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Physiology

10th edition

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- High-yield facts reinforce key concepts
- Targets what you really need to know
- Student-tested and reviewed

James P. Ryan ■ Michael B. Wang



Physiology

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Physiology

PreTest® Self-Assessment and Review
Tenth Edition

James P. Ryan, Ph.D.

Professor and Associate Chair
Department of Physiology
Temple University School of Medicine
Philadelphia, Pennsylvania

Michael B. Wang, Ph.D.

Professor and Associate Chair for Education
Department of Physiology
Temple University School of Medicine
Philadelphia, Pennsylvania

Student Reviewers

Christopher T. Lang

State University of New York—Buffalo
Buffalo, New York
Class of 2002

Hobart W. Walling, Ph.D., M.D.

Saint Louis University School of Medicine
Saint Louis, Missouri
Class of 2001

Junda C. Woo

State University of New York—Buffalo
Buffalo, New York
Class of 2002

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Introduction

Each *PreTest® Self Assessment and Review* allows medical students to comprehensively and conveniently assess and review their knowledge of a particular basic science, in this instance physiology. The 500 questions parallel the subject areas and degree of difficulty presented by the United States Medical Licensing Examination (USMLE) Step 1.

Each question is accompanied by the correct answer and its explanation. The explanation provides the reason why the correct answer is correct and, in many cases, the reason why the wrong answers are wrong. In addition, the explanation provides additional information relevant to the topic the question is designed to test. The references accompanying each question are from the major textbooks purchased by most medical students. 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 answer 150 of the questions in two and a half hours. Write the answers on a separate sheet of paper and then compare your answers to the ones provided in the book. The *PreTest®* can also be used as a review book. Answer a group of questions covering the same topic, check your answers, and then read the explanations and the referenced text pages. Whichever way you use the *PreTest®*, the most important part of your review is to be found in the explanations. The information in the explanations is designed to reinforce and expand on the material covered by the questions.

The High-Yield Facts found at the beginning of the book are not meant to be a complete list of all of the important facts, concepts, and equations necessary for understanding physiology. However, those that are included offer a solid foundation of the subjects they do cover and should be included in your review of physiology in preparation for a class test or for the Step 1 Examination. If you are not familiar with a section of the material presented in the High-Yield Facts, you should plan to do more reading. If, on the other hand, you have a good grasp of this material, you can feel confident in your knowledge of that topic.

Good luck on your exam.

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Physiology

PreTest® Self-Assessment and Review

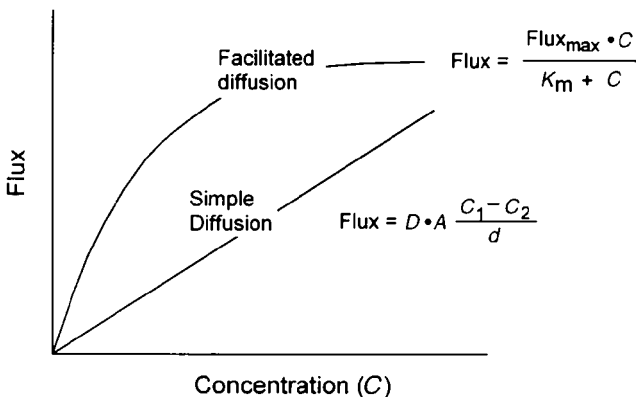
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High-Yield Facts in Physiology

CELLULAR PHYSIOLOGY

- Ions, nutrients, and waste material are transported across cell membranes by diffusion, osmosis, and active transport.

Simple diffusion is described by the Fick equation. Carrier-mediated diffusion, called *facilitated diffusion*, is described by the Michaelis-Menton equation (see figure below).



The flow of water through membranes by osmosis is described by the osmotic flow equation. Material dissolved in the water is carried across the membrane by solvent drag.

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

σ = reflection coefficient

L = hydraulic conductivity

π = osmotic pressure

The reflection coefficient (σ)

$$\sigma = 1 - \frac{P_{\text{solute}}}{P_{\text{water}}}$$

2 Physiology

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

The osmotic pressure (in units of mmHg) is calculated with the van't Hoff equation:

$$\pi = c \cdot R \cdot T$$

Cells shrink when placed in hypertonic solutions and swell when placed in hypotonic solutions. *Tonicity* is the concentration of nonpermeable particles. The following equation is used to calculate the steady state volume of the cell:

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

Active transport processes may be primary or secondary. Primary active transport processes, such as the Na-K pump, use the energy derived from the hydrolysis of ATP to transport materials against their electrochemical gradient. Secondary active transport processes, such as those that transport glucose and amino acids into renal or intestinal epithelial cells, use the energy from the Na⁺ electrochemical gradient.

