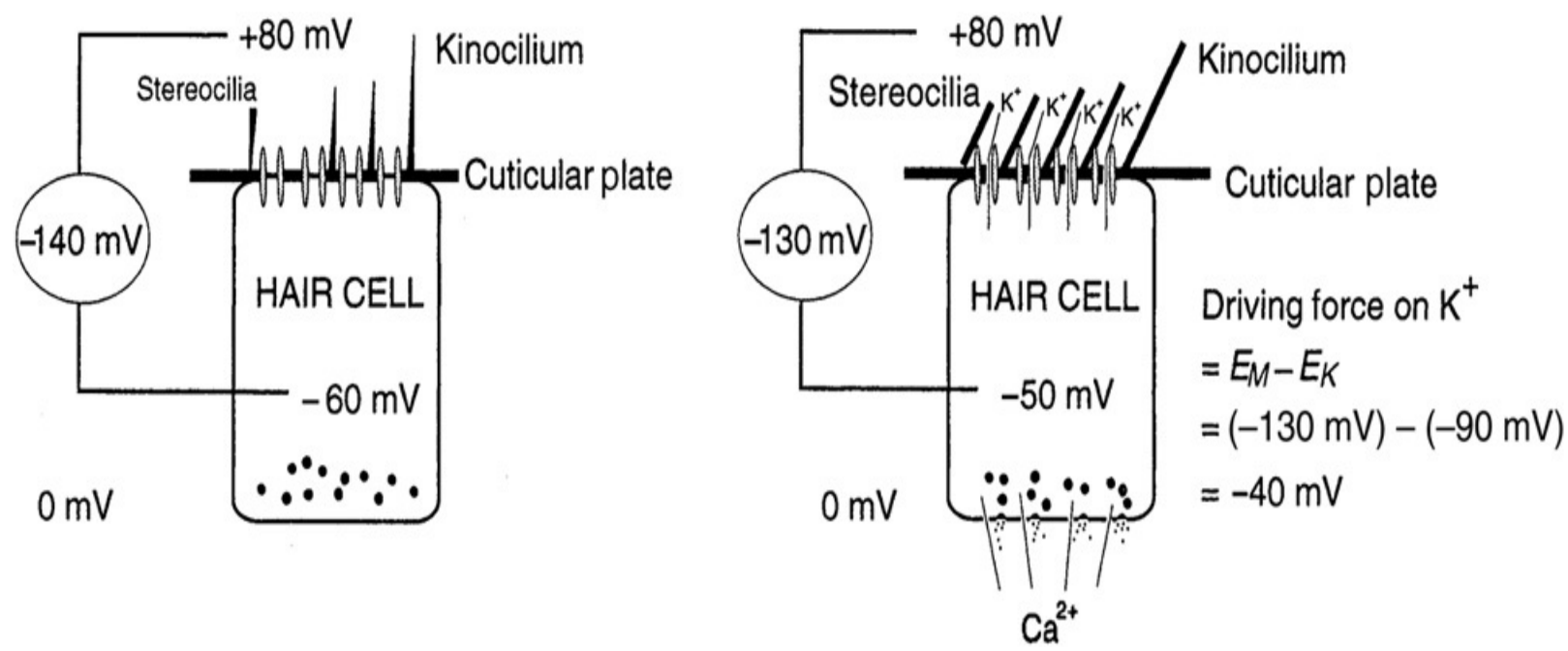


Figure 8
The auditory hair cell and K^+ channels.

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 apex of the cochlea, which are located on the more compliant portions of the basilar membrane.

Vestibular System

- 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.
- The vestibular system can be divided into the *vestibular apparatus* and central *vestibular nuclei*.
- The *vestibular apparatus* within the inner ear detects head motion and position and transduces this information to a neural signal.
- The *vestibular nuclei* are the cranial nuclei for the vestibular nerve. The vestibular nuclei are primarily concerned with maintaining the position of the head in space. The tracts that descend from these nuclei mediate head-on-neck and head-on-body adjustments.
- Nystagmus, the characteristic jerky movement of the eye observed at the start and end of a period of rotation, can be used as a diagnostic indicator of the integrity of the vestibular system.
- Nystagmus is a reflex that maintains visual fixation on stationary points while the body rotates. Nystagmus is not initiated by visual impulses and is present in blind individuals. When rotation starts, the eyes move slowly in a direction opposite to the direction of rotation, maintaining visual fixation (vestibulo-ocular reflex). When the limit of this movement is reached, the eyes quickly snap back to a new fixation point and then again move slowly in the other direction. The slow component is initiated by impulses from the vestibular labyrinths; the quick component is triggered by a center in the brainstem.
- When nystagmus is seen at rest, it is a sign of a pathology. Lesions to the vestibular system result in nystagmus and loss of balance.

Olfaction

A diagram of the olfactory pathway is shown in Figure 9.

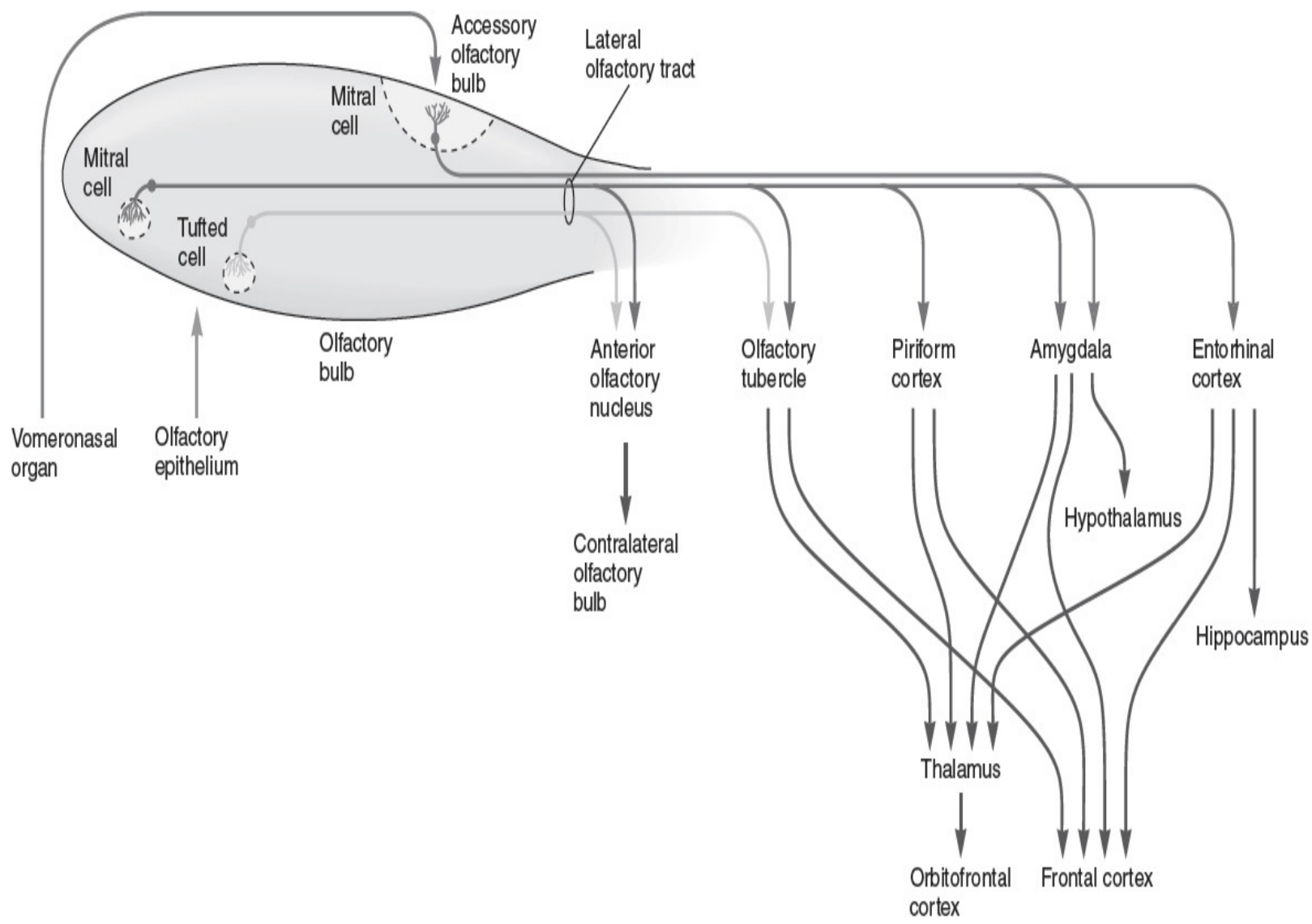


Figure 9

The olfactory pathway. (Reproduced, with permission, from Barrett et al. *Ganong's Review of Medical Physiology.* 24th ed. New York, NY: McGraw-Hill; 2012:219.)

- Olfactory sensory neurons are located in the olfactory epithelium within the nasal cavity, and their dendrites are exposed to odorant molecules, which bind to receptors and activate the neurons via G-proteins. The axons project through the cribriform plate, into the olfactory bulbs.
- Olfactory sensory information travels in the lateral olfactory stria to the olfactory cortex, including the anterior olfactory nucleus, olfactory tubercle, piriform cortex, the amygdala, and the entorhinal cortex.
- Anosmia may be associated with neurodegenerative diseases, including Parkinson disease and Alzheimer disease, as well as trauma, aging, and other factors.
- Decreased olfaction is also associated with hypogeusia (decreased taste).

Taste

- There are five basic types of taste: sweet, salty, bitter, sour, and umami. Umami was recently added, and has been described as savory (pleasant and sweet, but different from the standard sweet taste).
- 10,000 taste buds are organized into papillae on the tongue, pharynx, epiglottis, and palate.
- The anterior two-thirds of the tongue transmits taste information via the chorda tympani branch of the facial nerve (cranial nerve 7). The posterior tongue transmits taste information via the glossopharyngeal nerve (cranial nerve 9). The vagus nerve (cranial nerve 10) carries taste information from other areas to the brainstem.
- The taste fibers mentioned above unite at the nucleus of the tractus solitaries in the medulla and ascend in the ipsilateral medial lemniscus to the ventroposteromedial nucleus of the thalamus, then to the insula and frontal operculum in the brain.
- Second messenger systems for transmitting taste information is via several mechanisms, including ion channels and G-proteins.

Autonomic Nervous System

The autonomic nervous system (ANS) is the part of the peripheral nervous system responsible for homeostasis. Innervation to all organs is supplied by the ANS, except for skeletal muscle, which is innervated by the somatomotor nervous system. The ANS has two divisions—the *sympathetic* (thoracolumbar division) and the *parasympathetic* (craniosacral division) nervous systems. In addition, the ANS includes the enteric nervous system within the gastrointestinal tract.

Table 19 summarizes the responses of some effector organs to autonomic nerve activity, as well as the types of autonomic receptors mediating the responses.

TABLE 19. EFFECTOR ORGAN RESPONSES TO AUTONOMIC NERVOUS SYSTEM ACTIVITY

Effector Organs	Parasympathetic Nervous System	Sympathetic Nervous System	
		Receptor	Response
Eyes			
Radial muscle of iris	—	α_1	Contraction (mydriasis)
Sphincter muscle of iris	Contraction (miosis)		—
Ciliary muscle	Contraction for near vision		—
Heart			
SA node	↓ Heart rate	β_1	↑Heart rate
Atria and ventricle	↓Atrial contractility	β_1, β_2	↑Contractility
AV node and Purkinje	↓ Conduction velocity	β_1	↑Conduction velocity
Arterioles			
Skin, splanchnic vessels	—	α_1	Constriction
Skeletal muscle	—	α_1/β_2, M	Constriction/ Dilation
Systemic veins	—	α_1, α_2/β_2	Constriction/ Dilation
Bronchial smooth muscle	Contraction	β_2	Relaxation

Stomach and intestine			
Motility and tone	Increased	α_1, α_2, β_2	Decreased
Sphincters	Relaxation	α_1	Contraction
Secretion	Stimulation	—	
Gall bladder	Contraction	β_2	Relaxation
Adipose tissue	—	β_3	Lipolysis
Urinary bladder			
Detrusor	Contraction	β_2	Relaxation
Sphincter	Relaxation	α_1	Contraction
Uterus (pregnant)	—	α_1/β_2	Contraction/ Relaxation
Male sex organs	Erection	α_1	Ejaculation
Skin			
Pilomotor muscles	—	α_1	Contraction
Sweat glands	—	M	Secretion
Liver	—	α_1, β_2	Glycogenolysis
Pancreas			
Acini	Increased secretion	α	Decreased secretion
Islet cells	—	α/β_2	Decreased/ Increased secretion
Salivary glands	Profuse, watery secretion	α_1/β	Thick, viscous secretion/ Amylase secretion
Lacrimal glands	Secretion		—

↓ = decreased; ↑ = increased.
A dash means the target tissue is not innervated by this division of the autonomic nervous system.
(Reproduced, with permission, from Barrett et al. *Ganong's Review of Medical Physiology.* 24th ed. New York, NY: McGraw-Hill; 2012:260.)

MUSCULOSKELETAL PHYSIOLOGY

(*References: Barrett et al., pp 97-117. Widmaier et al., pp 250-291.*)

Three types of skeletal muscle fibers have been identified based upon their maximal shortening velocities and the predominant pathway used to form ATP, as summarized in Table 20.

TABLE 20. SKELETAL MUSCLE FIBER TYPES

	Slow-Oxidative Fibers (Type I)	Fast-Oxidative-Glycolytic Fibers (Type IIa)	Fast-Glycolytic Fibers (Type IIb)[a]
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

[a]Type IIb fibers are sometimes designated as type IIx in the human muscle physiology literature.
(Reproduced, with permission, from Widmaier EP, Raff H, Strang KT. *Vander's Human Physiology: The Mechanisms of Body Function*. 11th ed. New York, NY: McGraw-Hill; 2008:276.)

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 which, in turn, phosphorylates the 20,000-Da myosin light chains. 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) muscle is provided in Table 21.

TABLE 21. COMPARISON OF SKELETAL, SMOOTH, AND CARDIAC MUSCLE

Characteristic	Skeletal Muscle	Single-Unit Smooth Muscle	Multiunit Smooth Muscle	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[a]	++++	+	+	++
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	In some 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

[a]Number of plus signs (+) indicates the relative amount of sarcoplasmic reticulum present in a given muscle type.
(Reproduced, with permission, from Widmaier EP, Raff H, Strang KT. *Vander's Human Physiology: The Mechanisms of Body Function*. 11th ed. New York, NY:McGraw-Hill; 2008:292.)

RESPIRATORY PHYSIOLOGY

(*References: Barrett et al., pp 647-697. Levitzky, pp 1-264. Kaufman et al., pp 272-301. Widmaier et al., pp 434-474.*)

Partial Pressures

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

Room air contains 21% O_2 and 0.04% CO_2; the major constituent of the atmosphere is N_2 (~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 mm Hg, 0% H_2O vapor), the partial pressure of a gas (P_{gas}) is calculated as the product of the total pressure of the gas (ie, atmospheric pressure) and the fractional concentration of the gas (F_{Igas}), that is, the percent concentration expressed as a decimal.

$$P_{gas} = (P_{total})(F_{Igas}) = (P_{total})(\%gas/100)$$

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 (body temperature and pressure, saturated [BTPS], 98.6°F [37°C], 760 mm Hg, 100% H_2O vapor), that is, in tracheal (conducting airways), alveolar, and exhaled air and in arterial and venous blood, the H_2O vapor tension (PH_2O at 98.6°F [37°C] is 47 mm Hg) must be subtracted from the total pressure of 760 mm Hg before multiplying by the fractional concentration of a gas, as follows:

$$P_{gas} = (P_{total} - PH_2O)(F_{Igas}) = (P_{total} - 47\ mm\ Hg)(\%gas/100)$$

A summary of the partial pressures of the respiratory gases at sea level is presented in Table 22.

TABLE 22. PARTIAL PRESSURE OF RESPIRATORY GASES AT SEA LEVEL

(Barometric Pressure = 760 mm Hg)

Gases	Dry Inspired Air (Atmospheric)	Humidified Inspired Air (Dead Space)	Alveolar Air	Mixed Expired Air	Arterial Blood	Mixed Venous Blood
P_{O_2}	159 (20.93)	149 (20.93)	104 (14.6)	120 (16.8)	100	40
P_{CO_2}	0.3 (0.04)	0.3 (0.04)	40 (5.6)	27 (3.8)	40	46
P_{N_2}	600 (79)	563 (79)	569 (79.8)	566 (79.4)	573	573
PH_2O	0.0	47	47	47	47	47
Total	760	760	760	760	760	706

Note I: The partial pressures are given in mm Hg followed in parenthesis by the percentage concentration.
Note II: H_2O vapor is not expressed as a percentage of the total because the PH_2O is temperature dependent, not concentration dependent. The PH_2O at 98.6°F (37°C) is 47 mm Hg. This value must be subtracted from the total pressure of 760 mm Hg before multiplying by the fractional concentration of a gas when determining partial pressures of the gases anywhere in the body (BTPS), that is, in the humidified inspired air in the conducting airways (anatomic dead space), alveolar air, and exhaled air. 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.

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:

$$P_{AO_2} = P_IO_2 - (Pa_{CO_2}/R),$$

where R is the respiratory gas exchange ratio $(\dot{V}CO_2/\dot{V}O_2)$. Under normal circumstances, its value depends on metabolism and is equal to 0.8.

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:

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

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 dead space*.

The *physiological dead space* is the sum of the anatomical and alveolar dead spaces. The ratio of the physiological dead space 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_ECO_2) must have come from alveoli that are both ventilated and perfused.

$$V_D/V_T = Pa_{CO_2} - P_ECO_2/Pa_{CO_2}$$

The dead space 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:

$$Pa_{CO_2} = \dot{V}CO_2/\dot{V}_A$$

Thus, at a constant rate of CO_2 production,

Normal alveolar ventilation = normal $Paco_2$ (35–45 mm Hg)

Hyperventilation = decreased $Paco_2$ (<35 mm Hg)

Hypoventilation = increased $Paco_2$ (<45 mm Hg)

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 sub-atmospheric intra-alveolar 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 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. The four primary lung volumes and the four lung capacities (sum of two or more lung volumes) are shown in Figure 10.

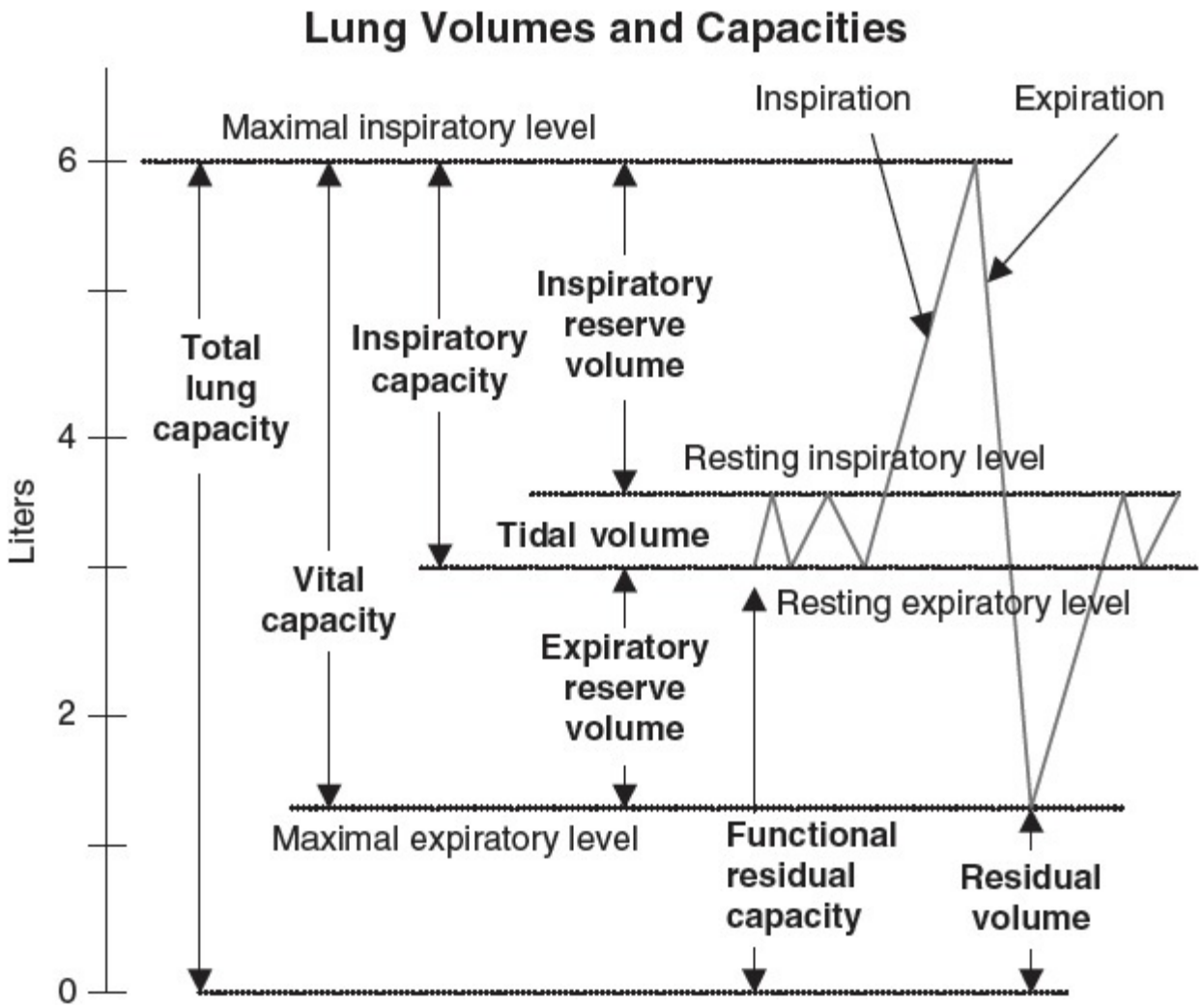


Figure 10

The four primary lung volumes (no overlap) are as follows:

1. *Tidal volume* (V_T): the volume of gas moving in and out of the lungs with each breath.
2. *Inspiratory reserve volume* (IRV): the maximum amount of gas that can be inspired over and above the tidal volume.
3. *Expiratory reserve volume* (ERV): the maximum amount of gas that can be expelled from the lungs after a normal tidal expiration.
4. *Residual volume* (RV): the amount of gas remaining in the lungs at the end of a maximum expiration.

The four lung capacities are as follows:

1. *Inspiratory capacity* (IC = V_T + IRV): the maximum volume of gas that can be inspired from the resting expiratory level.
2. *Functional residual capacity* (FRC = ERV + RV): the volume of gas remaining in the lungs at the end of a quiet (tidal) expiration; the volume of gas present in the lungs at the resting expiratory level.
3. *Total lung capacity* (TLC = V_T + IRV + ERV + RV): the volume of gas present in the lungs after a maximum inspiration, equal to the sum of the four primary lung volumes.
4. *Vital capacity* (VC = V_T + IRV + ERV): the maximum amount of gas that can be exhaled from the lungs after a maximal inspiration.

Note that the RV cannot be measured by spirometry, and thus neither can the capacities that contain the RV, that is, FRC and TLC.

The lungs and chest wall are elastic structures. The lungs tend to recoil inward from the chest wall at all lung volumes, creating a sub-atmospheric intrapleural pressure, which becomes more negative with increases in lung volume. Intrapleural pressure is normally about −5 cm H_2O at FRC, and decreases to about −30 cm H_2O 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 departitioning 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. Restrictive diseases are characterized by a decrease in all of the lung volumes and capacities.

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:

$$R_{aw} = \frac{\Delta P}{\dot{V}} = \frac{P_{atm} - P_{alv},\ \text{cm } H_2O}{\text{Flow rate, L/sec}}$$

R_{aw} can also be defined by Poiseuille law:

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

where l is the length, η is the viscosity, and r is the 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 decrease expiratory flow rates (peak flow, forced vital capacity [FVC], forced expiratory volume in 1 second [FEV_1], and FEV_1/FVC) and (2) to increase RV, FRC, and TLC.

The differences in pulmonary function findings in obstructive versus restrictive pulmonary impairment are summarized in Table 23.

TABLE 23. SUMMARY OF PF FINDINGS IN OBSTRUCTIVE VERSUS RESTRICTIVE IMPAIRMENT

PF Measurement	Obstructive Impairment	Restrictive Impairment
Residual volume, functional residual capacity	↑	↓
Total lung capacity	↑	↓
Inspiratory reserve volume, inspiratory capacity	N or ↓	↓
Forced vital capacity (FVC)	↓	↓
Forced expiratory volume in 1 second (FEV_1)	↓	↓
FEV_1/FVC	↓	N or ↑
Airway resistance	↑	N
Lung compliance	↑ (emphysema)	↓

N, normal; ↓, decreased; ↑, increased.

In restrictive diseases, FEV_1 and FVC are decreased because of the decrease in compliance and lower lung volumes, but the ratio of FEV_1/FVC is normal because airway resistance is normal.

Obstructive and restrictive diseases also cause characteristic changes in the configuration of the maximal expiratory flow–volume curves of the lung as shown in Figure 11.

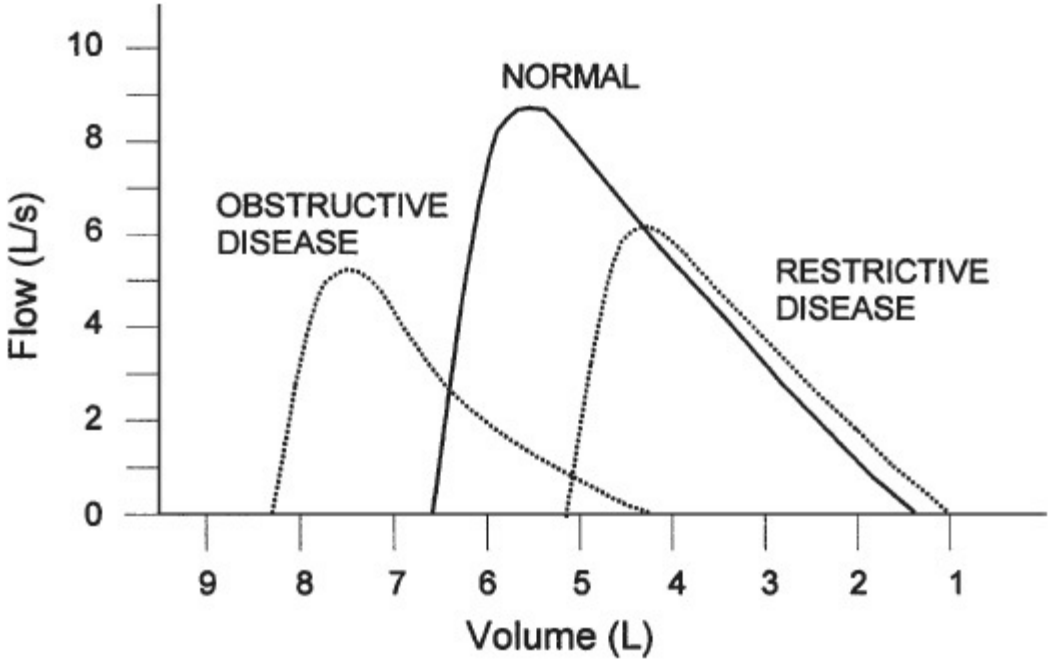


Figure 11

Maximal expiratory flow–volume curves representative of obstructive and restrictive pulmonary diseases. (Reproduced, with permission, from Levitzky MG. *Pulmonary Physiology*. 7th ed. New York, NY: McGraw-Hill; 2007:46.)

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 Table 24. There are also four different categories of hypoxemia.

TABLE 24. TYPES OF HYPOXIA

Classification	P_AO_2	PaO_2	A-a P_{O_2}	CaO_2	PvO_2	CvO_2	Normal PaO_2 with increased FIO_2?
Hypoxic hypoxia (hypoxemia)							
Low alveolar P_{O_2}	Low	Low	N	Low	Low	Low	Yes
Diffusion impairment	N	Low	High	Low	Low	Low	Yes
Right-to-left shunts	N	Low	High	Low	Low	Low	No
$\dot{V}/\dot{Q}$ mismatch	N	Low	High	Low	Low	Low	Yes
Anemic hypoxia							
Anemia	N	N	N	Low	Low	Low	
CO poisoning	N	N	N	Low	Low	Low	
Hypoperfusion hypoxia	N	N	N	N	Low	Low	
Histotoxic hypoxia	N	N	N	N	High	High	

N, normal.
(Reproduced, with permission, from Levitzky MG. *Pulmonary Physiology.* 7th ed. New York, NY: McGraw-Hill; 2007:181.)

CARDIOVASCULAR PHYSIOLOGY

(*References: Barrett et al., pp 110-114, 519-617. Kaufman et al., pp 31-59. Le et al., pp 253-265. Widmaier et al., pp 353-433.*)

Electrical Activity of the Heart

Action Potential

A schematic of the action potential of a cardiac muscle fiber is shown in Figure 12.

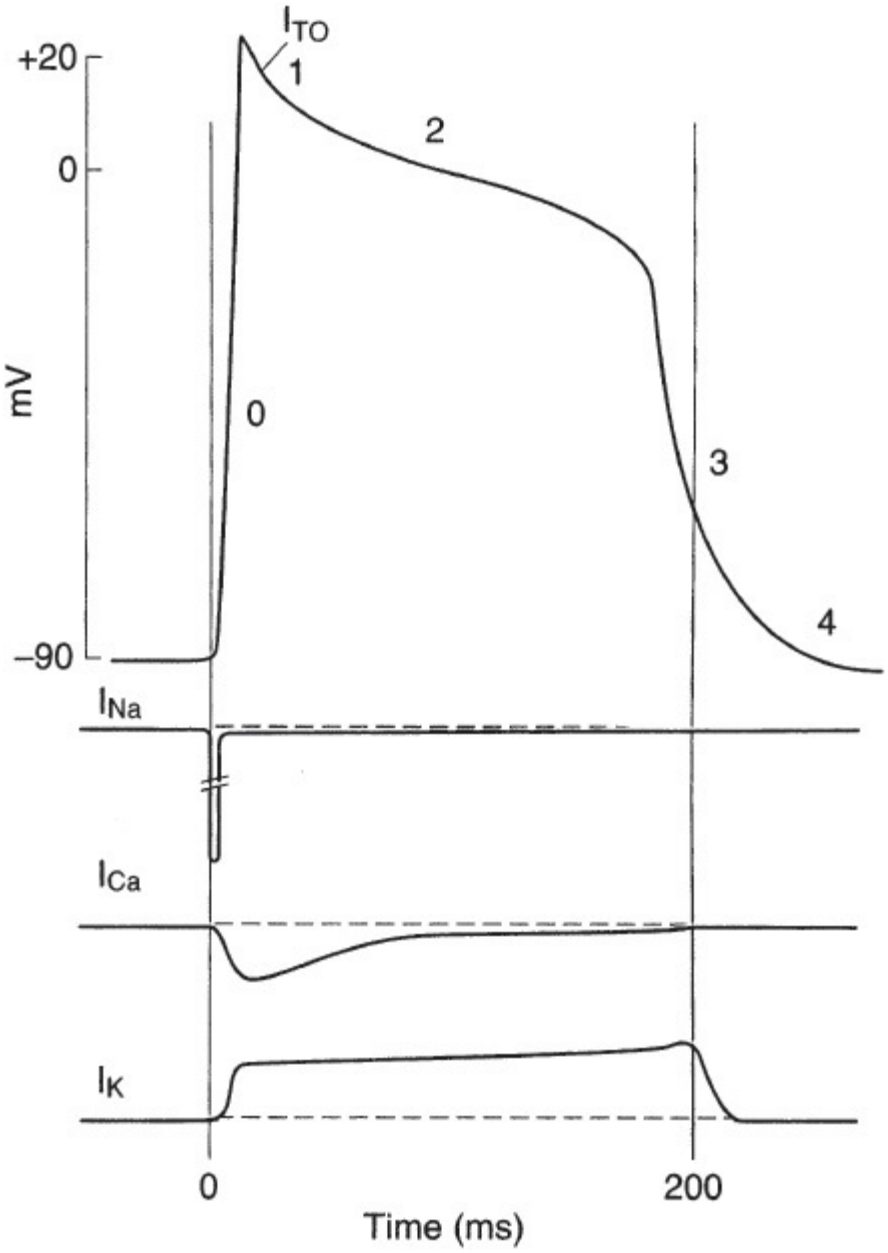


Figure 12

Top: Action potential of a cardiac muscle fiber. 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 Ganong, WF. *Review of Medical Physiology*, 22nd ed. New York: McGraw-Hill; 2005:80.)

Phase 0: The initial rapid depolarization and overshoot are produced by the activation of Na^+ channels.

Phase 1: The initial repolarization is produced by inactivation of Na^+ channels.

Phase 2: The plateau is caused primarily by the activation of Ca^{2+} channels.

Phase 3: The down stroke or final repolarization is caused by closure (inactivation) of the Ca^{2+} channels and K^+ efflux through various types of K^+ channels.

Phase 4: Resting membrane potential.

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. During phases 0 to 2 and a portion of phase 3, cardiac muscle cannot be excited again and, thus, is in the absolute refractory period. It remains in the relative refractory period until phase 4 (Figure 13). As such, tetanus does not occur like that seen in skeletal muscle.

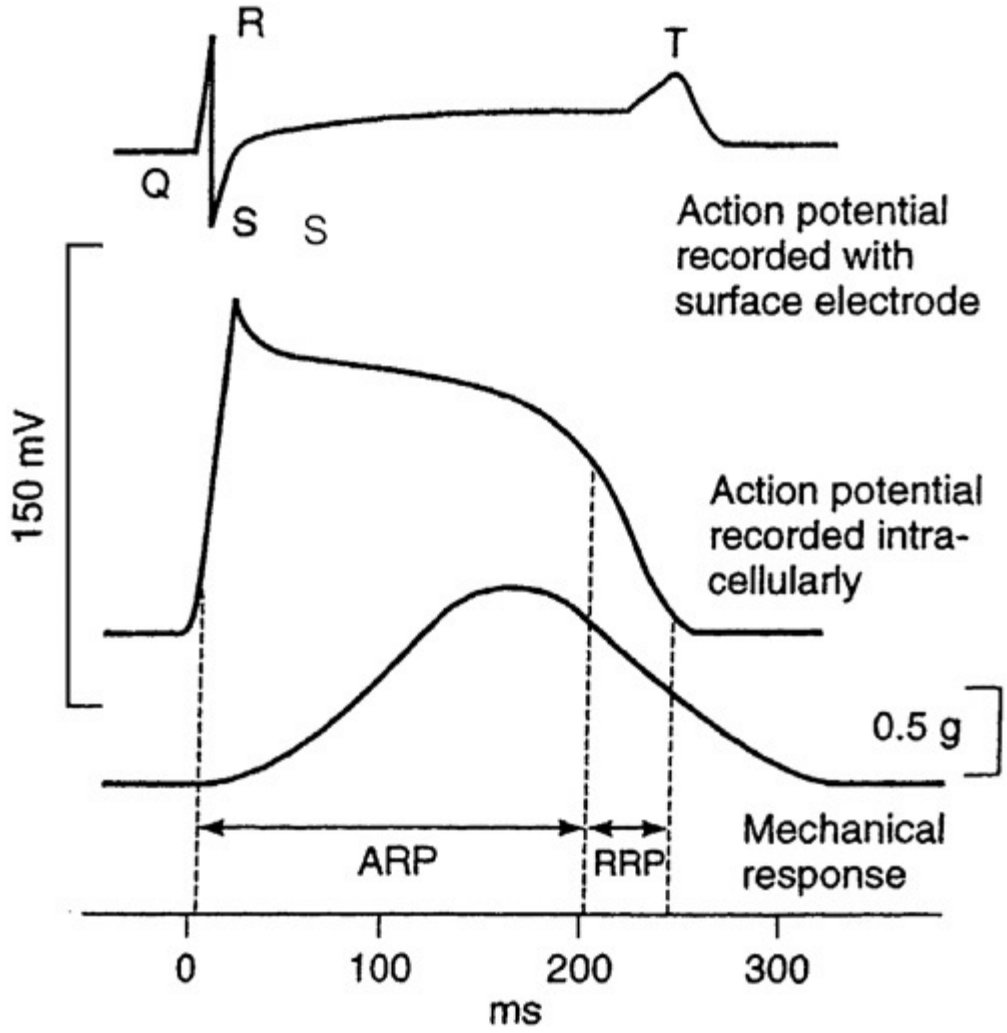


Figure 13

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.)

Electrocardiogram

Recording extracellularly, the electrocardiogram (ECG) represents the summed electrical activity of all of the cardiac muscle cells, as shown in Figure 14.

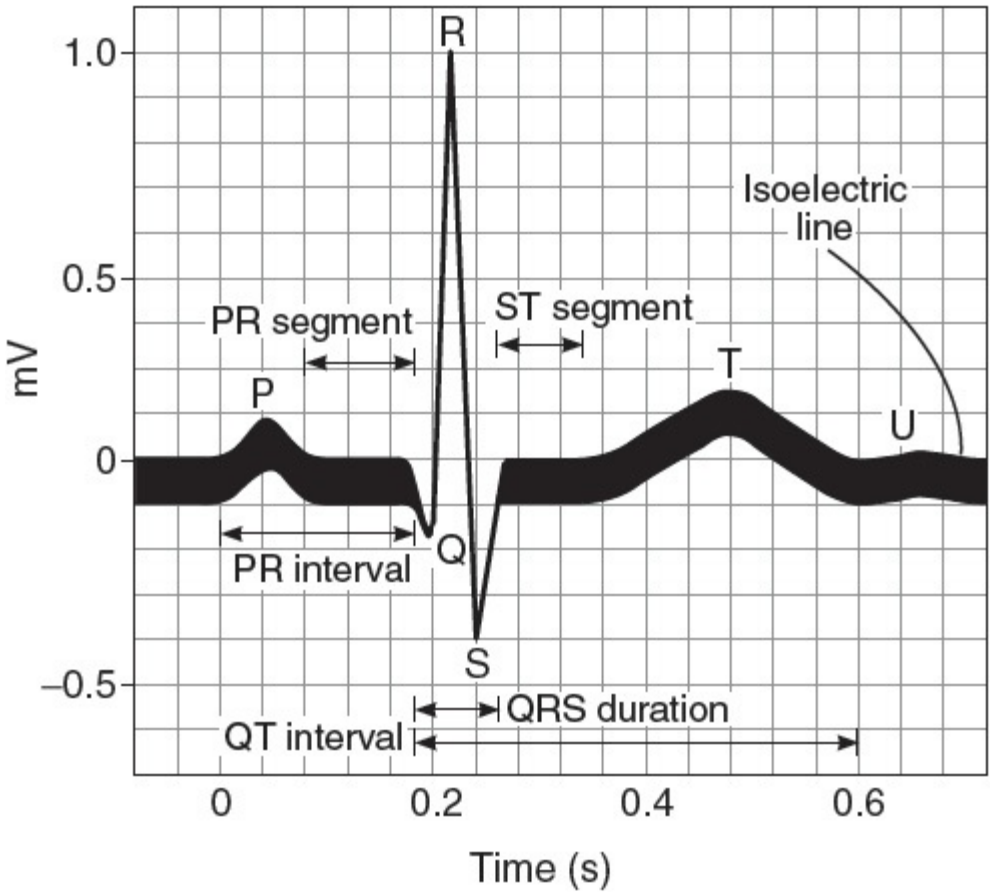


Figure 14

The ECG waves and intervals. (Reproduced, with permission, from Barrett et al. *Ganong's Review of Medical Physiology*. 24th ed. New York, NY: McGraw-Hill; 2012:526.)

The components and normal duration of the ECG are as follows:

- The P wave is produced by atrial depolarization, and normally lasts <0.10 seconds. (Lack of P waves suggests a disorganized atrial rhythm, a junctional rhythm, or a ventricular rhythm.)
- The QRS complex is produced by ventricular depolarization, and has a normal duration of <0.12 seconds. Normal sinus rhythm is usually a regular narrow-complex rhythm with each QRS complex preceded by a P wave.
- The ST segment is the time from the end of ventricular depolarization to the start of ventricular repolarization.
- The T wave corresponds to ventricular repolarization.
- The PR interval is the time for atrial depolarization and conduction through the atrioventricular (AV) node. The normal PR interval is 0.12 to 0.20 seconds.
- The QT interval is the time for atrial depolarization and conduction through the AV node. The normal PR interval is 0.12 to 0.20 seconds.

The mean electrical axis of depolarization (mean QRS vector) can be determined from the standard bipolar and the unipolar limb leads, as seen in Figure 15.

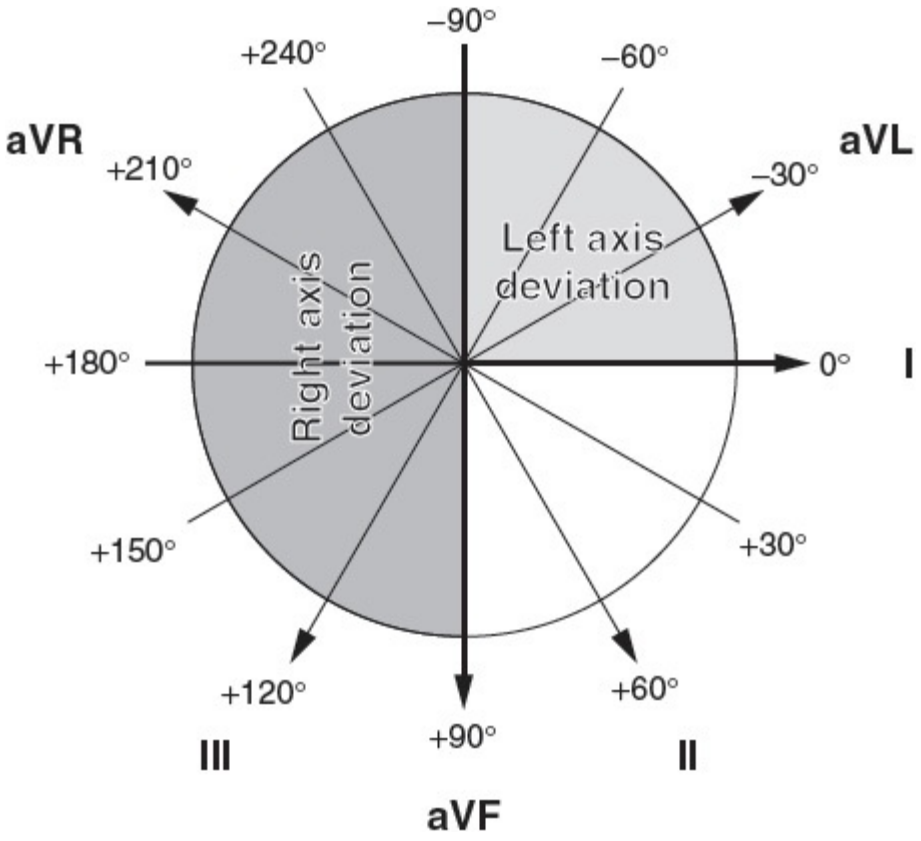


Figure 15

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

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 are shown in Figure 16, and include the following:

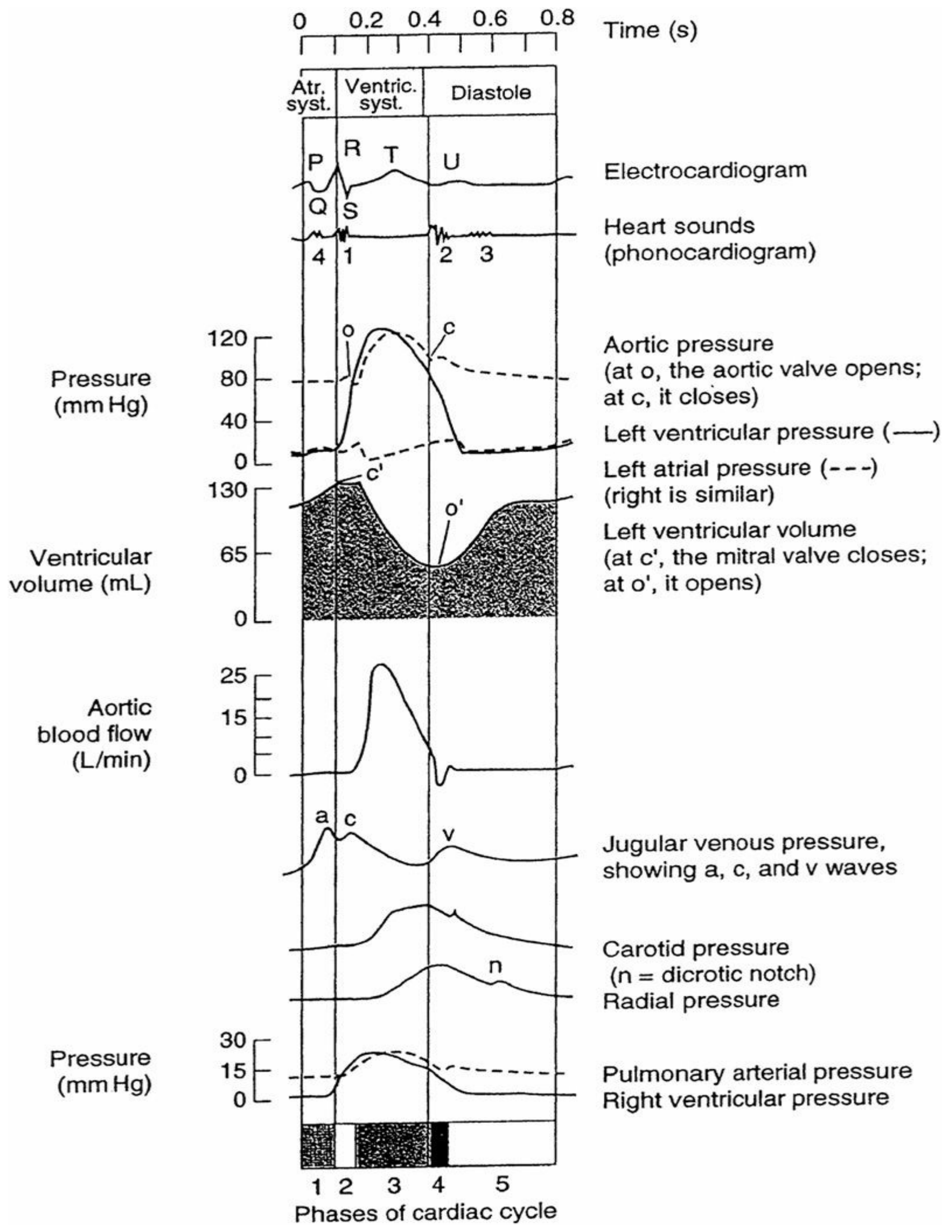

0
0.2
0.4
0.6
0.8
Time (s)
Atr. syst.
Ventric. syst.
Diastole
P
Q
R
S
T
U
Electrocardiogram
Heart sounds (phonocardiogram)
4
1
2
3
Pressure (mm Hg)
120
80
40
0
o
c
Aortic pressure (at o, the aortic valve opens; at c, it closes)
Left ventricular pressure (——)
Left atrial pressure (- - -) (right is similar)
Ventricular volume (mL)
130
65
0
c'
o'
Left ventricular volume (at c', the mitral valve closes; at o', it opens)
Aortic blood flow (L/min)
25
15
0
a
c
v
Jugular venous pressure, showing a, c, and v waves
n
Carotid pressure (n = dicrotic notch)
Radial pressure
Pressure (mm Hg)
30
15
0
Pulmonary arterial pressure
Right ventricular pressure
1 2 3 4 5
Phases of cardiac cycle

Figure 16

Events of the cardiac cycle at a heart rate 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; and 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. Atr. 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.)

- Atrial systole
- Ventricular systole, which comprises isovolumetric contraction, rapid ejection, and reduced ejection
- 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 Figure 17.

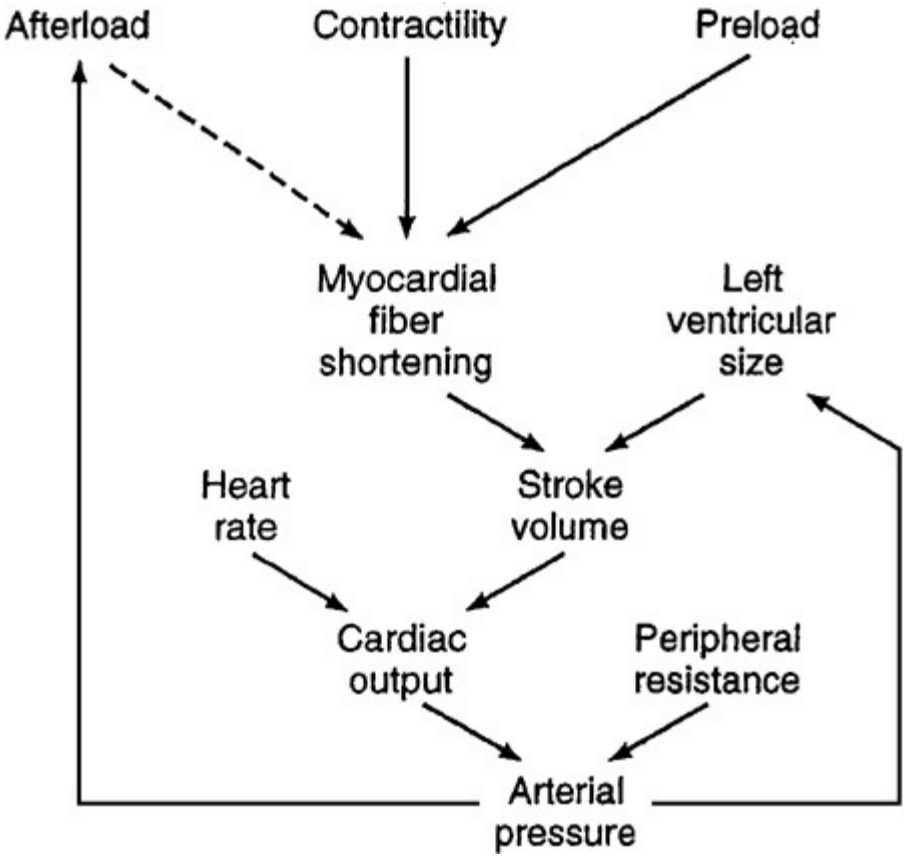


Figure 17

Solid arrows indicate increases and the *dashed arrow* indicates a decrease. (Reproduced, with permission, from Ganong WF. *Review of Medical Physiology*, 22nd ed. New York: McGraw-Hill; 2005:572.)

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 (eg, due to hemorrhage) by reflexly stimulating sympathetic activity to the heart and blood vessels, which increases heart rate, cardiac contractility, total peripheral resistance (TPR), and decreases venous compliance (Figure 18).

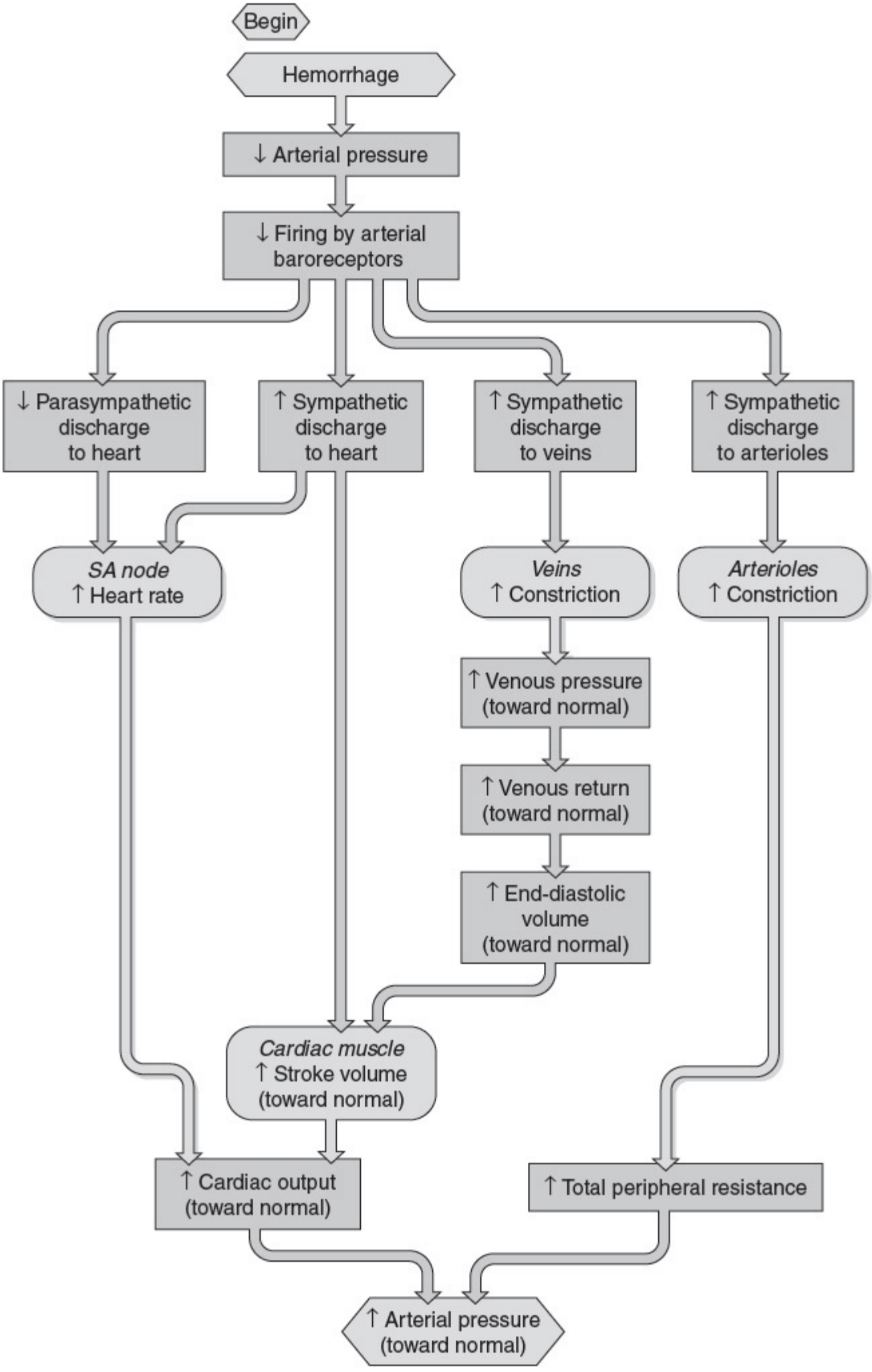

Begin
Hemorrhage
↓ Arterial pressure
↓ Firing by arterial baroreceptors
↓ Parasympathetic discharge to heart
↑ Sympathetic discharge to heart
↑ Sympathetic discharge to veins
↑ Sympathetic discharge to arterioles
SA node
↑ Heart rate
Veins
↑ Constriction
Arterioles
↑ Constriction
↑ Venous pressure (toward normal)
↑ Venous return (toward normal)
↑ End-diastolic volume (toward normal)
Cardiac muscle
↑ Stroke volume (toward normal)
↑ Cardiac output (toward normal)
↑ Total peripheral resistance
↑ Arterial pressure (toward normal)

Figure 18

(Reproduced, with permission, from Widmaier E, Hershel R, Strang K. *Vander's Human Physiology*. 11th ed. New York, NY:McGraw-Hill; 2008:410.)

Stroke volume (and thus cardiac output) is dependent on preload, afterload, and contractility. The relationship between preload (enddiastolic 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 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, as shown in Figure 19.

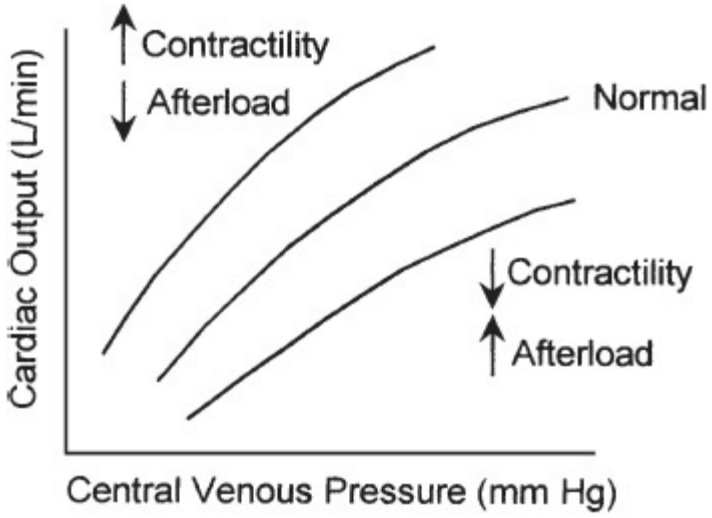


Figure 19

Preload is dependent on blood volume, venous compliance, and 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, as shown in Figure 20.

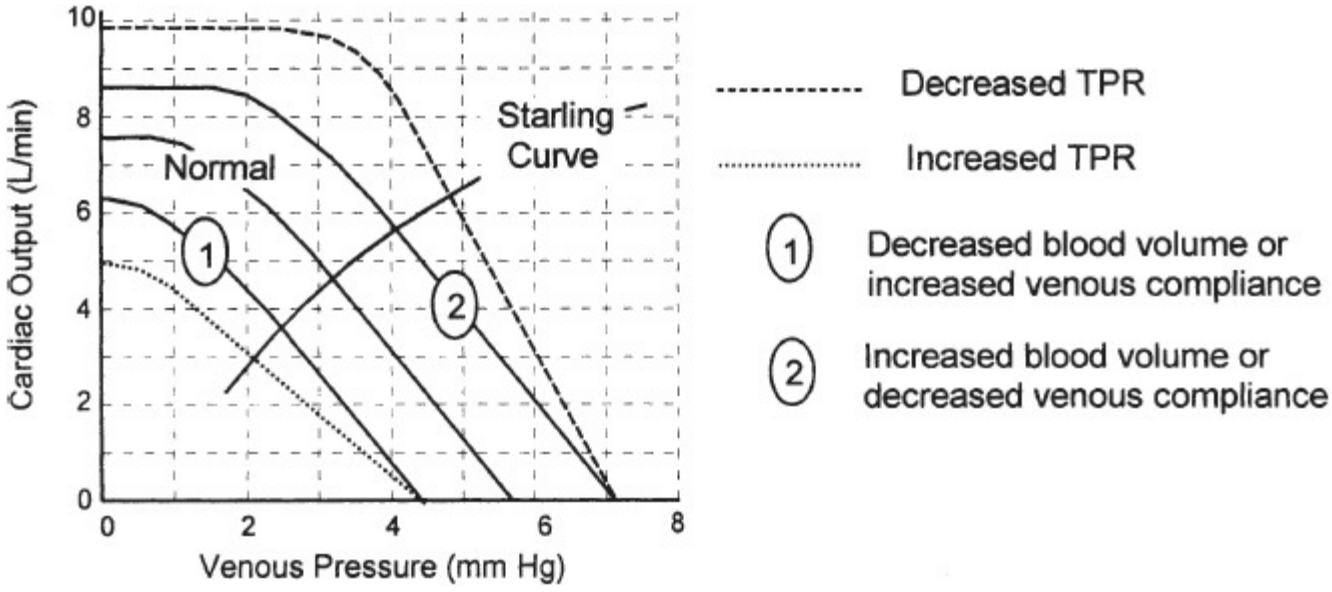


Figure 20

The change in pressure and volume within the heart during one cardiac cycle can be represented by a pressure–volume loop. 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 (Figure 21). If the coronary circulation cannot provide the necessary oxygen, ischemic pain (angina) results.

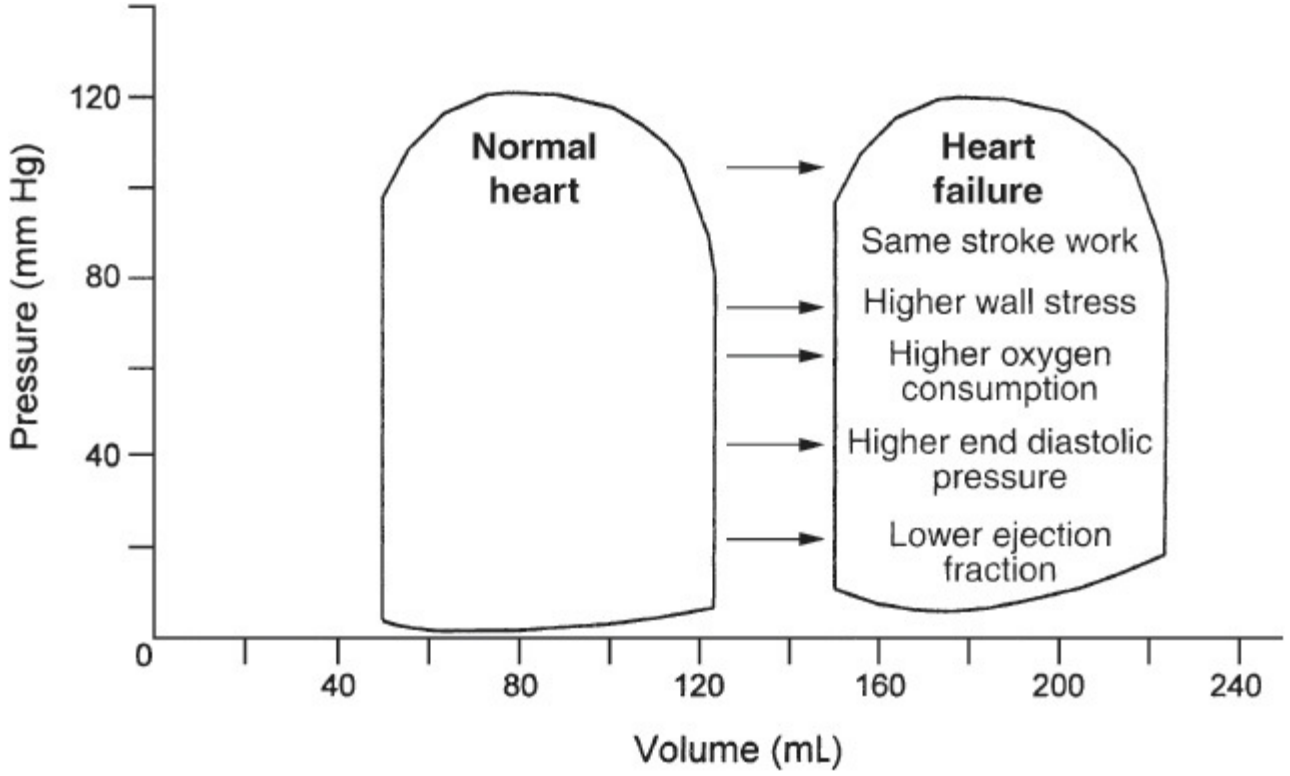


Figure 21

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, more than 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 Reynolds 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.

Examples of cardiac murmurs are as follows:

Systolic murmurs:
1. Aortic stenosis
2. Pulmonic stenosis
3. Mitral regurgitation
4. Tricuspid regurgitation
5. Ventricular septal defect

Diastolic murmurs:
1. Aortic regurgitation
2. Pulmonic regurgitation
3. Mitral stenosis
4. Tricuspid stenosis

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 the Starling law of capillary fluid balance:

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

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
- A decrease in plasma proteins, as during malnutrition, which decreases π_{cap}

• An increase in capillary hydrostatic pressure (P_{cap}), as in heart failure
• 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.

Regional Circulations

The characteristics of the regional circulations are summarized in Table 25.

TABLE 25. CHARACTERISTICS OF THE REGIONAL CIRCULATIONS

Organ	Cardiac Output (%)	Unique Characteristics	Primary Factors Regulating Blood Flow	Auto-regulation
Heart	5%	Largest arteriovenous O_2 difference. O_2 extraction is ~80% at rest, so ↑ O_2 demand must be met by ↑ coronary blood flow; large capillary density facilitates O_2 diffusion into myocardial cells	Local metabolites—O_2, adenosine, NO; Physical—most coronary flow during diastole due to systolic compression	Yes, important
Brain	15%	Organ that is least tolerant to ischemia and hypoxia; redundancy of arterial supply and venous drainage; blood–brain barrier	Local—CO_2 (1°), H^+, O_2; Physical—↑ intracranial pressure (Cushing reflex)	Yes, important but abolished by ↑ CO_2
Kidneys	20–25%	Highest blood flow per gram of tissue; lowest O_2 extraction (ie, arteriovenous O_2 difference); two sets of arteriolar vessels and two capillary beds arranged in series; only organ in which a large volume of fluid passes out of the blood vessels into the interstitial space (170 vs. 20 L/day in other areas)	Myogenic autoregulation and tubuloglomerular feedback; reflex activation/inhibition of sympathetic vasoconstrictor fibers on large arteries and afferent arterioles	Yes—major regulatory mechanism
Liver	25–30%	Dual blood supply via portal vein (~70%) and hepatic artery (~30%); organ with greatest share of systemic cardiac output	Sympathetic vasoconstrictor nerves (direct and reflex activation/inhibition)	Yes, can be demonstrated

Skin	5–10%; 10 × less if cold, ≥ 10 × more in heat ranging from 1 to 150 mL/ 100 g/min	Two types of resistance vessels: arterioles and AV anastomoses in fingertips, palms, toes, soles of feet, earlobes, nose, and lips; dense subdermal capillary and venous plexus is a blood reservoir	Sympathetic vasoconstrictor nerves—basal tone and reflex activation/inhibition by thermoreceptors, baroreceptors	Yes, in cutaneous arterioles but not AV anastomoses
Skeletal muscle	15–20% at rest; up to 80% during exercise	Large range of blood flow due to great mass and variation in metabolic rate; white muscle has lower basal and lower maximal flow rates than red muscle; blood volume is low at rest	Neural control predominates at rest; local metabolic vasodilation predominates during exercise—lactate, adenosine, K^+; physical—contraction compression	Yes, can be demonstrated; may be more avid during exercise
Lungs	100%	Hypoxia causes vasoconstriction so that only well-ventilated areas are perfused. In other organs, hypoxia causes vasodilation	Passive factors (eg, gravity, lung volume); hypoxia causes active vasoconstriction	No

GASTROINTESTINAL PHYSIOLOGY

(*Barrett et al., pp 453-518. Le at al., pp 319-323. Widmaier et al., pp 516-553.*)

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 including salivary α-amylase. Swallowing is coordinated by a swallowing center in the brain stem. 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 allow the food to enter the esophagus. During the esophageal phase, the lower esophageal sphincter 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 and a half hour. Solids cannot pass through the pyloric sphincter until they are broken into small pieces (<1 mm^3), and, therefore, emptying of solids takes from 1 to 3 hours.

Gastric emptying is slowed by the enterogastric reflex and the release of inhibitory hormones. The reflex and the secretion of hormones 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.

Carbohydrates, proteins, and fats are digested by several enzymes. Carbohydrate digestion is completed in the small intestine by pancreatic amylase and by oligosaccharides such as maltase, lactase, sucrase, and trehalase, which are located in the brush border of the small intestine. Proteins are broken down in the small intestine by enzymes from the pancreas (trypsin, chymotrypsin, elastase, and carboxypeptidase) and from aminopeptidase found in the intestinal brush border. Fat digestion occurs via pancreatic lipase and colipase.

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 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 sodium absorption. The source of water is both exogenous (oral input) and endogenous (gastrointestinal 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 jejunum and ileum, with less amounts of absorption occurring in the colon.

Some of the key functions of the stomach, small intestine, and colon are summarized below:

Stomach:
• Mucus secretion (mucus cells)
• Pepsinogen secretion (chief cells)
• HCl secretion (parietal cells)
• Intrinsic factor secretion (parietal cells)
• Gastrin secretion (G cells in antrum)
• Accommodation (receptive relaxation) and peristalsis

Small intestine:
• Iron absorption (duodenum)
• Folate absorption (duodenum)
• Bile acid absorption (ileum)
• Vitamin B_{12} absorption (ileum)
• Water reabsorption
• Carbohydrate, protein, fat absorption
• Segmentation (digestive period) and migrating motor complex (interdigestive period)

Colon:
• Absorption of sodium and water
• Net secretion of potassium and bicarbonate
• Vitamin synthesis from colonic bacteria
• Segmentation and mass action contraction

RENAL AND URINARY PHYSIOLOGY

(*Barrett et al., pp 671-696. Widmaier et al., pp 475-515.*)

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. As depicted in Figure 22, the three basic components of renal function are:

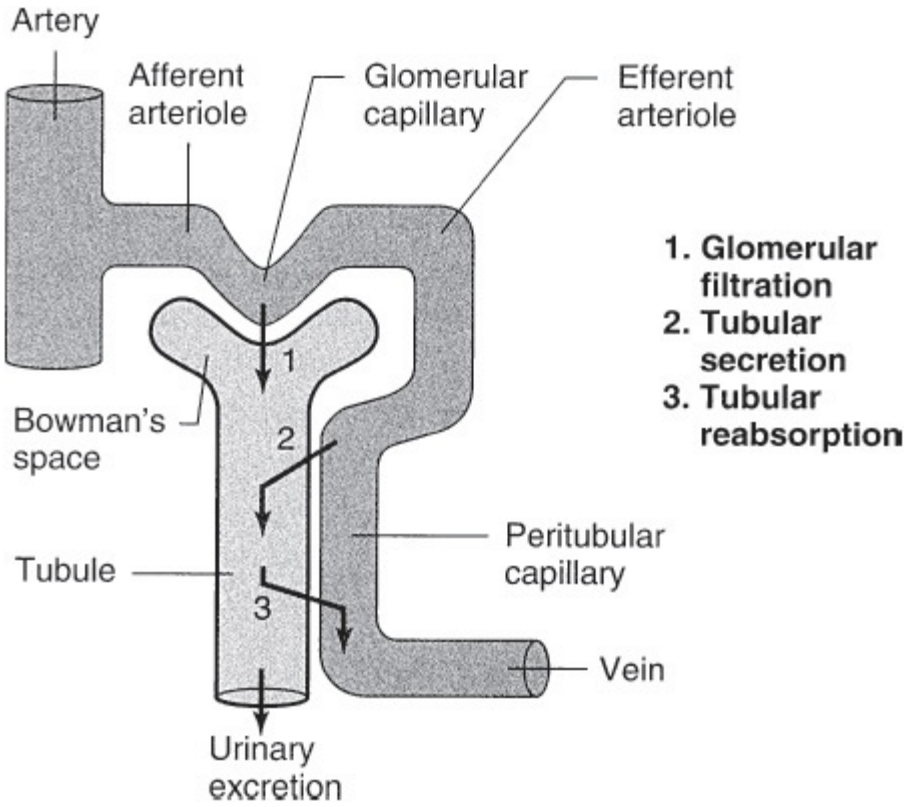


Figure 22

Basic components of renal function. (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.)

• Glomerular filtration
• Tubular reabsorption
• Tubular secretion

Each day, 160 to 180 L of fluid is filtered into the approximately 1 million nephrons in the human kidney. The glomerular filtration rate (GFR) is dependent on the Starling forces between the glomerular capillaries (cap) and Bowman capsule (BC):

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

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.

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:

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

where U_{conc} is the urinary concentration of material, P_{conc} is the plasma concentration of material, and V is the 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 inulin are 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 RPF. The clearance of the organic anion para-aminohippurate is used clinically to measure RPF:

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

The proximal tubule is responsible for reabsorbing most of the material filtered from the glomerulus, as shown in Table 26.

TABLE 26. PROXIMAL TUBULE REABSORPTION

Material	Reabsorbed (%)	Mechanism
Na^+	60–70	Na/H exchange Na-nutrient cotransport diffusion
K^+, urea, Cl^-	60–70	Diffusion and solving drug
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. 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–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:

- Bicarbonate ion reabsorption
- Titratable acid excretion (tubular secretion of H^+, which combines with filtered phosphate)
- Ammonium ion excretion (tubular secretion of H^+, which combines with filtered ammonia)

REPRODUCTIVE PHYSIOLOGY

(*Barrett et al., pp 391-429. Widmaier et al., pp 586-631.*)

Female Reproductive System

The reproductive system of women, unlike that of men, is characterized by regular cyclical changes in hormone secretion, ovarian function, and uterine events called the menstrual cycle.

The key events of the menstrual cycle are summarized in Table 27.

TABLE 27. SUMMARY OF THE MENSTRUAL CYCLE

Day(s)	Major Events
1–5	Estrogen and progesterone are low because the previous corpus luteum is regressing. *Therefore:* (a) Endometrial lining sloughs. (b) Secretion of FSH and LH is released from inhibition, and their plasma concentrations increase. *Therefore:* Several growing follicles are stimulated to mature.
7	A single follicle (usually) becomes dominant.
7–12	Plasma estrogen increases because of secretion by the dominant follicle. *Therefore:* Endometrium is stimulated to proliferate.
7–12	LH and FSH decrease due to estrogen and inhibin negative feedback. *Therefore:* Degeneration (atresia) of nondominant follicles occurs.
12–13	LH surge is induced by increasing plasma estrogen. *Therefore:* (a) Oocyte is induced to complete its first meiotic division and undergo cytoplasmic maturation. (b) Follicle is stimulated to secrete digestive enzymes and prostaglandins.
14	Ovulation is mediated by follicular enzymes and prostaglandins.
15–25	Corpus luteum forms and, under the influence of low but adequate levels of LH, secretes estrogen and progesterone, increasing plasma concentrations of these hormones. *Therefore:* (a) Secretory endometrium develops. (b) Secretion of FSH and LH is inhibited, lowering their plasma concentrations. *Therefore:* No new follicles develop.
25–28	Corpus luteum degenerates (if implantation of the conceptus does not occur). *Therefore:* Plasma estrogen and progesterone concentrations decrease. *Therefore:* Endometrium begins to slough at conclusion of day 28, and a new cycle begins.

(Reproduced, with permission, from Widmaier E, Hershel R, Strang K. *Vander's Human Physiology.* 11th ed. New York, NY: McGraw-Hill; 2008:625.)

Male Reproductive System

- The testes (male gonads) have a dual function: the production of germ cells (spermatogenesis) and the secretion of sex hormones (principally testosterone).
- Spermatogonia develop into mature spermatozoa in the seminiferous tubules via a process called spermatogenesis. This is a multistep process that includes maturation of spermatogonia into primary spermatocytes, which undergo meiotic division, resulting in haploid secondary spermatocytes. Several further divisions result in spermatids. Spermatids eventually mature into motile spermatozoa (sperm) to complete spermatogenesis; this last part of maturation is called spermiogenesis.
- Germ cells lining the seminiferous tubules must stay in contact with Sertoli cells to survive. Sertoli cells are large glycogen-containing cells that stretch from the basal lamina to the lumen of the seminiferous tubule. Tight junctions between Sertoli cells form a blood–testis barrier.
- Testosterone is synthesized from cholesterol in Leydig cells and is under the control of luteinizing hormone. Most testosterone is bound to albumin or to gonadal steroid-binding globulin in the plasma.
- The actions of testosterone include inhibitory feedback on pituitary LH secretion and hypothalamic GnRH secretion; development and maintenance of male secondary sex characteristics; protein-anabolic, growth-promoting effects; and, along with FSH, maintenance of spermatogenesis.
- Another hormone of testicular origin, inhibin B, is produced by the Sertoli cells and acts to inhibit FSH release from the anterior pituitary gland.
- 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. Erections are produced by the release of nitric oxide (NO), which inhibits the smooth muscle of the corpora cavernosa, allowing blood to fill the penis. NO is a potent vasodilator that acts by activating guanylyl cyclase, resulting in increased production of the second messenger, cyclic GMP. Normally, erection is terminated by sympathetic vasoconstriction of the penile arterioles.
- Ejaculation is a spinal reflex consisting of two phases—(1) emission, the movement of semen from the prostate into the urethra in response to sympathetic activation of the hypogastric nerves causing contraction of the smooth muscle of the vas deferens and seminal vesicles, and (2) ejaculation, the propulsion of the

semen out of the urethra by contraction of the bulbocavernosus muscle, a skeletal muscle, at the time of orgasm.

ENDOCRINE PHYSIOLOGY

(*Barrett et al., pp 297-390, 431-45. Kacsoh, pp. Widmaier et al., pp 311-352, 554-631.*)

The endocrine system consists of endocrine glands, as well as hormone-secreting cells located in various organs, that which secrete hormones, that is, "chemical messengers," which are carried by the blood to their site of action (target cells).

The pituitary gland (hypophysis), often referred to as the master gland, controls the secretion of many endocrine hormones, and in turn is mediated by the hypothalamus, as well as feedback control from peripheral hormones. The pituitary is divided into two parts based on its development. The posterior pituitary, or neurohypophysis, is a collection of axons from neurons that originate in the paraventricular and supraoptic nuclei of the hypothalamus. These hypothalamic neurons synthesize:

1. Oxytocin—responsible for milk ejection after childbirth, and uterine contraction during labor
2. Antidiuretic hormone also known as vasopressin increases water permeability of the renal collecting ducts, causing retention of water and increase in blood pressure.

The anterior pituitary, or the adenohypophysis, develops through evagination of Rathke's pouch. The anterior pituitary secretes six major hormones. The synthesis and release of these hormones are controlled by the hypothalamus. Six major hormones are secreted by the anterior pituitary under the control of the hypothalamus. These hypothalamic releasing hormones are secreted into the superior hypophyseal arteries, which form the primary capillary plexus in the median eminence. From the median eminence, the releasing hormones travel to the secondary plexus of the adenohypophysis via the long hypophyseal portal veins. At this point, the releasing hormones diffuse to the anterior pituitary cells to regulate release of pituitary hormones in conjunction with peripheral hormone feedback.

Table 28 summarizes a number of other endocrine glands, the hormones produced by each, and the major function of each hormone.

TABLE 28. SOME ENDOCRINE GLANDS AND HORMONES

Site Produced	Hormone	Major Function/ Control of
Adrenal gland		
Adrenal cortex	Glucocorticoids (cortisol; corticosterone)	Glucose metabolism; body's response to stress; regulation of immune system; development
	Aldosterone	Na^+ and K^+ excretion by kidneys; extracellular water balance
	Androgens (dehydroepiandrosterone; androstenedione)	Adrenarche; sex drive in women
Adrenal medulla	Catecholamines (epinephrine; norepinephrine)	Organic metabolism; cardiovascular function; response to stress ("fight-or-flight")
Thyroid gland	Thyroxine (T_4) and triiodothyronine (T_3)	Metabolic rate; stimulate activity of Na^+/K^+-ATPases throughout the body (calorigenic action); growth; brain development and function; permissive effects on catecholamines
Pancreas		
β-Cells of the islets of Langerhans	Insulin	Increases cellular entry, promotes storage, and inhibits synthesis and mobilization of glucose, amino acids, and fatty acids
α-Cells of the islets of Langerhans	Glucagon	Increases plasma glucose

(Modified, with permission, from Widmaier et al. *Vander's Human Physiology: The Mechanism of Body Function*. 11th ed. New York, NY: McGraw-Hill; 2011:314–315.)

One of the major functions of the endocrine system is to control growth. Growth is a complex process influenced not only by endocrine function but also by bone growth, genetics, and a variety of environmental factors, including nutrition. At least a dozen hormones directly or indirectly influence growth. The major hormones influencing growth and their principal actions are summarized in Table 29.

TABLE 29. MAJOR HORMONES INFLUENCING GROWTH

Hormone	Principal Action
Growth hormone (GH)	Major stimulus of postnatal growth: • Induces precursor cells to differentiate and secrete insulin-like growth factor 1 (IGF-1), which stimulates cell division • Stimulates liver to secrete IGF-1 • Stimulates protein synthesis
Insulin	• Stimulates fetal growth • Stimulates postnatal growth by stimulating secretion of IGF-1 • Stimulates protein synthesis
Thyroid hormones	• Permissive for GH's secretion and actions • Permissive for CNS development
Testosterone	• Stimulates growth at puberty by stimulating GH secretion • Causes eventual epiphyseal closure • Stimulates protein synthesis in males
Estrogen	• Stimulates GH secretion at puberty • Causes eventual epiphyseal closure
Cortisol	• Inhibits growth • Stimulates protein catabolism

(Reproduced, with permission, from Widmaier E, Hershel R, Strang K. *Vander's Human Physiology*. 12th ed. New York, NY: McGraw-Hill; 2011:344.)

Figure 23 presents a summary of overall target cell responses to (a) an increase in the plasma concentration of insulin, such as occurs in the absorptive state, and (b) a decrease in the plasma concentration of insulin, such as occurs in the postabsorptive state. Glucagon's effects oppose those of insulin.

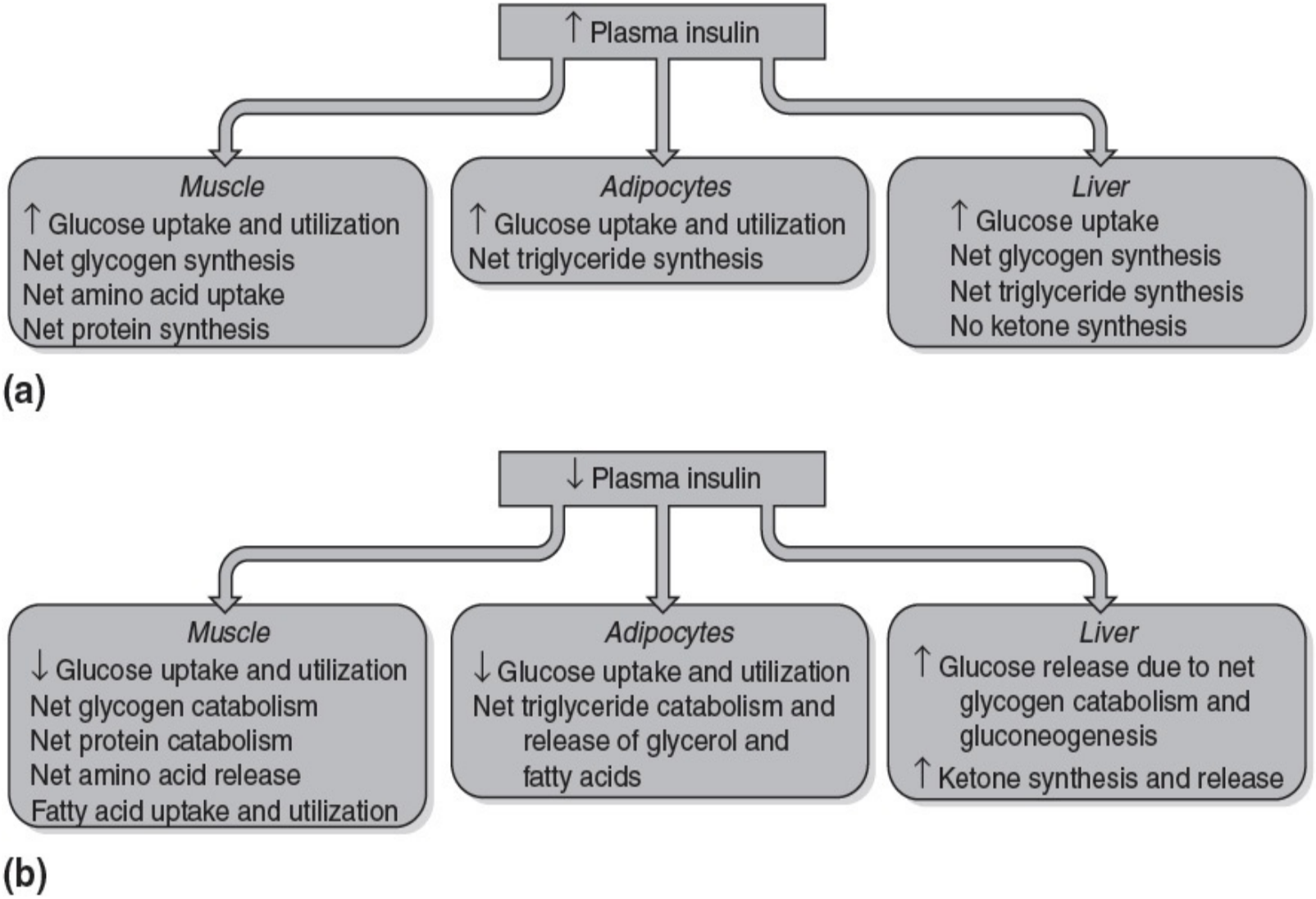


Figure 23

Effects of insulin on organic metabolism. (Reproduced, with permission, from Widmaier E, Hershel R, Strang K. *Vander's Human Physiology*. 11th ed. New York, NY: McGraw-Hill; 2008:572.)

Calcium and phosphate concentrations in the body are controlled by parathyroid hormone (PTH), calcitonin, and vitamin D concentrations (Table 30). PTH is essential for extracellular calcium homeostasis. Low levels of extracellular calcium, recognized by a G protein–coupled receptor, stimulate immediate PTH release. Vitamin D, however, is more effective in maintaining steady-state calcium levels. Calcitonin has limited physiologic significance in calcium homeostasis, and is typically more important as a tumor marker.

TABLE 30. HORMONES CONTROLLING CALCIUM AND PHOSPHATE CONCENTRATIONS

Hormone	Effect on Calcium	Effect on Phosphate	Location of action
Parathyroid hormone (PTH)	Increase	Decrease	Bone—stimulates osteoclasts to release calcium Kidney—calcium reabsorption and phosphate excretion, and calcitriol formation
Calcitonin	Decrease	Decrease	Bone—inhibits osteoclasts Kidney—increase calcium and phosphate excretion
Vitamin D (calcitriol)	Increase	Increase	Intestine—stimulates Ca^{2+}, phosphate, and Mg^{2+} absorption Bone—stimulates Ca^{2+} and phosphate release with the help of PTH Kidney—decreases Ca^{2+} and phosphate excretion

General Principles: Cellular Physiology

Questions

1. A 61-year-old man with erectile dysfunction asks his physician to prescribe Viagra® (sildenafil citrate; Pfizer Inc., Mission, KS, USA). Sildenafil 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. Cyclic guanosine monophosphate (cGMP)
b. cGMP phosphodiesterase (PDE)
c. Diacylglycerol
d. G protein
e. Guanylate cyclase

2. A 40-year-old male with acute promyelocytic leukemia is started on treatment with all-trans retinoic acid (ATRA). Which of the following characteristics of a hydrophobic hormone that binds to nuclear receptors is most important in governing its diffusibility through a cell membrane?

a. Diameter
b. Electrical charge
c. Lipid solubility
d. Molecular weight
e. Three-dimensional shape

3. An 83-year-old woman with sepsis develops multiorgan failure. Based on her blood urea nitrogen of >100 mg/dL, she is placed on continuous venovenous hemodialysis. Which of the following factors will increase the diffusive clearance of solutes across the semipermeable dialysis membrane?

a. Area of the membrane increases
b. Concentration gradient for the solutes decreases
c. Lipid solubility of the solutes decreases
d. Size of the solute molecules increases
e. Thickness of the membrane increases

4. A 48-year-old woman with advanced breast cancer presents with severe nausea, vomiting, and dehydration. She is not undergoing chemo-therapy currently. Laboratory findings reveal elevated serum-ionized calcium. Parathyroid hormone (PTH) levels are undetectable, but there is an increase in PTH-related peptide (PTHrP). The increased flow of calcium into the cell is an important component of the upstroke phase of the action potential in which of the following?

a. Cardiac ventricular muscle
b. Intestinal smooth muscle
c. Nerve cells
d. Presynaptic nerve terminals
e. Skeletal muscle

5. A 10-year-old boy sprains his ankle while running. History reveals that he has difficulty running, jumping, and keeping up with other children in races. His mother reports that she is also clumsy. Physical examination demonstrates foot drop, weakness, sensory loss, and reduced reflexes. The boy is found to have a decrease in nerve conduction velocity and an X-linked mutation of connexin 32, consistent with Charcot–Marie–Tooth (CMT) disease. The neuropathy and gait disorder result because connexin is an important component of which of the following?

a. Gap junction
b. Microtubule
c. Sarcoplasmic reticulum
d. Sodium channel
e. Synaptic vesicle

6. A 2-day-old infant starts having brief tonic–clonic seizures throughout the day. His neurological function in between seizures is normal, and he has no other medical or neurological problems. The history reveals no readily apparent causes for the seizures, though the mother recalled that her first baby also developed seizures shortly after birth that only lasted for 2 weeks, with no subsequent episodes or developmental problems. Genetic analysis revealed a mutation of voltage-gated K^+ channels consistent with a diagnosis of benign familial neonatal seizures. Which of the following would cause an immediate reduction in the amount of potassium leaking out of a cell?

a. Decreasing the extracellular potassium concentration
b. Decreasing the extracellular sodium concentration
c. Hyperpolarizing the membrane potential
d. Increasing the permeability of the membrane to potassium
e. Reducing the activity of the sodium–potassium pump

7. A 42-year-old woman consults a dermatologist to evaluate and treat the frown lines on her forehead just above the nose. After the treatment options are explained to her, the patient asks the dermatologist to administer botulinum type A (Botox). Botox smooths out glabellar lines by which of the following mechanisms?

a. Blocking the release of synaptic transmitter from α-motoneurons
b. Decreasing the amount of calcium released from the sarcoplasmic reticulum
c. Enhancing the enzymatic hydrolysis of acetylcholine at the neuromuscular junction
d. Increasing the flow of blood into facial muscles
e. Preventing the opening of sodium channels on muscle membranes

8. A 48-year-old executive was referred for a life insurance physical examination for his new corporation. His body mass index was 34, indicating clinical obesity, and his blood pressure was 145/92 mm Hg. Blood tests showed hyperlipidemia and hyperglycemia with normal insulin levels, consistent with type 2 diabetes mellitus (T2DM). T2DM adversely affects many cellular processes. Which of the following transport processes is a passive downhill process?

a. Calcium into the sarcoplasmic reticulum (SR)
b. Glucose into skeletal muscle and fat cells
c. Hydrogen into the lumen of canaliculi of the parietal cells of the stomach
d. Phosphate into epithelial cells lining the proximal tubule of the kidney
e. Sodium out of brain cells

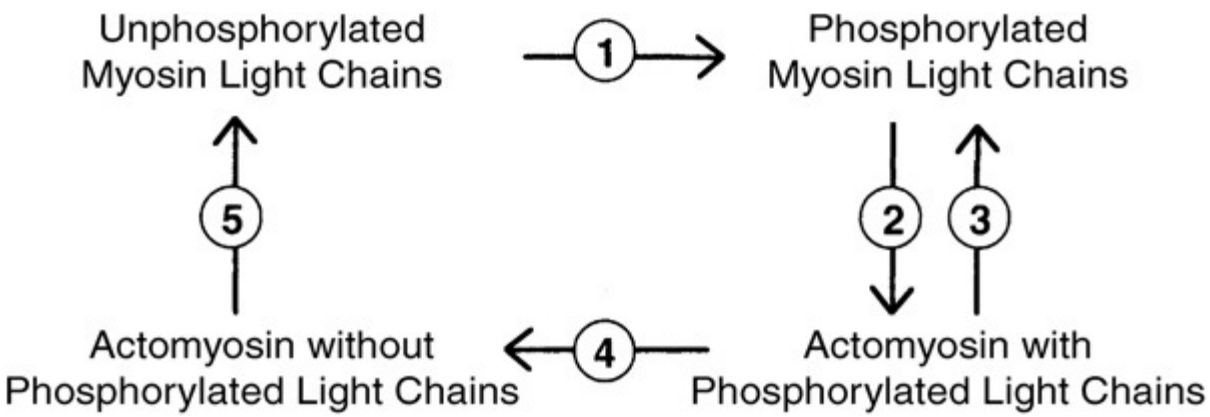
9. A 54-year-old woman undergoes a colonoscopy to screen for colon cancer. Biopsy of a polyp removed during the procedure reveals epithelial cell metaplasia, with some cells progressing toward malignant transformation. A high-fiber diet is prescribed to generate more short-chain fatty acids. The figure below illustrates the concentration of protonated short-chain fatty acids on either side of a colonic epithelial cell membrane. If the concentration of fatty acids on the outside surface of the cell doubles, the rate of diffusion of the short-term fatty acids will change from 10 mg/h to which of the following rates?

a. 5 mg/h
b. 10 mg/h
c. 15 mg/h
d. 20 mg/h
e. 30 mg/h

10. A 43-year-old pregnant woman develops preeclampsia at 32 weeks' gestation. Intravenous labetalol is given to reduce blood pressure, and magnesium sulfate, which blocks *N*-methyl-D-aspartate (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. Acetylcholine
b. Gamma-aminobutyric acid (GABA)
c. Glutamate
d. Glycine
e. Kainate

11. A 56-year-old woman presents with fatigue and malaise. Hepatomegaly and mild jaundice are evident upon physical examination. Blood tests reveal an increase in aspartate aminotransferase and the presence of anti–smooth muscle antibodies, suggestive of autoimmune hepatitis. Which of the steps in the chemical reactions that occur during cross-bridge cycling in smooth muscle shown below is responsible for relaxation of contracted smooth muscle and 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. A 14-year-old adolescent girl reports blood in her urine 2 weeks after she had a sore throat. She has uremia and a blood pressure of 160/90 mm Hg with peripheral edema, suggestive of volume expansion secondary to salt and water retention. 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 woman 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 the quantity of water she would have drunk to produce the observed hyponatremia?

a. 2.5 L
b. 3.5 L
c. 5 L
d. 6 L
e. 7 L

15. A 49-year-old man 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.

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 reports systolic blood pressure near 200 mm Hg earlier in the day and suspects a dissecting aneurysm, which is confirmed with a computed tomography (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. Activation of phospholipase A_2

b. Increased capillary membrane permeability
c. Increased formation of leukotrienes
d. Increased release of interleukin-1 (pyrogen) from granulocytes
e. Inhibition of the activation of nuclear factor-κB (NF-κB)

17. A 62-year-old man presents to the emergency room with an acute onset of aphasia and hemiparesis. A CT scan reveals an increase in intracranial fluid. Which of the following solutions will be most effective in reducing intracranial pressure (ICP) 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

General Principles: Cellular Physiology

Answers

1. The answer is a. (*Barrett, pp 62-63, 116, 151, 422-423, 596-597. Longo, pp 374-378.*) 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. Erections are produced by the release of nitric oxide (NO), which inhibits the smooth muscle of the corpora cavernosa, allowing blood to fill the penis. NO is a potent vasodilator that acts by activating guanylyl cyclase, resulting in increased production of the second messenger, cGMP. Sildenafil citrate (Viagra®) is an effective and selective inhibitor of cGMP PDE. By blocking the breakdown of cGMP, sildenafil prolongs the action of NO and erections. Sildenafil is most active against PDE5, the type of PDE found in the corpora cavernosa. Other cGMP PDE5 inhibitors used in the treatment of erectile dysfunction include tadalafil (Cialis®; Eli Lilly and Company, Indianapolis, IN, USA) and vardenafil (Levitra®; Bayer Pharmaceuticals Corporation, Leverkusen, North Rhine-Westphalia, Germany and GlaxoSmithKline, Brentford, Middlesex, United Kingdom). 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. G proteins are coupling molecules that link various receptors to nearby effector molecules, which, in turn, generate second messengers that mediate the hormone's actions. Inositol triphosphate (IP_3) is associated with the membrane phospholipid system for hormonal signal transduction. G-protein activation of the membrane-bound enzyme phospholipase C breaks down membrane phospholipids into diacylglycerol (DAG) and inositol triphosphate. DAG is a potent activator of protein kinase C.