- All cells have membrane potentials. The magnitude of the membrane potential is determined by the membrane permeability and ion 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 is calculated with Nernst's equation:

$$\left(E_{\text{ion}} = -60 \cdot \log \frac{\text{Conc}_{\text{in}}}{\text{Conc}_{\text{out}}} \right)$$

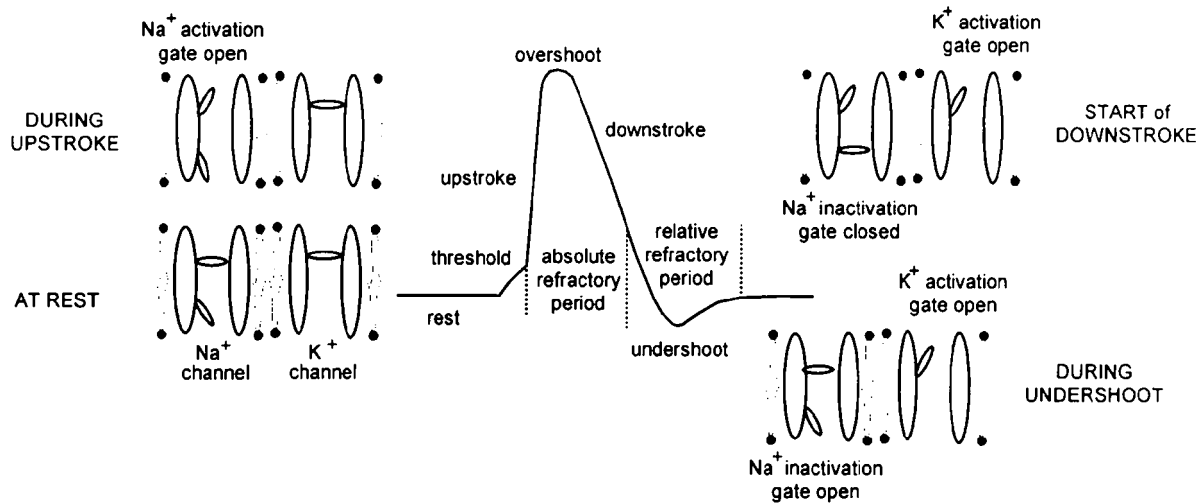
The resting potential is calculated with the transference equation:

$$\left(E_M = T_K \cdot E_{\text{Na}} + T_{\text{Na}} \cdot E_{\text{Na}} \right. \\ \left. T_K = \frac{g_K}{g_{\text{Na}} + g_K}; T_{\text{Na}} = \frac{g_{\text{Na}}}{g_{\text{Na}} + g_K} \right)$$

or with the Goldman equation:

$$E_M = -61 \cdot \log \frac{P_{\text{Na}} \cdot [\text{Na}]_{\text{in}} + P_K \cdot [\text{K}]_{\text{in}}}{P_{\text{Na}} \cdot [\text{Na}]_{\text{out}} + P_K \cdot [\text{K}]_{\text{out}}}$$

Action potentials are produced by voltage and time-dependent gates covering ion selective channels. Nerve and skeletal muscle membranes contain Na⁺ and K⁺ ion selective channels (see figure on p 3).



4 Physiology

- Cardiac muscle membranes contain Na^+ , K^+ , and Ca^{2+} ion selective channels.
- The upstroke (phase 0) is produced by the activation of Na^+ channels.
- The initial repolarization (phase 1) is produced by inactivation of Na^+ channels.
- The plateau (phase 2) is caused by the activation of Ca^{2+} channels and the closing of inward rectifying (anomalous) K^+ channels.
- The downstroke (phase 3) is caused by the activation of the delayed rectifier K^+ channels and the inactivation of Ca^{2+} channels (see figure on p 5).
- Increasing extracellular K^+ concentration depolarizes the membrane and reduces its excitability. Excitability is reduced because the depolarization inactivates Na^+ channels. The reduced excitability can lead to muscle weakness and cardiac arrhythmias.
- Synaptic transmission is used to transmit information from one cell to another cell. 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 the identity of the synaptic transmitter and the receptor (see figure on p 6).

Acetylcholine, which binds to the end plate of skeletal muscle cells, and glutamate and GABA, which bind to the postsynaptic membranes of many central nervous system membranes, open ion selective channels.

Norepinephrine and acetylcholine, which bind to the postsynaptic membranes of smooth muscle cells, produce their effect by activating a G protein which, in turn, activates an enzyme-mediated response.

- 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 (skeletal or cardiac muscle) or cell (smooth muscle; see figure on p 7).

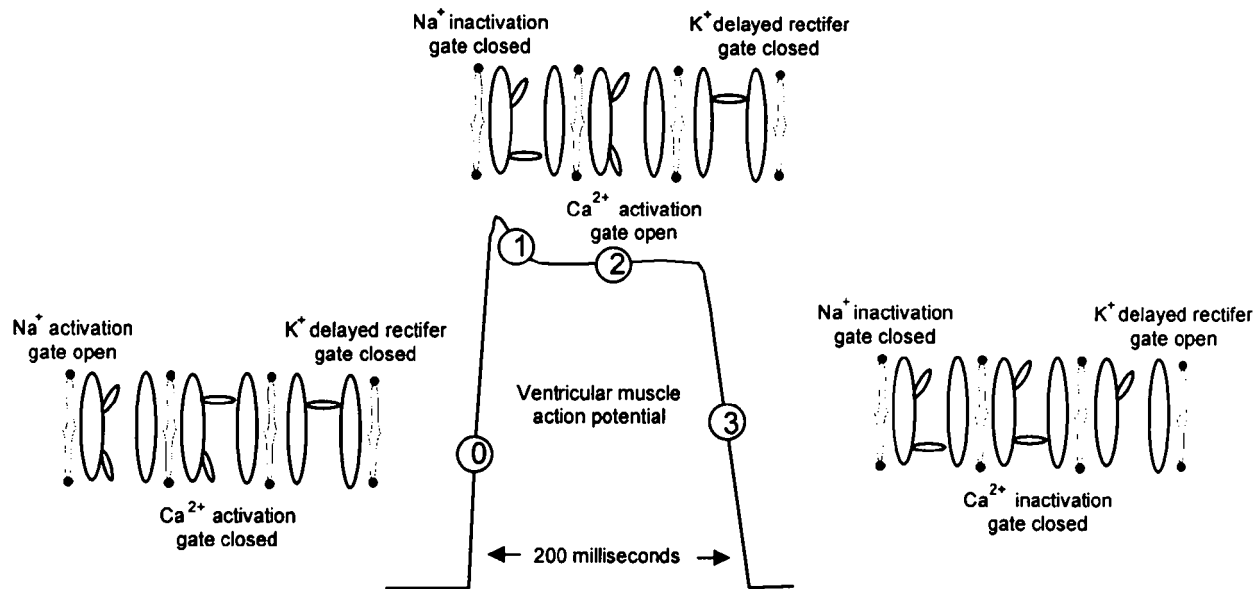
The initiation of contraction is called *excitation-contraction coupling*. In striated muscle, excitation-contraction coupling is initiated when Ca^{2+} binds to troponin. Troponin causes tropomyosin to move, thereby exposing the actin binding site to myosin (see figure on p 8).