2. The answer is c. (*Widmaier, pp 97-100.*) 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. Signal transduction pathways differ between water-soluble and lipid-soluble messengers (hormones). Lipid-soluble messengers, including steroid hormones, thyroid hormones, and vitamin derivatives such as retinoids (vitamin A) and vitamin D, interact with intracellular nuclear receptors, in contrast to water-soluble amino acid derivatives and peptide hormones, which interact with cell-surface membrane receptors. In promyelocytic leukemia, fusion of retinoic acid receptor alpha to other nuclear proteins causes aberrant gene silencing and prevents normal cellular differentiation. Treatment with the hormone retinoic acid reverses this repression and allows cellular differentiation and apoptosis to occur.

3. The answer is a. (*Barrett, p 7. Longo, pp 2322-2324. Widmaier, pp 96-100.*) The rate of diffusion is described by the Fick equation, as follows:

$$\text{Net flux} = A \times ([S_1] - [S_2]) \times D/d$$

where A is the area available for diffusion, $[S_1] - [S_2]$ is the concentration gradient of the substance across the membrane, d is the distance for diffusion, and D is the diffusion coefficient of the substance, which is equal to solubility coefficient/square root of gram molecular weight of the substance.

In other words, the flux of a molecule 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 molecule. During acute renal failure, dialysis is often used to support renal function until renal recovery occurs. Hemodialysis relies on the effectiveness of solute diffusion across a semipermeable membrane. There are various modalities of hemodialysis, including intermittent, slow, low-efficiency dialysis, and continuous hemodialysis.

4. The answer is b. (*Barrett, pp 114-117. McPhee and Hammer, pp 105, 467-470.*) 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. Hypercalcemia occurs in approximately 10% of all malignancies and is most commonly seen in solid tumors, particularly breast carcinoma, renal carcinoma, and squamous cell carcinomas (eg, esophagus and lung). Solid tumors usually produce hypercalcemia by secreting PTHrP. The resulting humoral hyper-calcemia mimics primary hyperthyroidism, but with no elevation in PTH.

5. The answer is a. (*Barrett, pp 43-45. Longo, pp 516-518, 3452-3455.*) 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. 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 neuromuscular disorders. Demyelinating forms of CMT are classified as CMT1 and axonal forms as CMT2. 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.

6. The answer is c. (*Barrett, pp 9-10, 276-278. McPhee and Hammer, pp 169-171.*) The amount of potassium moving 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. Answer (a) is incorrect because 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 (answer d). Decreasing the activity of the sodium–potassium pump (answer e) has no immediate effect on potassium efflux, but ultimately results in depolarization of the membrane, resulting in an increased flow of potassium out of the cell. Altering the extracellular sodium concentration (answer b) has no immediate effect on the flow of potassium across the membrane. Seizures are paroxysmal disturbances in cerebral function caused by an abnormal synchronous discharge of cortical neurons. The epilepsies are a group of disorders characterized by recurrent seizures. Benign familial neonatal seizures constitute a rare type of idiopathic epilepsy linked to autosomal dominant mutations of voltage-gated K^+ channels. The seizures are paroxysmal, generally appearing within the first week to month of life, and generally resolve spontaneously within days to weeks after onset. The seizures are brief tonic–clonic seizures with little or no postictal state. There are generally no resultant developmental problems, though there may be a predisposition to developing epilepsy later in life.

7. The answer is a. (*Barrett, p. 123. Longo, pp 1200-1203, 1776-1778.*) 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 toxins are used for a variety of cosmetic and therapeutic purposes. Generalized botulism-like weakness (iatrogenic botulism) is a rare complication of these procedures. Botulinum and tetanus toxin are released from the same class of bacteria (*Clostridium*). Illness begins with cranial nerve involvement and proceeds caudally to involve the extremities. Cases may be classified as food borne, wound botulism, and intestinal botulism. Because of its extraordinary potency, botulinum toxin has also been used as an agent of bioterrorism or biological warfare that could be acquired by inhalation or ingestion. Features of outbreaks suggesting deliberate release of botulinum toxin include infection with an unusual toxin type, outbreak of a large number of cases of acute flaccid paralysis with prominent bulbar palsies with a common geographic factor but without a common dietary exposure, or multiple simultaneous outbreaks without a common source. Tetanus toxin produces an increase in skeletal muscle contraction by blocking the release of inhibitory neurotransmitter from spinal interneurons.

8. The answer is b. (*Barrett, pp 50-54. Widmaier, pp 101-102, 106.*) Glucose is transported into skeletal muscle and fat cells by facilitated diffusion and thus does not require the direct or indirect use of energy. Several distinct transporters mediate the facilitated diffusion of glucose. Insulin increases the number of the glucose transporters expressed in skeletal muscle and adipose tissue, and thereby increases the rate of diffusion of glucose, though insulin is not necessary for the diffusion. In diabetes mellitus (DM), when insulin is not available (type 1 DM) or when the cells are unresponsive to insulin (T2DM), muscle and adipose tissue cannot efficiently transport glucose across their membranes, leading to the characteristic hyperglycemia that is the hallmark of DM. All of the answer choices describe transport systems that 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 Na^+–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 e. (*Barrett, p 7. Widmaier, pp 96-100, 115.*) Absorption of protonated short-chain fatty acids into enterocytes occurs by simple diffusion. Fick law states that the net rate of diffusional flux (J) of a substance is proportional to its concentration difference (Δc). Doubling the concentration of protonated short-chain fatty acids outside of the enterocytes 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. Short-chain fatty acids are released by the action of the colonic microflora on dietary fiber. These short-chain fatty acids promote survival of healthy colonic epithelium while inducing apoptosis in epithelial cells progressing toward malignant transformation.

10. The answer is c. (*Barrett, pp 138-145. Longo, pp 55-56, 2058-2059.*) Glutamate is the major neurotransmitter that mediates synaptic excitation in the central nervous system, and glutamate receptors are also known as excitatory amino acid receptors. The NMDA (*N*-methyl-D-aspartate) receptor channel is one of the five different classes of excitatory amino acid receptors. The NMDA receptor 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. The NMDA receptor is also unique in that glycine binding to the receptor is essential for the receptor to respond to glutamate. 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 definitive treatment for preeclampsia is delivery of the baby, which may mean a premature birth. In the interim, intravenous labetalol or hydralazine may be given to treat the maternal hypertension, though the risk of drug-induced maternal hypotension is reportedly less with labetalol. Magnesium sulfate is the treatment of choice for preventing and treating eclamptic seizures. Acetylcholine binding to nicotinic acetylcholine receptors opens ion channels conductive to Na^+ and K^+. Glycine and GABA are both inhibitory neurotransmitters that act on glycine and $GABA_A$ receptors, respectively, which are ligand-gated Cl^- channels. Binding of GABA to the metabotropic $GABA_B$ receptor activates a G-protein, which leads to activation of K^+ channels and inhibition of Ca^{2+} channels. Kainate is another type of glutamate receptor.

11. The answer is d. (*Barrett, pp 114-117. Widmaier, pp 280-282.*) Smooth muscle relaxes when Ca^{2+} is removed from the myoplasm and latch bridges detach from actin. 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 cross-bridges (Step 4). 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.

Smooth muscle autoantibodies (SMAs) are found in the sera of patients with autoimmune liver diseases, viral infections, certain cancers, heroin addicts, and female infertility. SMAs are classified according to their reactivity to microfilaments, microtubules, or intermediate filaments. Auto-antibodies to actin-like microfilaments appear specific for autoimmune hepatitis; autoantibodies to microtubules occur in infectious mononucleosis; and autoantibodies to intermediate filaments occur in infectious hepatitis, chickenpox, measles, and mumps. Autoimmune hepatitis is positive for both SMA and antinuclear antibodies (ANAs), whereas systemic lupus erythematosus is positive for ANA but not for SMA. A possible pathogenic role for SMAs seems unlikely because the autoantibodies are in the serum and the cytoskeletal antigens are in the cytoplasm. However, observations that serum autoimmune complexes may activate complement raise the possibility of antibody-mediated tissue damage by complement lysis.

12. The answer is c. (*Barrett, pp 7-9, 701-702. Kaufman, p 387. Longo, pp 343-349.*) 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. (*Barrett, pp 1-3, 6-7. Kaufman, pp 206, 26. Longo, pp 264, 341-343, 348-351, 2340.*) 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 with that in the intracellular water, increases; hypotonicity of the extracellular water decreases the proportion of water in the extracellular fluid. Poststreptococcal glomerulonephritis is an acute nephritic syndrome that typically affects children between the age of 2 and 14 years, although 10% of cases are patients older than 40. Throat infections with certain M-type streptococci antedate the glomerular disease by 1 to 3 weeks. Findings include hematuria, proteinuria and pyuria, red blood cell casts, edema, hypertension, and oliguric renal failure. Antibiotic treatment for streptococcus should be given to the patient and all cohabitants, as incidence in cohabitants is as high as 40%.

14. The answer is e. (*Barrett, pp 3-9, 310-31. Widmaier, pp 105-109, 115.*) After ingesting water, it is absorbed from the intestine, enters the plasma, and rapidly achieves osmotic equilibrium with the interstitial and intra-cellular compartments. Assuming that she had a normal osmolarity of 300 mOsm/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 mOsm/L. Assuming that her normal osmolarity of 300 mOsm was reduced to 250 mOsm by the ingestion of water, she drank approximately 7 L.

$$\begin{aligned}
\text{Osmolarity} &= \text{mOsm/volume} \\
300\ \text{mOsm/L} &= 60\ \text{kg} \times 60\% \times 300/\text{initial volume} \\
\text{Initial volume} &= 10{,}800\ \text{mOsm}/300\ \text{mOsm/L} = 36\ \text{L} \\
250\ \text{mOsm/L} &= 60\ \text{kg} \times 60\% \times 300/\text{new volume} \\
\text{New volume} &= 10{,}800\ \text{mOsm}/250\ \text{mOsm/L} \cong 43\ \text{L} \\
\text{Volume consumed} &= \text{new volume} - \text{initial volume} \\
&= 43\ \text{L} - 36\ \text{L} = 7\ \text{L}
\end{aligned}$$

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 d. (*Barrett, pp 7-8. Longo, pp 2325-2326. Widmaier, pp 105-107.*) 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. Dialysis is often used for the treatment of either acute or chronic kidney disease. Commonly accepted criteria for initiating patients on maintenance dialysis include marked uremia and reductions in glomerular filtration rate, hyperkalemia and/or acidosis that are unresponsive to medication, and persistent extravascular fluid expansion despite diuretic therapy. Hemo-dialysis is used in more than 90% of patients with end-stage renal disease in the United States, but no large-scale clinical trials have been completed to compare outcomes among patients randomized to either hemodialysis or peritoneal dialysis.

16. The answer is e. (*Barrett, pp 80, 367. Longo, p 2796.*) Evidence is accumulating that the transcription factor, NF-κB, plays a key role in the inflammatory response. NF-κB is a heterodimer that normally exists in the cytoplasm of cells bound to IκBα, which renders it inactive. Stimuli such as viruses, cytokines, and oxidants separate NF-κB from IκBα, and NF-κB 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-κB by increasing the production of IκBα, 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 their ability to stabilize lysosomal membranes and decrease the formation of bradykinin. Glucocorticoids inhibit the enzyme phospholipase A_2; 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 (inter-leukin 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.

17. The answer is e. (*Barrett, pp 7-9, 304. Longo, pp 2254-2257.*) Swelling or edema of the brain with a resultant elevation of ICP occurs with many types of brain injury. Interventions to lower ICP are ideally based on the underlying mechanism responsible for the elevated ICP. In head trauma, stroke, or brain metastases, use of osmotic diuretics to treat cytotoxic edema becomes an appropriate early step. 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 (ie, >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.

Questions

18. 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. Laboratory test results are as follows:

Serum Na^+ = 190 mmol/L (normal range = 135–142 mmol/L)
Serum K^+ = 4.5 mmol/L (normal range = 3.5–5 mmol/L)
Urine Na^+ = 18 mmol/L (normal range = 20–40 mmol/L)
Urine osmolality = 75 mOsm/kg (normal = 100 mOsm/kg)

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. These persistent clinical signs are most likely due to which of the following?

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

19. A 65-year-old man being treated with a beta-blocker and an angiotensin-converting enzyme (ACE) inhibitor for his heart failure presents to his cardiologist's office complaining of fatigue, weakness, shortness of breath, and an irregular heartbeat. An electrocardiogram (ECG) reveals atrial fibrillation, so his cardiologist adds digoxin to his treatment regimen, but tells the patient that he will need to get his blood drawn to check for low K^+ on a regular basis. Hypokalemia will increase the risk and severity of digitalis toxicity because of which of the following?

a. Hypopolarization of cardiac muscle membranes
b. Increased amplitude of cardiac muscle action potentials
c. Increased excitability of cardiac muscle cells
d. Increased inhibition of the $Na^+ - K^+$ pump
e. Increased removal of cardiac cytosolic Ca^{2+} via the $Na^+ - Ca^{2+}$ exchanger

20. A man calls 911 after finding his 19-year-old son in a comatose condition. A blood sample drawn in the emergency department shows the following results:

PaO_2 = 105 mm Hg	Na^+ = 135 mEq/L	BUN = 15 mg/dL
$PaCO_2$ = 24 mm Hg	K^+ = 5 mEq/L	Serum Cr = 1.2 mg/dL
pH = 7.31	Cl^- = 100 mEq/L	Blood glucose = 95 mg/dL
SaO_2 = 98%	HCO_3^- = 5 mEq/L	

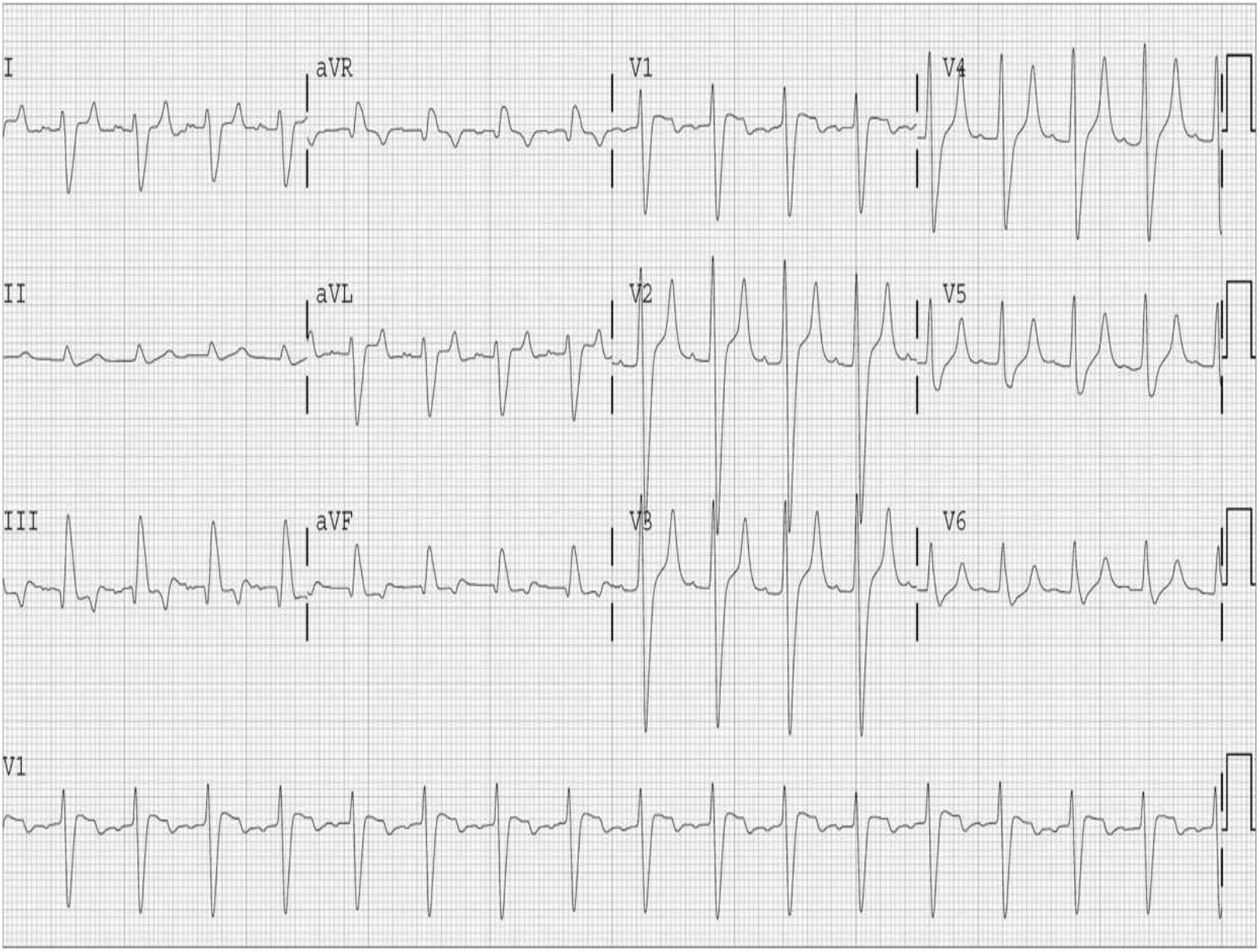
Which of the following is the most likely diagnosis?

a. Carbon monoxide poisoning
b. Diabetes mellitus
c. Ethylene glycol ingestion
d. Renal tubular acidosis
e. Respiratory arrest

21. A 55-year-old obese man with type 2 diabetes mellitus presents for his annual checkup. Serum lipoprotein analysis done after a 12-hour fast shows elevated low-density lipoprotein (LDL) and very low-density lipoproteins (VLDL), elevated triglycerides, and decreased high-density lipo-protein cholesterol. What contributes to the lipid abnormalities in type 2 diabetes mellitus?

a. Hyperglycemia increases triglyceride uptake into adipose tissue.
b. Insulin resistance increases triglyceride uptake into adipose tissue.
c. Insulin resistance and hyperglycemia decrease fatty acid flux to the liver and lipolysis.
d. Insufficient insulin action in adipose tissue decreases lipoprotein lipase activity.
e. Insufficient insulin action increases LDL receptor activity.

22. A 72-year-old woman with a history of hypertension presents to the emergency department with generalized weakness. Her medications include a potassium-sparing diuretic and an ACE inhibitor. Serum creatinine and BUN are elevated. The ECG is shown below. Which of the following electrolyte disturbances should be corrected to have the ECG return to normal?



(Reproduced, with permission, from Knoop KJ, Stack LB, Storrow AB, Thurman RJ. *The Atlas of Emergency Medicine.* 3rd ed. http://www.accessmedicine.com. Copyright © The McGraw-Hill Companies, Inc. All rights reserved.)

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

23. The friends of a 26-year-old man plan a bachelor's party for him in Las Vegas. After a round of golf, the group heads to the pool. They order several rounds of drinks over the next 4 hours and also order lunch poolside. Most of the group orders hamburgers and French fries, but the groom-to-be is watching his weight and opts for a club sandwich and a side of coleslaw. Later that night, they go for dinner and to the casinos, where they imbibe some more. Early the next morning, the groom-to-be becomes ill. He thinks it is just a hangover, but presents to the emergency department 36 hours later with persistent vomiting and orthostatic hypotension. Which of the following metabolic abnormalities are most likely present in this patient?

a. Hypokalemia, hypochloremia, and metabolic alkalosis
b. Hypokalemia, hypochloremia, and metabolic acidosis
c. Hyperkalemia, hyperchloremia, and metabolic alkalosis
d. Hyperkalemia, hyperchloremia, and metabolic acidosis
e. Normal serum electrolytes and acid–base balance

24. A 58-year-old man is transported to the emergency department due to impaired breathing and shortness of breath. Arterial blood gases show the following:

pH = 7.35
Pa_{O_2} = 60 mm Hg
Pa_{CO_2} = 60 mm Hg

$[HCO_3^-]$ = 31 mEq/L

Which of the following is the most likely diagnosis of this patient?

a. Alcoholic ketoacidosis
b. Anxiety-induced hyperventilation
c. Chronic obstructive pulmonary disease (COPD)
d. Narcotic overdose
e. Salicylate overdose

25. A 22-year-old female professional golfer collapses while waiting to tee off on the 16th hole of the LPGA Jamie Farr Classic Tournament. It was July in Toledo, OH, with the temperature in the 90s and 85% humidity. When the emergency medical technicians and tournament physicians arrived in a mobile clinic, the patient had a respiratory rate of 28 breaths per minute, heart rate of 120 beats per minute, blood pressure of 85/60, and temperature of 99°F. Her pupils were reactive. Her caddy reported that the golfer's face was very red, sweating profusely, eating a lot of ice chips, and making frequent trips to the bathroom. A stat blood sample showed a pH of 7.47, P_{CO_2} of 32 mm Hg, $[HCO_3^-]$ of 22 mEq/L, and a normal anion gap. Which of the following is a likely diagnosis?

a. Diabetes mellitus
b. Diarrhea
c. Heat exhaustion
d. Heat stroke
e. Vomiting

26. A 28-year-old student goes to Cancun, Mexico, for his spring break. After running on the beach the morning he was to return, he feels so thirsty that he takes a drink of water from a garden hose at the hotel. After his return, the man presents in the Student Medical Center reporting foul-smelling diarrhea and flatulence over the past 5 days. Stool cultures confirm an infection with the protozoan *Giardia lamblia*. Which of the following arterial blood gases would be expected in this patient?

	pH	P_{CO_2} (mm Hg)	$[HCO_3^-]$ (mEq/L)	Anion Gap (mEq/L)
a.	7.22	30	15	12
b.	7.22	30	15	25
c.	7.38	37	25	16
d.	7.51	49	38	12
e.	7.51	25	22	25

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 narcotic analgesic (Vicodin; Abbott Pharmaceuticals, Green Oaks, IL USA) was found next to the bathroom sink. Which of the following arterial blood gases are most consistent with her clinical presentation?

a. pH = 7.02, P_{CO_2} = 60 mm Hg, $[HCO_3^-]$ = 15 mEq/L, anion gap = 12 mEq/L
b. pH = 7.10, P_{CO_2} = 20 mm Hg, $[HCO_3^-]$ = 6 mEq/L, anion gap = 30 mEq/L
c. pH = 7.27, P_{CO_2} = 60 mm Hg, $[HCO_3^-]$ = 26 mEq/L, anion gap = 12 mEq/L
d. pH = 7.40, P_{CO_2} = 20 mm Hg, $[HCO_3^-]$ = 10 mEq/L, anion gap = 30 mEq/L
e. pH = 7.51, P_{CO_2} = 49 mm Hg, $[HCO_3^-]$ = 38 mEq/L, anion gap = 12 mEq/L

28. A 22-year-old man is planning to run a marathon when he goes to visit his brother in Denver, CO. Because of the high altitude, he decides to leave early for Denver 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. Plasma proteins are more ionized under alkalotic conditions, which provide more protein anion to bind with Ca^{2+}
e. Stimulation of Na^+/K^+ adenosine triphosphatase (ATPase) reduces the plasma concentration of free ionized Ca^{2+}

29. A 64-year-old patient with COPD develops jugular venous distention, ascites, and peripheral edema. A chest X-ray reveals cardiomegaly with marked enlargement of the right ventricle. A decrease in which of the following variables is the major cause of cor pulmonale in COPD?

a. Alveolar P_{CO_2}
b. Alveolar P_{O_2}
c. Arterial $[H^+]$

d. Pulmonary artery pressure
e. Pulmonary vascular resistance

30. A 78-year-old woman recovering from a stroke is observed to have altered mental status. She is taken from the nursing home to the emergency department, where physical examination shows signs of dehydration and laboratory test results show a blood glucose concentration of 600 mg/dL and plasma osmolarity of 340 mOsm/L. Which of the following physiological variables is likely increased in this patient?

a. Arterial pH
b. Alveolar P_{aCO_2}
c. Intracellular volume
d. Plasma sodium concentration
e. Urine volume

31. A 54-year-old man goes out to shovel the snow so that he can drive his wife to her doctor's appointment. After getting some chest pain and feeling shortness of breath, he thinks he better go in and rest for a while before finishing the task. When his wife comes downstairs, she finds him sitting with his head down on the morning paper at the kitchen table. When the ambulance arrives, he is still responsive, but has a cardiac and respiratory arrest en route to the hospital. Which of the following arterial blood gases would be expected given these findings?

a. $pH = 7.22$, $P_{aCO_2} = 60$ mm Hg, $[HCO_3^-] = 26$ mEq/L, anion gap = 12 mEq/L
b. $pH = 7.05$, $P_{aCO_2} = 60$ mm Hg, $[HCO_3^-] = 15$ mEq/L, anion gap = 25 mEq/L
c. $pH = 7.10$, $P_{aCO_2} = 20$ mm Hg, $[HCO_3^-] = 6$ mEq/L, anion gap = 30 mEq/L
d. $pH = 7.51$, $P_{aCO_2} = 49$ mm Hg, $[HCO_3^-] = 38$ mEq/L, anion gap = 14 mEq/L
e. $pH = 7.40$, $P_{aCO_2} = 20$ mm Hg, $[HCO_3^-] = 10$ mEq/L, anion gap = 26 mEq/L

32. A 21-year-old woman is admitted to the emergency department after ingesting a large dose of aspirin to try to get rid of her headache. The patient is diaphoretic and has the following blood gases: pH of 7.45, P_{aCO_2} of 17 mm Hg, and $[HCO_3^-]$ of 13 mmol/L. 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

33. A child makes a blue slush drink using a container of windshield wiper fluid in the garage. At first he acted like he was drunk, but about 6 hours later, he complained that he was having difficulty seeing. His parents rushed him to the poison control center at a nearby emergency department. Arterial blood gases shown below indicate that the child has which of the following acid–base disturbances?

$pH = 7.34$
$P_{aCO_2} = 29$ mm Hg
$[HCO_3^-] = 15$ mEq/L
Anion gap = 28 mEq/L

a. Compensated metabolic acidosis
b. Compensated metabolic alkalosis
c. Compensated respiratory alkalosis
d. Respiratory and metabolic acidosis
e. Uncompensated respiratory acidosis

34. A patient with Guillain–Barré syndrome develops paralysis of the respiratory muscles that increases P_{aCO_2} from 40 to 60 mm Hg 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 $[HCO_3^-]$ 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

35. 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 hyper-kalemia. In addition to the serum glucose and potassium, which of the following laboratory values would most likely be above normal?

a. Anion gap
b. Arterial P_{CO_2}

c. Blood volume
d. Plasma pH
e. Serum $[HCO_3^-]$

36. An 84-year-old woman 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 causes metabolic alkalosis?

a. Diarrhea
b. Hypoaldosteronism
c. Hypoxemia
d. Renal failure
e. Treatment with a loop diuretic

37. A 23-year-old woman 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. Diabetes
b. Hyperaldosteronism
c. Hyperventilation
d. Persistent diarrhea
e. Renal failure

38. 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 benzodiazepine after positron emission tomography 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. $pH = 7.28$, $Paco_2 = 20$ mm Hg, $[HCO_3^-] = 16$ mEq/L, anion gap = 25 mEq/L
b. $pH = 7.28$, $Paco_2 = 60$ mm Hg, $[HCO_3^-] = 26$ mEq/L, anion gap = 12 mEq/L
c. $pH = 7.44$, $Paco_2 = 25$ mm Hg, $[HCO_3^-] = 16$ mEq/L, anion gap = 12 mEq/L
d. $pH = 7.51$, $Paco_2 = 20$ mm Hg, $[HCO_3^-] = 24$ mEq/L, anion gap = 12 mEq/L
e. $pH = 7.51$, $Paco_2 = 49$ mm Hg, $[HCO_3^-] = 38$ mEq/L, anion gap = 12 mEq/L

39. A 25-year-old man training for a 10-km race runs at a moderate level of approximately 25% of his maximal oxygen consumption. During the increase in aerobic metabolism in the exercising skeletal muscles, most of the volatile acid entering the blood is buffered by which of the following?

a. Bicarbonate
b. Hemoglobin
c. Lactate
d. Phosphates
e. Plasma proteins

40. A 64-year-old man with a long history of type 2 diabetes mellitus presents at his internist's office with a chief complaint of weakness and fatigue. Serum chemistries are as follows: Na^+, 130 mEq/L; K^+, 6.3 mEq/L; HCO_3^-, 18 mEq/L; BUN, 43 mg/dL; creatinine, 2.9 mg/dL; and glucose, 198 mg/dL. The only medication the patient is currently taking is 5 mg glyburide twice daily. These electrolyte and acid–base disturbances are most likely the result of which of the following?

a. Hyperreninemia
b. Hypoaldosteronism
c. Hypocalcemia
d. Hypoventilation
e. Hypovolemia

41. A 60-year-old man presents with symptoms of vitamin B_{12} deficiency. Further diagnostic tests reveal that he has pernicious anemia. The underlying problem in pernicious anemia is which of the following?

a. Autoimmune destruction of chief cells in the gastric mucosa
b. Gluten-induced enteropathy
c. Inadequate dietary intake of cyanocobalamin
d. Infection with *Diphyllobothrium latum*
e. Lack of intrinsic factor

42. An 89-year-old nursing home resident exhibits signs of vitamin deficiency. At concentrations present in the diet, which of the following vitamins is absorbed primarily by diffusion?

a. Folate

b. Niacin
c. Vitamin B_{12}
d. Vitamin C
e. Vitamin D

43. A 69-year-old man is brought to the emergency department by his wife after he blacks out and falls, hitting his head on the kitchen floor. She indicates that he has been drinking beer all afternoon while watching the baseball game on television. Measurement of serum Na^+, glucose, BUN, and osmolality indicates 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	$Paco_2$	Anion Gap
a.	↑	↑	↑
b.	↓	↑	↑
c.	↑	↑	↓
d.	↓	↓	↑
e.	↑	↓	↓

44. A 65-year-old man with type 1 diabetes presents to the emergency department with impaired mental status and generalized muscle weakness. Laboratory tests reveal a blood glucose concentration of 500 mg/dL, an anion gap of 22 mmol/L, and a bicarbonate ion concentration of 14 mmol/L. Other expected blood values in this patient include an increase in which of the following?

a. Insulin
b. K^+
c. Na^+
d. $Paco_2$
e. pH

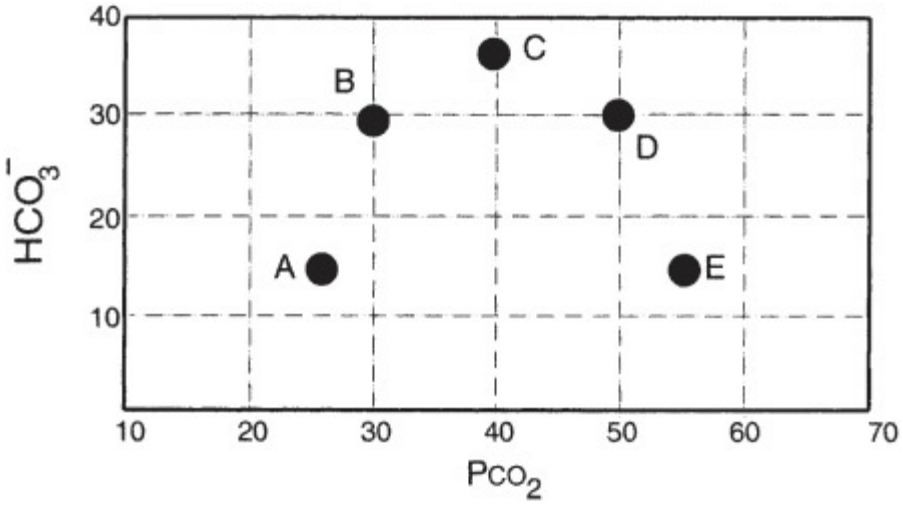
45. A patient comes into the emergency department exhibiting signs of hyperkalemia. The extracellular potassium of a hyperkalemic patient can be decreased by administering which of the following drugs?

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

46. A 22-year-old woman presents to the emergency department with nausea, abdominal pain, and vomiting, which has gotten progressively worse over the past 24 hours. On physical examination, her abdomen is soft and tender, but there is no guarding or rebound tenderness. Her temperature is 99.1°F, heart rate is 110 beats per minute, respiratory rate is 16 breaths per minute, and blood pressure is 135/85 mm Hg when lying down and 112/70 mm Hg while standing. Laboratory findings are as follows: WBC, 7.5; hemoglobin, 12 g/dL; Na^+, 140 mEq/L; K^+, 3.2 mEq/L; Cl^-, 95 mEq/L; and HCO_3^-, 37 mEq/L. Which of the following $Paco_2$ and pH values are consistent with these findings?

	$Paco_2$ (mm Hg)	pH
a.	25	7.70
b.	47	7.52
c.	40	7.40
d.	28	7.32
e.	60	7.20

47. A 25-year-old man, who is a medical student living in Rochester, MN, decides to go backcountry skiing in Colorado over spring break. Which of the following points on the graph below best represents the blood gas values obtained from the student 72 hours after his arrival in Aspen, CO (base altitude = 7945 ft)?



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

48. A 49-year-old man is brought to the emergency department with weakness, confusion, and shortness of breath. The ECG reveals QRS complex widening and flattened P waves typical of serum potassium concentrations exceeding 7.5 mEq/L. Which of the following conditions results in hyperkalemia?

a. Adrenal medullary stimulation
b. Diuretic therapy
c. Insulin administration
d. Metabolic alkalosis
e. Volume depletion

49. A 69-year-old man is brought to the emergency department by his son because of headache, nausea, and fatigue. The patient used to smoke two packs of cigarettes a day for the past 50 years before stopping 1 year ago, when he was diagnosed with small cell carcinoma of the lung. Laboratory tests reveal the following result: WBC, 8.3; blood glucose, 106 mg/dL; Na^+, 122 mEq/L; K^+, 4.1 mEq/L. His hyponatremia may be a result of excess secretion of which of the following?

a. Aldosterone
b. Arginine vasopressin
c. Atrial natriuretic hormone
d. Insulin
e. Norepinephrine

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 carpo-pedal spasm. Which of the following blood gas values will most likely be observed in this patient?

	$Paco_2$ (mm Hg)	$[HCO_3^-]$ (mM)
a.	50	40
b.	60	20
c.	40	30
d.	30	15
e.	20	20

51. A 27-year-old patient with insulin-dependent diabetes mellitus tells his roommate that he cannot afford to refill his insulin prescription until he gets a paycheck. The roommate offers to get it for him, but the patient assures him that he can wait until the weekend. When the roommate returns from a weekend trip on Sunday evening, he finds the man unresponsive on the couch. He calls 911. Which of the following arterial blood gases taken in the emergency department would be expected in this diabetic coma patient?

a. pH = 7.10, $Paco_2$ = 25 mm Hg, $[HCO_3^-]$ = 15 mEq/L, anion gap = 12 mEq/L
b. pH = 7.10, $Paco_2$ = 25 mm Hg, $[HCO_3^-]$ = 15 mEq/L, anion gap = 30 mEq/L
c. pH = 7.10, $Paco_2$ = 80 mm Hg, $[HCO_3^-]$ = 25 mEq/L, anion gap = 12 mEq/L
d. pH = 7.45, $Paco_2$ = 25 mm Hg, $[HCO_3^-]$ = 15 mEq/L, anion gap = 12 mEq/L
e. pH = 7.45, $Paco_2$ = 50 mm Hg, $[HCO_3^-]$ = 40 mEq/L, anion gap = 30 mEq/L

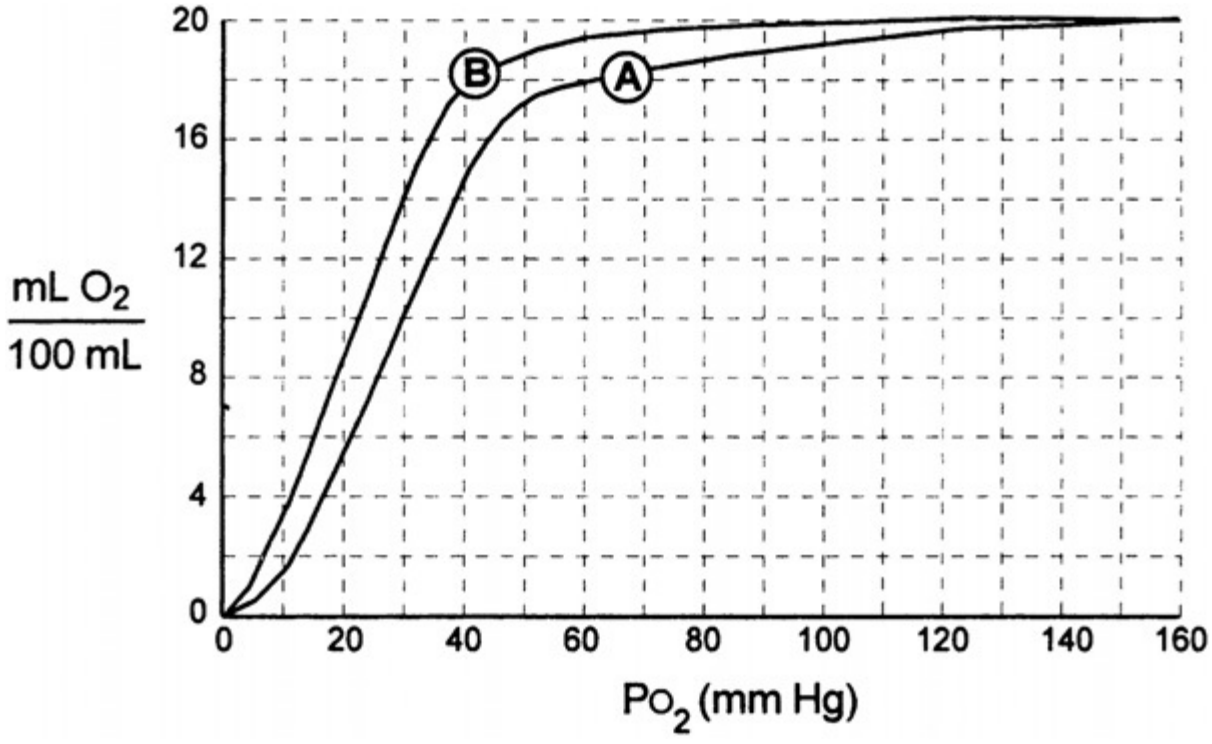
52. A 27-year-old man presents to the emergency department with asthmatic bronchitis that started 3 days ago. He is given an aerosolized bronchodilator treatment, which relieves his symptoms. Arterial blood gases following bronchodilator therapy demonstrate metabolic acidosis with a normal anion gap. These findings can be attributed to which of the following?

a. A decrease in plasma bicarbonate caused by renal compensation for the respiratory alkalosis that existed before treatment
b. A decrease in plasma chloride concentration resulting from the chloride shift after the treatment restored alveolar ventilation
c. An increase in citrate from the vehicle used in the bronchodilator preparation
d. An increase in lactic acid secondary to the hypoxemia that existed before treatment
e. A laboratory error

53. A group of medical students in the Wilderness Medicine Club leave after their exam for a hiking trip in the Rocky Mountains. After spending the night in a hotel in Denver, CO, they drive to the base camp (10,000 ft) the following day, where the guide decides to camp for the night to better acclimate to the altitude. Three of the students grow impatient and announce that they are going ahead to Mt. Elbert, the highest mountain in Colorado (14,400-ft altitude, barometric pressure = 447 mm Hg). About 3 hours later, one of the students returns in a panic to get medical help because his friends are disoriented, ataxic, short of breath, and vomiting. The guide calls for the search and rescue helicopter, which locates the hikers and takes them to the nearest emergency department. A diagnostic workup will likely show a decrease in which of the following values?

a. 2,3-Bisphosphoglycerate
b. Erythropoietin
c. $Paco_2$
d. pH
e. Pulmonary vascular resistance

54. A 19-year-old man presents at the emergency department complaining of shortness of breath. His oxyhemoglobin dissociation curve was shifted from that for normal hemoglobin A depicted in curve A in the figure below to curve B. This finding is consistent with which of the following conditions?



a. Carbon monoxide poisoning
b. Exercise
c. Hypoventilation
d. Increased body temperature
e. Recent transfusion with banked blood

55. A 28-year-old pregnant woman develops placental insufficiency at 27 weeks' gestation. It is determined that a preterm caesarian section will be required. 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 adrenal function
b. Fetal brain development
c. Fetal kidney development
d. Fetal lung maturity
e. Placenta gas exchange

56. A 25-year-old man, who is a fourth-year medical student at Louisiana State University School of Medicine in New Orleans, LA, enrolls in a month-long clinical elective at the University of Colorado School of Medicine in Denver, CO. Which of the following values will return toward normal after the student has acclimatized to the change in altitude?

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

57. A 27-year-old woman presents with nausea, vomiting, and tachypnea. Laboratory test results show the following:

$Pa_{O_2} = 105$ mm Hg
$Pa_{CO_2} = 30$ mm Hg
pH = 7.47
$[HCO_3^-] = 21$ mEq/L
[Hb] = 14 g/dL

These findings are consistent with which of the following conditions?

a. Anemia
b. Compensated metabolic alkalosis
c. Exercise hyperpnea
d. Pregnancy
e. Too rapid of ascent to high altitude

58. An 86-year-old man waiting to see his doctor is sitting in an examination room in which the air temperature is 21°C (70°F). He is 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 mechanisms?

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

Answers

18. The answer is a. (*Barrett, pp 374-375, 437, 700. Kaufman, pp 79-80. Le, pp 301, 306, 574. Longo, pp 2904-2907. Widmaier, p 492.*) Diabetes insipidus (DI) is a disease caused by decreased release of antidiuretic hormone (ADH) from the posterior pituitary or the inability of the kidney to respond 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 DI. 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, and systemic) or nephrogenic in etiology. Nephrogenic DI can be either acquired (renal disease, drugs, hypokalemia, and hypercalcemia) or familial. Diabetes mellitus (choice **b**), which results from a deficiency of the effects of insulin at the tissue level, is characterized by polyuria, hyperglycemia, and increased urine osmolarity from glycosuria. Hyperaldosteronism (choice **d**) is associated with hyponatremia and polyuria, and also hypokalemic alkalosis. Renal failure (choice **e**) is an inability to make urine. Hypothyroidism (choice **c**) is accompanied by constipation.

19. The answer is d. (*Barrett, p 524. Le, pp 229, 282, 284. Longo, pp 353, 356, 967, 1883-1886, 1908-1911. Widmaier, p 413.*) Digoxin is used to treat congestive heart failure because it increases cardiac contractility. Digoxin is also used to treat atrial fibrillation because it increases vagal tone, which depresses the sinoatrial node and slows conduction at the atrioventricular node. Digoxin produces its physiological effects by inhibiting Na^+/K^+-ATPase by blocking the K^+-binding site on the enzyme. As a result, intracellular Na^+ concentration increases, which reverses the direction of the Na^+/Ca^{2+} exchanger, such that less Ca^{2+} is removed from the cell and cytosolic $[Ca^{2+}]$ increases, which increases cardiac contractility. 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, which decreases excitability.

20. The answer is c. (*Kaufman, pp 240-242. Le, pp 487-488. Levitzky, pp 171-185. Longo, pp 363-368.*) This patient has a high anion gap metabolic acidosis. 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.

$$\begin{aligned}\text{Anion gap} &= [Na^+] - ([Cl^-] + [HCO_3^-]) \\ &= 135\ \text{mEq/L} - (100\ \text{mEq/L} + 5\text{mEq/L}) \\ &= 30\ \text{mEq/L}\end{aligned}$$

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. Diabetic ketoacidosis also causes a high anion gap metabolic acidosis, but the characteristic hyperglycemia is not present. Renal tubular acidosis results in a normal anion gap metabolic acidosis. Renal failure with uremia is another cause of high anion gap metabolic acidosis, but renal function is normal in this patient. Carbon monoxide poisoning and consequent lactic acidosis cause a high anion gap metabolic acidosis, but the requisite decline in oxygen saturation is not present. Respiratory arrest can be ruled out on the basis of the reduced $Paco_2$ and thus the absence of respiratory acidosis.

21. The answer is d. (*Barrett, p 439. McPhee and Hammer, pp 511, 518. Widmaier, pp 32-33, 86-87, 555-560, 581-583.*) Increased serum lipid levels may result from increased production, decreased clearance, or both. The principal lipid abnormality in diabetes is hypertriglyceridemia, which is due to increased VLDLs. VLDL levels are increased because of insufficient insulin action in adipose tissue, which results in decreased VLDL clearance as a result of decreased lipoprotein lipase activity. Triglyceride uptake into adipose tissue from plasma lipoproteins requires hydrolysis of triglyceride to fatty acids and glycerol by lipoprotein lipase, which is bound to the vascular endothelial surface. The activity of lipoprotein lipase varies in reciprocal fashion with that of cytoplasmic hormone-sensitive lipase, and thus is enhanced by insulin and decreased by catecholamines. Lipoprotein lipase is present in nearly every tissue and acts at the capillary surface as it does in adipose tissue.

22. The answer is d. (*Kaufman, pp 250-251. Le, p 487. Longo, pp 351-362.*) Several different types of drugs, most notably potassium-sparing diuretics and ACE inhibitors, can cause hyperkalemia, which can produce significant changes in the ECG. In elderly persons, a decline in renal function may also lead to hyperkalemia. 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 $\geq$7 mEq/L. As the plasma K^+ level rises, the first change on the ECG 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 sodium polystyrene sulfonate (Kayexalate; SanofiAventis US, Bridgewater, NJ USA), but takes hours to work. Hypokalemia is associated with U waves. Hypocalcemia may present with prolonged QT and ST intervals. Hypercalcemia is associated with a shortened QT interval and widened T waves. Hypermagnesemia presents with prolonged QT and ST intervals and increased QRS duration.

23. The answer is a. (*Kaufman, pp 243-244, 249-250. Longo, pp 351-354, 369-371.*) Analysis of serum electrolytes reveals low potassium (hypokalemia), low chloride (hypochloremia), and metabolic alkalosis. These abnormalities arise from two sources. First, gastric juice contains hydrogen, 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 individual'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.

24. The answer is c. (*Kaufman, pp 239-244. Levitzky, pp 171-181.*) The interpretation of the arterial blood gas is compensated respiratory acidosis. The primary disturbance is an elevation in arterial P_{CO_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 HCO_3^- concentration, returning the pH back into the normal range. Narcotic overdose would be associated with an acute, uncompensated respiratory acidosis. Anxiety-induced hyperventilation would lower arterial P_{CO_2} and increase arterial pH, characteristic of respiratory alkalosis. Ketoacidosis secondary to excessive alcohol ingestion, starvation, or diabetes would cause a metabolic acidosis with a compensatory decrease in arterial P_{CO_2}. Salicylate toxicity results in a combined respiratory alkalosis (due to direct stimulation of the medullary respiratory center) and metabolic acidosis (due to accumulation of organic acid).

25. The answer is d. (*Barrett, pp 316-321. Kaufman, p 387. Levitzky, pp 174-176, 180-181. Widmaier, pp 574-580.*) Heat exhaustion is a state of collapse (fainting) in a hot environment due to hypotension resulting from both a decrease in cardiac output (from depletion of plasma volume secondary to sweating) and a decrease in peripheral vascular resistance (due to marked dilation of cutaneous blood vessels). In other words, heat exhaustion occurs as a direct consequence of heat-loss mechanisms, which help to prevent increases in core temperature. Heat stroke results from a failure of thermoregulation and is associated with an increase in core body temperature. When diabetes mellitus leads to ketoacidosis and a diabetic coma, pH decreases and the anion gap increases. Diarrhea causes a normal anion gap metabolic acidosis. Vomiting causes metabolic alkalosis due to loss of acid.

26. The answer is a. (*Kaufman, pp 143, 208.*) Diarrhea causes a loss of bicarbonate, which increases plasma hydrogen ion concentration leading to metabolic acidosis, as evidenced by a reduction in plasma bicarbonate and a reduction in pH. Respiratory compensation as a result of peripheral chemoreceptor stimulation by the increased arterial $[H^+]$ causes the arterial Pa_{CO_2} to be decreased. Diarrhea is a normal anion gap type of metabolic acidosis because the loss of bicarbonate is replaced by an increase in serum chloride concentration, with no increase in the concentration of unmeasured anions, which makes choice (**a**) the correct answer rather than the high anion gap type of metabolic acidosis represented by choice (**b**), such that you might see in type 1 diabetes mellitus or lactic acidosis. Choice (**d**) is a metabolic alkalosis with respiratory compensation, and the interpretation of choice (**e**) is respiratory alkalosis combined with high anion gap metabolic acidosis. Choice (**c**) is normal acid–base status.

27. The answer is c. (*Kaufman, pp 239-243. Longo, pp 363-373.*) Narcotics used for the treatment of severe headache may depress the medullary respiratory center causing alveolar hypoventilation, as evidenced by an elevation in arterial P_{CO_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 completed, 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 d. (*Barrett, pp 377-378. Kaufman, pp 251-252. Levitzky, pp 172-173.*) 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 b. (*Le, pp 273, 549, 580. Longo, pp 1834-1835, 1913-1915.*) Cor pulmonale is defined as dilation and hypertrophy of the right ventricle in response to diseases of the pulmonary vasculature and/or lung parenchyma that are sufficient to cause pulmonary hypertension. Pulmonary hypertension is an increase in pulmonary artery pressure due to a rise in pulmonary vascular resistance. The major cause of pulmonary hypertension in COPD is increased pulmonary vasoconstriction due to alveolar hypoxia. Alveolar hypercapnia and acidosis in COPD also contribute to the development of pulmonary hypertension and cor pulmonale. COPD accounts for approximately half of the cases of cor pulmonale in North America.

30. The answer is e. (*Longo, pp 340, 2976-2981.*) 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 P_{CO_2}.

31. The answer is b. (*Barrett, pp 637, 692, 731, 734. Kaufman, pp 222-223. Levitzky, pp 171-175, 180-183. Longo, pp 288-295.*) 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 P_{CO_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 HCO_3^- and decreases pH. The normal anion gap of about 12 mEq/L, calculated as the difference between the concentration of Na^+ and major plasma anions, $Cl^- + HCO_3^-$, increases due to the increase in the unmeasured organic anion, lac-tate. Because both independently existing disorders cause acidosis, mixed respiratory and metabolic acidosis may cause dangerously low pH levels and a poor outcome.

32. The answer is c. (*Barrett, pp 253, 614-615. Longo, pp 288-291.*) Although reducing alveolar ventilation would increase P_{CO_2} toward its normal value, it is an inappropriate therapy in this circumstance. Aspirin has a p *Ka* of 3.5 and will rapidly cross the blood–brain barrier when it is in an unionized state. The alkaline pH resulting from the hyperventilation is keeping most of the aspirin in an ionized form, so 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.

33. The answer is a. (*Kaufman, pp 240-242. Le, pp 487-488. Longo, pp 288-295.*) The interpretation of the arterial blood gas is 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 also dissolved CO_2 and returns the pH toward the normal range. The predicted respiratory compensation for a simple metabolic acidosis is 1.2 mm Hg decrease in $Paco_2$ for every mEq/L decrease in $[HCO_3^-]$ or $Paco_2 = 1.5\ [HCO_3^-] + 8 \pm 2$ (Winter's formula). 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 with a normal value of approximately 12 mEq/L is consistent with an increase in formic acid, a metabolite of methanol, which is a constituent of windshield wiper fluid. After its initial effect of inebriation, the metabolic products of methanol may cause metabolic acidosis, blindness, and death after a characteristic latent period of 6 to 30 hours.

34. The answer is d. (*Levitzky, pp 171-180, 202-209. Longo, pp 371-372, 3473-3477.*) 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 mm Hg 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 mm Hg increase in $Paco_2$), which helps to return the pH toward normal.

35. The answer is a. (*Kaufman, 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.

36. The answer is e. (*Levitzky, pp 174-175. Longo, pp 369-371.*) Loop diuretics, such as furosemide (Lasix; Sanofi-Aventis US, Bridgewater, NJ USA), act by inhibiting the Na–K–2Cl symporter in the thick ascending limb of the loop of Henle. By inhibiting the transporter, loop diuretics reduce the reabsorption of NaCl and thus water, and also promote K^+ excretion. As a result, treatment with a loop diuretic causes hypokalemia and can cause metabolic alkalosis by inducing volume depletion. Volume depletion 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. Hypoaldosteronism would have the opposite effect. Loop 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.

37. The answer is b. (*Barrett, pp 380-381. Kaufman, pp 96-97. Longo, pp 280-284, 288-294.*) 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.

38. The answer is c. (*Kaufman, pp 243-244. Levitzky, pp 172-181. Longo, pp 371-373.*) Anxiety causes hyperventilation, which lowers $Paco_2$ and increases arterial pH, that is, respiratory alkalosis. Because the condition has persisted for several days, there has been adequate time for renal compensation to occur. 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, making choice (**c**) the correct answer over (**d**), which is acute, uncompen-sated respiratory alkalosis. The anion gap is normal in acute and compensated respiratory alkalosis. Choice (**e**) is metabolic alkalosis. Choice (**a**) is metabolic acidosis with respiratory compensation present. Choice (**b**) is an acute, uncompensated respiratory acidosis.

39. The answer is b. (*Barrett, pp 730-734. Levitzky, pp 165-167. Longo, pp 287-288.*) Aerobic metabolism produces 13,000 to 24,000 mmol of volatile acid (CO_2) per day. This yields close to that amount of H^+ ions produced per day via the reaction $CO_2 + H_2O \leftrightarrow H_2CO_3 \leftrightarrow H^+ + HCO_3^-$. The lungs excrete almost all of the CO_2 as it is formed. At the tissues, CO_2 diffuses into the red blood cells, where the enzyme carbonic anhydrase accelerates the above reaction. Non-bicarbonate buffers, primarily hemoglobin, buffer any CO_2 that accumulates in the blood. Phosphate, lactate, and plasma proteins are also non-bicarbonate buffers, but they buffer only a small portion of the volatile acid dissolving in the blood. Bicarbonate is not an effective buffer of volatile acid (from CO_2).

40. The answer is b. (*Kaufman, pp 89-91, 230-233. McPhee and Hammer, pp 598, 608-615, 621-622, 723.*) This patient probably has hyporeninemic hypoaldosteronism (type IV renal tubular acidosis), a disorder characterized by hyperkalemia and metabolic acidosis in association with mild chronic renal insufficiency, as evidenced by the elevate BUN and serum creatinine. The syndrome is thought to be due to impairment of renin secretion by the juxtaglomerular apparatus, associated with underlying renal disease, a common sequel to diabetes. As a result of the decreased renin concentration, mineralocorticoid deficiency occurs. 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 therefore results in a decrease in H^+ secretion, which leads to the production of metabolic acidosis (and hyperkalemia and hyponatremia). Hypoventilation would produce respiratory, not metabolic, acidosis. Hypovolemia causes an increase in aldosterone secretion, which can lead to an increase in H^+

secretion and metabolic alkalosis. Hypocalcemia does not directly affect acid–base balance.

41. The answer is e. (*Barrett, pp 457-461. Kaufman, pp 150-151. Longo, pp 866-868. Widmaier, pp 419, 527.*) The etiology of vitamin B_{12} (cobalamin) deficiency includes vegan diet, ileal resection, tapeworm (*Diphyllobothrium latum*), autoimmune, megaloblastic anemia, inflammation of the terminal ileum (Crohn disease), nitrous oxide, and bacterial overgrowth (vitamin B). The autoimmune cause of vitamin B_{12} deficiency is called pernicious anemia, in which antibodies are made against intrinsic factor and gastric parietal cells, resulting in impaired uptake of vitamin B_{12}. Cobalamin is an essential vitamin found in such foods as liver, fish, and dairy products, and thus vegans may have an inadequate dietary intake of the vitamin.

42. The answer is e. (*Barrett, p 485. Kaufman, p 98. Longo, pp 3093-3095.*) 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 low concentrations present in the diet (1 to 100 nM), transport of the water-soluble 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. The elderly and nursing home residents are particularly at risk for vitamin D deficiency because both the efficiency of vitamin D synthesis in the skin and the absorption of vitamin D from the intestine decline with age. The hypocalcemia and hypophosphatemia that accompany vitamin D deficiency result in osteomalacia, that is, impaired mineralization of bone matrix proteins, which increases skeletal fractures, a major contributor to mortality in the elderly.

43. The answer is d. (*Kaufman, pp 240-241. Levitzky, p 178. Longo, pp 366-367.*) Alcoholic ketoacidosis is associated with a high anion gap metabolic acidosis with a compensatory rise in alveolar ventilation, which lowers the arterial P_{CO_2}.

44. The answer is b. (*Kaufman, pp 63-65, 250-251. Le, pp 302-303.*) Hyperkalemia is frequently observed in patients with uncontrolled diabetic ketoacidosis. The hyperosmotic extracellular fluid draws water out of cells and K^+ follows the water by solvent drag. In addition, the lack of insulin decreases the ability of K^+ to enter cells. The normal compensation for metabolic acidosis is hyperventilation and decreased P_{CO_2}.

45. The answer is b. (*Kaufman, pp 231-232. Le, p 487. Longo, pp 355-359, e15-1-e15-3.*) 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.

46. The answer is b. (*Barrett, pp 647-648. Kaufman, pp 243-244. Le, pp 487-488. Levitzky, pp 175-180. Longo, pp 363, 369-371.*) The patient likely has a viral gastroenteritis with metabolic alkalosis (high bicarbonate, high pH) due to a loss of HCl from vomiting. There is also a higher than normal arterial P_{CO_2} (>45 mm Hg) produced by respiratory compensation for the alkalemia. The orthostatic blood pressure changes are indicative of volume depletion, which is a hallmark of saline-sensitive metabolic alkalosis.

47. The answer is a. (*Barrett, pp 649-651. Levitzky, pp 234-240.*) 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 P_{O_2} leads to a decrease in arterial P_{O_2}, a condition classified as hypoxic hypoxia or hypoxemia. Hypoxemia stimulates the peripheral chemoreceptors to increase ventilation, causing arterial P_{CO_2} to decrease and arterial pH to rise (respiratory alkalosis). After 72 hours, renal compensation for the respiratory alkalosis causes a decrease in renal H^+ excretion, which lowers plasma bicarbonate concentration.

48. The answer is e. (*Kaufman, pp 250-251. Longo, pp 343-344, 355-359.*) Hyperkalemia can result from an increased K^+ load, decreased K^+ excretion, or shift of K^+ from the intra- to the extracellular fluid. Volume depletion decreases distal tubular flow and NaCl delivery to the distal tubule, which decreases K^+ excretion, leading to hyperkalemia. Metabolic acidosis, insulin administration, and elevated epinephrine levels from stimulation of the adrenal medulla all promote the movement of K^+ into cells, and thus hypokalemia. Diuretic therapy may be associated with hypokalemia as a result of increased K^+ excretion, though K^+-sparing agents may maintain normokalemia. The most common cause of elevated potassium in laboratory 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.

49. The answer is b. (*Barrett, p 700. Kaufman, pp 299-300. Le, p 223.*) Arginine vasopressin, also known as 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 central nervous system disorders (head trauma, stroke, and encephalitis) and pulmonary disease (tuberculosis and pneumonia), ectopic ADH production by malignant tumors (paraneoplastic syndrome), and drug-induced stimulation of the hypothalamic–pituitary axis (vincristine, carbamazepine, and chlorprop-amide). Patients with SIADH usually improve with fluid restriction.

50. The answer is e. (*Barrett, pp 104-105. Kaufman, pp 283-284. Le, pp 487-488. Longo, pp 361-362, 3112-3114.*) 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 P_{aCO_2} of 30 mm Hg and a P_{aCO_2} of 15 mm Hg are consistent with respiratory alkalosis, only the combination of a P_{aCO_2} of 20 mm Hg and an HCO_3^- of 20 mM produces an alkaline pH (7.6). The combination of a P_{aCO_2} of 30 mm Hg and an HCO_3^- of 15 mM is metabolic acidosis.

51. The answer is b. (*Kaufman, pp 68-69, 239-242. Le, pp 303, 487-488. Longo, pp 363-366.*) In untreated type 1 diabetes mellitus, the generation of ketoacids

produces 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 Pa_{CO_2} and also dissolved CO_2 and returns the pH toward the normal range. The body does not overcompensate for an acid–base disturbance, and thus compensatory hyperventilation for metabolic acidosis would not increase pH above 7.4. 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 with a normal value of approximately 12 mEq/L is consistent with an increase in ketoacids, that is, acetoacetic acid and β-hydroxybutyric acid, in a diabetic patient.

52. The answer is a. (*Levitzky, pp 172-181.*) During the early stages of an asthmatic attack, patients often hyperventilate, producing a decrease in arterial CO_2 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 c. (*Barrett, pp 647-651. Le, p 552. Levitzky, pp 234-239.*) Hypoxemia at high altitude stimulates the peripheral chemoreceptors to increase ventilation, causing arterial P_{CO_2} 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. (*Barrett, pp 643-644. Le, pp 547-548. Levitzky, pp 145-155.*) Bank blood is low in 2,3-bisphosphoglycerate, which results in a higher affinity of hemoglobin for oxygen and a shift in the oxyhemoglobin dissociation curve to the left. An increase in body temperature or an increase in Pa_{CO_2} resulting from hypoventilation shifts the oxyhemoglobin dissociation to the right. During exercise, there is an increase in muscle temperature, carbon dioxide, and H^+, all of which shift the oxy-hemoglobin curve to the right and enhance oxygen release to the tissues. Although carbon monoxide shifts the curve to the left, the oxygen content (mL O_2/100 mL blood) would be less than normal because of a lower than normal % O_2 saturation.

55. The answer is d. (*Barrett, pp 631-632. Le, p 555. 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 approximately 75% of which is dipalmitoylphosphatidylcholine. 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 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 of the newborn, also known as hyaline membrane disease.

56. The answer is c. (*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 P_{O_2} remains low at high altitude because of the low inspired and alveolar P_{O_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 d. (*Barrett, p 444. Levitzky, pp 172-177. Longo, pp 372-373.*) The alveolar and arterial P_{CO_2} are determined by the rate of CO_2 production (VCO_2) divided by the rate of alveolar ventilation. Thus, at any given metabolic rate, hyperventilation is by definition a decrease in Pa_{CO_2}. Pregnancy produces hyperventilation because progesterone stimulates the brain stem respiratory centers to increase alveolar ventilation. The compensatory response to metabolic alkalosis is a decrease in alveolar ventilation (increased Pa_{CO_2}). During most levels of exercise, alveolar ventilation increases in proportion to carbon dioxide production such that the arterial P_{CO_2} remains normal; thus, the increased rate of alveolar ventilation in exercise is not hyperventilation, but it has been given a special term, *exercise hyperpnea*. At high altitude, PaO_2 would be lower than normal.

58. The answer is d. (*Barrett, pp 317-318. Widmaier, pp 575-578.*) 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.

Questions

59. A 21-year-old woman presents to her doctor's office indicating that she has been feeling very tired for the past 2 weeks and has recently developed a sore throat and fever. Urine output has been normal. Her temperature is 100.7°F (38.1°C) and blood pressure is 100/70 mm Hg. Lung fields are clear on auscultation, but there are exudates on the pharynx, the posterior cervical nodes are enlarged and tender, and she has splenomegaly. The white blood cell count is 20,000/μL with lymphocytosis and greater than 10% atypical lymphocytes. Rapid antigen testing for gram-negative bacteria is negative and serologic testing shows a positive reaction for heterophile antibody. Based on these findings, which of the following is the most likely diagnosis?

a. β-Hemolytic *Streptococcus* infection
b. Hepatitis B
c. Infectious mononucleosis
d. Influenza
e. Toxic shock syndrome

60. A 27-year-old African American man who is HIV+ presents with fever, waxing and waning mental status, petechiae, and hematuria. Blood analysis shows thrombocytopenia with normal prothrombin time (PT) and activated partial thromboplastin time (aPTT). Schistocytes are seen on the blood smear. Which of the following is the most likely basis for the pathogenesis of these findings?

a. Abnormal sequestration of platelets in the spleen
b. Decreased activity of the plasma metalloproteinase ADAMTS13
c. Deficiency of von Willebrand factor (vWF)
d. Drug-induced suppression of platelet production
e. Sickle cell anemia comorbidity

61. A 42-year-old patient 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 to prevent coagulation. Which of the following is the mechanism for citrate's anticoagulative action?

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

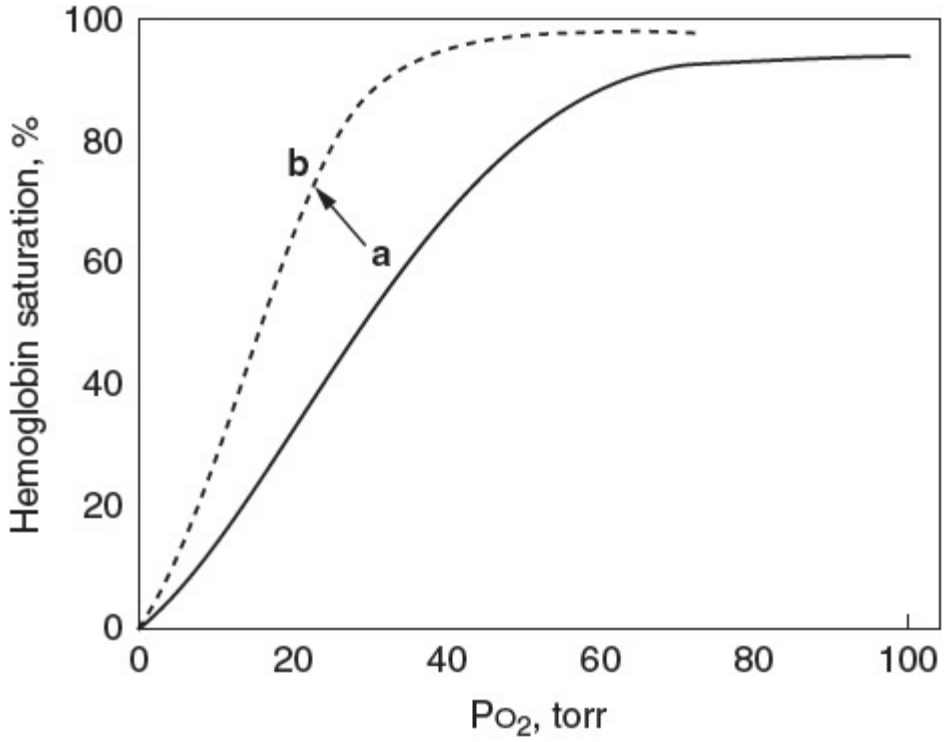
62. Preoperative evaluation of a 56-year-old man scheduled for knee replacement surgery reveals frequent bruising and a family history of a bleeding disorder, but no bleeding problems himself. The patient is found to have a normal PT, increased aPTT, and a Factor VIII activity level of 40%. These findings are indicative of which of the following conditions?

a. Bernard–Soulier syndrome
b. Glanzmann thrombasthenia
c. Hemophilia A
d. Hemophilia B
e. von Willebrand disease

63. A 44-year-old woman with a history of excessive menstrual bleeding and menstrual cycles that generally last over 7 days complains of increasing fatigue and cold extremities. Laboratory results reveal a hemoglobin (Hb) concentration of 6 g/dL. In this patient with anemia, which of the following would be reduced?

a. Arterial PO_2
b. Dissolved oxygen content
c. Oxygen extraction
d. Percent O_2 saturation in the arterial blood
e. Total arterial oxygen content

64. A 48-year-old man presents to the emergency department with chest pain and shortness of breath. His ECG shows ST-segment elevation and cardiac enzymes are elevated. After cardiac catheterization revealed 90% occlusion of his left anterior descending coronary artery, the patient is scheduled for coronary artery bypass graft surgery. During surgery, his oxygen saturation curve shifts from a to b, as shown in the figure below. Which of the following can best account for this shift?



a. A change in P_{CO_2} from 40 to 46 mm Hg
b. A change in pH from 7.4 to 7.3
c. A decrease in core body temperature from 37°C to 32°C
d. An increase in erythrocyte [2,3-bisphosphoglycerate]
e. Transfusion of blood with a higher P_{50} than normal

65. A 24-year-old woman presents to her family physician with intractable hiccups. The patient is instructed to breathe into and out of a bag in order to rebreathe exhaled CO_2. In the blood, the majority of CO_2 is transported as which of the following forms?

a. Bicarbonate
b. Carbaminohemoglobin
c. Carbonic acid
d. Carboxyhemoglobin
e. Dissolved CO_2

66. A 67-year-old woman with a history of venous thromboembolism is placed on warfarin (Coumadin; Bristol-Myers Squibb Company, New York, NY USA) 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?

a. Fibrinogen
b. Platelets
c. Protein C
d. Thrombin
e. Vitamin K

67. A 37-year-old man presents with low exercise tolerance. Blood work shows a normal hematocrit and Hb concentration but a decreased P_{50}. Which would be true of his oxyhemoglobin transport and dissociation?

a. Hb's affinity for oxygen is increased
b. O_2 loading at the alveolar-capillary level is less than normal
c. O_2 saturation is lower than normal at any Pa_{O_2}
d. O_2 unloading is increased at the tissue level
e. The differential diagnosis includes a point mutation resulting in increased binding of H^+ to his Hb chains.

68. A 35-year-old woman presents to her family physician's office with fatigue of at least 3 months' duration. Her only explanation is that keeping up with her twin 4-year-olds really tires her out, and she does not even have enough energy to make nutritious meals for her and her husband. Vital signs and ECG are normal, but a third heart sound is heard with auscultation and she is pale. Blood results are as follows: Hb, 8 g/dL; hematocrit, 30%; MCV, 115 fL; WBC, 8000/µL; platelets, 200,000/µL. A deficiency of which of the following substances can most likely account for these findings?

a. Folate
b. Glucose-6-phosphatase
c. Iron

d. Niacin
e. Zinc

69. A 65-year-old slightly cyanotic man presents to his physician complaining of pruritus and nose bleeds. A blood test reveals a hematocrit of 62%, leading to the diagnosis of polycythemia vera. Treatment includes aspirin to prevent thrombosis and periodic phlebotomy to reduce the hematocrit. The reduction in hematocrit is beneficial because it does which of the following?

a. Decreases cardiac output
b. Increases arterial oxygen content
c. Increases arterial oxygen saturation
d. Reduces blood velocity
e. Reduces blood viscosity

70. A 65-year-old man with chronic bronchitis is admitted to the emergency department with cyanosis and shortness of breath. Arterial and venous blood samples show the following:

Pa_{O_2}	50 mm Hg
Pa_{CO_2}	67 mm Hg
Pv_{O_2}	30 mm Hg
Sa_{O_2}	80%
Sv_{O_2}	50%
Hb	20 g/dL

What do these data reveal about the patient's gas exchange and transport?

a. Arteriovenous oxygen content difference is lower than normal
b. Dissolved CO_2 content in the arterial blood is lower than normal
c. Dissolved O_2 content in the venous blood is higher than normal
d. Oxygen extraction is higher than normal
e. Oxyhemoglobin content in the arterial blood is lower than normal

71. A 23-year-old man with a ruddy complexion presents with chief complaints of headache, dizziness, and lethargy. Blood analysis shows erythrocytosis and a P_{50} of 20 mm Hg. He denies any history of tobacco smoking and is unaware of any other exposure to carbon monoxide or nitrites. Which of the following is a probable cause for these findings?

a. α-Thalassemia-2
b. β-Thalassemia major
c. High-O_2 affinity hemoglobinopathy
d. Low-O_2 affinity hemoglobinopathy
e. Sickle cell trait

72. A 42-year-old woman presents to her doctor's office with heavy menstrual bleeding for up to 2 weeks' duration for each of the past five cycles. She also reports that she has a tendency to bruise easily, and has had several episodes of epistaxis over the past couple of months. Blood analysis shows: Hb, 8 g/dL; hematocrit, 24%; MCV, 70; platelet count, 230,000/μL. Which of the following is a likely cause of her bleeding disorder?

a. Aplastic anemia
b. Hemophilia
c. Nonsteroidal anti-inflammatory drugs
d. Vitamin B_{12} deficiency
e. von Willebrand disease

73. A 26-year-old 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?

a. Affinity of Hb for oxygen
b. Cardiac glycogen content
c. Cardiac output/kg body weight
d. Erythrocyte binding of 2,3-bisphosphoglycerate
e. Hb concentration

74. A 61-year-old man 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 PT of 19 seconds (normal, 11–14 seconds). The bruising and prolonged PT can be explained by a decrease in which of the following

vitamins?

a. A
b. C
c. D
d. E
e. K

75. 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. Kininogen
c. Plasminogen
d. Prothrombin
e. Thrombin

76. A 32-year-old woman presents to the emergency department with a chief complaint of acute shortness of breath and right-sided chest pain, which increases during inspiration. She does not have a cough or fever, and does not have a history of asthma or other respiratory disease. She has not been ill or immobile, but reports having taken oral contraceptives for 8 years until shortly before conceiving her first child about 2 years ago. The family history is notable for her mother who died of a pulmonary embolism. Her respiratory rate is 25 breaths/min and her heart rate is 110 beats/min. Chest x-ray is normal, but a ventilation/perfusion scan reveals a possible pulmonary embolism. Which of the following blood disorders is associated with a hypercoagulable state?

a. Activated protein C resistance
b. Antithrombin III (AT-III) excess
c. Disseminated intravascular coagulation (DIC)
d. Hypoprothrombinemia
e. Idiopathic thrombocytopenic purpura

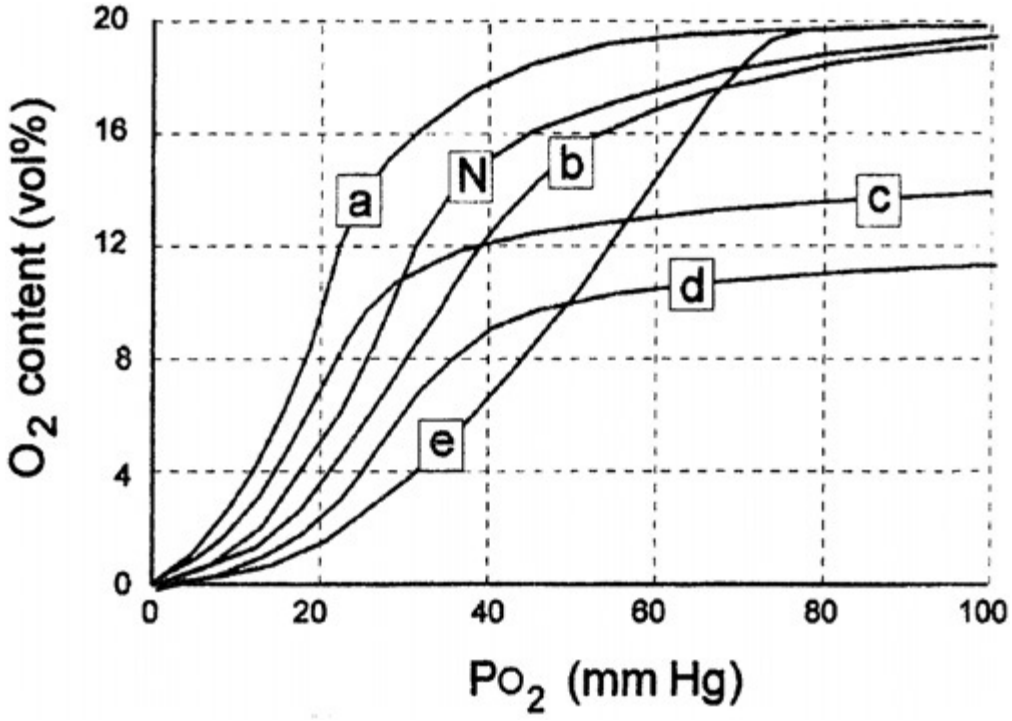
77. A 9-year-old African American boy is brought to the emergency department by his mother who states that he was complaining of muscle aches and pain while playing basketball, which became worse whenever he was running up and down the court. She reports that he was sick with a fever last week, but she thought he was feeling better so she let him go to his summer basketball camp. Blood tests show anemia, increased reticulocyte count, and crescent-shaped cells. Hb electrophoresis confirms the presence of HbS. The primary mechanism for the change in RBC shape during a sickle cell crisis is which of the following?

a. A decrease in erythrocyte volume during dehydration
b. A rightward shift in the oxyhemoglobin dissociation curve of HbS compared with normal
c. Low levels of erythropoietin
d. Polymerization of HbS as it is deoxygenated
e. The presence of antibodies against the red blood cell membrane

78. A 67-year-old man with chronic bronchitis is brought to the emergency department exhibiting labored breathing and cyanosis. The presence of cyanosis is due to which of the following?

a. Decreased O_2 unloading at the tissue capillary level
b. Decreased oxyhemoglobin content in the capillary blood
c. Decreased total arterial oxygen content
d. Increased concentration of deoxygenated Hb
e. Increased hematocrit

79. A 26-year-old pregnant woman is diagnosed with placenta previa, which requires premature delivery of her fetus of 28-week gestation. A blood sample is taken from both the mother and the newborn infant for determination of the oxyhemoglobin saturation curve. If curve N in the figure below is the oxyhemoglobin saturation curve of the mother who has normal HbA, which of the curves is most likely obtained from the premature infant?



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

Physiology of the Hematopoietic and Lymphoreticular Systems

Answers

59. The answer is c. (*Kaufman, pp 156, 204-206, 366. Le, pp 156-157, 568-569. Longo, pp 263, 469, 1467-1471.*) The diagnosis of infectious mononucleosis caused by the Epstein–Barr virus depends primarily on the detection of antibodies to the DNA virus with a heterophile agglutination assay (monospot slide test). Lymphocytosis with atypical lymphocytes is also a common laboratory finding in infectious mononucleosis. Millions visit primary care providers each year complaining of a sore throat. The overwhelming majority of patients with a recent-onset sore throat have acute pharyngitis of viral or bacterial etiology. The signs and symptoms accompanying acute pharyngitis are not reliable predictors of the etiologic agent, but the clinical presentation may be helpful in narrowing the possibilities. The primary goal of diagnostic testing is to separate streptococcal pharyngitis from other etiologies so that antibiotics can be prescribed more efficiently and judiciously.

60. The answer is b. (*Kaufman, p 162. Le, pp 95, 350-352. Longo, pp 965-973.*) The classic pentad of the presentation of thrombotic thrombocytopenic purpura (TTP) are fever, altered mental status, renal dysfunction, thrombocytopenia, and microangiopathic hemolytic anemia, though not all signs and symptoms have to be present. The pathogenesis of TTP is related to a deficiency of, or antibodies to, a plasma metalloproteinase, called ADAMTS13, which cleaves the ultrahigh-molecular-weight multi-mers of vWF produced by endothelial cells into smaller multimers. The ultrahigh-molecular-weight multimers of vWF initiate platelet aggregation and thrombosis. The etiology of TTP is infection (especially HIV and *Escherichia coli* O157:H7), pregnancy, malignancy, autoimmune disorders, and drug induced (antiplatelet agents, chemotherapy agents, contraceptives). TTP is a life-threatening emergency with mortality approaching 90% if left untreated. Plasmapheresis is the mainstay of treatment and transfusion with platelets is contraindicated. Fresh frozen plasma, which contains ADAMTS13, may help. Thrombocytopenia may also be caused by abnormal sequestration of platelets in the spleen or drug-induced suppression of platelet production, but there would be normal RBC morphology (not fragmented cells) in these conditions. A deficiency of vWF impairs hemostasis, but platelet count would be normal. Sickle cell anemia is a type of hemolytic anemia, but the peripheral smear in sickle cell anemia shows sickled erythrocytes, not schistocytes (helmet cells) typical of the microangiopathic hemolytic anemia in TTP or DIC. The presence of schistocytes with macroangiopathic anemia may be found with traumatic hemolysis from prosthetic metal heart valves or aortic stenosis.

61. The answer is e. (*Barrett, pp 542-544.*) 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.

62. The answer is c. (*Kaufman, pp 159-161. Le, pp 348-349, 359-360. Mason, Chapter 230.*) Hemophilia A is a disorder of coagulation caused by a deficiency of Factor VIII and is the most common cause of hemophilia in the United States, affecting 1 in 10,000 males. Hemophilia B is caused by a deficiency of Factor IX and is less common, affecting approximately 1 in 25,000 to 35,000 males. Together, these forms of hemophilia make up about 99% of patients with inherited coagulation factor deficiencies. Hemophilia A and B are clinically indistinguishable from each other, and specific factor testing must be done to identify the specific type of hemophilia. Both hemophilia A and B are X-linked disorders; therefore, this is overwhelmingly a disease of men, with women typically being asymptomatic carriers. A third of new cases of hemophilia A arise from a spontaneous gene mutation. Patients with factor activity levels of 5% to 40% are classified as having mild disease. They will usually bleed only after trauma, and those with factor activity levels of 25% to 50% may never be aware that they have hemophilia, or they might manifest unusual bleeding only after major surgery or severe trauma. Treatment of patients with hemophilia relies on either the replacement of missing factors or, for those who have mild Factor VIII deficiency, administering desmopressin, which is believed to cause release of vWF from endothelial storage sites. The increased amount of vWF is capable of carrying additional amounts of Factor VIII in the plasma. In patients with hemophilia, the PT, which measures the extrinsic coagulation cascade, is normal, whereas the aPTT, which measures the intrinsic coagulation cascade, is usually elevated, though may be normal in mild hemophilia. von Willebrand disease is the most common bleeding disorder, resulting from lack or functional defect of vWF. Bernard–Soulier syndrome (GpIb deficiency) and Glanzmann thrombasthenia (GpIIb/IIIa deficiency) are platelet disorders with impaired thrombogenesis.

63. The answer is e. (*Kaufman, pp 149, 272. Le, pp. 352-357. Levitzky, pp 153-154. Longo, pp 448-456.*) Anemia from chronic blood loss presents most often as iron-deficiency anemia. A reduction of iron stores decreases Hb synthesis. A reduction in the concentration of Hb reduces the oxy-hemoglobin 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 content, and the percent saturation of Hb with oxygen are all normal in anemia.

64. The answer is c. (*Le, pp 547-548. Levitzky, pp 146-152.*) Hypothermia increases Hb's affinity for oxygen, causing the oxyhemoglobin dissociation curve to shift to the left. With a leftward shift, the saturation of Hb with oxygen is greater than normal at any PO_2, as denoted by a lower P_{50} value than normal. Acidosis, hypercapnia (increased P_{CO_2}), and an increase in erythrocyte [2,3-bisphosphoglycerate] all cause rightward shifts of the oxyhemoglobin dissociation curve. Although bank blood has decreased 2,3-bisphosphoglycerate, if the transfused blood has a higher P_{50} than normal, then one would expect no shift or a rightward shift.

65. The answer is a. (*Barrett, pp 644-647.*) CO_2 is transported in arterial blood in three forms: as physically dissolved CO_2 (about 5%), in combination with the amino groups of Hb as carbaminohemoglobin (about 10%), and as bicarbonate ion, that is, 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 Hb.

66. The answer is e. (*Kaufman, p 160. Le, pp 95, 367, 553. Longo, pp 998, 2175.*) Warfarin is a vitamin K antagonist 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.

67. The answer is a. (*Le, p 548. Levitzky, pp 148-156.*) A decreased P_{50} denotes a leftward shift of the oxyhemoglobin dissociation curve and an increase in Hb'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 Hb binds the oxygen more tightly than normal. With a decreased P_{50}, oxygen saturation is higher than normal at any PO_2. Increased H^+ shifts the oxyhemoglobin dissociation curve to the right.

68. The answer is a. (*McPhee and Hammer, pp 119-120. Kaufman, pp 149-153. Le, p 354. Longo, pp 448-456.*) This patient has a macrocytic anemia found with folate or vitamin B_{12} deficiency. Iron-deficiency anemia, the most common type of anemia, and glucose-6-phosphate deficiency, the most common metabolic disorder of red blood cells, are both associated with microcytosis (low MCV). Niacin (vitamin B_3) and zinc deficiencies are causes of malabsorption. Niacin deficiency also presents with pellagra.

69. The answer is e. (*Kaufman, pp 171-172. Le, p 366. Longo, pp 456, 898-900.*) Polycythemia vera is a primary bone marrow disease in which an abnormally large number of red blood cells are produced. 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). Reduction of the red cell mass by phlebotomy is the first principle of therapy in polycythemia vera because it reduces blood viscosity, which removes a major source of complications and may also alleviate systemic hypertension, pruritus, and splenomegaly.

70. The answer is d. (*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 can 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 (PO_2 in mm Hg × 0.003 mL O_2/100 mL blood/mm Hg PO_2) and the oxyhemoglobin content ([Hb] × 1.34 mL O_2/g% Hb × % O_2 saturation). Arterial oxygen content in this patient is therefore 21.6 mL O_2/100 mL blood and venous oxygen content is 13.5 mL O_2/100 mL blood, with the a-v O_2 = 8.1 mL O_2/100 mL blood, compared with a normal value of approximately 5 mL O_2/100 mL blood.

71. The answer is c. (*Le, pp 349, 360, 578. Levitzky, pp 142-156.*) The P_{50} of the oxyhemoglobin curve is the oxygen tension at which half of the Hb is saturated with oxygen. The normal P_{50} of HbA is 27 mm Hg. A decreased P_{50} of 20 mm Hg indicates a higher-than-normal affinity for O_2, such as may occur with a number of inherited variants of Hb. The thalassemia syndromes are inherited disorders of Hb's globin chains. Severity is highly variable, but findings generally include hypochromia and microcytosis with varying degrees of anemia. Persons with sickle cell trait inherit the gene for normal HbA from one parent and the abnormal gene for HbS from the other parent. People with sickle cell trait generally have no manifestations of the disease, but can pass it on to their children.

72. The answer is e. (*Kaufman, pp 148-152. Longo, pp 971-972. McPhee and Hammer, pp 117-121.*) Because platelet count is normal, causes of thrombocytopenia, including aplastic anemia, vitamin B_{12} deficiency, and nonsteroidal anti-inflammatory drugs, can be ruled out, whereas a defect in platelet function is a likely cause of the bleeding disorder. von Willebrand disease is the most common inherited bleeding disorder. Hemophilia A is an X-linked recessive trait leading to a decrease in factor VIII. Females with the trait generally have 50% of the normal amount of the factor with no bleeding problems.

73. The answer is d. (*Barrett, p 559. Levitzky, pp 154-155.*) Fetal Hb (HbF) is chemically different from adult Hb (HbA) 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-bisphosphoglycerate, resulting in an increased affinity for oxygen, and a leftward shift of the oxygen dissociation curve of HbF. The greater affinity of Hb for oxygen is advantageous in the placental exchange of O_2 from maternal blood (Pao_2 = 100 mm Hg) to fetal blood (Pao_2 = 25 mm Hg). Despite the low arterial PO_2, the fetus is not hypoxic. Oxygen delivery in the fetus is enhanced by a higher Hb concentration than in the adult and a cardiac output that is two to four times higher than in the adult on a milliliter per kilogram basis. The fetal heart is protected by an increased cardiac glycogen content.

74. The answer is e. (*Barrett, pp 492-495. Kaufman, p 386. Le, pp 348, 359.*) Vitamin K denotes a group of lipophilic, hydrophobic vitamins that are essential for maintaining normal clotting of blood. Vitamin K is required for hepatic synthesis of seven proteins involved in blood coagulation (prothrombin [factor II], factors VII, IX, X, proteins C, S, and Z). Vitamin K is involved in the carboxylation of certain glutamate residues in these proteins to form gamma carboxyglutamate (Gla) residues that are involved in calcium binding. Vitamin K_1 (phylloquinone) and vitamin K_2 (menaqui-none) are normally produced by bacteria in the large intestine. Common causes of vitamin K deficiency include cholestasis and factors that limit fat absorption. Dietary deficiency is rare unless there is decreased production by normal flora, as may be seen in broad-spectrum antibiotic use.