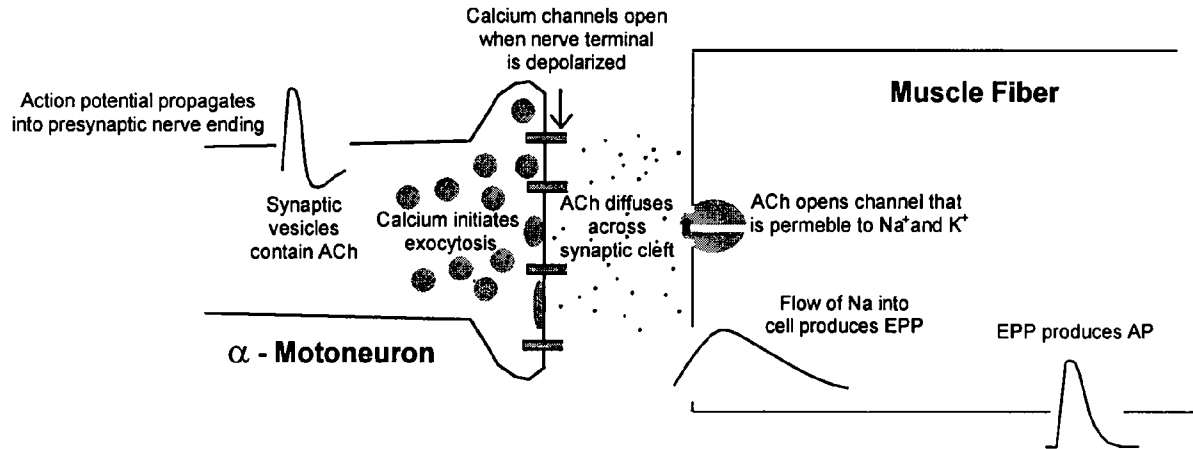
In skeletal muscle, Ca^{2+} is released from the sarcoplasmic reticulum (SR) when the muscle fiber depolarizes.

In cardiac muscle, Ca^{2+} is released from the SR by the Ca^{2+} that enters the cell during the cardiac action potential.

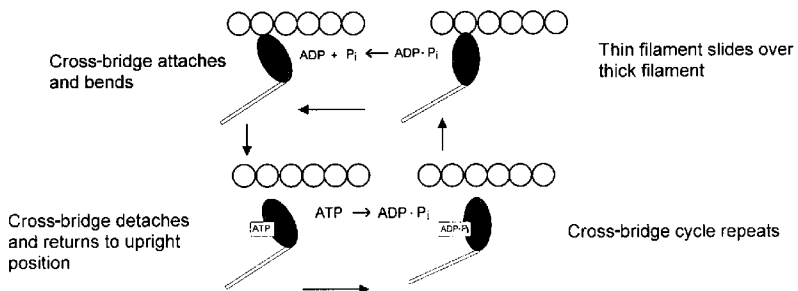
In smooth muscle, excitation-contraction coupling is initiated when Ca^{2+} binds to calmodulin.

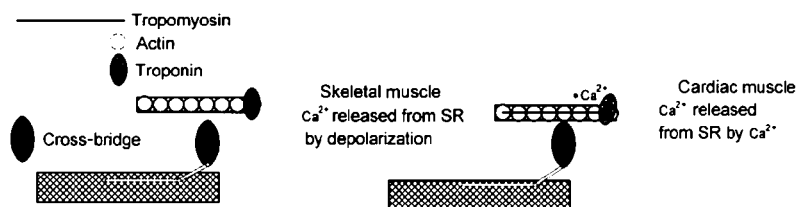
The Ca^{2+} -calmodulin complex activates myosin light chain kinase (MLCK) which, in turn, phosphorylates the 20,000-Da myosin light chains (LC_{20}). Cross-bridge cycling begins when the myosin light chains are phosphorylated.





Receptor	Enzyme	Enzyme Effect	Postsynaptic Response
Adrenergic Alpha ₁ (G _o)	Activation of phospholipase C	Formation of IP ₃ and DAG	IP ₃ releases calcium from SR DAG activates PKC Calcium activates arteriolar smooth muscle cells
Adrenergic Alpha ₂ (G _i)	Inhibition of adenylyl cyclase	Reduction in cAMP formation	Relaxes GI smooth muscle cells
Adrenergic Beta (G _s)	Activation of adenylyl cyclase	Formation of cAMP	cAMP activates PKA which: <ul style="list-style-type: none"> Increases Ca²⁺ entry into cardiac muscle cells and increases contractility Increases sequestration of Ca²⁺ in bronchiole smooth muscle cells and relaxes muscle
Cholinergic Muscarinic (M ₁)	Activation of phospholipase C	Formation of IP ₃ and DAG	IP ₃ releases calcium from SR DAG activates PKC Calcium activates GI smooth muscle cells



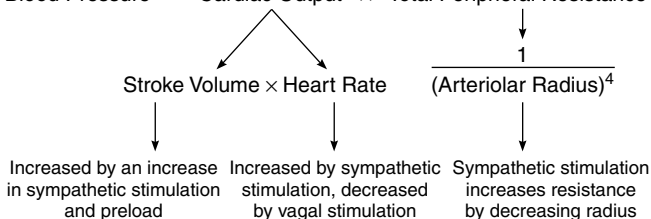


When dephosphorylated, the cross-bridges stay attached (or cycle slowly). The attached, slowly cycling cross-bridges are called latch bridges. Latch bridges allow smooth muscle to maintain force while minimizing energy expenditure.

CARDIAC AND VASCULAR PHYSIOLOGY

- The heart pumps the blood through the circulation. The cardiac output from the heart must be sufficient to perfuse all the organs and maintain a pressure adequate to perfuse the brain (see figure below).

$$\text{Mean Blood Pressure} = \text{Cardiac Output} \times \text{Total Peripheral Resistance}$$



Cardiac output can be measured using the Fick equation:

$$\text{CO} = \frac{\dot{V}\text{O}_2 \text{ (oxygen consumption)}}{(\text{Arterial O}_2 \text{ content} - \text{Venous O}_2 \text{ content})}$$

Resistance can be calculated using the Poiseuille equation:

$$R = \frac{8 \cdot \eta \cdot L}{\pi \cdot r^4}$$

η = viscosity

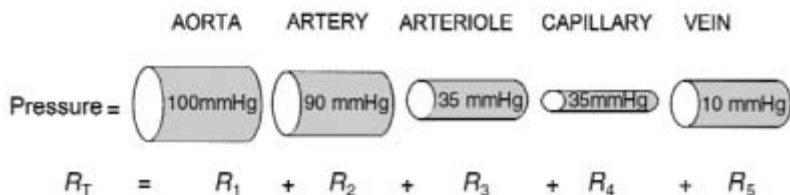
L = length

r = radius

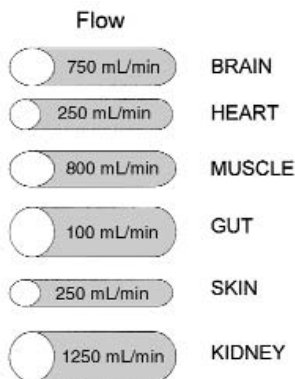
Because resistance is inversely proportional to the 4th power of the radius, TPR is controlled by small variations in the diameter of the arterioles.

Blood pressure is maintained by the baroreceptor reflex, which responds to a decrease in blood pressure by increasing heart rate, contractility, and TPR, and by decreasing venous compliance.

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 (see figure below).



The quantity of blood flowing into each organ is inversely proportional to the relative resistance of each organ. For example, at rest approximately 20% of the cardiac output flows through the skeletal muscles. During exercise, when the resistance of the skeletal muscle vessels decreases, over 80% of the cardiac output can flow through the skeletal muscles. The organs in the body are in parallel with each other (see figure below).



$$\frac{1}{R_T} = \frac{1}{R_1} + \frac{1}{R_2} + \frac{1}{R_3} + \frac{1}{R_4} + \frac{1}{R_5} + \frac{1}{R_6}$$

The velocity of blood through a vessel is proportional to the flow of blood through the vessel and inversely proportional to the area of the vessel:

$$v = \frac{Q}{A}$$

Increasing the velocity of blood can change flow from laminar (the fluid moves in a steady, orderly stream) to turbulent (the fluid movement is disorderly).

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.

Turbulence can be predicted from Reynolds number:

$$N_R = \frac{\rho \cdot D \cdot V}{\eta}$$

ρ = density

D = diameter

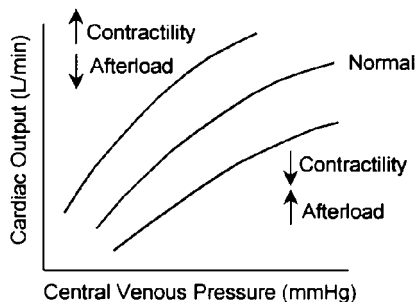
V = velocity

η = viscosity

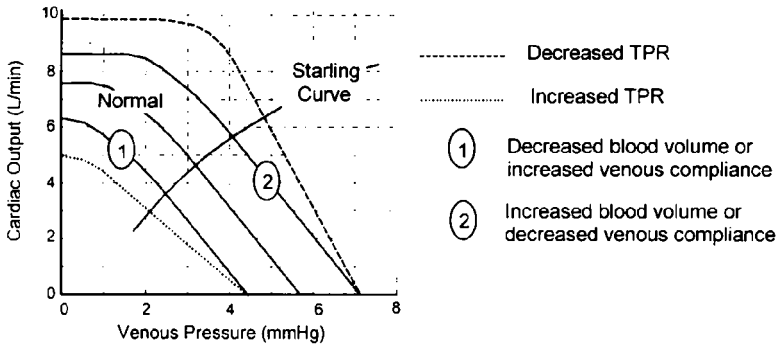
If Reynolds number exceeds 2000–3000, flow is likely to be turbulent.