75. The answer is c. (*Widmaier, pp 424-427.*) Plasminogen is the inactive precursor of plasmin, the proteolytic enzyme involved in clot dissolution. An infusion of tissue plasminogen activator soon after a heart attack (and possibly a thrombolytic 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 anticlotting agent found on endothelial cell surfaces.

76. The answer is a. (*McPhee and Hammer, pp 117-118, 134-135.*) Activated protein C resistance is the most common inherited hypercoagulable state. Up to 25% of patients who have venous thrombosis without an inciting event are found to have activated protein C resistance. Most of the cases are due to a single DNA base pair mutation in the gene for factor V in the coagulation cascade, known as factor V Leiden. AT-III inhibits the coagulation cascade at a different site than protein C; a deficiency of AT-III results in a hypercoagulable state due to an inability to inactivate factors II, IX, XI, and XII. Hyperprothrombinemia (not hypo) is the second most common cause of hereditary hypercoagulable state and the only one known to cause an overproduction of procoagulant factors, rather than a lack of adequate anticoagulation. DIC is an acquired coagulation defect that results in consumption of coagulation factors I, V, VIII, and XIII, causing bleeding and thrombosis. ITP is another bleeding disorder due to immune-mediated thrombocytopenia of unknown etiology.

77. The answer is d. (*Kaufman, pp 154-156. Le, pp 351, 356, 571. Longo, pp 854-857.*) Persons with sickle cell anemia have a homozygous substitution of valine for glutamine in the sixth position of theβ-hemoglobin chain. During periods of high oxygen consumption, the abnormal HbS polymerizes and distorts the normal shape of red blood cells. The sickled cells cause vaso-occlusion in multiple organs, leading to renal papillary necrosis and hematuria, acute chest syndrome, ischemic retinopathy, and functional asplenism and splenomegaly.

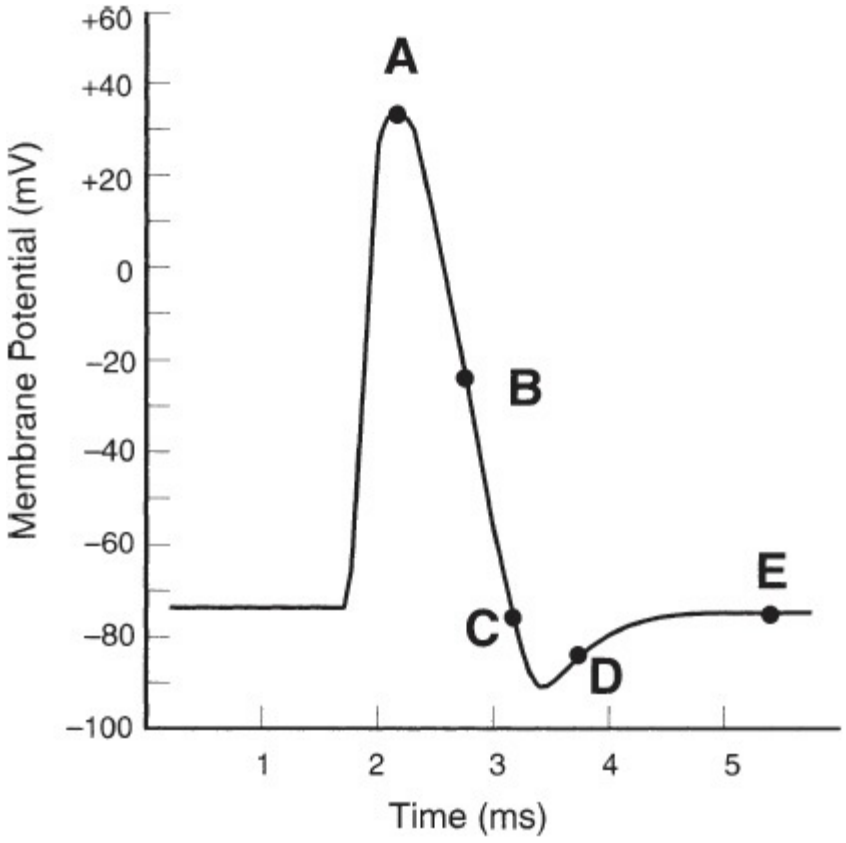
78. The answer is d. (*Le, pp 265, 578. Levitzky, p 156. Longo, pp 288-289.*) Cyanosis refers to a bluish color of the skin and mucous membranes resulting from an

increased concentration of desaturated (deoxygenated) Hb or of methemoglobin or sulfhemoglobin. In general, cyanosis becomes apparent when the concentration of reduced Hb in capillary blood exceeds 4 to 5 g/dL. The degree of cyanosis is modified by the color of the cutaneous pigment and the thickness of the skin, as well as the state of the cutaneous capillaries. For a person with a normal Hb 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 Hb), cyanosis may appear when only one-fourth of the Hb is desaturated (eg, if Hb concentration is 20 g/100 mL). In cyanotic, polycythemic patients, oxy-hemoglobin content and total oxygen content in the arterial and capillary blood are actually higher than normal. Thus, this individual may not be hypoxic. On the other hand, a person with anemia (a lower-than-normal concentration of Hb) may have a significant portion of the Hb desaturated without displaying cyanosis. This individual will not appear cyanotic but may be hypoxic. Hematocrit is usually increased in chronic bronchitis, but the increase in RBCs is not the cause of the cyanosis. Cyanosis may be subdivided into central and peripheral types, with the latter due to slowing of blood and greater extraction of oxygen from normally saturated arterial blood, such as may occur with exposure to cold air or water.

79. The answer is a. (*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 Hb. Normal Hb is 50% saturated at a PO_2 of approximately 27 mm Hg (the P_{50}), 75% saturated at a PO_2 of 40 mm Hg (the normal PO_2 of mixed venous blood), and 98% saturated at a PO_2 of 100 mm Hg (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}. HbA has two α and two β globin chains, whereas HbF has two α chains and two γ chains. The γ chains in HbF do not bind 2,3-bisphosphoglycerate, which results in the higher affinity for oxygen.

Questions

80. At which point on the action potential shown in the figure 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

81. An 82-year-old woman with end-stage renal disease is brought to the emergency department complaining of nausea, vomiting, muscle cramps, and generalized weakness. Laboratory analysis reveals significant hyper-kalemia. Elevations of extracellular potassium ion concentration will have which of the following effects on nerve membranes?

a. The activity of the Na^+–K^+ pump will decrease
b. The membrane potential will become more negative
c. The membrane will become more excitable
d. Potassium conductance will increase
e. Sodium conductance will increase

82. A 16-year-old adolescent boy is brought to the emergency room by ambulance after suffering a concussion during a football game. When he awoke, he was able to understand and follow commands, including repeating language spoken to him, but he had difficulty with spelling, mild word-finding difficulty, and difficulty understanding written language and pictures. His condition is most likely caused by damage to which of the following?

a. Angular gyrus in the categorical hemisphere
b. Arcuate fasciculus connecting Broca and Wernicke areas
c. Broca area in the frontal lobe
d. Hippocampus
e. Wernicke area at the posterior end of the superior temporal gyrus

83. A 13-year-old adolescent boy has no movement in his legs after falling out of a tree. Neurological examination shows the 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?

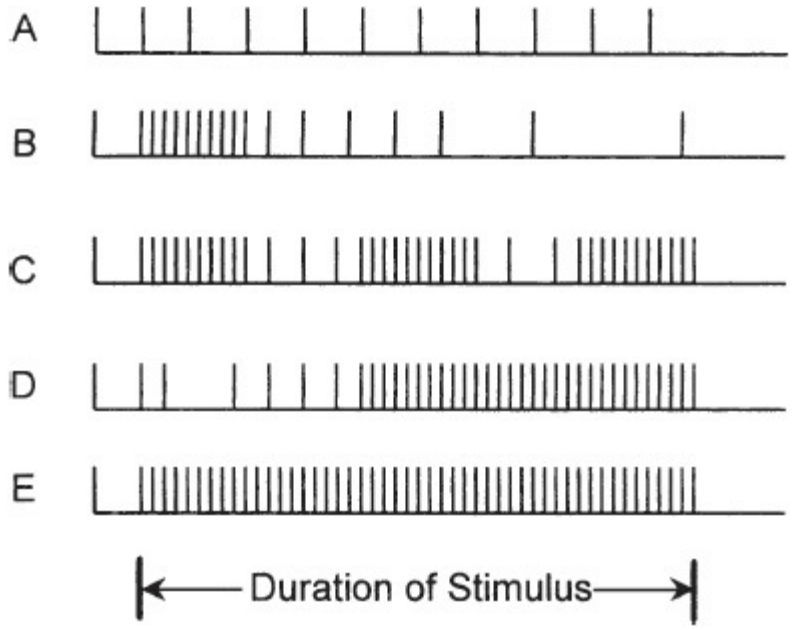
a. Detect the length of resting skeletal muscle
b. Generate activity in Ib afferent fibers
c. Maintain Ia afferent activity during contraction of muscle
d. Prevent muscles from producing too much force

e. Stimulate skeletal muscle fibers to contract

84. 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 a single dose of levodopa. This patient's neurological signs are most likely related to a lesion within which of the following?

a. Caudate nucleus and putamen
b. Cerebellum
c. Hippocampus
d. Premotor area
e. Substantia nigra

85. A 53-year-old man develops loss of pain and temperature sensation in his right leg and loss of proprioception in his left leg (Brown-Séquard syndrome). These symptoms appear 6 weeks following total prostatectomy for prostate cancer. A bone CT scan reveals metastases compressing the patient's left hemicord. His urologist refers him to a neurologist who wishes to confirm normal proprioception in the left leg. Which figure below illustrates the train of action potentials normally seen in a sensory nerve encoding the velocity of limb movement in response to sudden movement?

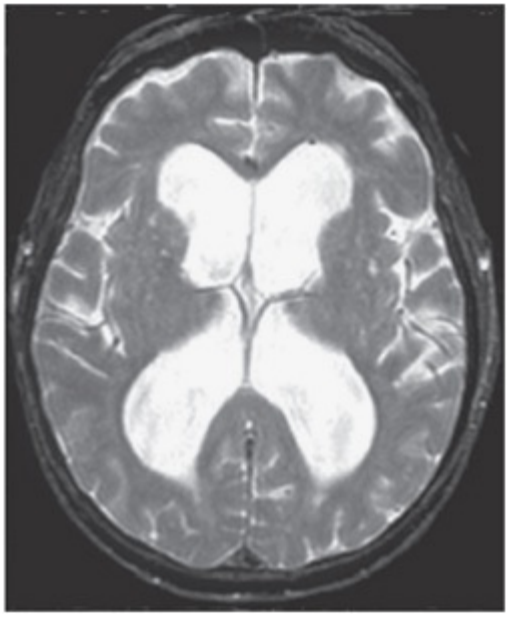


a. A
b. B
c. C
d. D
e. E

86. A 72-year-old man develops selective loss of the large pyramidal cells in the precentral gyrus and degeneration of the corticospinal and corticobulbar projections. Other neuronal systems are spared. He is told that the progression of the disease is variable, and that the worst prognosis is about a 3-year survival. The precentral gyrus and corticospinal and corticobulbar tracts are essential for which of the following?

a. Auditory identification
b. Kinesthesia
c. Olfaction
d. Vision
e. Voluntary movement

87. A 62-year-old woman with a history of multiple head injuries in the past becomes progressively more confused, and develops urinary incontinence and a gait disorder. An MRI of the brain (shown below) and lumbar puncture are performed. Intracranial pressure is found to be within normal limits. The patient's symptoms improved after ventriculoperitoneal shunting. Under normal conditions, which of the following statements correctly describes the cerebrospinal fluid (CSF)?



(MR image from Seeley WW, Miller BL. Dementia. In: Longo DL, Fauci AS, Kasper DL, Hauser SL, Jameson JL, Loscalzo J, eds. *Harrison's Principles of Internal Medicine.* 18th ed. Retrieved October 13, 2012, from http://www.accessmedicine.com/content.aspx?aID=9146233.)

a. It is absorbed into 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

88. A 78-year-old man 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. Basal ganglia
b. Cerebellum
c. Cortical motor strip
d. Eighth cranial nerve
e. Medulla

89. 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. High-amplitude electroencephalogram (EEG) waves
b. Hyperventilation
c. Low frequency EEG waves
d. Periods of loss of skeletal muscle tone
e. Slow but steady heart rate

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

91. 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, 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 infarction most likely affected which of the following?

a. Ia afferent fibers
b. Corticoreticular fibers
c. Corticospinal fibers
d. Reticulospinal fibers

e. Vestibulospinal fibers

92. A 27-year-old patient with a chief complaint of mild vertigo of 3-month 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. Lesion of the flocculonodular lobe of the cerebellum
c. Lesion of the spinocerebellum
d. Ménière syndrome
e. Psychogenic

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

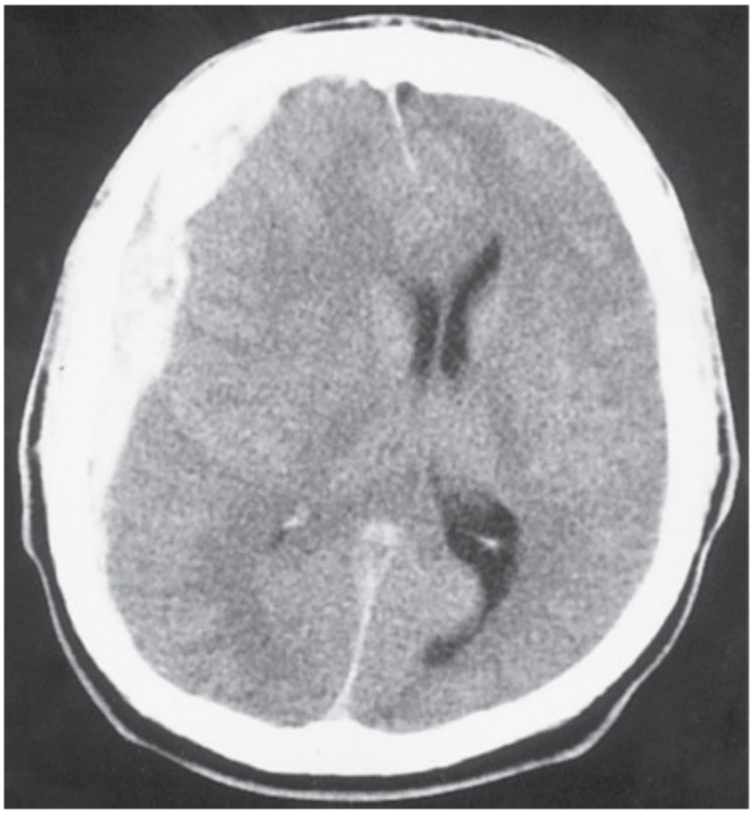
a. It disappears when a patient's eyes open
b. It is associated with deep sleep
c. It is replaced by slower, larger waves during REM sleep
d. It produces 20 to 30 waves per second
e. It represents activity that is most pronounced in the frontal region of the brain

94. A 29-year-old woman presents at the ophthalmologist's office complaining of slowly progressive loss of vision. Based on the visual field defect shown here, the ophthalmologist determines that the patient has a right-sided homonymous hemianopia. She refers the patient to a neurologist who orders a CT scan of the head. The CT scan demonstrates a high-density, space-occupying lesion, which is compressing which area of the brain?

a. Left optic nerve
b. Left optic tract
c. Optic chiasm
d. Right lateral geniculate nucleus
e. Right visual cortex

For Questions 95 and 96

An 84-year-old woman presents to her cardiologist's office complaining of hemiparesis that has worsened over the past 3 days. She is on anticoagulant therapy for atrial fibrillation. A noncontrast CT of the brain is shown below.



(CT image from Longo DL, Fauci AS, Kasper DL, Hauser SL, Jameson JL, Loscalzo J, eds. *Harrison's Principles of Internal Medicine*. 18th ed. New York: The McGraw-Hill Companies, Inc.; 2012, Fig. 378-3. http://www.accessmedicine.com/popup.aspx?aID=9147481.)

95. The CT findings reveal:

a. Amyloid angiopathy
b. Cerebral edema
c. Cerebral infarction
d. Subarachnoid hemorrhage
e. Subdural hematoma

96. On physical examination, stroking the plantar surface of her foot produces a reflex extension of the large toe rather than the expected flexion, which indicates damage to which of the following?

a. Basal ganglia
b. Brain stem
c. Cerebellum
d. Lower motoneurons
e. Upper motoneurons

97. A 59-year-old woman with an inherited neurodegenerative disease 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. Within which of the following areas of the brain the neuronal degeneration results in this presentation?

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

98. A 22-year-old woman presents at the student medical center with tachycardia and palpitations. She reports that she has been taking a diet supplement containing ephedrine that she purchased from an Internet site. Activation of the sympathetic nervous system by ephedrine causes smooth muscle contraction in which of the following?

a. Arterioles
b. Bronchioles
c. Ciliary bodies
d. Intestines
e. Pupils

99. A 27-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 structures?

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

100. An 86-year-old woman develops unilateral vesicular eruption on the trunk in a T_8 dermatomal pattern. 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. Krause ending
b. Meissner corpuscle
c. Merkel disk
d. Pacinian corpuscle
e. Ruffini ending

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 nuclei?

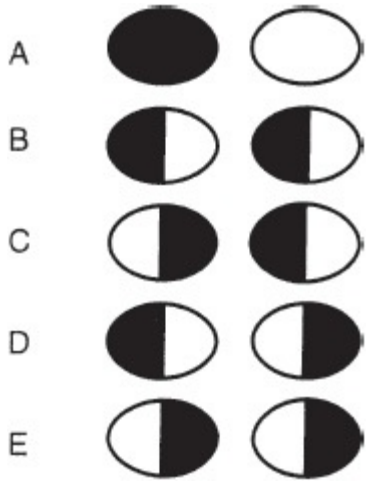
a. Arcuate
b. Lateral
c. Paraventricular
d. Suprachiasmatic
e. Ventromedial

102. A 48-year-old woman with multiple sclerosis (MS) and increasing spasticity is treated with an intrathecal infusion of baclofen, a $GABA_B$ agonist that mediates

presynaptic inhibition. Presynaptic inhibition in the central nervous system (CNS) affects the firing rate of α-motoneurons by which of the following mechanisms?

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

103. 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 an enlarged pituitary gland. She is 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

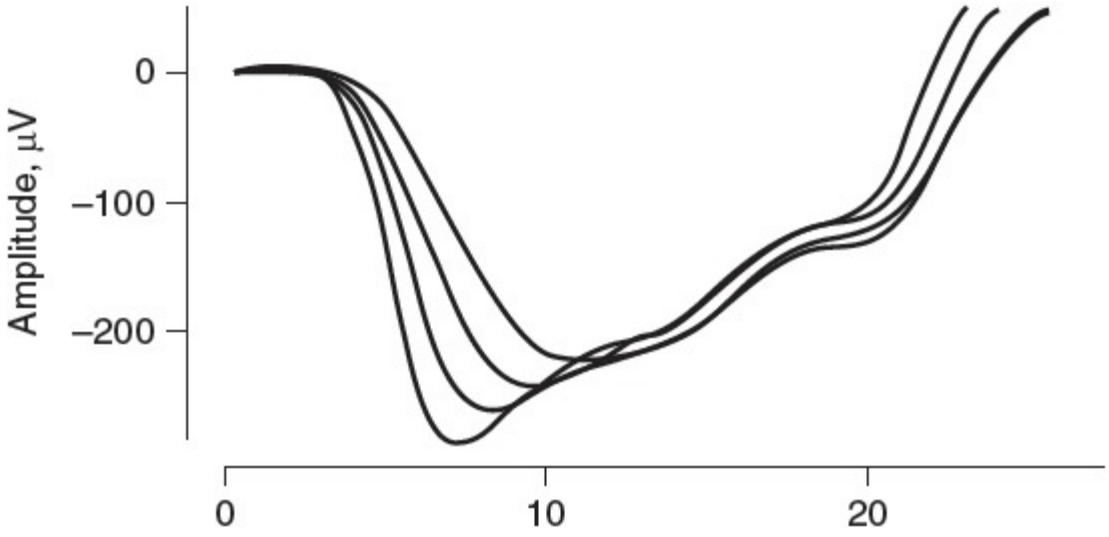
104. A 24-year-old man complains of fatigue, increased daytime somnolence, and periodic sudden loss of muscle tone. Polysomnography confirms the diagnosis of narcolepsy. Narcolepsy is associated with which of the following?

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

105. 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 102.2°F (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. Anterior hypothalamus
b. Arcuate nucleus
c. Lateral hypothalamus
d. Paraventricular nucleus
e. Posterior nucleus

106. A medical student is working in a sensory physiology laboratory during the summer after her first year. She is responsible for conducting electrophysiologic recordings from several types of sensory receptor cells. The intracellular recordings shown in the figure below were obtained from receptor cells in response to a specific stimulus. From which of the following sensory receptors were these recordings obtained?



(Photoreceptor recording from http://www.masseyeandear.org/research/ophthalmology/vision-research-landing-page/retina/retinal-function/).

a. Auditory receptors
b. Photoreceptors
c. Smell receptors
d. Taste receptors
e. Touch receptors

107. 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. Ischemic pain is associated with which of the following?

a. A beta (Aβ) sensory fibers
b. Afferent pathway in the neospinothalamic tract
c. Overstimulation of somatic touch receptors
d. Rapidly adapting receptors
e. Sensory fibers terminating within the substantia gelatinosa of the dorsal horn of the spinal cord

108. A 42-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. Ciliary body
b. Extraocular muscles
c. Iris
d. Pupils
e. Suspensory ligaments

109. 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. Amplifying sounds
b. Enhancing frequency discrimination
c. Filtering high-frequency sounds
d. Localizing sound
e. Protecting the ear from load sounds

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

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

112. A 27-year-old man with severe epilepsy, characterized by major convulsions and lapses of consciousness every few minutes, underwent experimental neurosurgery to help relieve his seizures. The operation had a significant, beneficial effect on the epilepsy, but led to a devastating memory deficit. He had normal procedural memory, maintained long-term memory for events that occurred prior to surgery, and his short-term memory was intact, but he could not commit new events to long-term memory (loss of declarative memory). Which of the following areas of the brain was bilaterally resected in this patient?

a. Cerebral cortex
b. Cingulate gyrus
c. Hypothalamus
d. Parietal lobe
e. Temporal lobe

113. A 68-year-old man with avitaminosis A presents with a chief complaint of night blindness (nyctalopia). Which of the following reactions in the retinal rods is caused directly by the absorption of light energy?

a. Decomposition of scotopsin
b. Dissociation of scotopsin and metarhodopsin
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 presents at a neurologist's office complaining of dizziness and a problem with his balance. He indicates that in a recent match, he suffered several blows to the ears. Which of the following normally happens when a person slowly rotates toward the right?

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

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

116. An 8-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. Absence of the pupillary response to light
b. Inequality of pupil size
c. Pupillary constriction (miosis)
d. Pupillary dilation (mydriasis)
e. Tonic pupil (slow redilation after exposure to light)

118. A 20-year-old woman 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. Damage to the central gustatory pathways

c. Damage to the gustatory afferent nerves
d. Impaired transport of the tastant to the receptor cells in the taste bud
e. Injury to the taste receptor cells

119. A 52-year-old man has a motor vehicle accident and closed head injury, after which he notes decreased sense of smell. Anosmia after head injury is most likely associated with which of the following?

a. Direct injury to the olfactory bulbs
b. Fractures of the cribriform plate
c. Low Glasgow coma scale
d. Recovery of olfaction over time to baseline
e. Shearing of the olfactory fila as they pass through the cribriform plate

120. A Jewish couple present at the pediatrician's office with concerns about their 6-month-old child. They report that the infant was perfectly fine for the first few months of life, but lately he is very easily startled by noise, he has difficulty swallowing, he can no longer hold his head up, and he had a seizure earlier in the day. On physical examination, the doctor also notes "cherry-red" spots in the child's eyes. These symptoms are due to the accumulation of harmful quantities of which of the following substances in the brain?

a. Beta-amyloid
b. Beta-hexosaminidase A
c. Ganglioside GM2
d. Sphingomyelin
e. Tau protein

121. A 24-year-old male 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. $GABA_A$
b. Glutamate
c. Histamine
d. Neurokinin 1 (NK-1, substance P)
e. Neuropeptide Y

122. 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. Glaucoma
c. Macular degeneration
d. Optic neuritis
e. Retinal detachment

123. 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 tries to stand up, but is unable to walk on the crossed leg, and feels tingling and pain. Which of the following explains the loss of motor function without the loss of pain sensation in the peripheral nerves?

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

124. Three weeks following a gastrointestinal (GI) infection with *Campylobacter jejuni*, a 60-year-old man develops weakness and tingling in his legs. Over the next few days, his legs and face become paralyzed, and he is hospitalized for Guillain–Barré syndrome (GBS). Which of the following is the most likely underlying cause of his motor paralysis?

a. Antibodies against nerve growth factor
b. Antibodies against oligodendrogliocytes
c. Demyelination of Aβ fibers
d. Demyelination of B fibers
e. Demyelination of C fibers

125. A 32-year-old woman from the IT department presents to the employee health clinic late in the afternoon complaining of fatigue, muscular weakness, and double vision. She indicates that the symptoms have been getting worse over the past 2 months and that she gets worse the longer she works at the computer screen. Cranial nerve examination discloses impaired movement of the right eye and bilateral ptosis, which worsen with repetitive eye movements. An MRI of the chest shows enlargement of the thymus gland. The neuropathy of this clinical presentation is most likely caused by antibodies against which of the following?

a. Acetylcholine
b. Acetylcholinesterase
c. Postsynaptic muscarinic acetylcholine receptors
d. Presynaptic nicotinic acetylcholine receptors in autonomic ganglia
e. Postsynaptic nicotinic acetylcholine receptors on the motor end plate

126. A 26-year-old woman presents with unilateral facial weakness. She states that whenever she tries to close her eyes, the upper eyelid on the affected side rolls upward. Electromyography on the affected side shows evidence of axonal degeneration. 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

127. 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 disease can be attributed to a paucity of which of the following neurotransmitters?

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

128. A 62-year-old man 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. Acetylcholine
b. Atropine
c. Curare
d. Dopamine
e. Epinephrine

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

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

130. A 19-year-old woman with a history of diplopia and paresthesia is diagnosed with MS. Immersion of an affected limb in a cold bath restores nerve conduction in many MS 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 amount of sodium entering the nerve with each action potential increases
b. The capacitance of the nerve fiber membrane is increased
c. The duration of the refractory period is increased
d. The potassium conductance of the membrane is increased
e. The membrane potential becomes more positive

131. A 37-year-old woman presents with severe migraine headaches that are accompanied by hemiparalysis. Genetic analysis confirms the suspicion of an inherited channelopathy. The membrane potential will depolarize by the greatest amount if the membrane permeability increases for which of the following ions?

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

132. A 65-year-old postgastrectomy patient presents to his gastroenterologist's office with fatigue, weakness in his legs, and frequent falls over the past several

months. His physical examination demonstrates increased deep tendon reflexes and decreased vibratory sense in his toes. Laboratory analysis reveals megaloblastic anemia and vitamin B_{12} deficiency. Which of the following mechanisms cause the neurological deficits characteristic of vitamin B_{12} deficiency?

a. Decreased folate concentration
b. Decreased myelin synthesis
c. Decreased Na^+–K^+ pump activity
d. Increased hyperphosphorylated microtubule protein tau
e. Production of antinerve antibodies (ANA)

133. A 52-year-old man presents at the oral surgeon's office with an abscessed tooth. Prior to surgery to extract the tooth, the patient is given a shot of procaine. Preventing the inactivation of sodium channels by local anesthetics will decrease which of the following?

a. Downstroke velocity of nerve cell action potentials
b. Duration of nerve cell action potentials
c. Magnitude of the overshoot in nerve cell action potentials
d. Relative refractory period of nerve cells
e. Upstroke velocity of nerve cell action potentials

134. A 13-year-old boy on the junior high wrestling team experienced attacks of proximal muscle weakness that lasted 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 on a diet and exercise regime. Genetic testing revealed an inherited channelopathy. Electrically excitable gates are normally involved in which of the following?

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

135. A 58-year-old man with a history of hypertension and renal disease presents at his physician's office with a complaint of headaches. His blood pressure is 190/115 mm Hg and laboratory results show an elevated plasma renin activity with hypernatremia. Which of the following best describes the sodium gradient across the nerve cell membrane?

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

136. A 19-year-old sexually active woman presents with lower abdominal pain for 1 week. Physical examination reveals a temperature of 101°F (38.33°C), tenderness on pelvic examination, 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. Endorphins
c. Serotonin
d. Somatostatin
e. Substance P

137. 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. Contraction of airway smooth muscle
b. Rate of depolarization in the SA node
c. Rate of glycogenolysis in the liver
d. Strength of ventricular muscle contraction
e. Transport of calcium into skeletal muscle fibers

138. A 10-year-old girl with type I diabetes develops a neuropathy of sensory neurons with free nerve endings. As a result, quantitative sensory testing will reveal higher-than-normal thresholds for detection of which of the following stimuli?

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

139. An 85-year-old man is brought to his doctor by his daughter. 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 because of old age or a more serious problem. Which of the following would provide the definitive diagnosis of Alzheimer disease?

a. Cerebral cortical atrophy on CT or MRI
b. Improved symptoms with cholinesterase inhibitors
c. Neuritic plaques containing A-beta (Aβ) amyloid bodies
d. Nonspecific slowing of the EEG
e. Presence of an apolipoprotein ε4 allele on chromosome 19

Answers

80. The answer is a. (*Barrett, pp 88-89.*) 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 does not 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.

81. The answer is d. (*Barrett, pp 88-89. Longo, pp 355-359.*) Because the resting membrane potential is related to the ratio of ICF to ECF K^+ concentration, an increase in extracellular K^+ partially depolarizes the cell membrane, that is, makes the membrane potential more positive. Depolarizing the membrane opens K^+ channels, causing an increase in membrane conductance to potassium. Prolonged depolarization, whether caused by an increase in extracellular K^+ or by an action potential, inactivates Na^+ channels and decreases the excitability of the nerve membrane, which manifests as weakness, and which may progress to flaccid paralysis. The activity of the Na^+–K^+ pump is reduced in hypokalemia, not in hyperkalemia.

82. The answer is a. (*Barrett, p 293. Le, p 420. Longo, pp 202-206.*) 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 he was able to understand and follow commands, but he had difficulty understanding written language and pictures. There may be mild word-finding difficulty with this aphasia as well. Anomic aphasia is the single most common language disturbance seen in head trauma, metabolic encephalopathy, and Alzheimer 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 or Wernicke areas. A lesion in Broca area leads to nonfluent aphasia, and would have resulted in a severe impairment in expressive language. Fluent aphasias are due to lesions in Wernicke 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. Damage to the arcuate fasciculus would be incorrect because the patient was able to verbally repeat language spoken to him.

83. The answer is c. (*Barrett, pp 229-232.*) The γ-motoneurons innervate the intrafusal fibers of the muscle spindle. 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. Golgi tendon organs generate Ib afferents, and prevent excessive force of contraction. Alpha motoneurons cause skeletal muscle contraction.

84. The answer is e. (*Barrett, pp 245-248. Le, pp 234, 416-417, 455-456, 569-571. Longo, pp 3317-3335.*) These findings are consistent with the presence of Parkinson disease, which is characterized by resting tremor rigidity and bradykinesia. It is caused by destruction of the dopa-mine-secreting neurons within the substantia nigra pars compacta. 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 disease, cerebellar disease is characterized by an intention tremor. In contrast to damage to the nigrostriatal dopaminergic system in Parkinson disease, Huntington disease results in a loss of the intrastriatal GABAergic and cholinergic neurons in the caudate nucleus and putamen of the basal ganglion, and is not responsive to treatment with L-dopa. Hippocampal lesions do not cause Parkinson disease.

85. The answer is b. (*Barrett, pp 229-232. Le, p 430. Longo, pp 191, 3367.*) The Ia afferents, which innervate the muscle spindles, have a phasic and tonic component. **B** illustrates the response of Ia afferents to 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. The patterns of sensory loss are often indicative of the level of nervous system involvement. In the spinal cord, segregation of fiber tracts and the somatotopic arrangement of fibers give rise to distinct patterns of sensory loss. Lesions that involve one-half of the spinal cord lead to loss of proprioception on the ipsilateral side and loss of pain and temperature sensation on the contralateral side. This presentation is called Brown-Séquard syndrome, which may be accompanied by contra-lateral hemiparesis with lesions in the high cervical spinal cord.

86. The answer is e. (*Barrett, pp 236-237. Longo, p 3350.*) 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. Olfaction is processed in the frontal lobe. Cortical localization of visual function is within the occipital lobes, and the optic tracts. Primary lateral sclerosis (PLS) is a rare disorder arising sporadically in midto-late life. PLS is characterized clinically by progressive spastic weakness of the limbs, preceded or followed by spastic dysarthria and dysphagia, indicating combined involvement of corticospinal and corticobulbar tracts. Sensory changes are absent and neither EMG nor muscle biopsy shows denervation.

87. The answer is d. (*Barrett, p 603. Le, p 426. Longo, p 3313.*) The concentrations of glucose and protein within the 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. CSF, 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 (not the epidural space) between the arachnoid mater and pia mater and is absorbed into the circulation by the arachnoid villi. Disturbances in CSF circulation or absorption result in hydrocephalus. Normal pressure hydrocephalus is characterized by dementia, urinary urgency and/or incontinence, and gait changes. It is important to recognize because it may be reversible with a removal of CSF via permanent shunt.

88. The answer is b. (*Barrett, pp 251-252. Le, pp 415, 417. Longo, p 193.*) 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. Lesions in the basal ganglia more commonly present with a resting tremor, such as seen in Parkinson disease. Lesions in the cortical motor strip would cause contralateral hemiparesis. Damage to the eighth (vestibulocochlear) nerve can result in symptoms such as hearing loss, nystagmus, and vertigo. Lesions in the medulla may compromise respiration and other autonomic functions.

89. The answer is d. (*Barrett, pp 274-276. Le, pp 61-62. Longo, pp 213-223.*) In a normal sleep cycle, a person passes through the three stages of non-REM 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 heartbeats and respiration and atonia (loss of muscle tone). Hypoventilation is characteristic of both REM and non-REM sleep because sleep depresses the central chemoreceptors. It is also the state of sleep in which dreaming occurs. High-amplitude EEG waves occur in the late stages of slow-wave sleep. EEG during REM sleep is low amplitude, high frequency.

90 The answer is e. (*Barrett, pp 229-232.*) The Ib afferents innervating the quadriceps muscles are activated when the quadriceps contracts 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.

91. The answer is b. (*Barrett, p 240. Le, p 428. Longo, pp 181-182.*) 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 brain stem. These brain stem fibers are normally inhibited by fibers originating in the cortex. Cutting the corticoreticular fibers releases the brain stem fibers from inhibition and results in spasticity. Cutting the fibers from the reticular formation, vestibular nuclei, or the Ia afferents will reduce the spasticity.

92. The answer is b. (*Barrett, pp 212, 250. Le, p. 446. Longo, pp 4178-4179. Widmaier, pp 219-220.*) 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 vestibulo-ocular reflex, which serves to maintain visual stability during head movement; a lesion of this area of the cerebellum may result in vertigo and nystagmus. In contrast, the spinocerebellum is involved in the coordination of limb movement. Pathologic vertigo is generally classified as peripheral (labyrinthine) or central (brain stem 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. Labyrinthitis and Méniére syndrome are examples of vertigo of peripheral origin. In psychogenic versus organic vertigo, nystagmus is absent during a vertiginous episode.

93. The answer is a. (*Barrett, pp 272-273. Le, p 445. Longo, pp e45-1-e45-3.*) As shown in the EEG below, in a totally relaxed adult with eyes closed, the major component of the EEG will be a regular pattern of 8 to 12 waves per second observed over the posterior (occipital) brain regions, called the α-rhythm or posterior dominant rhythm. The α-rhythm disappears when the eyes are opened. It is most prominent in the 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.

94. The answer is b. (*Barrett, pp 189-191. Le, p 441.*) The loss of vision on the right half of the visual field of both eyes (right-sided homonymous hemianopia) occurs because neurons from the left half of each of the retinas do not reach the visual cortex. This would result from a lesion of the left visual pathway distal to the optic chiasm, that is, the left optic tract, 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.

95. The answer is e. (*Le, p 424. Longo, pp 3290-3299, 3377-3380.*) Intracranial hemorrhage is often discovered on noncontrast CT imaging of the brain, which is preferred over routine MRI because CT is more sensitive for acute blood. Intracranial hemorrhages associated with anticoagulant therapy are often lobar or subdural. The noncontrast CT scan reveals a hyperdense clot that has an irregular border with the brain, characteristic of a subdural hematoma. Edema and infarction are not visible in the CT scan. Amyloid angiopathy is a degenerative disease of intracranial vessels seen in Alzheimer disease, which can cause lobar intracranial hemorrhage. Subarachnoid hemorrhages are produced by trauma and rupture of intracranial aneurysms.

96. The answer is e. (*Barrett, p 240. Le, p 432. Longo, pp 182, 3237.*) The plantar reflex is a cutaneous reflex elicited by stroking the lateral surface of the sole of the foot with a noxious stimulus such as a tongue blade, beginning near the end of the heel and moving across the ball of the foot to the great toe. The normal reflex consists of plantar flexion of the toes. With upper motoneuron lesions above the S1 level of the spinal cord, a paradoxical extension of the toe is observed, associated with fanning and extension of the other toes; this is termed an extensor plantar reflex or the Babinski sign. 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 motoneuron 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).

97. The answer is c. (*Barrett, pp 5245-5246. Le, pp 417, 556. Longo, pp 3330-3331.*) Huntington 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 disease; and those within the limbic system yield emotional disorders.

98. The answer is a. (*Barrett, pp 259-261.*) The catecholamine, norepinephrine (and epinephrine), activates 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 PIP_2 and produces IP_3 and DAG. The IP_3 causes the release of Ca^2 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. Ephedrine is both a direct and indirectly acting sympathomimetic amine. Its direct action to activate postsynaptic α-receptors and β-receptors is weak. Ephedrine's actions are primarily due to its effects as an indirect sympathomimetic, which involves its uptake into the presynaptic nerve terminal, where it is packaged and released with norepinephrine from the sympathetic nerve terminals. The effect of adding

ephedrine is to increase the number of vesicles released during each action potential and possibly to extend the duration of action of norepinephrine by prolonging its inactivation via the neuronal reuptake process. Therefore, the actions of norepinephrine are enhanced in the presence of ephedrine. There are no α-receptors in the bronchioles, pupils, or ciliary smooth muscles in the ciliary body of the eye, so norepinephrine does not cause contraction in these areas, but rather smooth muscle relaxation caused by activation of β-receptors in these tissues. Intestinal smooth muscles have α_2-adrenergic receptor, which mediates relaxation when bound to norepinephrine.

99. The answer is c. (*Barrett, pp 206-207. Longo, pp 248-250.*) 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. (*Barrett, pp 158-160.*) 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.

101. The answer is d. (*Barrett, p 309. Le, p 62. Longo, p 214.*) 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-hour 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 e. (*Barrett, pp 126-127. Widmaier, p 161.)* 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 pre-synaptic 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 d. (*Barrett, pp 189-191. Le, pp 436, 441. Longo, pp 227-228. McPhee and Hammer, pp 157-160. Widmaier, pp 208-210, 227.*) Compression of the optic chiasm by an enlarged pituitary gland, which may be caused by increased synthesis of thyroid-stimulating hormone (TSH) in response to decreased circulating thyroxine, 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. Bitemporal hemianopia resulting from symmetric compression of the optic chiasm may also occur with pituitary adenoma, meningioma, glioma, or aneurysm. Homonymous hemianopia (B or E), in which the loss of vision is on the same half of the visual field of both eyes, results from lesions of the contralateral optic tract. Loss of the medial half of both visual fields (C) is called binasal hemianopia; this visual field defect is uncommon, but may occur in glaucoma, bitemporal retinal disease (eg, retinitis pigmentosa), or a tumor or aneurysm compressing both optic nerves. Total blindness of the left eye (A) would result from a complete lesion of the left optic nerve.

104. The answer is b. (*Barrett, p 276. Le, p 62. Longo, p 220.*) 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.

105. The answer is a. (*Barrett, p 309. Le, p 414.*) 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. The posterior hypothalamus regulates catecholamine secretion. The paraventricular nucleus regulates TSH secretion. The lateral hypothalamus regulates thirst, and the arcuate nucleus exerts neuroendocrine control of prolactin secretion.

106. The answer is b. (*Barrett, pp 182-184.*) The photoreceptors (rods and cones) are unique because they are the only type of sensory cells that are depolarized at rest (ie, in the dark) and hyperpolarized in response to their adequate stimulus (ie, when exposed to light). 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.

107. The answer is e. (*Barrett, p 15 Le, p 428. Longo, pp 93-97.*) Activating nociceptors on the free nerve endings of C fibers produces ischemic pain. The C fibers synapse on interneurons located within the substantia gelatinosa (laminas 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.

108. The answer is a. (*Barrett, p 188. Le, pp 321, 439. Widmaier, pp 204-205.*) The ciliary body contains the ciliary muscle, which changes the shape of the lens when your eyes focus on something, a process called accommodation. 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. Contraction of the ciliary muscle, which causes short-range focus, is mediated by M_3 cholinergic muscarinic receptors, and relaxation of the ciliary muscle, which causes long-range focus, is mediated by β_2-adrenergic receptors. The muscles of the iris control the size of the pupils, and the extraocular muscles control the position of the eye in the socket. Sympathetic activation causes dilation of the pupil (mydriasis) by stimulating α_1-adrenergic receptors, which lead to contraction of the radial muscle in the iris of the eye. Parasympathetic stimulation causes constriction of the pupil (miosis) due to contraction of the circular muscle in the eye mediated by M_3 cholinergic muscarinic

receptors.

109. The answer is a. (*Barrett, p 206. Widmaier, pp 213-215.*) 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 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.

110. The answer is c. (*Barrett, pp 202-203. Widmaier, pp 215-216.*) 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.

111. The answer is b. (*Barrett, pp 211-212, 183-184. Widmaier, p 201.*) 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.

112. The answer is e. (*Barrett, pp 283-285.*) The patient underwent bilateral surgical removal of the amygdala, large portions of the hippocampal formation, and portions of the association area of the temporal cortex. An audio recording by National Public Radio from the 1990s of the patient talking to scientists is available at http://www.npr.org/templates/story/story.php?storyId=7584970. He died in 2008. His case was the first to bring attention to the critical role of the temporal lobes in formation of long-term declarative memories and to implicate this region in the conversion of short- to long-term memories. Later work showed that the hippocampus is the primary structure within the temporal lobe involved in this conversion. Because the patient retained memories from before surgery, his case also shows that the hippocampus is not involved in the storage of declarative memory.

113. The answer is c. (*Barrett, pp 183-184.*) 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 a. (*Barrett, pp 211-212.*) 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 stereo-cilia 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 e. (*Barrett, p 188. Longo, p 224. Widmaier, pp 204-205.*) 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 that presbyopia is caused by ciliary muscle paralysis.

116. The answer is a. (*Barrett, p 184.*) 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 (hyper-polarizes). 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 c. (*Barrett, p 260. Le, pp 233, 439, 449. Widmaier, p 205.*) 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 (eg, 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 c. (*Barrett, p 222. Longo, pp 244-246.*) 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 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 e. (*Longo, p 244.*) "The physiologic basis for most head trauma-related smelling losses is the shearing and subsequent scarring of the olfactory fila as they pass from the nasal cavity into the brain cavity. The cribriform plate does not have to be fractured or show pathology for smell loss to be present. Severity of trauma, as indexed by a poor Glasgow Coma Rating on presentation, and the length of posttraumatic amnesia, is associated with a higher risk of olfactory impairment. Fewer than 10% of posttraumatic anosmic patients recover age-related normal function over time."

120. The answer is c. (*Le, pp 112, 566. http://www.ninds.nih.gov/disorders/taysachs/taysachs.htm. http://www.ninds.nih.gov/disorders/niemann/niemann.htm.*) Tay–Sachs disease is a fatal autosomal recessive lipid storage disorder in which harmful quantities of a fatty substance called ganglioside GM2 build up in tissues and nerve

cells in the brain. The condition is caused by insufficient activity of the enzyme beta-hexosaminidase A, which catalyzes the biodegradation of acidic fatty materials known as gangliosides. Gangliosides are made and biodegraded rapidly in early life as the brain develops. Infants with Tay–Sachs disease appear to develop normally for the first few months of life. Then, as nerve cells become distended with fatty material, a relentless deterioration of mental and physical abilities occurs. The child becomes blind, deaf, and unable to swallow. Muscles begin to atrophy and paralysis sets in. Other neurological symptoms include dementia, seizures, and an increased startle reflex to noise. A much rarer form of the disorder occurs in patients in their 20s and early 30s and is characterized by an unsteady gait and progressive neurological deterioration. Persons with Tay–Sachs also have "cherry-red" spots in their eyes. The incidence of Tay–Sachs is particularly high among people of Eastern European and Ashkenazi Jewish descent. Patients and carriers of Tay–Sachs disease can be identified by a simple blood test that measures beta-hexosaminidase A activity. Both parents must carry the mutated gene in order to have an affected child. In these instances, there is a 25% chance with each pregnancy that the child will be affected with Tay–Sachs disease. Prenatal diagnosis is available if desired. Another inherited lipid storage disease is Niemann–Pick (NP) disease. NP has four types. In types A and B, insufficient activity of the enzyme sphingomyelinase causes the buildup of toxic amounts of sphingomyelin, a fatty substance present in every cell of the body. Types C and D are characterized by a defect that disrupts the transport of cholesterol between brain cells and are caused by a lack of the NPC1 or NPC 2 proteins. Beta-amyloid plaques and neurofibrillary tangles of tau protein accumulate in the brains of patients with Alzheimer disease.

121. The answer is a. (*Barrett, pp 143, 149-151.*) Gamma-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. Gluta-mate is the major excitatory transmitter in the brain. Neuropeptide Y is an excitatory neurotransmitter that has a stimulatory effect on food intake. CNS 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. (*Kaufman, p 348. Le, p 441. Longo, pp 230, 232-235.*) 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 amaurosis fugax. Amaurosis 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 MS. 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.

123. The answer is b. (*Barrett, pp 92-93.*) 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. Aβ 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. Aβ 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.

124. The answer is c. (*Barrett, pp 92-93. Kaufman, pp 343-344. Le, pp 136, 412, 444, 569. Longo, pp 3473-3477.*) GBS is an acute, rapidly evolving inflammatory 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 Aβ 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 *C. jejuni*. A similar proportion is 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 immunosympathectomy. Oligodendrocytes are involved in myelin formation in the CNS, whereas Schwann cells are involved in myelin formation in peripheral nerves.

125. The answer is e. (*Barrett, p 129. Kaufman, pp 318-319. McPhee and Hammer, pp 175-176, 186-187, 701-702. Longo, pp 3480-3485. Widmaier, pp 276-277, 661, 664.*) Myasthenia gravis is an autoimmune disease in which circulating antibodies against the postsynaptic nicotinic acetylcho-line receptors on the motor end plate 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 administration of acetylcholinesterase inhibitors, immunosuppressive agents, and plasmapheresis or intravenous immunoglobulin.

126. The answer is c. (*Barrett, pp 87-92. Longo, pp 3362-3363.*) The conduction velocity of an action potential along an axon is proportional to the axon's diameter for both nonmyelinated and myelinated axons. For any given axon diameter, conduction velocity is greater in myelinated than in nonmyelinated fibers. Propagation via saltatory conduction in myelinated fibers is faster than propagation in nonmyelinated fibers of the same axon diameter because less charge leaks out through the myelin-covered sections of the membrane. Conduction velocities range from about 0.5 m/s for small-diameter unmyelinated fibers to about 100 m/s for large-diameter myelinated fibers. 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. Bell palsy is the most common form of facial paralysis. This idiopathic disorder has a fairly abrupt onset with maximal weakness attained within about 48 hours. MRI may reveal swelling of the geniculate ganglion and facial nerve. If denervation is evident on electromyography indicating axonal degeneration, it can take up to 3 months or longer for regeneration and recovery to occur.

127. The answer is b. (*Barrett, pp 245-248. Le, pp 413, 416-417, 569-571. Longo, pp 3317-3321.*) Parkinson 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 disease. The diagnosis of Parkinson disease can generally be made with at least two of the cardinal signs of parkinsonism, which are resting tremor, paucity and slowness of movement (bradykinesia), rigidity, and postural instability (falls).

128. The answer is b. (*Barrett, p 261.*) 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 down the heart. The bradycardia can be prevented by administering atropine, which blocks the muscarinic receptors on the SA node.

129. The answer is e. (*Barrett, pp 87-89. Kaufman, pp 246-247.*) 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.

130. The answer is a. (*Barrett, pp 87-92. Le, p 444.*) 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 MS, 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.

131. The answer is c. (*Barrett, pp 87-92. Longo, p 3325. Widmaier, pp 142-156.*) When the permeability of a particular ion is increased, the membrane potential moves toward the equilibrium potential for that ion. The equilibrium potential for sodium (+60 mV) is much greater than the resting membrane potential. Thus, increasing the permeability for sodium causes a large depolarization. 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 resting potentials of neurons and the action potentials responsible for impulse conduction are generated by ion currents and ion channels. Disorders of ion channels, that is, channelopathies, are responsible for a growing number of neurologic diseases. Mutations in Na^+, K^+, and Ca^{++} channels that alter ion permeability are associated with migraine and epilepsy.

132. The answer is b. (*Le, pp 93, 354. Longo, pp 3374, 3467. Widmaier, pp 418-419, 527.)* Vitamin B_{12} is necessary for normal neurological function because it is involved in myelin synthesis and repair. Vitamin B_{12} deficiency causes damage to the white matter of the spinal cord and peripheral neuropathy. Treatment consists of vitamin B_{12} administration. Although folate may be an adequate substitute for treatment of the megaloblastic anemia characteristic of vitamin B_{12} deficiency, folate should not be used instead of vitamin B_{12} because the neurological deficits will persist and progress. Vitamin B_{12} does not modulate the sodium/potassium pump. Tau hyper-phosphorylation causes neuritic tangles, as seen in the brains of dementia patients. Vitamin B_{12} or its deficiency does not stimulate formation of ANA.

133. The answer is a. (*Barrett, pp 87-91. Widmaier, p 152.*) 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 down 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.

134. The answer is d. (*Barrett, pp 49, 54. Longo, p 3325.*) 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 sarcoplasmic reticulum 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.

135. The answer is e. (*Barrett, pp 8, 51-53, 87-91. McPhee and Hammer, pp 615-618. Widmaier, pp 100-104.*) 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. Recall that transference is a measure of an ion's relative conductance:

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

where T is the transference and g is the conductance.

136. The answer is e. (*Barrett, p 150. Le, pp 173. Longo, pp 1104-1107.*) 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 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, motoneurons, and sympathetic post-ganglionic 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, both of which are 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.

137. The answer is a. (*Barrett, pp 145-147, 357-358, 447. Longo, pp 2709-2710.*) 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 and activation of protein kinase A.

138. The answer is d. (*Barrett, pp 92-93, 158-160.*) Free nerve endings are small diameter nerves that contain receptors for temperature, pain, and crude touch. 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.

139. The answer is c. (*Kaufman, pp 324-325. Longo, pp 3305-3309. McPhee and Hammer, pp 178-181.*) The presence of an apolipoprotein **ε**4 allele on chromosome 19, especially in the homozygous 4/4 state, is an important risk factor for Alzheimer disease, and cortical atrophy on CT or MRI is a diagnostic sign of Alzheimer disease. Also, cholinesterase inhibitors may be used to improve memory in Alzheimer disease by increasing available levels of acetylcholine. However, the definitive diagnosis of Alzheimer disease 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 disease 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 disease, alcohol dependence, alcoholism, or other drug/medication intoxication.

Questions

140. 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. Laboratory findings include increased creatine phosphokinase, 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. How does repetitive stimulation of a skeletal muscle fiber cause an increase in contractile strength?

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

141. A 62-year-old man presents with a hypokinetic movement disorder characterized by paucity and slowness of voluntary movement (bradykinesia). Which of the following characterizes the order of recruitment during normal voluntary movement?

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

142. A 35-year-old woman having an anxiety attack collapses. The emergency medical technician who arrives on the scene notes that she is hyperventilating and has facial and carpopedal spasms. What causes increased excitability of nerves and muscle membranes that can lead to continuous contraction of skeletal muscle fibers?

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

143. A 32-year-old woman undergoing an appendectomy develops malignant hyperthermia following halothane anesthesia. What changes in skeletal muscle cause body temperature to increase in this condition?

a. An increase in the refractory period of the α-motoneurons
b. Inability of skeletal muscle cells to repolarize
c. Excess calcium release from the SR during muscle contraction
d. Production of endogenous muscle pyrogens
e. Rapid repetitive firing of the presynaptic terminals of α-motoneurons

144. A 47-year-old man 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 demonstrates negative birefringent urate crystals and elevated 24-hour urinary uric acid levels. For maintenance therapy, which of the following agents would be best to treat his condition?

a. Allopurinol
b. Aspirin
c. Colchicine
d. Nonsteroidal anti-inflammatory drugs
e. Uricosurics

145. A 35-year-old woman presents at her ophthalmologist's office with a chief complaint of bilateral drooping eyelids. A complete history reveals that the woman has also been experiencing generalized fatigue and weakness that only improves if she takes frequent naps. The ophthalmologist suspects a synaptogenic basis for the ptosis and refers her to a neurologist. The patient is found to have circulating antibodies to nicotinic acetylcho-line receptors on the motor endplate. A drug is administered that increases the force of muscle contraction but causes bradycardia in the patient. What is the most likely mechanism of action of the drug?

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

146. An 8-year-old girl experiences two to three episodes of proximal muscle weakness a day. The attacks are precipitated by rest following exercise and last 1 to 2 hours. Serum potassium concentration during the attack of weakness is normal. Which of the following is most likely to cause the muscle weakness in periodic hyperkalemic paralysis?

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

147. A 16-year-old adolescent 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 delays the metabolism of fatty acids.
b. Creatine increases muscle glycogen concentration.
c. Creatine increases plasma glucose concentration.
d. Creatine is converted to phosphorylcreatine.
e. Creatine prevents dehydration.

148. An 18-month-old boy presents with delayed dentation, short stature, difficulty and painful walking, and bowing of the legs. The history reveals that he has been breast-fed, but that he has not been receiving daily vitamin D supplementation. A defect in which of the following can explain his findings?

a. Blood supply to the haversian canals
b. Bone formation by osteoblasts
c. Bone resorption by osteoclasts
d. Calcification of the bone matrix
e. Composition of bone collagen

149. A 12-year-old boy 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. Actin to β-dystroglycan
b. Actin to the Z lines
c. β-Dystroglycan to laminin
d. Z lines to M lines
e. Z lines to the sarcolemma

150. A 20-year-old man presents with a 6-month history of lower back pain of insidious onset, as well as morning low back stiffness that lasts several hours. He reports that the pain improves with exercise but not with rest, and often wakens him at night; when it is relieved, he gets up and walks around. A pelvic MRI reveals sacroiliitis with edema in the juxtaarticular bone marrow, synovium, and joint capsule and interosseous ligaments. Which of the following best describes ankylosing spondylitis?

a. Descending progression of endochondral ossification and cartilaginous erosion in the spine.
b. It affects women more than men.
c. Its occurrence is correlated with the histocompatibility antigen, HLA-B27.
d. Peak onset is usually between ages 50 and 60 years.
e. Symptoms worsen with the use of tumor necrosis factor-α (TNF-α) inhibitors.

For Questions 151 and 152, refer to the following case.
A 24-year-old medical student is an avid bodybuilder who lifts weights approximately 2 to 3 hours per day.

151. Which of the following best describes the action potential of skeletal muscle during his workout?

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

152. Which of the following best describes the contractile response of skeletal muscle?

a. More tension is produced when the muscle contracts isometrically than isotonically.
b. Muscle contraction starts after the action potential is over.
c. Muscle length decreases to a greater extent in isometric than in isotonic contractions.
d. Repeated stimulation decreases the magnitude of the muscle contraction.
e. The duration of the action potential exceeds the duration of skeletal muscle contraction.

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

For Questions 154 and 155, refer to the following case.
A 26-year-old male golfer presents with a chief complaint of muscle stiffness, pain, and cramping that occurs when walking uphill, and is worse when he is carrying his golf bag. He has had these symptoms for a while, but attributed them to just being out of shape until he noticed that his urine was burgundy colored following intense exercise.

154. The differential diagnosis includes McArdle disease, which results from a deficiency of which of the following enzymes?

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

155. The patient undergoes a forearm exercise test, and a normal rise in venous lactate is measured. Based on this additional finding, which of the following causes exercise intolerance and myoglobinuria?

a. Carnitine palmitoyltransferase II (CPT II) deficiency
b. Hypokalemic periodic paralysis (HypoKPP)
c. Hypothyroidism
d. Phosphofructokinase deficiency
e. Inclusion body myositis

156. An 87-year-old man presents with acute pain and swelling of the right knee. He is subsequently diagnosed with calcium pyrophosphate dihydrate (CPPD) deposition (pseudogout) after joint aspiration. Which of the following would be expected with CPPD deposition?

a. Aspiration reveals weakly negative birefringent crystals.
b. Rhomboid crystals are not seen in the aspirate.
c. There is decreased production of inorganic pyrophosphate.
d. The knee is the most commonly affected joint.
e. The temporomandibular joint (TMJ) is commonly involved.

157. A 28-year-old man qualifies to run the Boston marathon. He undertakes an endurance training regimen designed to improve marathon performance. Which of the following properties is greater in Type I compared to Type IIb/x skeletal muscle fibers, thereby promoting distance running success?

a. Diameter of the muscle fibers
b. Force of contraction
c. Glycolytic capacity
d. Oxidative capacity
e. Speed of contraction

158. A 26-year-old medical student walks briskly down the hallway to grand rounds while eating a hamburger and fries on the way. What is the major difference in the contractile responses occurring in his smooth versus skeletal muscles?

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

159. A 62-year-old woman presents to her primary care physician with a 2-month history of stiffness and aching in her neck, shoulders, and hips. She is referred to a rheumatologist. After doing a battery of tests, he diagnoses the woman with polymyalgia rheumatica and not fibromyalgia. Which of the following findings is characteristic of polymyalgia rheumatica?

a. Absence of response to prednisone
b. Antibodies to vascular smooth muscle
c. Increased serum creatine kinase (CK) levels
d. Increased erythrocyte sedimentation rate (ESR)
e. Persistent muscle weakness

Musculoskeletal Physiology

Answers

140. The answer is b. (*Barrett, pp 104-105. Kaufman, pp 311, 317-318. Longo, pp 186, 428-429, 3509-3510. Widmaier, pp 265-266.*) Each time a skeletal muscle fiber is stimulated by an α-motoneuron, enough Ca^{2+} is released from its SR 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. The skin findings, along with limitation in rising from a seated position or combing hair, are suggestive of proximal muscle weakness, characteristic of dermatomyositis.

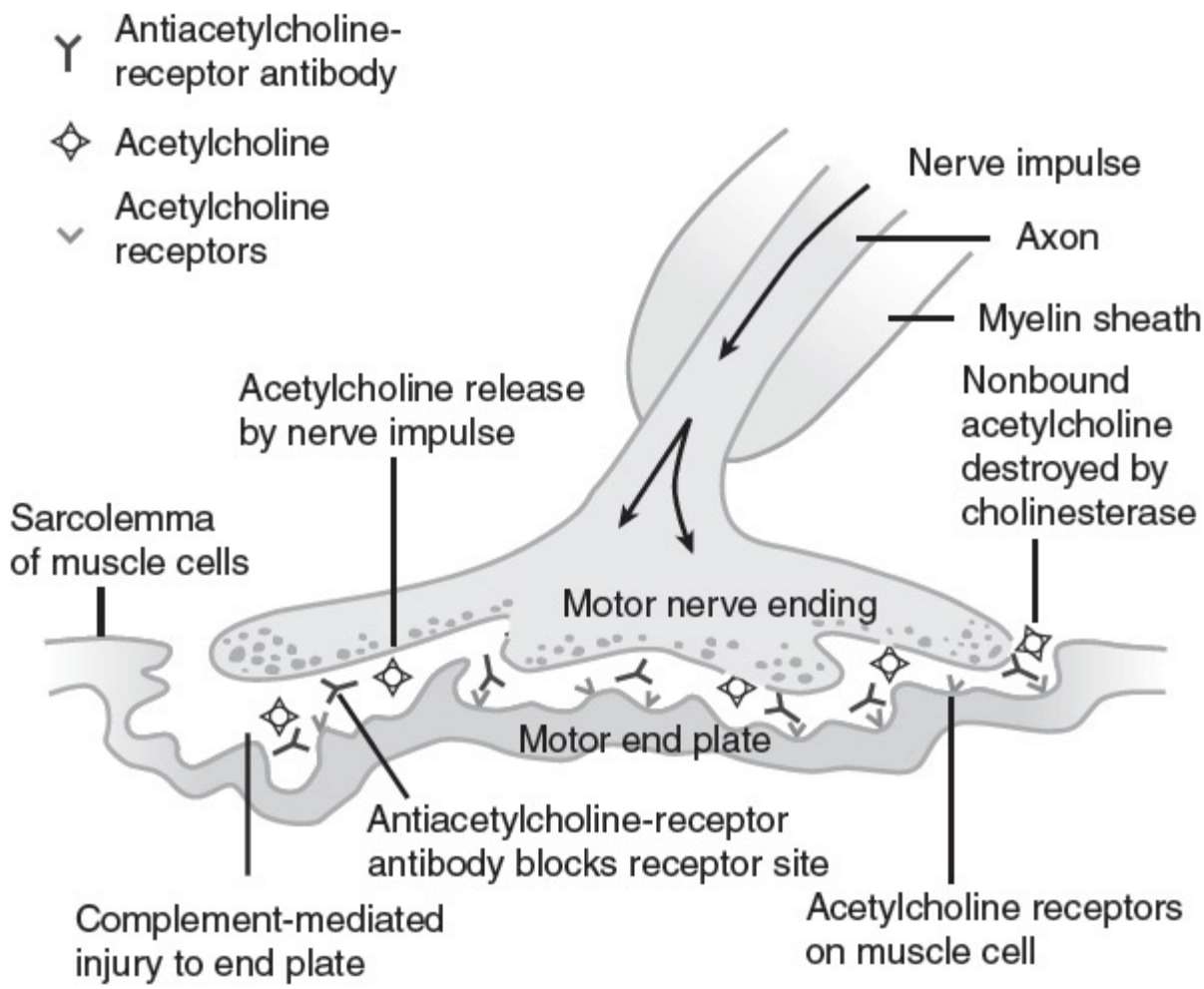
141. The answer is e. (*Barrett, pp 106-109. Widmaier, pp 269-272, 278.*) During most normal reflex or voluntary movements, small spinal moto-neurons are recruited before large motoneurons. In general, small, weak, slow, fatigue-resistant muscle fibers are innervated by small spinal moto-neurons, whereas large spinal motoneurons innervate large, fast, strong, easily fatigable muscle fibers. The slow fatigue-resistant muscle fibers have a dense capillary network for perfusion and use mitochondrial oxidative metabolism to produce adenosine triphosphate (ATP).

142. The answer is c. (*Barrett, pp 88-91, 104-105. Widmaier, pp 265-266.*) 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.

143. The answer is c. (*Barrett, pp 105, 320. Le, pp 279, 453, 455. Longo, pp 144, 147, 525. Widmaier, p 288.*) Malignant hyperthermia is a life-threatening increase in metabolic rate and body temperature attributed to a mutation of the ryanodine receptor in skeletal muscle. The ryanodine receptor, or calcium release channel on the 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.

144. The answer is a. (*Barrett, p 13. Le, pp 391, 406, 569, 572, 574. Kaufman, pp 182, 323-324.*) 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.

145. The answer is b. (*Barrett, pp 105, 127-129. Kaufman, pp 342-343. Le, pp 233, 394. McPhee and Hammer, pp 168-169. Widmaier, pp 276-278, 661.*) Myasthenia gravis is an autoimmune disorder of neuromuscular transmission. The major clinical features are fluctuating fatigue and weakness that improve after a period of rest and after administration of acetylcholinesterase inhibitors. Muscles with small motor units, such as ocular muscles, are most often affected. In severe cases, all muscles are weak, including the diaphragm and intercostal muscles, and death may result from respiratory failure. In 90% of patients, circulating antibodies to the nicotinic acetylcholine receptors on the motor end plate are present. The antibodies block acetylcholine binding and receptor activation (see the following figure).



(Reproduced, with permission, from McPhee SJ, Hammer GD: *Pathophysiology of Disease: An Introduction to Clinical Medicine.* 6th ed: http://www.accessmedicine.com. Copyright © The McGraw-Hill Companies, Inc. All rights reserved.)

In addition, the antibodies cross-link receptor molecules, increasing receptor internalization and degradation. Bound antibody also activates complement-mediated destruction of the postsynaptic region, resulting in simplification of the end plate, characterized by structural abnormalities such as sparse, shallow, and abnormally wide or absent synaptic clefts and a 70% to 90% decrease in the number of receptors per end plate in affected muscles. The number and size of the presynaptic vesicles are normal. Electrophysiologic studies show a decreased response to acetylcholine applied to the postsynaptic membrane. Acetylcholine released at the nerve ending by the nerve impulse normally binds with acetylcholine receptors. This evokes the action potential in the muscle. In myasthenia gravis, antiacetylcholine receptor antibody binds to the acetylcholine receptor and inhibits the action of acetylcholine. Bound antibody evokes immune-mediated destruction of the end plate. Treatment has reduced the mortality rate from approximately 30% to 5% in generalized myasthenia gravis. The two basic strategies for treatment that stem from knowledge of the pathogenesis are to increase the amount of acetylcholine at the neuromuscular junction and to inhibit immune-mediated destruction of acetylcholine receptors. By preventing metabolism of acetylcholine, cholinesterase inhibitors can compensate for the normal decline in released neurotransmitter during repeated stimulation. By increasing the duration of time acetylcholine remains in the synaptic cleft, acetylcholine can bind to the end-plate receptors for a longer time, which increases the magnitude of the end-plate potential and the probability of it generating an action potential. The greater the action potential force rate, the greater the force of muscle contraction. Increasing the amount of acetylcholine released by the α-motoneurons, 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. Decreasing extracellular Ca^{2+} will increase the excitability of skeletal muscle fibers but does not have a direct effect on contractile force.

146. The answer is c. (*Longo, pp 3225, 3504-3506.*) Periodic hyperkalemic paralysis is a disorder of muscle membrane excitability resulting from a sodium channel disorder. 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.

147. The answer is d. (*Barrett, pp 106-107.*) Phosphorylcreatine 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 phosphorylcreatine in muscle may increase the amount of ATP that can be produced and therefore enhance performance.

148. The answer is d. (*Barrett, pp 379-380. Le, pp 94, 294, 387, 575. Longo, pp 602, 3092-3095.*) 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. Although breast feeding is the preferred nutritional source for infants, breast-fed infants require daily vitamin D supplementation. In addition to dietary vitamin D deficiency, 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 $1,25(OH)_2D_3$, which is also usually inherited as an autosomal recessive disorder.

149. The answer is a. (*Barrett, pp 100-101. Le, pp 86, 566, 569. Longo, pp 3491-3494.*) 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 and Becker muscular dystrophy are two types resulting from mutations in the dystrophin gene.

150. The answer is c. (*Kaufman, pp 311, 317-319. Le, pp 194, 392, 406, 570, 578. Longo, pp 135, 2774-2777.*) Ankylosing spondylitis (AS) is a chronic systemic inflammatory disorder of unknown cause that primarily affects the axial skeleton; peripheral joints and extraarticular structures may also be involved. The disease is associated with the HLA-B27 antigen and is seen more commonly in men than in women, usually manifesting between ages 20 and 30. The pathogenesis of AS is incompletely understood, but the response of the disease to blockade of TNF-α indicates that this cytokine plays a major role in the immunopathogenesis. Sacroiliitis is often the earliest manifestation, though acute anterior uveitis, which occurs in ~40% of patients, may antedate the spondylitis. Ascending progression of inflammatory granulation, endochondral ossification, and cartilaginous erosion, often followed by bony ankylosis, leads to the "bamboo spine." Diffuse osteoporosis is seen in the spine as the disease progresses.

151. The answer is e. (*Barrett, pp 101-102. Widmaier, pp 257-259.*) 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 (not uptake) of Ca^{2+} from the lateral sacs of the SR 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.

152. The answer is a. (*Barrett, pp 101-106. Widmaier, pp 254-269.*) 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.

153. The answer is b. (*Barrett, pp 104-105. Le, pp 86, 566. Longo, pp 2682-2683. Widmaier, pp 265-266, 276, 277.*) 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 Mg^{2+} 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.

154. The answer is e. (*Le, pp 111, 566. Longo, pp 3199-3203, 3502.*) In McArdle disease, glycogen accumulates in skeletal muscles because of a deficiency of myophosphorylase (muscle glycogen phosphorylase). Without adequate myophosphorylase, patients cannot break down their muscle glycogen to provide the energy for muscle contraction, except during normal activity or mild exercise. Thus, they have a greatly reduced exercise tolerance. McArdle (type V glycogenosis) is 1 of the 12 types of glycogen storage diseases, all resulting in abnormal glycogen metabolism and an abnormal accumulation of glycogen within cells. Type V glycogen storage disease is an autosomal recessive disorder. It is by far the most common of the glycolytic defects associated with exercise intolerance. The burgundy-colored urine results from myoglobinuria secondary to rhabdomyolysis.

155. The answer is a. (*Longo, pp 3198-3203, 3487-3518.*) The diagnostic evaluation of intermittent weakness subdivides the various disorders into those associated with myoglobinuria or not. If myoglobinuria is present, a forearm exercise test is indicated to measure venous lactate levels. If there is a reduction in lactic acid rise, a glycolytic defect should be considered. If there is a normal lactate rise, that rules out glycolytic deficiencies, such as myophosphorylase or phosphofructokinase deficiency, and suggests a metabolic energy deficiency due to impaired fatty acid utilization, as lipid is an important muscle energy source during rest and prolonged, submaximal exercise. CPT II deficiency is the most common cause of recurrent myoglobinuria, and is more common than the glycolytic defects. Onset is usually in the teenage years or early 20s, and is much more common in men than in women (5:1). The diagnosis requires direct measurement of muscle CPT or genetic testing. Episodic weakness with onset after age 25 is almost never due to HypoKPP, and HypoKPP is not associated with myoglobinuria. Most muscle disorders cause persistent weakness, including polymyositis, dermatomyositis, inclusion body myositis, and most types of muscular dystrophies. Muscle cramps, pain, and stiffness are common in hypothyroidism, but there is no rhabdomyolysis, and thus no myoglobinuria.

156. The answer is d. (*Le, p 391. Longo, pp 2167-2168.*) The knee is the most commonly affected joint in patients with CPPD deposition. The elbow, shoulder, and wrists are also affected, but involvement of the TMJ is rare. There is an increased production of inorganic pyrophosphate, and joint aspiration reveals rhomboid, rod-shaped, or rectangular crystals that are weakly positive in birefringence.

157. The answer is d. (*Barrett, pp 106-107. Widmaier, pp 269-271.*) Skeletal muscle is a heterogeneous tissue made up of three different fiber types—Type I (slow-twitch, slow oxidative, red), Type IIa (intermediate, fast-twitch, fast oxidative glycolytic, white), and Type IIb/x (fast-twitch, fast glycolytic, white). Other properties of Type I compared with Type II fiber types are smaller diameter, less fatigability, decreased force of contraction, and decreased speed of contraction.

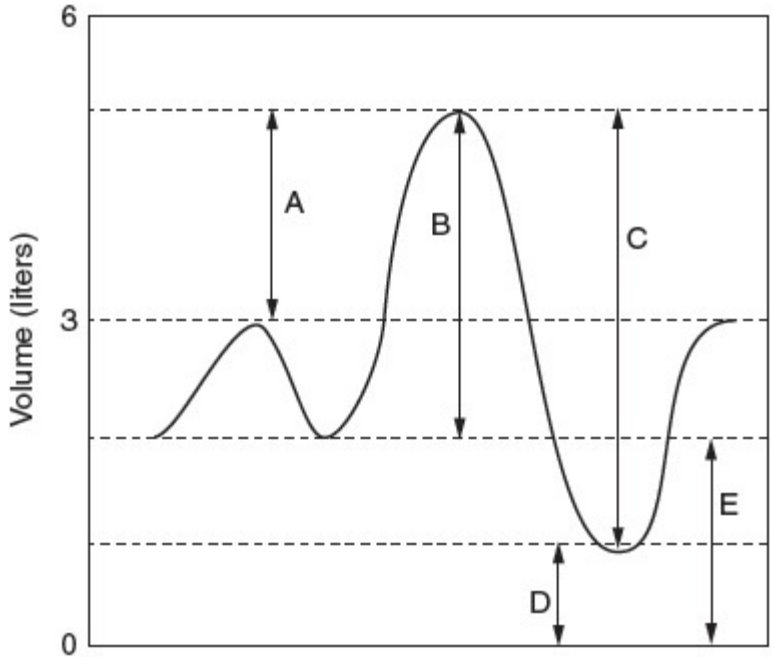
158. The answer is c. (*Barrett, pp 97-110, 114-117. Widmaier, pp 250-285.*) The greatest difference in excitation–contraction coupling between skeletal muscle and smooth muscle involves the role of calcium in initiating contraction. In smooth muscle, calcium binds to and activates calmodulin, which, by activating myosin light chain kinase, catalyzes the phosphorylation of the 20,000-Da myosin light chain. 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 muscles, 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.

159. The answer is d. (*Le, pp 393, 580. Longo, pp 2795-2796, 3489.*) Polymyalgia rheumatica is almost always seen in patients older than 50 years and can be seen in isolation or in patients with giant cell arteritis. CK levels are not increased with the disease, and while patients may have stiffness and pain, muscle weakness is not seen and electromyography and muscle biopsy are normal. The characteristic laboratory finding in polymyalgia rheumatica is an elevated ESR. There is generally a prompt therapeutic response to low-dose prednisone.

Questions

160. A healthy 30-year-old woman is referred for a life insurance physical exam. History reveals that she has never smoked and vesicular breath sounds are heard at the periphery of the lung with auscultation. In the patient's spirometry tracing below, the expiratory reserve volume (ERV) equals which of the following?



a. C
b. D
c. E
d. C + D
e. E – D

161. A group of third-year medical students accompanied a medical mission team to Peru, South America. After arriving at the airport in Bolivia, they hiked to a remote mountain village in the Andes at an elevation of 18,000 ft. With a barometric pressure of 380 mm Hg at this altitude, what would be the resulting P_{O_2} of the dry inspired air?

a. 160 mm Hg
b. 100 mm Hg
c. 80 mm Hg
d. 70 mm Hg
e. 38 mm Hg

162. 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 the first-year resident obtains an arterial blood sample from the patient, the glass plunger slides back, drawing an air bubble into the syringe before it is handed to the blood gas technician for analysis. How does exposure to room air affect the measured values of P_{O_2} and P_{CO_2} in arterial blood?

a. The measured values of both Pa_{O_2} and Pa_{CO_2} will be higher than the patient's actual values.
b. The measured values of both Pa_{O_2} and Pa_{CO_2} will be lower than the patient's actual values.
c. The measured Pa_{O_2} will be higher and the measured Pa_{CO_2} will be lower than the patient's actual blood gas values.
d. The measured Pa_{O_2} will be lower and the measured Pa_{CO_2} will be higher than the patient's actual blood gas values.
e. The measured values of Pa_{O_2} and Pa_{CO_2} will accurately reflect the actual values.

163. A 68-year-old woman with pulmonary fibrosis presents with a complaint of increasing dyspnea while performing activities of daily living. She is referred for pulmonary function testing to assess the progression of her disease. Which of the following laboratory values is consistent with her diagnosis?

a. Decreased diffusing capacity of the lung
b. Increased residual volume
c. Decreased forced expiratory volume exhaled in 1 second (FEV_1)/forced vital capacity (FVC)
d. Increased lung compliance
e. Increased airway resistance corrected for lung volume

164. A 34-year-old woman presents in the emergency department with tachypnea and shortness of breath of acute onset. The history reveals that she has been taking oral contraceptives for 9 years. A lung scan demonstrates a perfusion defect in the left lower lobe. Which of the following occurs if the blood flow to alveolar units is totally obstructed by a pulmonary thromboembolism?

a. The $\dot{V}/\dot{Q}$ 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 dead space.

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

Tidal volume = 600 mL
Respiratory rate = 12/min
Vital capacity = 5000 mL
P_{aO_2} = 90 mm Hg
P_{aCO_2} = 40 mm Hg
P_ECO_2 = 28 mm Hg

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

a. 0.3 mL

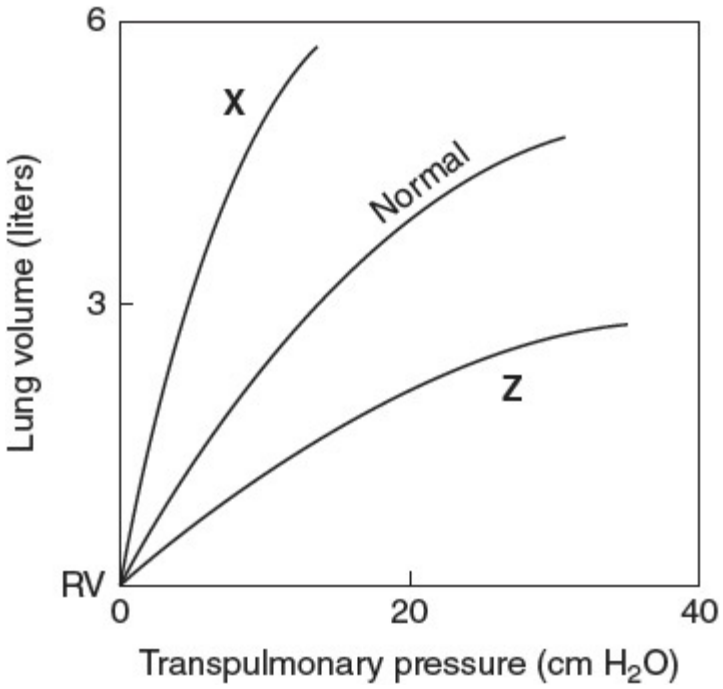
b. 150 mL

c. 180 mL

d. 420 mL

e. 7200 mL

166. 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. Asthma

b. Emphysema

c. Dyspnea with aging

d. Newborn with lecithin to sphingomyelin (L/S) ratio greater than 2

e. Pulmonary edema

167. A 6′3″ tall, 140-lb, 20-year-old man 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. The physical exam revealed decreased tactile fremitus, hyperresonance, and diminished breath sounds. A chest x-ray revealed a 55% pneumothorax of the right lung, which was attributed to rupture of a bleb on the surface of the lung. What changes in lung function occur as a result of a pneumothorax?

a. The chest wall on the affected side recoils inward.

b. The intrapleural pressure in the affected area equals to atmospheric pressure.

c. The trachea deviates away from the affected lung.

d. There is hyperinflation of the affected lung.

e. The $\dot{V}/\dot{Q}$ ratio on the affected side increases above normal.

168. An insulation worker presents with a chief complaint of dyspnea on exertion. Pulmonary function test is consistent with a restrictive impairment. His arterial P_{O_2} is normal at rest but hypoxemic during exercise stress testing. Which of the following is the most likely explanation for the decline in the patient's P_{aO_2} during exercise compared with rest?

a. A decreased partial pressure gradient for O_2 diffusion during exercise
b. A decreased surface area for diffusion during exercise
c. An increase in hemoglobin's affinity for O_2 during exercise resulting in more oxygen being transported as oxyhemoglobin and less in the dissolved state
d. An increased uptake of oxygen from the blood by exercising skeletal muscles
e. An underlying diffusion impairment coupled with a decrease in pulmonary capillary transit time during exercise

169. 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 FIO_2 of 40%, a control rate of 15 breaths per minute, 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

170. A 26-year-old man training for a marathon reaches a workload that exceeds his anaerobic threshold. If he continues running at or above this workload, which of the following will increase?

a. Alveolar ventilation
b. Arterial pH
c. P_{aCO_2}
d. Plasma $[HCO_3^-]$
e. Firing of the central chemoreceptors

171. A medical student waiting for her first patient interview at the clinical skills center becomes very anxious and increases her rate of alveolar ventilation. If her rate of CO_2 production remains constant, which of the following will decrease?

a. pH
b. P_{aO_2}
c. P_{aCO_2}
d. $\dot{V}/\dot{Q}$
e. Alveolar–arterial P_{O_2} difference

172. 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 FIO_2 of 1.0. An arterial blood sample taken 20 minutes later reveals a P_{O_2} of 350 mm Hg, a P_{CO_2} of 36 mm Hg, and a pH of 7.32. At a barometric pressure of 757 mm Hg, 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 mm Hg
b. 355 mm Hg
c. 576 mm Hg
d. 665 mm Hg
e. 712 mm Hg

173. A 58-year-old woman experiences an acute exacerbation of asthma, which causes her breathing to become labored and faster. As a result, which of the following changes in airflow is expected?

a. Flow in the trachea and upper airways will become more laminar.
b. The pressure gradient required for airflow will increase.
c. The resistance to airflow will decrease.
d. The resistance to airflow will increase linearly with the decrease in airway radius.
e. Reynolds number will decrease.

174. A 27-year-old woman at 30 weeks of gestation goes to the obstetrician for a prenatal visit. During the visit, she expresses concern that she has been breathing faster than usual. Lab results revealed the following:

Pa_{O_2} = 105 mm Hg	Tidal volume = 480 mL
Pa_{CO_2} = 30 mm Hg	Respiratory rate = 30 breaths/min
pH = 7.47	R = 0.8
$[HCO_3^-]$ = 20 mEq/L	[Hb] = 12 g%
$P_{E}CO_2$ = 18 mm Hg	Anion gap = 12 mEq/L

Based on the data, what conclusions can you draw about the level of the patient's alveolar ventilation?

a. Alveolar ventilation exceeds her minute ventilation.

b. Alveolar ventilation is inadequate due to rapid, shallow breathing.

c. Alveolar ventilation is less than her dead space ventilation.

d. Alveolar ventilation matches the increased CO_2 production during pregnancy.

e. Alveolar ventilation is greater than normal.

175. A newborn of 28 weeks of gestation develops respiratory distress syndrome. Mechanical ventilation on 100% O_2 with 10 cm H_2O of positive end-expiratory pressure (PEEP) does not provide sufficient oxygenation. After porcine surfactant is instilled via a fiberoptic bronchoscope, the Pa_{CO_2}, fraction of inspired oxygen (FIO_2), and shunting improve impressively. The improvements in respiratory function occurred because surfactant increased which of the following?

a. Alveolar surface tension

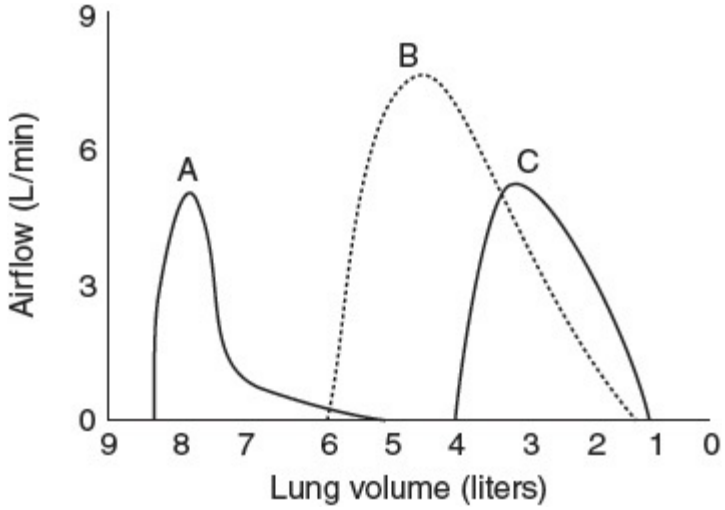
b. Bronchiolar smooth muscle tone

c. Lung compliance

d. The pressure gradient needed to inflate the alveoli

e. The work of breathing

176. In the maximal expiratory flow–volume curves below, curve A would be typical of which of the following clinical presentations?



(Modified from Levitzky MG. *Pulmonary Physiology*. 7th ed. New York, NY: McGraw-Hill; 2007:46.)

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 who 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 that he was exposed to asbestos for approximately 10 years when he worked in a factory in his 30s.

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 exam. He has never smoked, but is tired that morning, and does not use much effort while exhaling.

177. A 14-year-old adolescent girl presents with a lump in the neck. Fine needle aspiration biopsy reveals acinic cell carcinoma of the parotid gland. During the parotidectomy, there is compression injury of the glossopharyngeal nerve. As a result, which of the following respiratory reflexes will be impaired?

a. Aortic baroreceptor reflex

b. Carotid body chemoreceptor reflex

c. Hering–Breuer inflation reflex

d. Irritant airway reflex

e. Juxta pulmonary capillary (J) receptor reflex

178. A 30-year-old woman 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:

$Pa_{O_2} = 67$ mm Hg	$Sa_{O_2} = 90\%$
$Pa_{CO_2} = 60$ mm Hg	$Pv_{O_2} = 30$ mm Hg
pH = 7.27	$Sv_{O_2} = 55\%$
$[HCO_3^-] = 26$ mEq/L	$\dot{V}o_2 = 350$ mL/min
[Hb] = 15 g%	$Ca_{O_2}–Cv_{O_2} = 7$ mL O_2/100 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

179. A 63-year-old woman is required to undergo pulmonary function testing as part of a life insurance health assessment. The occupational medicine physician orders the testing to be done in both the upright and supine positions. In the upright position, which of the following variables will be lower in the apex compared with the base of the lung?

a. Pa_{CO_2}
b. Lung compliance
c. Pulmonary vascular resistance (PVR)
d. Resting lung volume (functional residual capacity [FRC])
e. $\dot{V}/\dot{Q}$ ratio

180. A 68-year-old woman convalescing from surgery developed fever, hypoxemia, and shortness of breath. She was given 100% O_2 for 30 minutes, and the laboratory results were as follows:

$Pa_{O_2} = 95$ mm Hg	$[HCO_3^-] = 22$ mEq/L
$Pa_{CO_2} = 33$ mm Hg	[Hb] = 15 g%
pH = 7.46	$Sa_{O_2} = 95\%$

The response to 100% O_2 reveals that the patient has which of the following?

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

181. A 67-year-old man who is a candidate for cardiac transplantation undergoes cardiac catheterization to assess his hemodynamic status. Findings include:

Pulmonary artery pressure (PAP) = 35 mm Hg
Cardiac output = 4 L/min
Left atrial pressure (LAP) = 15 mm Hg
Right atrial pressure = 10 mm Hg

Which of the following values is his PVR?

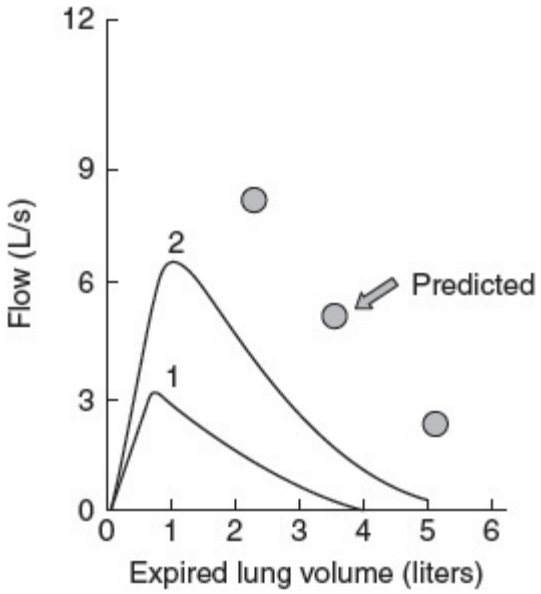
a. 0.16 L/min/mm Hg
b. 0.2 L/min/mm Hg
c. 5 mm Hg/L/min
d. 6.25 mm Hg/L/min

182. A 36-year-old woman is found comatose at her home and is life-flighted to the nearest regional medical center. Blood gases reveal a normal Pa_{O_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. Hypoventilation
d. Low $\dot{V}/\dot{Q}$ ratio
e. Right-to-left shunt

183. A 22-year-old male presents with a nonproductive cough, wheezing, and dyspnea. While doing a FVC maneuver, he generated curve 1 in the figure below. After receiving an aerosolized medication, he generated curve 2 while repeating the vital capacity 10 minutes later. Compared to curve 1, the greater flow rates measured after

exhaling 3 L on curve 2 can be attributed to an increase in which of the following?



a. Airway radius
b. Airway resistance
c. Dynamic compression of the airways
d. Effort exerted in contracting the expiratory muscles
e. Intrapleural pressure

184. 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 compared with the term infant?

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

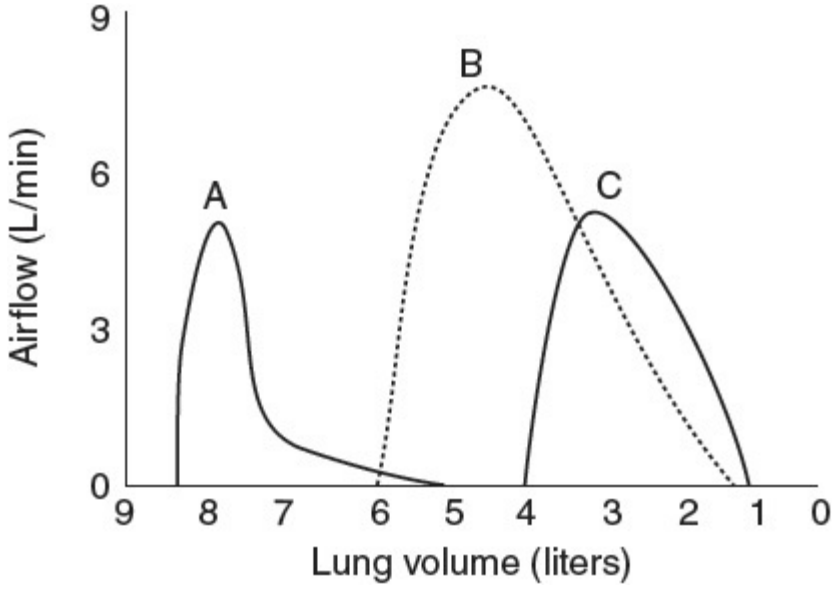
185. A 62-year-old man with congestive heart failure (CHF) develops increasing shortness of breath in the recumbent position. A chest x-ray reveals cardiomegaly, horizontal lines perpendicular to the lateral lung surface indicative of increased opacity in the pulmonary septa, and lung consolidation. Pulmonary edema in CHF is promoted by which of the following?

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

186. A 76-year-old patient with emphysema presents for his annual pulmonary function testing to assess the progression of his disease. As a result of alveolar septal departitioning in emphysema, there is a decrease in which of the following?

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

187. A 54-year-old man with severe asbestosis reports worsening of his dyspnea. Pulmonary function tests are ordered and the patient is instructed to take in a maximal inspiration and then to exhale 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:



(Modified from Levitzky MG. *Pulmonary Physiology*. 7th ed. New York, NY: McGraw-Hill; 2007:46.)

The patient's MEFV curve is consistent with which of the following sets of values?