- Stroke volume (and cardiac output) is dependent on preload, afterload, and contractility.

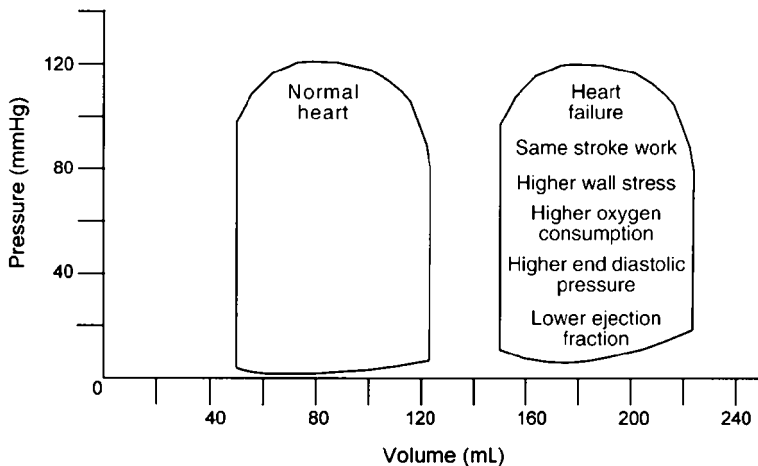
The relationship between preload and stroke volume (or cardiac output) is represented by a Starling curve. The Starling curve is shifted up and to the left by an increase in contractility or a decrease in afterload. The Starling curve is shifted down and to the right by a decrease in contractility or an increase in afterload (see figure below).



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 (see figure below).



The change in pressure and volume within the heart during one cardiac cycle can be represented by a pressure-volume loop (see figure below).



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:

$$\text{Stroke work} = \text{MLVSP} \cdot \text{SV}$$

Stroke work is equal to the area within the pressure-volume loop.

The energy required to eject the blood is dependent on the stroke work and the wall stress.

Wall stress is proportional to systolic pressure and the radius of the ventricle and inversely proportional to the thickness of the ventricular wall (law of Laplace):

$$\text{Wall stress} = \frac{P \cdot r}{\text{Thickness}}$$

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

- Fluid exchange across capillaries is dependent on Starling forces:

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

Normally, the fluid filtered from the capillaries is returned to the circulation by the lymphatic system. Fluid accumulation in the interstitial space is referred to as *edema*.

Edema can result from:

An increase in capillary permeability, as during an inflammatory response

A decrease in plasma proteins, as during malnutrition

An increase in capillary pressure, as in heart failure (the increased end-diastolic pressure that occurs in heart failure causes the increase in capillary pressure)

A blockage of the lymphatic circulation

PULMONARY PHYSIOLOGY

- Air is moved in and out of the lungs by the movement of the diaphragm and chest. During inhalation, the diaphragm descends and the rib cage moves up and out. The expansion of the lungs creates a negative intra-alveolar pressure (with respect to atmospheric pressure) which draws air into the alveoli. The air moving into the lung with each breath is called the *tidal volume*. The amount of air moving into the lung per minute is called the *minute ventilation*.

Minute ventilation (V_{\min}) = Tidal volume (V_T) · Breathing frequency (f)

At the end of inspiration, the air within the conducting airways is called the *anatomical dead space air* and does not contribute to gas exchange. The fresh air entering the alveoli each minute is called the *alveolar ventilation*.

Alveolar ventilation (\dot{V}_A) = ($V_T - V_D$) · f

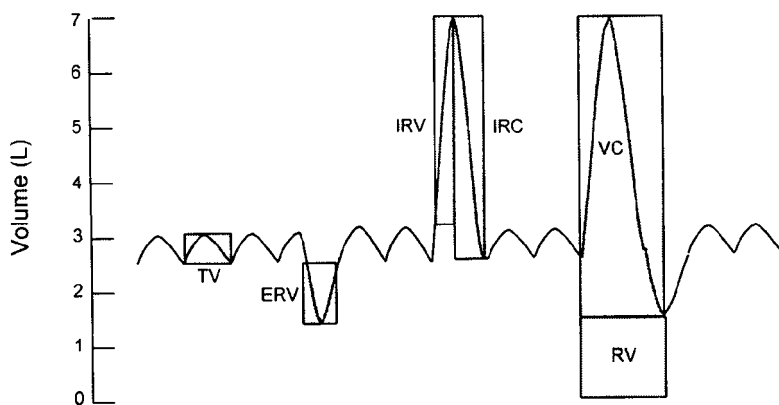
The physiological dead space is the sum of the anatomical and alveolar dead spaces. It is calculated with Bohr's equation:

$$V_D = V_T \cdot \left(\frac{F_{aCO_2} - F_{eCO_2}}{F_{aCO_2}} \right)$$

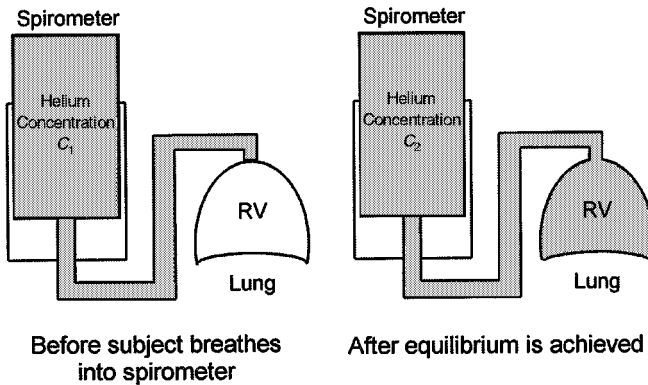
The anatomical dead space (in mL) is approximately equal to the weight (in pounds).

The alveolar dead space (areas of the lung that are ventilated but not appropriately perfused) is typically zero.

- The gas moving in and out of the lungs is measured with spirometry. Tidal volume is the gas moving in and out of the lungs with each breath. The maximum amount of gas that can be expelled from the lungs after breathing in as far as possible is called the *vital capacity*. The maximum amount of gas that can be expelled from the lungs after a normal breath is called the *expiratory reserve volume*. The maximum amount of gas that can be inhaled at the end of a normal breath is called the *inspiratory capacity*. The maximum amount of gas that can be inhaled at the end of a normal inspiration is called the *inspiratory reserve volume* (see figure below).



The gas remaining in the lung at the end of maximum expiration (the residual volume) cannot be measured by spirometry. It is measured using the helium dilution technique (see figure below).



A known amount of helium is placed in a spirometer. The subject is connected to the spirometer when the volume in his or her lung is at the residual volume. After equilibration is achieved, the concentration of helium in the spirometer is measured. The following equation is then used to calculate the RV.

$$RV = V_{\text{Spirometer before equilibration}} \left(\frac{C_{\text{Spirometer before equilibration}}}{C_{\text{Spirometer after equilibration}}} - 1 \right)$$

The equation calculates whatever volume is in the lung when the subject begins to breathe into the spirometer. Therefore, the helium dilution technique can be used to measure any lung volume. For example, if the subject is connected to the spirometer at the end of a normal expiration, the FRC is calculated.

The *FRC* is the amount of gas in the lung at the end of a normal breath. It equals the RV + ERV.

The *total lung capacity* (TLC) is the amount of gas in the lung after a maximum inspiration. It equals RV + VC.

- The partial pressure of a gas is measured after water has been removed. Therefore, the partial pressure is calculated as a fraction of the atmospheric pressure remaining when the partial pressure of water vapor is subtracted.

$$F_{\text{gas}} \cdot (P_{\text{atm}} - P_{\text{H}_2\text{O}}) = F_{\text{gas}} \cdot (P_{\text{atm}} - 47 \text{ mmHg})$$

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

$$F_{aCO_2} = (\dot{V}_{CO_2} / \dot{V}_a)$$

$$P_{aCO_2} \propto (\dot{V}_{CO_2} / \dot{V}_a)$$

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

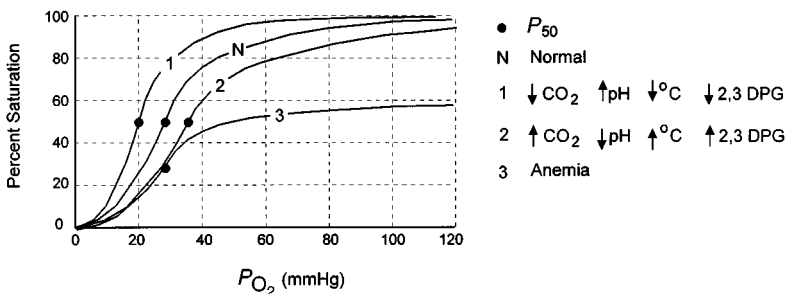
$$P_{aO_2} = P_{iO_2} - (P_{aCO_2} / R)$$

$$R = (\dot{V}_{CO_2} / \dot{V}_{O_2})$$

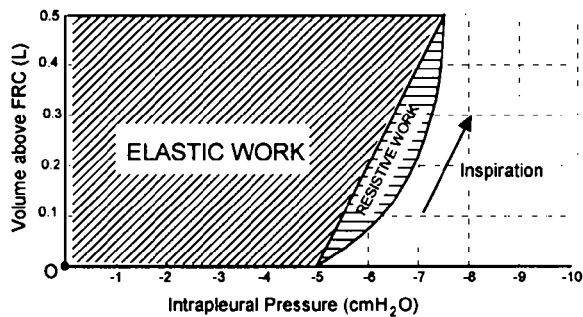
R is the respiratory gas exchange ratio. Under normal circumstances its value depends on metabolism and is equal to 0.8. When the P_{iO_2} is 100%, the value of R used in the alveolar gas equation is 1.0.

- The lung is an elastic organ that resists stretching. To expand the lungs, the inspiratory muscles must overcome the recoil force of the lungs and the resistance of the airways to airflow. The intrapleural pressure is a measure of the elastic and resistive work done by the inspiratory muscles. Expiration is usually passive. That is, the inspiratory muscles relax and the recoil force of the lungs expels the gas. Gas flow during expiration can be increased by contracting the expiratory muscles. However, the maximum expiratory flow is limited by airway compression (see figure below).

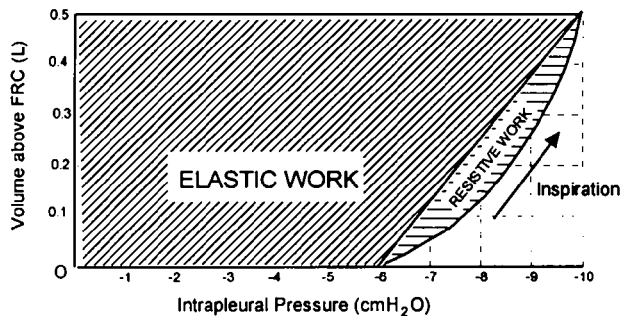
The work done by the lung can be represented by a pressure-volume loop. In restrictive airway disease (e.g., fibrosis), elastic work increases; in obstructive airway disease (e.g., asthma), resistive work increases (see figure on p 16).