	FVC (L)	FVC (% predicted)	FEV_1 (L)	FEV_1 (% predicted)	FEV_1/FVC
a.	4.2	85	3.4	90	81
b.	4.2	85	2.1	32	50
c.	3.1	48	2.8	50	90
d.	3.1	48	2.0	40	65
e.	1.5	25	1.0	20	67

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

a. Increase blood flow from the right atrium into the left atrium across the foramen ovale
b. Increase blood flow to the fetal lungs
c. Increase fetal P_{O_2}
d. Shift the fetal oxyhemoglobin dissociation curve to the right
e. Increase the lecithin/sphingomyelin ratio in the amniotic fluid

189. A person with CHF and progressive shortness of breath is admitted to the hospital for cardiac transplantation surgery. Hemodynamic recordings made with a Swan–Ganz catheter were as follows:

Mean pulmonary artery pressure (PAP): 35 mm Hg
Mean left atrial pressure (LAP): 20 mm Hg
Pulmonary artery wedge pressure (PAWP): 25 mm Hg
Cardiac Output: 3 L/min

On a previous admission, the patient's LAP was 15 mm Hg and cardiac output was 4 L/min. What can be deduced from these data?

a. Cardiac contractility is lower than on the previous admission.
b. Left ventricular preload is lower than on his previous admission.
c. Net fluid absorption into the pulmonary capillaries is increased.
d. Pulmonary capillary hydrostatic pressure is lower than normal.
e. Pulmonary vascular resistance is lower than normal at present.

190. A 68-year-old man with chronic obstructive pulmonary disease (COPD) 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 O_2 mask delivering 40% O_2. 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 P_{CO_2} had increased from 55 to 70 mm Hg, and his Pa_{O_2} increased from 55 to 70 mm Hg. Oxygen therapy most likely resulted in which of the following?

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

191. 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 was best to take him to the emergency department to be evaluated for possible hypoxia. Blood values obtained from the professor while he was breathing room air were as follows:

Hb: 16 g/dL	Sa_{O_2}: 97.5%
Pa_{O_2}: 102 mm Hg	Pv_{O_2}: 65 mm Hg
Pa_{CO_2}: 27 mm Hg	Sv_{O_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 diffusion across the alveolar–capillary membrane
c. Impaired hemoglobin oxygen transport
d. Impaired oxygen delivery
e. Impaired oxygen utilization

192. A 42-week gestation infant is delivered by cesarean section. Which of the following occurs with the baby's first diaphragmatic respiration?

a. All of the fetal vascular channels functionally close.
b. Pa_{O_2} increases.
c. Pulmonary capillary hydrostatic pressure increases.
d. Pulmonary vascular resistance increases.
e. Systemic vascular resistance decreases.

193. 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 FEV_1/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. Arterial P_{CO_2}
b. Arterial pH
c. Elastic recoil of the chest wall
d. Hemoglobin concentration
e. Plasma bicarbonate concentration

194. An 18-year-old male college freshman living in a dormitory contracts meningitis, which causes a centrally mediated increase in his respiratory rate. The pacemaker neurons responsible for respiratory rhythmogenesis are located in which of the following regions of the brain?

a. Apneustic center in the pons
b. Central chemoreceptors in the medulla
c. Inspiratory neurons in the dorsal respiratory group
d. Pontine respiratory groups
e. Pre-Bötzinger complex in the ventral respiratory group

195. 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 FIO_2 of 0.5 and an arterial blood gas sample reveals a P_{O_2} of 160 mm Hg and a P_{CO_2} of 40 mm Hg. His alveolar oxygen tension, at a barometric pressure of 747 mm Hg and a respiratory exchange ratio (*R*) of 0.8, is approximately what?

a. 100 mm Hg
b. 200 mm Hg
c. 300 mm Hg
d. 400 mm Hg
e. 500 mm Hg

196. A 68-year-old man who has COPD presents to his pulmonologist with fatigue, dyspnea at rest, and peripheral edema. His blood gases on room air are Pa_{O_2} = 60 mm Hg, Pa_{CO_2} = 60 mm Hg, and pH = 7.36. His alveolar–arterial (A–a) O_2 gradient, at a barometric pressure of 760 mm Hg and a respiratory exchange ratio (R) of 0.8, is approximately what?

a. 5 mm Hg
b. 10 mm Hg
c. 15 mm Hg
d. 20 mm Hg
e. 25 mm Hg

197. A 45-year-old man presents with severe back pain that he attributes to an injury from operating a jackhammer for his job as a cement worker. An MRI of the spine confirms a herniated disk. The patient reports that he has smoked one to two packs of cigarettes a day for 30 years, so the neurosurgeon requests pulmonary function studies prior to the patient's back surgery. During a forced expiration, the patient generates an intrapleural pressure of 20 mm Hg. The patient's equal pressure point will move closer to the mouth and forced expiratory volume will increase if there is an increase in which of the following?

a. Airway resistance
b. Airway smooth muscle tone
c. Expiratory effort
d. Inspired lung volume
e. Lung compliance

198. A healthy, 24-year-old man is prescribed sustained-release bupropion (Zyban) for smoking cessation. Three weeks later, he presents to his family physician with intermittent fever and a generalized rash, at which time the bupropion is discontinued. A month later, he develops a dry, intermittent cough and dyspnea. Which of the following pulmonary function results is consistent with allergic bronchospasm?

a. A decreased FEV_1/FVC
b. A decreased residual volume
c. An increased diffusing capacity
d. An increased FVC
e. An increased lung compliance

199. A 5-month-old infant 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 Pa_{CO_2} was increased, but decreased during hyperoxia. Which of the following is the most likely cause of this infant's apnea?

a. Bronchospasm
b. Decreased irritant receptor sensitivity
c. Diaphragmatic fatigue
d. Dysfunctional central chemoreceptors
e. Peripheral chemoreceptor hypersensitivity

200. A 66-year-old woman presents with a chief complaint of shortness of breath accompanying alternating chills and spiking fever. She has an increase in heart rate and respiratory rate. The right lower lobe is dull to percussion and increased vocal fremitus and bronchovesicular breathing are auscultated over this region.

Ventilation–perfusion ($\dot{V}/\dot{Q}$) abnormalities occurring in a patient with lobar pneumonia will generally cause a decrease in which of the following?

a. Alveolar ventilation
b. Anion gap
c. Arterial pH
d. Arterial P_{O_2}
e. A–a gradient for oxygen

201. A 72-year-old man with CHF, paroxysmal nocturnal dyspnea, and orthopnea is referred for pulmonary function test 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. Blood flow
b. Lung compliance
c. Pa_{CO_2}
d. Ventilation
e. $\dot{V}/\dot{Q}$ ratio

202. A 65-year-old smoker develops a squamous cell bronchogenic carcinoma that metastasizes to the tracheobronchial and parasternal lymph nodes. The chest x-ray is consistent with accumulation of fluid in the pulmonary interstitial space. Flow of fluid through the lymphatic vessels will be decreased if there is an increase in which of the following?

a. Capillary oncotic pressure
b. Capillary permeability
c. Capillary pressure

d. Central venous pressure
e. Interstitial protein concentration

203. A 24-year-old presents with a chief complaint of fatigue and daytime somnolence. His wife has noticed that he stops breathing for periods of 30 to 60 seconds while he is sleeping and that this happens many times throughout the night. His physician orders pulmonary function testing including ventilatory response curves and polysomnography. The tests confirm apneic episodes during sleep. During a ventilatory responsiveness test, his alveolar ventilation increased as predicted in response to breathing 5% CO_2, but his ventilatory response to breathing 16% O_2 was depressed. Which of the following conditions are consistent with these findings?

a. Central hypoventilation syndrome (Ondine curse)
b. Decreased central chemoreceptor sensitivity
c. Decreased peripheral chemoreceptor sensitivity
d. Obstructive sleep apnea
e. Spinal cord injury affecting the fourth cervical vertebra

204. A 57-year-old woman presents with dyspnea on exertion. Pulmonary function studies with plethysmography demonstrate an increased resting oxygen consumption and work of breathing. Which of the following will decrease the oxygen consumption of the respiratory muscles?

a. A decrease in airway resistance
b. A decrease in diffusing capacity of the lung
c. A decrease in lung compliance
d. An increase in rate of respiration
e. An increase in tidal volume

205. An 18-year-old man is life-flighted to a Level 1 trauma center after being thrown from his motorcycle. It is determined that he has a brain tran-section above the pons. How will this lesion affect the control of breathing in this patient?

a. All breathing movements will cease.
b. The central chemoreceptors will no longer be able to exert any control over ventilation.
c. The peripheral chemoreceptors will no longer be able to exert any control over ventilation.
d. The Hering–Breuer reflex will be abolished.
e. The limbic system will no longer be able to exert any control over ventilation.

206. A 48-year-old coal miner complains of shortness of breath and a productive cough. He has smoked one to two 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 lungs and chest wall recoil away from each other throughout a tidal breath.
d. The lungs and chest wall recoil in the same direction throughout a tidal breath.
e. A small volume of air leaves the pleural space during a tidal breath.

207. A 47-year-old man presents with a 7-day history of fever, productive cough, and shortness of breath. A chest x-ray reveals consolidation in the right lower lobe and culture of the sputum is positive for *Klebsiella pneumoniae*. Blood gases reveal hypoxemia but not carbon dioxide retention. Which of the following would be increased in this patient?

a. Alveolar–arterial P_{O_2} difference
b. Diffusing capacity of the lung
c. Lung compliance
d. Physiological dead space
e. $\dot{V}/\dot{Q}$

208. A 57-year-old man undergoes total knee replacement for severe degenerative joint disease. Four days after surgery, he develops an acute onset of shortness of breath and right-sided pleuritic chest pain. He is now in moderate distress with a respiratory rate of 28 breaths per minute, tidal volume of 450 mL, heart rate of 120 bpm, and blood pressure of 125/85 mm Hg. Arterial blood gases on room air at a barometric pressure of 760 mm Hg and *R* of 0.8 were Pa_{O_2} = 60 mm Hg, SaO_2 = 90%, Pa_{CO_2} = 30 mm Hg, pH = 7.50, $[HCO_3^-]$ = 22 mEq/L, and P_ECO_2 = 10 mm Hg. The right lower extremity is healing well, but is red, tender, warm to touch, and has 2+ pitting edema. The most likely cause of these postoperative findings is:

a. Atelectasis
b. Pneumonia
c. Pneumothorax
d. Pulmonary embolism
e. Sepsis

209. Several months after recovering from mononucleosis, a 26-year-old man develops weakness and tingling in both legs. Three days later, he is hospitalized when his legs become paralyzed. A conduction block in the peripheral Aβ, sensory fibers and the finding of autoantibodies to Schwann cell gangliosides confirm the diagnosis of

Guillain–Barré syndrome. The next day the weakness and paralysis ascended to his upper extremities and trunk. Stat arterial blood gas results indicated the need for mechanical ventilation. Which of the following sets of values is consistent with acute respiratory muscle paralysis?

	pH	P_{aCO_2} (mm Hg)	$[HCO_3^-]$ (mmol/L)
a.	7.24	30	13
b.	7.24	60	26
c.	7.35	60	32
d.	7.52	25	21
e.	7.55	48	34

210. A 37-year-old woman is admitted to the hospital with severe kyphoscoliosis and respiratory muscle weakness. Which of the following physiological variables is most likely decreased in this patient?

a. Airway resistance
b. Alveolar surface tension
c. Arterial carbon dioxide tension
d. Chest wall compliance
e. FEV_1/FVC

For Questions 211 and 212, refer to the following case.

A 32-year-old man 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 as follows:

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

211. 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%

212. What is the patient's oxygen consumption?

a. 200 mL/min
b. 210 mL/min
c. 220 mL/min
d. 230 mL/min
e. 240 mL/min

213. An 83-year-old woman is found unresponsive by her son approximately 3 hours after she returned to her hospital room following gall bladder surgery. The nurse reported that the patient had asked for her pain medications and said she was going to rest for a while. Arterial blood gases reveal hypercapnia and hypoxemia. Which of the following is the most likely cause of the high arterial P_{CO_2} ?

a. Decreased alveolar dead space
b. Decreased metabolic activity
c. Hypoventilation
d. Hypoxemia
e. $\dot{V}/\dot{Q}$ inequality

214. A 29-year-old man with AIDS presents with a painful, red, swollen area on top of his shin, which is warm to the touch. He has a fever, tachypnea, and tachycardia, and is hospitalized and started on IV antibiotics. His condition progresses rapidly to septicemia and septic shock. He is transported to the ICU, intubated, and started on mechanical ventilation. A Swan-Ganz catheter is inserted to monitor pulmonary hemodynamics and lung fluid balance. Which of the following conditions will cause a decrease in PVR?

a. Alveolar hypoxia
b. Decreased pH in the pulmonary artery
c. Increased cardiac output
d. Inflation of the lungs to total lung capacity

e. Sympathetic stimulation of the pulmonary vessels

215. 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. Alveolar ventilation increases
b. Arterial pH decreases
c. Arterial lactate level increases
d. Pa_{CO_2} decreases
e. Pa_{O_2} increases

216. A 56-year-old woman presents to her physician complaining of fatigue, headaches, and dyspnea on exertion. She states that she sometimes gets blue lips and fingers when she tries to exercise. Pulmonary function tests reveal 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. CHF
b. COPD
c. Fibrotic lung disease
d. Polycythemia
e. Pulmonary embolism

217. A 49-year-old farmer develops 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 (CSF) pH is normal
d. Central chemoreceptors are depressed
e. Arterial oxygen tension is normal

218. 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 of the following statements best characterizes lung compliance?

a. It decreases with advancing age.
b. It increases when there is a deficiency of surfactant.
c. It increases in patients with pulmonary edema.
d. It is equivalent to $\Delta P/\Delta V$.
e. It is inversely related to the elastic recoil properties of the lung.

219. 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. A decrease in the metabolic rate of the surrounding brain tissue
b. A decrease in the P_{O_2} of blood flowing through the brain
c. An increase in the P_{CO_2} of blood flowing through the brain
d. An increase in the pH of the CSF
e. Hypoxemia, hypercapnia, and metabolic acidosis

220. 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. Airway diameter
b. Anatomic dead space
c. Compliance of the lungs
d. Elastic work of breathing
e. Resistive work of breathing

221. A 28-year-old woman 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?

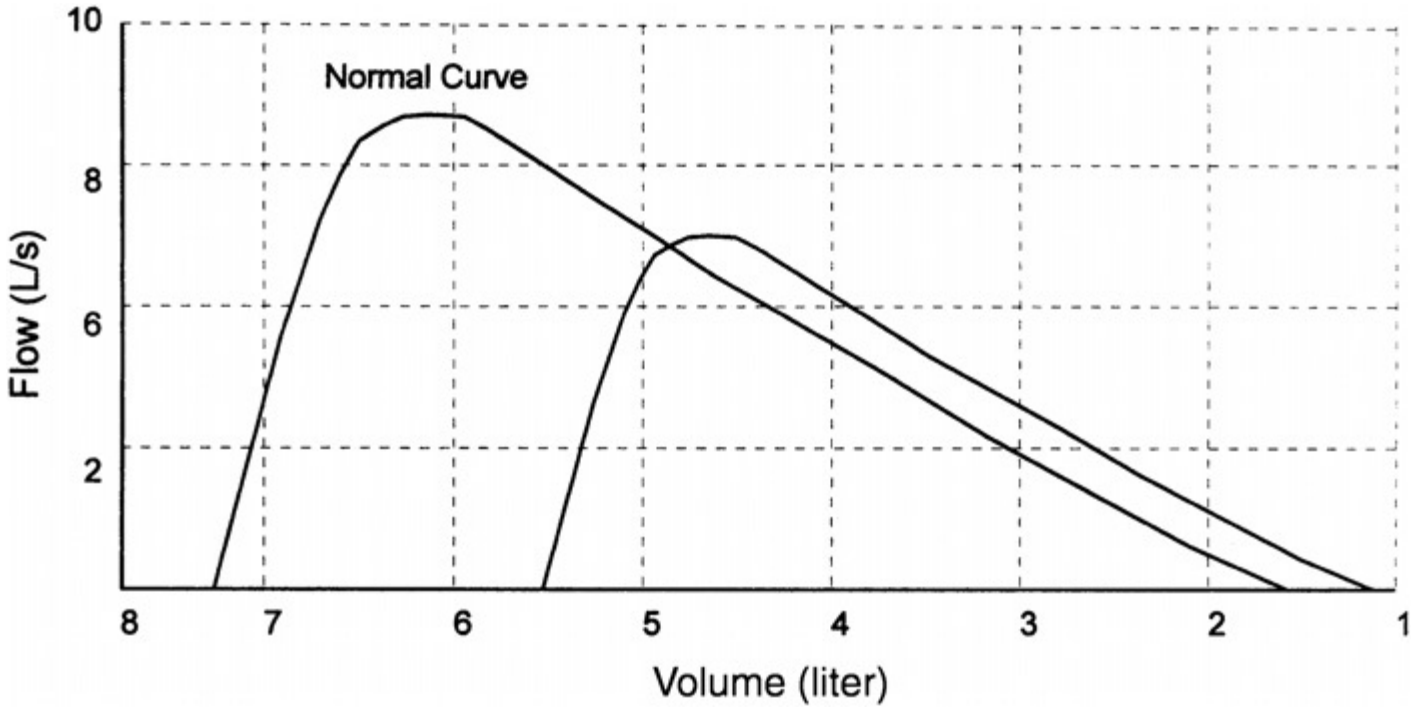
a. The alveoli at the base of the lung have more surfactant.
b. The alveoli at the base of the lung are more compliant.

c. The alveoli at the base of the lung have higher $\dot{V}/\dot{Q}$ 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.

222. A 21-year-old woman presents with cough and shortness of breath. The physician conducts a pulmonary function screening test in his office, and the patient generates the maximum flow–volume curve shown to the right of the normal curve in the diagram below. These findings are consistent with which of the following conditions?



a. Asthma

b. Chronic bronchitis

c. Cystic fibrosis

d. Decreased effort

e. Sarcoidosis

223. A 56-year-old man presents for his annual physical examination. His BMI has increased from 28 to 33 over the past year and the fat deposition is mainly around the abdomen. His blood pressure has increased from 125/85 to 140/95 mm Hg since the last visit. Other physical findings are unremarkable and he and his spouse state that he does not snore. Past medical history and social history are insignificant except for his sedentary lifestyle. Exercise stress testing is ordered prior to placing the patient on a regular exercise regimen. Aerobic exercise causes which of the following changes in pulmonary physiology?

a. Diffusing capacity of the lungs increases.

b. Mean PAP decreases.

c. Overall $\dot{V}/\dot{Q}$ ratio of the lungs decreases.

d. Pulmonary blood flow decreases.

e. PVR increases.

224. A 43-year-old woman develops shortness of breath following a cholecystectomy. Bronchial breath sounds and crackles are heard over all lung fields and the lungs are dull on percussion. A chest x-ray demonstrates a pattern of diffuse opacification characteristic of atelectasis. Intrapulmonary shunting will cause which of the following changes in arterial blood gas values?

	pH	$Paco_2$	Pao_2
A.	↑	↓	↑
B.	↑	↓	↓
C.	↓	↓	↓
D.	↓	↑	↓

a. A

b. B

c. C

d. D

225. A 49-year-old coal miner presents with dyspnea, a nonproductive cough, and decreased exercise tolerance. Lung function tests reveal the following: total lung capacity = 3.34 L (56% of predicted), residual volume = 0.88 L (54% of predicted), and FVC = 1.38 L (30% of predicted). His arterial P_{O_2} is 68 mm Hg. Which of the following values will be approximately normal?

a. Diffusing capacity
b. FEV_1/FVC ratio
c. FRC
d. Lung compliance
e. $\dot{V}/\dot{Q}$ ratio

226. A 43-year-old woman with a history of asthma presents to the emergency department with an acute asthma attack after her bronchodilator inhaler ran out the day before. Airway resistance is greater at which of the following?

a. At low lung volumes compared with high lung volumes
b. At lower values for Reynolds number
c. During inspiration compared with expiration
d. In the total cross-section of the small airways compared with the total cross-section of the central airways
e. With laminar flow than with turbulent flow

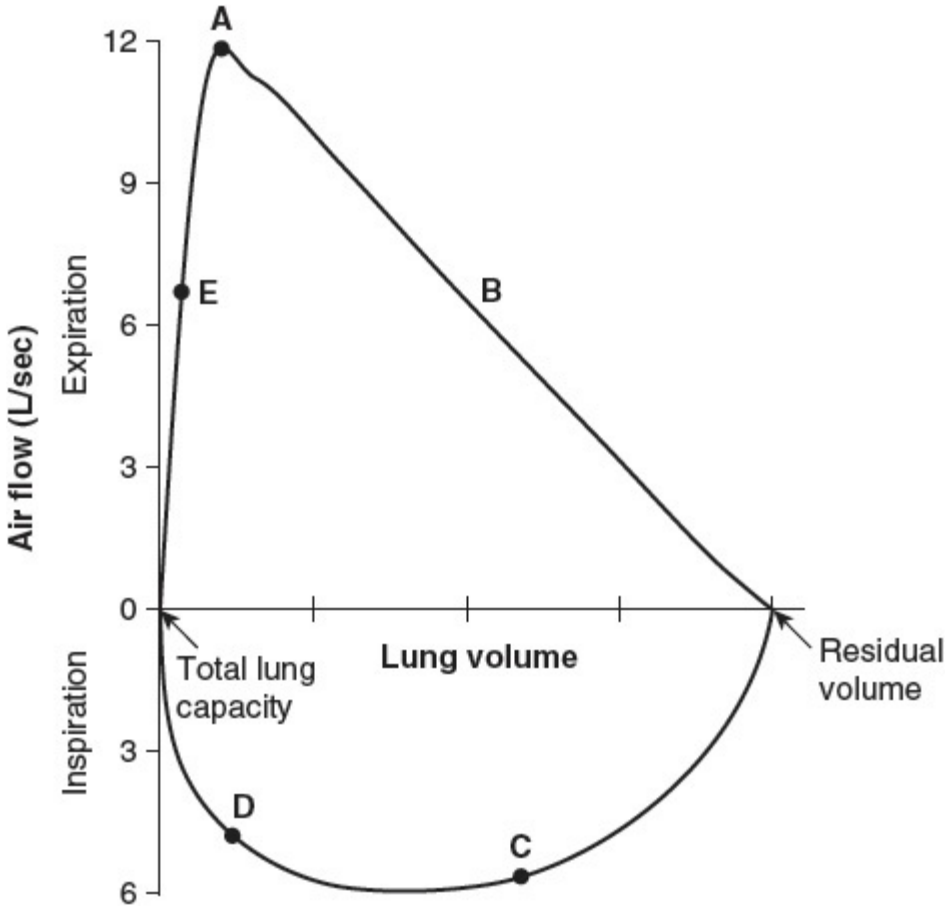
227. A 78-year-old woman presents to her family physician's office with a chief complaint of fatigue and shortness of breath. The doctor indicates that he wants her to go to the hospital to get some pulmonary function tests, but there is one who is able to do in the office. A spirometer can be used to directly measure which of the following?

a. FRC
b. Peak flow rate
c. Residual volume
d. Total lung capacity
e. Vital capacity

228. 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. A–a gradient for O_2
b. $Paco_2$
c. Pao_2
d. Oxygen dissolved in blood
e. Oxygen combined with hemoglobin

229. An 18-year-old woman 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 shown below will airflow remain constant despite an increased respiratory effort?


A
12
9
E
B
6
3
Air flow (L/sec)
Expiration
0
Total lung
capacity
Lung volume
Residual
volume
Inspiration
3
D
C
6

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

Answers

160. The answer is e. (*Barrett, p 629. Le, p 546. Levitzky, pp 54-57. McPhee and Hammer, p 212.*) 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 FRC and the residual volume, designated as E and D, respectively. The FRC is the volume of gas remaining in the lungs following a passive, tidal exhalation. The residual volume is the volume of gas remaining in the lungs following a maximal expiration. The inspiratory reserve volume is designated by A, the inspiratory capacity (IC) by B, and the vital capacity (VC) by C in the figure.

161. The answer is c. (*Barrett, pp 634, 649-650. Levitzky, pp 71-73, 234-235.*) 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 O_2 in dry atmospheric air equals the fractional concentration of oxygen (FIO_2) times the atmospheric (barometric) pressure. At sea level, the barometric pressure is 760 mm Hg, yielding a PIO_2 of 160 mm Hg. At high altitude, the barometric pressure decreases in proportion to the decreased weight of the air above it. At an elevation of 18,000 ft in the Peruvian Andes, the barometric pressure is 380 mm Hg, yielding a PIO_2 of 80 mm Hg. Once inside the respiratory tract, the inspired air becomes warmed and humidified. The partial pressure of H_2O vapor is temperature dependent rather than concentration dependent and at body temperature (37°C) it is 47 mm Hg. The presence of H_2O vapor reduces the partial pressure of the other gases in the atmosphere, and the PH_2O 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 PIO_2 in the conducting airways is 0.21 (760-47) or 150 mm Hg, whereas, at 18,000 ft, the humidified, tracheal P_{O_2} would be 0.21 (380-47) or 70 mm Hg.

162. The answer is c. (*Barrett, p 634. Levitzky, pp 71-73.*) Room air contains 21% O_2 and 0.04% CO_2, yielding a PIO_2 of 160 mm Hg and a $PICO_2$ of 0.3 mm Hg. Thus, if a sample of arterial blood is equilibrated with room air, the measured Pa_{O_2} will have an inaccurately high reading and the Pa_{CO_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.

163. The answer is a. (*Barrett, pp 629-631, 635. Kaufman, pp 275-276. Le, pp 547, 555. Levitzky, pp 44-46, 58, 137-141, 265, 550. Longo, p 2093.*) 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 law of diffusion. Pulmonary fibrosis is characterized by a decrease in lung compliance and an increase in lung elastic recoil ("stiff" lungs), which results in findings typical of a restrictive impairment. Pulmonary function test values characteristic of a restrictive impairment include a decrease in all lung volumes and capacities and a ratio of the FEV_1 to the total FVC that is normal or increased. Airway radius is decreased, and thus airway resistance is increased, at lower lung volumes, but in restrictive disorders, the airway resistance is normal when corrected for lung volume in contrast to obstructive disorders, in which an increased airway resistance is a hallmark of the functional impairment.

164. The answer is b. (*Barrett, pp 636-637. Le, p 553. Levitzky, pp 114-117. McPhee and Hammer, pp 217-221, 237-242.*) A pulmonary thromboembolism results in areas of the lung that are ventilated, but not perfused, yielding $\dot{V}/\dot{Q}$ ratios of infinity and an increase in alveolar dead space. When the $\dot{V}/\dot{Q}$ 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 $\dot{V}/\dot{Q}$ ratio equal to 0, and having P_{AO_2} values that equilibrate with the mixed venous blood.

165. The answer is c. (*Le, p 546. Levitzky, pp 67-71.*) Physiological dead space is the volume of the respiratory tract that is ventilated but not perfused by the pulmonary circulation. The Bohr equation for determination of the ratio of the physiologic dead space (V_D) to the tidal volume (V_T) is:

$$V_D/V_T = PaCO_2 - P_ECO_2/PaCO_2$$

$$V_D/V_T = 40 - 28/40 = 0.3$$

$$V_D/V_T \times V_T = V_D$$

$$0.3 \times 600\ mL = 180\ mL$$

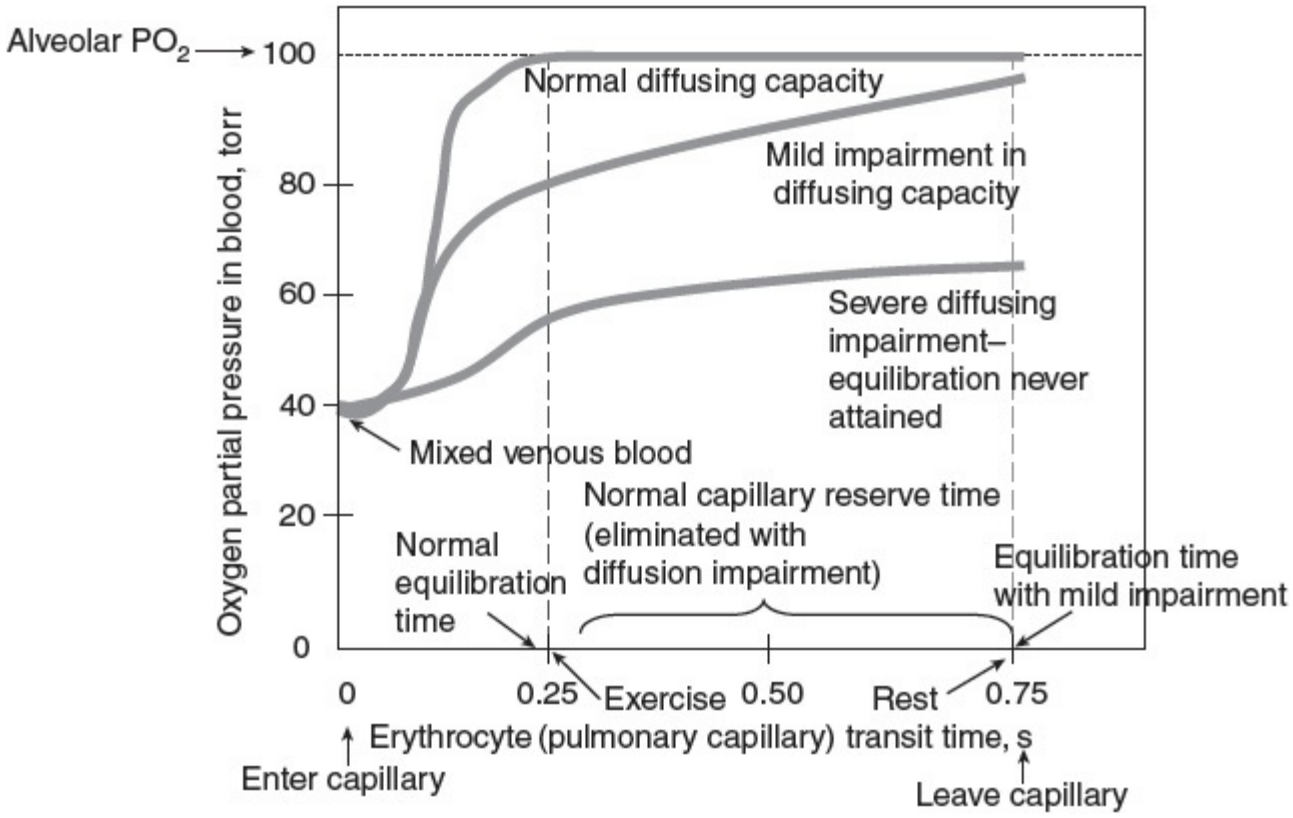
Physiological dead space volume is equal to the sum of the anatomic dead space and the alveolar dead space. Anatomic dead space, which represents the volume of the conducting airways (nose → terminal bronchioles), can be measured using the Fowler technique, but it is often estimated as 1 mL per pound of body weight. Alveolar dead space represents the volume of alveoli that are ventilated but not perfused. Because there is normally no alveolar dead space, physiologic dead space volume approximates anatomic dead space volume in persons with normal lung function.

166. The answer is e. (*Barrett, pp 629-632. 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. Curve Z has a lower slope than normal, and thus is characteristic of a pressure–volume curve in an individual with decreased lung compliance. In pulmonary edema, the abnormal accumulation of fluid in the lungs causes a restrictive pulmonary impairment characterized by decreased lung compliance. The increase in airway resistance in asthma is not associated with an increase (or decrease) in lung compliance. In emphysema, alveolar septal departitioning causes the destruction of elastic fibers, which decreases the elastic recoil of the lungs, thereby increasing lung compliance (curve X). Emphysematous changes in the lungs also occur in aging. An L/S ratio ≥2 indicates normal biochemical maturation of the

lung in utero, with normal surfactant production and lung compliance (normal curve). If the L/S ratio is less than 2, such as may occur in preterm infants, there is an increased incidence of respiratory distress syndrome of the newborn, a restrictive impairment that would be characterized by curve Z.

167. The answer is b. (*Kaufman, pp 294-295. Le, pp 557, 561. Levitzky, pp 12-14, 113-117. Longo, p 2181.*) 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. With collapse of the lung, the $\dot{V}/\dot{Q}$ ratio on the affected side decreases. The trachea shifts toward the affected lung in a spontaneous pneumothorax and away from the affected lung in a tension pneumothorax.

168. The answer is e. (*Levitzky, pp 135-137.*) The time course for oxygen transfer across the alveolar-capillary (A-C) membrane is shown in the graph below. At the entry of the pulmonary capillary, the partial pressure of oxygen starts at the P_{O_2} of the mixed venous blood, about 40 mm Hg, and rises fairly rapidly, reaching equilibration with the alveolar P_{O_2} within about 0.25 of a second, or about one-third of the time the blood is in the pulmonary capillary at a normal resting cardiac output (called the pulmonary capillary transit time or erythrocyte transit time = 0.75 s). Once equilibration occurs and the P_{O_2} in the pulmonary capillary blood equals the alveolar P_{O_2}, there is no partial pressure gradient (ΔP) for further oxygen transfer across the A-C membrane. The time between equilibration and when an erythrocyte leaves the pulmonary capillary is referred to as pulmonary capillary reserve time (~0.5 s at a resting cardiac output). Because of the pulmonary capillary reserve time at rest, even individuals with mild-to-moderate diffusion impairment may have sufficient transfer of oxygen across the A-C membrane by the time an erythrocyte leaves the pulmonary capillary, such that the blood exits with a P_{O_2} in the normoxic range. More severe diffusion impairments, on the other hand, may slow down oxygen transfer to the extent that equilibration of pulmonary capillary and alveolar P_{O_2} is never reached and the blood leaving the pulmonary capillary is hypoxemic. During exercise, as cardiac output increases, pulmonary capillary transit time decreases to as fast as ~0.25 s. When diffusing capacity is normal, the decreased pulmonary capillary transit time does not decrease oxygen transfer across the A-C membrane because the equilibration time for O_2 transfer across the A-C membrane is also approximately ~0.25 s. However, because there may not be any pulmonary capillary reserve time during exercise, even mild diffusion impairments may manifest hypoxemia during exercise. *Note*: hemoglobin's affinity for O_2 decreases during exercise, particularly in the working skeletal muscle, where there are increases in temperature, P_{CO_2}, and $[H^+]$. Skeletal muscle does consume more oxygen during exercise, but that does not account for the differences in oxygen transfer across the A-C membrane in persons with varying levels of pulmonary diffusing capacity.



Effects of impaired diffusion on equilibration time & capillary reserve time for oxygen diffusion across the A-C membrane. (Adapted from Levitzky, p 36).

169. The answer is d. (*Barrett, p 633. Levitzky, pp 65-67.*) Alveolar ventilation $\dot{V}_A$ equals the tidal volume (V_T) minus the dead space volume (V_D) times the breathing frequency (f). The dead space volume can be estimated as 1 mL/lb of body weight.

$$\dot{V}_A = (V_T - V_D) \times f$$
$$\dot{V}_A = (500\ \text{mL} - 125\ \text{mL}) \times 15\ \text{breaths per minute}$$
$$\dot{V}_A = 5625\ \text{mL/min}$$

170. The answer is a. (*Barrett, pp 666-669. 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 $[HCO_3^-]$. The increased $[H^+]$ stimulates the peripheral (not central) chemoreceptors to increase alveolar ventilation more proportionally than the increase in carbon dioxide production, resulting in a decrease in P_{ACO_2}.

171. The answer is c. (*Levitzky, pp 73-75.*) Because the dead space air does not participate in gas exchange, the entire output of CO_2 in the expired gas comes from the alveolar gas. Accordingly, alveolar (and arterial) P_{CO_2} can be expressed in terms of CO_2 output and alveolar ventilation according to the following equation:

$$P_{ACO_2} = PaCO_2 = \dot{V}CO_2/\dot{V}_A$$

Thus, an increase in alveolar ventilation at a constant rate of carbon dioxide production will lower $PACO_2$ and $PaCO_2$. Hyperventilation increases P_{AO_2} and PaO_2, with no change in the alveolar–arterial P_{O_2} difference. The $\dot{V}/\dot{Q}$ will be normal or increased.

172. The answer is d. (*Kaufman, pp 208-209, 215, 277-278. Le, pp 146, 550, 579, 575. Levitzky, p 75. Longo, pp 1671-1673.*) 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 mm Hg, F_{IO_2} = 1.0 (100% O_2), $PaCO_2$ 36 mm Hg, and R = 0.8, then

$$P_{AO_2} = (1.0)(757 - 47) - (36/0.8)$$
$$= 710 - 45 = 665 \text{ mm Hg}$$

Pneumocystis is an opportunistic fungal pulmonary pathogen that is an important cause of pneumonia in immunocompromised hosts. HIV patients with a CD4+ cell count below 200/μL 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.

173. The answer is b. (*Levitzky, pp 32-35. McPhee and Hammer, p 215.*) An increased velocity of airflow will increase turbulent airflow, as predicted by an increased Reynolds 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 law.

174. The answer is e. (*Levitzky, pp 65-75.*) Alveolar ventilation is the volume of air entering and leaving the alveoli per minute. Alveolar ventilation is less than the minute ventilation (minute volume) because the last part of each inspiration remains in the conducting airways and does not reach the alveoli. The minute ventilation is the product of tidal volume and respiratory rate (14,400 mL/min). Alveolar ventilation cannot be measured directly but must be calculated by subtracting dead space ventilation from minute ventilation. The ratio of the physiological dead space volume to the tidal volume (V_D/V_T) can be calculated using the Bohr equation ($PaCO_2$ $P_ECO_2/PaCO_2$), and then multiplied by the V_T to yield the dead space volume, which when multiplied by the respiratory rate yields the dead space ventilation (5760 mL/min). Thus, alveolar ventilation in this patient is 8640 mL/min. The adequacy of alveolar ventilation is determined by the alveolar air equation, which states that the $PaCO_2$ is approximately equal to the rate of carbon dioxide production divided by the rate of alveolar ventilation. At a normal rate of alveolar ventilation, $PaCO_2$ is in the normal range of 35 to 45 mm Hg. Assuming a constant rate of carbon dioxide production, a decrease in alveolar ventilation (hypoventilation) causes a higher $PaCO_2$ than normal (ie, >45 mm Hg) and a rate of alveolar ventilation that is greater than normal (hyperventilation) "blows off" excessive CO_2 causing $PaCO_2$ to decrease below normal (ie, <35 mm Hg). Thus, in this patient, the $PaCO_2$ of 30 mm Hg indicates that she is hyperventilating. If her increase in alveolar ventilation matched an increased carbon dioxide production, then $PaCO_2$ would be in the normal range.

175. The answer is c. (*Levitzky, pp 26-28. Longo, pp 2205-2209.*) 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. Although surfactant replacement therapy has proven to be beneficial in respiratory distress syndrome of the newborn, surfactant replacement therapy is not currently recommended in acute respiratory distress syndrome based on clinical evidence against efficacy of the therapy.

176. The answer is a. (*Levitzky, pp 44-46. Longo, pp 2093-2094, 2151-2160.*) Cigarette smoking is the major cause of 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 MEFV curve. Decreased effort would decrease flow rates during the effort-dependent portion of a MEFV curve, but not during the effort-independent portion.

177. The answer is b. (*Barrett, pp 660-661, 664-665. Levitzky, pp 195-201. Longo, pp 220, 548-551, 1220-1221.*) The afferent pathway from the carotid body chemoreceptors is the Hering nerve, a branch of cranial nerve IX, the glossopharyngeal nerve. The vagus nerve constitutes the afferent pathway from the aortic baroreceptors, the J receptors, the irritant airway receptors, and the rapidly adapting stretch receptors mediating the Hering–Breuer inflation reflex.

178. The answer is a. (*Barrett, pp 649-653. Levitzky, pp 181-184.*) 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

$$(\dot{V}O_2/CaO_2 - CvO_2)$$

is 5 L/min, which is normal. In histotoxic hypoxia, oxygen extraction is impaired, and thus $CaO_2 - CvO_2$ would be less than normal and SvO_2 would be greater than normal.

179. The answer is b. (*Barrett, pp 632-633, 636. Levitzky, pp 125-127. Longo, pp 1589-1592.*) Hydrostatic pressure increases with vertical distance from the apex to the base of the upright lung. The lower hydrostatic pressure in the apex results in a lower (more subatmospheric) intrapleural pressure, which increases the resting lung volume (ie, FRC). This places the apex on a portion of the pressure–volume curve of the lung with a decreased slope (decreased compliance) compared with the base. As a result of the greater compliance in the dependent regions of the lung, the base in the upright position receives a greater ventilation per unit volume upon inspiration from FRC. The greater hydrostatic pressure in the base results in a greater PAP, which decreases PVR by recruitment and distension, thereby increasing pulmonary blood flow in going from the apex to the base. Because the effects of gravity (hydrostatic pressure) are greater for blood than air as blood is more dense, the increase in perfusion exceeds the increase in ventilation at the base, and the $\dot{V}/\dot{Q}$ ratio decreases from a high of about 3.3 at the top of the upright lung to approximately 0.65 at the base of the upright lung. An area with a higher $\dot{V}/\dot{Q}$ has more gas exchange, and thus Pa_{CO_2} is lower and Pa_{O_2} is higher in the apex compared with the base.

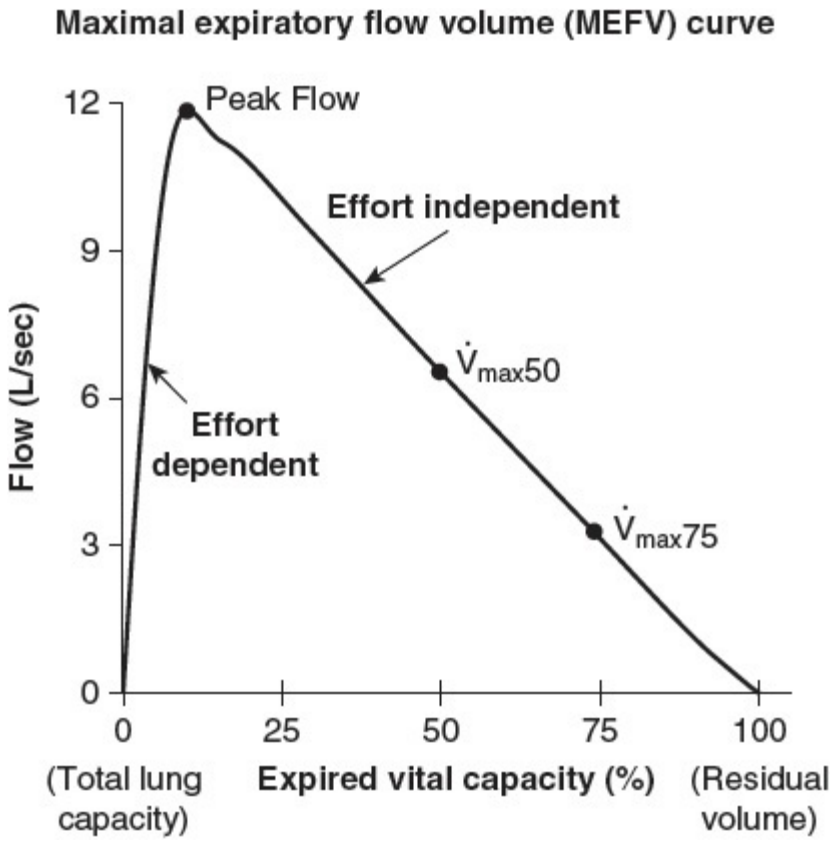
180. The answer is d. (*Barrett, pp 649-653. Le, pp 550-551. Levitzky, pp 181-184.*) The classification of the causes of hypoxemia (low Pa_{O_2}) are (1) reduced P_{AO_2} (alveolar hypoventilation or reduced PIO_2 found at high altitude or with breathing low concentrations of oxygen), (2) diffusion impairment, (3) ventilation/perfusion inequality, and (4) right-to-left shunting (venous admixture). Left-to-right shunting does not cause hypoxemia. Administration of 100% O_2 corrects the hypoxemia caused by alveolar hypoventilation, diffusion impairment, or ventilation/perfusion inequality, but not due to right-to-left shunting (venous admixture). Alveolar hypoventilation would have an increased Pa_{CO_2}. In carbon monoxide poisoning, the SaO_2 would be lower than normal. On 100% O_2, the Pa_{O_2} should be ≥ 500 mm Hg and the A–a P_{O_2} difference should be ≤100 mm Hg. This patient's Pa_{O_2} is only 95 mm Hg on 100% O_2, indicating the presence of right-to-left shunting, that is, areas of the lung that are perfused but not ventilated ($\dot{V}/\dot{Q}$ ratio = 0). Postoperative complications such as pneumonia, pulmonary edema, and atelectasis are all causes of intrapulmonary right-to-left shunts.

181. The answer is c. (*Le, p 549. Levitzky, pp 90-91.*) PVR is calculated as:

$$\text{PVR} = \Delta P/\dot{Q} = \text{Mean PAP} - \text{mean LAP/pulmonary blood flow}$$
$$= 35 - 15 \text{ mm Hg}/4 \text{ L/min} = 5\text{mm Hg/L/min}$$

182. The answer is b. (*Barrett, pp 649-653. Kaufman, p 272. Le, pp 547, 550. Levitzky, pp 153-156, 181-184. Longo, pp 229-231.*) Hemoglobin has 240 × greater affinity for carbon monoxide than for oxygen. Thus, in carbon monoxide poisoning, the amount of dissolved oxygen, as reflected by the Pa_{O_2}, may be normal, but the saturation of hemoglobin with oxygen will be lower than expected for a given Pa_{O_2}. In anemia, hemoglobin concentration is reduced, but the saturation of hemoglobin O_2 is normal. Hypoventilation, $\dot{V}/\dot{Q}$ mismatch with low $\dot{V}/\dot{Q}$ units, and right-to-left shunting are all causes of hypoxemia (decreased Pa_{O_2}).

183. The answer is a. (*Levitzky, pp 32-36, 44-48. Longo, pp 2091-2094.*) Reversibility of airway obstruction is assessed by the change in expiratory flow rate before and after administration of a bronchodilator drug, such as a β_2-adrenergic agonist, which increases airway radius, thereby decreasing airway resistance and increasing expiratory airflow as predicted by Poiseuille law. Increasing the effort of muscular contraction on exhalation would increase expiratory airflow on the effort-dependent portion of the MEFV curve, but not the effort-independent portion, as delineated in the figure below. Regardless of increased effort, flow rates decrease during the effort-independent portion of a maximal expiration due to dynamic compression of the airways by the positive intrapleural pressure generated by a forced (active) expiration.



184. The answer is c. (*Barrett, pp 615-616. Le, p 252.*) In the fetal circulation, PVR is increased compared with 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 approximately 25 mm Hg, which causes hypoxic pulmonary vasoconstriction. As a result, 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.

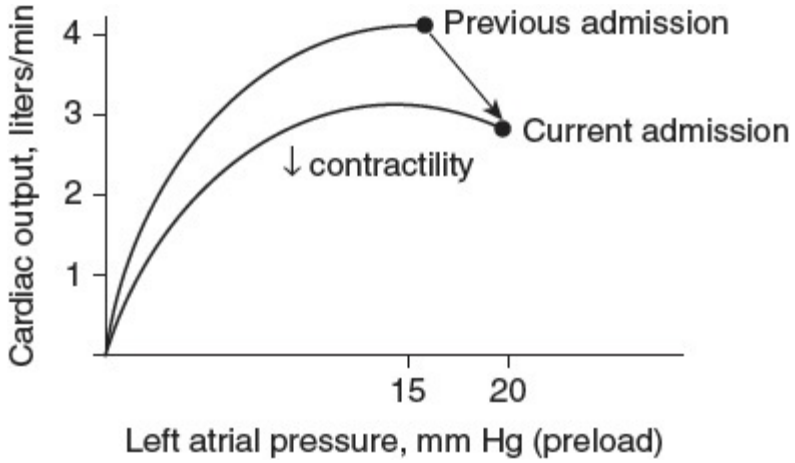
185. The answer is c. (*Le, p 273. Levitzky, pp 107-110. Longo, pp 280-281, 2236-2238. McPhee and Hammer, pp 233-237.*) In CHF, left ventricular dysfunction increases left ventricular end-diastolic pressure, which raises LAP, pulmonary venous pressure, and pulmonary capillary pressure, which is the hydrostatic pressure tending to drive fluid movement out of the pulmonary capillaries, according to Starling law. Thus, pulmonary edema, generally limited to the interstitium of the lungs, is a hallmark of CHF. All of the other responses would act to decrease fluid movement out of the capillary, in accordance with Starling law.

186. The answer is c. (*Le, pp 554, 556. Levitzky, pp 22-23, 37-58, 137-140. Longo, pp 2151-2160.*) 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 law. Alveolar septal departitioning with destruction of pulmonary capillaries results in enlargement of the air spaces distal to the terminal bronchioles and an increase in alveolar dead space, 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 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.

187. The answer is c. (*Levitzky, pp 44-46. Longo, pp 2091-2094.*) Curve C is the 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 FEV_1/FVC ratio to be normal or increased above the normal value of 0.7 (which eliminates choices d and e).

188. The answer is e. (*Le, pp 544, 555.*) Maturation of surfactant production in fetal lungs is accelerated by glucocorticoid hormones, which increases the L/S ratio of the amniotic fluid. Lecithin (dipalmitoylphosphatidylcholine) 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.

189. The answer is a. (*Barrett, pp 547-550. Kaufman, pp 22-24. Levitzky, pp 107-110. Longo, pp 1702-1707.*) The elevated LAP, which is normally approximately 5 mm Hg, is indicative of an increase in left ventricular preload. Plotting LAP (preload) and cardiac output in the cardiac function curves below demonstrates that cardiac contractility has decreased since the previous admission. PVR, calculated as (mean PAP − mean LAP)/cardiac output, is (35 – 20)/3 = 5 mm Hg/L/min, which is higher than normal [(15 − 5 mm Hg)/5 L/min = 2 mm Hg/L/min]. PAWP measured with a Swan-Ganz catheter is an index of the pulmonary capillary hydrostatic pressure. Normal PAWP is ≤12 mm Hg. An elevated PAWP of 25 mm Hg is indicative of an increased pulmonary capillary hydrostatic pressure, which will drive fluid movement out of the pulmonary capillaries according to Starling law, thereby decreasing net fluid reabsorption into the pulmonary capillaries.



190. The answer is a. (*Barrett, pp 653-654, 661. Kaufman, pp 282-283. Levitzky, pp 156, 181-182, 202-209. Longo, pp 2157-2160. McPhee and Hammer, p 222.*) 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 Pa_{O_2} stimulating the peripheral chemoreceptors (hypoxic drive) becomes the primary drive to breathe in chronic hypercapnia. Although supplemental oxygen is the only pharmacologic therapy demonstrated to decrease mortality in patients with COPD, administration of too high of an oxygen concentration can raise Pa_{O_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 Pa_{CO_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.

191. The answer is e. (*Barrett, pp 649-653. Le, p 550. Levitzky, pp 181-184.*) Cyanide impairs oxidative phosphorylation, which impairs the ability of the tissues to utilize oxygen causing hypoxia. In histotoxic hypoxia, oxygen extraction (CaO_2–CvO_2) is impaired, as evidenced by greater-than-normal values of PVO_2 (normal = 40 mm Hg) and SVO_2 (normal = 75%). The patient is not hypoxemic and does not have a diffusion defect because Pa_{O_2} is not lower than normal (80 to 100 mm Hg). 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.

192. The answer is b. (*Barrett, 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 Pa_{O_2} increases, which attenuates the hypoxic pulmonary vasoconstriction present in the fetus, causing PVR and pressures to decrease. The increased Pa_{O_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 approximately 48 hours (though ductal flow is reversed from that in fetal life).

193. The answer is b. (*Levitzky, pp 20-23, 41-42. Longo, pp 2084, 2182-2184.*) The low FVC 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 Pa_{CO_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.

194. The answer is e. (*Barrett, pp 657-658. Levitzky, pp 189-195, 207-209.*) 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 in an area called the ventral respiratory group. 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.

195. The answer is c. (*Barrett, pp 634-635. Le, pp 550, 582. Levitzky, pp 75, 264.*) The alveolar oxygen tension is calculated using the modified alveolar gas equation:

$$P_{AO_2} = P_{IO_2} - Pa_{CO_2}/R$$
$$P_{AO_2} = [0.5 \times (747 - 47 \text{ mm Hg})] - 40 \text{ mm Hg}/0.8$$
$$P_{AO_2} = 350 \text{ mm Hg} - 50 \text{ mm Hg} = 300 \text{ mm Hg}$$

196. The answer is c. (*Levitzky, pp 75, 181-182, 264.*) The A–a O_2 gradient is the partial pressure difference between the alveolar gas and arterial blood. The Pa_{O_2} has been measured. The alveolar oxygen tension must be calculated using the modified alveolar gas equation:

$$P_{AO_2} = P_{IO_2} - Pa_{CO_2}/R$$
$$P_{AO_2} = [0.21 \times (760 - 47 \text{ mm Hg})] - 60 \text{ mm Hg}/0.8$$
$$P_{AO_2} = 150 \text{ mm Hg} - 75 \text{ mm Hg} = 75 \text{ mm Hg}$$
$$(A–a)\ O_2 \text{ gradient} = 75 \text{ mm Hg} - 60 \text{ mm Hg} = 15 \text{ mm Hg}$$

The patient's low arterial oxygen tension (hypoxemia; hypoxic hypoxia) results from a low P_{AO_2} due to hypoventilation (as evidenced by the elevated Pa_{CO_2}), and thus the (A–a) O_2 gradient is within the normal range.

197. The answer is d. (*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.

198. The answer is a. (*Levitzky, pp 32-48.*) Bronchospasm increases the resistance to airflow, which makes it more difficult to expel gas rapidly from the lung during expiration; therefore, although both FEV_1 and vital capacity decrease, the percent of gas expelled in 1 second as a function of the total amount that can be expelled (the FEV_1/FVC ratio) also decreases dramatically. Obstructive disease also produces air trapping, which increases the residual volume, FRC, and total lung capacity.

199. The answer is d. (*Barrett, pp 659-669. Kaufman, pp 285-286. Levitzky, pp 199-200, 202-211. Longo, pp 2186-2189.*) The central chemoreceptors play the major role in providing the normal drive to breathe. They respond to changes in $[H^+]$ in the CSF, which are brought about by changes in arterial P_{CO_2}. The failure of CO_2 to significantly 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 P_{O_2} was increased (hyperoxia) and increased slightly in response to an increase in arterial P_{CO_2}. 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.

200. The answer is d. (*Barrett, pp 651-652. Le, pp 557, 560, 579. Levitzky, pp 113-116, 174-175, 180-183, 210-211. Longo, pp 2130-2141.*) $\dot{V}/\dot{Q}$ mismatches will cause arterial oxygen levels (Pa_{O_2}) to decrease. A decreased Pa_{O_2} will stimulate the peripheral chemoreceptors, which, in turn, will increase alveolar ventilation and decrease Pa_{CO_2}. The decreased Pa_{CO_2} will cause a respiratory alkalosis (increased pH). Hypoxemia may also cause lactate levels to rise, increasing the anion gap (and blunting the rise in pH). The fall in Pa_{O_2} causes the A–a gradient to rise.

201. The answer is e. (*Barrett, pp 632-633. Le, p 566. Levitzky, pp 125-128.*) 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 $PACO_2$ lower and P_{AO_2} higher than they are at the base.

202. The answer is a. (*Levitzky, pp 107-110. McPhee and Hammer, pp 233-236.*) 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.

203. The answer is c. (*Barrett, pp 662, 672-677, 686-688. Levitzky, pp 205-209. Longo, pp 1665-1668.*) 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 acute 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. The central chemoreceptors are unresponsive to hypoxemia (acute or chronic). In addition, the central chemoreceptors do not mediate the increase in ventilation in response to a decrease in arterial pH because the blood–brain barrier is relatively impermeable to hydrogen ions.

204. The answer is a. (*Levitzky, pp 49-51. McPhee and Hammer, pp 216-217.*) 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.

205. The answer is e. (*Levitzky, pp 189-198.*) Transection of the brainstem above the pons would prevent any changes in ventilation from 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.

206. The answer is c. (*Barrett, pp 213-214. Le, p 547. Levitzky, pp 12-23, 29-32.*) 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 within the pleural space. When one reaches lung volumes in excess of approximately 70% of the total lung capacity, the chest wall recoil is also inward.

207. The answer is a. (*Levitzky, pp 164-181.*) Pneumonia and other pulmonary infiltrative diseases cause a decreased $\dot{V}/\dot{Q}$, which results in hypoxemia and an increase in the alveolar–arterial Po_2 difference (A–a Po_2). There is no carbon dioxide retention because the hypoxemia stimulates carotid body chemoreceptors causing reflex hyperventilation and a decreased $Paco_2$. Pneumonia and other pulmonary infiltrative diseases are associated with a decrease in lung compliance, making the lungs more difficult to inflate. The presence of alveolar exudate would tend to decrease diffusing capacity of the lung. Physiological dead space is characterized by a $\dot{V}/\dot{Q}$ of ∞, not a decreased $\dot{V}/\dot{Q}$, as seen in pneumonia.

208. The answer is d. (*Le, pp 546, 549, 553. Longo, pp 2170-2177.*) All of these are postoperative complications, but the presentation is most closely associated with the development of a pulmonary thromboembolism secondary to venous stasis in the extremity. The patient's dead space-to-tidal volume ratio is 0.67 in contrast to a normal value in the range from 0.2 to 0.4. The increase in dead space ventilation indicates that there is an increase in the volume of the respiratory track that is ventilated, but not perfused. Pulmonary embolism is a dead space–producing disease, whereas pneumonia, atelectasis, and pneumothorax are all shunt-producing diseases, that is, they increase the volume of the respiratory track that is perfused but not ventilated.

209. The answer is b. (*Kaufman et al., pp 239-245. Levitzky, pp 171-181. Longo et al., pp 363-371.*) Respiratory muscle paralysis causes an acute, uncompensated respiratory acidosis. The primary disturbance is an elevation in arterial Pco_2 due to alveolar hypoventilation from the impaired mechanics of breathing. 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. In acute respiratory acidosis, the plasma HCO_3^- concentration increases 1 mmol/L for every 10 mm Hg increase in $Paco_2$ due to intracellular buffering. In chronic respiratory acidosis (eg, in COPD), the kidneys compensate for the acidosis by increasing the net excretion of H^+, which increases the plasma $[HCO_3^-]$ by 0.4 mmol/L for every mm Hg increase in $Paco_2$, which helps return the pH back into the normal range (*choice c*). The interpretation of *choice a* is metabolic acidosis, in which there is a lower than normal pH due to a primary decrease in plasma $[HCO_3^-]$, with compensatory hyperventilation that decreases arterial Pco_2. *Choice d* represents acute respiratory alkalosis, in which hyperventilation lowers arterial Pco_2 and increases arterial pH; plasma $[HCO_3^-]$ decreases 0.2 mmol/L for every mm Hg decrease in $Paco_2$ due to intracellular buffering. *Choice e* is compensated metabolic alkalosis.

210. The answer is c. (*Levitzky, pp 65-67, 73-75, 171-172.*) A decrease in alveolar ventilation results in an increased $Paco_2$. Alveolar hypoventilation in this patient is likely due to shallow breathing from abdominal pain or depressed respirations secondary to pain medication. 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. $\dot{V}/\dot{Q}$ inequality causes hypoxemia, and thus reflex hyper-ventilation. At a constant tidal volume and respiratory rate, a decrease in the dead space volume would increase alveolar ventilation, and thus lower the $Paco_2$.

211 and 212. The answers are b for 211 and e for 212. (*Levitzky, pp 120-122, 263.*) The fraction of the pulmonary blood flowing bypassing the lung (the shunt, $\dot{Q}_s$) compared with the total pulmonary blood flow ($\dot{Q}_T$) is calculated using the following equation:

$$\dot{Q}_S/\dot{Q}_T = C_cO_2 - C_aO_2/C_cO_2 - C_VO_2$$
$$= \frac{19\ \text{mL/dL} - 18\ \text{mL/dL}}{19\ \text{mL/dL} - 14\ \text{mL/dL}}$$
$$= 0.2$$

where C_c is the end pulmonary capillary blood oxygen content, CaO_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% to 5% of the cardiac output. In this case, there is a 20% shunt.

The oxygen consumption can be calculated if the cardiac output and the difference between the arterial and venous oxygen content are known using the Fick equation:

$$\dot{V}O_2 = CO \times (C_aO_2 - C_vO_2)$$
$$= 6000\ \text{mL/min} \times (18\ \text{mL/dL} - 14\ \text{mL/dL})$$
$$= 240\ \text{mL/min}$$

213. The answer is d. (*Le, p 550. Levitzky, pp 23, 171-173. Longo, p 278.*) Kyphoscoliosis is a deformity of the spine involving both lateral displacement (scoliosis) and anteroposterior angulation (kyphosis), which decrease the compliance of the chest wall. Decreased chest wall compliance and respiratory muscle weakness cause inadequate alveolar ventilation, which leads to an accumulation of carbon dioxide and a decrease in arterial pH (respiratory acidosis). Restrictive impairments are characterized by a decrease in all lung volumes and capacities, but a normal or increased ratio of FEV_1 to FVC.

214. The answer is c. (*Levitzky, pp 90-102, 105-107.*) Increasing cardiac output causes PVR to passively decrease due to two mechanisms— distention of perfused vessels and recruitment of more parallel vascular beds. Cardiac output is often elevated in septic shock, which differentiates it from hypovolemic and cardiogenic shock. Decreasing alveolar P_{O_2} causes hypoxic pulmonary vasoconstriction and a rise in PVR. Increasing alveolar P_{CO_2} or pulmonary artery H^+ concentration also causes PVR to rise. The sympathetic nervous system exerts little effect on PVR under physiologic conditions, but stimulation of sympathetic nerves will constrict the pulmonary vessels, causing increased PVR. At high lung volumes, the pulmonary capillaries ("alveolar" vessels) are stretched and compressed causing an increased PVR; this is true with spontaneous respirations and occurs even more so with positive pressure ventilation.

215. The answer is a. (*Barrett, pp 666-669. Levitzky, pp 228-233*). During moderate aerobic exercise, oxygen consumption and CO_2 production increase, and alveolar ventilation increases in proportion. Thus, Pa_{CO_2} (and Pa_{O_2}) does 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 approximately 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 arterial lactate and a decrease in the pH of the blood.

216. The answer is d. (*Levitzky, pp 130-140. Longo, pp 456, 898-900.*) The diffusing capacity is the volume of gas transported across the lung per minute per mm Hg 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 and by the reaction with hemoglobin. Increases in the diffusing capacity can be produced by increasing the concentration of hemoglobin within the blood (polycythemia). The approach to the patient with polycythemia includes determination of not only hematocrit but also red cell mass, erythropoietin levels, arterial oxygen saturation, and hemoglobin's affinity for oxygen in order to distinguish among the various causes. The diffusing capacity of the membrane can be calculated by rearranging Fick law of 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 CHF.

217. The answer is e. (*Kaufman, p 272. Levitzky, pp 153-154, 183.*) 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 why 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) P_{CO_2}, causing CSF pH to rise. Carboxyhemoglobin has a cherry-red color.

218. The answer is e. (*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.

219. The answer is c. (*Barrett, pp 661, 665-667. Levitzky, pp 207-209.*) 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 the ECF is affected by the P_{CO_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 Pa_{O_2} or blood oxygen content but rather depressed by long-term or severe decreases in oxygen supply.

220. The answer is e. (*Le, pp 233, 544, 564. Levitzky, pp 32-36, 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 dead space but has no significant effect on the lung compliance, and thus does not affect the elastic work of breathing.

221. The answer is b. (*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 3 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 $\dot{V}/\dot{Q}$ ratio is lower at the base than at the apex in a normal lung.

222. The answer is e. (*Le, p 569. Levitzky, pp 44-46.*) A restrictive impairment in which lung elastic recoil is increased and lung compliance is decreased, such as occurs in sarcoidosis, shifts the normal MEFV 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.

223. The answer is a. (*Levitzky, pp 86-98, 130-132, 228-234.*) 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 law of diffusion. The increased perfusion of the lungs is accompanied by an even greater increase in ventilation, so the $\dot{V}/\dot{Q}$ 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 PAPs increase slightly during exercise because of the increased pulmonary blood flow and blood volume.

224. The answer is b. (*Levitzky, pp 181-184. Longo, pp 2199-2200.*) Type III respiratory failure occurs as a result of lung atelectasis, which commonly occurs in the perioperative period. Following general anesthesia, decreases in FRC lead to collapse of dependent lung units. This leads to intrapulmonary shunting (areas that are perfused but not ventilated). When the $\dot{V}/\dot{Q}$ ratio is 0, there is no gas exchange and arterial oxygen tension decreases. The hypoxemia stimulates the peripheral chemoreceptors to increase respiratory drive, causing a respiratory alkalosis. Perioperative atelectasis can be treated by frequent changes in position, chest physiotherapy, aggressive control of incisional or abdominal pain, and intermittent positive-pressure breathing. Typical chest examination findings in atelectasis with a patent airway include bronchial, rather than the normal vesicular, breath sounds heard at the lung bases and the presence of crackles, an adventitious (abnormal) breath sound in which there are discontinuous, typically inspiratory sounds on inspiration created by the alveoli and small airways opening and closing with respiration.

225. The answer is b. (*Le, p 555. Levitzky, pp 41-46. Longo, p 2125.*) 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 FEV_1/FVC ratio that is close to normal. All lung volumes and capacities are decreased in patients with restrictive lung disease. 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 $\dot{V}/\dot{Q}$ abnormalities is indicated by the hypoxemia and need for supplemental oxygen.

226. The answer is a. (*Levitzky, pp 32-40.*) As lung volume decreases, intrapleural pressure increases in accordance with Boyle law. The greater intrapleural pressure decreases the radial traction on the airways, thereby decreasing airway diameter and increasing airway resistance. During a forced expiration or at residual volume, the intrapleural pressure actually becomes 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.

227. The answer is e. (*Levitzky, pp 41, 54-59.*) 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 vital capacity, which is the maximal amount of gas that can be expired following a maximal inspiration. Spirometry cannot be used to measure the volume of the gas that remains in the lungs following a maximal expiration (residual volume), and thus cannot directly measure the lung capacities that contain the residual volume, that is, the FRC and the total lung capacity. The peak flow rate is the maximal rate at which the volume of gas is exhaled. The measurement of flow rate requires a pneumotach, an instrument that integrates exhaled volume to derive the flow rate, or by a peak flow meter that patients can use at home, which are calibrated to record exhaled flow rates.

228. The answer is a. (*Levitzky, pp 113-116, 122-127, 181-184.*) Areas with low $\dot{V}/\dot{Q}$ ratios produce hypoxemia or a decreased Pa_{O_2}, which leads to (a) a decrease in the dissolved oxygen content of the blood and (b) a decrease in Pa_{CO_2}, due to stimulation of the peripheral chemoreceptors. At lower Pa_{O_2} levels, arterial oxygen saturation is decreased, which decreases the oxyhemoglobin content. Because the mixed alveolar P_{O_2} is normal and the arterial P_{O_2} is less than normal, the A–a gradient is greater than normal.

229. The answer is b. (*Levitzky, pp 44-46.*) A MEFV curve is generated during a FVC 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 MEFV 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.

Questions

230. During which interval on the electrocardiogram (ECG) below does the aortic valve close?

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

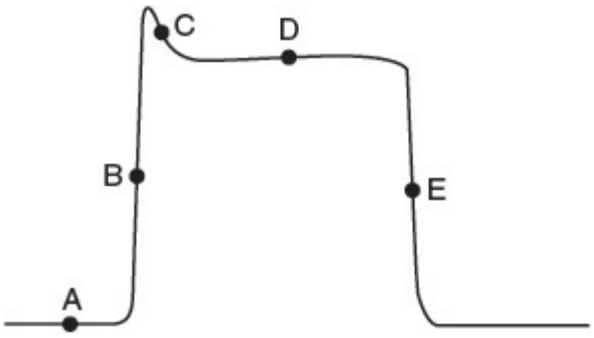
231. A 56-year-old woman presents for her annual physical examination. Her physician auscultates a late systolic crescendo murmur with a midsystolic click. The murmur is best heard over the apex, is loudest at S_2, is shortened with squatting, and is longer and more intense when venous return is decreased by standing or a Valsalva maneuver. 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. Ventricular end-diastolic pressure
e. Ventricular end-diastolic volume

232. 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. An afterload-reducing medication is prescribed. Which of the following values would provide the best measure of the effectiveness of the medication in reducing left ventricular afterload in aortic stenosis?

a. Left ventricular end-diastolic pressure
b. Left ventricular mean systolic pressure
c. Mean arterial blood pressure
d. Pulmonary capillary wedge pressure
e. Total peripheral resistance

233. 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

234. During a routine physical examination, a 32-year-old woman is found to have second-degree heart block. Which of the following ECG recordings is consistent with her diagnosis?

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

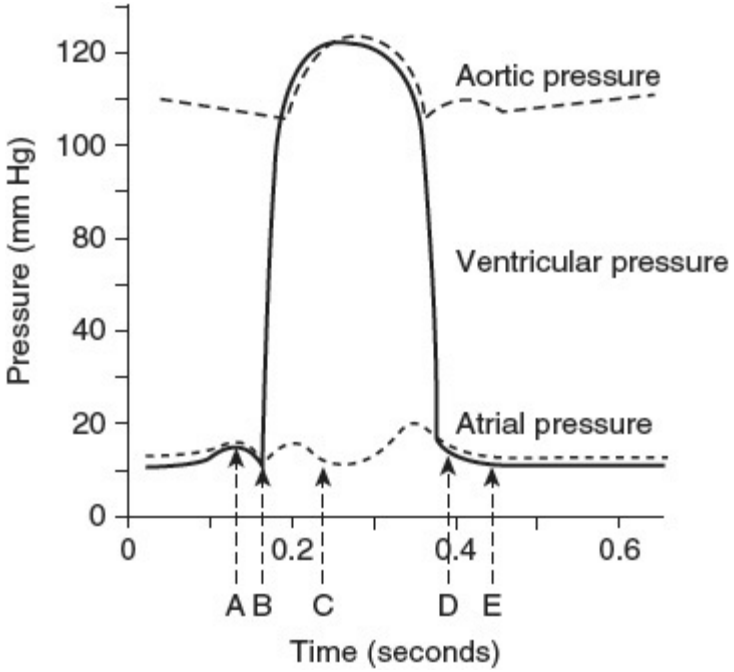
235. The spouse of a 58-year-old man calls 911 because her husband complains of chest pain radiating down his left arm. He is transported to the emergency department, where an ECG and cardiac enzymes indicate a recent myocardial infarction. The man undergoes cardiac catheterization, including coronary 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. Aorta and capillaries
b. Left atrium and left ventricle
c. Left ventricle and aorta
d. Pulmonary artery and left atrium
e. Right atrium and right ventricle

236. A 55-year-old man reports several episodes of syncope and worsening exercise intolerance over the past year. Of the following, which is the most likely diagnosis?

a. Sinus arrhythmia
b. First-degree heart block
c. Second-degree heart block
d. Third-degree heart block
e. Multifocal atrial tachycardia

237. In the hemodynamic pressure tracings below, rapid ventricular filling begins at which point?



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

238. An 82-year-old woman was admitted to the hospital with ascites, peripheral edema, and shortness of breath. Cardiac catheterization was conducted and the following values were obtained:

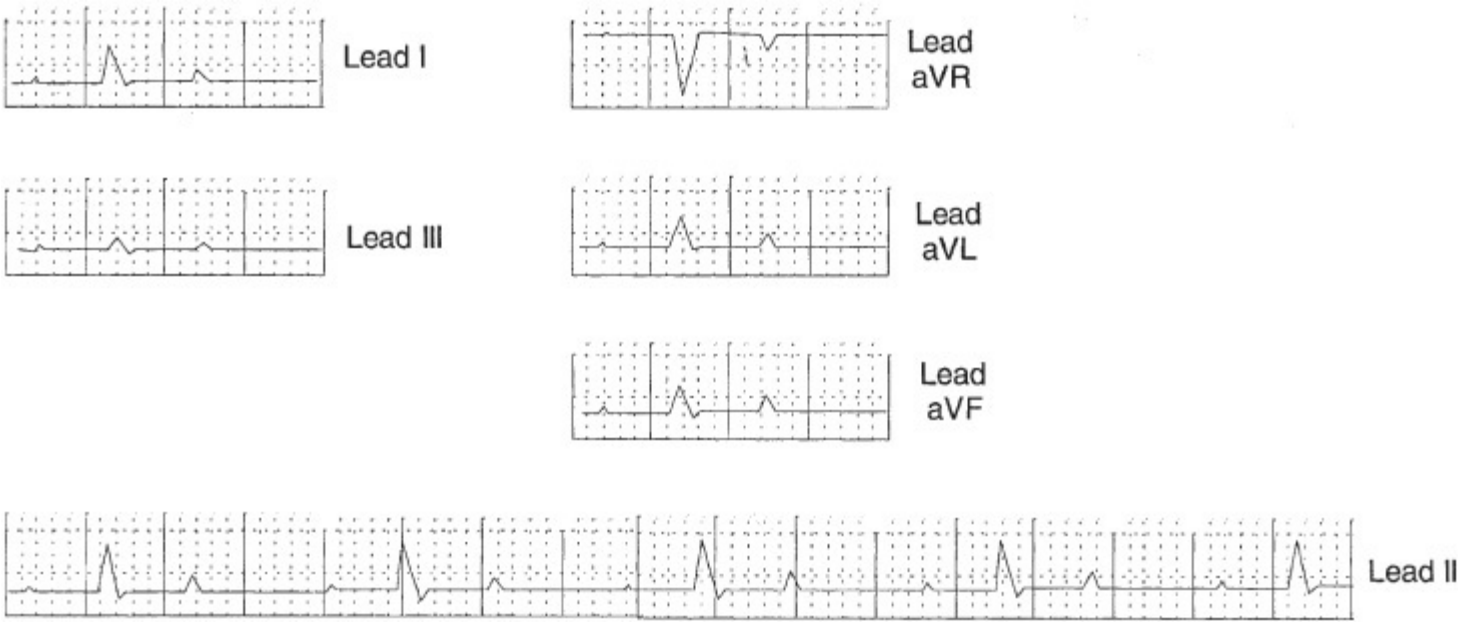
Pulmonary vein O_2 content = 20 mL O_2/100 mL blood
Pulmonary artery O_2 content = 12 mL O_2/100 mL blood
Oxygen consumption (VO_2) = 280 mL/min
Stroke volume = 40 mL

What is the woman's cardiac output?
a. 2.86 L/min
b. 3.5 L/min
c. 7.0 L/min
d. 8.0 L/min
e. 9.24 L/min

239. A 66-year-old man 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. Of the following, which is the most likely diagnosis?

a. Aortic regurgitation
b. Aortic stenosis
c. Mitral valve prolapse
d. Pulmonary regurgitation
e. Pulmonic stenosis

240. The following six-lead frontal ECG was performed as part of an annual heath maintenance physical examination. Which of the following is the mean electrical axis (MEA) of the patient?



a. −10 degrees
b. +10 degrees
c. +20 degrees
d. +40 degrees
e. +70 degrees

241. 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 physiologist starts the patient on a walking regimen. During exercise in cardiac transplant patients, cardiac output increases primarily due to an increase in which of the following?

a. Arterial blood pressure
b. Heart rate
c. Stroke volume
d. TPR
e. Venous compliance

242. A patient complaining of an irregular heartbeat is referred for a cardiac electrophysiological study. Propagation of the action potential through the heart is fastest in which of the following cardiac structures?

a. SA node
b. Atrial muscle
c. Atrioventricular (AV) node
d. Purkinje fibers
e. Ventricular muscle

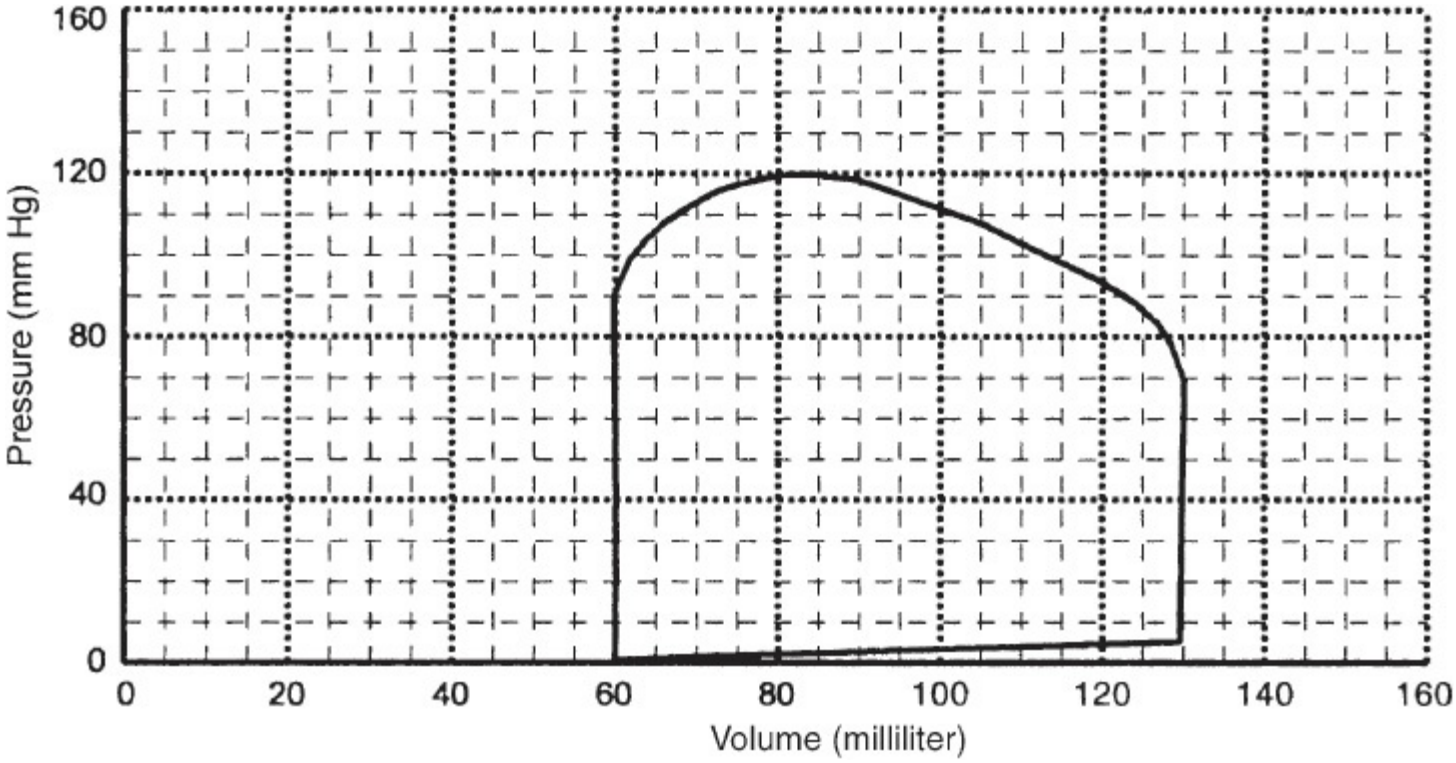
243. A 75-year-old woman presents with fatigue and orthopnea. Rales are heard widely over both lung fields. After several days of furosemide to treat the patient's fluid retention, lisinopril therapy is initiated. Which of the following is primarily responsible for the improvement in her condition with lisinopril?

a. An increase in cardiac contractility
b. An increase in ventricular end-diastolic pressure
c. An increase in ventricular wall thickness
d. A reduction in heart rate
e. Stabilization of cardiac remodeling

244. 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. Doubled
d. Increased by 50%
e. Increased 16-fold

245. A patient undergoes cardiac catheterization to assess his left ventricular function prior to thoracic surgery. What is his ejection fraction percentage, as determined from the left ventricular pressure–volume curve illustrated below?



a. 34%
b. 46%
c. 54%
d. 60%
e. 75%

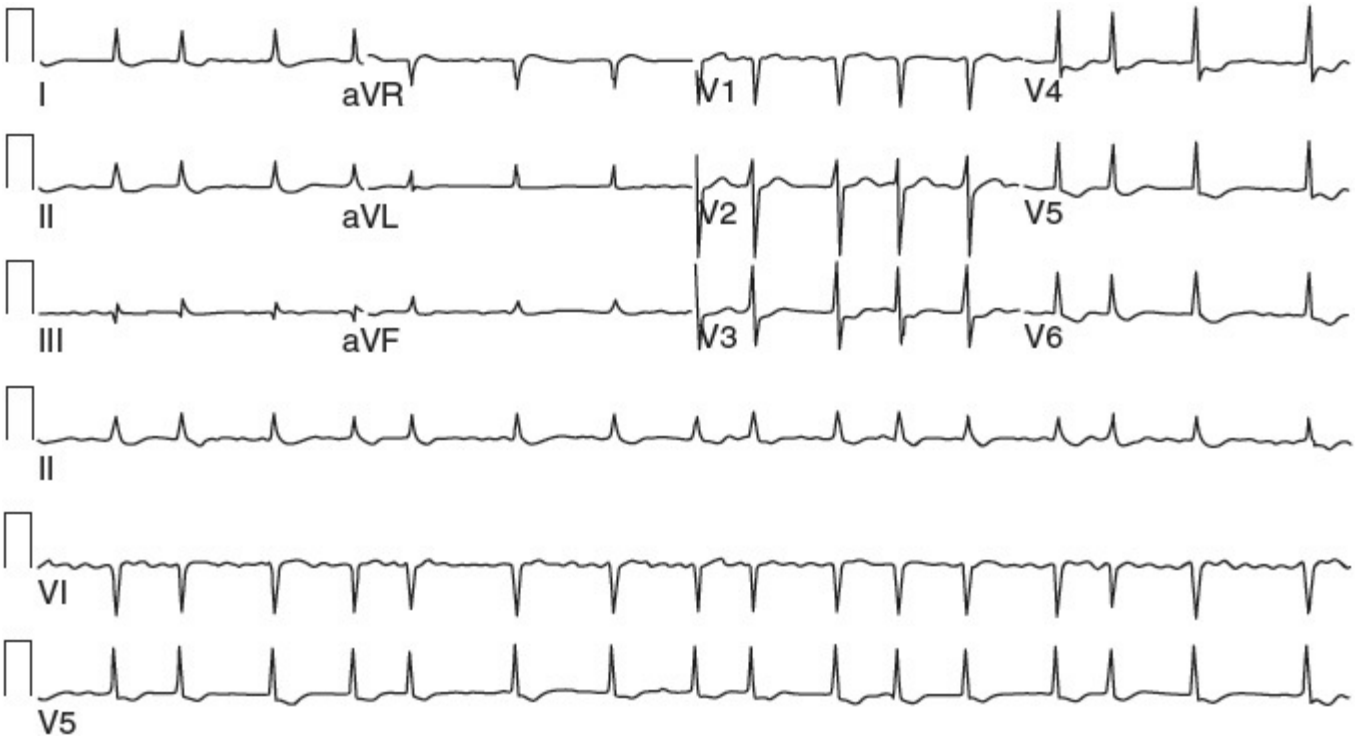
246. A 72-year-old man is hospitalized with a history of respiratory distress, fever, and fatigue. An ECG reveals ST-segment and T-wave abnormalities and echocardiography shows an ejection fraction of 30%. Over the next several days, significant peripheral edema develops. The edema is most likely caused by which of the following?

a. Decreased capillary permeability
b. Decreased arterial pressure
c. Increased central venous pressure
d. Increased lymphatic flow
e. Increased plasma protein concentration

247. 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. Isovolumetric relaxation
c. Rapid ejection
d. Rapid ventricular filling
e. Systole

248. A 57-year-old man complains of palpitations that are relieved by pressing on his eyeball. His ECG is shown below. An increase in which of the following is most likely to accompany this condition?



(Reproduced, with permission, from Crawford MH. *Current Diagnosis & Treatment: Cardiology*, 3rd ed. New York: McGraw-Hill; 2009:260.)

a. Left atrial pressure
b. MAP
c. Stroke volume
d. Sympathetic tone
e. Venous a wave

249. 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 normal 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 closing of the pulmonic valve
e. Delayed opening of the mitral valve

250. A 68-year-old man presents for his quarterly cardiology examination. Upon auscultation, a third heart sound is heard. Of the following conditions, which is the most likely cause of an S_3?

a. Aortic regurgitation
b. Aortic stenosis
c. Heart failure
d. Right bundle branch block
e. Tricuspid regurgitation

251. A 23-year-old woman presents with fatigue. She is found to have a mid-systolic murmur and higher-than-normal cardiac output. The differential diagnosis based on these findings includes which of the following?

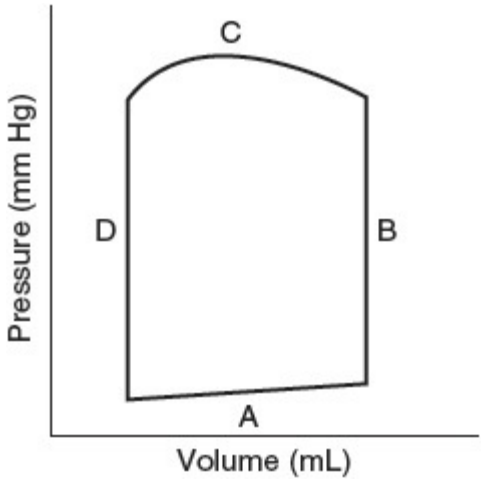
a. Anemia
b. Cardiac tamponade
c. Mitral regurgitation
d. Mitral stenosis
e. Third-degree heart block

252. A 22-year-old woman with lightheadedness and recurrent syncope is taken to the emergency department. Her symptoms are relieved by intravenous atropine administration. Antagonism of cholinergic muscarinic receptors causes an increase in which of the following physiologic variables?

a. Heart rate
b. PR interval
c. Stroke volume

d. TPR
e. Ventricular contractility

253. A 58-year-old woman presents for evaluation of headaches. Her blood pressure is 170/70 mm Hg. Her physical examination is otherwise unremarkable except for a diastolic murmur heard best over the left sternal border. During which phase of the pressure–volume loop below does the murmur occur?



a. Segment A
b. Segment B
c. Segment C
d. Segment D

254. Physical examination of a 41-year-old IV drug 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. Aortic regurgitation
b. Atherosclerosis
c. Mitral stenosis
d. Tachycardia
e. Tricuspid regurgitation

255. A 50-year-old woman complains of intermittent chest discomfort. She is given an exercise stress test to determine if the angina is a result of myocardial ischemia. The test will be considered positive if which of the following occurs?

a. An increase in mean arterial pressure
b. Depression of the ST-segment
c. Tachycardia
d. A diastolic murmur
e. Widening of the QRS complex

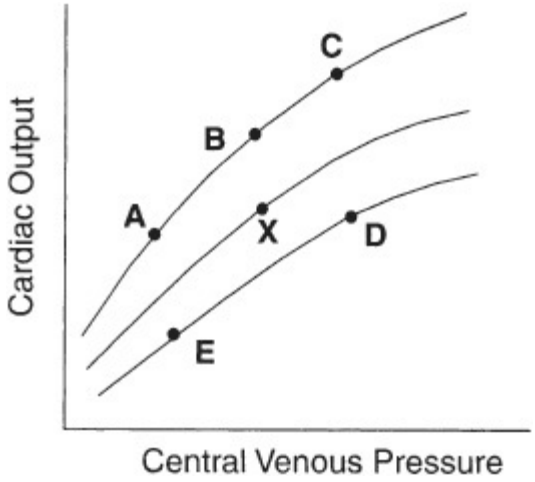
256. A 64-year-old woman is postoperative day 1 after a cholecystectomy. She suddenly stands up after being supine since the operation. As a result, which of the following hemodynamic variables will increase?

a. Heart rate
b. Mean arterial pressure
c. Stroke volume
d. Venous return
e. Ventricular end-diastolic volume

257. 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?

a. Aortic coarctation
b. Left ventricular hypertrophy
c. Mitral regurgitation
d. Pulmonary vasoconstriction and hypertension
e. Systemic hypertension

258. A 74-year-old black man with a past medical history significant for two previous myocardial infarctions presents with atrial fibrillation. His ejection fraction by echocardiography is 25%. Which of the shifts in the cardiac function curves shown below are consistent with the changes in ventricular function that occur before and after digitalis administration in a patient with congestive heart failure (CHF) assuming that normal function is depicted by the curve on which an **X** is marked?



a. A → B
b. C → X
c. D → X
d. E → D
e. E → X

259. A 19-year-old man 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. Aorta
b. Arteries and arterioles
c. Capillaries
d. The heart
e. Venules and veins

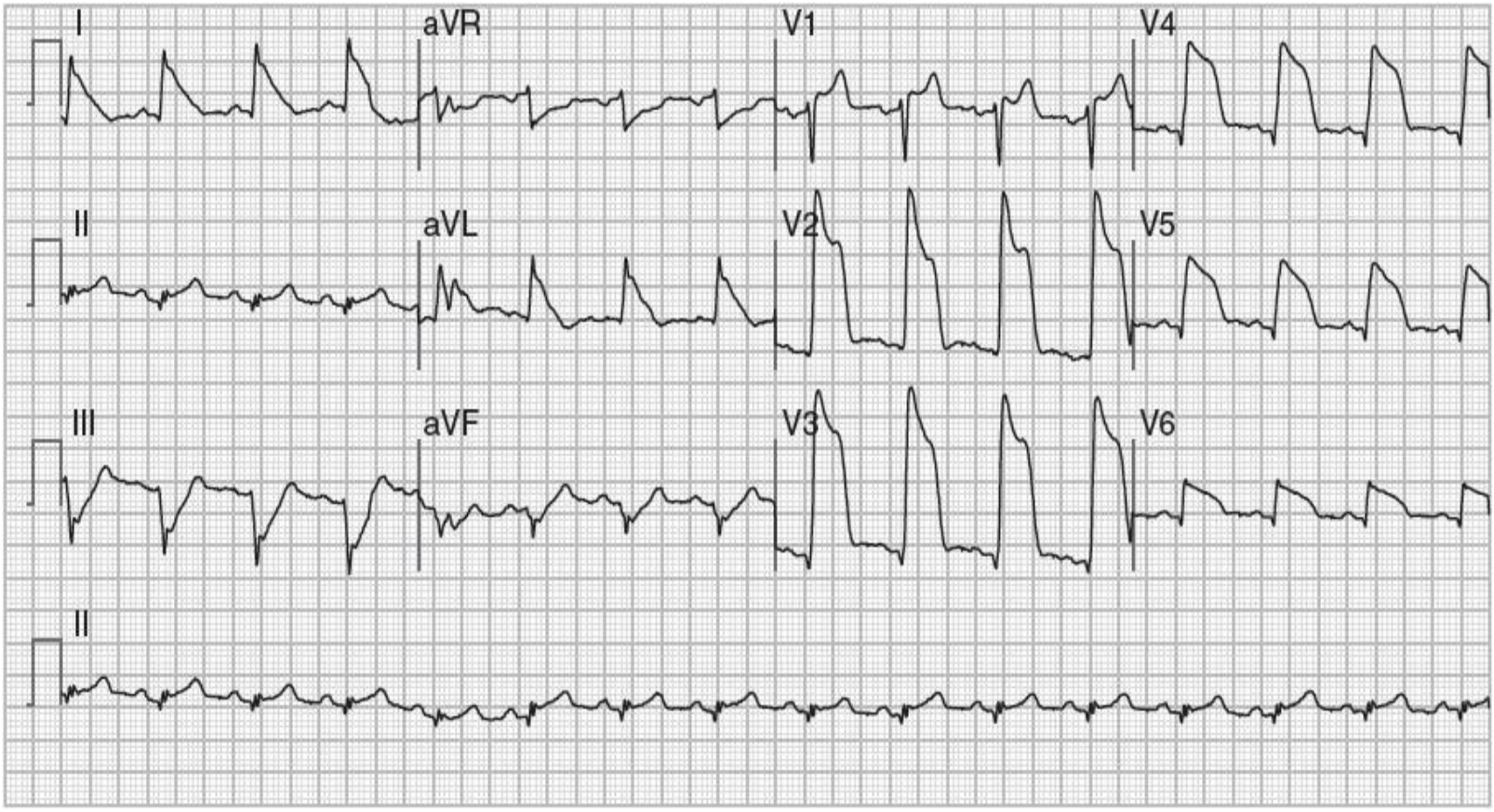
260. An 84-year-old woman presents with paroxysmal dizziness, syncope, confusion, and fatigue. Her heart rate did not change when the patient was instructed to perform a Valsalva maneuver. A 24-hour Holter monitor revealed periodic episodes of sinus bradycardia. Phase 4 of the pacemaker potential of SA nodal cells is caused by which of the following?

a. A decrease in the activity of the Na–K pump
b. A decrease in the flow of potassium out of the cell
c. An increase in the activity of the Na/Ca exchanger
d. An increase in the flow of calcium into the cell
e. An increase in the flow of sodium into the cell

261. During auscultation of a patient with long-standing hypertension, the physician notes that the splitting of the second heart sound is reversed with P_2 occurring before A_2. Which of the following is a common ECG finding accompanying paradoxical splitting of the second heart sound?

a. Left bundle branch block
b. Right bundle branch block
c. Sinus arrhythmia
d. Sinus bradycardia
e. Sinus tachycardia

262. A 56-year-old man was admitted to the hospital with angina and diaphoresis. A myocardial infarction is suspected, and a 12-lead ECG is ordered and shown below. The ECG is most effective in detecting a decrease in which of the following?



(Reproduced, with permission, from Fauci AS, Braunwald E, Kasper DL, et al. *Harrison's Principles of Internal Medicine*. 17th ed. New York: McGraw-Hill; 2008:e19-e25.)

a. Coronary blood flow
b. Ejection fraction
c. Mean blood pressure
d. Total peripheral resistance
e. Ventricular contractility

263. 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. A decrease in stroke volume
b. An increase in arterial compliance
c. An increase in heart rate
d. An increase in total peripheral resistance
e. Stiffening of the arteries

264. A 75-year-old woman makes an appointment to see her physician because of exertional dyspnea and an episode of syncope while dancing with her husband at their granddaughter's wedding. A systolic ejection murmur is auscultated that radiates to the carotid arteries. Her signs and symptoms are most likely due to which of the following?

a. Aortic regurgitation
b. Aortic stenosis
c. Mitral stenosis
d. Pulmonic regurgitation
e. Tricuspid stenosis

265. A 68-year-old sedentary, obese man 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 this patient?

a. Heart rate
b. Pulmonary capillary hydrostatic pressure
c. Systemic vascular resistance
d. Venous compliance
e. Ventricular contractility

266. A pacemaker is inserted in a patient in order to treat a prolonged PR interval detected on the ECG. Which of the following normally occurs during the PR interval?

a. The cardiac action potential passes through the AV node
b. The mitral and aortic valves are both closed
c. There is no change in the voltage tracing on the ECG
d. The second heart sound is heard
e. The ventricles are contracting

267. A 36-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 unifocal premature ventricular complexes (PVCs). Which of the following may predispose an athlete to the occurrence of PVCs?

a. An accessory bundle of Kent
b. Atrial fibrillation
c. Bradycardia
d. Inverted P waves
e. Sinus tachycardia

268. 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 cardiologist because of suspected heart failure. Which of the following is most consistent with a diagnosis of CHF?

a. Decreased heart rate
b. Decreased left ventricular energy consumption
c. Decreased pulmonary arterial wedge pressure
d. Increased left ventricular ejection fraction
e. Increased left ventricular wall tension

269. 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. Decreased arterial blood pressure
b. Decreased total peripheral resistance
c. Increased central venous pressure
d. Increased heart rate
e. Sympathetic-mediated positive inotropy

270. A 47-year-old man is brought to the emergency department because he had chest pain, was short of breath, and fainted at the gym during his daily workout. A prominent systolic ejection click and crescendodecrescendo systolic murmur is heard over the right sternal border. Which of the following findings is consistent with the patient's most likely diagnosis?

a. Decreased cardiac oxygen consumption
b. Decreased left ventricular systolic pressure
c. Decreased pulse pressure
d. Increased arterial blood pressure
e. Increased ejection fraction

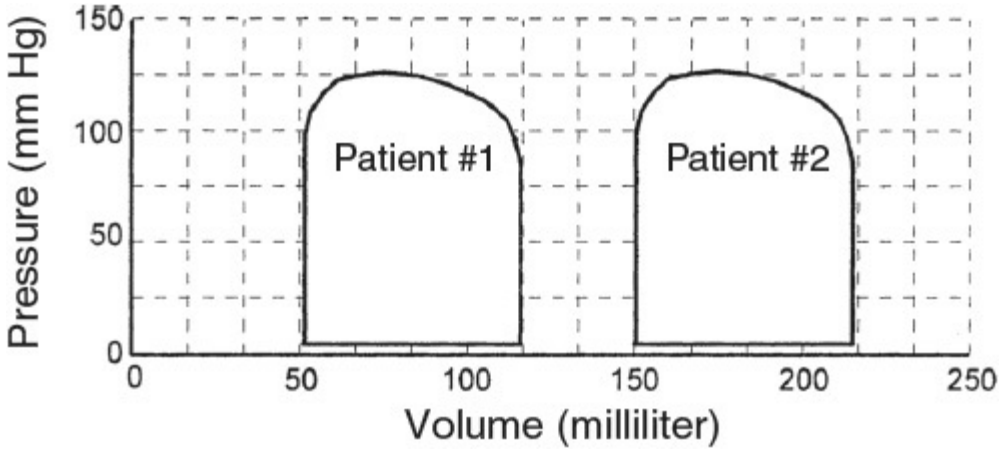
271. A patient with an inferior MI develops a stable bradycardia of 50 beats per minute (bpm). The cardiologist orders an ECG to evaluate whether there is sinus node dysfunction or an AV conduction disturbance. The diagnosis of a first-degree heart block is made in which of the following cases?

a. Asynchrony of P waves and QRS complexes
b. Fixed, prolonged PR interval followed by a nonconducted QRS complex at regular intervals
c. Normal PR interval, normal QRS complexes, increased R-R interval
d. Prolonged PR interval with every P wave followed by a QRS complex
e. The PR interval is progressively prolonged until a QRS complex is dropped

272. A 67-year-old man with a history of rheumatic heart disease presents with difficulty breathing when he exercises, which has worsened over the last year. Auscultation reveals a holosystolic murmur at the left 5th intercostal space along the midclavicular line. The murmur is loudest at the apex, radiates to the axilla, and is enhanced during expiration and when the patient is instructed to make a fist. Which of the following findings is most likely to be present?

a. Decreased arterial pressure
b. Decreased left ventricular preload
c. Increased cardiac output
d. Increased pulse pressure
e. Increased v wave

273. Ventricular pressure–volume curves are determined in two different patients, as illustrated below. Which of the following variables is greater in patient #1?



a. Afterload
b. Cardiac efficiency
c. Preload
d. Stroke volume
e. Stroke work

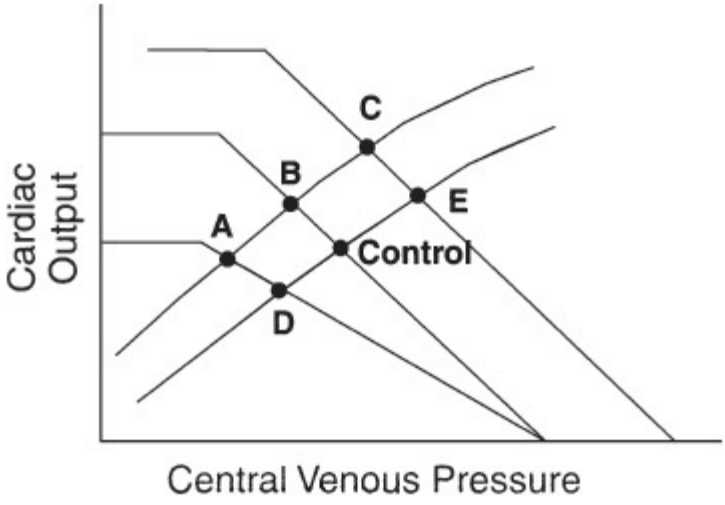
274. During a routine physical examination, a 35-year-old man is found to have a blood pressure of 170/105 mm Hg. The history reveals episodes of headache accompanied by palpitations, diaphoresis, and anxiety. Which of the following is the best initial pharmacotherapy for this patient's most likely diagnosis?

a. α-Adrenergic agonist
b. α-Adrenergic antagonist
c. β-Adrenergic agonist
d. β-Adrenergic antagonist
e. Glycoprotein IIb/IIIa antagonist

275. A 43-year-old man comes to his physician complaining of exhaustion and shortness of breath. After completing the physical examination, the physician suspects the patient may be suffering from pericardial tamponade. Which of the following observations led to the physician's putative diagnosis?

a. Bradycardia
b. Expiratory rales
c. Hypertension
d. Pulsus paradoxus
e. Third heart sound

276. Cardiac and vascular function curves were generated in a patient undergoing several maneuvers to evaluate his cardiac and cardiovascular reserves. Starting from the control point in the figure below, 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

277. A 40-year-old woman with metabolic syndrome is prescribed a low-calorie diet and 30 minutes of daily aerobic exercise. Sympathetic stimulation during exercise has which of the following effects on the heart?

a. A decrease in the cytosolic concentration of Ca^{2+} during systole
b. A decrease in intracellular concentration of cyclic AMP
c. An increase in the activity of the sarcoplasmic reticulum (SR) calcium pump
d. An increase in the duration of diastole
e. An increase in the duration of systole

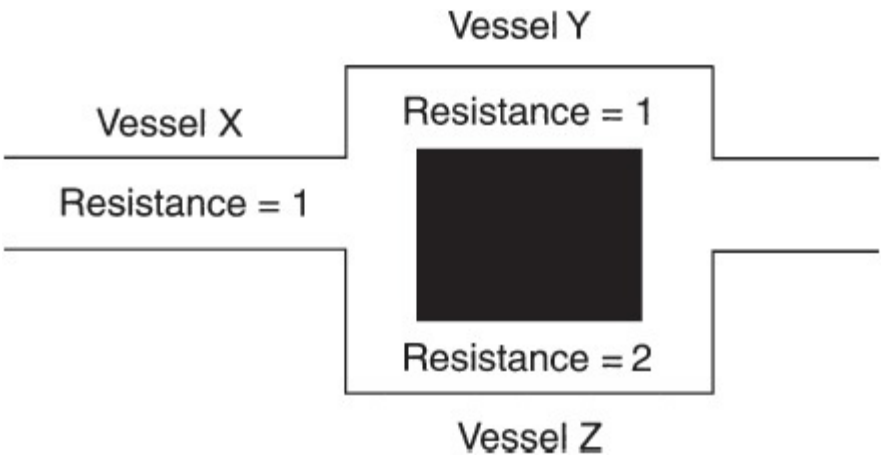
278. A 37-year-old patient is brought to the emergency department in shock. A decision is made to treat anaphylactic shock rather than hypovolemic shock based on an increase in which of the following variables?

a. Cardiac output
b. Heart rate
c. Serum creatinine
d. Total peripheral resistance
e. Ventricular contractility

279. 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. Diastolic pressure
b. Pulmonary vascular resistance
c. Stroke volume
d. Systemic vascular resistance
e. Venous compliance

280. 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?

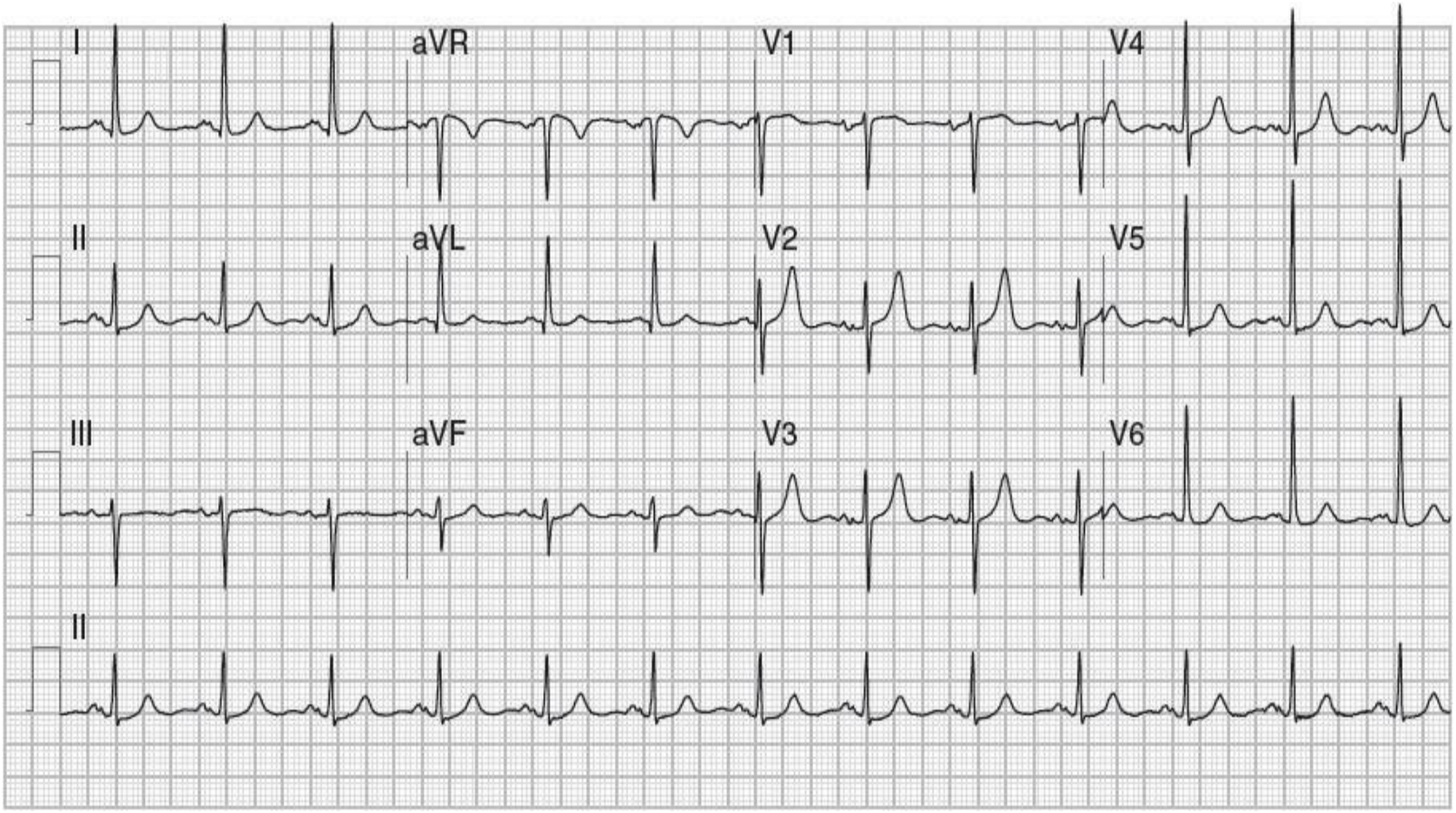


a. 1:1
b. 2:1
c. 3:1
d. 3:2
e. 4:3

281. 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 decrease.
b. Blood pressure and heart rate increase.
c. Blood pressure and heart rate remain constant.
d. Blood pressure decreases and heart rate increases.
e. Blood pressure increases and heart rate decreases.

282. A 75-year-old woman presents to her primary care physician's office in follow-up for her hypertension of 25 years. She is currently on losartan. Her ECG is shown below.



(Reproduced, with permission, from Fauci AS, Braunwald E, Kasper DL, et al. *Harrison's Principles of Internal Medicine*. 17th ed. New York: McGraw-Hill; 2008:e19-e28.)

Considering the history and ECG findings, this patient's left ventricular wall stress will be decreased by an increase in which of the following?

a. Contractility of the left atrium
b. Left ventricular end-diastolic volume
c. MAP
d. Thickness of the free wall of the left ventricle
e. TPR

283. A 47-year-old man with type II diabetes reports for his 6-month checkup. His doctor prescribes a daily 30-minute routine of walking at a brisk pace. During aerobic exercise, blood flow remains relatively constant to which of the following organs?

a. Brain
b. Heart
c. Kidneys
d. Skeletal muscle
e. Skin

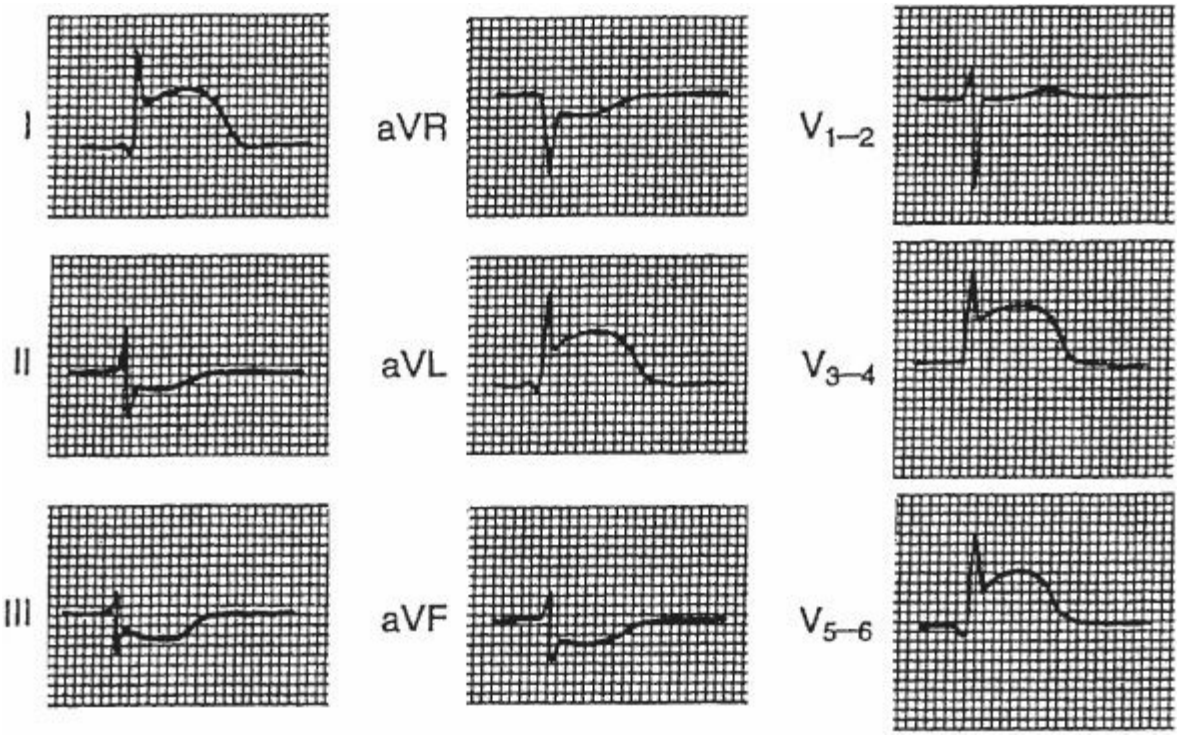
284. During which interval on the ECG below does the bundle of His depolarize?

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

285. A 56-year-old man presents with complaints of fatigue and headaches. During physical examination, he is found to have a wide pulse pressure. Which of the following conditions causes pulse pressure to increase?

a. Aortic stenosis
b. Arteriosclerosis
c. Heart failure
d. Hemorrhage
e. Tachycardia

286. 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 ECG changes are consistent with a diagnosis of which of the following?



a. Anterior infarction
b. Hyperkalemia
c. Hypokalemia
d. Posterior infarction
e. Ventricular premature beat

287. A 63-year-old woman presents to the emergency room with complaints of dyspnea, an elevated jugular venous pulse, and bilateral lower extremity edema. She is prescribed captopril. Which of the following best describes a beneficial effect of this drug?

a. Afterload is decreased
b. Arteriolar vasoconstriction is augmented
c. Bradykinin is reduced
d. A nonproductive cough can develop
e. Survival is decreased

288. A 29-year-old woman presents at the office of her obstetrician/gynecologist with breast tenderness. She reports that her last menstrual period was 6 weeks ago. An assay for human chorionic gonadotropin in her urine is positive. During pregnancy, which of the following is true of the maternal and fetal circulations?

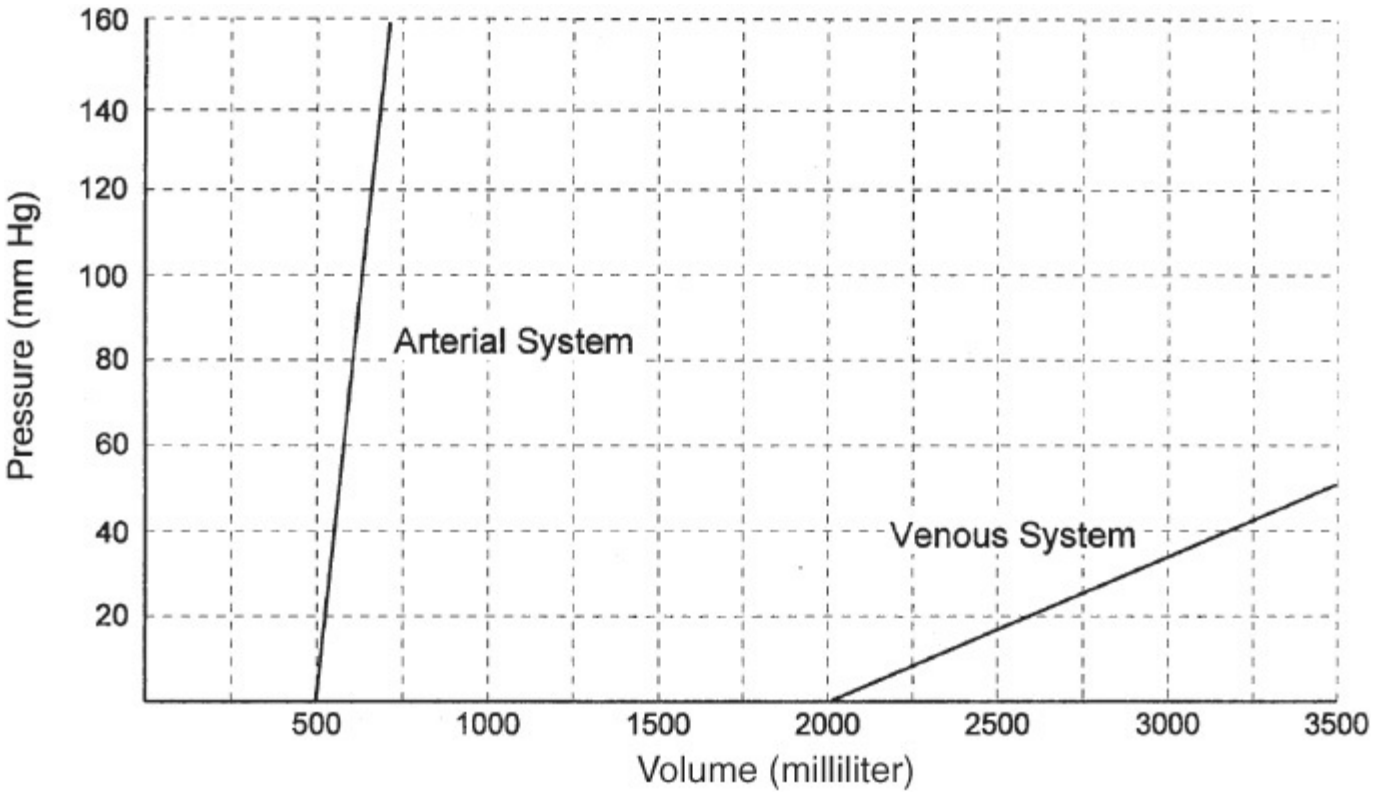
a. Fetal CO_2 that diffuses across the placenta is removed by the maternal uterine arteries.
b. The oxygen dissociation curve for fetal hemoglobin is shifted to the right of that of maternal hemoglobin A.
c. The highest partial pressure of oxygen in the fetus is in the umbilical arteries.
d. The majority of the fetal cardiac output goes to the placenta.
e. Uterine blood flow doubles.

289. 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?

a. Bradycardia
b. Low hematocrit
c. Metabolic alkalosis
d. Polyuria

e. Warm skin

290. 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?

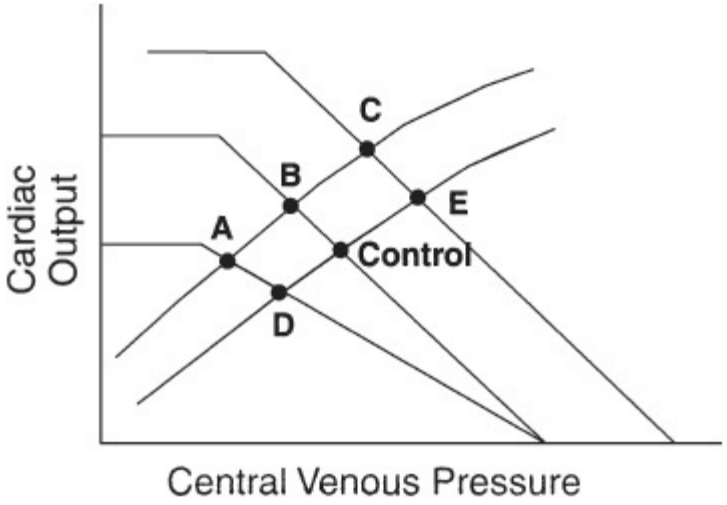


a. 15:1
b. 10:1
c. 1:1
d. 1:10
e. 1:20

291. A 6-day-old baby girl undergoes a routine physical examination. 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. Which of the following best describes the in utero function of the most likely structure causing the murmur?

a. It allows blood to flow from the aorta to the pulmonary artery.
b. It delivers oxygenated blood from the placenta to the left ventricle.
c. It diverts oxygenated blood away from the lungs to the aorta.
d. It is a high-resistance conduit, which helps to maintain normal fetal blood pressure.
e. It is located in the septum between the left and right atrium.

292. 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?

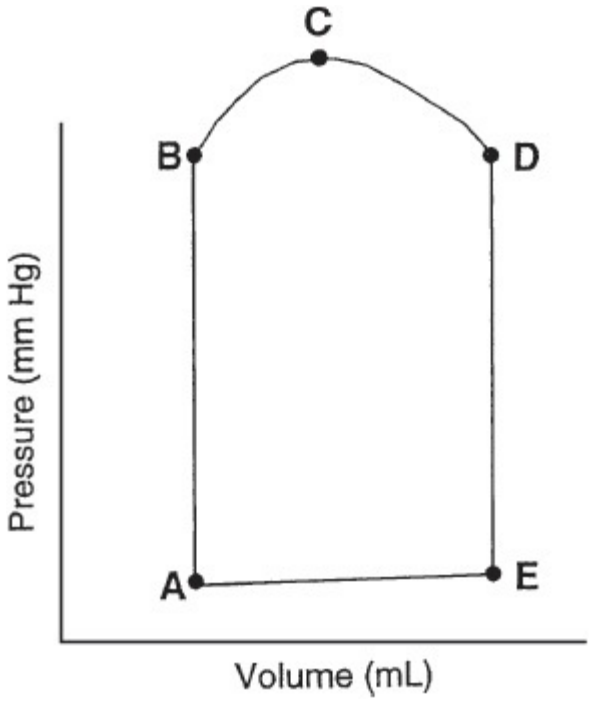


a. A
b. B
c. C
d. D
e. E

293. 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. High velocity of blood within the carotid artery
b. Increase in blood viscosity
c. Increase in hematocrit
d. Lengthening of the carotid artery
e. Widening of the carotid artery

294. In the pressure–volume loop below, systole begins at which of the following points?



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

295. 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. Adenosine

b. Antidiuretic hormone
c. Atrial natriuretic peptide
d. β_2-Adrenergic agonist
e. Nitric oxide

296. A 28-year-old woman gave birth without complications 48 hours ago to a term 8-lb 12-oz boy. Which of the following best describes the functional closure of the ductus arteriosus?

a. It causes blood to flow from the aorta into the pulmonary artery.
b. It is independent of gestational age.
c. It is the final event required for conversion of the transitional circulation in the newborn to the adult circulatory pattern.
d. It occurs due to hypoxic pulmonary vasoconstriction.
e. It precedes functional closure of the foramen ovale.

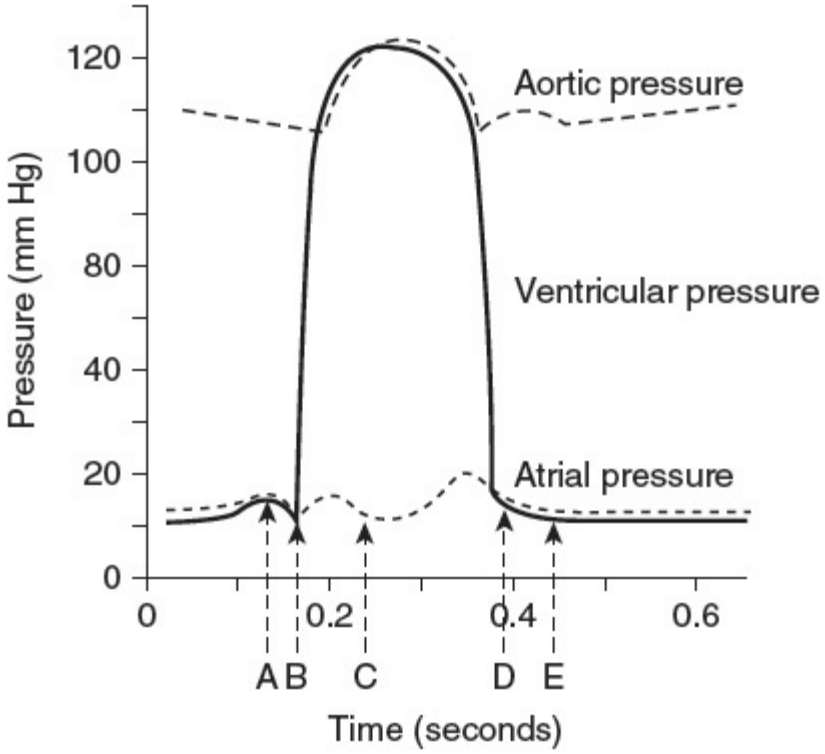
297. A 32-year-old man is diagnosed with primary hypertension. His physician recommends a drug for hypertension that acts by decreasing vascular smooth muscle contractile activity without affecting ventricular contractility. Which of the following is the most likely site of action for the drug?

a. β-Adrenergic receptors
b. Calmodulin
c. Troponin
d. Tropomyosin
e. Protein kinase A

298. A 59-year-old man 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. Activity of the L-type calcium channels
b. Activity of the sodium–potassium pump
c. Concentration of calcium within the SR
d. Diastolic stiffness of the ventricular muscle cells
e. Duration of the ventricular muscle action potential

299. A 72-year-old male is undergoing a preoperative evaluation prior to scheduled hip replacement surgery. He states that he has felt well and has no complaints other than the osteoarthritis in his right hip. During your cardiac examination, you auscultate an S_1 and S_2. At which time point in the figure below is S_1 auscultated?



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

300. A 62-year-old man with a history of diabetes mellitus and hypertension arrives in the emergency room with substernal chest pain for the last hour. He is given intravenous nitroglycerin to help reduce the pain. Which of the following would be expected with the use of this drug?

a. Arterial blood pressure is increased.
b. Coronary blood flow is decreased.
c. Left ventricular wall stress is increased.
d. Myocardial oxygen demand is decreased.
e. Venous return to the heart is increased.

301. During a clinical elective, a second-year medical student auscultates the heart of a patient, which reveals normal S_1 and S_2 heart sounds with no murmurs. In correlating the physical examination with the cardiac cycle, when does the highest coronary blood flow per gram of left ventricular myocardium occur?

a. At the beginning of diastole
b. At the beginning of isovolumic contraction
c. When aortic blood flow is highest
d. When aortic pressure is highest
e. When left ventricular pressure is highest

302. A 64-year-old man was admitted to the hospital with edema and CHF. 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. Myosin light chain kinase
c. Titin
d. Tropomyosin
e. Troponin

303. A 22-year-old man with no history of congenital heart disease has a normal physical examination prior to entering the military. Which of the following characteristics is most similar in the systemic and pulmonary circulations of this patient?

a. Afterload
b. Blood volume
c. Peak systolic pressure
d. Preload
e. Stroke work

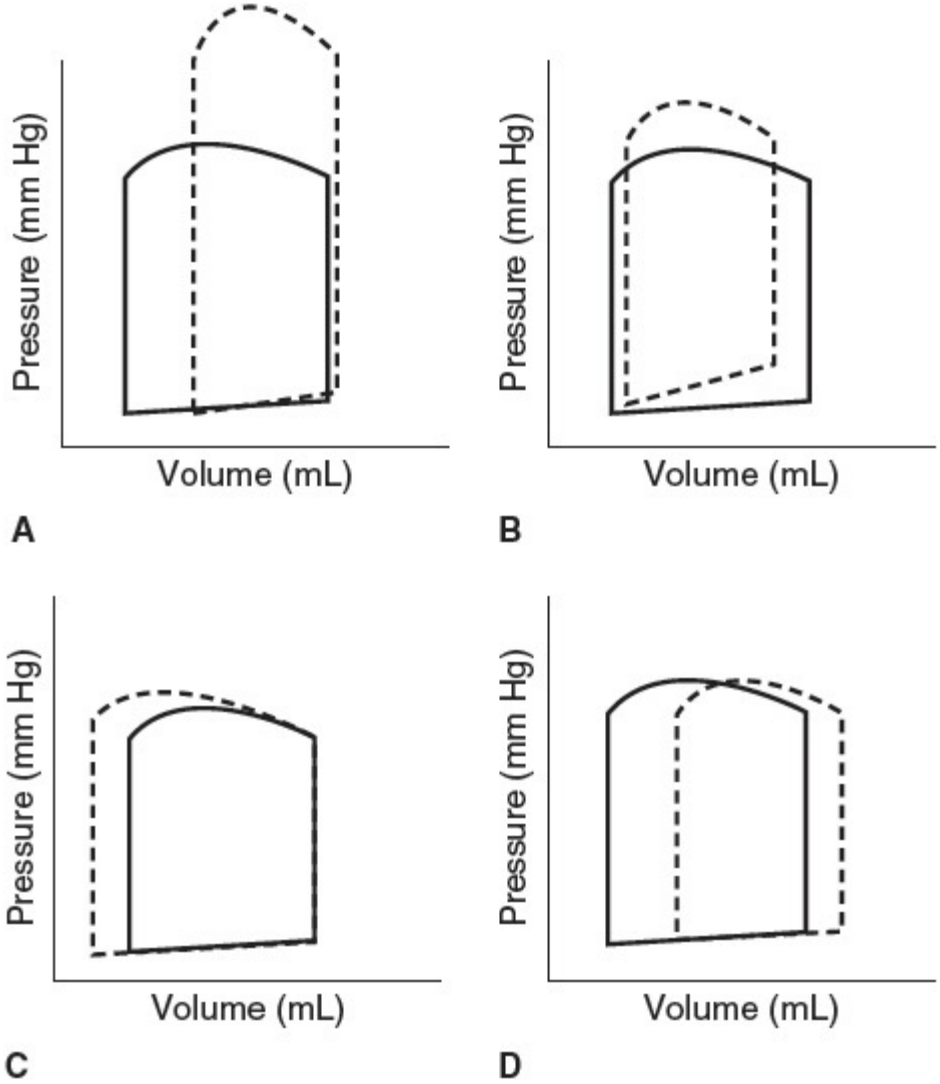
304. A 22-year-old woman is recovering from an upper respiratory infection with Coxsackie B virus when her condition worsens and she becomes increasingly dyspneic. An echocardiogram reveals global hypokinesis and an ejection fraction of 25%. Which of the following is the underlying process in this patient's most likely diagnosis?

a. Global ventricular hypertrophy
b. Hypertrophy of the interventricular septum
c. Narrowing of the descending aorta
d. Vegetations on the cardiac valves
e. Ventricular dilation

305. A 58-year-old man with a history of several months of exertional chest pain presents for evaluation. He also has severe arthritis in his knees bilaterally and is unable to undergo exercise stress testing. Thus, you elect to conduct a chemical stress test with dipyridamole to investigate the nature of his chest pain. Momentarily after administering the drug he begins to experience severe retrosternal chest pain and ST-segment depression in the anterior leads of the ECG. What is the most likely mechanism of this patient's chest pain?

a. Bradycardia
b. Coronary blood redistribution
c. Coronary vasospasm
d. Occlusive coronary embolus
e. Pulmonary embolism

306. A 61-year-old gentleman experiences progressive dyspnea on exertion over the last few weeks. He also complains of swelling of his lower extremities and increased fatigue. After an echocardiogram is performed, he is diagnosed with dilated cardiomyopathy. Which of the following options represents this patient's pressure–volume loop, where the solid line represents the healthy baseline and the dotted line represents dilated cardiomyopathy?



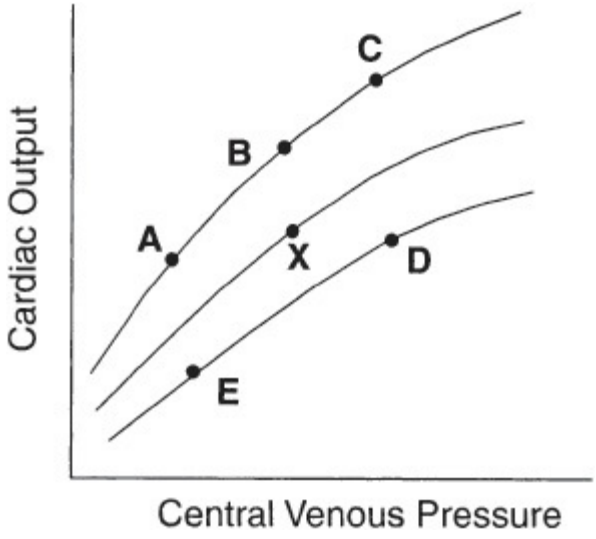
307. A healthy 3-year-old girl presents for a health maintenance examination. Her developmental history is unremarkable and her immunizations are up to date. Upon cardiac auscultation, there are no murmurs, rubs, or gallops, and an S_1 and an S_2 are heard. S_2 is split at a fixed interval and does not vary with respiration. Which of the following conditions is most likely present in this patient?

a. Atrial septal defect
b. Bicuspid aortic valve
c. Coarctation of the aorta
d. Dilated ventricles
e. Normal cardiac variant

308. A 58-year-old woman with idiopathic pulmonary hypertension presents with right ventricular hypertrophy and cor pulmonale. Her ECG shows positive QRS complexes in leads V_1, III, and aVF, and equiphasic QRS complexes in lead aVR. Which of the following is her mean QRS vector?

a. −150 degrees
b. −120 degrees
c. +60 degrees
d. +90 degrees
e. +120 degrees

309. A 59-year-old obese woman is referred for cardiac stress testing before beginning an exercise and diet regimen. Baseline recordings resulted in the generation of point X on the cardiac function curves shown below. Which point is most likely to represent her cardiac function as she achieves a new steady-state during treadmill exercise?



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

Answers

230. The answer is e. (*Le, p 256. McPhee and Hammer, pp 250-253. Widmaier, pp 367-371.*) 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 corresponds to the end of the T wave (segment E) on the ECG recording.

231. The answer is e. (*Barrett, pp 546-547. Le, pp 254, 259. Longo, pp 1805, e-13-4. Widmaier, pp 372-373.*) Preload is the degree to which the myocardium is stretched before it contracts, that is, the length of the sarcomere at the end of diastole. Recall the Frank–Starling law that states that the energy of contraction is proportional to the initial length of the cardiac muscle fiber (preload). In vivo, the variable most directly related to sarcomere length during end diastole is ventricular end-diastolic volume (*choice e*). Blood volume (*choice a*) can influence preload through changes in end-diastolic volume. Central venous pressure (*choice b*), pulmonary capillary wedge pressure (*choice c*), and left ventricular end-diastolic pressure (*choice d*) are indices of preload, but end-diastolic volume is the most direct reflection of changes in end-diastolic fiber length (preload). Mitral valve prolapse is the most frequent valvular lesion, which can be caused by myxomatous degeneration, rheumatic fever, or chordae rupture. It is generally benign, but can predispose to infective endocarditis. Both Valsalva maneuver and standing decrease venous return to the heart, thereby decreasing left ventricular diastolic filling (preload) and causing more laxity on the chordae tendineae. This allows the mitral valve to prolapse earlier in systole, leading to an earlier systolic click (ie, closer to S_1) and a longer murmur.

232. The answer is b. (*Barrett, pp 546-547. Le, p 254. Longo, pp 1937-1941. McPhee and Hammer, pp 265-268.*) 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 (*choice b*) would therefore be the best index of afterload on the left ventricle in vivo. MAP (*choice c*) is normally the same as mean ventricular systolic 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 TPR (*choice e*) can influence afterload by causing changes in MAP, 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. Also, following a hemorrhage, TPR is high, whereas afterload (MAP) is low. Pulmonary capillary wedge pressure (*choice d*) and left ventricular end-diastolic pressure (*choice a*) are estimates of the volume of blood in the ventricle during diastole and are indices of preload.

233. The answer is d. (*Barrett, pp 522-523. Le, p 260. Longo, pp 1860-1861. McPhee and Hammer, pp 250, 253-255.*) The plateau phase (phase 2, *choice d*) is the result of the influx of calcium. Although calcium channels begin to open during the upstroke (phase 0, *choice b*), the greatest numbers of calcium channels open during the plateau. The upstroke is primarily dependent on the opening of Na^+ channels. The initial repolarization (phase 1, *choice c*) is dependent on the inactivation of Na^+ channels and the opening of a transient K^+ channel. Repolarization (phase 3, *choice e*) is produced by the inactivation of Ca^{2+} channels and the activation of the delayed rectifier K^+ channels. The resting membrane potential (phase 4) is determined largely by I_{K+} and is represented in the diagram by *choice a*.

234. The answer is c. (*Barrett, pp 529-530. Kaufman, pp 6-8, 44-45. Le, pp 283, 289-290. Longo, ch 232: pp 1867-1877.*) Conduction abnormalities can produce first-degree, second-degree, or third-degree AV heart block. 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) but a QRS complex always follows each P wave. 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 third-degree heart block, *trace B*, 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 complexes) are completely dissociated. *Trace A* and *trace E* do not illustrate any degree of AV heart block.

235. The answer is c. (*Barrett, pp 539-544, 577. Le, p 256. Widmaier, pp 367-371.*) 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 (*choice c*). 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 (*choice a*). Because the mitral valve is closed during ventricular ejection, there is a pressure difference between the left ventricle and left atrium (*choice b*). Similarly, because the tricuspid valve is closed during ventricular ejection, there is an appreciable pressure difference between the right ventricle and the right atrium (*choice e*). 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 (*choice d*), which is necessary to generate the pressure gradient that drives pulmonary blood flow.

236. The answer is d. (*Barrett, pp 529-534. Kaufman, pp 57-58. Le, pp 262-263. Longo, pp 1870-1877, 1886-1887.*) 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 (*choice d*) 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 bpm. 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 bpm with periods of asystole that may last a minute or more. The resultant cerebral ischemia causes dizziness and fainting (Stokes–Adams syndrome). Aside from syncope, other important associations with third-degree heart block include Lyme disease and neonates of mothers with systemic lupus erythematosus. Sinus arrhythmia (*choice a*) 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. This arrhythmia is not pathological and not associated with syncope. First-degree heart block (*choice b*) is defined as a higher-than-normal PR interval (greater than 0.2 seconds) but no “missed” QRS complexes. Second-degree

heart block (*choice c*) occurs when the action potential fails to reach the ventricles some, but not all, of the time. Syncope may occur in second-degree heart block, but it is not as common as in third-degree heart block; therefore, *choice d* is the best answer. Multi-focal atrial tachycardia (*choice e*) is a heart rate above 100 bpm with at least three different P-wave morphologies and varying PR intervals, and is not commonly associated with syncope.

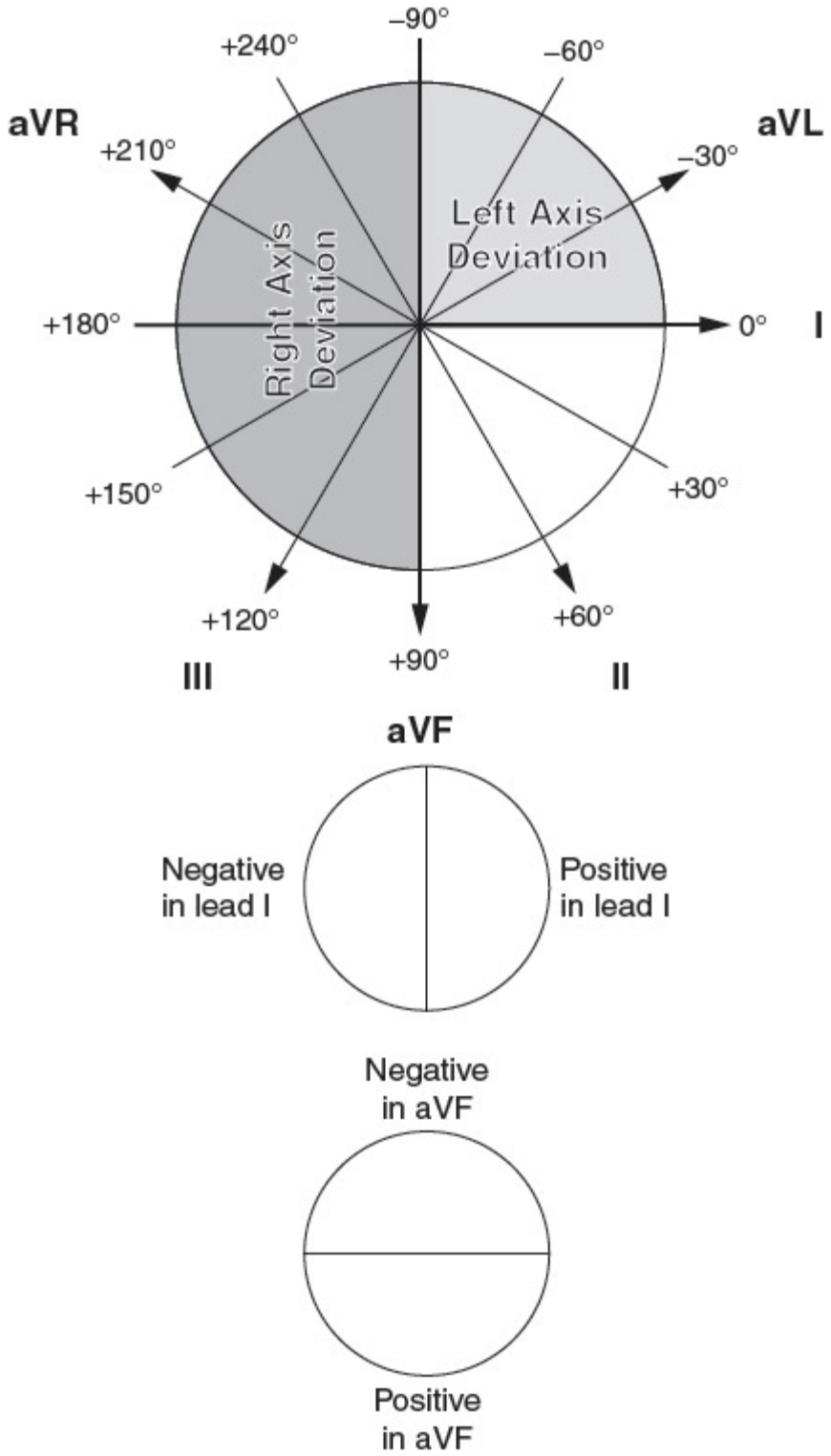
237. The answer is d. (*Barrett, pp 539-544. Le, p 256. Widmaier, pp 367-371.*) The graph illustrates the development of pressure in the aorta, the left atrium, and the left ventricle during a single cardiac cycle. At point time D, the pressure within the left ventricle is less than the pressure in the 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 (time A). At time B, the atrial and ventricular pressure curves separate as the mitral valve closes and isovolumetric contraction occurs. At time E, ventricular filling begins to slow.

238. The answer is b. (*Barrett, pp 545-546. Le, pp 253, 582.*) Cardiac output (CO) can be calculated using the Fick equation, where VO_2 is the steady-state oxygen consumption by the body and a-v O_2 is the difference in arterial O_2 content and mixed venous O_2 content. Blood in the pulmonary veins is oxygenated "arterial" blood, and blood in the pulmonary artery is fully mixed venous blood.

$$\begin{aligned} CO &= \dot{V}O_2/\text{a-v } O_2 \\ &= \frac{280 \text{ mL/min}}{20 \text{ mL/100 mL} - 12 \text{ mL/100 mL}} \\ &= \frac{280 \text{ mL/min}}{8 \text{ mL/100 mL}} \\ &= 280 \text{ mL/min} \times 100 \text{ mL/8 mL} \\ &= 3500 \text{ mL/min} \\ &= 3.5 \text{ L/min} \end{aligned}$$

239. The answer is a. (*Barrett, pp 544-545. Le, pp 284-285. Longo, pp 1929-1950.*) 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. Aortic stenosis, *choice b*, produces a systolic murmur and thus inconsistent with the described clinical presentation. Mitral valve prolapse, *choice c*, yields a systolic murmur with a midsystolic click. Pulmonary regurgitation, *choice d*, is a diastolic murmur but would not produce the systemic blood pressure findings described in the question stem. Pulmonic stenosis, *choice e*, would produce a systolic murmur as blood flows out of the right ventricle into the pulmonary artery.

240. The answer is d. (*Barrett, p 528. Kaufman, p 57. Longo, pp 1832-1835.*) The 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. The left ventricular myocardium is normally more massive than the right resulting in a slight leftward deflection of the MEA in healthy subjects. Normally the MEA ranges from −30 to +100 degrees. The MEA is approximately perpendicular to the axis of the limb lead, which is approximately isoelectric, with either a no discernible QRS deflection or where equal parts of the QRS are above and below baseline. In this case, the lead closest to isoelectric is 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 and +30 degrees. A good strategy for estimating the MEA is to use the net deflection in lead I and lead aVF to find the quadrant in which the MEA falls, as shown in the figures below:



If lead I shows a net positive deflection of the QRS complex (more area above the baseline than below), then the MEA must fall in one of the two right-sided quadrants. Conversely, if lead I shows a net negative deflection, then the MEA will be in one of the two left-sided quadrants. Similarly, the direction of net deflection of the QRS complex in lead aVF determines whether the MEA will fall in the upper two or lower two quadrants. Taking both pieces of information together will yield the specific quadrant the MEA falls in. Applying this method to the question stem where there are net positive deflections in leads I and aVF, we can determine that the MEA lies in the bottom right quadrant and thus is between 0 and +90 degrees. This determination is helpful because it rules out *choice a* and *choice e*.

241. The answer is c. (*Barrett, pp 550-552, 582-583. Widmaier, pp 407-410.*) Normally, cardiac output increases during exercise primarily due to sympathetically mediated increases in heart rate. Cardiac allografts are denervated such that the sympathetic nervous system is disconnected from the heart, and thus heart rate (*choice b*) does not increase appreciably during exercise in cardiac transplant patients. Patients with transplanted hearts are able to increase their cardiac output during exercise in the absence of cardiac innervation through increases in stroke volume (*choice c*). The mechanisms for the increase in stroke volume are an increase in preload (Frank–Starling mechanism) and myocardial contractility (from circulating catecholamines). Preload is the degree of stretch on ventricular myocar-dial cells as determined by the volume of blood within the ventricles at the end of diastole. During isotonic exercise, venous return is increased by the pumping action of muscles, a decrease in venous compliance (not increased, *choice e*) due to constriction of the veins by sympathetic stimulation, and increased respirations. In addition, because of vasodilation in the contracting muscles, total peripheral resistance is decreased (not increased, *choice d*). An increase in arterial pressure (ie, afterload, *choice a*) would decrease stroke volume and thus cardiac output.

242. The answer is d. (*Barrett, pp 521-524. McPhee and Hammer, pp 247-250. Widmaier, pp 361-363.*) The most rapid conduction of the action potential occurs

through the Purkinje fibers (*choice d*) of the His-Purkinje system. The slowest conduction occurs in the AV node (*choice c*). Pacemaker cells located within the SA node (*choice a*) 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 HisPurkinje 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. Conduction is slow in ventricular muscle (*choice e*) and this is why ventricular arrhythmias produce wide QRS complexes on an ECG, since conduction is propagating through slow myocardial tissue instead of fast, specialized conduction tissue like the His-Purkinje system. The order of fastest conduction to slowest conduction is as follows: the Purkinje fibers (*choice d*) at 4 m/sec, atrial (*choice b*) and ventricular muscle (*choice e*) at 1 m/sec, and the SA (*choice a*) and AV (*choice c*) nodes at 0.05 m/sec.

243. The answer is e. (*Longo, pp 1901-1906.*) Ventricular remodeling refers to the changes in left ventricular mass, volume, and shape and the composition of the heart that occur after cardiac injury or abnormal hemodynamic loading conditions. Left ventricular remodeling contributes to the progression of heart failure. Angiotensin-converting enzyme (ACE) inhibitors can relieve the symptoms of heart failure with a depressed ejection fraction by stabilizing or reversing cardiac remodeling (*choice e*). This effect is due not only to angiotensin suppression by inhibition of ACE but also to bradykinin upregulation by inhibition of kininase II. An increase in ventricular end-diastolic pressure (*choice b*) would not result from administration of lisinopril and would result in further decompensation of the patient's CHF, not an improvement. Similarly, increased wall thickness (*choice c*) is a sign of progression of heart failure, not an improvement. An increase in cardiac contractility (*choice a*) would improve heart failure. Lisinopril is neither a positive inotropic agent nor a negative chronotropic agent (*choice d*).

244. The answer is e. (*Barrett, p 575. Le, pp 255, 582.*) 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.

245. The answer is c. (*Barrett, p 540. Le, pp 254, 582.*) The ejection fraction (EF) is equal to the stroke volume (SV) divided by the end-diastolic volume (EDV), and the SV is equal to the EDV minus the end-systolic volume (ESV).

$$EF = SV/EDV = EDV - ESV/EDV$$

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 (54%).

246. The answer is c. (*Barrett, pp 581-582. Le, pp 265, 582.*) Net filtration from capillaries is dependent on the Starling forces and capillary permeability according to the following equation:

$$\text{Net filtration} = K_f\,[(P_{capillary} - P_{tissue}) - (\pi_{capillary} - \pi_{tissue})],$$

where K_f is the filtration coefficient of the membrane, and it is directly proportional to capillary permeability; $P_{capillary}$ and P_{tissue} are the hydrostatic pressures in the capillary and tissue (interstitial space), respectively; and $\pi_{capillary}$ and π_{tissue} are the osmotic (colloid oncotic) pressures in the capillary and interstitial space, respectively. Increasing central venous pressure (*choice c*) increases the capillary hydrostatic pressure ($P_{capillary}$), which increases the filtration of fluid from the systemic capillaries, leading to edema. All of the other choices will cause a decrease in filtration.

247. The answer is b. (*Barrett, pp 539-544. Le, p 256. Widmaier, pp 367-371.*) Closure of the semilunar valves (aortic and pulmonic valves) marks the beginning of the isovolumetric relaxation (*choice b*) phase of the cardiac cycle and is responsible for the second heart sound (S_2). 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. The first heart sound (S_1) is created by closure of the AV valves (tricuspid and mitral) during isovolumetric contraction (*choice a*) and occurs during diastole, not systole (*choice e*). Rapid ejection (*choice c*) produces neither S_1 nor S_2, but can produce a murmur via increased turbulent flow over a narrowed orifice. Rapid ventricular filling (*choice d*) can produce a gallop rhythm on auscultation with the addition of S_3 (sometimes pathological) or S_4 (always pathological).

248. The answer is a. (*Barrett, pp 531-532. Le, pp 262, 282, 577. Longo, pp 1880-1882.*) The ECG shows the irregular rhythm of atrial fibrillation. 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 (*choice a*). The venous a wave (*choice e*) 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, not an increase (*choice c*). Arterial blood pressure (*choice b*) typically falls because of inadequate filling of the ventricles and the resulting decrease in stroke volume. The oculocardiac reflex is a decrease in heart rate that occurs when pressure is applied to the eyeball via connections between the ophthalmic branch of the trigeminal nerve (afferents) and the vagus nerve (efferents) to the SA node. Decreased heart rate results from increased parasympathetic stimulation of atrial musculature, not increased sympathetic tone (*choice d*). The oculocardiac reflex is similar to carotid sinus massage whereby stimulation of afferents of the glossopharyngeal nerve interface with vagal efferents leading to increased parasympathetic output to the heart.

249. The answer is d. (*Barrett, pp 544. Kaufman, p 27. Le, p 257. Longo, pp 1826-1827.*) 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, but the distinction of these two events is not always perceptible. However, during inspiration, intrathoracic pressure falls, increasing venous return to the right heart and increasing preload on the right heart, resulting in a larger stroke volume. This causes the delay in the closure of the pulmonic valve, not the aortic valve (*choice c*), and a prolongation of the interval between the two components of the second heart sound. This is a normal finding and is termed "physiological splitting." Splitting of S_2 can also occur in pathological conditions where closure of the pulmonic valve is delayed, such as in a right bundle branch block or pulmonic stenosis. This is termed "wide splitting" of S_2 since it is present throughout the respiratory cycle. Closure of the mitral valve (*choice e*) and tricuspid valves is associated with the first heart sound (S_1). Inspiration causes an increase in heart rate, not a decrease (*choice a*). This is known as respiratory sinus arrhythmia. The negative intrathoracic pressure during inspiration draws blood into the pulmonary circulation and decreases pulmonary venous return to the left heart, decreasing left ventricular stroke volume, not increasing (*choice b*).

250. The answer is c. (*Barrett, pp 544-545. Kaufman, pp 22-38. Le, pp 256-259. Longo, pp 1826-1830.*) The third heart sound (S_3) occurs during the rapid filling phase of ventricular diastole. S_3 can be a normal finding in children, young adults, and pregnant women. In older patients, it usually signifies heart failure (*choice c*). A

left-sided S_3 in patients with chronic heart failure is predictive of cardiovascular morbidity and mortality. Aortic regurgitation (*choice a*) is associated with a diastolic murmur that occurs immediately following S_2 and is characterized as high-pitched "blowing" decrescendo murmur. Aortic stenosis (*choice b*) and tricuspid regurgitation (*choice e*) produce systolic murmurs. Right bundle branch block (*choice d*) is not associated with an S_3, but is associated with wide splitting of S_2.

251. The answer is a. (*Barrett, pp 574-576. Longo, pp 1826-1830, e13-1-e13-10. Le, pp 256-259, 275.*) In anemia (*choice a*), the reduced hematocrit reduces blood viscosity, which increases the velocity and thus the turbulence of blood flow, which makes systolic murmurs common. An increased velocity of blood flow in anemia is also due to higher than normal heart rate and cardiac output, which is a compensatory response to increase oxygen delivery to the tissues in the face of reduced arterial oxygen content. An increased velocity of blood flow and turbulence can also result from flow through a narrowed orifice, such as a stenotic heart valve. It is helpful to stratify murmurs into systolic and diastolic. During systole, the AV valves (tricuspid and mitral) close and blood is ejected from the ventricles as the semilunar valves (aortic and pulmonic) open. If there is a murmur during systole, the AV valves have not closed as they should (tricuspid or mitral regurgitation), the semilunar valves are narrowed (aortic or pulmonic stenosis), or there is a higher than normal velocity of blood flow across normal valves (eg, anemia). However, the systolic murmur of mitral regurgitation (*choice c*) is either early systolic (acute mitral regurgitation) or holosystolic, and cardiac output would be decreased. Third-degree heart block (*choice e*) may be associated with a mid-systolic murmur, but cardiac output would not be increased. During diastole, the semilunar valves should close and the AV valves should open to allow filling of the ventricles. If a diastolic murmur is present, then there is either semilunar (aortic or pulmonic) regurgitation, or AV valve (tricuspid or mitral) stenosis (*choice d*). In cardiac tamponade (*choice b*), cardiac output is reduced due to decreased filling of the heart; heart sounds are "distant" due to accumulation of fluid within the pericardium.

252. The answer is a. (*Le, pp 230-231. Longo, pp 171-177, 1867-1870.*) Although the cause of the patient's 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 in the parasympathetic nervous system 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 (*choice a*). Atropine causes a decrease in the PR interval by enhancing conduction through the AV node (dromotropic effect); atropine does not increase the PR interval (*choice b*). Stroke volume (*choice c*), TPR (*choice d*), and ventricular contractility (*choice e*) are primarily under the control of the sympathetic, rather than the parasympathetic, nervous system, and thus are not directly affected by the parasympatholytic effects of atropine.

253. The answer is a. (*Barrett, pp 539-545. Kaufman, pp 36-37. Le, pp 258-259. Longo, pp 1942-1946.*) A wide pulse pressure and a diastolic murmur heard best over the aortic area is highly suggestive of aortic regurgitation. The classic rapidly rising "water hammer" pulse associated with aortic regurgitation can result in involuntary head bobbing in addition to headaches. The murmur of aortic regurgitation is generated as blood flows backward from the aorta to the left ventricle through an incompetent aortic valve. This occurs during the filling phase of diastole (*segment A*), after isovolumetric relaxation (*segment D*) The other two answer choices correspond to systolic phases of the cardiac cycle, isovolumetric contraction (*segment B*), and ejection (*segment C*).

254. The answer is e. (*Barrett, pp 544-545. Kaufman, pp 22-38. Le, pp 256-259. Longo, pp 1826-1830.*) Early systolic murmurs begin with the first heart sound and end in mid-systole. The higher-than-normal height of the jugular blood column (jugular venous pulse or JVP) 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 IV drug abusers with infective endocarditis. Mitral stenosis (*choice c*) and aortic regurgitation (*choice a*) produce diastolic murmurs. Atherosclerosis (*choice b*) can lead to heart failure and an elevated jugular venous pulse, but it would be unlikely to produce a systolic murmur and thus is not the best answer. Tachycardia (*choice d*) can produce a systolic murmur if blood flow through the heart rises above a critical value, but it is unlikely to cause elevated jugular venous pressure, so it is not the best answer.

255. The answer is b. (*Le, p 296. Longo, pp 2001-2002.*) A stress test is conducted by asking the 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 (*choice b*). MAP (*choice a*) and heart rate (*choice c*) normally rise during exercise, and would not indicate a positive test. The presence of a diastolic murmur (*choice d*) or conduction abnormalities (eg, *choice E*) in the ECG is not diagnostic of ischemic heart disease. The exercise test will also be terminated if dizziness, dyspnea, or ventricular tachycardia develops or if blood pressure falls.

256. The answer is a. (*Longo, pp 172-173. Widmaier, pp 400-407.*) When a person rises suddenly, 500 to 1000 mL of blood pools in the lower extremities and splanchnic circulation. As a result, there is a transient decrease in venous return (*choice d*), ventricular end-diastolic volume (*choice e*), stroke volume (*choice c*), cardiac output, and blood pressure (*choice b*). The decreased blood pressure elicits the baroreceptor reflex, leading to an increase in sympathetic activity and decreased vagal nerve activity. The reflex increases heart rate (*choice a*), as well as TPR and cardiac contractility. These changes in the cardiovascular system limit the fall in blood pressure.

257. The answer is d. (*Barrett, pp 615-616. Longo, p 1924.*) 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 approximately 5% to 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 P_{O_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 P_{O_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 (*choice C*), causing the persistence of the right-to-left flow of blood across the ductus arteriosus, which exacerbates the hypoxemia, and causes cyanosis. Left ventricular hypertrophy (*choice b*) is not associated with persistent fetal circulation; right ventricular hypertrophy (RVH), however, is part of another cyanotic congenital heart disease, tetralogy of Fallot (RVH, pulmonary stenosis, ventricular septal defect (VSD), and overriding aorta). Aortic coarctation (*choice a*) is a congenital cardiovascular lesion, but does not cause cyanosis. Systemic hypertension (*choice e*) and mitral regurgitation (*choice c*) also do not cause cyanosis.

258. The answer is c. (*Barrett, pp 540, 546-553. Le, pp 254-255, 282. Longo, pp 1808-1809.*) Cardiac output is the product of stroke volume and heart rate. The stroke volume is a function of preload, afterload, and contractility. A cardiac function curve is an in vivo plot of the cardiac length–tension relationship in which an index of tension development (in this case, cardiac output) is plotted against an index of end-diastolic fiber length, that is, preload (in this case, central venous pressure). For any given curve, increasing preload increases stroke volume and thus cardiac output (the Frank–Starling relationship). The curve above the normal curve will result from an increase in contractility or a decrease in afterload. The curve below the normal curve will result from a decrease in contractility (eg, with CHF) or an increase in afterload. Because this patient has CHF, point E or D must be the initial starting point for the vignette. Digitalis is a cardiac glycoside that increases contractility, causing a point on the lower curve to shift up and to the left, such that there is an increased stroke volume (and thus cardiac output) at a lower preload. Thus, *choice c* is the best answer. In reality, digitalis would seldom return myocardial function to normal, so there would more likely be another curve between points D and X, reflecting improved performance with higher contractility than point D but not reaching point X (see *Le, p 254*). Digitalis derivatives such as digoxin have classically been used to treat CHF because of their ability to increase intracellular stores of Ca^{2+} and thus exert a positive inotropic effect, but they are now used in a secondary role to treat systolic dysfunction and slow down the ventricular rate in CHF patients with atrial fibrillation. *Choice d* is incorrect because even though cardiac output has increased in shifting from E to D, cardiac contractility, which is independent of load, has not changed; rather, the increase in cardiac output has resulted from an increase in preload. Similarly, *choice a* is incorrect because there is no increase in contractility when moving along the same curve from A to B, along the curve to a lower cardiac output. *Choice e* is the most reasonable wrong answer, showing a shift from E to X, to a higher cardiac output, as would be expected after treatment with an inotropic agent like digitalis; however, this shift also indicates an increase in central venous pressure (preload), which would not be expected. The shift in *choice b* would be expected, for example, if there were a decrease in blood volume with either an increase in afterload or a negative inotropic effect.

259. The answer is e. (*Barrett, pp 577-585. Widmaier, pp 377-396.*) The total circulating blood volume is approximately 70 mL/kg, about two-thirds of which is found in the venules and veins (*choice e*), compared to only one-third in the arteries and arterioles (*choice b*). 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 shunts blood into the arterial system, increasing perfusion of vital organs such as the heart and brain. Although the heart (*choice d*) pumps the redistributed blood to vital organs, this choice is incorrect, since the blood volume came from the capacitance vessels of the venous system. The aorta (*choice a*) contains 2% of blood volume, and the capillaries (*choice c*) contain 5%, and thus do not contribute as much to this redistribution as the venous system which contains over 65% of blood volume.

260. The answer is e. (*Barrett, pp 522-523. Le, p 260.*) The slope of phase 4 of the action potential in the SA node determines heart rate. The automaticity of the SA and AV nodes is due to the spontaneous slow diastolic depolarization occurring in phase 4, which is caused by the activation of a Na^+ channel that increases the flow of sodium into the cell (*choice e*). This channel is activated when the membrane hyperpolarizes, in contrast to the Na^+ channel responsible for phase 0 of the ventricular action potential, which is activated when the cell depolarizes. Neither the Na–K pump (*choice a*) nor the Na/Ca exchanger (*choice c*) is involved in phase 4 depolarization. Calcium conductance (*choice d*) does not change during phase 4, but is responsible for the upstroke phase of the pacemaker potential. Potassium conductance decreases during phase 4 depolarization and thus the flow of potassium out of the cell is diminished (*choice b*); however, this change in potassium current is not responsible for phase 4 depolarization.

261. The answer is a. (*Le, p 257. Longo, pp 1826-1827, 1835, e13-8-e13-9.*) The aortic valve (A_2) normally closes before the pulmonic valve (P_2). During expiration, the aortic (A_2) and pulmonic (P_2) components of the second heart sound are normally separated by <30 ms and are heard as a single sound. During inspiration, the splitting interval widens, and A_2 and P_2 are clearly separated into two distinct sounds, considered normal physiological splitting. Sinus arrhythmia (*choice c*) 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. Splitting of S_2 will be reversed by any condition that delays the closing of the aortic valve. The most common causes of reversed (paradoxical) splitting is left bundle branch block in which activation of the left ventricle is delayed (*choice a*) or aortic stenosis. A right bundle branch block (*choice b*) would delay P_2, thus causing increased physiological splitting, termed a "wide split." Increases or decreases in heart rate (*choice d* and *choice e*) do not alter the normal pattern of semilunar valve closure.

262. The answer is a. (*Barrett, pp 534-537. Kaufman, pp 18-20. Le, pp 269, 271. Longo, pp 1836-1838.*) 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 ECG presented shows marked ST-segment elevation in leads I, aVL, and V_1 to V_6, indicative of acute myocardial infarction. The electrical activity of the heart does not reflect changes in ejection fraction (*choice b*), blood pressure (*choice c*), total peripheral resistance (*choice d*), or ventricular contractility (*choice e*), although all of these can be altered by changes in coronary blood flow.

263. The answer is e. (*Barrett, pp 578-579. Widmaier, pp 379, 407-410.*) Pulse pressure is the difference between the systolic and diastolic pressures that occur during the cardiac cycle. The most important factors determining the magnitude of the pulse pressure are (1) stroke volume, (2) speed of ejection of the stroke volume, and (3) arterial compliance. An increase in the stiffness of the arteries (*choice e*), such as occurs in arteriosclerosis that progresses with advancing age, will increase pulse pressure. Stiffening of the arteries decreases, not increases, arterial compliance (*choice b*). An increased stroke volume would increase pulse pressure, not a decreased stroke volume (*choice a*). If heart rate increases (*choice c*), stroke volume and therefore pulse pressure may decrease. An increase in total peripheral resistance (*choice d*) will slow down flowing out of blood from the aorta during systole and therefore decrease pulse pressure.

264. The answer is b. (*Barrett, pp 544-545. Kaufman, pp 31-38. Le, pp 258-259. Longo, pp 1937-1941.*) Patients with aortic stenosis (*choice b*) are usually asymptomatic until the aortic valve orifice becomes significantly narrowed. The systolic murmur auscultated is due to the turbulent flow of blood across the aortic valve during ventricular systole. Dyspnea, angina, and syncope are major symptoms that can be associated with it. In contrast, aortic regurgitation (*choice a*), mitral stenosis (*choice c*), pulmonic regurgitation (*choice d*), and tricuspid stenosis (*choice e*) are all diastolic murmurs.

265. The answer is e. (*Barrett, pp 546-550. Le, pp 214, 254-255. Widmaier, pp 371-375, 406.*) This patient is in cardiogenic shock from a massive myocardial infarction. Recall that stroke volume is influenced by ventricular preload, afterload, and contractility. Increasing ventricular contractility (*choice e*) will increase stroke volume. Increasing heart rate (*choice a*) will decrease ventricular filling and stroke volume. Increasing systemic vascular resistance (*choice c*) would increase arterial pressure and afterload and therefore decrease stroke volume. Increased venous compliance (*choice d*) would cause more blood to pool in capacitance vessels, decreasing preload and thus stroke volume. Increased pulmonary capillary wedge pressure (*choice b*), although present in this patient as evidenced by his pink, frothy sputum from acute cardiogenic pulmonary edema, does not result in increased stroke volume.

266. The answer is a. (*Barrett, pp 524-526. Le, pp 256, 261. Longo, pp 1831-1834. McPhee and Hammer, pp 250-253. Widmaier, pp 364-371.*) The PR interval starts at the beginning of the P wave and ends at the beginning of the QRS complex. During the P-R interval, AV conduction occurs, including depolarization of the atria, the AV node (*choice a*), the bundle of His, and the Purkinje fibers. The PR interval precedes ventricular contraction (*choice e*), which occurs during and following the QRS complex. The mitral and aortic valves close (*choice b*) after the QRS complex has begun, during the phase of isovolumetric contraction. The second heart sound (*choice d*) occurs at the end of systole, which occurs after the PR interval. The PR interval includes the P wave, and thus is not isoelectric (*choice c*). The normal duration of the PR interval is 120 to 200 ms (average 180 ms) at a heart rate of 70 bpm, and shortens to an average of 140 ms at a rate of 130 bpm.

267. The answer is c. (*Barrett, pp 530-533. Kaufman, pp 38-43. Le, pp 261-262. Longo, p 1890.*) In normal conduction, all cardiac impulses originate at the SA node and the intrinsic rates of the other structures in the conduction system are slower than the SA node. The intrinsic firing rate of the SA node is approximately 60 to 100 bpm. The intrinsic rate for the AV node is 40 to 60 bpm. The intrinsic rate for the Purkinje system is about 20 to 40 bpm. In the case of a sinus rhythm with occasional PVCs, the PVCs most likely originate from ventricular pacemaker cells in the Purkinje system. A unifocal PVC results when the depolarization is triggered from one site in the ventricle such that the premature QRS complexes on the ECG look the same. Multifocal PVCs arise when more than one site in the ventricles initiate depolarization, which is manifest as different shaped PVCs on the ECG, and generally results from increased automaticity of ectopic foci. Because of their lower intrinsic rate, ventricular pacemaker cells are usually reset with each beat and do not produce ventricular activation. However, when the sinus rhythm is <60 bpm (bradycardia, *choice c*), there may be time for these pacemaker cells to reach threshold and produce a ventricular contraction. Bradycardia is a normal rhythm variant in well-trained athletes resulting from aerobic conditioning. In Wolff–Parkinson–White (WPW) syndrome, AV conduction via an accessory bundle of Kent (*choice a*) bypasses the AV node and manifests with a characteristic upslope of the QRS complex known as a delta wave; although there may be wide QRS complexes, WPW does not result in VPBs. Atrial fibrillation (*choice b*) does not result in PVCs, but can cause palpitations. Although an inverted P wave (*choice d*) can occur following a PVC (if the action potentials propagate into the atria), this would be a result rather than a cause of the premature contractions. Sinus tachycardia (*choice e*) is a higher-than-normal firing rate of the SA node, and thus a ventricular pacemaker cell with its low intrinsic rate would not take over as a pacemaker and cause a PVC in sinus tachycardia.

268. The answer is e. (*Barrett, pp 540, 545-552, 576, 577. Kaufman, pp 22-24. Le, pp 254-255, 273. Longo, pp 1903-1904.*) The decrease in left ventricular contractility in heart failure causes the ejection fraction to decrease (not increase, *choice d*) resulting in an increase in left ventricular end-diastolic volume. The resultant increase in the radius of the dilated ventricle increases wall tension (*choice e*) according to the Laplace relationship, $T = Pr/w$, where T = tension, P = systolic pressure, r = ventricular radius, and w = ventricular wall thickness. This compensatory increase in wall tension comes at the cost of an increase in energy consumption (not a decrease, *choice b*). In heart failure, an increase in left ventricular end-diastolic pressure causes an increase in pulmonary capillary hydrostatic pressure as reflected in the measurement of pulmonary arterial wedge pressure using a balloon-tipped pulmonary artery catheter (not a decrease, *choice c*). The increased pressure in the pulmonary circulation promotes fluid filtration out of the pulmonary capillaries and is responsible for the characteristic pulmonary edema associated with heart failure. Heart rate is increased (not decreased, *choice a*) by an increase in sympathetic nerve activity that accompanies heart failure.

269. The answer is d. (*Barrett, pp 545-552. Le, pp 253-255. Longo, pp 1998-1999. Widmaier, pp 372-376.*) Factors promoting a decrease in stroke volume are (1) a decrease in preload, (2) an increase in afterload, and (3) a decrease in cardiac contractility. Preload is the degree of stretch on the myocardium before contraction and afterload is the resistance against which blood is ejected. Although heart rate is not a direct determinant of stroke volume, increasing heart rate (*choice d*) decreases the time for filling during diastole, and thus may decrease preload and compromise stroke volume. All of the other choices promote an increase in stroke volume. Increasing central venous pressure (*choice C*) will increase stroke volume by increasing preload. Decreasing afterload by decreasing blood pressure (*choice a*), which may result from decreasing total peripheral resistance (*choice b*), will increase stroke volume. A sympathetic mediated increase in contractility (positive inotropy, *choice e*) will increase stroke volume.

270. The answer is c. (*Barrett, pp 551-552, 578, Kaufman, pp 32, 35. Le, pp 258-259, 570, 578. Longo, pp 279-280, 1826-1828, 1937-1941, e13-1-e13-4, e13-8.*) Exertional syncope, angina, and dyspnea associated with a systolic ejection click and murmur over the aortic valve area (right second intercostal space) suggests aortic stenosis until proven otherwise. In aortic stenosis, the obstruction to left ventricular outflow causes stroke volume and ejection fraction to decline (not increase, *choice e*). The decreased stroke volume leads to a decrease in pulse pressure (*choice c*). The resistance of the stenotic aortic valve increases systolic ventricular pressure (not decreased, *choice b*); in addition, a mean systolic pressure gradient occurs across the valve with systolic ventricular pressure being much higher than the aortic pressure (*choice d*). The increased afterload created by the stenotic valve causes an increase in cardiac oxygen consumption, not decreased (*choice a*). Approximately 80% of adult patients with symptomatic valvular aortic stenosis are male.

271. The answer is d. (*Kaufman, pp 41-43. Le, pp 262-263. Longo, pp 1870-1874.*) A first-degree heart block refers to slowing of the conduction velocity through the AV node, which is manifest as prolongation of the PR interval (*choice d*). There are two types of second-degree heart blocks—Mobitz I (Wenckebach) denoted by progressive prolongation of the PR interval until a QRS complex is dropped (*choice e*) resulting in an irregular rhythm and Mobitz II, a more dangerous dysrhythmia manifest as a fixed, prolonged PR interval followed by a nonconducted QRS complex at regular intervals (*choice b*). A third-degree block occurs when the action potential never reaches the ventricle, such that there is complete asynchrony (dissociation) of atrial and ventricular activity (*choice a*); under these conditions, pacemakers within the ventricle produce ventricular contraction, but the rate is very slow at the intrinsic ventricular rate of around 40 bpm. Sinus bradycardia is represented on the ECG as normal P waves, QRS complexes, and PR interval, but a slow rate as denoted by an increase in the R-R interval (*choice c*).

272. The answer is e. (*Barrett, pp 543-544. Kaufman, pp 32-34. Le, pp 258-259, 274, 579. Longo, pp 1827-1828, 1934-1936, e13-1-e13-8.*) With a history of rheumatic heart disease and a holosystolic murmur heard over the mitral area, this patient likely has mitral regurgitation. Regurgitation of the mitral valve results in backward flow of blood from the left ventricle to the left atrium during systole, resulting in an increased left atrial pressure, which is manifest as an increased *v* wave (*choice e*) in a jugular pressure recording. Blood pressure is typically normal in patients with chronic mitral regurgitation, not decreased (*choice a*). Left ventricular preload is increased (not decreased, *choice b*), and this elicits 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 (*choice d*) or cardiac output (*choice c*).

273. The answer is b. (*Longo, pp 1805-1809.*) End-diastolic volume or preload (*choice c*) is higher in patient #2. Because both ventricles eject the same stroke volume (*choice d*) at the same pressure (*choice a*), they perform the same stroke work (*choice e*). Efficiency is defined as work divided by energy consumption. Cardiac energy consumption is directly related to wall stress. 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. Thus, cardiac efficiency is greater in patient #1 (*choice b*).

274. The answer is b. (*Barrett, p 358. Kaufman, pp 43-44, 97-98. Le, pp 223, 237, 286, 297, 304, 446, 570, 575, 581. Longo, pp 2693-2697.*) Pheochromocytoma is a tumor of the adrenal medulla characterized by an excessive release of catecholamines, which are agonists at both α- and β-adrenergic receptors. 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 (*choice b*) will cause a decrease in TPR and a decrease in blood pressure. An irreversible α-adrenergic antagonist (eg, phenoxybenzamine) is thus administered first to avoid a hypertensive crisis. A β-adrenergic antagonist is then given to slow down the heart rate but administering a β-adrenergic antagonist alone (*choice d*) would lead to unopposed catecholamine stimulation of α receptors in vessel walls, increasing TPR and blood pressure to dangerously high levels. The administration of α-adrenergic or β-adrenergic agonists (*choices a and c*) would only make the problem of excess adrenergic stimulation worse. Glycoprotein IIb/IIIa antagonists (*choice e*) inhibit platelet function and are used in patients with coronary heart disease, not in the treatment of hypertension.

275. The answer is d. (*Kaufman, p 29. Le, p 275. Longo, pp 1972-1976.*) 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. As little as 200 mL of fluid can cause this critical state if developed acutely but up to 2000 mL can be accommodated if developed chronically. The three principal features of cardiac tamponade comprising Beck triad are hypotension, jugular venous distension, and muffled heart sounds. Pulsus paradoxus (*choice d*) is a clinical sign in which there is an abnormally large decrease (>10 mm Hg) 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 left 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 due to the increased fluid in the pericardial space. Instead, the blood pushes against the intraventricular septum and bulges into the left ventricle, greatly reducing the volume of blood that can enter the left ventricle. Systemic hypotension, not hypertension (*choice c*) occurs in cardiac tamponade due to impaired ventricular filling. A third heart sound (*choice e*) is not a feature of cardiac tamponade, but instead occurs in situations of ventricular dilation such as dilated cardiomyopathy. Tachycardia (not bradycardia, *choice a*) is generally present in cardiac tamponade. Rales (*choice b*) may be present in cardiac tamponade, but this is a nonspecific finding and thus not the best answer.

276. The answer is e. (*Klabunde, pp 113-117. Le, pp 254-255.*) The diagram represents the cardiac (ventricular) function and vascular function curves. For the cardiac function (Starling) curves (D→E and A→C), cardiac output is plotted 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 three vascular function curves (including points A→D, B→Control, and C→E) plot central venous pressure as a function of cardiac output. 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 cardiac and vascular function curves intersect represents the central venous pressure and cardiac output of the cardiovascular system. The shift from the control 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. 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. With exercise, there is an increase in contractility and a decrease in TPR and venous compliance, consistent with a shift from control to *point C*. The shift from control to *point D* reflects an increase in TPR, rotating the venous function curve counter-clockwise at no change in contractility. The shift from control to *point A* reflects an increase in TPR and contractility.

277. The answer is c. (*Barrett, pp 139, 146-147, 260-261, 547-550. Klabunde, pp 41-48. Le, p 254. Longo, pp 1803-1807. Widmaier, pp 373-375.*) Sympathetic stimulation of the heart increases the activity of the SR Ca^{2+} pump (*choice c*). Sympathetic stimulation also increases the rate of SA nodal firing, which increases heart rate, and decreases the duration of both systole and diastole (not increases, *choices c* and *d*). Norepinephrine secreted by the sympathetic nerve endings binds to β_1-adrenergic receptors, activating a Gs protein, which activates adenylyl cyclase and increases the intra-cellular concentration of cyclic AMP (not decreases, *choice b*). 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. Thus, there is an increase in the concentration of Ca^{2+} during systole, not a decrease (*choice a*). Cyclic AMP also increases the active transport of Ca^{2+} to the SR, which accelerates relaxation and shortens systole.

278. The answer is a. (*Barrett, p 548. Le, p 214. Longo, pp 270, 2216, 2709-2710.*) Shock is the clinical syndrome that results from inadequate tissue perfusion, and is usually accompanied by hypotension, that is, MAP <60 mm Hg in a previously normotensive person. Shock can be classified into hypovolemic, distributive (including anaphylactic, septic, and neurogenic), cardiogenic, and obstructive subtypes. Each subtype is treated differently, so it is important to be able to distinguish between them. In hypovolemic shock, the primary disturbance is a decrease in blood volume. Since blood volume declines, preload, stroke volume, and thus cardiac output fall. In an effort to return blood pressure to normal (recall the relationship MAP = CO × TPR), the body constricts blood vessels, raising total peripheral resistance (TPR) (*choice d*) and heart rate with sympathetic stimulation. In distributive shock (including anaphylaxis), the primary problem is a dilation of peripheral blood vessels, lowering TPR. In anaphylaxis, this dilation is due to the degranulation of mast cells and release of prostaglandins in an allergic type 1 hypersensitivity response to an antigen. While TPR falls in anaphylactic shock, the body raises cardiac output (*choice a*) in an attempt to maintain blood pressure. In both hypovolemic and distributive shock, the baroreceptor reflex increases ventricular contractility (*choice e*) and heart rate (*choice b*). Also, in both hypovolemic and distributive shock, blood is shunted away from the kidney, decreasing renal blood flow and glomerular filtration, and increasing serum creatinine as a result (*choice c*). In cardiogenic shock, the primary problem is a decrease in cardiac output due to a decrease in ventricular contractility; the body responds by constricting blood vessels and increasing TPR to compensate.

279. The answer is c. (*Barrett, pp 550-552. Widmaier, pp 267-268.*) During exercise, sympathetic stimulation of the heart increases heart rate and myocardial contractility. Sympathetic stimulation also decreases in venous compliance (not increase, *choice e*), which increases venous return to the heart, and contributes to an increased stroke volume by a Frank–Starling mechanism. Cardiac output increases during exercise primarily due to an increase in heart rate, though there is a modest increase in stroke volume (*choice c*). Systolic pressure increases, but diastolic pressure decreases (not increases, *choice a*) due to a fall in systemic vascular resistance (not an increase, *choice d*), which is caused by dilation of the blood vessels within the exercising muscles. The increased cardiac output (pulmonary blood flow) passively dilates the pulmonary vessels, causing a decrease in pulmonary vascular resistance (not an increase, *choice b*).

280. The answer is d. (*Klabunde, pp 103-105. Le, p 255.*) 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.

$$Q_{\text{Vessel Y}} \propto 1/1;\ Q_{\text{Vessel Z}} \propto 1/2$$

$$Q_{\text{Vessel Y}}/Q_{\text{Vessel Z}} = \frac{1/1 \times 2/1}{1/2 \times 2/1}$$

$$= 2/1$$

$$Q_{\text{Vessel X}} = Q_{\text{Vessel Y}} + Q_{\text{Vessel Z}} = 2 + 1 = 3$$

$$Q_{\text{Vessel X}}/Q_{\text{Vessel Y}} = 3/2$$

281. The answer is e. (*Barrett, pp 574-577. Le, p 264. Longo, pp 2255-2257.*) An increased intracranial pressure compresses the cerebral vessels, thereby reducing cerebral blood flow. The increase in intracranial pressure stimulates the vasomotor center and produces an increased systemic blood pressure that may lead to a restoration of cerebral blood flow. The increased blood pressure induces bradycardia (*choice e*) mediated by the baroreceptor reflex. This response to increased intracranial pressure is part of Cushing triad, which includes hypertension, bradycardia, and respiratory depression.

282. The answer is d. (*Barrett, pp 576-577. Longo, pp 1834-1835.*) 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* is the radius of the ventricle (determined by end-diastolic volume), and *w* is 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 (*choice b*) will increase wall stress. Wall stress will also be increased if total peripheral resistance (*choice e*) is increased or mean arterial pressure (*choice c*) is increased because, under both conditions, the heart will have to develop more pressure. Increasing atrial contractility (*choice a*) would increase ventricular filling and end-diastolic volume, increasing wall stress. Losartan is an angiotensin II receptor (type AT_1) antagonist that helps to lower blood pressure, as well as reduce left ventricular hypertrophy. The *R* wave of ≥ 11 mm in aVL along with the findings of the S wave in V_1 + R wave in V_5 of ≥35 mm are suggestive of left ventricular hypertrophy.

283. The answer is a. (*Widmaier, pp 407-410.*) Blood flow to the brain (*choice a*) 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 (*choice d*). Coronary blood flow (*choice b*) increases to meet the increased metabolic needs of the heart. Blood flow to the gut, the kidneys (*choice c*), and the nonexercising muscles is reduced by sympathetic constriction of the arterioles leading to these organs. Blood flow to the skin (*choice e*) is increased to prevent overheating.

284. The answer is b. (*Barrett, pp 524-529. Le, p 261. Longo, pp 1831-1834. Widmaier, p 362.*) The bundle of His depolarizes during the PR segment (*segment B*), 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; *segment D*, the ST segment, represents the time interval during which all of the ventricular muscle is depolarized; and *segment E*, the T wave, represents ventricular repolarization.

285. The answer is b. (*Barrett, pp 544-545. Longo, p 2047. Widmaier, p 379.*) Pulse pressure is directly proportional to the stroke volume and inversely proportional to arterial compliance. Pulse pressure increases in arteriosclerosis because stiffening of the arteries causes arterial compliance to decrease. Stroke volume is decreased with tachycardia (*choice e*), hemorrhage (*choice c*), and heart failure (*choice b*), reducing pulse pressure in all three cases. In aortic stenosis (*choice a*), the stroke volume is decreased and the rate of ejection of blood from the ventricle is slowed down. Aortic regurgitation, on the other hand, does cause a widened pulse pressure.

286. The answer is a. (*Barrett, pp 534-537. Kaufman, pp 16-20. Longo, pp 351-355. Le, pp 269-271.*) 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, when 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. Hyperkalemia (*choice b*) results in peaked T waves and narrow QRS complexes at mildly elevated levels progressing to wide QRS complexes and ventricular fibrillation at severely elevated levels. Hypokalemia (*choice c*) results in ST-segment depression at modestly depressed levels and the appearance of inverted T waves and of U waves at more severely depressed levels. A posterior myocardial infarction (*choice d*) can be difficult to detect since there are no leads directly posterior to the heart analogous to the anterior precordial leads. It can, however, be suspected with reciprocal changes in the anterior leads such as ST depression in leads V_{1-3}. A ventricular premature beat (*choice e*) is an isolated ventricular systole that occurs from electrical activity originating in the ventricles instead of the atria. It manifests on the ECG as a single wide QRS complex occurring with no preceding P wave and usually has a different MEA from the remainder of the ECG. Further, a ventricular premature beat should not be associated with ischemic ECG findings such as ST elevation or ST depression.

287. The answer is a. (*Barrett, pp 540, 702-704. Kaufman, p 26. Le, p 502. Longo, pp 1906-1913. Widmaier, pp 411, 497-498.*) Angiotensin converting enzyme (ACE) inhibitors such as captopril are a mainstay of treatment for CHF and their use has been shown to increase survival (*choice e*). ACE inhibitors interfere with the renin–angiotensin system by blocking the conversion of angiotensin I to angiotensin II. Because angiotensin II is a potent vasoconstrictor, inhibiting this conversion leads to arteriolar vasodilation, thus reducing afterload (*choice a*). Arteriolar vasoconstriction is inhibited, not augmented (*choice b*). They also appear to stabilize ventricular remodeling. Bradykinin levels (*choice c*) are increased with the use of ACE inhibitor and a nonproductive cough (*choice d*) is a side effect as a result.

288. The answer is d. (*Barrett, pp 559, 614-616. Le, pp 251-252.*) During pregnancy, uterine blood flow increases 20-fold, not just 2× (*choice e*). The fetus derives its oxygen from the maternal arterial blood supply by gas exchange across the placenta, which constitutes 40% to 60% of the fetal cardiac output (*choice d*). The umbilical vein draining the placenta therefore has the highest oxygenation in the fetus, with a P_{O_2} of approximately 30 mm Hg and 80% oxygen saturation, not the umbilical arteries (*choice c*), which have a low oxygen saturation. Fetal CO_2 that diffuses across the placenta is removed by the maternal blood through the uterine veins, not the uterine arteries (*choice a*). The oxygen dissociation curve for fetal hemoglobin is shifted to the left of that for maternal hemoglobin A, which promotes greater oxygen loading at the placental level.

289. The answer is b. (*Barrett, pp 548, 580-585. Le, p 265. Longo, p 2216. Widmaier, pp 405-406, 416, 433.*) 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 (*choice b*). The increased arteriolar constriction lowers blood flow to the kidney causing urine formation to decrease, not increase (*choice d*). Sympathetic stimulation causes peripheral constriction and produces sweating, resulting in the classic sign of hemorrhage: cold, pale skin, not warm skin (*choice e*). The baroreceptor reflex increases heart rate and thus bradycardia would not occur (*choice a*). In states of low perfusion such as shock, there is decreased oxygen supply to the tissues and cells are forced to switch to anaerobic glycolysis in order to make ATP. This results in increased lactic acid production and thus metabolic acidosis, not metabolic alkalosis (*choice c*).

290. The answer is e. (*Widmaier, p 377.*) 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.

$$\text{Arterial compliance} = \Delta V/\Delta P = 250 \text{ mL}/160 \text{ mm Hg} = 1.56 \text{ mL/mm Hg}$$
$$\text{Venous compliance} = \Delta V/\Delta P = 1500 \text{ mL}/50 \text{ mm Hg} = 30 \text{ mL/mm Hg}$$
$$\text{Arterial compliance/Venous compliance} = 1.56 \text{ mL/mm Hg}/30 \text{ mL/mm Hg} = 1{:}19.2 \text{ (choice e)}$$

291. The answer is c. (*Barrett, pp 559, 614-616. Le, pp 251-252, 266-267.*) The vignette describes the classic presentation of a child with a patent ductus arteriosus. In utero, the ductus arteriosus is a low-resistance arterial vessel through which highly oxygenated blood flows from the pulmonary artery to the aorta, bypassing the lungs (*choice c*). 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. Under normal conditions, 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 (*choice a*). 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, but this is a late finding, which would occur long after 6 days after birth. *Choice e* describes the foramen ovale, which diverts blood away from the lungs across the atrial septum in utero, but would not cause the clinical presentation described if it persisted postnatally as a patent foramen ovale. *Choice b* does not describe the function of a known fetal structure, although the umbilical vein supplies oxygenated blood from the placenta to the right (not left) atrium by way of the ductus venosus. The ductus arteriosus is not primarily involved in regulating fetal blood pressure (*choice d*).

292. The answer is c. (*Klabunde, pp 113-117. Le, pp 254-255.*) This diagram depicts cardiac (ventricular) function and vascular 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 TPR 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 (*point C*) represents the central venous pressure and cardiac output of the cardiovascular system under these conditions. *Point A* shows an upward shift of the cardiac function curve and an increase in TPR, but it is known that TPR decreases during exercise. *Point B* shows an upward shift in the cardiac function curve, but no change in the venous function curve as would be expected to occur during exercise. *Point D* shows no change in the cardiac function curve and an increase in TPR; during exercise, the cardiac function curve shifts upward due to increases in contractility. *Point E* shows no change in the cardiac function curve but an increase in blood volume as would occur in states of renal salt retention or overtransfusion, but would not occur during exercise.

Cardiac (ventricular) function curve determinants:

- Afterload: increases in afterload shift the cardiac function curve down and decreases in afterload shift it up.
- Contractility: increases in contractility shift the cardiac function curve up and decreases in contractility shift it down.

Venous function curve determinants:

- Blood volume: increases in blood volume shift the venous function curve rightward and decreases in blood volume shift it leftward.
- Total peripheral resistance (TPR): increases in TPR rotate the venous function curve counter-clockwise about its x-intercept (flatter). Decreases in TPR rotate the venous function curve clockwise about its x-intercept (steeper).

293. The answer is a. (*Barrett, pp 544, 573-577. Longo, pp 3282-3287. Widmaier, pp 356-358.*) Under conditions of increased velocity above the critical threshold, blood flow becomes turbulent and audible; this is known as a murmur when it occurs within the heart and a bruit when it occurs in the vasculature. In this patient, turbulence and consequently the bruit were produced by the high velocity of blood (*choice a*) within the stenotic area of the carotid artery, as predicted by Reynolds number. The widening of a vessel associated with aneurysms (*choice e*) can also produce bruits, but these are not relieved by endarterectomy. An increase in hematocrit (*choice c*) or blood viscosity (*choice b*) would decrease Reynolds number and decrease the tendency for turbulent flow. Lengthening of the carotid artery (*choice d*) would not have any effect on blood turbulence.

294. The answer is e. (*Barrett, pp 539-542. Le, p 256. Longo, pp 1808-1809.*) 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. 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. *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.

295. The answer is b. (*Widmaier, pp 315, 325-326, 384, 498-501.*) Antidiuretic hormone (*choice b*), also known as vasopressin, is a powerful vasoconstrictor in addition to its effect of decreasing plasma osmolality via renal water retention. All the other listed substances cause vasodilation.

296. The answer is c. (*Barrett, pp 614-616. Le, p 252, 267.*) Functional closure of the ductus arteriosus is the final event required for conversion of the transitional circulation in the newborn to the adult circulatory pattern (*choice c*). At birth, with the onset of extrauterine respiration and elimination of the placental circulation, functional closure of the foramen ovale (*choice e*) and the ductus venosus occur immediately, whereas functional closure of the ductus arteriosus generally begins within a few hours after birth, and is not complete until about 48 to 72 hours. Immediately after birth, flow through the ductus switches, with blood flowing from the aorta to the pulmonary artery, but this ceases when the ductus closes (*choice a*). 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, *choice D*). Ductal sensitivity to oxygen is age dependent (*choice b*), 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.

297. The answer is b. (*Barrett, pp 57-58, 97-116. Le, pp 231, 385-386. Longo, pp 1800-1802.*) 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, 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 (*choice a*) may lower blood pressure by acting on β_2 receptors and relaxing vascular smooth muscle, they also increase the rate and strength of the heartbeat by acting on β_1 receptors. Troponin (*choice c*) and tropomyosin (*choice d*) are found only in skeletal and cardiac muscle and not found in smooth muscle. Protein kinase A (*choice e*) is found in all types of muscle and thus drugs acting at this site could affect cardiac muscle variables such as contractility.

298. The answer is c. (*Longo, pp 1802-1807.*) Phospholamban is a protein contained within the SR that inhibits the activity of the SR calcium pump. Inactivation of phospholamban results in an increase in calcium sequestration by the SR, which would increase the concentration of calcium within the SR, thereby increasing the force of the ventricular contraction. Decreasing phospholamban would not elicit any of the effects described in the other answer choices.

299. The answer is b. (*Barrett, pp 539-544. Le, pp 256. Widmaier, pp 367-371.*) S_1 is generated by two components, mitral valve closure (M_1), and tricuspid valve closure (T_1). M_1 and T_1 generally occur in such rapid succession that they cannot be distinguished as separate sounds with a standard bedside stethoscope. S_1, unlike S_2, should thus not be split under normal conditions. Splitting of S_1 is a sign of a pathological condition such as a right bundle branch block, when the tricuspid valve closes (T_1) later than the mitral valve due to a conduction delay to the right ventricle. On the time–pressure graph, a valve opens or closes at each major point of inflection or intersection of pressure curves. At time *B*, ventricular pressure begins to exceed atrial pressure causing each AV valve (mitral and tricuspid) to close, which prevents backflow of blood and results in the S_1 heart sound. Time *A* represents atrial systole, a small elevation in atrial pressure to aid in filling of the ventricles prior to the beginning of ventricular systole. No valves open or close at time *C* or *E*.

300. The answer is d. (*Le, p 280. Longo, pp 2006-2008. Widmaier, p 415.*) Nitrates are commonly used for the treatment of angina and coronary artery disease. Nitroglycerin is a vasodilator because it releases nitric oxide in smooth muscle causing an increase in cyclic GMP and vascular smooth muscle relaxation. Nitroglycerin dilates the coronary arteries, thereby increasing coronary blood flow (not decreasing, *choice b*). Arteriolar dilation lowers TPR, thereby lowering arterial blood pressure (not increasing, *choice a*) and the work the heart must do to eject blood, which decreases myocardial oxygen demand (*choice d*). The decrease in myocardial oxygen consumption is primarily due to systemic venodilation, which decreases venous return (not increases, *choice e*) and ventricular end-diastolic volume (preload). The decreased end-diastolic volume decreases the radius of the ventricle and thus decreases left ventricular wall stress (not increased, *choice c*) in accordance with the law of Laplace— $T = P \times r/w$, where wall stress, that is, tension (T), is proportional to the pressure (P) and radius (r) and inversely proportional to the thickness of the ventricle wall (w).

301. The answer is a. (*Barrett, pp 610-612. Widmaier, pp 373-378.*) 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. Flow is highest just at the beginning of diastole (*choice a*) 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 not being compressed by the contracting myocardium. The second heart sound is due to closure of the aortic and pulmonic valves at the beginning of diastole. During systole, when the ventricle is contracting (*choice b* and *e*) and aortic pressure (*choice d*) and flow (*choice e*) are highest, coronary vascular resistance increases substantially and the first heart sound is auscultated due to closure of the mitral and tricuspid valves. Flow is highest just at the beginning of diastole (*choice a*) 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. The second heart sound is due to closure of the aortic and pulmonic valves at the beginning of diastole.

302. The answer is c. (*Barrett, pp 97-100. Longo, pp 1802-1807.*) Titin (*choice c*) 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. Calmodulin (*choice a*), troponin (*choice e*), tropomyosin (*choice d*), and myosin light chain kinase (*choice b*) are all involved in muscle contraction but are not as important as titin in the passive compliance of cardiac muscle.

303. The answer is d. (*Barrett, pp 603, 627-628, 636-638. Le, p 549. Longo, pp 1808-1809. Widmaier, pp 355, 370-371.*) 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. Although the left and right preloads are not identical, they are very similar as reflected by an average right atrial pressure of 2 mm Hg and a left atrial pressure of 5 mm Hg. In contrast, the resistance of the pulmonary vasculature is much lower than that of the systemic circulation, yielding much lower pressures in the pulmonary artery than the aorta (mean pulmonary artery pressure = 15 mm Hg; mean aortic pressure = 90 mm Hg). Thus, the afterload (*choice a*) and stroke work (*choice e*) 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 (*choice c*) is higher on the left side (120 mm Hg) than on the right side (25 mm Hg). 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 (*choice b*).

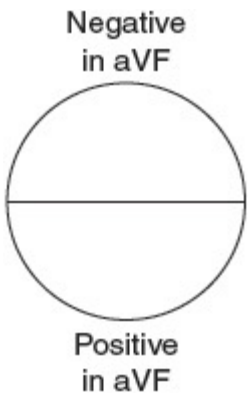
304. The answer is e. (*Le, pp 158, 579. Longo, pp 238, 1952-1956.*) This patient is showing classic signs of dilated cardiomyopathy caused by myocarditis. This clinical picture is commonly caused by viruses, most commonly Coxsackie B virus, which causes ventricular dilation (*choice e*) through a variety of mechanisms including degradation of myocardial structural proteins such as dystrophin. Hypertrophy of the interventricular septum (*choice b*) occurs in hypertrophic obstructive cardiomyopathy, which is the most common cause of death of otherwise healthy young athletes, but is usually asymptomatic. Global ventricular hypertrophy (*choice a*) occurs in hypertensive heart disease, but as the ventricular walls thicken the ejection fraction often becomes supraphysiologic, not decreased. Narrowing of the descending aorta (*choice c*) occurs in coarctation of the aorta, but does not present in this fashion. Vegetations on the cardiac valves (*choice d*) occur in infective endocarditis, but do not generally cause a reduced ejection fraction.

305. The answer is b. (*Le, p 269. Longo, p 2005.*) The patient described is experiencing the coronary "steal" phenomenon after being provoked with a vasodilator (dipyridamole). The coronary circulation normally demonstrates autoregulation in response to increased energy demand. For example, during exercise, the coronary arteries dilate to increase blood flow to meet the increased metabolic demand of the myocardium. This ability to increase blood flow is known as coronary reserve. Dilation during exercise occurs in response to products of metabolism, including low O_2, and elevated CO_2, H^+, K^+, and lactate. Under conditions of partially occlusive atherosclerosis in an isolated coronary vascular bed, blood flow is reduced at rest. In response, the diseased artery becomes progressively dilated as the occlusion worsens. This continues until the artery is maximally dilated at rest, while the other disease-free arteries remain at normal diameters. If a vasodilator is given under these circumstances, as in certain chemical stress tests, all the coronary arteries become maximally dilated. The effect is to shunt or "steal" blood flow from the diseased vascular bed and redistribute it to the newly dilated arteries (*choice b*), producing ischemia (as evidenced by the ST depression) in the myocardium supplied by the diseased artery. Coronary vasospasm (*choice c*) is also known as Prinzmetal angina and is nonexertional in nature, and relieved by vasodilators such as dipyridamole, not provoked by them. Vasodilators do not generally cause bradycardia (*choice a*). Although it is possible that the patient is experiencing ischemia due to an occlusive coronary embolus (*choice d*), the temporal relationship to the administration of the vasodilator argues that it is more likely due to coronary "steal." Pulmonary emboli (*choice E*) do not generally produce ST-depression on the ECG unless they are massive enough to cause right heart strain, and the temporal relation of the patient's chest pain to the administration of the vasodilator again makes coronary "steal" more likely.

306. The answer is d. (*Barrett, pp 547-549. Klabunde, pp 67-74. Le, pp 150, 256, 272, 567. Longo, pp 1806-1809, 1942-1944.*) Dilated cardiomyopathy is the most common cardiomyopathy, accounting for 90% of cases. Dilated cardiomyopathy is characterized by an increased end-diastolic volume and decreased ejection fraction due to dilated ventricles and decreased contractility. Only *choice d* demonstrates these changes with a rightward shift of the pressure–volume loop to a higher end-diastolic volume and a narrower loop representing a decreased stroke volume. *Choice a* represents the changes that would be seen in aortic stenosis. There is no change in end-diastolic volume, but peak systolic volume is significantly increased due to increased afterload from the stenotic valve. *Choice b* represents the changes that would be seen in impaired relaxation of the myocardium such as in left ventricular hypertrophy or diastolic heart failure. As shown, there is impaired filling of the heart demonstrated by a steepening of the bottom portion of the pressure–volume loop and a decreased end-diastolic volume. *Choice c* demonstrates an increase in ejection fraction with no change in end-diastolic volume. This is seen in instances of increased contractility such as during the response to exercise.

307. The correct answer is a. (*Barrett, pp 544-545. Le, p 257. Longo, pp e13-8-e13-9.*) The S_2 heart sound is generated by the aortic valve closure (A_2) and the pulmonic valve closure (P_2), which are nearly synchronous events in healthy individuals when intrathoracic pressure is equilibrated such as after expiration. When intrathoracic pressure is negative, as in inspiration, blood is drawn into the pulmonary circulation, which delays closure of the pulmonic valve, and thus A_2 and P_2 become discernible as separate sounds resulting in a normal physiological split of S_2. However, splitting of S_2 should only occur during inspiration in healthy individuals and this split should disappear during expiration. The patient is described as having a split of S_2 that occurs throughout the respiratory cycle, known as a fixed split. Fixed splitting occurs in conditions such an atrial septal defect (*choice a*). Fixed splitting occurs because pressure equilibrates across both atria due to the septal defect regardless of the respiratory phase. Dilated ventricles (*choice d*) occur in heart failure and dilated cardiomyopathy and are commonly associated with an S_3 gallop. Fixed splitting is never a normal finding (*choice e*). Coarctation of the aorta (*choice c*) does not result in a fixed split of S_2 but can result in early-onset hypertension and differential blood pressure readings in upper and lower extremities. A bicuspid aortic valve (*choice b*), the most common congenital heart defect, can result in aortic stenosis later in life. However, aortic stenosis manifests as a systolic ejection murmur, not as a fixed split of S_2.

308. The answer is e. (*Barrett, p 528. Kaufman, p 57. Longo, pp 1831-1839.*) 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. It is helpful to think of the MEA as a vector that can be broken down into its component parts, analogous to the *x* and *y* components of a vector in a Cartesian coordinate system. The deflection in lead aVF is analogous to the *y*-axis, but since the positive pole of aVF is inferior to the heart, a positive deflection in lead aVF would indicate the MEA points downward. This places the MEA within the range of 0 and 180 degrees, ruling out *choice a* and *choice b*.



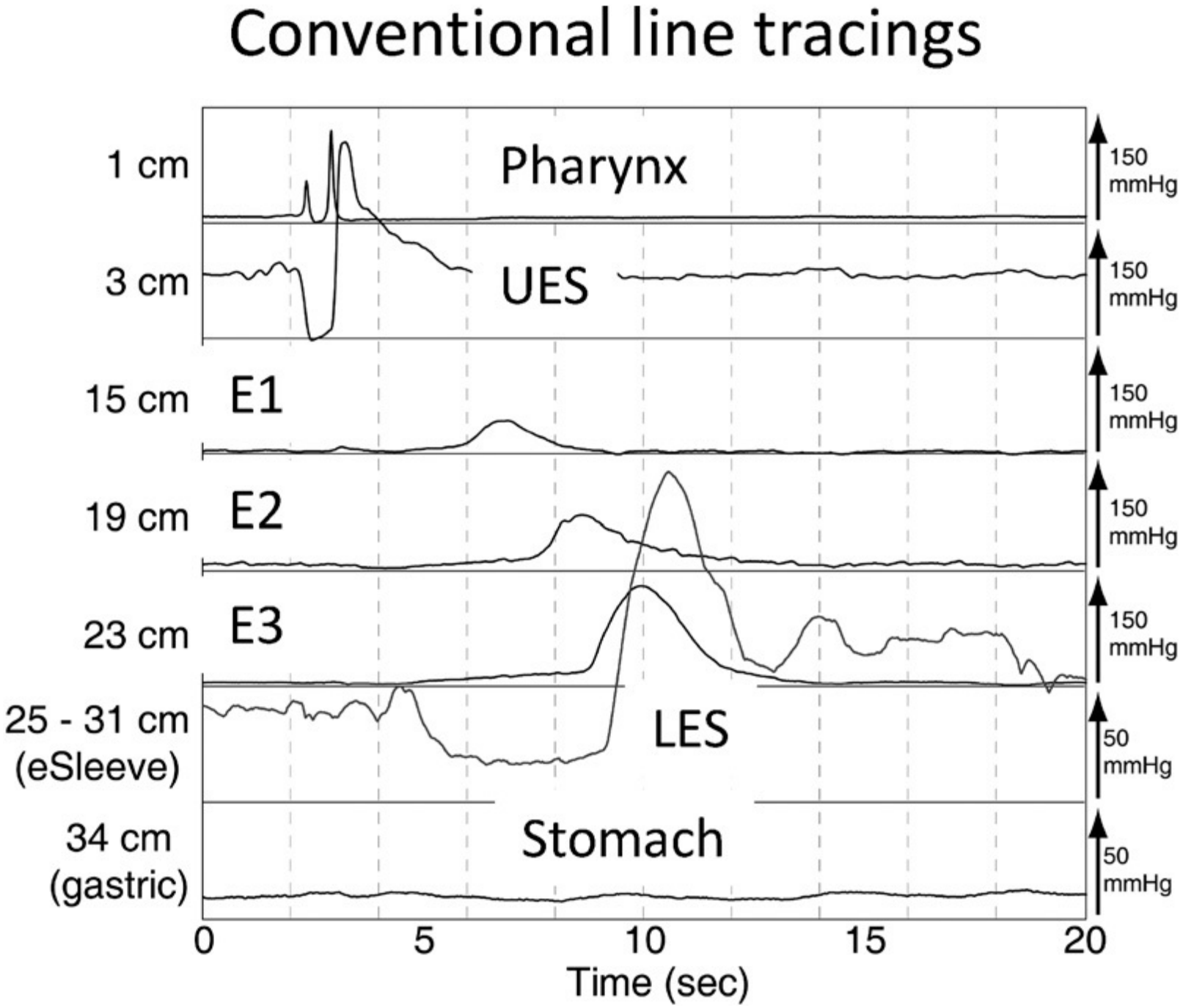
If the mean orientation of the depolarization vector is at right angles to a given lead axis, a biphasic (equally positive and negative) deflection will be recorded.

Therefore, the equiphasic QRS complex in lead aVR indicates that the mean QRS vector is 90 degrees away from +210 degrees. If the QRS complex is positive in leads III and aVF, the MEA must move toward +120 and +90 degrees, respectively. Thus, the mean QRS vector must be +120 degrees (*choice e*). Right axis deviation (mean QRS vector to the right of 110 degrees) is characteristic of the right ventricular strain or hypertrophy associated with pulmonary hypertension. The positive QRS complex in lead V_1 is also characteristic of right axis deviation.

309. The answer is c. (*Barrett, pp 540, 546-553. Le, pp 254-255. Longo, pp 1808-1809.*) During isotonic exercise, there is an increase in sympatho-adrenal activity that increases cardiac output and contractility, which will shift the normal operating point (X) to a Starling curve above the normal curve. *Choice c* is the best choice among the points on that curve because sympathetically mediated venoconstriction, coupled with the respiratory and muscle pumps, will also increase venous return and thus preload, whereas *choice b* represents an increase in contractility at a constant preload and *choice a* represents increased contractility but decreased preload. *Choice d* and *choice e* are incorrect because they represent a shift to a curve with a lower cardiac output and contractility.

Questions

310. A 58-year-old woman has a 6-month history of substernal chest pain and heartburn. She has been taking over-the-counter omeprazole with minimal relief. Conventional esophageal manometry is performed to measure pressures during a test swallow as shown below.



(Reproduced, with permission, from Longo DL, Fauci AS, Kasper DL, Hauser SL, Jameson JL, Loscalzo J. *Harrison's Principles of Internal Medicine*. 18th ed. New York, NY: McGraw-Hill; 2012:2428.)

Which of the following causes relaxation of the lower esophageal sphincter (LES) in response to swallowing?

a. Circulating gastrin
b. Inhibitory sympathetic nerve input to the LES
c. Intrinsic myogenic tone of circular smooth muscle
d. Release of acetylcholine from the myenteric plexus
e. Release of vasoactive intestinal peptide and nitric oxide from inhibitory ganglionic neurons

311. A 52-year-old man with diabetes mellitus type 1 has persistent nausea and vomiting due to gastroparesis with gastroesophageal reflux disease (GERD). Which of the following best describes the function of gastric emptying?

a. Acidification of the antrum increases gastric emptying.

b. Hyperosmolality of duodenal contents initiates a decrease in gastric emptying.
c. Meals containing fat empty faster than carbohydrate-rich food.
d. Solids empty more rapidly than liquids.
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 last month as the date she has scheduled for her licensure examination approaches. Which of the following best describes small intestinal motility?

a. Contractile activity is initiated in response to bowel wall distention.
b. Contractile frequency is constant from duodenum to terminal ileum.
c. Migrating motor complexes (MMCs) occur during the digestive period.
d. Peristalsis is the only contractile activity that occurs during feeding.
e. Vagotomy abolishes contractile activity during the digestive period.

313. An 18-year-old man with pernicious anemia lacks intrinsic factor, which is necessary for the absorption of cyanocobalamin. Vitamin B_{12} is absorbed primarily in which portion of the gastrointestinal (GI) tract?

a. Stomach
b. Duodenum
c. Jejunum
d. Ileum
e. Colon

314. A 27-year-old woman 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. Electroneutral NaCl transport
b. Sodium–bile salt cotransport
c. Sodium–glucose coupled cotransport
d. Sodium–hydrogen countertransport
e. Sodium–phosphorous countertransport

315. A 37-year-old man 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. Colon
b. Duodenum
c. Liver
d. Pancreas
e. Stomach

316. A 35-year-old male smoker presents with burning epigastric pain that is most pronounced on an empty stomach. In addition to peptic ulcer disease and gastric acid hypersecretion, the patient has a paroxysmal rise in serum gastrin in response to intravenous (IV) secretin. Normally, basal acid output is increased by which of the following?

a. Acidification of the antrum
b. Acidification of the duodenum
c. Administration of an H_2-receptor antagonist
d. Alkalinization of the antrum
e. Vagotomy

317. A 42-year-old man develops a gastric carcinoma affecting the proximal third of his stomach. He is scheduled for a partial gastrectomy of the affected region. Which of the following processes will be most affected by the surgery?

a. Receptive relaxation
b. Peristalsis
c. Retropulsion
d. Segmentation
e. Trituration

318. A 37-year-old man with AIDS presents with a fever, anorexia, weight loss, and GI bleeding. Physical examination reveals a palpable abdominal mass. Endoscopy and biopsy reveal a proximal small-bowel malignancy requiring 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

319. A 63-year-old woman has an intractable duodenal ulcer failing all previous treatments. After consultation with a surgeon, a laparoscopic vagotomy is performed. Subsequently, the patient experiences nausea and vomiting after ingestion of a mixed meal. Which of the following best explains her symptoms?

a. Decreased gastric emptying of liquids
b. Decreased gastric emptying of solids
c. Increased gastric emptying of liquids
d. Increased gastric emptying of solids
e. Increased gastric emptying of solids and liquids

320. A 17-year-old adolescent boy who is being treated with the macro-lide antibiotic erythromycin complains of nausea, intestinal cramping, and diarrhea. The side effects are the result of the antibiotic binding to receptors in the GI tract that recognize which GI hormone?

a. Cholecystokinin
b. Enterogastrone
c. Gastrin
d. Motilin
e. Secretin

321. 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

322. A 57-year-old woman 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. Decreased glucose absorption
b. Decreased water content of the feces
c. Increased bile acid concentration in the enterohepatic circulation
d. Increased excretion of fatty acids
e. Increased iron absorption

323. A 67-year-old man 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. Chymotrypsin
c. Colipase
d. Lipase
e. Trypsin

324. After a recent viral illness, a 20-year-old woman develops bilateral facial swelling consistent with parotitis. Which of the following best describes the salivary glands?

a. Approximately 4 L of saliva is secreted per day.
b. Salivary α-amylase preferentially hydrolyzes 1:6α over 1:4α linkages.
c. Cranial nerve VIII passes through the parotid gland.
d. Starch digestion begins in the mouth via salivary α-amylase.
e. The parotid gland is the most mucinous of the salivary glands.

325. 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

326. A 43-year-old woman presents with dysphagia to solids and liquids, bland regurgitation, and diffuse chest pain of 2 months duration. During this time, she has lost about 20 pounds. The patient is scheduled for esophageal imaging and motility testing. The esophagogram during a barium swallow shows a dilated esophagus with an area of distal stenosis and esophageal manometry tracings during a wet swallow shows a high lower esophageal sphincter (LES) opening pressure and uncoordinated peristalsis.

These findings are consistent with which of the following diagnoses?

a. Achalasia
b. Diffuse esophageal spasm
c. GERD
d. Schatzki ring
e. Zenker diverticulum

327. A 42-year-old salesman presents with the chief complaint of intermittent midepigastric pain that is relieved by antacids or eating. Gastric analysis reveals that basal and maximal acid outputs exceed normal values. The gastric acid hypersecretion can be explained by an increase in the plasma concentration of which of the following?

a. Cholecystokinin
b. Gastrin
c. Secretin
d. Somatostatin
e. Vasoactive intestinal peptide

328. A 70-year-old woman presents with abdominal pain, microcytic anemia, and weight loss. Colonoscopy with biopsy confirms colon cancer. Which of the following best describes colonic function?

a. Absorption of Na^+ in the colon is under hormonal control by aldosterone.
b. Bile acids enhance absorption of water from the colon.
c. Net absorption of HCO_3^- occurs in the colon.
d. Net absorption of K^+ occurs in the colon.
e. The luminal potential in the colon is positive.

329. A 42-year-old woman presents to the emergency room with right upper quadrant pain that developed after eating dinner. She is diagnosed as having cholecystitis. Which of the following would be expected with 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.

330. 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. Decreased gastric emptying of liquids
c. Decreased gastric emptying of solids
d. Increased bicarbonate secretion in the duodenal bulb
e. Increased maximal acid output

331. A 43-year-old woman 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. Her generalized decrease in intestinal absorption can be attributed to which of the following?

a. Decreased gastric emptying
b. Decreased intestinal motility
c. Decreased intestinal surface area
d. Increased enterohepatic circulation of bile
e. Increased migrating motor complexes

332. 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 recommends cimeti-dine (Tagamet) because it is inexpensive and over the counter. Which of the following best describes the pharmacological blockade of histamine H_2 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 cells.

333. A 37-year-old man is admitted to the hospital due to an exacerbation of his Crohn's disease with severe inflammation of the ileum. Which of the following would be seen?

a. Decreased bile acid pool size
b. Decreased release of secretin
c. Increased absorption of dietary fats
d. Increased colon absorption of water
e. Increased vitamin B_{12} absorption

334. A 47-year-old man takes esomeprazole for his "acid indigestion." Which of the following best describes the use of substituted benzimidazole derivatives?

a. They are not effective as part of a treatment regimen for *Helicobacter pylori.*
b. They are not used in the treatment of Zollinger–Ellison syndrome.
c. They are water-soluble compounds.
d. They decrease gastrin levels.
e. They inhibit H–K-ATPase in parietal cells.

335. 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. Bile salts
b. Folate
c. Iron
d. Lactose
e. Protein

336. A 62-year-old woman is prescribed the prostaglandin E agonist, misoprostol, along with a NSAID for her severe bilateral osteoarthritis of the knees. What is the purpose of the misoprostol?

a. Antagonizes H_2 receptors
b. Enhances LES relaxation, thereby preventing NSAID-induced dysphagia
c. Increases colonic water reabsorption, thereby preventing diarrhea
d. Inhibits bicarbonate secretion into the gastric mucous gel
e. Prevents NSAID-induced gastric ulcers

337. An 18-year-old college student reports that she experiences severe abdominal bloating and diarrhea within 1 hour of consuming dairy products. A subsequent hydrogen breath test is abnormal. The diarrhea and bloating can best be explained by which of the following?

a. A decrease in exocrine pancreatic secretion
b. A deficiency in the brush border enzyme lactase
c. Carbohydrate-induced secretory diarrhea
d. Decreased carbohydrate absorption
e. Decreased intestinal surface area

338. 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 of 12 mmol/hour (normal: <5 mmol/hour). The steatorrhea is most likely due to which of the following?

a. Decreased gastric acid secretion
b. Decreased pyloric sphincter tone
c. Decreased secretion of intrinsic factor
d. Delayed gastric emptying
e. Inactivation of pancreatic lipase due to low duodenal pH

339. A 42-year-old obese woman 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 gall-bladder contraction in the digestive period?

a. Acid-induced release of motilin from the small intestine
b. Acid-induced release of secretin from the small intestine
c. Amino acid-induced release of motilin from the small intestine
d. Distension-induced release of glucagon from the small intestine
e. Fat-induced release of cholecystokinin from the small intestine

340. A 20-year-old woman with type 1 diabetes mellitus presents with symptomatic hyperglycemia. The patient is started on 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

341. A 31-year-old man presents to the emergency department with the symptoms of heartburn and difficulty swallowing. Esophageal manometry reveals an inflamed esophageal mucosa and a hypotensive LES. A diagnosis of GERD is made and the patient is subsequently treated with a proton pump inhibitor. Normally, which of the following is most likely regarding reflux of gastric acid into the esophagus?

a. It inhibits esophageal bicarbonate secretion.
b. It inhibits gastric acid secretion.
c. It inhibits gastric motility.
d. It initiates primary esophageal peristalsis.
e. It initiates secondary esophageal peristalsis.

342. A 56-year-old man presents with postprandial diarrhea persisting since an ileal resection. The gastric surgeon suspects bile acid malabsorption. Which of the following best describes bile acid function?

a. They are essentially water insoluble.
b. The majority of bile acids are 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.

343. A 26-year-old man 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 acid pool size
b. Increased bile salt reabsorption
c. Increased colonic microbiota
d. Increased chylomicron formation
e. Increased lipase secretion

344. A 14-year-old ballerina reports that she has chronic diarrhea. A detailed history reveals that she frequently drinks skim milk, she does not use laxatives, and she has noticed that her condition improves when she fasts for religious observances. In contrast to secretory diarrhea, which of the following is most likely seen with osmotic diarrhea?

a. It is caused by bacterial toxins.
b. It is characterized by an increase in the stool osmotic gap.
c. It is the result of decreased electroneutral sodium absorption.
d. It is the result of increased crypt cell secretion.
e. It occurs only in the colon.

345. 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. Colon
b. Duodenum
c. Ileum
d. Jejunum
e. Stomach

346. A 42-year-old man presents to the emergency room with epigastric abdominal pain associated with nausea and vomiting. The history reveals that he was binge drinking that evening. He is diagnosed with acute pancreatitis. Which of the following best describes pancreatic function in this patient?

a. Pancreatic lipase converts triglycerides into fatty acids and glycerol.
b. Phospholipase A_2 may be prematurely activated by trypsin.
c. Secretin inhibits HCO_3^- secretion from the pancreas.
d. Serum amylase would be decreased in this patient.
e. Serum lipase would be decreased in this patient.

347. A 47-year-old woman with hypermenorrhea develops an iron-deficiency anemia requiring iron supplements. Which of the following best describes 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 into enterocytes by a ferroportin transporter on the apical membrane.
d. Iron is transported in the blood bound to transferrin.
e. Iron is oxidized from the ferrous to the ferric state during absorption.

348. A patient with alcoholic cirrhosis presents to the emergency room with hematemesis. After stabilizing him with IV fluids, the gastroenterolo-gist administers an analog of which of the following agents to inhibit gastric acid secretion and visceral blood flow?

a. Acetylcholine
b. Gastrin
c. Histamine
d. Pepsin
e. Somatostatin

349. A patient has vomiting and severe watery diarrhea after eating spoiled shellfish. IV 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. Electrolyte absorption in the small intestine is primarily electrogenic.
b. Osmotic equilibration of chyme occurs in the ileum.
c. The majority of water and electrolyte absorption occurs in the jejunum.
d. The small intestine and colon have similar absorptive capacities.
e. The toxin produced by *V. cholerae* decreases cyclic AMP in intestinal epithelial cells.

350. A 38-year-old man has dinner one evening at his favorite steakhouse. Several hours later, the chyme reaches the duodenum. After secretion of trypsinogen into the duodenum, the enzyme is converted into its active form, trypsin, by which of the following?

a. Alkaline pH
b. Chymotrypsin
c. Enteropeptidase
d. Pancreatic lipase
e. Procarboxypeptidase

351. An 18-year-old woman 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 laboratory values would most likely be found in a patient with infectious hepatitis?

a. A decrease in both direct and indirect plasma bilirubin
b. A decrease in plasma alkaline phosphatase
c. An increase in both direct and indirect plasma bilirubin
d. An increase in plasma alkaline phosphatase
e. An increase in plasma bile acids

352. A 27-year-old female patient with a history of IBS presents with a chief complaint of flatulence. Gas within the colon is primarily derived from which of the following sources?

a. Air pockets in diverticula
b. CO_2 liberated by the interaction of HCO_3^- and H^+
c. Diffusion from the blood
d. Fermentation of undigested oligosaccharides
e. Swallowed atmospheric air

353. A 60-year-old woman presents to her family physician with complaints of paresthesias in her lower legs bilaterally. On physical examination she is found to have a shiny tongue. During the workup, a complete blood count reveals a macrocytic anemia with hypersegmented neutrophils on peripheral smear. She is subsequently diagnosed with pernicious anemia. With respect to cobalamin-intrinsic factor binding in a normal individual, nearly all binding of cobalamin to intrinsic factor occurs in which of the following organs?

a. Stomach
b. Duodenum
c. Jejunum
d. Ileum
e. Colon

354. A 29-year-old internal medicine resident has a breakfast buffet after a long night of call. The rate of gastric emptying increases with an increase in which of the following?

a. Acidity of duodenum
b. Fat content of duodenum

c. Intraduodenal volume
d. Intragastric volume
e. Osmolality of duodenum

355. 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. Cholecystokinin
b. Gastrin
c. Glucagon-like polypeptide 1 (GLP-1)
d. Serotonin
e. VIP

356. A 53-year-old man 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 the symptoms in this patient?

a. Decreased esophageal motility
b. Decreased LES tone
c. Decreased upper esophageal sphincter tone
d. Delayed gastric emptying
e. Hiatal hernia

357. 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 normal bowel movements in newborns?

a. Defecation reflex
b. Gastrocolic reflex
c. Gastroileal reflex
d. Intestinointestinal reflex
e. Peristaltic rushes

358. 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. Gluten-free diet
c. High-fiber diet
d. Lactose-free diet
e. Low-salt diet

359. A 47-year-old woman presents to her primary care physician with jaundice. She is found to have elevated levels of direct (conjugated) plasma bilirubin. Which of the following is the most likely diagnosis?

a. Crigler–Najjar syndrome type I
b. Crigler–Najjar syndrome type II
c. Gilbert syndrome
d. Hemolytic anemia
e. Obstruction of the common bile duct

360. A morbidly obese man presents with hypertension, hyperlipidemia, and type 2 diabetes mellitus. Dietary fat, after being processed, is extruded from the mucosal cells of the GI tract into the lymphatic ducts in the form of which of the following?

a. Chylomicrons
b. Free fatty acids
c. Diglycerides
d. Monoglycerides
e. Triglycerides

361. After a long workout, a third-year medical student drinks a bottle of an electrolyte-containing sports drink. Which of the following is the major mechanism for absorption of sodium from the small intestine?

a. Cotransport with HCO_3^-
b. Electrogenic transport
c. Na^+–K^+ exchange
d. Neutral NaCl absorption
e. Solvent drag

362. A 42-year-old healthy man takes a daily multivitamin to complement his diet. Which of the following is required for absorption of the fat-soluble vitamins contained in his supplement?

a. Chymotrypsin
b. Intrinsic factor
c. Pancreatic amylase
d. Pancreatic lipase
e. Secretin

363. Following gastric bypass surgery, a patient presents with crampy abdominal discomfort 15 to 30 minutes after meals, accompanied by nausea, diarrhea, belching, tachycardia, palpitations, diaphoresis, and light-headedness. These symptoms most likely arise from which of the following?

a. Decreased emptying of hyperosmotic gastric contents
b. Decreased insulin release
c. Hyperglycemia
d. Increased secretion of cholecystokinin
e. Release of VIP and motilin

364. A 61-year-old woman presents with diarrhea, abdominal pain, and flushing. Urinary excretion of the serotonin metabolite, 5-hydroxyindoleacetic acid, 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. A decrease in the fat content of the feces
c. An increase in the absorption of iron
d. An increase in the concentration of bile acid in the enterohepatic circulation
e. An increase in the water content of the feces

365. Twenty years ago, a 65-year-old man underwent vagotomy for his refractory peptic ulcer disease. As a result, which of the following GI motor activities will be affected most?

a. Distention-induced intestinal segmentation
b. Migrating motor complexes
c. Orad stomach accommodation
d. Secondary esophageal peristalsis

366. A 33-year-old woman who has been taking large doses of NSAIDs for her menstrual cramps presents with burning epigastric pain that is worse after eating. Which of the following is the major factor that protects the duodenal mucosa from damage by gastric acid?

a. Bicarbonate contained in bile
b. Duodenal bicarbonate secretion
c. Endogenous mucosal barrier of the duodenum
d. Hepatic bicarbonate secretion
e. Pancreatic bicarbonate secretion

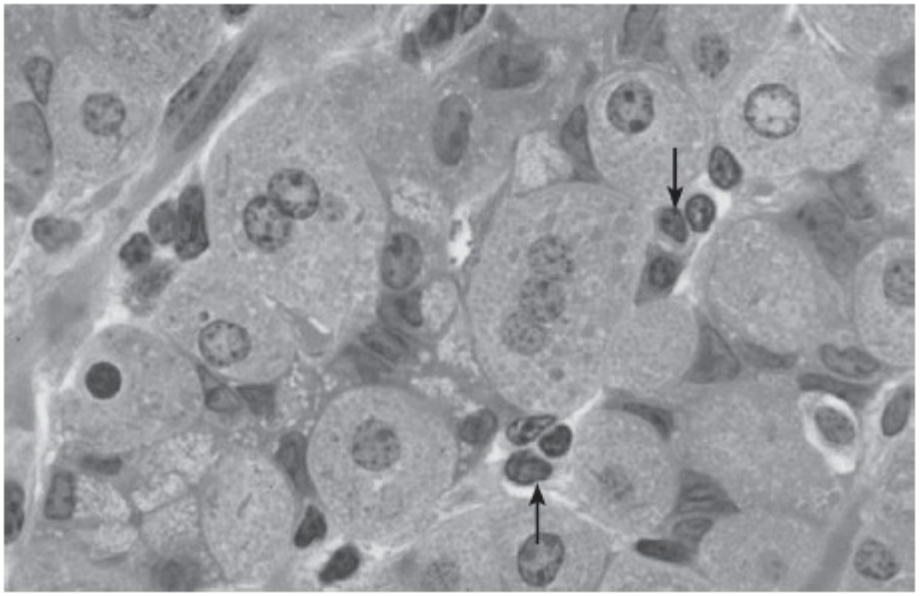
367. Gastric emptying studies performed on a 49-year-old woman who has vomiting shortly after eating reveal a normal rate of liquid emptying, but a prolonged time for emptying of solids. Which of the following best explains these findings?

a. Colonic obstruction
b. Increased amplitude of antral contractions
c. Inflammation of the proximal small intestine
d. Pyloric stenosis
e. Sectioning of the vagus nerves to the stomach

368. A full-term newborn infant with abdominal distention has not had a bowel movement for 5 days. An x-ray of the abdomen shows a narrowed colon, bowel obstruction, and dilated intestine above the obstruction. A suction rectal biopsy is done at the bedside. The pathology report indicates the absence of ganglion cells and the presence of nonmyelinated nerves in the biopsy segment. What is the underlying cause of the bowel obstruction in this patient?

a. Activation of intestinal opioid receptors
b. Carcinoid tumor
c. Impaired endothelin B receptor function
d. Impaired gastrocolic reflex
e. Increased activity of splanchnic sympathetic nerves

369. In the light microscopic slide shown below obtained from a biopsy of the stomach, which of the following is secreted by the cell type identified by the arrows?



http://www.vetmed.vt.edu/education/curriculum/vm8304/lab_companion/histo-path/vm8054/labs/Lab18/EXAMPLES/Exfuncel.htm

a. Gastrin
b. Hydrochloric acid
c. Intrinsic factor
d. Mucus
e. Pepsinogen

Gastrointestinal Physiology

Answers

310. The answer is e. (*Barrett, pp 500-501. Le, p 324. Longo et al., pp 297-300, 304-307, 2428. Toy, http://www.accessmedicine.com/casecontent.aspx?aid=510003309&tabid=1.*) Unlike the rest of the esophagus, the muscle of the gastroesophageal junction (LES) is tonically active (contracted) at rest and relaxes on swallowing. In contrast to the proximal esophagus, which consists of striated muscle directly innervated by lower motor neurons of the vagus nerve, the distal esophagus and LES are composed of smooth muscle and are controlled by excitatory and inhibitory neurons within the esophageal myenteric plexus. The inhibitory ganglionic neurotransmitters causing relaxation are vasoactive intestinal peptide and nitric oxide. Contraction is produced by neurotransmitters of the excitatory ganglionic neurons, namely, acetylcholine and substance P. The tonic activity of the LES is associated with a high pressure that limits reflux of gastric contents into the esophageal body. Intrinsic (myogenic) properties of the circular smooth muscle of the LES contribute to the resting tone. The normal esophageal manometry findings, along with the finding that the chest and epigastric pain do not respond to PPI, suggest that etiologies other than GERD should be considered. Cardiac disease would be the most concerning, and should be ruled out first.

311. The answer is b. (*Barrett, pp 502-503. Le, p 324. Longo, pp 301-307, 2985. Widmaier, pp 536-538.*) Gastroparesis is delayed emptying of food from the stomach, and is a common cause of 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 a. (*Barrett, pp 497-500, 504-505. Le, p 329. Longo, pp 308-309, 2496-2501. Widmaier, pp 542-548.*) 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, is very intense peristaltic waves that may occur in intestinal obstruction. The basal electrical rhythm (BER) is the spontaneous rhythmic fluctuation in membrane potential in the smooth muscle along the GI tract. The BER itself rarely causes muscle contraction; contractions occur only 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 approximately 12 BER cycles per minute in the duodenum and proximal jejunum and 8 cycles per minute in the distal ileum. During fasting between periods of digestion, cycles of motor activity, called migrating motor complexes (MMCs), 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. (*Barrett, pp 458, 485, 492-494. Le, pp 93, 320, 322, 354, 429. Longo, pp 862-871.*) Most vitamins are absorbed in the upper small intestine, but active absorption of vitamin B_{12} (cobalamin) occurs primarily in the terminal ileum. Vitamin B_{12} binds with intrinsic factor, a glycoprotein secreted by the parietal cells of the gastric mucosa. The vitamin B_{12}-intrinsic factor complex is propelled along the small intestine to the terminal ileum, where specific active transporters located on the enterocyte microvilli bind the vitamin B_{12}-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, leading to lack of intrinsic factor. Other causes of vitamin B_{12} deficiency include malabsorption (sprue, enteritis, *Diphyllobrothium latum*), removal of the intrinsic factor-secreting tissue (gastrectomy, gastric bypass surgery), or by diseases/absence of the terminal ileum (Crohn's disease). Binding of the vitamin B_{12}-intrinsic factor complex requires Ca^{2+}. Although vitamin B_{12} and folate absorption is Na^+ independent, all seven of the other water-soluble vitamins are absorbed by carriers that are Na^+ cotransporters. A second mechanism for cobalamin absorption is passive, occurring equally through buccal, duodenal, and ileal mucosa; this process is rapid but extremely inefficient, with <1% of an oral dose being absorbed by this process.

314. The answer is a. (*Kaufman, pp 142-144. Le, p 168. Longo, pp 308-312, 1084-1090.*) 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.

315. The answer is a. (*Barrett, pp 466-468. Longo, pp 351-355, 363-369.*) Excessive loss of fluid from the GI tract can lead to dehydration and electrolyte and acid–base disturbances that depend on the origin of the fluid loss. Because the pancreas, liver, ileum, and colon secrete bicarbonate, excessive loss of fluids from these organs leads to metabolic acidosis. Generally, plasma K^+ increases in metabolic acidosis due to H^+–K^+ exchange, but because the colon secretes potassium, the acidosis from excess fluid loss from the colon is accompanied by hypokalemia. Intestinal loss of K^+ due to diarrhea is globally important in light of the worldwide prevalence of infectious diarrheal disease. Noninfectious GI processes such as celiac disease, ileostomy, and chronic laxative abuse can also lead to significant hypokalemic, metabolic acidosis, as can colonic pseudo-obstruction (Ogilvie syndrome), which is associated with a secretory diarrhea with abnormally high potassium content caused by marked activation of colonic K secretion. Loss of gastric juice results in hypokalemic, metabolic alkalosis. The hydrogen ion and potassium ion concentration of gastric juice exceeds that of the plasma. As a result, excess gastric fluid loss leads to metabolic alkalosis accompanied by hypokalemia.

316. The answer is d. (*Barrett, pp 457-461, 468-469. Kaufman, pp 114-117. Le, pp 319-321, 327, 341, 333, 373. Longo, pp 111, 2438-2454.*) Alkalinization 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 cells in the GI 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, PPI, and vagotomy all reduce acid secretion. ZES has a triad of peptic ulcer disease, gastric acid hypersecretion, and an elevated gastrin level. In ZES, a pancreatic acinar cell adenoma (gastrinoma) is the site for the synthesis and secretion of large amount 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 neoplasia type I (MEN I). PPIs (omeprazole,

lansoprazole) are the treatment of choice for peptic ulcer disease in ZE, and have decreased the need for total gastrectomy.

317. The answer is a. (*Barrett, pp 502-504. Le, pp 325, 327, 577, 580. Longo, p 2402. Widmaier, pp 533-538, 542-543.*) Increases in intragastric volume normally are not associated with large increases in intragastric pressure because of receptive relaxation, also known as the accommodation reflex, which is vagally mediated. 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.

318. The answer is e. (*Barrett, pp 455-507. Longo, pp 308-309, 603, 775-776, 845, 2402. Widmaier, pp 538-539, 541-543.*) 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, and 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. Removal of these reflexes decreases pancreatic secretion and gallbladder emptying and increases gastric emptying and acid output.

319. The answer is b. (*Barrett, pp 502-504. Longo, pp 2452-2453. Widmaier, pp 536-538.*) 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.

320. The answer is d. (*Barrett, p 472. Le, pp 176, 180, 242. Widmaier, pp 314, 543.*) Motilin is the GI 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.

321. The answer is b. (*Barrett, pp 377-378, 485. Le, p 352. Longo, pp 2438-2454.*) 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 (eg, hypergastrinemia) or reduced inhibitory feedback (ie, 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 and the microcytic anemia is the result of reduced stores of iron.

322. The answer is d. (*Barrett, pp 465-466, 479, 484-485.*) 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 (*choice d*). 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 (not decrease, *choice b*). Essentially all glucose is absorbed across the wall of the small intestine before the remains of a meal reach the terminal ileum (*choice a*). Iron is primarily absorbed in the duodenum (*choice e*). The majority of the bile acid pool circulates between the small intestine and the liver; most bile acids are absorbed in their conjugated forms from the terminal ileum, so removal of the terminal ileum would decrease, not increase (*choice c*), bile acid concentration in the enterohepatic circulation.

323. The answer is d. (*Barrett, pp 478-485. Le, p 322.*) 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 (*choice d*). Lipase is secreted as an active enzyme but full activity of lipase requires the protein cofactor colipase, as well as an alkaline pH, bile salts, and fatty acids. Colipase (*choice c*) is secreted in an inactive proform and is activated in the intestinal lumen by trypsin (*choice e*), which, along with chymotrypsin (*choice b*), is endopeptidase involved in protein digestion. Amylase (*choice a*) is involved in the digestion of carbohydrates.

324. The answer is b. (*Barrett, pp 477-481. Le, pp 320, 322.*) Starch digestion begins in the mouth via α-amylase. Salivary and pancreatic α-amylases hydrolyze 1:4α linkages but spare 1:6α and terminal 1:4α linkages (opposite of *choice b*), such that the end products of α-amylase digestion are the disaccharides maltose and α-limit dextrins that require further digestion. The parotid gland is the most serous (not mucinous, *choice e*) of the salivary glands and cranial nerve VII (*choice c*), not VIII, runs through the parotid (though it does not innervate the gland). Approximately 1.5 L of saliva is secreted per day, not 4 L (*choice a*).

325. The answer is c. (*Barrett, pp 434-435. Le, p 322.*) The transport protein responsible for the sodium-dependent glucose transport in the small intestine is termed the SGLT 1 (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 SGLT 1 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 SGLT 1 and SGLT 2. Glut-5 is the membrane transporter located on the apical portion of the enterocyte responsible for the facilitated entry of fructose into the cell.

326. The answer is a. (*Farrokhi and Vaezi, pp 38-45. Kaufman, pp 110-114. Le, p 324.*) Achalasia is a neurogenic disorder of esophageal motility with the absence of normal peristalsis and impaired relaxation of the LES in response to deglutition. The barium esophagogram demonstrates a dilated esophagus with a sharply tapered "birds beak" narrowing of the terminal esophagus. Esophageal manometry shows normal to increased pressure in the LES with no relaxation in response to swallowing. The etiology is unknown, but achalasia is thought to arise from scarring (nerve damage) in Auerbach plexus. An association with viral infections and autoantibodies against myenteric plexus has been reported, but the causal relationship remains unclear. Endoscopy should be done to rule out malignancy as a cause of

the achalasia. Treatment is strictly palliative with excellent palliation available in over 90% of patients. Current pharmacological (nitroglycerin, endoscopic injection of botulinum toxin) and surgical (balloon dilation, myotomy) therapeutic options are aimed at reducing LES pressure and promoting esophageal emptying of retained food and liquids. Primary achalasia "is a rare disease with an annual incidence of approximately 1/100,000 and a prevalence rate of 10/100,000, but frequent enough to be encountered at least once by every gastroenterologist." (*Farrokhi and Vaezi, p 38*.) Diffuse esophageal spasm (*choice b*) is another esophageal motility disorder characterized by frequent nonperistaltic contractions. The barium esophagogram has a classic "corkscrew" pattern and esophageal manometry shows high amplitude in the esophagus, sometimes including the proximal esophagus. GERD may be caused by decreased esophageal motility and a relaxed or incompetent LES, but is not associated with aperistalsis. In GERD, acidic gastric contents enter the esophagus in contrast to neutral regurgitation in achalasia. Schatzki ring (*choice d*) is a narrow lower esophageal ring-like growth at the gastroesophageal junction associated with dysphagia to solids only. Zenker diverticulum (*choice e*) is a pharyngeal or esophageal pouch due to a defect in the muscular wall of the posterior hypopharynx. The outpouching of the esophagus can be seen on a barium swallow. The clinical signs and symptoms include sensation of food getting "stuck on the way down," regurgitation/vomiting of food days after it was eaten, frequent aspiration, and halitosis.

327. The answer is b. (*Barrett, pp 457-461. Kaufman, pp 114-117. Le, pp 319-320, 327. Longo, pp 2438-2457, 3057-3065*.) 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. The 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, vasoactive intestinal peptide, secretin, and cholecystokinin inhibit gastric acid secretion.

328. The answer is a. (*Barrett, pp 466-468. Le, p 332*.) Both the absorption of Na^+ and the 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 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^-.

329. The answer is d. (*Barrett, pp 516-517. Kaufman, pp 122-123. Le, p 339*.) 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.

330. The answer is e. (*Le, p 327. Longo, pp 2438-2454*.) 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 enterogastrones to gastric emptying and gastric acid secretion. Absent inhibitory input, basal and maximal acid outputs are increased, and gastric emptying of liquids and solids is increased. Bicarbonate secretion is significantly decreased in the duodenal bulb of patients with an active duodenal ulcer compared to control subjects.

331. The answer is c. (*Barrett, pp 482-483, 491. Kaufman, pp 144-145. Le, p 326*.) Gluten-sensitivity enteropathy, also known as celiac sprue, is characterized by an autoimmune-induced decrease in the absorptive surface area of the small intestine in response to gluten and other proteins in grain foods. Findings include antibodies to gliadin and tissue transglutaminase (serum levels used for screening). 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.

332. The answer is a. (*Barrett, pp 493-496. Le, pp 327, 340-342. Longo, pp 244-245*.) Histamine (H_2) receptor antagonists inhibit both gastrin-induced and vagal-mediated secretion of acid. Secretion of acid by gastric parietal 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.

333. The answer is a. (*Barrett, pp 465-466, 479, 484-485. Kaufman, pp 134-136. Le, p 328. Longo, pp 2477-2494*.) 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.

334. The answer is e. (*Kaufman, pp 113-117. Le, pp 340-341. Longo, pp 306-307, 2447-2456*.) Esomeprazole and other substituted benzimidazole derivatives are known as proton pump inhibitors (PPIs), which covalently bind and irreversibly inhibit H^+/K^+-ATPase. These agents are lipophilic compounds, which, upon entry into the parietal cells of the stomach, are protonated and trapped within the acid environment of the tubulovesicular and canalicular system. The most potent acid inhibiting agents available, PPIs inhibit all phases of gastric acid secretion. Onset of action is rapid, with a maximal acid inhibitory effect between 2 and 6 hours. Basal and secretagogue-stimulated acid production is inhibited >95% after 1 week of therapy. The half-life of PPIs is approximately 18 hours. PPIs are used for the treatment of all gastric acid–related conditions, such as peptic ulcer disease, gastritis, esophageal reflux, and Zollinger-Ellison syndrome. They are used in conjunction with various antibiotics as treatment for the eradication of *H. pylori*. Mild to moderate hypergastrinemia has been observed in patients taking these drugs. Omeprazole and lansoprazole are the PPIs that have been used the longest. Esomeprazole, the S-enantiomer of omeprazole, is the newest member of this class.

335. The answer is a. (*Barrett, pp 465-466, 479, 484-485. Longo, pp 2477-2494*.) 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 steatorrhea. 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. Iron, folate, carbohydrate, and protein absorption occur primarily in the upper portions of the small intestine.

336. The answer is e. (*Kaufman, pp 114-118. Le, p 341. Longo, pp 2447-2451.*) Misoprostol is used in the prevention of NSAID-induced gastric ulcers by maintaining the gastric mucosal barrier, which can become compromised with prostaglandin inhibitors such as NSAIDs. Misoprostol enhances bicarbonate secretion into the gastric mucous gel. Diarrhea is the most common side effect of misoprostol. Misoprostol is effective in the prophylaxis of NSAID-related mucosal injury. Other prophylactic agents include PPIs and selective COX-2 inhibitors. Only PPIs can heal active gastric or duodenal ulcers, independent of whether NSAIDs are discontinued.

337. The answer is b. (*Barrett, pp 478-480. Longo, pp 305-306, 313, 316, 2465. Widmaier, p 547.*) 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.

338. The answer is e. (*Barrett, pp 483-485.*) 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.

339. The answer is e. (*Barrett, p 516. Le, p 319. Longo, pp 2461-2462. Widmaier, p 530.*) The delivery of food into the small intestine is characterized by prompt emptying of the gallbladder, resulting from fat-induced release of cholecystokinin. Secretin (*choice b*) stimulates pancreatic bicarbonate secretion. Glucagon (*choice d*) is involved in nutrient metabolism and motilin (*choice a* and *choice c*) is an interdigestive hormone responsible for migrating motor complex activity.

340. The answer is b. (*Barrett, p 440. Le, pp 288, 303, 305.*) 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.

341. The answer is e. (*Barrett, pp 500-501. Kaufman, pp 113-114. Le, p 324. Longo, pp 304-307, 2427-2428, 2433-2435. Widmaier, p 532.*) 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. In GERD, esophageal motility is decreased, not gastric motility, though gastric emptying is delayed.

342. The answer is d. (*Barrett, pp 464-465. Longo, pp 2460-2465.*) 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 in the liver from cholesterol. Secondary bile acids, deoxycholic acid and lithocholic acid, are produced by biotransformation of primary bile acids in the intestine by colonic bacterial enzymes. Prior to secretion into the duodenum in bile, 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. The majority of bile acid is absorbed via a Na–K-ATPase in the terminal ileum.

343. The answer is a. (*Barrett, pp 483-484. Le, pp 90, 326. Longo, pp 313-317, 2460-2475.*) 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, decreased intestinal absorptive surface area (such as occurs in celiac sprue), or inability to form chylomicrons (such as in abetalipoproteinemia). 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.

344. The answer is b. (*Kaufman, pp 142-144. Longo, pp 312-317, 2460-2461.*) 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 ($290 - 2[Na^+ + K^+]$) 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. In contrast to osmotic diarrhea, secretory diarrhea has a normal stool osmotic gap and is not remedied with fasting. The other major pathophysiologic mechanisms of chronic diarrhea include steatorrheal, inflammatory, infectious, dysmotile, radiation injury, and factitial causes.

345. The answer is a. (*Barrett, p 485. Longo, pp 317, 2465.*) The colon is the major site for the generation and absorption of SCFAs. 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.

346. The answer is b. (*Barrett, pp 461-464. Kaufman, pp 118-121. Le, pp 115, 326, 334, 339-340, 472, 580. Longo, pp 2637-2639.*) Phospholipase A_2 cleaves a fatty acid off phosphatidylcholine (PC) to form lyso-PC, which damages cell membranes. Premature activation of phospholipase A_2 by trypsin is hypothesized to cause acute pancreatitis. In pancreatitis, pancreatic digestive enzymes leak into the circulation and thus serum amylase and lipase would be expected to be increased; the elevations are greater in acute pancreatitis than in chronic pancreatitis. Gallstones are the most common cause of pancreatitis. Alcohol, drugs, hypertriglyceridemia, and endoscopic retrograde cholangiopancreatography are other common causes. Pancreatic lipase converts triglycerides to monoglycerides and free fatty acids; gastric lipase converts triglycerides to fatty acids and glycerol. Secretin stimulates bicarbonate secretion from the pancreas.

347. The answer is d. (*Barrett, pp 485-486. Widmaier, p 528.*) 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.

348. The answer is e. (*Barrett, p 472. Kaufman, p 127. Le, pp 306, 341. Longo, pp 320-321. Widmaier, pp 533-534.*) 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. The analog octreotide (Sandostatin®, Novartis Pharmaceuticals, Basil, Switzerland), however, can be administered subcutaneously to inhibit the secretion of gastrin and gastric acid and decrease 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 cells). Gastrin secretion is stimulated by the amino acids and peptides produced by pepsin's action in protein digestion.

349. The answer is d. (*Barrett, pp 62, 466-468. Kaufman, pp 1242-1243. Le, pp 124, 136, 168. Longo, pp 1289-1293.*) Most water and electrolyte absorption occurs in the jejunum, with the duodenum serving primarily as the site of osmotic equilibration of chyme. In the period between meals, sodium and chloride are absorbed together from the lumen by the coupled activity of a sodium/hydrogen exchanger and a chloride/bicarbonate exchanger in the apical membrane in an electroneutral mechanism. In contrast to the small intestine, the colon has a limited capacity to absorb water and most water absorption in the colon occurs in the proximal colon. The toxin produced by *V. cholerae* increases cyclic AMP in intestinal epithelial cells.

350. The answer is c. (*Barrett, pp 461-464. Widmaier, pp 538-539.*) 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 chymotrypsinogen and other proenzymes into their active forms.

351. The answer is c. (*Barrett, pp 513-514. Kaufman, pp 128-131, 221, 379. Longo, pp 2537-2557.*) 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.

352. The answer is d. (*Barrett, p 502. Longo, pp 2496-2497. Widmaier, pp 543-544.*) Gas within the colon is derived primarily from fermentation of undigested material by intestinal bacteria to produce CO_2, H_2, 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 N_2 present in intestinal gas and is influenced by the atmospheric pressure. While many patients with IBS complain of increased flatus, most produce no more than that seen in normal individuals.

353. The answer is b. (*Barrett, p 485. Kaufman, pp 150-151. Le, pp 320, 322. Longo, p e37-1.*) Intrinsic factor is secreted by the parietal cells of the gastric mucosa. Cobalamin, also known as vitamin B_{12}, is provided almost entirely from animal products in the human diet. Gastric digestion of food liberates cobalamin where, at low pH, it binds primarily to R-binder protein, derived primarily from salivary secretions. In the duodenum, pancreatic proteases release cobalamin from the R-binder protein where cobalamin then rapidly complexes (binds) with intrinsic factor and is transported along the gut to the terminal ileum, where it is absorbed via specific receptors located on the villus tip cells that bind the cobalamin-intrinsic factor complex. In this patient, the neurologic symptoms, glossitis, and findings on the peripheral smear are characteristic of cobalamin deficiency.

354. The answer is d. (*Barrett, pp 502-503. Widmaier, pp 536-538.*) 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.

355. The answer is c. (*Barrett, pp 442-446. Widmaier, pp 314, 529, 563.*) 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.

356. The answer is b. (*Barrett, pp 500-501. Kaufman, pp 113-114. Le, p 324. Longo, pp 304-307, 2427-2428, 2433-2435. Widmaier, p 532.*) 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 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 composed of smooth muscle at the junction of the esophagus and the stomach.

357. The answer is b. (*Barrett, pp 506-507. Widmaier, p 543.*) 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. The defecation reflex (*choice a*) refers to the sudden distention of the walls of the rectum produced by mass movement of fecal material into the rectum. The gastroileal reflex (*choice c*) refers to the relaxation of the cecum and passage of chyme through the ileocecal valve when food leaves the stomach. The intestinointestinal reflex (*choice d*) 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. Peristaltic rushes (*choice e*) are very intense peristaltic waves that may occur with intestinal obstruction.

358. The answer is b. (*Barrett, p 491. Kaufman, pp 144-145. Le, p 326. Longo, pp 2467-2471, 2693, 2676. Widmaier, p 527.*) 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 enter-opathy. 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.

359. The answer is e. (*Barrett, pp 513-514. Le, p 336.*) 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. All other choices are found in conditions with an increase in the indirect (unconjugated) form of bilirubin.

360. The answer is a. (*Barrett, pp 29-31, 483-485. Le, pp 115-116, 326. Widmaier, pp 524-527.*) Long-chain fatty acids are extruded from enterocytes in the form of chylomicrons into the lymphatic system. Chylomicrons represent triglycerides and esters of cholesterol that have been invested in the intestinal mucosa with a coating of phospholipid, protein, and cholesterol. 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. Triglycerides are hydrolyzed to monoglycerides and taken into mucosal cells.

361. The answer is d. (*Barrett, p 62, 466-468.*) Absorption of sodium is the primary absorptive event in the small intestine. Absorption of Na^+ is necessary for absorption of water and other electrolytes. Although multiple pathways exist for the absorption of Na^+, neutral absorption is the major mechanism. Neutral absorption may occur in two ways: Na^+ cotransported with Cl^- and in exchange for H^+ ions.

362. The answer is d. (*Barrett, p 485. Widmaier, p 527.*) Absorption of the fat-soluble vitamins (A, D, E, 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.

363. The answer is e. (*Barrett, pp 502-503. Longo, pp 2453-2454.*) The dumping syndrome consists of a series of GI and vasomotor signs and symptoms and occurs in patients in whom part of the stomach has been removed, in whom the jejunum has been anastomosed to the stomach, or those who have undergone vagotomy and drainage (especially Bill-roth procedures). Two phases of dumping, early and late, can occur. Early dumping occurs within 15 to 30 minutes after meals, and is characterized by crampy abdominal discomfort, diarrhea, belching, tachycardia, palpitations, diaphoresis, light-headedness, and rarely syncope. These symptoms arise from rapid emptying of a hyperosmotic meal into the small intestine, which promotes the movement of an abundance of water into the gut, producing significant hypovolemia and hypotension. Release of vasoactive GI hormones (VIP, motilin, neurotensin) is also theorized to play a role in early dumping. The late phase of dumping typically occurs 90 min to 3 hours after eating. Vasomotor symptoms, including light-headedness, sweating, palpitations, tachycardia, and syncope, predominate in this phase. The late phase of dumping is attributed to hypoglycemia secondary to excessive insulin release. Dietary modification is the cornerstone of treatment.

364. The answer is e. (*Barrett, pp 483-485. Le, pp 90, 326. Longo, pp 313-317, 2460-2475.*) 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, hind-gut). Small intestinal (midgut) carcinoid tumors arise from the argentaffin 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 (cutaneous flushing, diarrhea, bronchospasm, right heart valvular lesions), which is manifested when they metastasize, but only occurs in 5% to 10% of carcinoid tumors.

365. The answer is c. (*Barrett, pp 479-482, 494-495. Widmaier, pp 540-541, 548-550.*) Orad stomach accommodation (receptive relaxation) depends exclusively on an intact vago-vagal reflex. Vagal innervation of the GI 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 GI 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.

366. The answer is a. (*Kaufman, pp 114-117. Le, pp 327-328. Longo, pp 2444-2447, 2450-2451. Widmaier, pp 544-545.*) Epigastric pain that worsens after eating a meal suggests a duodenal versus gastric ulcer. Normally, 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.

367. The answer is d. (*Barrett, pp 502-504. Longo, pp 301-304. Widmaier, pp 535-538.*) 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.

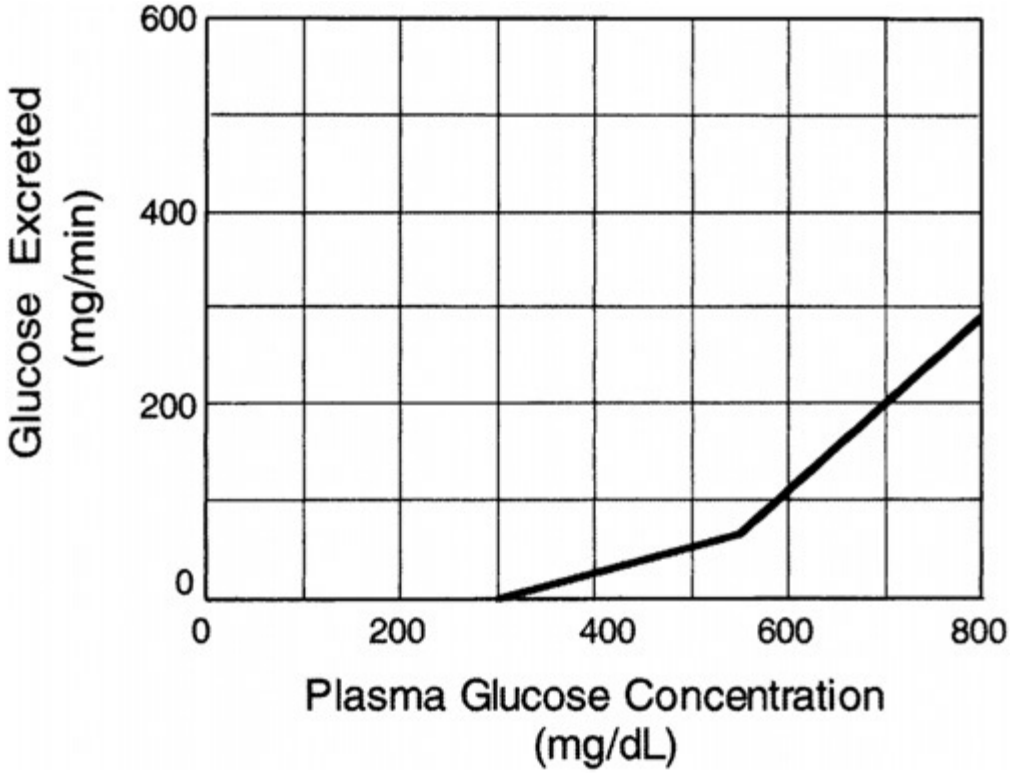
368. The answer is c. (*Barrett, pp 504-507.*) Hirschsprung disease or aganglionic megacolon is an inherited disorder of abnormal colonic motility due to a congenital absence of the ganglion cells in both the myenteric and submucous plexuses of a segment of the distal colon, as a result of failure of the normal cranial-to-caudal migration of neural crest cells during development. The action of endothelins on the endothelin B receptor is necessary for normal migration of certain neural crest cells. Megacolon develops in knockout mice lacking endothelin B receptors. In addition, one cause of congenital aganglionic megacolon in humans appears to be a mutation in the endothelin B receptor gene. The disease is typically diagnosed in infancy, and affects as many as 1 in 5000 live births. The absence of peristalsis in patients with this disorder causes feces to pass the aganglionic region with difficulty, and children with the disease may defecate as infrequently as once every 3 weeks. Findings also include abdominal distention, anorexia, and lassitude. The symptoms of Hirschsprung disease can be relieved completely if the aganglionic portion of the colon is

resected and the portion of the colon above it anastomosed to the rectum. If an extensive segment is involved, patients may require a colectomy.

369. The answer is e. (*Widmaier, p 533*.) The cells identified are chief cells, which secrete pepsinogen. The large, round, multinucleated cells are parietal cells, which secrete hydrochloric acid and intrinsic factor. Other cells found in the stomach include mucous cells, which secrete mucus, and enteroendocrine cells, which secrete gastrin.

Questions

370. A 65-year-old man with uncontrolled type 2 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

371. A 16-year-old girl presents for her annual high school athletic physical. She states that she seems more tired than usual, she has been having muscle cramps in her calves, and her legs get very weak and sore after running and playing soccer. Her blood pressure is 160/100 mm Hg, and her ECG shows a prolonged QT interval and the presence of a U wave. Blood analysis shows hypokalemia, metabolic alkalosis, and decreases in plasma renin activity and aldosterone concentration. Her clinical condition is reversed after she is placed on the diuretic amiloride. Based on this finding, which of the following renal transport processes is the major defect causing her metabolic disorder?

a. Greater than normal sodium reabsorption by the proximal tubules
b. Greater than normal sodium reabsorption by the cortical collecting ducts
c. Inability of the distal nephron to secrete hydrogen
d. Inability of the distal nephron to secrete potassium ion
e. Inability to concentrate urine

372. 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 (BUN) 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:

Urine flow rate = 1 mL/min
Urine [uric acid] = 36 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

373. A 69-year-old man 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 (ACE) 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 prerenal origin associated with increased renin secretion by the kidney. A stimulus for increasing renal renin secretion is an increase in which of the following?

a. Angiotensin II
b. Atrial natriuretic peptide (ANP)
c. GFR
d. Mean blood pressure
e. Sympathetic nerve activity

374. A patient with uncontrolled hypertension is placed on a new diuretic targeted to act on 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. Facilitated diffusion
b. Na^+/H^+ exchange
c. Na^+–glucose cotransport
d. Na^+–K^+ pump
e. Solvent drag

375. A 28-year-old woman presents to her physician's office with fatigue, malaise, and orthostatic dizziness. When asked what medications she is taking, she stated that she has been taking 800 mg ibuprofen four to six times a day for painful menstrual cramps. Serum creatinine was elevated to 2.1 mg/dL. Which of the following is most likely to produce an increase in GFR in patients with acute renal failure?

a. Administration of angiotensin II
b. Contraction of glomerular mesangial cells
c. Dilation of afferent arterioles
d. Increased renin release from the juxtaglomerular apparatus
e. Volume depletion

376. 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 = 5L
Total glucose = 375 g
Total creatinine = 2.4 g

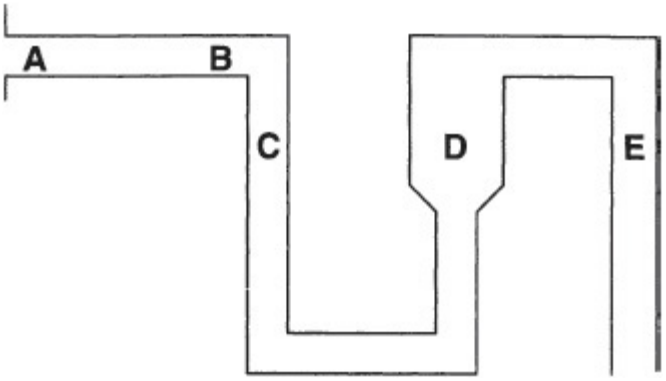
The patient's GFR is approximately which of the following?

a. 75 mL/min
b. 100 mL/min
c. 125 mL/min
d. 200 mL/min
e. 275 mL/min

377. An 83-year-old woman with a history of hypertension presents to her family physician's office with oliguria. Serum creatinine and BUN are elevated and a computed tomography (CT) reveals that the patient's left kidney is hypoplastic. Renal function studies are performed to assess the renal handling of various substances. Substance X is injected into an arterial line. All of substance X appears in the urine and none is detected in the renal vein. What do these findings indicate about the renal handling of substance X?

a. It must be filtered by the kidney.
b. It must be reabsorbed by the kidney.
c. Its clearance is equal to the GFR.
d. Its clearance is equal to the renal plasma flow (RPF).
e. Its urinary concentration must be higher than its plasma concentration.

378. A 60-year-old woman presents to her gynecologist with progressive fatigue, weakness, and diffuse bony pain. She has been postmenopausal for 5 years, and her medical history is notable for hypertension and recurrent kidney stones. Physical examination is insignificant except for a slight dorsal kyphosis. A bone scan confirms osteoporosis. Serum calcium and parathyroid hormone (PTH) are increased and serum phosphate is decreased. PTH increases Ca^{2+} reabsorption at which of the points along the nephron pictured below?



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

379. 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 her filtration fraction?

a. 0.05
b. 0.15
c. 0.25
d. 0.35
e. 0.45

380. 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

381. 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). In patients with the syndrome of inappropriate antidiuretic hormone (SIADH), which of the following will increase?

a. Intracellular volume
b. Plasma oncotic pressure
c. Plasma osmolarity
d. Plasma sodium concentration
e. Urine flow

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 RPF?

Renal artery *p*-aminohippuric acid (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. A 46-year-old man presents to his physician with a 12-week history of frontal headaches. 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 hypertonic urine
b. A higher-than-normal flow of hypotonic urine
c. A lower-than-normal flow of hypertonic urine
d. A lower-than-normal flow of hypotonic urine
e. A normal flow of hypertonic urine

384. 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 = 1 L/day
Plasma sodium = 125 mmol/L
Plasma potassium = 4 mmol/L
Urine osmolality = 385 mOsm/L
Urine sodium = 125 mmol/L
Urine potassium = 25 mmol/L

Which of the following is the 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

385. A 28-year-old woman with systemic lupus erythematosus is brought to the emergency department after developing hypokalemic paralysis. Arterial blood gas analysis shows a Pa O_2 of 102 mm Hg and a pH of 7.1. She is diagnosed with type I renal tubular acidosis (RTA) 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. Anion gap
b. Aldosterone secretion
c. Net acid excretion
d. Serum bicarbonate
e. Urine ammonium

386. 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. Decreased GFR
b. Decreased secretion of urea by the distal tubules
c. Increased reabsorption of urea by the proximal tubules
d. Increased renal blood flow (RBF)
e. Increased synthesis of urea by the liver

387. A 52-year-old man presents to his internist for a 6-month checkup following diuretic therapy and recommended diet changes for his essential hypertension. His blood pressure is 145/95 mm Hg and serum aldosterone levels are increased. Aldosterone secretion is increased when there is a decrease in the plasma concentration of which of the following?

a. Adrenocorticotropic hormone (ACTH)
b. Angiotensin II
c. Potassium
d. Renin
e. Sodium

388. A 76-year-old man presents at the emergency department with headache, vomiting, shortness of breath, insomnia, and confusion. He is found to be oliguric with an increased BUN and creatinine. Urine-specific gravity is low and there is proteinuria. Which of the following statements concerning the normal renal handling of proteins is correct?

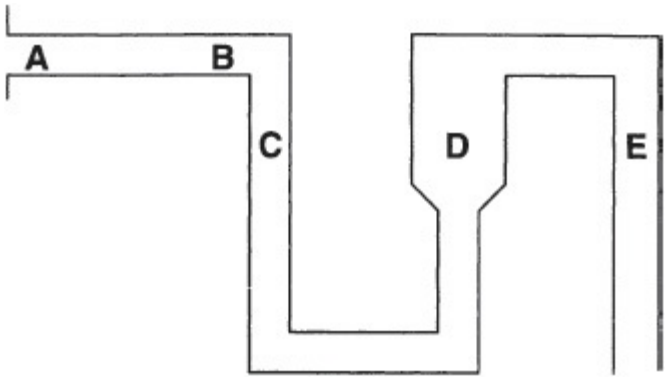
a. Proteins are more likely to be filtered if they are negatively charged than if they are uncharged.
b. Proteins can be filtered and secreted but not reabsorbed by the kidney.

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.

389. A 92-year-old man presents with dehydration following 4 days of persistent diarrhea. Under this circumstance, hypotonic fluid would be expected in which of the following?

a. Glomerular filtrate
b. Proximal tubule
c. Ascending limb of the loop of Henle
d. Cortical collecting tubule
e. Distal collecting duct

390. A 10-year-old boy is brought to the emergency department with a brief history of severe, excruciating left flank pain, nausea, vomiting, and hematuria. The patient has had one similar episode in the past that brought him to the emergency department a few months ago. The boy also has a family history of recurrent kidney stones. Urinalysis showed hematuria and microscopic evaluation of the urinary sediment showed hexagonal crystals. An abdominal radiograph of the patient demonstrated the appearance of a faintly, opaque, ground glass stone in the left ureter. The patient's reoccurring clinical presentation is likely due to a defect in amino acid reabsorption in the kidney. What part of the kidney is responsible for the majority of amino acid reabsorption?



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

391. An 18-year-old man 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 best describes the action or secretion of renin?

a. It converts angiotensin I to angiotensin II.
b. It converts angiotensinogen to angiotensin I.
c. It is secreted by cells of the proximal tubule.
d. Its secretion is stimulated by increased mean renal arterial pressure.
e. Its secretion leads to loss of sodium and water from plasma.

392. A patient with multiple myeloma develops type II RTA with a defect in proximal tubular bicarbonate reabsorption. Which of the following structural features distinguishes the epithelial cells of the proximal tubule from those of the distal convoluted tubule?

a. The distal tubule has a thicker basement membrane.
b. The distal tubule has fewer tight intercellular junctions.
c. The distal tubule has more microvilli.
d. The proximal tubule forms the juxtaglomerular apparatus.
e. The proximal tubule has a more extensive brush border.

393. A 63-year-old hospitalized woman becomes oliguric and confused. A blood sample is drawn to measure her glucose concentration, which is found to be 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 areas of the nephron?

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

394. A 56-year-old man with hypertension presents with complaints of flushing and orthostatic hypertension. Blood analysis reveals an increased plasma renin activity and hyperlipidemia. Urinalysis reveals a decreased GFR and an increase in urinary albumin excretion. Gadolinium-enhanced three-dimensional magnetic resonance angiography is suggestive of renal artery stenosis. Measurement of RBF and a renal arteriogram are ordered to evaluate the patient for atherosclerotic renal vascular disease (ARVD = renal artery stenosis and ischemic nephropathy). The effective RPF, determined from the clearance of PAH, is less than the true RPF because of which of the following?

a. The calculated clearance of PAH depends on the urinary flow rate.
b. The cortical and medullary collecting ducts are able to reabsorb some PAH.
c. The fraction of PAH filtered is less than the filtration fraction.
d. The measured value of the plasma PAH concentration is less than the actual PAH concentration.
e. The plasma entering the renal vein contains a small amount of PAH.

395. A 64-year-old elementary school teacher complains of a strong sense of urinary urgency followed by incontinence of large amounts of urine as she tries to rush to the bathroom. She also states that she has had urinary frequency as well as nocturia over the last week. Her past medical history is insignificant, but she was recently diagnosed with a urinary tract infection last week. The patient is diagnosed with an overactive bladder with urinary incontinence. She is treated with behavioral training and oxybutynin. What neurotransmitter is responsible for initiating bladder (detrusor) contraction?

a. Acetylcholine
b. Epinephrine
c. GABA
d. Norepinephrine
e. Serotonin

396. A 14-year-old girl with polycystic kidney disease has a decrease in both GFR and RBF. The nephrologist wants to administer a drug that will increase both GFR and RBF. Both GFR and RBF would increase if which of the following occurred?

a. The efferent and afferent arterioles are both constricted.
b. The efferent and afferent arterioles are both dilated.
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.

397. A 47-year-old woman presents for her annual physical examination. A year ago, the patient started a diet and exercise regimen when her blood pressure was 130/85 mm Hg. She has lost 10 lb and reduced her BMI to 25 kg/m^2, but her blood pressure on this visit is found to be 145/98 mm Hg. The patient is started on a combination of a low dose of hydrochlorothiazide with the K^+-sparing diuretic, triamterene. The amount of potassium excreted by the kidney will decrease if which of the following occurs?

a. Circulating aldosterone levels increase.
b. Dietary intake of potassium increases.
c. Distal tubular flow increases.
d. Na^+ reabsorption by the distal nephron decreases.
e. The excretion of organic ions decreases.

398. A 23-year-old woman presents with burning epigastric pain. A careful history reveals that the burning is exacerbated by fasting and improved with meals. The woman is prescribed the H_2-receptor antagonist, cimeti-dine, for suspected peptic ulcer disease. Cimetidine may also have an adverse effect on proximal tubular function. Which of the following substances is more concentrated at the end of the proximal tubule than at the beginning of the proximal tubule?

a. Bicarbonate
b. Creatinine
c. Glucose
d. Phosphate
e. Sodium

399. A 69-year-old man with chronic hypertension presents to his physician's office. His blood pressure is 165/105 mm Hg despite treatment with a diuretic, β-blocker, and an angiotensin receptor antagonist. It is decided that a fourth drug is needed for the patient's resistant hypertension, and he is prescribed the vasodilator diltiazem, a calcium channel antagonist. The effect of decreasing the resistance of the afferent arteriole in the glomerulus of the kidney is to decrease which of the following aspects of renal function?

a. Filtration fraction
b. Glomerular filtration rate
c. Oncotic pressure of the peritubular capillary blood
d. Renal plasma flow
e. Renin release from juxtaglomerular cells

400. A 17-year-old male presents with fatigue, muscle cramps, and joint pain. Blood analysis reveals hypokalemia, hypomagnesemia, and hypochloremic metabolic alkalosis, and urinalysis reveals decreased urinary chloride and calcium. The clinical findings suggest a loss-of-function mutation of the SLC12A3 gene encoding the

thiazide-sensitive sodium–chloride cotransporter (NCCT). Electrically neutral active transport of sodium and chloride occurs in which of the following areas of the nephron?

a. Cortical collecting duct
b. Descending limb of the loop of Henle
c. Distal tubule
d. Medullary collecting duct
e. Thin ascending limb of the loop of Henle

401. A 36-year-old African American man presents with low renin essential hypertension. Renin release from the juxtaglomerular apparatus is normally inhibited by which of the following?

a. Aldosterone
b. β-Adrenergic agonists
c. Increased pressure within the afferent arterioles
d. Prostaglandins
e. Stimulation of the macula densa

402. A 44-year-old woman presents with abdominal pain, fever, and chills. Physical examination reveals costovertebral angle tenderness, previously undiagnosed hypertension, and a mid-systolic click. Urine culture shows bacteriuria and free water clearance is positive, indicating excretion of dilute urine. The ability of the kidney to excrete concentrated urine will increase if which of the following occurs?

a. The activity of the Na^+–K^+ pump in the loop of Henle increases.
b. The flow of filtrate through the loop of Henle increases.
c. The glomerular capillary pressure increases.
d. The permeability of the collecting duct to water decreases.
e. The reabsorption of Na^+ by the proximal tubule decreases.

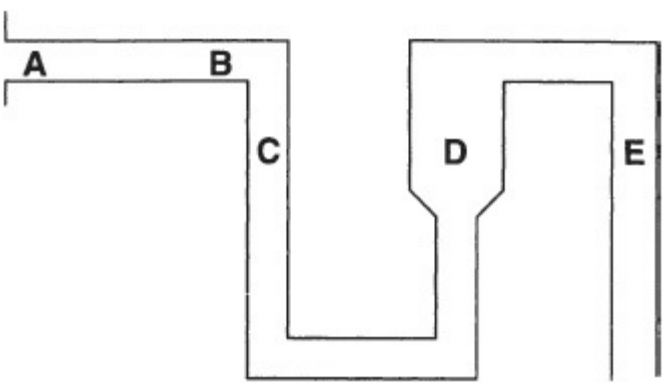
403. A patient undergoing surgery develops an increase in the secretion of ACTH, cortisol, and aldosterone. Which of the following statements best characterizes the actions of aldosterone in the kidney?

a. It increases hydrogen ion reabsorption from the distal convoluted tubules.
b. It increases potassium ion reabsorption from the distal convoluted tubules.
c. It increases sodium ion reabsorption in the proximal tubule.
d. It increases the number of active epithelial sodium channels (ENaCs) in the collecting ducts.
e. It produces its effect by activating cyclic adenosine monophosphate (cAMP).

404. A 44-year-old African American woman with a medical history of hypertension and diabetes mellitus presents to the clinic for her routine examination. At her last visit, her blood pressure was 150/95 despite trying to control her blood pressure with diet and exercise, so the patient was placed on lisinopril. She also takes metformin for her diabetes. Today, the patient's blood pressure has decreased to 130/80. Routine laboratory work indicates that she has a blood glucose of 120 mg/dL, serum creatinine of 1.0 mg/dL, and urinary microalbumin of <30 mg. What effect does angiotensin II have on the glomerular filtration rate (GFR)?

a. Decreases GFR because of constriction of the afferent arteriole
b. Decreases GFR because of dilation of the efferent arteriole
c. No change in GFR because of equal constriction of the afferent and efferent arteriole
d. Increases GFR because of dilation of the afferent arteriole
e. Increases GFR because of constriction of the efferent arteriole

405. A 27-year-old man with bipolar disorder presents to his psychiatrist complaining that since he started his lithium treatment 6 months ago, he is frequently thirsty and gets up three or four times each night to urinate. Head–neck examination reveals slightly dry mucous membranes. Urinalysis reveals polyuria with a dilute urine. Serum ADH is normal. A diagnosis of lithium-induced nephrogenic diabetes insipidus is suspected. In the absence of ADH or when the kidney lacks responsiveness to ADH, the luminal Na^+ concentration will be lowest at which of the points along the nephron shown schematically in the diagram below?



a. A

b. B
c. C
d. D
e. E

406. 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 collecting ducts to water

407. A 16-year-old pregnant girl is admitted to the hospital in labor. Her blood pressure is 130/85 mm Hg, and her plasma creatinine is 2.7 mg/dL (normal 0.6 to 1.2 mg/dL). Renal ultrasonography demonstrates severe bilateral hydronephrosis. Which of the following is the most likely cause of this patient's high creatinine levels?

a. Coarctation of the renal artery
b. Hypovolemia
c. Hyperproteinemia
d. Increased sympathetic nerve activity
e. Ureteral obstruction

408. 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 ibuprofen (Motrin) for pain. Laboratory data reveal the following: BUN, 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%

409. A patient with chronic obstructive lung disease and cor pulmonale is given acetazolamide to inhibit carbonic anhydrase, along with a thiazide diuretic. How does the distal nephron differ functionally from the proximal tubule?

a. The distal nephron has a more negative intraluminal potential than the proximal tubule.
b. The distal nephron is less responsive to aldosterone than the proximal tubule.
c. The distal nephron is more permeable to hydrogen ion than the proximal tubule.
d. The distal nephron secretes more hydrogen ion than the proximal tubule does.
e. The distal nephron secretes less potassium than the proximal tubule does.

410. An 82-year-old man who recently suffered head trauma from a car accident presents with polyuria and polydipsia. Blood analysis reveals hypernatremia and urinalysis shows hypotonicity and an increased free water clearance. In which of the following conditions is an increased free water clearance a hallmark of the disease?

a. Diabetes insipidus
b. Diabetes mellitus
c. Diuretic therapy
d. Heart failure
e. Renal failure

411. A 58-year-old man is hospitalized following an acute myocardial infarction. Several days later, the patient's 24-hour urine output is lower than normal. An increase in which of the following contributes to a reduced urine flow in a patient with congestive heart failure and reduced effective circulating volume?

a. ANP
b. Renal natriuretic peptide (urodilatin)
c. Renal perfusion pressure
d. Renal sympathetic nerve activity
e. Sodium delivery to the macula densa

412. A 58-year-old man 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 GFR would result from which of the following?

a. A decrease in the concentration of plasma protein
b. An increase in afferent arteriolar pressure
c. An increase in RBF

d. Compression of the renal capsule
e. Constriction of the efferent arteriole

413. A patient has suffered from persistent diarrhea lasting for 7 days. Which of the following would be decreased in this patient?

a. Anion gap
b. Filtered load of HCO_3^-
c. H^+ secretion by the distal nephron
d. Production of ammonia by the proximal tubule
e. Production of new bicarbonate by the distal nephron

414. A 27-year-old graduate student from China presents at the Student Medical Center for mandatory tuberculosis screening. Quantiferon testing is positive and physical examination reveals cough, cachexia, and mild respiratory distress. Chest x-ray reveals a cavitary lesion in the right upper lobe. Blood analysis reveals a serum sodium of 118 mg/dL and an increased ADH concentration. As a result, the permeability of the collecting duct will be increased to which of the following?

a. Ammonium ion
b. Hydrogen ion
c. Potassium ion
d. Sodium ion
e. Urea

415. A 54-year-old woman presents with profound fatigue, ankle edema, and paroxysmal nocturnal dyspnea. Filtration fraction may be increased in patients with heart failure due to an increase in which of the following?

a. Afferent arteriolar resistance
b. Efferent arteriolar resistance
c. Hydrostatic pressure within Bowman capsule
d. Plasma oncotic pressure
e. Renal blood flow

416. A 29-year-old man expresses concern about his upcoming skiing trip to Breckenridge, Colorado (elevation = 10,000 ft). He states that every time he goes there, he gets high altitude sickness that is relieved when he is given oxygen. The family physician gives the patient a prescription for oxygen to use when he arrives in Colorado, as well as a prescription for acetazolamide to take for 2 days prior and throughout his 4-day trip. Carbonic anhydrase inhibitors exert their diuretic effect by inhibiting the reabsorption of Na^+ in which of the following parts of the nephron?

a. The proximal tubule
b. The thick ascending limb of loop of Henle
c. The distal convoluted tubule
d. The cortical collecting duct
e. The outer medullary collecting duct

417. 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 RBF to decrease?

a. Acetylcholine
b. Angiotensin II
c. ANP
d. Dopamine
e. Nitric oxide

418. A 19-year-old man presents for his annual football physical examination. He is asymptomatic but urinalysis reveals macroscopic hematuria. Microscopic examination is positive for deformed erythrocytes and RBC casts. Where in the renal–urinary system is the most likely origin of the blood in his urine?

a. Bowman capsule
b. Glomerulus
c. Peritubular capillaries
d. Renal artery
e. Urinary bladder

419. A 55-year-old hypertensive patient is placed on a potassium-sparing diuretic. Which of the following mechanisms of action are characteristic of potassium-sparing diuretics?

a. Inhibition of H^+ secretion in the proximal tubule
b. Inhibition of Na–Cl cotransport in the early portion of the distal tubule
c. Inhibition of Na–K–2Cl cotransport in the medullary thick ascending limb of loop of Henle
d. Inhibition of Na^+ reabsorption via Na channels in the collecting tubules

e. Inhibition of vasopressin secretion

For Questions 420 and 421, refer to the following case.

A 39-year-old woman with chronic kidney disease secondary to a longstanding history of type I diabetes mellitus and hypertension presents to the nephrologist for follow-up of her hypertension. The patient was recently started on amiloride. Her review of systems is positive for muscle weakness and some chest pain during the last 2 weeks. Her blood pressure is 155/92 mm Hg and an ECG reveals tall, peaked T waves. Blood results show a pH of 7.25, Na^+ 140, Cl^- 120, HCO_3^- 18, K^+ 6.0, and decreased aldosterone and plasma renin activity. Urinary ammonium (NH_4^+) excretion is decreased.

420. Which of the following statements best describes renal ammonia (NH_3)?

a. NH_3 is classified as a titratable acid.
b. NH_3 excretion reduces the concentration of bicarbonate in the plasma.
c. Renal NH_3 synthesis is decreased in hyperkalemia.
d. The majority of NH_3 is produced by epithelial cells in the distal nephron.
e. The tubular epithelial cells are impermeable to NH_3.

421. In type IV RTA, the excretion of which of the following urinary electrolytes is increased?

a. Cl^-
b. H^+
c. K^+
d. Na^+
e. NH_4^+

422. A patient with renal failure presents to the clinic with increasing fatigue for the past month. Based on a thorough history and physical, as well as diagnostic testing, it is determined that the symptoms are caused by the loss of a hormone produced by the kidney. Which of the following is the most likely diagnosis?

a. Acidosis
b. Anemia
c. Edema
d. Hypertension
e. Uremia

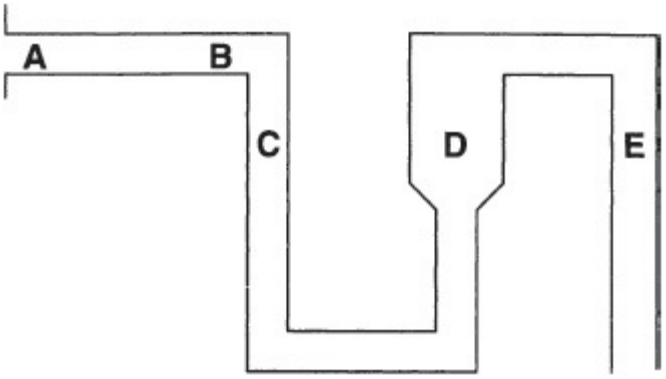
423. A patient with congestive heart failure presents with jugular venous distention, ascites, and peripheral edema. Blood work shows elevated levels of plasma ANP. ANP increases Na^+ excretion by which of the following mechanisms?

a. Contracting afferent arterioles
b. Decreasing GFR
c. Decreasing sodium reabsorption by the inner medullary collecting duct
d. Increasing permeability of the apical membrane of the collecting duct epithelial cells
e. Increasing sodium reabsorption by the proximal tubules

424. 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. Adenosine
b. Aldosterone
c. Angiotensinogen
d. Antidiuretic hormone (ADH)
e. Renin

425. A 42-year-old man presents with fatigue, loss of stamina, and frequent urination. He is not taking any medications currently. Physical examination is normal except for a blood pressure of 165/95 mm Hg. Serum electrolytes show sodium, 152 mEq/L; potassium, 3.1 mEq/L; chloride, 112 mEq/L; and bicarbonate, 32 mEq/L. Aldosterone concentration is elevated and plasma renin activity is low, consistent with primary hyperaldosteronism. Aldosterone increases Na^+ reabsorption at which of the point depicted in this schematic diagram of the nephron?



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

426. A 39-year-old man presents with severe writhing back pain, hematuria, and nausea. An intravenous pyelogram 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. Angiotensin
c. Norepinephrine
d. Parathyroid hormone (PTH)
e. Vasopressin

427. A 41-year-old woman presents with hemoptysis and hematuria. Laboratory findings include markedly elevated BUN, creatinine, and erythrocyte sedimentation rate. Serum is positive for antiproteinase-3 ANCA, and negative for antiglomerular basement membrane antibody, suggesting Wegener granulomatosis rather than Goodpasture disease. Urinalysis reveals proteinuria and RBC casts, in addition to the hematuria. Progressive renal failure makes it difficult for the patient to excrete a normal dietary potassium load. Which of the following will produce the greatest increase in potassium secretion?

a. A decrease in circulating blood volume
b. A decrease in renal blood flow
c. A decrease in urine flow rate
d. An increase in distal nephron sodium concentration
e. An increase in sympathetic nerve activity

428. A 36-year-old man suffers third-degree burns over 70% of his body while responding to a three-alarm fire. His effective circulating volume and renal perfusion pressure drop precipitously and the concentration of NaCl in the intraluminal fluid in the kidney decreases. These conditions cause the juxtaglomerular apparatus to release which of the following hormones?

a. Adenosine
b. Aldosterone
c. Angiotensinogen
d. ADH
e. Renin

429. Renal and pulmonary biopsies in a 35-year-old woman with Wegener's granulomatosis demonstrate glomerulonephritis and a granulomatous vasculitis in the lungs. In adults, which of the following is greater in the pulmonary circulation compared to the renal circulation?

a. Arterial pressure
b. Blood flow
c. Capillary hydrostatic pressure
d. Capillary oncotic pressure
e. Vascular resistance

430. A 65-year-old man presents in the emergency department with a fracture of his right arm after slipping and falling on the ice. He reports that he has had back pain for the past 6 months. Blood results show Hb = 9 g/dL; hematocrit = 30%; BUN = 35 mg/dL; creatinine = 3 mg/dL. Urinalysis shows pH >5.3 and is positive for Bence Jones proteins. The patient is diagnosed with type II (proximal) RTA secondary to multiple myeloma. The transport of H^+ into the proximal tubule is primarily associated with which of the following?

a. Excretion of ammonium ion
b. Excretion of potassium ion
c. Reabsorption of bicarbonate ion

d. Reabsorption of calcium ion
e. Reabsorption of phosphate ion

431. A 57-year-old woman with chronic cardiac failure presented at the University Medical Center to participate in a clinical research study on the genetics of heart failure. Genetic analysis showed an increase in ADH gene expression and associated hypothalamic biosynthesis of the hormone, in addition to increased release of the hormone from the posterior pituitary. In the presence of ADH, the filtrate will be isotonic to plasma in which part of the kidney?

a. Ascending limb of the loop of Henle
b. Descending limb of the loop of Henle
c. Cortical collecting tubule
d. Medullary collecting tubule
e. Renal pelvis

432. A hypertensive patient develops chronic renal failure from progressive nephrosclerosis. Which of the following is associated with chronic renal failure?

a. A decrease in the excretion of creatinine
b. A decrease in the fractional excretion of sodium
c. A decrease in net acid excretion
d. An increase in free water clearance
e. A normal anion gap

433. A 65-year-old male with a past medical history of COPD, hypertension, diabetes mellitus type II, and hypercholesterolemia presents to the emergency department with swelling of the legs and feet and shortness of breath. After complete history, physical exam, and appropriate diagnostic testing, it is determined that the patient is experiencing volume overload as a result of an acute exacerbation of congestive heart failure. The patient is started on oxygen therapy, nebulizer treatments, and intravenous furosemide, which increases sodium reabsorption in the thin ascending limb of the loop of Henle via which of the following mechanisms?

a. Na^+ Cl^- cotransport
b. Na^+/H^+ exchange
c. Na^+/K^+ exchange
d. $Na^+ - K^+ - 2Cl^-$ cotransport
e. Na^+/nutrient cotransport

434. A 28-year-old woman with blood pressures that have ranged from 155-190/70-100 during her last two visits to her family physician is started on lisinopril. When her blood pressure worsened on lisinopril, she was referred to a nephrologist for uncontrolled hypertension. Her blood pressure was 170/95 and a renal ultrasound showed a greater than 50% reduction in vessel diameter. Based on the laboratory data shown below, what is her estimated renal blood flow?

Serum inulin = 2 mg/dL
Urinary inulin = 10 mg/mL
Serum PAH = 6 mg/dL
Urinary PAH = 20 mg/mL
Urine flow = 1.2 mL/min
Hematocrit = 40%
Hemoglobin = 13

a. 400 mL/min
b. 600 mL/min
c. 667 mL/min
d. 1000 mL/min
e. 1250 mL/min

Answers

370. The answer is e. (*Barrett, pp 682-683. Widmaier, p 485.*) 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. The filtered load of a substance is calculated by multiplying the GFR by the plasma concentration of the substance. For example, in this patient, 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.

371. The answer is b. (*Barrett, pp 681-682, 690-691. Kaufman, p 266. McPhee and Hammer, pp 442-443. Widmaier, pp 503-504.*) The patient is treated with amiloride, a potassium sparing diuretic, which blocks sodium channels in the principal cells of the cortical collecting ducts thus limiting sodium reabsorption. Sodium reabsorption in the cortical collecting ducts is normally under the control of aldosterone. In patients with Liddle syndrome, the cortical collecting ducts reabsorb excess Na^+ despite low levels of aldosterone and renin in the plasma, because of a mutation in the genes for the renal ENaCs, which increases ENaC activity and sodium retention. Metabolic alkalosis, hypokalemia, and hypertension are also present secondary to the increased sodium (and water) reabsorption. An inability of the distal nephron to secrete hydrogen (*choice d*) would cause RTA type I. An inability to concentrate urine (*choice e*) occurs when patients are treated with loop diuretics like furosemide, which prevents the kidney from developing medullary hypertonicity, thus limiting the reabsorption of water and the production of concentrated urine. The amount of sodium reabsorbed in the proximal tubules is relatively constant (*choice a*) at roughly 60% of the filtered amount, primarily as a result of Na^+/H^+ exchange. The inability of the distal nephron to secrete potassium ion (*choice c*) would result in hyperkalemia, not hypokalemia as described in the case presentation.

372. The answer is e. (*Barrett, pp 677-679. Le, pp 480, 582. Longo, pp 2284, 3185, 3221. Widmaier, pp 486-487.*) Clearance is a measure of how much plasma is totally cleared of a substance. It is calculated using the following formula:

$$\text{Clearance} = U_x V/P_x,$$

where U = Urine concentration of substance x
V = Urine volume/time
P = Plasma concentration of substance x

Thus, the clearance of uric acid in this patient can be calculated as follows:

$$\text{Clearance} = U_{\text{uric acid}} \times V/P_{\text{uric acid}} = 36 \text{ mg/dL} \times 1 \text{ mL/min}/0.6 \text{ mg/dL}$$
$$= 60 \text{ mL/min}$$

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 anti-oxidant 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.

373. The answer is e. (*Barrett, pp 644, 705-706. Le, p 485. Widmaier, pp 497-499.*) Renin secretion is stimulated by the sympathetic nerves innervating the juxtaglomerular apparatus. Sympathetic nerve activity increases when baroreceptors sense low blood pressure. Increasing mean blood pressure (*choice d*) decreases sympathetic activity, thereby decreasing renin secretion. Angiotensin II (*choice a*) decreases renin release through a negative feedback loop by binding to AT1 receptors on the juxtaglomerular cells to increase intracellular Ca^{2+} concentration, which inhibits renin secretion. ANP (*choice b*) also decreases renin release. Increases in GFR (*choice c*) sensed by the macula densa lead to the secretion of a mediator, perhaps adenosine or ATP, which contracts the afferent arteriole (tubuloglomerular feedback) and decreases renin release. Decreases in GFR lead to an increase in renin release.

374. The answer is d. (*Barrett, pp 681-682. Le, p 483.*) Na^+ is pumped out of renal epithelial cells by the Na^+–K^+ pump located on the basolateral surface of the cells. The Na^+/H^+ exchanger and the Na^+–glucose cotrans-porter are located on the apical surface of the epithelial cells. Na^+ is transported from the peritubular spaces to the capillaries by solvent drag.

375. The answer is c. (*Barrett, p 679. McPhee and Hammer, pp 459-469.*) GFR is directly proportional to glomerular capillary hydrostatic pressure, RPF, and the surface area for diffusion between the glomerular capillary and Bowman space. Dilation of afferent arterioles causes an increase in glomerular capillary hydrostatic pressure and, therefore, an increase in GFR. Nonsteroidal anti-inflammatory drugs (NSAIDs) can induce acute renal failure in patients dependent on prostaglandin-mediated vasodilation of the afferent arteriole to maintain renal perfusion. Contraction of the mesangial cells (*choice b*) causes a decrease in the surface area for diffusion between the glomerular capillary and Bowman space. Administration of angiotensin II (*choice a*) generally causes a decrease in GFR due to renal vasoconstriction, which decreases RPF, perfusion pressure, and glomerular capillary hydrostatic pressure. In addition, angiotensin II contracts mesangial cells, particularly at higher concentrations. However, angiotensin II constricts efferent arterioles to a greater extent than the afferent arterioles, which offsets the decline in

glomerular capillary hydrostatic pressure and may maintain GFR. Angiotensin II also increases the sensitivity of tubuloglomerular feedback, which acts to prevent excessive rises in GFR. Volume depletion (*choice e*) causes increased renin release from the juxtaglomerular cells (*choice d*), leading to an increase in angiotensin II and thus a reduction in GFR.

376. The answer is d. (*Barrett, pp 678-680. Le, pp 480-481, 582. Widmaier, p 487.*) GFR is approximately equal to the clearance of creatinine. In this case,

$$\text{Creatinine clearance} = \text{creatine excreted/plasma creatinine concentration}$$
$$\text{Creatinine clearance} = 2.4 \text{ g/day}/0.8 \text{ mg/dL} = 300 \text{ L/day}$$
$$= 300{,}000 \text{ mL/day} = 300{,}000 \text{ mL}/24 \text{ h}$$
$$= 300{,}000 \text{ mL}/1440 \text{ min} = 208 \text{ mL/min}$$

377. The answer is d. (*Barrett, pp 676-677. Le, pp 480, 582. Widmaier, p 487.*) 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 which case the clearance of the substance equals RPF. The clearance would not equal the GFR (*choice c*) because the normal filtration fraction is 20%, which would not totally clear the plasma concentration of substance. None of the substance is reabsorbed (*choice b*) because none of the substance is detected in the renal vein. If the substance is bound to plasma proteins, it can be secreted without being filtered (*choice a*). 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 (*choice e*).

378. The answer is d. (*Barrett, pp 377-383. McPhee and Hammer, pp 443, 465-470, 476-480, 483-484. Widmaier, pp 503-504.*) Parathyroid hormone (PTH) acts in the kidney to stimulate Ca^{2+} reabsorption and to inhibit phosphate reabsorption. Although most of the filtered Ca^{2+} is reabsorbed in the proximal tubule, the regulation of Ca^{2+} excretion by PTH occurs in the medullary thick ascending limb and the distal convoluted tubule, where the action of PTH increases Ca^{2+} reabsorption. The major effect of PTH inhibits on phosphate handling is to promote its excretion by inhibition of sodium-dependent phosphate transport in the proximal and distal tubules. PTH also increases urinary excretion of bicarbonate through its action on the proximal tubule, which may produce proximal RTA. These physiological responses to PTH are the basis for hypophosphatemia and hyperchloremic acidosis commonly observed in patients with hyperparathyroidism. Primary hyperparathyroidism, in which there is excessive secretion of PTH in relation to serum calcium, accounts for most cases of hypercalcemia in the outpatient setting. The *PRAD1* gene, which produces the cell-cycle regulatory protein D1 cyclin, has been implicated in the pathogenesis of primary hyperparathyroidism.

379. The answer is c. (*Barrett, pp 680-681. Le, pp 481, 582.*) 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 percentage of the arterial concentration that is filtered (and, therefore, the fraction of plasma filtered) is

$$3 \text{ mg/mL}/12 \text{ mg/mL} = 0.25$$

Filtration fraction is normally 0.16 to 0.20. When there is a fall in systemic blood pressure, the GFR falls less than the RPF because of efferent arteriolar constriction, and thus the filtration fraction rises.

380. The answer is d. (*Barrett, pp 711-717. Widmaier, pp 508-511.*) Net acid excretion is the amount of acid excreted each day. It is calculated using the following formula:

$$\text{Net acid excretion (NAE)} = (\text{TA} + NH_4^+ - HCO_3^-) \times V$$
$$\text{NAE} = (24 \text{ mEq/L} + 38 \text{ mEq/L} - 2 \text{ mEq/L}) \times 1.2 \text{ L/day}$$
$$= 72 \text{ mEq/L/day}$$

Almost all of the acid excreted is buffered by either phosphate, called titratable acid, or 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. Ammonia is produced in renal cells from glutamine and may either (1) diffuse into the tubular lumen down its concentration gradient and combine with H^+ produced by cells from CO_2 and H_2O or (2) combine with H^+ within the renal cell and then secreted into the tubular fluid by the Na^+/NH_4^+ exchanger. 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.

381. The answer is a. (*Barrett, pp 697-700. Kaufman, pp 80, 182, 299. Le, pp 233, 301, 306, 576, 580.*) SIADH can occur as a paraneoplastic process in patients diagnosed with small cell lung cancer. The increased secretion of 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 (*choice d*), osmolarity (*choice c*), and oncotic pressure (*choice b*). The decreased extracellular osmolarity causes water to flow from the extracellular fluid compartment into the intracellular fluid compartment, increasing intracellular volume (*choice a*). Because more water is being reabsorbed, less is excreted and urine flow (*choice e*) is decreased.

382. The answer is c. (*Barrett, pp 676-677. Le, pp 480-481, 582.*) The clearance of PAH is a good estimate of RPF because, under normal circumstances, almost all (more than 90%) of the PAH passing through the kidney is excreted. This is due to the fact that PAH is both freely filtered and excreted by proximal tubule cells, but is not reabsorbed.

$$C_{PAH} = U_{PAH} \times \dot{V}/P_{PAH}$$
$$= (25 \text{ mg/mL} \times 1.5 \text{ mL/min})/6 \text{ mg}/100 \text{ mL}$$
$$= 625 \text{ mL/min}$$

If the clearance of PAH is 90% of the actual RPF, then the true RPF is approximately 695 mL/min.

383. The answer is b. (*Barrett, pp 697-700. Kaufman, pp 79-80. Le, pp 301, 306, 574. Longo, pp 340, 343, 350-351, 2904-2906. McPhee and Hammer, pp 536, 538, 540-542.*) The presence of a mass in the posterior pituitary, coupled with the presentation of thirst and nocturia, suggests that the patient has a central diabetes insipidus with inadequate pituitary secretion of ADH. As a result of decreased ADH, the urine will have a low tonicity. A patient with diabetes insipidus often presents with polyuria, polydipsia, and dehydration. Due to the inability to reabsorb water, the patient may also have serum hyperosmolarity due to hypernatremia. On MRI, the absence of the normal bright spot in the region of the posterior pituitary further supports the diagnosis.

384. The answer is a. (*Barrett, p 690.*) Free water clearance is the amount of water excreted in excess of that required to excrete urine that is isoosmotic to plasma. When the urine is concentrated, the value of C_{H_2O} is negative, indicating that solute-free water is retained in the body. In other words, the amount of water excreted is less than that required to excrete urine that is isoosmotic to plasma. When the urine is dilute, the value of C_{H_2O} is positive, indicating that solute-free water is excreted. Free water clearance is calculated using the following formula:

$$\text{Free water clearance } (C_{H_2O}) = \text{urine flow} - \text{osmolar clearance } (C_{osm})$$

where

$$C_{osm} = U_{osm} \times \text{urine flow}/P_{osm},$$

$$U_{osm} = 2(U_{Na^+} + U_{K^+}),$$

and

$$P_{osm} = 2 \times [Na^+]$$

The urine osmolarity is estimated from the concentration of effective osmoles, that is, sodium and potassium, because these electrolytes determine the shift of water between intracellular and extracellular compartments. The total measured osmolarity is not used because it includes urea, which has no effect on body fluid distribution. Similarly, effective plasma osmolarity is used in calculating free water clearance, rather than total plasma osmolarity.

$$\begin{aligned} C_{H_2O} &= \text{urine flow} - [2(U_{Na^+} + U_{K^+}) \times \text{urine flow}/P_{osm}] \\ &= 1 \text{ L/day} - [2(125 + 25 \text{ mOsm/kg } H_2O) \times 1 \text{ L/day}/2 \\ &\quad \times 125 \text{ mOsm/kg } H_2O] \\ &= 1 \text{ L/day} - 1.2 \text{ L/day} = -0.2 \text{ L/day} \end{aligned}$$

This patient has a negative free water clearance, and thus she is producing concentrated urine. This means that she is diluting her plasma despite her low serum sodium. The negative free water clearance is probably caused by the combination of diuretics and antidepressants, which stimulate the release of ADH. The serum hypotonicity (250 mOsm/L) causes brain swelling, accounting for her signs and symptoms.

385. The answer is a. (*Le, p 488. Kaufman, pp 240-241, 266.*) The rise in H^+ and fall in HCO_3^- that occurs in type I (distal) RTA does not increase the anion gap because the decrease in HCO_3^- is accompanied by an increase in Cl^-. (Remember, the anion gap is calculated by subtracting the sum of the chloride concentration and bicarbonate concentration from the concentration of sodium.) 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 HCO_3^- 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.

386. The answer is a. (*Barrett, p 693. Le, pp 486, 495. Longo, pp 97, 335, 2295, 2320, 2368.*) Urea is synthesized primarily in the liver. Its excretion is dependent on its concentration in plasma and the GFR. 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. Most of the secretion of urea into the tubules occurs in the proximal tubules, not in the distal tubules. Ingestion of large amounts of ibuprofen does not increase the synthesis of urea. In this scenario, RBF will be decreased due to renal artery vasoconstriction resulting from the inhibition of prostaglandin synthesis by ibuprofen.

387. The answer is e. (*Barrett, pp 53, 364, 371-375.*) 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 zona glomerulosa cells, which opens voltage-gated Ca^{2+} channels, increasing intracellular Ca^{2+}. ACTH stimulates aldosterone synthesis and secretion via increases in cAMP and protein kinase A. The stimulatory effect of ACTH on aldosterone secretion is usually transient, declining in 1 to 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.

388. The answer is e. (*Barrett, pp 685-679, 681, 692-693. Kaufman, p 265. McPhee and Hammer, pp 445, 451-452.*) Sympathetic stimulation causes renal vasoconstriction, which reduces GFR and thus the transit time of glomerular filtrate; this favors diffusion of proteins across the basement membrane and protein excretion. Approximately two-thirds of the 40 to 150 mg of protein excreted per day by the kidney is derived from plasma proteins; the remaining one-third is derived from the tubular secretion (*choice c*) of Tamm-Horsfall protein, a mucoprotein 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 (*choice a*) because the fenestrated capillary epithelium serves as a size barrier and the basement membrane consisting predominantly of negatively charged heparin sulfate serves as a charge barrier for negatively charged proteins (*choice a*). Most of the filtered protein is reabsorbed in the proximal tubule (*choice b*) 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. The presence of protein in the urine indicates glomerular dysfunction. Progressive elevation of BUN serum creatinine results in uremia, a clinical syndrome manifested by headache, vomiting, dyspnea, insomnia, and delirium progressing to convulsions and coma.

389. The answer is c. (*Barrett, pp 699, 701-702*.) When a person is dehydrated, the decrease in extracellular fluid volume is sensed by stretch receptors in the low pressure receptors in the great veins, right and left atria, and pulmonary vessels, leading to an increase in vasopressin (ADH) secretion from the posterior pituitary. The ascending limb of the loop of Henle is not affected by ADH and remains impermeable to water; thus, 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. In the presence of ADH, the cortical and medullary collecting tubules become permeable to water due to the insertion of aquaporin channels in the luminal membrane, and the filtrate within these portions of the nephron reaches osmotic equilibrium with the interstitial fluid surrounding them.

390. The answer is a. (*Barrett, pp 681-683*.) Like glucose reabsorption, amino acid reabsorption occurs primarily in the early portion of the proximal convoluted tubule. Proximal tubular amino acid reabsorption of amino acids resembles that in the intestine. The main carriers in the apical membrane cotransport Na^+, whereas the carriers in the basolateral membranes are not Na^+ dependent and the amino acids leave by passive or facilitated diffusion into the interstitial fluid. The proximal tubule is responsible for nearly 100% of the reabsorption of glucose, amino acids, and bicarbonate. Proximal tubular cells have a brush border that serves to significantly increase the surface area for reabsorption. Patients with a hereditary defect of renal tubular amino acid reabsorption, specifically cystine, ornithine, lysine, and arginine, develop cystinuria. Cystinuria is an autosomal recessive disorder which causes excess amounts of cystine in the urine, which can lead to the precipitation of cystine kidney stones. These kidney stones are often described as being "hexagonal" in shape on microscopic evaluation. Stone analysis will confirm the diagnosis, but the diagnosis should be suspected in patients with a strong family history of kidney stones and a young age of onset. Treatment includes high fluid intake and urinary alkalinization as the solubility of cystine is pH dependent, with a p K a of approximately 8.1.

391. The answer is b. (*Barrett, pp 372-373, 702-706*.) Renin 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. Renin is secreted by the juxtaglomerular cells (near the afferent arterioles) in response to sympathetic nervous system stimulation, decreased renal arterial pressure, and decreased salt delivery to the distal convoluted tubule. The aortic and carotid baroreceptors sense a decrease in arterial pressure, which triggers a signal in the renal sympathetic nerves that stimulates the granular cells to release renin. Activation of beta-1 adrenergic receptors on these cells stimulates renin secretion via a cAMP- and protein kinase A-dependent process. The juxtaglomerular cells serve as intrarenal baroreceptors that deform in response to changes in afferent arteriole blood pressure and are stimulate to release renin when arterial blood pressure falls. The amount of sodium chloride leaving the thick ascending limb and entering into the distal convoluted tubule can also stimulate the release of renin. The amount of sodium chloride in the tubule at this point is sensed by the macula densa cells of the juxtaglomerular apparatus. If there is an abundance of salt delivery to the cells of the macula densa, renin production decreases. It is thought that this is due to increased uptake of NaCl by the cells with subsequent osmotic swelling, which causes the release of transmitters that inhibit renin release. On the other hand, when salt delivery to the macula densa cells is decreased, renin secretion is increased.

392. The answer is e. (*Barrett, pp 673-674. Longo, pp 2280-2286, 2298*.) 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. The proximal tubule also has an extensive network of intracellular channels. Although a few microvilli are present in the distal convoluted tubule, there is no distinct brush border. 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.

393. The answer is a. (*Barrett, pp 682-683*.) Glucose is reabsorbed along with Na^+ in the early portion of the proximal tubule via a secondary active transport process. Normally, essentially all filtered glucose is reabsorbed. In diabetes mellitus, hyperglycemia results in a tubular filtration load that exceeds and glycosuria ensues. The renal threshold for glucose is the plasma level at which glucose first appears in the urine. The predicted renal threshold is approximately 300 mg/dL, that is, the transport maximum (T_{max}) for glucose of 375 mg/min divided by the GFR (normally ~125 mL/min). However, the actual renal threshold is only approximately 200 mg/dL because the $T_{\max}$ for glucose is not identical in all tubules.

394. The answer is e. (*Barrett, pp 676-677, 683-684. Longo, pp 1811-1812*.) The clearance of PAH would equal the true RPF only if the kidney reabsorbs all of the filtered PAH, that is, if no PAH appears in the renal vein. Because the kidney is able to reabsorb only approximately 85% to 90% of the filtered PAH, some PAH appears in the renal vein, and the PAH clearance is less than the true RPF. A number of clinical trials have focused on the rate of urinary albumin excretion as an early and powerful predictor of atherosclerotic vascular disease. Renal artery stenosis (RAS) accounts for approximately 5% of cases of hypertension. The most common cause of renal artery stenosis in the middle-aged and elderly is an atheromatous plaque at the origin of the renal artery. ARVD with renal artery stenosis and ischemic nephropathy stimulate renin release and increase sympathetic activity, resulting in the frequently described flushing, rapid blood pressure swings, and autonomic instability. The low GFR in these patients is a strong independent predictor of cardiovascular risk; in other words, patients with ARVD are more likely to suffer from stroke, myocar-dial infarction, or heart failure than to progress to end-stage renal disease. Gadolinium-enhanced 3D-MRA has replaced previous imaging modalities as the most sensitive and specific test for RAS. The most definitive diagnostic procedure is contrast-enhanced arteriography.

395. The answer is a. (*Barrett, pp 693-695. Widmaier, pp 487-488*.) The sacral parasympathetic pathways mediate contraction of the detrusor smooth muscle and relaxation of the outflow region, which causes micturition. The preganglionic parasympathetic neurons are located in the sacral parasympathetic nucleus in the spinal cord at the level of S2–S4. The axons pass through the pelvic nerves to synapse with postganglionic nerves near or within the walls of the bladder and urethra. The ganglionic neurotrans-mission is mediated by acetylcholine acting on nicotinic receptors. The postganglionic neurons mediate the excitatory input to the normal human detrusor by releasing acetylcholine, which acts on muscarinic receptors causing bladder contraction (*choice a*). The pelvic nerves also convey para-sympathetic fibers to the outflow region, which have an inhibitory effect on the smooth muscle sphincters that also aids in micturition through a nitric oxide–related pathway. The catecholamines, epinephrine (*choice b*) and norepinephrine (*choice d*), relax the detrusor muscle. Incontinence is the involuntary loss of urine, and is generally classified

as stress incontinence (due to sneezing, coughing, exercise), urge incontinence (associated with the desire to urinate), or mixed. This patient has urge incontinence. Anticholinergics, such as oxybutynin or tolterodine, along with behavioral modifications, such as timed voiding and double voiding, would be useful first-line treatment options of her urge incontinence. Any irritation to the bladder or urethra, for example, a bacterial infection, can cause urge incontinence. The internal urethral sphincter as the base or neck of the bladder is innervated by sympathetic neurons, which constrict the sphincter to prevent urination. GABA (*choice c*) inhibits the micturition reflex via its action as an inhibitory neurotransmitter in the CNS. Serotonin (*choice e*) has been shown to be involved in the control of micturition by inhibiting voiding at the level of the Raphe nucleus; serotonin has not been shown to be active at the level of the bladder.

396. The answer is b. (*Barrett, pp 677-681, 687, 702. Le, p 498. Widmaier, pp 482-484.*) The renal artery pressure and the resistance of the renal vascular bed determine renal blood flow (RBF). 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. GFR will increase if glomerular capillary pressure increases. This can occur if the afferent arteriolar resistance decreases or if the efferent arteriolar resistance increases.

397. The answer is d. (*Barrett, pp 691-692. Longo, pp 342-343, 351, 2054-2055.*) 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. Low-dose thiazide diuretics, such as hydrochlorothiazide, are often used as first-line antihypertensive agents, and are often combined with a potassium-sparing diuretic to prevent hypokalemia. Health-promoting lifestyle modifications are recommended for individuals with prehypertension and as an adjunct to therapy in hypertensive individuals.

398. The answer is b. (*Barrett, pp 678-679. Longo, pp 2447-2448, 2283-2285.*) Because creatinine is not reabsorbed from the tubule, its concentration rises as water is reabsorbed. The H_2 receptor antagonist, cimetidine, competes with creatinine for proximal tubule transport by the organic cation pathways. This may elevate serum creatinine levels, but this change does not reflect changes in GFR. Phosphate (*choice d*) is almost completely reabsorbed in the proximal tubule, so its concentration decreases along the length of the tubule. The concentrations of glucose (*choice c*) and bicarbonate (*choice a*) are also less at the end of the proximal tubule than at the beginning. 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 (*choice e*) does not normally change as the filtrate flows through the proximal tubule.

399. The answer is e. (*Barrett, pp 674-680. Longo, pp 2056-2058. Widmaier, pp 480-484.*) Decreased pressure or stretch in the afferent arteriole is one of three primary stimuli for increasing renin secretion. RPF, filtration fraction, the oncotic pressure, and the filtration rate all increase when the afferent arteriolar resistance is decreased. The RBF 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 GFR is proportional to the glomerular capillary pressure and the RPF. Because both of these increase, so does the GFR. Vasodilators are used in the treatment of hypertension to improve both cardiovascular and renal outcomes. The concomitant use of an ACE inhibitor or angiotensin receptor antagonist protects against the effects of renin on angiotensin generation or action, respectively.

400. The answer is c. (*Barrett, pp 681-682, 686-687. Longo, pp 353, 370, 2284-2285, 2357, 2360-2362.*) The distal convoluted tubule reabsorbs approximately 5% of the filtered NaCl via an electrically neutral thiazide-sensitive Na^+/Cl^- cotransporter on the apical membrane. Loss-of-function mutations of the SLC12A3 gene encoding the thiazide-sensitive apical Na^+/Cl^- cotransporter (NCCT or TSC) causes Gitelman's syndrome, an autosomal recessive salt-wasting disorder associated with hypokalemic alkalosis, hypomagnesemia, hypocalciuria, and decreased urine chloride. The thick ascending limb of loop of Henle 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.

401. The answer is c. (*Barrett, pp 372-373, 702-706. Longo, pp 2042-2059.*) Juxtaglomerular 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 juxtaglomerular cells. Renin release is increased in response to increased activity in the sympathetic neurons innervating the kidney. Prostaglandins, particularly PGI_2 and PGE_2, 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.

402. The answer is a. (*Barrett, pp 686-690. Kaufman, pp 265-266. Longo, pp 2051, 2053, 2355-2361.*) 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 thick ascending limb of 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. Patients with autosomal dominant polycystic kidney disease typically present in their 30s or 40s with flank pain. Complications include recurrent urinary tract infections and pyelonephritis, and cardiovascular complications, including hypertension, valvular disorders (especially mitral valve prolapse and aortic regurgitation), and berry aneurysms (subarachnoid hemorrhage). Approximately 50% of patients will develop end-stage renal disease, requiring dialysis or renal transplantation.

403. The answer is d. (*Barrett, pp 360-361, 364, 370-375, 682, 690-691, 701-702.*) Aldosterone is a steroid hormone synthesized in the zona glomerulosa of the adrenal gland, which acts to increase the reabsorption of Na^+ (and H_2O) from the urine, sweat, saliva, and colon, thereby expanding extracellular fluid volume. In the kidneys, aldosterone, and other steroids with mineralocorticoid activity, acts primarily on the principal (P) cells of the collecting ducts, where the final 3% of filtered

sodium is reabsorbed via ENaC in the apical membrane. Aldosterone acts to increase the number of active ENaCs in the collecting ducts. The molecular mechanism for this is that aldosterone binds to a cytoplasmic receptor and the steroid–hormone complex moves to the nucleus where it activates the genome by altering the transcription of mRNAs, which in turn increases the production of proteins that alter cell function. The aldosterone-stimulated proteins have two effects—a rapid effect to increase the number of active ENaCs by increasing the insertion of these channels into the cell membrane from a cytoplasmic pool, which takes 10 to 30 minutes to develop, and a slower effect to increase the synthesis of ENaCs. Among the genes activated by aldosterone is the early response gene for serum- and glucocorticoid-regulated kinase, a serine-threonine protein kinase, which increases ENaC activity. Aldosterone also increases the mRNAs for the three subunits that constitute ENaCs. The peak effect of aldosterone on Na^+ reabsorbed takes 90 to 140 minutes, indicating that it depends on the synthesis of new protein by a genomic mechanism. Under the influence of aldosterone, increased amounts of Na^+ are in effect exchanged for K^+ and H^+ in the collecting ducts, producing a K^+ diuresis and an increase in urine acidity; this "exchange," however, is not via the ENaC channels.

404. The answer is e. (*Barrett, pp 679-681, 691, 701-706. Le, pp 483, 485-486. Longo, pp 2281-2282, 2294.*) Angiotensin II binds to ATII receptors on the vascular smooth muscle cells of the efferent arteriole causing vascular constriction, which increases the capillary hydrostatic pressure resulting in increased glomerular filtration. Angiotensin II is formed from angiotensin I in a reaction catalyzed by ACE. Angiotensin II is part of the renin–angiotensin–aldosterone system, which is stimulated in patients with low blood volume or low blood pressure in an effort to increase blood volume and blood pressure. Lisinopril is an ACE inhibitor that blocks the formation of angiotensin II and is one of the primary medications used to treat high blood pressure. ACE inhibitors are first-line treatment options in hypertensive patients with medical comorbidities, such as diabetes, and individuals of African American descent. In addition, ACE inhibitors have been shown to slow down renal damage in patients with microalbuminuria, as determined by a urinary microalbumin level of 30 to 300 mg. Urinary microalbumin is a more sensitive test when compared to urinary protein levels to indicate protein wasting in early renal failure. Angiotensin II does not decrease GFR because of constriction of the afferent arteriole. Angiotensin II constricts the efferent arteriole, but not the afferent arteriole. Thus, ACE inhibitors, which block the formation of angiotensin II, cause efferent arteriolar dilation. NSAIDs do constrict the afferent arteriole and decrease GFR by inhibiting prostaglandin-mediated vasodilation of the afferent arteriole, and the resultant increase in RBF and GFR.

405. The answer is e. (*Barrett, pp 313, 685, 697-701. McPhee and Hammer, pp 542-544.*) The ascending limb of the loop of Henle dilutes the fluid within the nephron by reabsorbing Na^+ without water. In the absence of ADH, or when the nephron is resistant to 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. Diabetes insipidus is a syndrome of polyuria resulting from the inability to concentrate urine and thus to conserve water due to a lack of action of ADH. Diabetes insipidus is classified as central (affecting the synthesis or secretion of ADH) or nephrogenic (due to loss of the kidney's ability to respond to circulating ADH). Both types of diabetes insipidus have hereditary and acquired causes.

406. The answer is e. (*Barrett, pp 279, 665-668, 686-687. Le, pp 483, 485-486. Widmaier, pp 384, 492, 494.*) Because one of its principal physiologic actions is water retention by the kidney, vasopressin is often called antidiuretic hormone (ADH). ADH increases the permeability of the collecting ducts of the kidney so that water more readily enters the hypertonic interstitium of the renal pyramids. Thus, the concentration of solutes in the urine is increased and urine volume decreases. The overall effect is therefore retention of water in excess of solute. The mechanism by which vasopressin (ADH) exerts its antidiuretic effect is via V_2 receptors and involves the translocation of aquaporin-2 from cytoplasmic endosomes and insertion of the channels into the apical (luminal) membranes of the principal cells of the collecting ducts. The vasoconstrictor effects of vasopressin are mediated by V_{1A} receptors. Vasopressin has no effect on GFR, and because it increases water reabsorption, it would decrease urine formation.

407. The answer is e. (*Barrett, pp 680, 693. Le, pp 479, 481. McPhee and Hammer, p 303. Widmaier, pp 476-477, 480.*) The most likely cause of acute renal failure in this patient is ureteral obstruction, as evidenced by the swelling of the kidneys. Ureteral obstruction in this patient is most likely due to mechanical compression of the urinary collection system and ureters by the gravid uterus. In addition, the elevated progesterone levels in pregnancy cause decrease ureteral motility. The ureteral obstruction raises the hydrostatic pressure within Bowman 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.

408. The answer is d. (*Kaufman, pp 256-259. Le, p 486.*) The fractional excretion (FE) is the fraction of the filtered load that is excreted. It is calculated using the following formula:

$$\text{FE} = \text{amount excreted/amount filtered} = (U_{Na} \times \dot{V})/(P_{Na} \times \text{GFR})$$

$$\text{Because GFR} = (U_{creatinine} \times \dot{V}/P_{creatinine})$$

$$\text{FE} = (U_{Na} \times \dot{V})/[P_{Na} \times (U_{creatinine} \times \dot{V}/P_{creatinine})]$$

$$= (U_{Na} \times P_{creatinine})/(P_{Na} \times U_{creatinine})$$

$$= 33\ \text{mM} \times 7.5\ \text{mg/dL}/135\ \text{mM} \times 90\ \text{mg/dL} = 0.02$$

Fractional excretion is used to distinguish between a prerenal state (due to decreased kidney perfusion) 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 ibuprofen (Motrin). NSAIDs can cause acute renal failure by inhibiting the renal production of prostaglandins, which maintain GFR by dilating the afferent arterioles.

409. The answer is a. (*Barrett, pp 681-692. Le, p 499. Longo, pp 2280-2288.*) The site of action of acetazolamide is the proximal convoluted tubule and the site of action of the thiazides is the distal convoluted tubule. 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^-.

410. The answer is a. (*Barrett, pp 690, 693, 700. McPhee and Hammer, pp 536, 538, 540-542.*) 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} = urine flow – C_{osm}. Free water clearance is positive when the urine is dilute (more than a sufficient amount of water is excreted), and it 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 (*choice a*), very little water is reabsorbed in the distal nephron, and, therefore, the free water clearance is very high. 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 (*choice b*) than in diabetes insipidus. With diuretic therapy (*choice c*), 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. In heart failure (*choice d*) or renal failure (*choice e*), very little free water can be generated even if the urine is dilute because the GFR is decreased. Diabetes insipidus can be due to (1) diseases of the CNS or head trauma affecting the synthesis or secretion of vasopressin (central diabetes insipidus); (2) diseases of the kidneys with loss of the kidney's ability to respond to circulating vasopressin (nephrogenic diabetes insipidus); or (3) pregnancy, which increases the metabolic clearance of vasopressin.

411. The answer is d. (*Barrett, pp 540, 677-678, 706-708. Kaufman, pp 15, 22-24. Longo, pp 290-294, 345, 354, 1901-1907, 2031. McPhee and Hammer, pp 257-265. Widmaier, pp 504-505.*) Patients with congestive heart failure frequently have a paradoxical increase in NaCl and water retention despite an increase in extracellular fluid volume. An increase in renal sympathetic nerve activity promotes a decrease in NaCl and water excretion by decreasing GFR, increasing renin secretion, and increasing tubular NaCl reabsorption. All of the other factors cause an increase in NaCl and water excretion.

412. The answer is d. (*Barrett, pp 678-681. Longo, pp 334-335, 2281-2282, 2293-2295, 2309.*) 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% to 95% of malignant neoplasms arising from the kidney.

413. The answer is b. (*Barrett, pp 716-717. Longo, pp 344-345, 363-366, 368. Widmaier, pp 506-511.*) Persistent diarrhea will result in a metabolic acidosis, due to the loss of the bicarbonate-rich secretions originating from the pancreas and gallbladder. The ensuing metabolic acidosis will decrease the plasma concentration of HCO_3^-, 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.

414. The answer is e. (*Barrett, pp 688-689, 700. Longo, pp 344-349. McPhee and Hammer, pp 540-542.*) ADH increases the permeability of the collecting ducts 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. The cardinal clinical presentation in patients with the syndrome of inappropriate ADH secretion (SIADH) is hyponatremia without edemas. SIADH is due to the secretion of ADH in excess of what is appropriate for plasma osmolality or intravascular volume depletion. Tuberculosis is one of the many causes of SIADH.

415. The answer is b. (*Barrett, p 681. Le, p 481. Longo, pp 290-293.*) The filtration fraction is defined as the ratio of GFR to RBF. In heart failure, efferent arteriolar constriction mediated by increased renal sympathetic nerve activity and angiotension II causes an increase in glomerular capillary (hydrostatic) pressure, which increases GFR, as well as a decrease in peritubular hydrostatic pressure. In addition, the increased renal vascular resistance decreases RBF. Thus, filtration fraction is increased, which increases the colloid osmotic pressure in the peritubular capillaries, thereby enhancing salt and water reabsorption in the proximal tubule and the ascending limb of the loop of Henle, which contributes to the formation of edema. An increase in afferent arteriolar resistance, such as occurs with inhibition of vasodilatory prostaglandins by NSAIDS, will decrease glomerular capillary pressure and, therefore, the filtration fraction. Increasing the plasma oncotic pressure or the hydrostatic pressure within Bowman capsule will decrease the filtration fraction because both of these Starling forces oppose filtration. Increasing RBF at a constant GFR causes a decrease in the filtration fraction.

416. The answer is a. (*Barrett, pp 647, 650-651, 692. Levitzky, p 238.*) Carbonic anhydrase is the enzyme that catalyzes the formation of CO_2 and H_2O from HCO_3^- and H^+. In the proximal tubule, the efficient reabsorption of bicarbonate requires the presence of carbonic anhydrase. Carbonic anhydrase inhibitors like acetazolamide prevent the formation of CO_2 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. Acetazolamide taken for a few days before ascending to high altitude can prevent the symptoms of acute mountain sickness. The mechanisms are unclear, but likely relate to (1) prevention of fluid retention via diuresis, (2) production of metabolic acidosis from decreased bicarbonate reabsorption, which may offset the respiratory alkalosis at high altitude, and (3) inhibition of hypoxic pulmonary vasoconstriction.

417. The answer is b. (*Barrett, pp 676-678, 702-706.*) Blood flow through the kidney is controlled by numerous humoral agents. Angiotensin II decreases RBF. It vasoconstricts efferent arterioles more than afferent arterioles, which helps to maintain GFR 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 ACE 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 RBF. Dopamine synthesized in the kidney increases RBF and sodium excretion. Acetylcho-line and ANP also produce renal vasodilation and an increase in RBF.

418. The answer is b. (*Kaufman, pp 261-263. Le, pp 489, 572-573, 578.*) Abrupt onset hematuria with RBC casts is pathognomonic of any glomerulonephritis, also known as nephritic syndrome. Immunoglobulin A (IgA) nephropathy is the most common glomerulonephritis. It generally presents in young men during or after a viral infection or after trauma or exercise. Pathologically, IgA nephropathy has immune complex deposition of IgA and C3 in the mesangial matrix, hence the alternative name, mesangial proliferative glomerulonephritis. There is no effective treatment.

419. The answer is e. (*Barrett, p 692. Longo, pp 343, 352-355, 1907-1908.*) The so-called potassium-sparing diuretics act in the collecting duct by inhibiting Na^+ reabsorption via Na channels either by blocking the aldosterone receptor (spironolactone) or by directly inhibiting the channels (amiloride). By inhibiting Na^+ reabsorption in the collecting tubules, a diuresis can be produced without an excess loss of K^+. Furosemide and other loop diuretics inhibit the Na–K–2Cl cotransporter in the medullary thick ascending limb of loop of Henle, which causes a marked natriuresis and kaliuresis. Thiazides act by inhibiting Na–Cl cotransport in the early portion of the distal tubule, which increases the amount of Na^+ in the filtrate flowing through the distal nephron. The increased Na^+ load in the distal nephron results in an increased Na^+ reabsorption and, as a result, an increased K^+ secretion. The carbonic anhydrase inhibiting drugs such as acetazolamide (Diamox) inhibit acid secretion by decreasing the supply of carbonic acid. As a result, there is an increase in both Na^+ and K^+ excretion.

420. The answer is c. (*Barrett, pp 21-22, 712-713.*) Ammonia (NH_3) is produced from the amino acid glutamine in the epithelial cells of the renal tubules (mainly the proximal tubules). Hyperkalemia inhibits ammonia synthesis in the proximal tubule. Normally, the rate of NH_3 production increases during acidosis, which is important for increasing the total amount of H^+ ion that can be excreted in a given volume of urine. NH_3 is lipid soluble and freely diffuses across cell membranes down its concentration gradient into the tubular lumen, and because of the high p K_a (9.2) of the reaction, essentially all of it combines with H^+ to form NH_4^+, which maintains the driving force for more NH_3 to passively diffuse into the lumen. In addition, NH_4^+ may be formed within renal tubular cells and then be secreted via the Na^+/NH_4^+ counter transporter into the lumen and excreted. The NH_4^+ in the tubular lumen is "trapped" and excreted because the tubules are impermeable to this cation. The excretion of excess acid in the form of NH_4^+ contributes to the renal compensation for respiratory acidosis and nonrenal metabolic acidosis. In type IV RTA, this compensatory mechanism is inhibited by the presence of hyperkalemia. The kidney also increases the concentration of serum bicarbonate as a result of this reaction to further compensate for the acidosis. H^+ is formed in the proximal tubule cells along with bicarbonate from carbon dioxide and water, a reaction that is catalyzed by carbonic anhydrase. H^+ is then secreted by the Na^+/H^+ antiporter or by H^+-ATPase into the tubular lumen, where it combines with ammonia and is excreted, as described above. Bicarbonate, on the other hand, moves from the tubule cells into the peritubular capillaries; this bicarbonate is deemed "new bicarbonate" because the bicarbonate that is added to the serum is not a result of reabsorption of filtered bicarbonate. Ammonia is not classified as a titratable acid. The most common form of titratable acid excreted is dihydrogen phosphate ion ($H_2PO_4^-$).

421. The answer is d. (*Barrett, pp 711-717. Kaufman, p 266. Le, p 488. Longo, pp 368-369, 2280-2293.*) The combination of hyperkalemia and hyperchloremic (normal anion-gap) metabolic acidosis is characteristic of type IV RTA, and is often seen in patients with diabetic nephropathy. Type IV RTA is caused by aldosterone resistance or deficiency, and is also called hyporeninemic hypoaldosteronism. In this case, the patient's RTA is likely due to the amiloride therapy. Amiloride is a potassium-sparing diuretic that acts on the principal cells of the collecting ducts to inhibit aldosterone-induced sodium reabsorption, thereby increasing Na^+ excretion. As a result, potassium secretion from the principal cells is decreased, as is hydrogen ion secretion from intercalated cells, leading to hyperkalemia and metabolic acidosis. Hyperkalemia inhibits ammoniagenesis in the epithelial cells of the proximal tubule, which further decreases H^+ excretion, contributing to the acidosis. Both the acidosis and the hyperkalemia are out of proportion to the impairment of GFR in type IV RTA. Hyperkalemia may be a life-threatening electrolyte imbalance if extreme and not managed appropriately. Common acute manifestations of hyperkalemia include muscle weakness and ECG changes, which could potentially progress to life-threatening arrhythmias. ECG changes in hyperkalemic patients include peaked T-waves, QRS widening, and sinusoidal wave patterns.

422. The answer is b. (*Barrett, pp 709-710.*) The kidney produces a number of important hormones such as erythropoietin, 1,25-(OH)2-vitamin D, renin, and prostaglandins. Erythropoietin is necessary for the normal production of red blood cells and is released from the endothelial cells of the peritubular capillaries in response to hypoxia. 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. Decreased conversion of 1-OH-vitamin D to 1,25-(OH)2-vitamin D in patients with chronic renal failure leads to renal osteodystrophy or secondary hyperparathyroidism. Renin production in patients with chronic renal failure is actually increased due to decrease in GFR leading to decrease salt delivery to the macula densa cells of the distal convoluted tubule. This activates the renin–angiotensin–aldosterone system, which increases blood pressure as well as sodium and water retention leading to fluid overload/edema. Uremia is a clinical syndrome marked by large increases in BUN and creatinine, which develops as a later complication of chronic renal failure when kidney function is markedly reduced. The syndrome is characterized by nausea, vomiting, asterixis, and encephalopathy. Metabolic acidosis is also a complication of chronic renal failure due to failure of the kidneys to excrete the daily acid load.

423. The answer is c. (*Barrett, pp 706-708. Le, p 485.*) 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 dilating afferent arterioles and relaxing mesangial cells, both of which increase glomerular filtration and thus the filtered load of Na^+. There is also experimental evidence that ANP decreases sodium reabsorption in the proximal tubular brush border membrane, an effect mediated by ANP's effect on dopamine.

424. The answer is a. (*Barrett, pp 684-685. Longo, pp 2281, 2287-2294.*) The macula densa senses the chloride concentration of the fluid flowing from the ascending limb of loop of Henle 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.

425. The answer is e. (*Barrett, pp 690-691, 701-708. Le, pp 483, 485-486.*) 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. Up to 15% of patients diagnosed as having essential hypertension have primary hyperaldosteronism. The ratio of plasma aldosterone concentration to plasma renin activity is high in primary aldosteronism and low in secondary hyperaldosteronism, in which plasma renin activity is high.

426. The answer is d. (*Barrett, pp 377-379. Le, p 486.*) Inorganic phosphorus (P_i) in the plasma is filtered in the glomeruli, and 85% to 90% of the filtered phosphate is reabsorbed. Active transport in the proximal tubule accounts for most of the reabsorption and involves two related sodium-dependent secondary active transport systems—NaP_i-IIa and NaP_i-IIc. The NaP_i-IIa cotransporter is electrically neutral, requiring two Na^+ molecules for every HPO_4^{2-} molecule that it transports. The transporter is inhibited by 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.

427. The answer is d. (*Barrett, pp 691-692. Kaufman, pp 262-263, 291, 322-323. Le, pp 483, 489-492.*) 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 RBF 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.

428. The answer is e. (*Barrett, pp 701-706. Le, pp 485-486. Longo, pp 341-344.*) The juxtaglomerular apparatus is responsible for releasing renin when the effective circulating blood volume is decreased. The juxtaglomerular apparatus releases renin when the Cl^- concentration in the luminal fluid bathing the macula densa is decreased or when renal perfusion pressure 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 RBF by constricting the afferent arteriole and, therefore, the blood flow through the glomerular capillary. Decreased renal perfusion accounts for 40% to 80% of acute renal failure. The etiologies of prerenal failure include any cause of decreased circulating blood volume (burns, diarrhea, diuretics, and GI hemorrhage), volume sequestration (pancreatitis, rhabdomyolysis, and peritonitis), or decreased effective arterial volume (cardiogenic shock, sepsis).

429. The answer is b. (*Barrett, pp 636-637, 676-678. 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 approximately 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 because the concentration of albumin is essentially the same.

430. The answer is c. (*Barrett, pp 709-711. Kaufman, p 266. Le, p 488. Longo, pp 368, 2284, 2357-2365.*) In the proximal tubule, a large amount of H^+ ion is secreted into the tubule lumen via a Na^+–H^+ exchanger, which secretes H^+ into the lumen in exchange for Na^+. Most of the secreted 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. In type II RTA, a defect in proximal tubular bicarbonate reabsorption causes normal anion gap metabolic acidosis and bicarbonate wasting in the urine (increased pH). Multiple myeloma, heavy metals, and carbonic anhydrase inhibitors are causes of type II RTA. The most common presenting symptom of multiple myeloma is bone pain and compression fractures. Bence-Jones proteins in the urine are pathognomonic.

431. The answer is c. (*Barrett, pp 686-691.*) ADH (vasopressin) increases the water permeability of the cortical and medullary collecting tubules and ducts and allows the filtrate to reach osmotic equilibrium with the interstitial fluid surrounding the nephron segment. 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.

432. The answer is a. (*Barrett, pp 679-681, 690, 692-693. Kaufman, pp 263-266.*) The excretion of creatinine, which is neither reabsorbed nor secreted in any significant amount, is dependent on filtration, which is in turn dependent on RPF. The decrease in RPF 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 nonfunctioning nephrons in renal failure. For each doubling of the serum creatinine, the GFR has decreased by 50%. Interestingly, the remaining nephrons adapt to renal failure. Even creatinine secretion can be increased, so the plasma creati-nine concentration does not increase proportionally to the amount of renal damage. 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. The nitrogenous products of metabolism are retained in the blood (azotemia or uremia), causing an increased 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.

433. The answer is d. (*Barrett, pp 548, 681-682, 692.*) The patient is suffering from volume overload as a result of an acute exacerbation of congestive heart failure. Treatment consists of supportive measures and significant diuresis to help remove some of the excess water that has caused this patient's pulmonary edema and shortness of breath, as well as the patient's peripheral edema. The most common method to induce diuresis in these patients is to place them on IV loop diuretics such as furosemide, ethacrynic acid, and bumetanide. This class of medications induces a powerful diuresis by inhibiting sodium reabsorption in the thin ascending limb of the loop of Henle. In this segment, sodium reabsorption is driven by the Na^+–K^+–$2Cl^-$ cotransporter on the luminal membrane and is responsible for the reabsorption of 30% of the filtered sodium. These electrolytes are reabsorbed without water, as this segment of the tubule is impermeable to water. As a result, the tubular fluid osmolarity in this segment decreases as more electrolytes are reabsorbed. This section is extremely important for the development of the countercur-rent exchange mechanism and overall water reabsorption. By being impermeable to water, this section creates a hyperosmotic interstitium, which in turn increases water reabsorption in the adjacent distal tubule and collecting duct. However, when loop diuretics such as furosemide are given, the Na^+–K^+–$2Cl^-$ cotransporter is blocked which inhibits the formation of the hyperosmotic interstitium resulting in a decrease in water reabsorption in the distal tubule and collecting duct and subsequent diuresis. Na^+/nutrient cotransport and Na^+/H^+ exchange are the two principal mechanisms for Na^+ reabsorption in the proximal tubule. The Na^+/nutrient cotransport processes accounts for the reabsorption of all the filtered glucose and amino acids. The Na^+/H^+ exchange occurs in the proximal tubule in a mechanism that is directly linked to the reabsorption of bicarbonate ion. These mechanisms of sodium reabsorption are responsible for approximately 60% of the reabsorption of filtered sodium in the kidneys. Na^+ Cl^- cotransport is the method of sodium reabsorption in the distal tubule and collecting duct and reabsorbs 7% of the overall total of filtered sodium. Thiazide diuretics such as hydrochlorothiazide work on this section by inhibiting these Na^+ Cl^- cotransporters. Na^+/K^+ exchange occurs in the principal cells of the collecting duct. Here, Na^+ and water are reabsorbed and potassium is excreted under the control of aldosterone. Aldosterone is a steroid hormone synthesized in the zona glomerulosa of the adrenal gland that increases Na^+ channels in the luminal membrane and Na^+/K^+-ATPase in the basal membrane to increase sodium reabsorption. This section reabsorbs roughly 3% of the overall filtered sodium.

434. The answer is c. (*Barrett, pp 676-677.*) To calculate RBF, one may use the following equation:

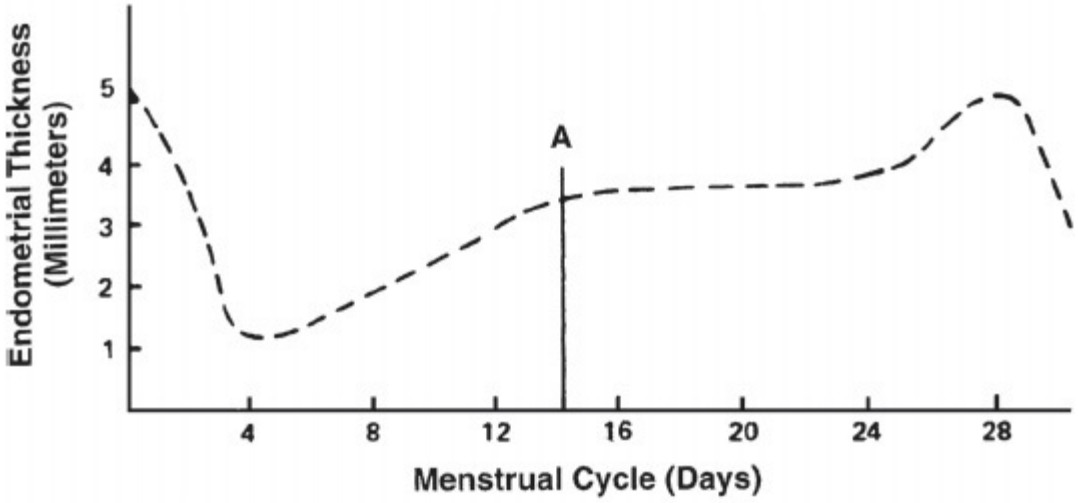
$$\text{RBF} = \text{RPF}/1 - \text{hematocrit}$$
$$\text{RPF} = U_{PAH} \times V/P_{PAH}$$
$$\text{RPF} = (20\ \text{mg/mL} \times 1.2\ \text{mL/min})/6\ \text{mg}/100\ \text{mL} = 400\ \text{mL/min}$$
$$\text{RBF} = 400\ \text{mL/min}/(1-0.40) = 667\ \text{mL/min}$$

RPF can be determined by calculating the clearance of PAH. PAH can be used to estimate RPF because it is both filtered and actively secreted in the proximal tubule but not reabsorbed. Inulin, on the other hand, may be used to estimate GFR because inulin is freely filtered but neither reabsorbed nor secreted. The calculated RPF must then be divided by the plasma volume, as estimated by the calculation of 1 – hematocrit, to determine the RBF.

This patient most likely has renal artery stenosis secondary to fibrodysplasia. Evidence for this diagnosis includes labile hypertension that is worsened with ACE inhibitors in a young female. ACE inhibitors make hypertension worse in patients with bilateral renal artery stenosis by limiting vasoconstriction of the efferent artery. Vasoconstriction of the efferent arteriole in these patients helps preserve kidney function by increasing the perfusion pressure and the GFR. With stenosed renal arteries, afferent flow cannot be increased and angiotensin II is the only mechanism by which to preserve renal function by increasing filtration. ACE inhibitors, such as lisinopril, prevent the conversion of angiotensin I to angiotensin II and thus perfusion pressure decreases, which severely diminishes any remaining kidney function in these patients.

Questions

435. 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. Early proliferative phase
b. Menses
c. Mid-luteal phase
d. Ovulation
e. Secretory phase

436. A 15-year-old boy presents for his annual athletic physical exam. 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 best describes spermatogenesis?

a. Leydig cell secretion of testosterone requires follicle-stimulating hormone (FSH).
b. Luteinizing hormone (LH) acts directly on Sertoli cells to promote cell division.
c. Mature spermatozoa are present at birth, but cannot be released until puberty is reached.
d. Spermatogenesis requires a temperature lower than internal body temperature.
e. Spermatogenesis requires continuous release of gonadotropin-releasing hormone (GnRH).

437. A 19-year-old female presents to her primary care physician with significant weight loss and secondary amenorrhea. She has a high-intensity exercise regimen, is preoccupied with food, and seems to have an irrational fear of gaining weight. Decreased production of which of the following hormones leads to amenorrhea in anorexia nervosa?

a. Human chorionic gonadotropin (hCG)
b. Estradiol
c. Gonadotropin releasing hormone (GnRH)
d. Progesterone
e. Prolactin

438. A 32-year-old man taking chlorpromazine for his schizophrenia presents with diminished libido and decreased beard growth. His blood prolactin level of 75 µg/L confirms the diagnosis of hyperprolactinemia. Which of the following is true regarding prolactin?

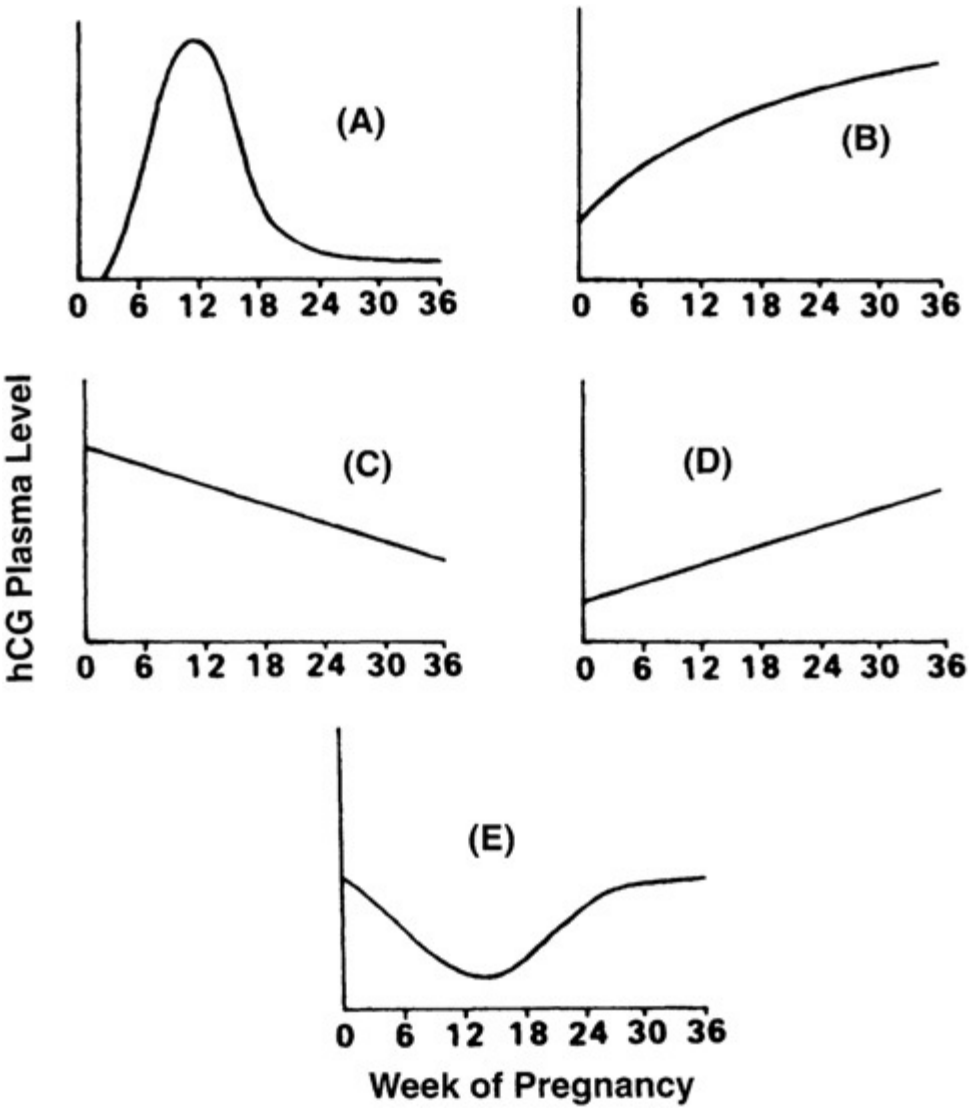
a. Prolactin causes milk ejection during suckling.
b. Prolactin inhibits GnRH secretion by the hypothalamus.
c. Prolactin inhibits gonadotropin secretion by the pituitary gland.
d. Prolactin inhibits growth of breast tissue.
e. Serum prolactin levels are much higher in women than in men.

439. A 22-year-old woman presents to the obstetrician-gynecologist's office with complaints of painful menstruation accompanied by profuse menstrual flow. The doctor prescribes ibuprofen and an oral contraceptive. Biological actions of estrogens include a decrease in which of the following?

a. Duct growth in the breasts
b. Libido
c. Ovarian follicular growth
d. Serum cholesterol levels

e. Uterine smooth muscle motility

440. A 34-year-old woman discovers that she is pregnant using a home pregnancy test that detects the presence of hCG in the urine. Which of the curves shown below approximates the level of this hormone during pregnancy?



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

441. A 26-year-old man with Klinefelter's syndrome has seminiferous tubule dysgenesis. Which of the following is a function of Sertoli cells in the seminiferous tubules?

a. Expression of surface LH receptors
b. Maintenance of the blood–testis barrier
c. Secretion of FSH into the tubular lumen
d. Secretion of testosterone into the tubular lumen
e. Synthesis of estrogen after puberty

442. A 23-year-old woman who has been training for a marathon presents with secondary amenorrhea. A pregnancy test is negative, so the woman is started on the orally active opioid blocker naltrexone, which restores ovulation and menses. Ovulation is caused by a sudden increase in the secretion of which of the following hormones?

a. Estrogen
b. FSH
c. GnRH
d. LH
e. Progesterone

443. 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 best describes implantation of the zygote in the uterine wall?

a. Involves infiltration of the endometrium by the syncytiotrophoblast
b. Is inhibited by secretion of progesterone from the corpus luteum
c. Occurs 3 to 5 days after fertilization
d. Occurs when the embryo consists of approximately 128 cells
e. Precedes formation of the zona pellucida

For Questions 444 and 445, refer to the following case.

A 28-year-old woman develops nausea and breast tenderness after missing her menstrual period. A digital home pregnancy test is positive. Other than lower back pain, occasional headaches, and frequent urination, the pregnancy progresses to the second trimester without complications.

444. With respect to hormonal changes during pregnancy, which of the following is the source of estrogen and progesterone during the first 2 months of pregnancy?

a. Anterior pituitary
b. Corpus luteum
c. Ovary
d. Placenta
e. Posterior pituitary

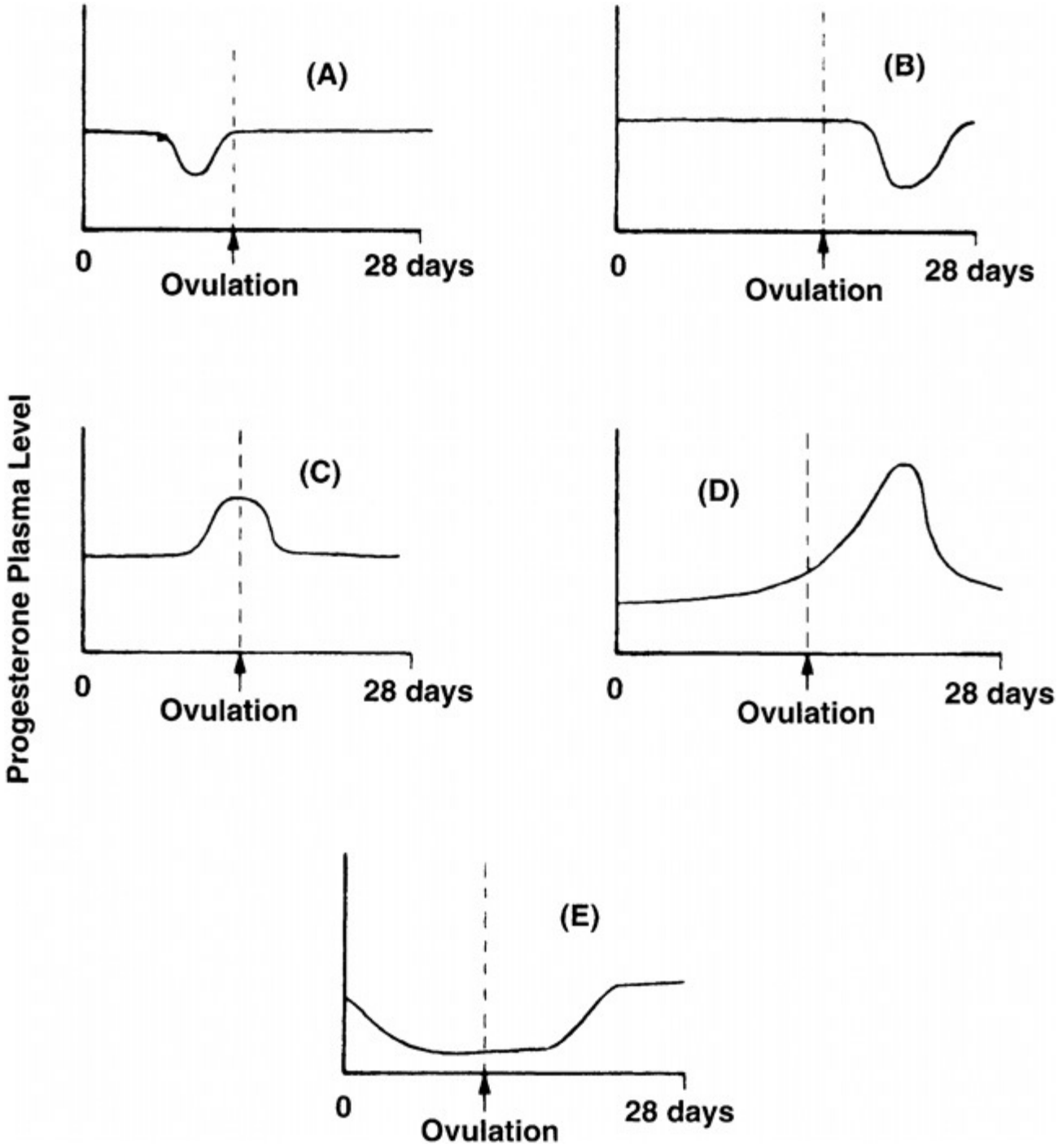
445. Which of the following is the source of estrogen and progesterone during the last 7 months of pregnancy?

a. Anterior pituitary
b. Corpus luteum
c. Ovary
d. Placenta
e. Posterior pituitary

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 beer would relax her and allow her milk to flow more readily, but it has not helped, even with drinking up to a six pack a day. Which of the following hormones is involved in the ejection of milk from a lactating mammary gland?

a. Estrogen
b. Growth hormone
c. Oxytocin
d. Progesterone
e. Prolactin

447. 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

For Questions 448 and 449, refer to the following case.

A 30-year-old woman with polycystic ovarian syndrome uses an estrogen/progesterone combination for androgen excess and endometrial protection.

448. Administration of estrogens in women will do which of the following?

a. Cause cervical mucus to become thicker and more acidic
b. Decrease bone density
c. Limit the growth of ovarian follicles
d. Produce cyclic changes in the vagina and endometrium
e. Retard ductal proliferation in the breast

449. Which of the following best describes progesterone?

a. Plasma levels of progesterone increase during menses.

b. Plasma levels of progesterone decrease after ovulation.
c. Plasma levels of progesterone remain constant after implantation.
d. Progesterone is secreted by the corpus luteum.
e. Progesterone secretion by the placenta increases at week 6 of gestation.

450. 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. Androstenedione
b. Androsterone
c. Dihydrotestosterone
d. Müllerian-inhibiting substance (MIS)
e. Testosterone

451. A 12-year-old girl presents to her pediatrician's office because she has not yet begun her menstrual periods and she lacks breast development. After evaluation, she is found to have Turner's syndrome. Which of the following best describes a patient with Turner's syndrome?

a. It is not associated with hypothyroidism.
b. It is not associated with renal abnormalities.
c. Ovarian dysgenesis (streak ovary) is characteristic.
d. Tall stature is common.
e. The most common karyotype is 45,X/46,XX mosaicism.

452. A 55-year-old woman is experiencing the signs and symptoms of menopause. Her gynecologist discusses with her the possibility of hormone replacement therapy (HRT). Which of the following are effects of postmenopausal HRT?

a. Increases the risk of osteoporosis
b. Reduces the incidence of hot flashes
c. Reduces the risk of breast cancer
d. Reduces the risk of coronary artery disease and stroke
e. Returns the menstrual cycle pattern to normal

453. A 29-year-old woman delivers a 7-lb 6-oz baby girl without complication. She begins to produce and eject breast milk a few days later. Prolactin secretion is tonically suppressed in nonpregnant women by which of the following hormones?

a. Dopamine
b. Estrogen
c. FSH
d. LH
e. Progesterone

454. 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.

455. 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?

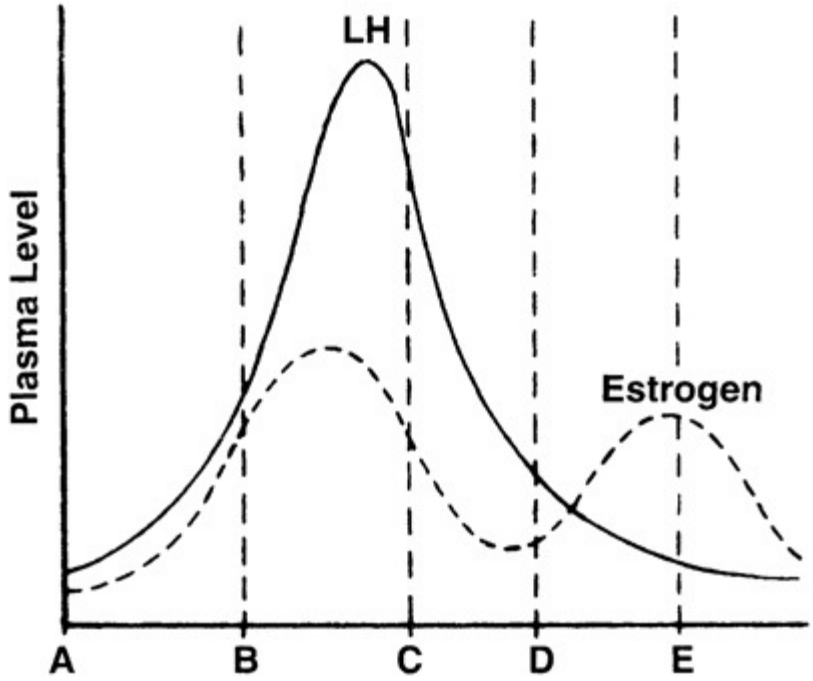
a. Decreased production of cortisol and corticosterone
b. Hypercapnia
c. Increased conversion of glucose to glycogen
d. Increased hematocrit
e. Reduced circulating gonadotropin levels

456. A couple presents at the fertility center with concerns 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. A drop in body temperature

b. An increase in serum estrogen levels
c. An increase in serum FSH levels
d. An increase in serum LH levels
e. An increase in serum progesterone levels

457. 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

458. A 35-year-old woman presents to 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 an ovarian cancer and may need 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 6th 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. Growth hormone–releasing hormone and corticotropin-releasing hormone
d. Human chorionic somatomammotropin and hCG
e. Progesterone and hCG

459. A 54-year-old man is prescribed finasteride, a 5-alpha reductase inhibitor, for his benign prostatic hypertrophy. Why is his pregnant wife instructed to not even handle the medication?

a. Blocking the production of dihydrotestosterone will interfere with normal sexual differentiation of the penis, scrotum, and prostate in male fetuses.
b. Inhibiting 5-alpha reductase in utero will impair SRY gene expression and consequently development of the testes.
c. Inhibiting 5-alpha reductase in utero will lead to precocious puberty in both sexes.
d. Inhibiting 5-alpha reductase in utero impairs secretion of MIS.
e. Inhibiting 5-alpha reductase in utero will cause regression of the Wolffian ducts such that a male fetus develops female genitalia.

Answers

435. The answer is d. (*Barrett, pp 401-406. Longo, pp 3031-3033. Widmaier, pp 611-612.*) 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. The endometrial lining is almost completely shed during menses (days 1 to 5). The endometrial lining of the uterus undergoes proliferation of both glandular epithelium and supporting stroma from the 5th to the 14th day of the menstrual cycle. Ovulation occurs at around day 14 (point A on the graph) in response to estrogen secretion by the ovary. Following ovulation, the endometrium becomes highly vascularized and slightly edematous and the glands become coiled and begin to secrete a clear fluid; this is known as the secretory or luteal phase. Late in the secretory phase, the stroma undergoes pseudodecidual reaction in preparation for potential pregnancy. When ovulation is not followed by implantation of a fertilized ovum, the corpus luteum regresses, withdrawing hormonal support for the endometrium.

436. The answer is d. (*Barrett, pp 420-422, 428. Longo, pp 805, 3018.*) 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 89.6°F (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 approximately 10% of newborn infants, 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 spermatocytes does not begin until adolescence. Throughout the reproductive life of the human male, 100 to 200 million sperms are produced daily. Of critical importance to the hormonal regulation of spermatogenesis is the pulsatile release of GnRH 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.

437. The answer is c. (*Barrett, pp 314, 398-399, 412-413. Longo, pp 636-640. Widmaier, pp 613-614.*) Amenorrhea in patients with anorexia nervosa is hypothalamic in origin due to decreased production of GnRH and subsequent low levels of FSH, LH, and plasma estrogen in women (and testosterone in men). The decreased production of GnRH 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.

438. The answer is b. (*Barrett, pp 333-334, 400, 416-417. Longo, pp 2886-2889. Widmaier, pp 623-625.*) 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 milk production from the breast and inhibition of the effects of gonadotropins. The function of prolactin in normal males is unsettled, but excess prolactin causes impotence, 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 hyper-secretion 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.

439. The answer is d. (*Barrett, pp 391, 406-409. Le, p 442. Longo, pp 388, 3030-3031. Widmaier, pp 611-613.*) 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 and has a protective effect against osteoporosis.

440. The answer is a. (*Barrett, pp 414-415. Widmaier, pp 619-620.*) 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 of gestation.

441. The answer is b. (*Barrett, pp 397, 419-429. Longo, pp 3046-3050.*) 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.

442. The answer is d. (*Barrett, pp 412-413. Longo, pp 3028-3033. Widmaier, pp 603-610.*) 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 physiological 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.

443. The answer is a. (*Barrett, pp 413-414. Widmaier, pp 616-617, 625.*) 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.

444 and 445. The answers are b for 444 and d for 445. (*Barrett, pp 413-416. Widmaier, pp 614-620, 629-631.*) 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.

446. The answer is c. (*Barrett, pp 151, 311-312, 323, 333-335. Longo, p 2218. Widmaier, pp 623-626.*) A combined neurogenic and hormonal reflex involving oxytocin, a posterior pituitary hormone, causes the actual ejection ("let-down") of milk from breast tissue. 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. Milk secretion is regulated by prolactin, a pituitary hormone secreted throughout pregnancy and after parturition. Suckling on breast tissue is the stimulus that leads to milk secretion. Adequate amounts of growth hormone are required to provide the nutrients that are essential for milk production by breast tissue. Although estrogen and progesterone are essential for the physical development of breast tissue during pregnancy, both hormones inhibit milk secretion.

447. The answer is d. (*Barrett, pp 409-410. Widmaier, pp 606-610.*) There is a marked increase in progesterone secretion following ovulation. When ovulation is not followed by implantation of a fertilized ovum, progesterone secretion declines as the corpus luteum involutes.

448. The answer is d. (*Barrett, pp 406-409, 414-416. Widmaier, p 613.*) Estrogens cause the mucus secreted by the cervix to become thinner and more alkaline and to exhibit a fernlike pattern upon drying. 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. Estrogen helps maintain bone density.

449. The answer is d. (*Barrett, pp 409-410, 414-416. Widmaier, p 613.*) Progesterone is secreted by the corpus luteum. The plasma level of progesterone is low during 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.

450. The answer is c. (*Barrett, pp 397, 419-429. Longo, pp 3046-3051. Widmaier, p 601.*) The testosterone metabolite dihydrotestosterone 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 of 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 MIS, also known as anti-Müllerian hormone, 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 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.

451. The answer is c. (*Barrett, p 397. Le, p 445. Longo, pp 3046-3051.*) Gonadal dysgenesis is characteristic of Turner's syndrome. Most females have primary amenorrhea and lack pubertal development. The 45,X karyotype is most common and short stature is also typically seen. Renal manifestations, such as horseshoe kidney, are also frequently observed. In addition, other abnormalities include bicuspid aortic valve, coarctation of the aorta, hypertension, and hypothyroidism.

452. The answer is b. (*Longo, pp 52-53, 755, 987, 3040-3045, 1990. Widmaier, pp 639-640.*) 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 (ie, 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 HRT. 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.

453. The answer is a. (*Barrett, pp 323, 333-335.*) In nonpregnant women, the secretion of prolactin is kept tonically suppressed by secretion of dopa-mine 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.

454. The answer is a. (*Barrett, pp 413-415. Le, p 444. Widmaier, pp 614-620.*) The corpus luteum in the ovary at the time of fertilization fails to regress and instead enlarges in response to stimulation by 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.

455. The answer is e. (*Barrett, pp 413-415. Widmaier, pp 614-625.*) 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.

456. The answer is e. (*Barrett, pp 401-406. Le, pp 442-443. Widmaier, pp 605-610.*) 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.

457. The answer is c. (*Barrett, pp 438-439. Widmaier, pp 605-613.*) Ovulation takes place just after the peak of the LH and estrogen curves, which occurs on approximately the 14th 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. There is a sharp preovulatory rise in plasma concentration of estrogen, followed by a second rise due to estrogen secretion by the post-ovulatory corpus luteum.

458. The answer is a. (*Barrett, pp 413-416. Le, pp 448-449.*) 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.

459. The answer is a. (*Widmaier, pp 590-593, 599-602, 613-614.*) Finasteride and other 5-alpha reductase inhibitors can be absorbed by pregnant women and cross the placenta to enter the fetal circulation. These drugs would block the production of dihydrotestosterone in target tissues with 5-alpha reductase activity, thereby interfering with the development of normal sexual differentiation of the penis, scrotum, and prostate in male fetuses. The male and female gonads derive embryologically from the same site—the urogenital ridge—and are undifferentiated until the 6th week of uterine life. In the genetic male, the testes begin to develop during the 7th week when the SRY gene on the Y chromosome is expressed in the urogenital ridge cells. The SRY gene codes for the SRY protein, which initiates a sequence of gene activation ultimately leading to formation of the testes in the urogenital ridge. In the absence of the Y chromosome, and thus the SRY gene, testes do not develop, but ovaries begin to develop at same site at about 11 weeks. The internal duct system and external genitalia of the fetus are also capable of developing into either sexual phenotype. The primitive reproductive tract consists of the Wolffian ducts and the Müllerian ducts. In the male, the Wolffian ducts persist and the Müllerian ducts regress; the opposite occurs in the female.

Questions

460. A 49-year-old male patient with AIDS and declining CD4 counts has an increased frequency of systemic infections and develops sick euthyroid syndrome. Which of the following would be expected with normal thyroid function?

a. T_4 is formed from T_3 by the process of monodeiodination.
b. T_4 is the physiologically active hormone.
c. Thyroid-stimulating hormone (TSH) is secreted from the posterior pituitary.
d. TSH initiates thyroid hormone secretion via activation of nuclear receptors in thyroid gland cells.
e. TSH secretion is regulated primarily by the pituitary level of T_3.

461. A 43-year-old man 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. Adrenocorticotropic hormone (ACTH)
b. Antidiuretic hormone (ADH)
c. Follicle-stimulating hormone (FSH)
d. Growth hormone
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 best describes parathyroid hormone (PTH)?

a. It acts directly on bone cells to increase Ca^{2+} resorption and mobilize Ca^{2+}.
b. It acts directly on intestinal cells to increase Ca^{2+} absorption.
c. It is synthesized and secreted from the oxyphil cells in the parathyroid glands.
d. It increases phosphate reabsorption in the renal proximal tubular cells.
e. Its secretion is increased in response to an increase in plasma-free Ca^{2+} concentration.

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. Adrenal cortex
b. Anterior pituitary
c. Breast
d. Hypothalamus
e. Posterior pituitary

464. A 33-year-old major league baseball player takes human growth hormone to increase his performance. Which of the following best describes human growth hormone?

a. It decreases lipolysis.
b. It has a long half-life.
c. It inhibits protein synthesis.
d. It stimulates production of somatomedins (insulin-like growth factors I and II [IGF-I and II]) by the liver, cartilage, and other tissues.
e. Its secretion is stimulated by somatostatin and inhibited by ghrelin.

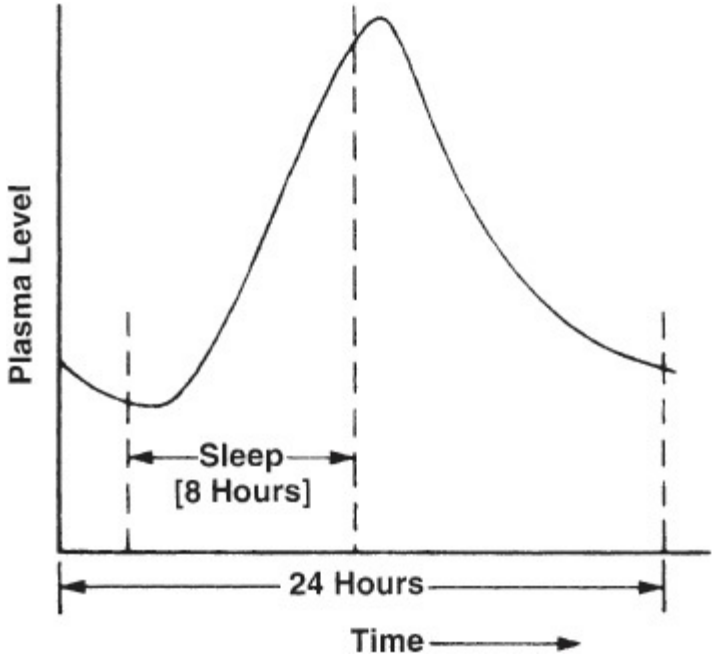
465. A 28-year-old woman presents with complaints of vision changes, frequent pressure-like headaches, polyuria, and polydipsia. An MRI of the brain showed a tumor at the posterior pituitary stalk. Which hormone abnormality would be expected?

a. Decreased ACTH leading to secondary adrenal insufficiency
b. Decreased ADH leading to diabetes insipidus
c. Decreased luteinizing hormone (LH) leading to irregular ovulation
d. Decreased α-melanocyte-stimulating hormone leading to changes in skin pigmentation
e. Decreased TSH leading to hypothyroidism

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 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. Cortisol
b. Estrogen
c. Insulin
d. PTH
e. Thyroxine

468. 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 U of insulin per day. Which aspect of glucose transport is enhanced by insulin?

a. Transport across the tubular epithelium of the kidney
b. Transport against a concentration gradient
c. Transport into adipocytes
d. Transport into the brain
e. Transport through the intestinal mucosa

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 potbelly 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. Monoiodotyrosine
b. Thyroglobulin
c. Thyroid peroxidase
d. Thyroxine
e. Triiodothyronine

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 and TSH. Thyroid hormone therapy is ordered. Physiologically active thyroxine exists in which of the following forms?

a. As a glucuronide
b. Bound to albumin
c. Bound to globulin
d. Bound to prealbumin
e. Unbound

471. A 35-year-old woman presents to her primary care physician with weakness and fatigue for the past 6 months. Before this current episode, she used to be a very active runner, but has not had the strength or energy to work out in the last few weeks. Despite this decrease in exercise, she has lost 10 lb over this time, and also reports a decreased appetite. She has also had two presyncopal episodes in the last 2 weeks and has noticed that her skin appears darker than usual. Laboratory tests show:

Sodium: 125
Potassium: 5.5
Renin: Elevated

Aldosterone: Suppressed
Serum ACTH: >100 pg/mL
ACTH stimulation test: Cortisol 10 µg/dL

What is the best description of the patient's fluid and osmolarity status?

a. Hyposmotic volume contraction
b. Hyposmotic volume expansion
c. Hyperosmotic volume contraction
d. Hyperosmotic volume expansion
e. Isosmotic volume contraction

472. A 3-year-old patient with DiGeorge 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. Bones
b. Intestine
c. Kidney
d. Skeletal musculature
e. Thyroid gland

473. A 20-year-old man presents with increasing daytime somnolence. A 24-hour sleep study showing a sudden onset of rapid eye movement (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. Free fatty acids
b. Growth hormone
c. Hypoglycemia
d. Hyperglycemia
e. Somatostatin

474. A 50-year-old alcoholic man presents with cirrhotic liver disease and chronic pancreatitis. He has been experiencing nausea for the past several days, and not eating. As a result of an elevation in his blood glucagon levels, which of the following will occur?

a. Inhibition of adenylate cyclase
b. Inhibition of insulin secretion
c. Inhibition of phospholipase C
d. Stimulation of gluconeogenesis in the liver
e. Stimulation of glycogenolysis in muscle

475. A patient with 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. Enhancing potassium entry into cells
c. Increasing plasma amino acid concentration
d. Reducing urine formation
e. Stimulating gluconeogenesis

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 is decreased during periods of stress.
b. It is inhibited by aldosterone.
c. It is stimulated by glucocorticoids.
d. It is stimulated by epinephrine.
e. It shows a circadian rhythm in humans.

477. A patient with tuberculosis becomes confused and complains of muscle cramps and nausea. Laboratory results show a plasma sodium concentration of 125 mEq/L, serum osmolarity of 200 mOsm/kg, urine osmolarity of 1,500 mOsm/kg, urine sodium of 400 mEq/d, and a normal blood volume. These clinical findings are consistent with which of the following?

a. Decreased secretion of aldosterone
b. Decreased secretion of ADH
c. Increased secretion of aldosterone
d. Increased secretion of ADH
e. Increased secretion of atrial natriuretic peptide

478. A 65-year-old woman with metastatic small cell lung cancer presents to the emergency department with nausea, vomiting, and tachycardia. She is diagnosed as

having Addison disease. Which of the following is most consistent with a patient in this condition?

	Serum Na	Serum K	Blood glucose	Blood pressure
a.	Increased	increased	decreased	decreased
b.	Decreased	increased	increased	decreased
c.	Decreased	increased	decreased	decreased
d.	Increased	decreased	increased	decreased
e.	Decreased	decreased	increased	increased

479. An abdominal computed tomography (CT) in a 50-year-old patient with Conn's syndrome (primary hyperaldosteronism) shows multiple small adrenocortical masses. Which of the following clinical findings are most likely present?

a. Decreased extracellular fluid volume
b. Hyperkalemia
c. Hypertension
d. Increased concentrating ability of the kidney
e. Increased hematocrit

480. A 75-year-old woman 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. Calcitonin
b. Calcium
c. Phosphate
d. Potassium
e. Sodium

481. A 29-year-old man complains of weight gain, decreased energy, dry skin, and brittle hair for the past 6 months. He was diagnosed with hypothyroidism and started on synthetic thyroid hormone. A decrease in which of the following laboratory values would be expected as result of starting treatment?

a. Free T_4
b. Plasma cholesterol
c. Plasma iron
d. TSH
e. Vitamin A

482. A 37-year-old woman presents with exophthalmus and an enlarged thyroid gland. The levels of free thyroxine in her blood are elevated. Other clinical findings of Graves' disease include which of the following?

a. Anorexia
b. Bradycardia
c. Decreased sweating
d. Increased basal metabolic rate
e. Increased weight gain

483. A 20-year-old man with diabetes 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. Brain
c. Cardiac muscle
d. Skeletal muscle
e. 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 TSH, and decreased free T_4 levels. Which of the following is also likely to be associated with her hypothyroid state?

a. Decreased body mass index
b. Heat intolerance
c. Increased metabolic rate
d. Sleepiness
e. Tachycardia

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. Aspirin to treat fever
b. β-Adrenergic antagonist therapy to block sympathomimetic symptoms
c. Iodine followed by propylthiouracil to block release and synthesis of thyroid hormone
d. Oral hydration to correct volume depletion
e. T_3 administration to induce negative feedback inhibition of T_4

486. A 13-year-old boy presents for short stature. He was growing appropriately; however, 2 years ago, his primary pediatrician noticed he dropped two percentiles on his growth chart. The patient reports he is much smaller than his friends and has not noticed any pubertal changes such as enlargement of testes or development of axillary or pubic hair. What laboratory test abnormality would you expect to see?

a. Decreased ACTH
b. Decreased IGF-I
c. Increased gonadotropins
d. Increased growth hormone
e. Increased thyroxine

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 is suggestive of islet cell carcinoma. Which of the following best describes the islets of Langerhans?

a. They are found primarily in the head of the pancreas.
b. They contain six distinct endocrine cell types.
c. They constitute approximately 30% of the pancreatic weight.
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 diagnosis of diabetes. As a result of insulin deficiency, which of the following will most likely occur?

a. Decreased fatty acid release from adipose tissue
b. Decreased intracellular α-glycerophosphate in liver and fat cells
c. Enhanced glucose uptake and use except by brain tissue
d. Increased cellular uptake of glucose
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 total T_4, 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 an adrenocortical tumor.
b. She has been subjected to chronic stress.
c. She has been treated with ACTH and TSH.
d. She has been treated with T_3 and cortisol.
e. She is in the third trimester of pregnancy.

490. A 13-year-old girl presents for her annual sports physical exam. Her height is measured at 50 in (>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 about growth and development is most likely?

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.

491. A 57-year-old postmenopausal woman takes calcium and vitamin D supplements daily to prevent osteoporosis. Which of the following best describes vitamin D?

a. 1,25 $(OH)_2$-vitamin D production increases when PTH secretion decreases.
b. It is a water-soluble vitamin.
c. It is converted to 1,25 $(OH)_2$-vitamin D in the liver.
d. The physiologically active form of vitamin D is 1,25 $(OH)_2$-vitamin D.
e. Vitamin D deficiency is seen in areas with high sun exposure.

492. A 22-year-old woman with insulin-dependent diabetes mellitus presents to the emergency department with nausea, vomiting, and a blood glucose of 600. She is found to have diabetic ketoacidosis (DKA). Which of the following is true regarding patients with DKA?

a. Intracellular potassium levels are increased.

b. Intravenous fluids correct the acidosis.
c. Respiratory rate decreases.
d. Serum potassium levels are decreased.
e. Serum potassium levels are increased.

493. A 34-year-old patient with chronic asthma is started glucocorticoid therapy. The treatment may result in bone loss because glucocorticoids do which of the following?

a. Increase calcium absorption from the gastrointestinal tract
b. Increase osteoblast growth
c. Inhibit bone formation
d. Inhibit bone resorption
e. Suppress vitamin D activation

494. Radiation treatment for a pituitary tumor in an 8-year-old boy results in complete loss of pituitary function. As a result, the child is likely to experience which of the following symptoms?

a. Accelerated growth spurts
b. Hyporeflexia
c. Hyperactivity
d. Increased responsiveness to stress
e. Sexual precocity

495. A 36-year-old male computer programmer works for a company that has just been acquired in a corporate takeover. He experiences symptoms of tachycardia, palpitations, and an irregular heartbeat, particularly at night. His plasma catecholamine levels are found to be increased, which may result from which of the following?

a. Changing from the standing to the supine position
b. An increase in blood glucose
c. An increase in blood pressure
d. An increase in blood volume
e. An increase in plasma cortisol

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. Enhanced wound healing
b. Increased ACTH secretion
c. Increased corticotropin-releasing hormone (CRH) secretion
d. Increased gluconeogenesis
e. Increased insulin sensitivity in muscle

497. An 80-year-old man reports increasing dyspnea, which worsens with exertion. The cardiologist orders an echocardiogram, brain natriuretic peptide, and atrial natriuretic peptide (ANP) to evaluate possible congestive heart failure. Which of the following is most likely with ANP?

a. ANP acts only on the distal nephron to increase urine flow.
b. ANP constricts afferent renal arterioles.
c. ANP enhances ADH secretion.
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. Decreased lipolysis
c. Decreased protein synthesis
d. Hypoglycemia
e. Insulin resistance

499. Sulfonylurea treatment in a 53-year-old type 2 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. Bradycardia
b. Dry skin
c. Insomnia
d. Loss of fine motor skills

e. Satiety

500. 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 laboratory findings of hypercalcemia and elevated urinary catecholamines suggest the possibility of MEN II. Which of the following is the hallmark of pheochromocytoma?

a. Dry skin
b. Hypertension
c. Hypoglycemia
d. Lethargy
e. Weight gain

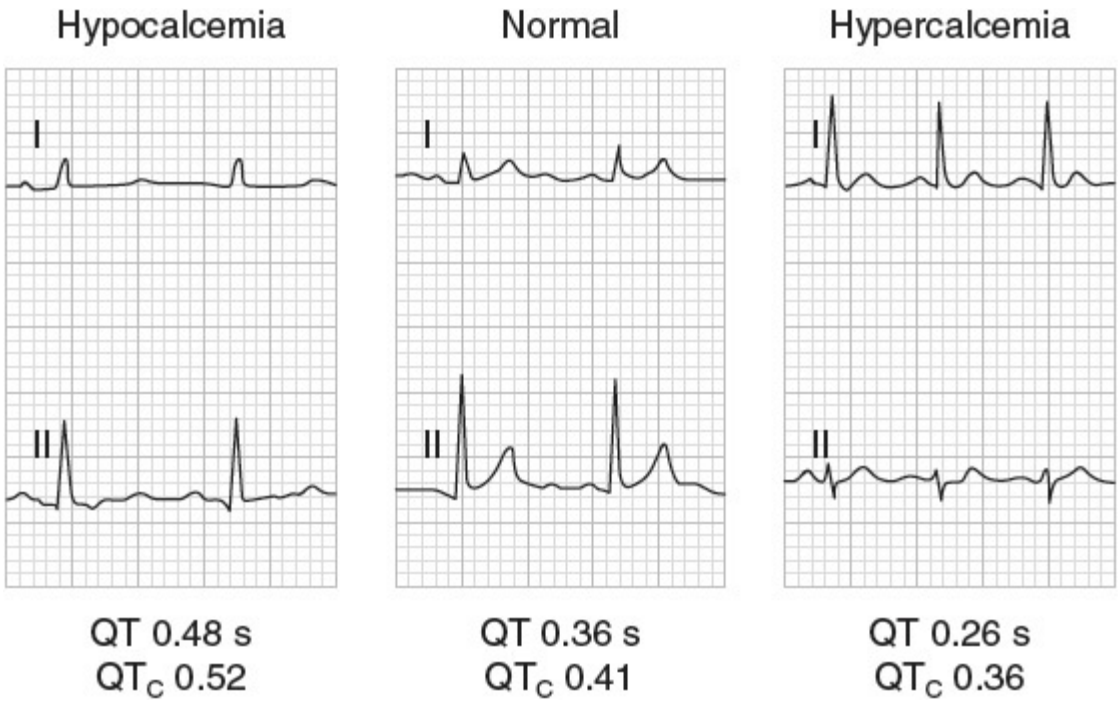
Endocrine Physiology

Answers

460. The answer is e. (*Barrett, pp 317-324. Longo, pp 2225-2227.*) 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 cyclic adenosine monophosphate (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.

461. The answer is b. (*Barrett, pp 277-279, 377.*) ADH, also called argi-nine vasopressin, is secreted from the posterior lobe of the pituitary gland (neurohypophysis) into the general circulation from the endings of supra-optic neurons in the hypothalamus. ACTH, FSH, growth hormone, and prolactin are all secreted by the anterior pituitary gland (adenohypophysis) into the portal hypophyseal circulation from the endings of arcuate and other hypothalamic neurons.

462. The answer is a. (*Barrett, pp 360-370. Kaufman, pp 88-89, 232-233.*) PTH, secreted by the chief cells of the parathyroid gland, is essential for calcium and phosphate homeostasis. PTH directly binds to receptors on osteoblasts to increase levels of intracellular cAMP, which activates a signaling pathway to stimulate osteoclastic osteolysis to liberate calcium from the bone into the blood. Osteoclasts do not have PTH receptors and are indirectly mediated by PTH via interaction with osteoblasts. PTH also increases calcium absorption from the gut, although that effect is the result of PTH-mediated increases in renal 1,25-dihydroxycholecalciferol (active vitamin D). 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. A prolonged QT interval is typical of hypocalcemia, whereas a shortened QT interval is seen with hypercalcemia.



(Reproduced, with permission, from Longo AS, Braunwald E, Kasper DL, et al. *Harrison's Principles of Internal Medicine.* 17th ed. New York: McGraw-Hill; 2008:1396.)

463. The answer is b. (*Barrett, pp 380-389. Kacsoh, pp 151-161. Kaufman, 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, explaining the patient's complaint of lactation. Human growth hormone also has intrinsic lactogenic activity, contributing to the development of gynecomastia and lactation in this male patient. Acromegaly can be caused by hypothalamic tumors that secrete growth hormone–releasing hormone (GHRH), but these are rare. Posterior pituitary releases oxytocin and ADH, which are not involved in this case. Adrenal cortex tumors release corticotropins leading to Cushing's syndrome, primary aldosteronism, or rarely virilization. Tumors of the breast would not explain this patient's skeletal features.

464. The answer is d. (*Barrett, pp 381-389. Widmaier, pp 347-349, 576.*) Growth hormone 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 IGF-I (somatomedin C) and IGF-II. Growth hormone release is stimulated by 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. Growth hormone 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. Growth hormone also has a protein anabolic effect. Growth hormone is metabolized rapidly; the half-life of circulating growth hormone in humans is 6 to 20 minutes.

465. The answer is b. (Barrett, *pp 665-668. Kacsoh, pp 274-277.*) This patient is suffering from diabetes insipidus most likely caused by a craniopharyngioma at the posterior pituitary stalk. A tumor at this location will interfere with ADH release due to compression and destruction of the axonal tracts originating in the supraoptic nucleus of the hypothalamus. Central diabetes insipidus results from insufficient release of ADH leading to polyuria, polydipsia, increased serum sodium concentration, and osmolality. Central diabetes insipidus has many etiologies, and can be treated with desmopressin (DDVAP) and ADH analog. Patients may show signs of other pituitary abnormalities based on the tumor location, but in this case, the tumor was visualized on the pituitary stalk, which carries the axons of the hypothalamus to the posterior pituitary specifically. All other hormones mentioned are secreted from the anterior pituitary.

466. The answer is c. (*Barrett, pp 338, 342-346.*) The fetal cortex synthesizes primarily dehydroepiandrosterone. Because it lacks 3β-hydroxysteroid dehydrogenase, the enzyme that converts pregnenolone to progesterone (the initial step in both glucocorticoid and mineralocorticoid synthesis). This steroid 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. (*Longo, pp 2192-2193. Barrett, pp 372-374.*) Cortisol is a 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. The other hormone options do not demonstrate diurnal periodicity over a 24-hour period.

468. The answer is c. (*Barrett, pp 316-321. Kacsoh, pp 199-205. Kaufman, pp 63-65. Longo, pp 2275-2283.*) Insulin increases glucose uptake by adipocytes. Glucose is transported into cell by either facilitated diffusion via GLUT transport proteins or secondary active transport via Na^+–glucose cotransporters. Insulin increases the number of GLUT4 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. Patients with diabetes have increased susceptibility to infections due to decreased efficacy of granulocytes despite normal number. Patients with type 1 diabetes mellitus must use insulin. They cannot use oral hypoglycemic agents because they do not have functional pancreatic β cells. Type 1 diabetes mellitus is commonly referred to as juvenile diabetes; however, it can present later in life and should not be ruled out due to patient's age.

469. The answer is b. (*Longo, pp 2224-2226. Barrett, pp 317-322, 328-329.*) 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 tyro-sine residues in thyroglobulin. The iodinated tyrosine residues gradually become coupled to form thyroxine (T_4), the major secretion product of the thyroid. Triiodothyronine (T_3) is also secreted from the thyroid, but in significantly less amount. T_3 is more potent than T_4. Monoiodotyrosine is not secreted; it is a precursor of T_3 and T_4. Thyroid peroxidase is a catalytic enzyme involved in the peroxidation, iodination, and coupling of the iodotyrosyl residues. 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. (*Barrett, pp 321-323. Kaufman, pp 81-83.*) Only the free unbound form of thyroxine is physiologically active. Circulating thyroxine can be bound to albumin, thyroxine-binding prealbumin, 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 a. (*Longo, pp 2956-2958.*) This patient has adrenocortical insufficiency, or Addison's disease, a disorder that affects the adrenal glands causing decreased production of adrenocortical hormones, including aldosterone, cortisol, and dehydroepiandrosterone. Adrenocortical insufficiency may be caused by a destructive process that directly affects the adrenal glands or by a condition that interferes with adrenocortical hormone synthesis. Autoimmune destruction of the adrenal glands is the most common cause of Addison disease in the United States and is associated with numerous other autoimmune disorders such as Hashimoto thyroiditis and polyglandular autoimmune syndromes. Patients with Addison disease commonly present with an insidious onset of fatigue and weakness associated with mucocutaneous hyperpigmentation and postural hypotension due to deficiency in both mineralocorticoids and glucocorticoids. The abnormal laboratory results are a result of decreased aldosterone production. Aldosterone is a steroid hormone that increases protein synthesis in the principal and intercalated cells of the distal tubule. Aldosterone enters principal cells and interacts with cytosolic aldosterone receptors. The aldosterone-bound receptors interact with nuclear DNA to promote gene expression. The aldosterone-induced gene products activate sodium channels (luminal surface) and sodium/potassium pumps (basolateral surface) to increase sodium reabsorption. The sodium reabsorption is balanced by the secretion of potassium (from principal cells) and hydrogen (from intercalated cells). As a result of the lack of aldosterone in adrenocortical insufficiency, patients will have a hyposmotic volume contraction as there will be a decrease in ECF volume and ECF osmolarity caused by decreased Na^+ reabsorption. Also, hyperkalemia results because of decreased K^+ secretion and metabolic acidosis occurs because of decreased H^+ secretion. Addison disease may be diagnosed by serum chemistry, elevated renin levels without subsequent elevation in aldosterone, elevated serum ACTH with low levels of cortisol, and an inadequate response in cortisol production after ACTH stimulation. Hyperosmotic volume contraction (*choice c*) occurs in situations of excessive sweating. Sweat is hyposmotic due to relatively more water lost than salt. Excessive sweating therefore raises ECF osmolarity and decreases ECF volume. Hyperosmotic volume expansion (*choice d*) occurs with excessive NaCl intake; NaCl raises the osmolarity of the ECF causing water to shift from the ICF to the ECF causing volume expansion. Hyposmotic volume expansion (*choice b*) occurs in syndrome of inappropriate antidiuretic hormone secretion (SIADH) where the ECF osmolarity decreases and ECF volume increases due to excess water reabsorption. Isosmotic volume contraction (*choice e*) is characteristic of patients suffering from gastroenteritis and diarrhea, in which the fluid lost is generally isotonic.

472. The answer is a. (*Longo, pp 413, 2057. Barrett, pp 390-392. Kacsoh, pp 156-159.*) The main function of the parathyroid gland is to maintain a constant ionized calcium level in the extracellular fluid. PTH increases plasma calcium levels most rapidly by mobilizing bone calcium. PTH binds to receptors on osteoblasts, which in turn activate osteoclastic activity to release calcium into the bloodstream. PTH also increases renal tubular reabsorption of calcium, but this is not the most rapid action. PTH activates the conversion to functional vitamin D at the kidney, which leads to increased calcium absorption in the intestine, but this does not occur rapidly and is dependent on dietary intake of calcium.

473. The answer is c. (*Barrett, pp 384-385. Kaufman, p 71.*) Synthesis and secretion of growth hormone by the anterior pituitary is regulated by a variety of metabolic factors, many of which act to alter the balance between release of GHRH and somatostatin (SS) from the hypothalamus. Among the stimuli that increase

growth hormone secretion are (1) conditions in which there is a deficiency of energy substrate (eg, hypoglycemia, exercise, and fasting); (2) stressful stimuli (eg, fever and various psychological stresses); (3) an increase in arginine and some other amino acids (eg, protein meal); (4) glucagon; (5) L-dopa and dopamine receptor agonists; (6) estrogens and androgens; and (7) going to sleep. Stimuli that decrease growth hormone secretion include somatostatin, REM sleep, glucose, cortisol, free fatty acids, and growth hormone itself.

474. The answer is d. (*Barrett, pp 328-330. Kaufman, pp 114-117. Longo, pp 1969-1973.*) 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 cAMP, 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 b. (*Barrett, pp 318-321.*) 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; however, 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 e. (*Barrett, pp 345, 349, 351-354.*) The secretion of ACTH occurs in several irregular bursts during the day; the peak occurs early in the morning prior to wakening and the minimum secretion in the evening. Circulating cortisol levels reflect the diurnal pattern. ACTH secretion is mediated by hypothalamic secretion of CRH into the hypothalamichypophyseal portal capillary system. In addition to basal rhythm, physical or mental stress will lead to increased ACTH secretion within minutes. ACTH is also regulated through feedback inhibition by its end products, such as glucocorticoids. Aldosterone, a mineralocorticoid, is not controlled by ACTH. Epinephrine also does not have any effect on ACTH secretion.

477. The answer is d. (*Barrett, pp 246-247, 378-379, 729-730. Kaufman, pp 77-78, 226-228. Widmaier, pp 502-503.*) An increase in ADH is associated with isovolemic, hypotonic hyponatremia, and an increase in both urine osmolarity and urine sodium. The etiology of 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 c. (*Barrett, pp 360-361. Kaufman, pp 89-91. Widmaier, p 344.*) This patient has primary adrenal insufficiency due to bilateral adrenal destruction from a metastatic lung cancer. These patients are tired, chronically hypotensive, and lose weight due to mineralocorticoid and glucocorticoid deficiencies. The deficiency of cortisol results in hypoglycemia. The deficiency of the mineralocorticoids (aldosterone) results in hyponatremia and hyperkalemia from the loss of aldosterone's effect on the distal tubules of the kidney and subsequent volume depletion that takes place. Insulin production increases to correct hyperkalemia, which further contributes to hypoglycemia.

479. The answer is c. (*Barrett, pp 354-360. Kacsoh, pp 406-409, 417-418.*) 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 c. (*Barrett, pp 367-370. Kaufman, pp 87-88, 233-234.*) 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 b. (*Barrett, pp 458-459, 308-313. Kacsoh, pp 338-343.*) Thyroid hormones are considered calorigenic because they increase the O_2 consumption in almost all tissues except the brain, testes, uterus, lymph nodes, spleen, and anterior pituitary. In primary hypothyroid patients, one would expect increased TSH and decreased free T_4. Once corrected with thyroid hormone therapy, TSH and T_4 will normalize. With adequate circulating levels of thyroid hormone, the plasma cholesterol decreases because there is an increase in low-density lipoprotein receptors on hepatic cells, which increases hepatic removal of cholesterol from circulation. Decreased levels of cholesterol can be seen before the metabolic rate rises, which indicates the independent action of the stimulation of O_2 consumption. Thyroid hormones are required for the conversion of carotene to vitamin A; therefore, with adequate circulating T_3 and T_4, vitamin A levels will increase. In hypothyroid patients, accumulation of carotene in the bloodstream leads to yellowish tint of the skin. Plasma iron concentration relies heavily on the daily intestinal absorption of iron, the state of the iron stores in the body, and erythropoiesis in the bone marrow. Iron levels are usually relatively stable in the body, but hypothyroid patients can suffer anemia due to decreased absorption of iron and folate. With adequate levels of thyroid hormone, one would expect an increase in plasma iron levels and see increased erythropoiesis.

482. The answer is e. (*Barrett, pp 308-313. Kaufman, pp 78-81. Longo, pp 2233-2237.*) Graves' disease is an autoimmune disease, accounting for 60% to 80% of hypothyroid cases; it occurs more commonly in women. Antibodies target the TSH receptor to stimulate increased production of T_3 and T_4, thus increasing circulating levels of thyroid hormone. As a result, the basal metabolic rate can increase 60% to 100% above normal. Thyroid hormone stimulates nuclear transcription of a large number of genes in many cells of the body, leading to increased functional cell activity and metabolism. The increased metabolic activity in patients with hyperthyroidism is accompanied by increased food intake, yet decreased body weight. The generalized increase in cellular activity results in increased sweat production and increased heart rate. Exophthalmos, protrusion of the eyeballs, occurs as result of swelling of tissues in the orbits.

483. The answer is b. (*Barrett, pp 320-328.*) 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. (*Barrett, pp 309-313. Kaufman, 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. (*Barrett, pp 309-313. Kaufman, pp 82-83.*) Thyroid storm is an exaggerated manifestation of hyperthyroidism. Thyroid storm is a medical emergency and mortality is high (20–50%) even with correct treatment. After primary stabilization of the airway, breathing and oxygenation, circulation, and fluid balance, treatment includes administration of beta-blockers (eg, propranolol) to block adrenergic effects such as tachycardia, arrhythmias, myocardial infarction, and cardiovascular collapse. Beta-blockers also prevent peripheral conversion of T_4 to the more potent T_3. Propylthiouracil (PTU) or methimazole is given promptly to block synthesis of new thyroid hormone. Only after PTU has been in the patient's system for approximately 2 hours can iodine be given. If iodine is administered before PTU, more thyroid hormone will be synthesized, worsening the patient's condition. Aspirin displaces T_4 from the thyroid-binding protein; therefore, acetaminophen is the preferred treatment for fever. T_3 and T_4 inhibit the release of thyrotropin-releasing hormone from the hypothalamus, which regulates TSH secretion from the anterior pituitary. T_3 and T_4 should not be administered during thyroid storm. The patient should receive hydration; however, this is an emergent situation, and therefore two 14-gauge IVs should be started to initiate circulatory access and IV hydration.

486. The answer is b. (*Barrett, pp 380-387. Kacsoh, pp 304-306.*) Short stature is a common complaint seen by pediatric endocrinologists and is most likely due to growth hormone deficiency. Usually it is suspected once when a child drops two percentiles on the growth chart. Growth hormone stimulates bone growth and advancement of bone age. Severe cases of growth hormone deficiency lead to dwarfism; milder cases lead to short stature. Growth hormone is difficult to measure in a patient as it is pulsatile and usually highest in concentration around 3 to 4 AM. Therefore, it is not a reliable test for measuring a patient's growth hormone level. Instead IGF-I, a growth factor whose secretion is stimulated by growth hormone, is used because its levels are relatively stable and easy to measure. A patient with growth hormone deficiency will have a decreased level of IGF-I. This can be easily treated with growth hormone injections during childhood until the epiphyseal plates close (around the same time as puberty). Hypothyroidism can also be a cause of poor growth in children; therefore, TSH, free T_4, and T_3 should be part of the assessment. Cushing's syndrome, elevated ACTH, is a very common cause of growth failure in children. ACTH, cortisol, and electrolyte levels should be part of the evaluation. In female patients, a karyotype is ordered to rule out Turner's syndrome. This patient has not started pubertal development as evidenced by no change in testicular volume or development of secondary sexual hair. Therefore, his gonadotropins (FSH and LH) are probably not elevated. Sex hormones can induce growth hormone secretion, which likely contributes to the elevated levels of growth hormone during puberty leading to the growth spurt.

487. The answer is e. (*Barrett, pp 315-317. Kaufman, pp 70-71.*) 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. (*Barrett, pp 318-324. Kaufman, pp 65-69.*)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 e. (*Barrett, pp 424-426.*) 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 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. Elevated blood pressure is expected in the third trimester of pregnancy due to increased fluid. However, in most pregnant women, blood pressure actually decreases during the second trimester.

490. The answer is a. (*Barrett, 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 IGF-I increases throughout childhood and stimulates growth hormone's peripheral actions, such as cell proliferation and growth in many different cell types, including chondrocytes within growth plates. IGF-I is often measured instead of growth hormone, because growth hormone is released in a pulsatile fashion with a half-life of 14 minutes. IGF-I stays in the system much longer and, therefore, is a more reliable way to measure than the growth hormone. 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.

491. The answer is d. (*Barrett, pp 387-389. Widmaier, pp 354-355.*) 1,25 (OH)2-vitamin D is the physiologically active form of vitamin D and the conversion to this form occurs in the kidney, not in the liver. It is a fat-soluble vitamin with metabolism occurring in the skin with exposure to sunlight. When PTH secretion increases, so does the production of 1,25 (OH)2-vitamin D.

492. The answer is e. (*Longo, pp 2282-2284. Barrett, pp 340-343.*) Patients with DKA have an increased serum potassium at presentation. This is not due to an excess of potassium stores, but is the result of the shift of potassium out of the cells and hydrogen ions into the cells as intracellular buffering to reduce the acidosis. Thus, intracellular potassium is actually low and needs to be replaced as the acidosis resolves. Kussmaul respirations (rapid, deep breathing) occur as carbon dioxide is exhaled. While IV fluids help with the intravascular volume depletion that occurs with DKA (due to glucosuria), only insulin therapy can correct the acidosis.

493. The answer is c. (*Longo, pp 1641, 2365-2367. Barrett, 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 b. (*Barrett, pp 396-397, 404-409. Kaufman, pp 72-76. Le, p 325.*) Radiation treatment likely produces panhypopituitarism in the young child. Sexual maturation and growth during development will not occur because of low levels of growth hormone, FSH, LH, IGF-I, TSH and thyroid hormones, and gonadal hormones. The cortisol response to stress is decreased due to low ACTH levels. The decrease in TSH and thyroid hormones causes hypoactivity, lethargy, fatigue, weakness, and decreased reflexes.

495. The answer is e. (*Barrett, 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 d. (*Barrett, pp 366-372. Kaufman, pp 89-91. Widmaier, p 344.*) 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–insulinrequiring cells. Cortisol retards wound healing. It also decreases CRH and ACTH secretion by feedback inhibition.

497. The answer is d. (*Barrett, pp 460-462, 723. Widmaier, pp 509-510.*) 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 e. (*Barrett, pp 400-404. Kaufman, pp 74-75.*) 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. (*Barrett, pp 344-346, 353-354. Kaufman, pp 69-70. Widmaier, p 580.*) 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, convulsion, and loss of consciousness. Increased sympathetic activity can produce sweating, tachycardia, hunger, and anxiety.

500. The answer is b. (*Longo, pp 2269-2273. Barrett, pp 360, 642. Kaufman, 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 extra-adrenal, 10% are malignant, and 10% are familial, inherited as an autosomal dominant trait either alone or in combination with MEN II.

Bibliography

Barrett KE, Barman SM, Boitano S, Brooks HL, eds. *Ganong's Review of Medical Physiology*. 24th ed. New York, NY: The McGraw-Hill Companies, Inc.; 2012.

Farrokhi F, Vaezi MF. Idiopathic (primary) achalasia. *Orphanet J Rare Dis*. 2007; 2:38-46. Available at: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2040141/pdf/1750-1172-2-38.pdf.

Kacsoh B. *Endocrine Physiology*. New York, NY: The McGraw-Hill Companies, Inc.; 2000.

Kaufman MS, Stead LG, Rusovici A. *First Aid for the Medicine Clerkship*. 3rd ed. New York, NY: The McGraw-Hill Companies, Inc.; 2010.

Klabunde RE. *Cardiovascular Physiology Concepts*. 2nd ed. Philadelphia, PA: Lippincott Williams & Wilkins/Wolters Kluwer; 2011.

Le T, Bhushan V, Kulkarni VT, Sochat MM. *First Aid for the USMLE Step 1 2013*. New York, NY: The McGraw-Hill Companies, Inc.; 2013.

Levitzky MG. *Pulmonary Physiology*. 7th ed. New York, NY: The McGraw-Hill Companies, Inc.; 2007.

Longo DL, Fauci AS, Kasper DL, Hauser SL, Jameson JL, Loscalzo J, eds. *Harrison's Principles of Internal Medicine*. 18th ed. New York, NY: The McGraw-Hill Companies, Inc.; 2012.

Manson W, Hemphill RR, Kempton CL. Hemophilias and von Willebrand Disease. In: Tintinalli JE, Stapczynski JS, Cline DM, Ma OJ, Cydulka RK, Meckler GD, eds. *Tintinalli's Emergency Medicine: A Comprehensive Study Guide*. 7th ed. New York, NY: McGraw-Hill; 2011: Chapter 230. Available at http://www.accessmedicine.com/content.aspx?aID=6386401. Accessed February 3, 2013.

McPhee SJ, Hammer GD. *Pathophysiology of Disease: An Introduction to Clinical Medicine*. 6th ed. New York, NY: The McGraw-Hill Companies, Inc.; 2010.

Widmaier EP, Raff H, Strang KT. *Vander's Human Physiology*. 12th ed. New York, NY: The McGraw-Hill Companies, Inc.; 2011.

Index

Please note that index links point to page beginnings from the print edition. Locations are approximate in e-readers, and you may need to page down one or more times after clicking a link to get to the indexed material.

Note: Page numbers followed by "*t*" indicate table and page numbers followed by "*f*" indicate figure.

A

Abdomen, CT scan, 267
Abdominal aorta, 267
Abdominal bloating, complaint of, 339
Abdominal computed tomography (CT), 457
Abdominal cramps, complaint of, 339
Abdominal distension, 340, 353
Abdominal pain, 392, 462
Abdominal surgery
  patient's physiological dead space, 207
    Bohr equation, 207
  preoperative evaluation and testing, 207
Aβ fibers, demyelination of, 160
Accommodation reflex, 33
ACE inhibitor, 414
Acetazolamide, 391
Acetylcholine, 31, 198, 386
  metabolic breakdown of, 191
Acid–base balance and disorders, 15-19, 69, 115
  characteristics of, 19*t*
  compensation for, 19
Acid–base/electrolyte disorder, 337
  colon, 337
Acquired immunodeficiency syndrome (AIDS), 210, 227, 451
Actin–myosin interactions, 203
Action potential, 27-29
  components of, 28*f*
Activated partial thromboplastin time(aPTT), 126
Activated protein C resistance, 132
Active transport, 1
Acute flaccid paralysis, 87
Acute promyelocytic leukemia
  all-*trans* retinoic acid (ATRA), 77
  questions regarding, 77
  treatment of, 77
Addison's disease, 12, 457, 462, 468
Adenohypophysis, 72, 464
Adenosine, 396
Adenosine triphosphate (ATP), 196
ADH gene expression, 399
Adipocytes, transport, 454
Adrenal cortex gland, 12, 73*t*
Adrenal glands, 73*t*
Adrenal medulla, 73*t*
Adrenocorticotropic hormone(ACTH), 389
Adult circulatory pattern, transitional circulation, 290
Aerobic exercise, 231, 283
Aerobic metabolism, 102, 118, 199
Afferent arterioles, 388
  dilation of, 377
After-depolarization, 29

After-hyperpolarization, 29
Airway obstruction, 244
  reversibility of, 244
Airway resistance, 49, 232, 241, 242
  effect of, 50
  measurement of, 50
  respiratory muscles, oxygen consumption of, 224
Airway smooth muscle, construction of, 164
Alcohol abuse, 340
Alcoholic cirrhosis, 347
Aldosterone, 12, 15, 68, 118, 397, 416
  concentration, 397
  principal function of, 119
  receptor, 423
  secretion of, 12, 383, 408
Aldosterone-stimulated proteins, 416
Allopurinol, 190, 197
All-*trans* retinoic acid (ATRA), 77
Alveolar–arterial (A–a) O_2 gradient, 221
Alveolar–arterial PO_2 difference (A–a PO_2), 225, 252
Alveolar–capillary interface, 256
Alveolar-capillary (A-C) membrane, 238, 255
  oxygen transfer, 238
Alveolar dead space, 45, 237
Alveolar hyperventilation, causes of, 23*t*
Alveolar hypoventilation, 219, 242
  causes of, 22*t*
  chronic obstructive pulmonary disease (COPD), 219
Alveolar hypoxia, 115, 123
Alveolar oxygen tension, 210, 221, 249
Alveolar septal departitioning, 246
  in emphysema, 216
Alveolar ventilation, 47, 209, 210, 211, 228, 240, 241, 254
  breathing, 211
  CO_2 production, rate of, 210
  hypoventilation, 241, 242
  pulmonary exercise stress testing, 228
Alveoli, 45
Alzheimer disease, 39, 166, 171, 180, 187
  questions regarding, 165
Amaurosis fugax, 180
Amniotic fluid, 108
α-Adrenergic antagonist, 279
α-Amylase digestion, 359
α-Glycerophosphate, 474
α-Motoneurons, 79, 144, 152, 170, 199
Anaerobic threshold, 209, 240, 255
Anaphylactic shock, 281
Anaphylaxis, 320
Anemia, 133, 137, 138, 163, 270
Anemic hypoxia, 50, 242
Angina, 275
Angiotensin, 415
Angiotensin-converting enzyme (ACE), 12, 94, 112, 304, 324, 377
Angiotensin II, 117, 394, 403, 417, 422
Angiotensinogen, 385
Angiotensin receptor antagonist, 388
Angular gyrus, 144

Anion gap, 100, 107, 111, 116, 382
Ankle sprain, 78
Ankylosing spondylitis (AS), 200
Anorexia nervosa, 432, 461
Anosmia, 39, 158
ANP secretion, increase of central venous pressure due to, 463
Anterior infarction, 285
Anterior pituitary, 452
Anterior pituitary tumor, 456
  wound healing and hypertension, 456
Anteroposterior angulation, 254
  Antidiuretic hormone (ADH), 11, 13, 68, 72, 110, 289, 380, 418, 451, 464
  diabetes insipidus, 452
Antinuclear antibodies (ANAs), 89
Antiphospholipid antibody syndrome, 148
Antiproteinase-3 ANCA, 398
Antrum, alkalinization of, 337, 357
Anxiety disorder, 463
Aorta, left, 263
Aortic arch, 57
Aortic regurgitation, 265
  diastolic murmur, 265
Aortic stenosis, 136, 276, 301, 307, 314
Aortic valve, 313
  electrocardiogram (ECG), 261
Apolipoprotein, 187
Arginine vasopressin, 68, 106, 121, 464
Arterial blood, 206, 301
  gases, 100, 105-107, 206, 225
  pressure, 55-61, 306
Arterial carbon dioxide tension, 226
Arterial compliance, 325
Arterial hypoxia, 310
Arterial oxygen saturation, 256, 259
Arterial oxygen tension, 228, 249
  carbon monoxide poisoning, 228
Arterial PO_2, 209
  shortness of breath, 222
Arterial/venous systems, 325
  pressure-volume curves for, 287
Arteries, stiffening of, 275
Arteriolar vasoconstriction, 324
Arterioles, 151
Arteriosclerosis, 7, 284
Aspartate aminotransferase, 81
Aspirin, 129, 197
  sensitivity, 209
Asthma, 132
  acute, 232
  airflow, 210
  airway resistance, 232
  exacerbation of, 210, 234
  lung volumes, 232
Asthmatic bronchitis, 107
Asthmaticus respiratory failure, 209
Ataxia, 169
Atherosclerosis, 309

Atherosclerotic renal vascular disease (ARVD), 386
Atrial depolarization, 323
Atrial fibrillation, 94, 306, 315
Atrial natriuretic peptide (ANP), 12, 68, 69, 463
Atrial pressure, left, 269
Atrial septal defect, 295
Atrial systole, 55
Atropine, 161, 308
Auditory hair cell, 37*f*
Autoimmune destruction, 468
Autoimmune hepatitis, 81, 89
Autonomic nervous system (ANS), 39
  effector organ responses to, 40*t*-41*t*
Avitaminosis A, 157
AV node, 300
  cardiac action potential, 276

B

Babinski sign, 171
Baclofen, 152
Ballismus, 34*t*
"Bamboo spine", 201
Baroreceptor reflex, 325
Baroreceptors, 57
Basal electrical rhythm (BER), 355
Basal ganglia, 31, 33, 169, 171, 183
  diseases, 34*t*
Basalis of Meynert, 187
Basal laminas, 7
Beats per minute (bpm), 278
Beck triad, 318
Bell palsy, 182
Bence Jones proteins, 399
Benign prostatic hypertrophy, 442
Benzodiazepines, 101, 180
Bernard–Soulier syndrome (GpIb deficiency), 137
Beta-1 adrenergic receptors, 411
β-Dystroglycan, 192
Beta-hexosaminidase A, 179
Bicarbonate, contained in bile, 352
Bicarbonate ion, reabsorption, 399
Bile, 65
Bile acids, 369
  conservation of, 363
  function of, 345
  pool size, 345
Bile ductm obstruction of, 350
Biopsy, 338
  segments, 353
Biphasic deflection, 334
Bipolar disorder, 390
2,3-Bisphosphoglycerate, 123, 131, 137, 139, 142
Blood analysis, 386, 388, 392
Blood–brain barrier, 116, 167, 168
Blood gases reveal hypoxemia, 225
Blood pressure
  arterial, 55-61
  heart rate, 282

Blood–testis barrier, 71
Blood transfusion, 126
Blood urea nitrogen (BUN), 78, 376
Blood vessels, occlusion of, 61
Body mass index (BMI), 79, 231
Body temperature and pressure, saturated (BTPS), 43
Bohr effect, 25, 26
Bohr equation, 47, 237
Bone marrow disease, 138
Bone matrix, calcification of, 192, 200
Bones, hypoparathyroid state, 455
Botulinum toxin, 87
Botulinum type A (Botox), 79
Bowel movements, in newborns, 350
Bowel obstruction, 353
Bowel wall distention, contractile activity, 336
Bowman capsule, 67
Boyle's law, 47
Bradycardia, 191
  premature ventricular complexes (PVCs), 277
Bradykinesia, 161, 167
Bradykinin, 186
Brain
  diabetes, 458
    type II, 283
  functions of major part of, 32*t*
  tumor, 451
Breast
  cancer, 78
  development, 439
  feeding, 200
  tenderness, 436
    menstrual period, 436
Breathing
  elastic work of, 229
  mechanics of, 47-50
Breath, shortness of, 207
Breckenridge, 394
Bronchial breath, sounds and crackles, 231
Bronchial smooth muscle, 229
Brown-Séquard syndrome, 145, 168

C

Calcitonin, 75, 75*t*
Calcium
  Ca^{2+} resorption, 451
  calcium pyrophosphate dihydrate (CPPD), 194
  channels, 298
  concentration of, 290
  conductance, 312
  homeostasis, 75
  osteoporosis, 461
Calmodulin, 290, 330
Campylobacter jejuni, 160, 181
Capillary fluid balance, 61-62
  Starling law of, 62
Capillary hydrostatic pressure, 62, 416
Capillary oncotic pressure, parasternal lymph nodes, 223

Carbamazepine, 122
Carbaminohemoglobin, 26, 137-138
Carbohydrate digestion, 65
Carbohydrate-rich meal, 349
Carbon-di-oxide (CO_2), 128
  retention, 225, 252
  transport, in the blood, 26, 137
Carbonic anhydrase, 394, 422
  inhibitors, 394
Carbon monoxide poisoning, 111, 130, 138, 228
Carboxyhemoglobin, 228, 256
Carcinoid tumors, 373
Cardiac allografts, 303
Cardiac catheterization, 127, 265, 268, 277
Cardiac cycle
  mechanical events of, 55, 56*f*
  physical examination, 292
Cardiac disease, 354
Cardiac efficiency, 279
Cardiac energy consumption, 318
Cardiac enzymes, 263
Cardiac examination, 291
Cardiac failure, chronic, 399
Cardiac function, 280
  curves, 296
Cardiac murmurs
  diastolic, 61
  systolic, 61
Cardiac muscles
  action potential of, 52*f*
  characteristic of, 44*t*
Cardiac output, 270, 321
  pulmonary hemodynamics and lung fluid, 227
  septic shock, 255
  shock, 281
Cardiac output (CO), 25, 109, 301
Cardiac oxygen consumption, 317
Cardiac remodeling, stabilization of, 267
Cardiac stress testing, 296
Cardiac tamponade, 318
Cardiac transplant patients, 266
  stroke volume, 266
Cardiac/venous function, baseline and exercise levels, 288
Cardiac/ventricular function, 326
Cardiology examination, 270
Cardiomyopathy, 294
Cardiovascular complications, 416
Cardiovascular physiology
  arterial blood pressure and cardiac output, 55-61
  capillary fluid balance, 61-62
  cardiac cycle, 55
  electrical activity of the heart
    action potential, 52-53
    electrocardiogram, 54-55
  femoral popliteal bypass, 289
  pressure–volume loop, 289
  regional circulations, 62
    characteristics of, 63*t*-64*t*

Cardiovascular reserves, 280
Cardiovascular responses, 281
Carnitine palmitoyltransferase II (CPT II) deficiency, 194
Carotid artery blood, 288
Carotid body chemoreceptor reflex, 213
Carotid endarterectomy, 288
Carotid sinus, 57
Carpopedal spasm, 106
Cartesian coordinate system, 333
Cataracts, 7
Catecholamine, 172
Cell arteritis, 83
  Cell-to-cell communication, 7
Cellular physiology
  intercellular connections and communication, 7-9
  membrane transport mechanisms, 1-7
Cell volume, 6*f*
Central nervous system disorders, 121, 152
Central venous pressure, 268, 297, 312
Cerebellum, 88
Cerebral cortex, 249
Cerebrospinal fluid (CSF), 146, 168
Charcot–Marie–Tooth (CMT) disease, 78
Chemotherapy, 78
Chest, 47
  discomfort, complaints of, 272
  pain, 263, 278, 293, 335
  wall recoil, 252
    tidal breath, 224
Chewing, 62
Chloride shift, 26
Chlorpromazine, 433
Chlorpropamide, 122
Cholecystectomy, 272
  heart rate, 272
  shortness of breath, 231
Cholecystokinin contraction, 362
Cholesterol, loss of, 345
Choline phospholipid, 123
Chromophores, 33
Chromosomal analysis, 438
Chronic bronchitis, 130, 141
Chronic obstructive pulmonary disease (COPD), 96, 98, 161, 219, 221
  alveolar hypoventilation, 219
  cigarette smoking, 242
Chylomicrons, 351, 371
Chyme, 65
Cialis®. *See* Tadalafil
Cigarette smoking, 242
Cimetidine, 387
Circadian rhythm, 152
  in humans, 456
Clostridium, 87
Clouston syndrome, 7
Clumsiness, 219
Cobalamin, 119, 369
Cobalamin-intrinsic factor binding, 349
Cochlea, 156

Colchicine, 197
Colon, 353
  absorptive capacities, 347
  acid-base/electrolyte disorder, 337
  cancer, 80
  functions of, 66
  short-chain fatty acids (SCFAs), 346
Colonic bacteria metabolize lactose, 364
Colonoscopy, 80
Colorado, 394
Coma, ethanol-induced, 103
Computed tomography (CT), 83
Confusion, 213, 274, 383
Congenital heart disease, history of, 292
Congestive heart failure (CHF), 216, 273, 396
  cardiac contractility, 218
  cardiac transplantation surgery, 218
  diagnosis of, 277
  digitalis administration, 273
  left atrial pressure (LAP), 218
  paroxysmal nocturnal dyspnea, 223
  physician complaining, 277
  pulmonary capillary hydrostatic pressure, 216
  pulmonary edema, 216
  shortness of breath, 218
Connexins, 7, 86
  mutations, 7
Connexons, 7, 86
Conn's syndrome, 457, 471
Contraceptives, 435
Conventional esophageal manometry, 335
Coronary blood flow, 275, 322
  abnormalities in, 313
Coronary blood redistribution, 293
Coronary occlusion, 132
Coronary reserve, 332
Coronary vasospasm, 332
Cor pulmonale, 115
Corpus luteum, 436
  ovary, 449
  progesterone, secretion, 438
  progesterone to sustain, 440
Cortical collecting tubule, 399
Corticoreticular fibers, 148
Cortisol, 74, 453, 477
  administration of, 462
Cough, 244
  airway radius, 215
  chronic, 350
  shortness of breath, 225
Coumadin, 128
Coxsackie B virus, 293
Creatine, 191
Creatinine, 387
  clearance, 404
Crohn disease, 119
Cross-bridge cycling, 43, 89, 189
Cushing's syndrome, 460, 465

Cushing triad, 322
Cutaneous vasoconstriction, 124
Cyanosis, 141-142, 272, 326
Cyclic adenosine monophosphate (cAMP), 464
Cyclic guanosine monophosphate (cGMP), 77
Cystinuria, 410

D

Dalton's law, 43
Dark patches, 462
Dehydration, 12, 458
Dehydroepiandrosterone, 453
Dementia, 187
Desmopressin, 466
Desmosomes, 7
Diabetes
  diagnosis of, 460
  insulin deficiency, 460
  screening, 454
Diabetes insipidus (DI), 12, 93, 110, 420
Diabetes mellitus, 419
  history of, 291
  type 1, 122, 336, 395
    questions regarding, 165
  type 2, 79, 88, 94, 102, 283, 351, 400
    insulin-dependent, 106
Diabetic ketoacidosis (DKA), 100, 111, 461
Diacylglycerol (DAG), 84
Dialysis, 78
  peritoneal, 82
Diamox inhibit acid secretion, 423
Diaphoresis, 275, 279
Diaphragm, 47
Diaphragmatic respiration
  in extrauterine life, 248
  PaO_2 increases, 220, 248
Diarrhea, 93, 97, 113, 114, 118, 131, 340, 345, 392
  filtered load of HCO^-_3, 393
Diastole, beginning, 292
Diastolic dysfunction, 292
Diastolic pressure, 265
Diazepam, 180
Dietary deficiency, 140
Dietary fat, 351
Diffusing capacity, 216
Diffusion
  definition of, 1
  kinetics of, 2
  types of, 1
DiGeorge congenital thymic aplasia, 455
Digoxin, 110
Dihydrotestosterone, 438
  production of, 442
Dilated cardiomyopathy, 332
Dilated intestine, 353
Dipalmitoylphosphatidylcholine, 123
Diphyllobothrium latum, 119, 356
Diplopia, 162

Dipyridamole, 331
Distal nephron, 391, 421
  sodium concentration, 398
Distal tubule, 388
Distension-mediated vago-vagal reflexes, 358
Diuretic therapy, 420
Dizziness, 219, 310, 377, 462
Dopamine, 161, 439
  prolactin secretion, 439
Dromotropic effect, 308
Drug abuser, 271
Dry inspired air, PO_2 of, 206
Dry lips, physical examination, 337
Dry skin, 463
Duchenne muscular dystrophy, 193
Ductus arteriosus, 325, 328
  functional closure of, 290
Duodenum, 339, 349
Dysfunctional central chemoreceptors, ventilatory response test, 222
Dysgeusia, 158, 178
Dysmetria, 169
Dysphagia, 341
Dyspnea, 206, 213, 285, 294, 310, 463
  airway radius, 215, 244
  arterial pH, 220
  on exertion, 224
  insulation worker, 209
Dystroglycans, 200
Dystrophin, 200
Dystrophin–glycoprotein complex, 200

E

Ears, chambers of, 36
ECG recordings, diagnosis, 263
Echocardiography, ejection fraction, 273
Ectodermal stem cells, 373
Edema, 62
Efferent arteriolar resistance, 393
Eisenmenger syndrome, 326
Ejaculation, 71
Ejection fraction (EF), 305
Elastic fibers, 246
Electrical charge, 77
Electrocardiogram (ECG), 54-55, 94, 95, 105
Electrolyte imbalances, 162
Electromyography, 161
Electroneutral NaCl transport, 337
End-diastolic volume (EDV), 305
Endochondral ossification, 201
Endocrine physiology, 71-75
Endometrium, 446
  cyclic changes, 438
Endorphins, 186
Endoscopy, 338
Endothelin B receptor
  function, 353
  gene, 374
End-systolic volume (ESV), 305

Enterohepatic circulation, 65
Enteropeptidase, 348, 368
Enzymatic digestion, 446
Epigastric abdominal pain, 346
  nausea and vomiting, 346
Epinephrine, 15, 104, 120, 186, 187, 470
Epistaxis, 131
Epithelial sodium channels (ENaCs), 389
Epstein–Barr virus, 135, 181
Erectile dysfunction
  medicines for treatment of, 84
  questions regarding, 77
Erythrocyte sedimentation rate (ESR), 195
Erythrocytosis, 130
Erythrokeratoderma variabilis, 7
Erythropoietin, 424
Escherichia coli, 136, 337
Esophageal manometry, 360
Esophageal peristalsis, 345
Esophagogram, 341
Estriol, 446
Estrogens, 74, 442
  administration of, 438
  in women, 438
Ethylene glycol ingestion, 94
Excitation–contraction coupling, 41-43, 201
Exercise hyperpnea, 124
Exercise stress testing, for lungs diffusing capacity, 231
Exertion
  fatigue/headaches/dyspnea, complaints for, 228
  insulation worker, 209
Exertional dyspnea, 276
Exertional syncope, 316
Expiratory reserve volume (ERV), 205
Extracellular fluid (ECF), 5-7, 9, 13, 166
  composition of, 11*t*
  pH of, 257
Extracellular osmolarity, 406
Eyes
  dilation of the pupil, 176
  night blindness (nyctalopia), 157
  painless vision loss, 180
  pupil, cholinergic stimulation of, 158
  pupillary constriction (miosis), 158
  questions regarding, 157
  retinal detachment, 159
  retinal rods, 157
  stiffening of the lens, 157

F

Facial swelling, with parotitis, 340
Facilitated diffusion, 1
Factor V Leiden, 141
Fat cells, 79
Fatigue, 208, 267, 377, 382, 388, 392, 455
  complaints of, 284
  history of, 268
  peripheral chemoreceptor sensitivity, decreased, 223

Fatty acids, 88
excretion of, 339
Feces, water content of, 352
Feet, swelling of, 220
Female reproductive system, 69
Fertility center, 440
Fertilization, 447
Fetal adrenal cortical activity, 453
Fetal cardiac output, 286
Fetal CO_2, 324
Fetal Hb (HbF), 139
Fetal lungs, glucocorticoid hormones, 246
Fever, 379
alveolar–arterial PO_2 difference, 225
history of, 268
Fibromyalgia, 195
Fick equation, 2, 25, 85, 254
Fick law, 88, 246
of diffusion, 258
First-degree heart block, 300
Flatulence, 348
Fluid and electrolyte balance and disorders, 11-15
Focal adhesions, 7
Folate, 129
Fractional excretion (FE), 418
Fracture, arm, 399
Frank–Starling law, 297, 304, 311
Free water clearance, 406
Furosemide, 117

G

Gadolinium-enhanced 3D-MRA, 412
Gadolinium-enhanced three-dimensional magnetic resonance angiography, 386
Gait disorder, 146
Gallbladder, 65
contraction, 362
Gallstones, 367
Gamma-amino butyric acid (GABA), 31, 89, 159, 180
Gamma carboxyglutamate, 140
Ganglioside GM2, 159
Gangliosides, 179
Gap junction, 7, 78, 86
Gas-exchanging airways, 47
Gastric acid, 65, 352
hypersecretion, 337
Gastric bypass surgery, 351
Gastric carcinoma, 338
Gastric emptying, 349, 352, 362
hyperosmolality of, 336
Gastric emptying, of solids, 338
Gastric smooth muscle, contraction of, 357
Gastrin, 368
Gastrinoma, 357
Gastrin secretion, 355
Gastrocolic reflex, 350
Gastroenterologist administers, 347
Gastroesophageal junction, 354
Gastroesophageal reflux disease (GERD), 336

Gastrointestinal (GI) infection, 160
Gastrointestinal physiology, 62-66
Gastrointestinal (GI) tract, 336, 339
  bleeding, 338
  hormone, 339, 372
  motor activities, 352
  mucosa, 357
Gastroparesis, 336
Germ cells, 69, 71, 432
Giardia lamblia, 97
Glabellar lines, 79
Glanzmann thrombasthenia, 137
Glasgow Coma Rating, 179
Glaucoma, 180
Glomerular capillaries, 67
Glomerular filtration rate (GFR), 66, 67, 68, 321, 375, 383, 389, 396
Glomerular permeability, 409
Glomerulus, 66, 394
Glossopharyngeal nerve, compression injury, 213
Glucagon, 72, 365, 460
Glucagon-like polypeptide 1 (GLP-1), 349
Glucocorticoids, 83, 92, 476
  therapy, 461
Gluconeogenesis, 365, 477
  increased, 462
Glucose, 79, 467
  concentration, 385
  and galactose malabsorption, 340
  transport, 1, 87
Glucose-6-phosphate, 473
  deficiency of, 138
Glutamate, 80
Gluten-free diet, 350
Gluten-sensitivity enteropathy, 362
Glycogenolysis, 470
Glycosuria, 110
Golgi tendon, 167
Gonadal dysgenesis, 448
Gonadotropin releasing hormone (GnRH), 432
  secretion by hypothalamus, 433
Gout, 197
G-proteins, 39, 84, 175, 187
Gram-negative bacteria, 125
Graves' disease, 458, 472
Growth hormone–releasing hormone (GHRH), 465
Growth hormones (GH), 74*t*, 463, 465, 466
Gs protein, 320
Guillain–Barré syndrome, 100, 160, 226
Gustatory afferent nerves, 158
Gynecologist, 439

H

Hair cells
  depolarization of, 176
  questions regarding, 176, 177
Headaches, 219, 271, 279, 382, 383, 452, 463
  complaints of, 284
  hypotonic urine, 381

Hearing, sense of, 36
Heart
  cardiac cycle, 55
  electrical activity of action potential, 52-53
    electrocardiogram, 54-55
  failure of, 60
  palpitations, 277
  sounds, 270
  wall stress, 60
Heartbeat, irregular, 462
Heart block
  first-degree, 278
  third-degree, 264
Heartburn, 335
Heart failure, 270
  medications for, 290
  progression of, 304
  symptoms of, 305
Heart rate, syncope, 270
Heat stroke, 97, 113
Helicotrema, 173
Helmet cells, 136
Hematocrit, 128, 141
Hematopoietic and lymphoreticular systems
  CO_2 transport in the blood, 26
  oxygen transport in the blood, 20-25
  questions related to, 125-134
  reaction of hemoglobin and oxygen, 25-26
Hematuria, 392, 397, 398
Heme moiety, 25
Hemidesmosomes, 7
Hemiparalysis, 162
Hemispheric stroke, 83
Hemodialysis, 78, 85
Hemodynamic pressure, rapid ventricular, 264
Hemoglobin (Hb), 20, 23, 24, 102
  affinity for oxygen, 128, 239
  amino groups of, 137
  deoxygenated, 133
  oxygen transport, 248
Hemoglobinopathy, high-O_2 affinity, 130
Hemolytic anemia, 136
Hemophilia A, 126, 136
Hemoptysis, 233, 398
Hemorrhage, 57, 171
Hemorrhagic shock, 286
  low hematocrit, 286
Henderson–Hasselbalch equation, 15, 113, 114, 116, 122, 253
Henle loop, ascending limb of, 384
Heparin, 140
Hepatitis, 348
Hepatomegaly, 81
Hering–Breuer reflex, 224, 252
  control of breathing, 224
Heterophile agglutination assay, 135
Heterophile antibody, 125
High-fiber diet, 80
High-output congestive heart failure, 459

Hirschsprung disease, 374
His-Purkinje system, 299, 304
HLA-B27 antigen, 200
Holter monitor, 274
Homonymous hemianopia, 149, 171, 174
Hormone replacement therapy (HRT), 439
Hormones
  controlling calcium and phosphate concentrations, 75*t*
  influencing growth, 74*t*
Huntington chorea, 172
Huntington disease, 34*t*
Hyaline membrane disease, 124
Hydraulic conductivity, 4
Hydrostatic pressure, 243
  capillary, 62
  interstitial, 62
5-Hydroxyindoleacetic acid, 352
Hyperaldosteronism, 101, 110, 385, 425, 471
Hypercalcemia, 12, 86
Hypercapnia, arterial blood gases, 227
Hypercapnic respiratory failure, 209
Hypercholesterolemia, 459
Hypergastrinemia, 359
Hyperglycemia, 12, 79, 88
Hyperkalemia, 91, 95, 100, 111, 121, 424
  causes of, 15, 17*t*-18*t*
  conditions for, 105
  inhibition of ammoniagenesis, 424
    ammonia synthesis, 423
  medicine for treatment of, 104
  questions regarding, 104, 105
Hyperkalemic paralysis, 191, 199
Hyperkalemic renal failure, 456
Hyperlipidemia, 79, 351
Hypermenorrhea, 347
Hypernatremia, 12, 13, 164
  causes of, 14*t*
  questions regarding, 106
Hyperosmotic solutions, 6
Hyperosmotic volume expansion, 469
Hyperoxia, 250
Hyperpigmentation, 468
Hyperprothrombinemia, 141
Hyperpyrexia, 459
Hyperresonance, 208
Hypersecretion, of growth hormone, 465
Hypertension, 83, 95, 272, 274, 275, 283, 290, 351, 378, 382, 389, 395, 400, 402, 457, 463
  efferent arteriole, 389
  history of, 291
  left bundle branch block, 274
Hypertensive patient, 395
Hyperthermia, 25
  malignant, 197
Hypertonic, 428
Hypertriglyceridemia, 111
Hyperventilation, 241
Hypoaldosteronism, 40, 117, 119
Hypocalcemia, 112, 200, 358, 451

Hypochloremia, 96
Hypogeusia, 39
Hypoglycemia, 116, 456, 463, 477
Hypokalemia, 94, 96, 121, 323, 376, 402
  causes of, 15, 16*t*-17*t*
Hypokalemic alkalemia, 101
Hypokalemic alkalosis, 110
Hypokalemic paralysis, 382
Hypokinetic movement disorder, 189
Hyponatremia, 12, 13, 82, 162
  causes of, 14*t*
Hypoosmotic solutions, 6
Hypoparathyroid state, 455
Hypoperfusion, 50
Hypophosphatemia, 397
Hypoplastic left kidney, 381
Hyporeflexia, radiation treatment for, 462
Hyporeninemic hypoaldosteronism, 119
Hyposmotic volume contraction, 455
Hypotension, 83, 318, 340
Hypothalamic neurons, 72
Hypothalamus, 154, 174, 249
Hypothermia, 26, 137
Hypothyroidism, 12, 153
Hypotonic fluid, 384
Hypotonic hyponatremia, 470
Hypotonic solutions, 5
Hypouricemia, 402
Hypoventilation, 169
Hypovolemia, 12, 119
  causes of, 13*t*
Hypovolemic hypotension, 379
Hypovolemic shock, 281
Hypoxemia, 121, 123, 227, 242, 251. *See also* Hypoxic hypoxia
  arterial blood gases, 227
  carbon monoxide poisoning, 214
  gall bladder surgery, 227
  stimulations, 252
Hypoxia
  anemic hypoxia, 242
  classification of, 50
  oxygen utilization, impaired, 219
  signs of, 213
  types of, 51*t*
Hypoxic hypoxia, 50, 121, 213, 242
Hypoxic pulmonary vasoconstriction, 245

I

Iatrogenic botulism, 87
Ibuprofen, 383
Idiopathic epilepsy, 87
Ileum, 336
Immunizations, 295
Immunosympathectomy, 181
Indomethacin, 197
Inflammatory bowel disease, chronic, 339
Infranodal block, 300
Inhibin B, 71

Inositol triphosphate (IP_3), 84
Intracranial pressure (ICP), 83, 92
Insomnia, 383
Inspiratory capacity (IC), 235
Inspiratory reserve volume, 235
Insulin, 15, 72, 120
  effects on organic metabolism, 74*f*
  principal action, 74*t*
  resistance, 463, 477
  secretion, 349
Insulin-independent glucose uptake, 458
Intercellular connections and communication, 7-9
  principal mechanisms for, 8*t*-9*t*
Interstitial hydrostatic pressure, 62
Interstitial (extravascular) water, 9
Interventricular septum, hypertrophy of, 331
Intestinal enterocyte, 340
Intracellular fluid (ICF), 9, 166
  composition of, 11*t*
Intracellular volume, 81, 90
Intracranial pressure, 282
Intragastric volume, 349
Intrapulmonary shunting, 231
Intravenous fluid, 6
Intravenous labetalol, 80
Intravenous (IV) secretin, 337
Iodinated tyrosine residues, 467
Ionic equilibria, 27
Iron
  anemia caused by deficiency of, 347
  blood bound, transferrin, 347
Irritable bowel syndrome (IBS), 336
Ischemic pain, 155
Isosmotic solutions, 6
Isotonic solutions, 6
Isovolumetric relaxation, 269

J

JAK2-STAT pathway, 461, 475
Jaundice, 81, 348
Joint disease, 225
Jugular venous distension, 318
Jugular venous pulse (JVP), 285, 309
Juxtaglomerular apparatus, 398, 426
Juxtaglomerular cells (JG cells), 12, 410

K

K^+ channels, 37*f*
Ketoacidosis, 113, 120
Ketogenesis, 365
Ketones, 460
Kidney
  chronic disease, 395
  functional unit of, 66
  perfusion, 418
  stones, 384
Kinesthesia, 168
Kininogens, 140

Klebsiella pneumoniae, 225
Klinefelter's syndrome, 435, 438
Knee replacement, 225
  surgery for, 126
Kussmaul respirations, 476
Kyphoscoliosis, 254
  muscle weakness, 226
Kyphosis, 254. *See also* Anteroposterior angulation

L

Labyrinthitis, 170
Langerhans, 460
Language disorders, caused by memory loss, 167
Lansoprazole, 357
Laparoscopic vagotomy, 338
Laplace's law, 60
Latch bridges, 43
Lecithin, 246
  amniotic fluid, sphingomyelin ratio in, 218
  synthesis of, 123
Left atrial pressure (LAP), 214
Lesions, 33
Lethargic, 380
Levitra®. *See* Vardenafil
Leydig cells, 71
LH, opioid blocker naltrexone, 435
Lieberkühn, 373
Lipase, 340
Lipolytic pancreatic enzyme, 359
Lipoprotein
  lipase activity, 94
  mixture, 246
Lisinopril, 400, 417
  therapy, 267
Lithium therapy, for bipolar disorder, 459
Liver
  gluconeogenesis, stimulation, 456
  intracellular α-glycerophosphate in, 460
Loop of Henle, 68, 117
Low-density lipoprotein (LDL), 94
Lower esophageal sphincter (LES), 341
  swallowing, 335, 354
Lung
  asbestosis and pulmonary fibrosis, 242
  with auscultation, 205
compliance, 49
    flow–volume curves, 229
    hydrostatic pressure, 243
    pulmonary function testing, 213
    respiratory distress syndrome, 211, 242
    ventilation/perfusion scan, 230
  diffusing capacity of, 206, 231
  elastic recoil, 257
    properties of, 49, 229
  emphysematous changes, 238
  function tests, FEV_1/FVC ratio, 232
  inspired lung volume, 221
  obstructive *versus* restrictive impairment, 50*t*

pneumothorax, 208
pressure–volume curve of, 208
pulmonary edema, 208
pulmonary surfactant, 242
volumes and capacities, 48-49, 48*f*
Lung cancer, 457
intracellular volume, 380
Lung–chest wall system, 252
Lymphatic ducts, 351
Lymphocytosis, 125, 135

M

McArdle disease, 194, 202
Magnesium sulfate, 89
Malabsorption syndrome, 371
Malaise, 377, 458
Male fetuses, sexual differentiation of, 442
Male reproductive system, 69-71
Mammalian nerve fibers, 180
Mannitol therapy, 12, 83, 92
Maternal arterial blood supply, 324
Maternal immune system, 446
Maximal expiratory flow-volume (MEFV) curve, 212, 217
airflow, 212
FEV_1/FVC ratio, 246
pulmonary function tests, 217
Mean electrical axis (MEA), 266
Mediated transport, 1, 4
Melatonin, 152
Membrane permeability coefficient, 2
Membrane potentials, 27
hyperpolarizing, 79
Membrane transport
classification of, 1, 2*t*
mechanisms of, 1-7
osmotic pressure difference, 4
Menaquinone, 140
Méniére syndrome, 170
Meningitis, 220
Menopause, symptoms, 439
Menstrual bleeding, 127
Menstrual cramps, 352
NSAIDs, 352
Menstrual cycle, 69, 70*t*, 127, 443
Mental retardation, 448
Metabolic acidosis, 100, 122
causes of, 21*t*
questions regarding, 107
Metabolic alkalosis, 96, 101, 376, 402
causes of, 20*t*
Metabolic syndrome, 281
Methacholine, 257
Methacholine-induced bronchoconstriction, 257
Methemoglobinemia, 243
MHC class II antigen HLA-DQ2, 350
Michaelis–Menten equation, 4
Microcytic anemia, 339
Microcytosis, 138

Migrating motor complexes (MMCs), 355
Minute ventilation, 45
Miosis, 158
Misoprostol, 364
Mitral regurgitation, 308
Mitral stenosis, 309
Mononucleosis, infectious, 125
Monospot slide test. *See* Heterophile agglutination assay
Morning after pill, 435
Motilin, 339
  release of, 351
Motor cortex, 31
Müllerian ducts, 450
  regression, 448
Multiple endocrine neoplasia type I (MEN I), 357, 463
Multiple myeloma, 385
Multiple rib fractures, 390
Multiple sclerosis (MS), 152
Multisystem processes
  acid–base balance and disorders, 15-19
  body fluid compartments, 9-11
  fluid and electrolyte balance and disorders, 11-15
  questions regarding, 93-109
Murmur, 261, 269
  crescendodecrescendo systolic, 278
  diastolic, 271
  holosystolic, 278
  mid-systolic, 270
  pressure–volume loop, 271
  systolic ejection, 276
  utero function, 287
Muscles
  contractions, 355
  cramps, 388, 457
  dystrophy, 192, 200
  glycogen phosphorylase, 202
  lactate spills, 240
  relaxation, 161
  weakness, 378, 385
Musculoskeletal physiology, 41-43
  questions regarding, 189-195
Myasthenia gravis, 182, 197, 199
Mydriasis, 176
Myelin synthesis, 132
Myocardial contractility, 304
Myocardial infarction, 262, 263, 275
  stroke volume, 277
Myocardial oxygen, 291
Myoclonic epilepsy, 7
Myogenic properties, 354
Myoglobinuria, 194, 202
Myophosphorylase, 194, 202
Myopia, 159, 180
Myosin light chains (LC20), 328

N

Na^+ channels, 298
NaCl absorption, 356

Na^+–K^+ pump, 1, 94, 184, 377
Na^+/nutrient cotransport processes, 429
Narcolepsy, 174
  diagnosis of, 153
Narcotic analgesic, 98
Na^+ reabsorption, 377, 387
  distal nephron decreases, 387
Nasal polyps, 209
National Collegiate Athletic Association (NCAA), 458
Nausea, 219, 397, 457
  macrolide antibiotic erythromycin complains of, 339
Nephritic syndrome, 422
Nephrologist, 387
Nephrosclerosis, 399
Nernst equation, 86
Nerves
  classification of, 31*t*
  functions of, 29-31
  spike potential of, 28
  types of, 30*t*
Nervous system, 255
  dysfunction, 477
Net acid excretion (NAE), 405
Neuritic plaques, 165
Neurocardiogenic syncope, 299
Neurologic examinations, 288
Neurophysiology
  action potential, 27-29
  autonomic nervous system (ANS), 39
  central and peripheral, 31
  control of movement, 31-33
  functions of nerves, 29-31
  ionic equilibria and membrane potentials, 27
  questions related to, 143-165
  special senses
    hearing, 36
    olfaction, 37-39
    sight, 33-35
    taste, 39
    vestibular system, 36-37
Neutral NaCl absorption, 351
Newborn, transitional circulation in, 290
Niacin, 138
Niemann–Pick (NP) disease, 179
Night blindness (nyctalopia), 157
Nitric oxide (NO), 71, 84, 413, 422
  inhalation, 226
Nitroglycerin, 329
N-methyl-D-aspartate (NMDA) receptors, 80, 88
Node of Ranvier, 29
Noninfectious GI processes, 356
Nonsteroidal anti-inflammatory drugs (NSAIDs), 403
Norepinephrine, 172
Nuclear factor-κB (NF-κB), inhibition of the activation of, 83, 92
Nyctalopia (night blindness), 157
Nystagmus, 37

O
Obstructive disease, 250
Obstructive lung disease, chronic, 391
Oculocardiac reflex, 307
Ogilvie syndrome, 356
Olfactory fila, 158
Olfactory sensory system, 37-39
Oligodendrocytes, 181
Oligosaccharides, 65
Opsin, 33
Optic neuritis, 180
Optic tracts, 149
Orad stomach accommodation, 352, 373
Oral contraceptives, 207
Oral rehydration, 356
Organ of Corti, 36
Oropharynx, physical examination of, 337
Orthopnea, 267
Orthostatic
  hypertension, 386
  hypotension, 96
Osmol, 5
Osmolality, 10, 90, 91
Osmolarity, 5
Osmosis, diagrammatic representation of, 4*f*
Osmotic diarrhea, 366
Osmotic flow equation, 4
Osmotic pressure, 5
Osteoarthritic vertebral changes, 452
Osteoarthritis, 291
Osteoclasts, 464
Osteoporosis, 201
  calcium and vitamin D supplements, 461
Ovarian dysgenesis, characteristic of, 439
Ovary, corpus luteum, 449
Overhydration, 12
Ovulation, 431, 443
  endometrial thickness, menstrual cycle, 431
Oxygen consumption, 227, 265
Oxygen content, in arterial and venous blood, 24*t*
Oxygen therapy, 400
Oxygen transport, in the blood, 20-25
Oxyhemoglobin, 24, 128, 139, 142, 256
  dissociation curve, 24*f*, 25-26, 108, 137
  saturation curve, 134
Oxytocin, 72
  breast feeding, 436

P
Pacemaker, 276
Pacemaker cells, 299
  pre-Bötzinger complex in, 249
Pacemaker neurons, respiratory rhythmogenesis in, 220
Pacinian corpuscle, 173
Palpitations, 462, 463
  complaints of, 269
Pancreas, 73*t*
Pancreatic amylase, 65

Pancreatic enzyme secretion, 338
Pancreatic function, 346
Pancreatic lipase, 351, 367
Pancreatic weight, 460
Pancreatitis, chronic, 456
Paralysis of legs, 226
Paraneoplastic syndrome, 122
Parasternal lymph nodes, squamous cell bronchogenic carcinoma, 223
Parathyroid hormone (PTH), 75, 75*t*, 78, 379, 397, 451
Paresthesias, 162, 349
Parkinson disease, 34*t*, 39, 161, 167, 169, 172, 182, 187
Parotidectomy, 213
Parotitis, facial swelling, 340
Paroxetine, 382
Paroxysmal dizziness, 274
Paroxysmal nocturnal dyspnea, 393
Partial pressures, 43-45
  of respiratory gases, 45, 46*t*
Patient's oxygen consumption, 227
PCO_2, of blood flowing, 229
Pellagra, 138
Pelvic inflammatory disease, 186
Pepsinogen, 353
Peptic ulcer disease, 337, 352
Peripheral chemoreceptor sensitivity, 223
Peritoneal dialysis, 82
Pernicious anemia, 355
Phenylethanolamine-*N*- methyltransferase (PNMT), 476
Pheochromocytoma, 318, 463, 478
pH of plasma, calculation of, 15
Phosphate, 458
  renal clearance, 397
Phosphatidylcholine (PC), 367
Phospholamban, 290
Phospholipase A_2 trypsin, prematurely activated, 346
Phosphorylcreatine, 199
Photoisomerization, 177
Photopigments, components of, 33
Photoreceptors, 33, 35*f*, 154
  hyperpolarization of, 35
Phylloquinone, 140
Physiological dead space, 47
Pilocarpine, 158
Pituitary function, loss of, 462
Pituitary glands, 72, 153
Pituitary tumor, radiation treatment for, 462
Placenta gas exchange, 108
Placenta previa, 134
Plasma bilirubin, 350, 371
Plasma concentration, 401
Plasma cortisol, 462, 467
Plasma creatinine, 391
Plasma hormone levels, 441
Plasma membranes, 5
Plasma metalloproteinase, 135
Plasma osmolality, 11, 12
Plasmapheresis, 136
Plasma proteins, 62, 114

Plasma (intravascular) water, 9
Plasminogen, 132, 140
Pmeprazole, 357
Pneumocystis infection, 210
Pneumonia, 226, 253
  postoperative complications, 244
Pneumothorax, 62, 253
  lung function, 208
Poiseuille's law, 49, 241, 244, 246, 305
Polycystic kidney disease, 415
Polycystic ovarian syndrome, 438
Polycythemia, 141, 256
Polycythemia vera, 129, 138
Polydipsia, 452
Polymyalgia rheumatica, 195, 204
Polysomnography, 153
Polyuria, 110, 452
Positive end-expiratory pressure (PEEP), 211
Positron emission tomography, 101
Posterior pituitary gland, 11
Posterior pituitary hormone, 447
Postprandial diarrhea, 345
Postrenal renal failure, 418
Poststreptococcal glomerulonephritis, 90
Postsynaptic cells, 31
Postsynaptic nicotinic acetylcholine receptors, 160
Potassium, 86, 103
  secretion, regulation of, 15
Potassium-sparing diuretic, 395
PRAD1 gene, 405
Preeclampsia, 80, 89
Pregnancy, 109, 124
  corpus luteum, 436
  hormonal changes, 436
  physiological changes, 440
  prevention, 435
  question related to, 131
  test for
    hCG in urine, 434
    negative, 435
  third trimester, 460
  urine sample, 440
Premature ventricular complexes (PVCs), 277
  bradycardia, 277
  sinus rhythm, 277
Prerenal failure, etiologies of, 427
Presbyopia, 178
Presynaptic inhibition, 152
Primary lateral sclerosis (PLS), 168
PR interval, 276, 298
  with P wave, 278
Prinzmetal angina, 332
Progesterone, 124, 442
Progesterone secretion, 437
Prolactin secretion, 439
Promyelocytic leukemia, 85
Proprioception, 145
Propylthiouracil (PTU), 473

Prostaglandins, 415
Prostate cancer, 145
Protein dystrophin, 192
Protein excretion, 383
Protein kinase C, 84
Prothrombin time (PT), 126
Proton pump inhibitors (PPIs), 363
Proximal tubular amino acid, reabsorption of, 410
Proximal tubular bicarbonate, reabsorption of, 385
Proximal tubular cells, 410
Proximal tubule, 385
Pseudohyperkalemia, 121
PTH-related peptide (PTHrP), 78
Pulmonary artery, 331
Pulmonary artery pressure (PAP), 214
Pulmonary biopsies, 398
  blood flow, 398
Pulmonary blood flow, 299
  noninvasive color Doppler ultrasound studies, 215
Pulmonary capillary wedge pressure, 298
Pulmonary circulations, 427
  preload, 292
Pulmonary edema, 237
  fluids, 221
  pressure-volume curve, 208
Pulmonary embolism
  arterial blood, 225
  fatigue/headaches/dyspnea, 228
Pulmonary fibrosis, 206, 212, 236
Pulmonary function, 224
  tests for, 209, 220
    fatigue and shortness of breath, 233
    maximal expiratory flow–volume (MEFV) curve, 217
    vital capacity, 233
  tidal inspiration and expiration, 224
Pulmonary hypertension, 310
  idiopathic, 295
Pulmonary hypertension, 115
Pulmonary infiltrative diseases, 253
Pulmonary regurgitation, 301
Pulmonary thromboembolism, 207, 236, 253
  alveolus, O_2 of, 207
Pulmonary vasculature, 328
Pulmonary vasoconstriction, 272
Pulmonic stenosis, 301
Pulmonic valve, closing of, 270
Pulse pressure, 323
Pulsus paradoxus, 280, 318
Pupil, cholinergic stimulation of, 158
Purkinje fibers, 267, 304
Pyloric sphincter, 65
Pyloric stenosis, 352

Q

QRS complexes, 278, 299
QRS deflection, 302
Quantiferon testing, 393

R

Rabies, 181
Radiation treatment, 476
Rales, 319
Raphe nucleus, 413
Rapid eye movements (REM), 147, 169, 456
Rathke's pouch, 72
Reabsorption, 426
Receptive relaxation, 338
Red blood cells, 138
Reduced circulating gonadotropin levels, 440
Reissner membrane, 36
Renal 1,25-dihydroxycholecalciferol, 464
Renal ammonia (NH_3), 395
Renal and urinary physiology, 66-69
Renal artery stenosis (RAS), 412
Renal biopsies, 398
  blood flow, 398
Renal blood flow (RBF), 400, 413
  endogenous substances, 394
Renal capsule, compression of, 392
Renal epithelial cells, 377
Renal failure, 396
  acute, 419
Renal nephrons, 401
Renal plasma flow (RPF), 67, 68, 378
Renal sympathetic nerve activity, 392
Renal tubular acidosis, type IV, 119
Renal ultrasonography, 391
Renal-urinary system, 394
Renin, 12
  hypertension, 388
  release from juxtaglomerular cells, 388
Renin–angiotensin–aldosterone system, 117
Renin–angiotensin system, 12, 324
Reproductive endocrinologist, 440
Reproductive physiology
  female reproductive system, 69
  male reproductive system, 69-71
Respiratory acidosis, 248, 255
  causes of, 22*t*
Respiratory alkalosis, 121
  causes of, 23*t*
Respiratory bronchioles, 45
Respiratory compensation, 113
Respiratory distress syndrome. *See also* Hyaline membrane disease
  acute, 242
  history of, 268
  Lung compliance, 211
  newborn, 242
Respiratory gases
  exchange ratio of, 45
  partial pressure of, 45, 46*t*
Respiratory muscles
  oxygen consumption of, 224
  paralysis of, 253
  weakness of, 226, 254
Respiratory physiology

breathing, mechanics of, 47-50
hypoxia and hypoxemia, 50-51
partial pressures, 43-45
passive, tidal expiration, 235
ventilation, 45-47
Retina of the eye, 33
Retropulsion, 357
Reynolds number, 61, 241, 327
Rheumatic heart disease, 278, 317
increased *v* wave, 278
Rhodopsin, 33, 177
Rhomboid, 194
Rickets, 200
Right ventricular hypertrophy (RVH), 311
Ruffini ending, 152, 173

S

Sacral parasympathetic pathways, 412
Sacroiliitis, 201
Salivary α-amylase, 340
Sarcoglycans, 200
Sarcoidosis, 230
pulmonary function screening test, 230
Sarcolemma, 192
Sarcoplasmic reticulum (SR), 42
calcium, concentration of, 290
calcium pump, 281, 329
Scala media, 36
Scala tympani, 36
Scala vestibuli, 36
Schatzki ring, 361
Schwann cell, 181-182
cytoplasm, 86
Scoliosis, 254
Secrete insulin, 460
Sepsis, 78
Septic shock, cardiac output, 255
Serotonin metabolite, 352
Sertoli cells, 71
basal lamina, 445
secretion of MIS, 448
in seminiferous tubules, 435
Serum ADH, 390
Serum calcium, 379
Serum cholesterol levels, 433
menstrual flow, 433
Serum creatinine, 377
Serum hypotonicity, 407
Serum lipoprotein, 94
Serum osmolarity, 457
Serum potassium levels, 461
Serum progesterone levels, 440
Serum proteins, 445
Severe epigastric pain, 340
Severe idiopathic cardiomyopathy, 266
Severe tachycardia, 459
Severe watery diarrhea, 347
Sex hormones, 449

SGLT 1, severe diarrhea, 340
Short-chain fatty acids (SCFAs), 346
Shortness of breath, 383
Shunt fraction, 227
Sickle cell anemia, 136, 139, 141
Sight, sense of, 33-35
Signal transduction pathways, 85
Sildenafil citrate, 77, 84
Sinus arrhythmia, 313
Sinus bradycardia, periodic episodes of, 274
Sinusitis, 233
Sinus node dysfunction, 278
Sinus rhythm, 277
Sinus tachycardia, 315
Sjögren syndrome, 178
Skeletal muscle fibers, 79, 86
  action potential of, 193
  characteristic of, 44*t*
  contractile response of, 193
  questions related to, 193, 195
  series elastic component (SEC), 196
  types of, 42*t*
SLC12A3 gene encoding, 415
Sleep apnea, repeated episodes of, 222
Sleepiness, 459
Sleep–wake cycle, 173
Small intestine
  absorption of sodium, 351
  absorptive capacities, 347
  functions of, 66
  removal of, 338
Smooth muscle autoantibodies (SMAs), 89
Smooth muscles
  characteristic of, 44*t*
  intestinal, 78, 85
Sodium, 162
  aldosterone secretion, 383
  conductance, 143
Sodium cyanide, 219
Sodium-dependent phosphate transport, 404
Sodium reabsorption, 396, 401, 415
  by cortical collecting ducts, 376
Solute migration, 5
Somatomedins, production of, 452
Somatostatin, 347
Special senses
  hearing, 36
  olfaction, 37-39
  sight, 33-35
  taste, 39
  vestibular system, 36-37
Spermatids, 69
Spermatogenesis. *See* Germ cells
Spermatogonia, 69, 443
Sphingomyelin, 123, 246
Spike potential, 28
Spondylitis, 192
Squamous cell bronchogenic carcinoma, 223

Stagnant hypoxia, 50, 243
Standard temperature and pressure dry (STPD), 43
Starling curves, 57, 59, 319, 334
Starling forces, 420
Starling law, of capillary fluid balance, 62
Steatorrhea, 345
Stokes–Adams syndrome, 300
Stomach
  functions of, 66
  gastric carcinoma, 338
Stool osmotic gap, 346
Streak ovary, characteristic of, 439
Streptococcal pharyngitis, 135
Striatum, 151
Stroke volume (SV), 57, 281, 305, 323
Stroke work, 60
Subarachnoid hemorrhage, 416
Subdural hematoma, 150
Substance P, 164
Substantia nigra, 144
Succinylcholine, 161
Suction rectal biopsy, 353
Sulfonylurea treatment, 463
Swallowing, 62
Swan–Ganz catheter, 218
Sweat, vaporization of, 109
Sympathetic nerve activity, 403
Sympathetic nervous system, 303
Sympathetic stimulation, 281, 320, 321
Syncope, 270, 274, 300
  episode of, 276
Syndrome of inappropriate antidiuretic hormone (SIADH), 12, 121, 122, 380, 421
Systemic circulations, preload, 292
Systemic hypertension, 311
Systemic hypotension, 319
Systolic
  and diastolic pressures, 313
  ejection, prominent, 278
    decreased pulse pressure, 278
  murmur, 314
  pressure, 275, 321

T

Tachycardia, 213, 272, 319, 462
Tachypnea, 207
Tadalafil, 84
Tardive dyskinesia, 34*t*
Taste, types of, 39
Tau hyperphosphorylation, 184
Tay–Sachs disease, 179
Tectorial membrane, 36
Terminal ileum, removal of, 339
Testes (male gonads), 69
Testosterone, 71, 74*t*
Tetanus, 202
Tetany
  hypocalcemic, 122
  symptoms of, 114

Thalassemia syndromes, 139
Thermoregulation, progesterone affects, 449
Thiazide diuretics, 429
Thiazides, 423
Thiazide-sensitive sodium–chloride cotransporter (NCCT), 388
Thoracic surgery, 268
Threshold intensity, 28
Thrombin, 140
Thrombocytopenia, 126, 136
Thrombotic thrombocytopenic purpura (TTP), 135, 136
Thyroglobulin, 454
Thyroid follicles, 454
Thyroid function, 451
Thyroid gland, 73*t*
  physical examination, 454
  unbound, 454
Thyroid hormone, 458, 473
  block release and synthesis of, 459
  decreased IGF-I, 459
Thyroid hormones, 74*t*, 471
Thyroid-stimulating hormone (TSH), 174
  secretion, 451
Thyroxine, 458
Thyroxine-binding globulin (TBG), 468
Tidal volume, 45
Titin, 292
Tobacco smoking, 130
Tonic–clonic seizures, 79, 87
Tonicity, 5
Total body water (TBW), 9
Total peripheral resistance (TPR), 57, 327
Toxin ingestion, 12
Tracheobronchial, squamous cell bronchogenic carcinoma, 223
Tractus solitaries, 39
Transducin, 35, 158, 175
Tricuspid regurgitation, 271
Triiodothyronine, 467
Trituration (grinding), 357
Tropomyosin, 329
Troponin, 42, 328
Trypsinogen secretion, 348
Tuberculosis, 421, 457
Tubular reabsorption, 66, 68*t*
Tubular secretion, 66
Tumor marker, 75
Turbulent flow, 61
Turner's syndrome, 439

U

Ulcer disease, 337
Undigested oligosaccharides, fermentation of, 348
Urea, 393
Uremia, 12, 82, 425
Uric acid, 190, 197
Uricosurics, 197
Urinalysis, 384, 399
Urinary electrolytes, 395
Urinary excretion, 352

Urinary microalbumin, 417
Urinary urgency, 386
Urine cultures, 396
Urine isotonic, 419
Urine osmolarity, 407
Urine output, decreased, 391
Urine sodium, 457
Urine titratable acids, 380

V

Vagina, cyclic changes, 438
Vagus nerve, 306
Valsalva maneuver, 261, 274, 297
Valvular defects, 263
Van't Hoff equation, 5
Vardenafil, 84
Vascular function, 280
Vasodilators, 332
Vasomotor symptoms, 372
Vasopressin, 72, 328, 418, 427
  secretion, 390
    inhibition of, 395
    on kidney, 390
Veins, 273
Venous admixture, 237
Venous thromboembolism, 128, 449
Ventilation, 45-47
Ventilation–perfusion ($\dot{V}/\dot{Q}$)
  abnormalities, 222
  paroxysmal nocturnal dyspnea, 223
Ventilatory response testing, 222, 223
  PCO_2 of blood flowing, 229
Ventral respiratory group, pre-Bötzinger complex in, 220
Ventricle, left, 263
Ventricular action potential, 297
Ventricular contractility, 276
Ventricular dilation, 293
Ventricular ejection fraction, 277
Ventricular end-diastolic volume, 261, 310
Ventricular hypertrophy, 333
Ventricular muscle, 292
Ventricular pressure–volume curves, 268, 279
Ventricular relaxation, 55
Ventricular septal defect (VSD), 311
Ventricular systole, 55
Ventricular tachycardia, 310
Ventricular wall stress, 283
  left ventricle, free wall of thickness, 283
Venules, 273
Very low-density lipoproteins (VLDL), 94, 111
Vessel, resistance of, 282, 321
Vestibular apparatus, 36, 37
Vestibular nuclei, 36, 37
Vestibular system, 36-37
Vestibulo-ocular reflex, 37, 170
Viagra®. *See* Sildenafil citrate
Vibrio cholerae, 347

Vincristine, 122
Viral illness, 340
Vital capacity (VC), 235
Vitamin A, 85
Vitamin B_{12}, 102, 119, 138, 163, 184, 336, 355
Vitamin D, 75, 75*t*, 85, 192, 200
  absorption by diffusion, 103, 119
  osteoporosis, 461
Vitamin K, 126, 128, 131, 140
  deficiency, 350
Vomiting, 338, 347, 348, 383
Von Willebrand disease, 131, 137

W

Warfarin, 128, 148
Water balance, regulation of, 68
Water reabsorption, 415
Weakness, 455
Wegener's glomerulonephritis, 233
  A–a gradient for O_2, 233
Wegener's granulomatosis, 398
Weight gain, complains, 458
Wheezing, airway radius, 215, 244
Wilson disease, 34*t*
Wolffian ducts, 450
Wolff–Parkinson–White (WPW) syndrome, 315

X

Xanthine oxidase, 197
Xerostomia, 178
X-linked Charcot–Marie–Tooth disease, 7

Z

Zinc deficiencies, 138
Zona adherens, 7
Zona glomerulosa cells, 15
Zona occludens, 7