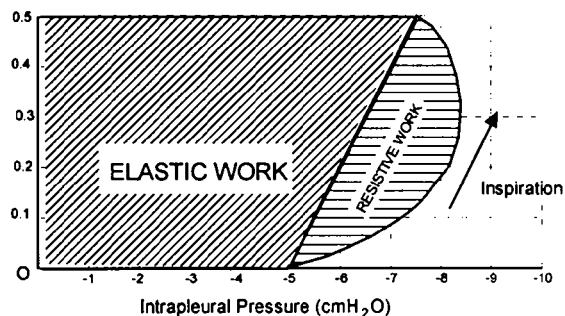
NORMAL



RESTRICTIVE



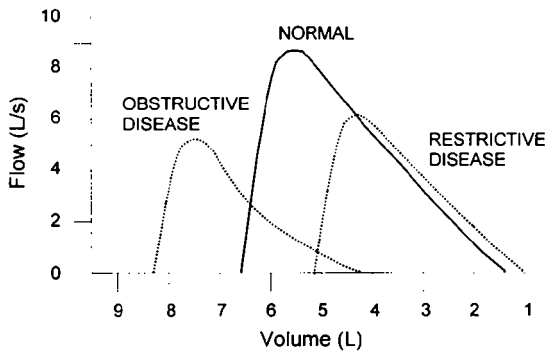
OBSTRUCTIVE



During active expiration, the alveolar pressure is the sum of the recoil force of the lung and the positive intrapleural pressure produced by the expiratory muscles. The intra-airway pressure decreases from the alveoli to the mouth. When the intrapleural pressure equals the intra-airway pressure (the equal pressure point) at a point along the airway where airway collapse can occur, increases in expiratory effort no longer increase expiratory flow (see figure on p 18).

Increases in lung compliance and/or increases in expiratory effort move the equal pressure point closer to the lung.

Maximum expiratory flow rates are lower in both obstructive and restrictive lung diseases.

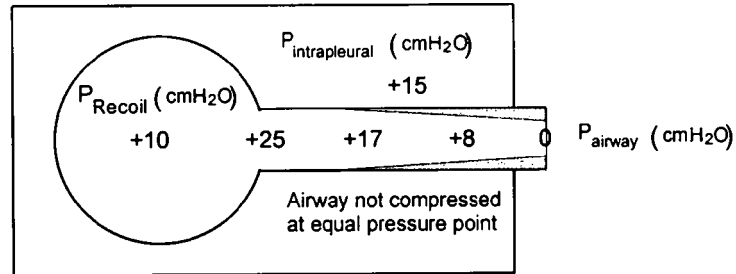


- Gas exchange across the alveolar-capillary membrane is very efficient. Under all but the most serious diffusion abnormalities (such as pulmonary edema), pulmonary capillary blood-gas tensions are in equilibrium with alveolar-gas tensions. Mixed venous blood returning from the systemic circulation has a PvO_2 of 40 mmHg and a $PvCO_2$ of 46 mmHg. Arterial blood has a PaO_2 of 95 mmHg and a $PaCO_2$ of 40 mmHg. The central chemoreceptors maintain $PaCO_2$ at 40 mmHg. The peripheral chemoreceptors will increase ventilation (and reduce $PaCO_2$ below 40 mmHg) if PaO_2 falls below 60 mmHg or if arterial pH is reduced by a metabolic acidosis.

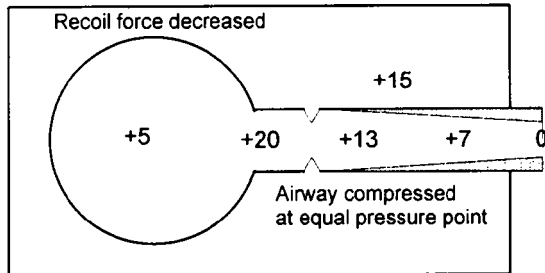
Most of the oxygen delivered to the blood is bound to hemoglobin ($Hb O_2$); a much smaller amount is dissolved in the blood. The amount of dissolved oxygen can be calculated if the PaO_2 is known:

$$\text{Dissolved } O_2 \text{ (mL } O_2/100 \text{ mL)} = 0.003 \cdot PaO_2$$

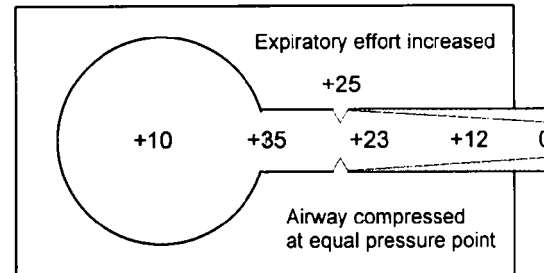
NORMAL



EMPHYSEMA



ASTHMA



The amount of O_2 combined with hemoglobin can be determined from the oxy-hemoglobin saturation curve or, if the saturation of hemoglobin is known, can be calculated:

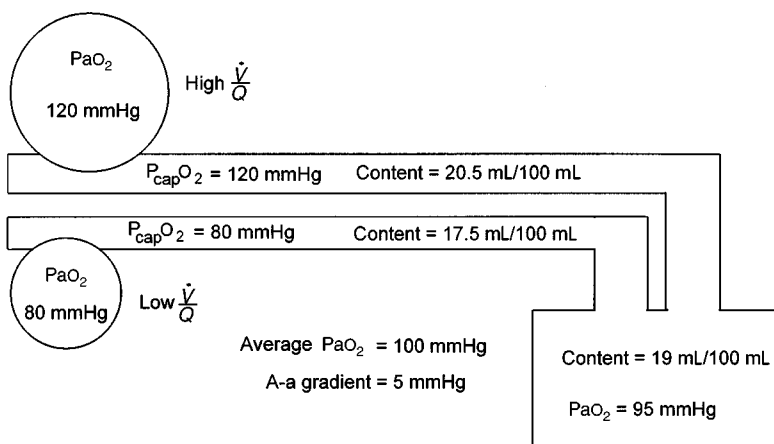
$$HbO_2 \text{ (mL } O_2/100 \text{ mL)} = \% \text{ sat} \cdot \text{g of Hb} \cdot 1.34$$

Hemoglobin is 97% saturated at the normal PaO_2 (95 mmHg); 75% saturated at the normal $P\bar{v}O_2$ (40 mmHg); and 50% saturated at 27 mmHg. The PaO_2 at which hemoglobin is 50% saturated is called the P_{50} .

The hemoglobin saturation curve shifts to the right when PCO_2 , temperature, H^+ concentration, or 2,3-DPG concentration increases. Shifting the curve to the right makes it easier for O_2 to dissociate from hemoglobin in the tissues. Interestingly, CO causes the Hb saturation curve to shift to the left, making it more difficult for oxygen to dissociate in the tissues.

The \dot{V}/\dot{Q} ratio affects the degree to which hemoglobin is saturated with oxygen.

The normal \dot{V}_A of 4 L/min and cardiac output of 5 L/min produces a normal \dot{V}/\dot{Q} ratio of 0.8. Areas of the lung with increased ratios are referred to as *alveolar dead space*; areas of the lung with decreased ratios are referred to as *intrapulmonary shunts*. Because areas of the lung with low \dot{V}/\dot{Q} ratios cannot compensate for areas of the lung with high \dot{V}/\dot{Q} ratios, the \dot{V}/\dot{Q} ratio abnormalities result in low arterial PO_2 and lead to a large A-a gradient for oxygen (see figure below).



GASTROINTESTINAL PHYSIOLOGY

- The first stage in the digestion and absorption of food is chewing and swallowing. Chewing and swallowing can be initiated voluntarily or involuntarily. Chewing breaks food into small pieces and mixes them with salivary secretions. Swallowing is coordinated by a swallowing center in the brainstem. During the oral phase of swallowing, the tongue pushes the food into the pharynx; during the pharyngeal phase, peristaltic contractions and relaxation of the upper esophageal sphincter (UES) allow the food to enter the esophagus; during the esophageal phase, the lower esophageal sphincter (LES) relaxes and the food is propelled into the stomach by primary peristalsis. A secondary peristaltic wave, initiated by the presence of food in the smooth muscle, clears the esophagus of any food not propelled into the stomach by primary peristalsis.
- The stomach breaks food into small pieces and mixes the pieces with gastric secretions to produce a paste-like material called *chyme*. Liquids and chyme are forced through the pylorus by a rise in gastric pressure. Liquids empty from the stomach in one half-hour. Solids cannot pass through the pyloric sphincter until they are broken into small pieces (less than 1 mm³), and, therefore, emptying of solids takes from 1 to 3 h.

Gastric Functions		
Function	Orad Stomach	Caudad Stomach
Motility	Tone	
	Receptive relaxation	Trituration
Secretion	Accommodation	Emptying of solids
	Emptying of liquids	Reflux barrier
	HCl	
	Intrinsic factor	
	Mucus	Gastrin
	Pepsinogen	

Gastric emptying is slowed by the enterogastric reflex and the release of an inhibitory hormone called enterogastrone. The reflex and the secretion of enterogastrone are evoked by the presence of acid or fats in the duodenum.

The secretion of gastric acid by the parietal cells is regulated by paracrine (histamine), neural (vagus nerve), and hormonal (gastrin) influences.

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

Intestinal Phase of Digestion		
Stimulus	Mediator	Response
Partially digested nutrients	CCK	Pancreatic enzyme secretion Gallbladder emptying Decreased gastric emptying
Acid	Enterogastrone and enterogastric reflex Secretin	Decreased gastric emptying Decreased gastric acid secretion Pancreatic/hepatic HCO_3^- secretion Decreased gastric acid secretion
Osmoles or distension	Enterogastrone and enterogastric reflex	Decreased gastric emptying Decreased gastric acid secretion

Sodium Transport Mechanisms in the Small Intestine			
Nutrient-Coupled Small intestine	Na^+/H^+ Exchange Jejunum	Neutral Ileum and colon	Electrogenic Colon

Functions of Small Intestine			
	Duodenum	Jejunum	Ileum
Motility		Segmentation (digestive period) Migrating motor complex (interdigestive period)	
Secretion Digestion	CCK and secretin	Intraluminal and brush border Nutrients, water, and electrolytes	HCO_3^-
Absorption	Iron and folate	Folate	Bile acids and vitamin B_{12}

Nutrient Digestion and Absorption		
Nutrient	Digestion	Absorption
Carbohydrates	Intraluminal (salivary, pancreatic amylase)	Active (glucose and galactose)
	Intestinal brush border enzymes	Passive (fructose)
Proteins	Intraluminal (gastric pepsin, pancreatic peptidases)	Active (amino acids and di- and tripeptides)
	Intestinal brush border enzymes	
Lipids	Intracellular (cytosolic peptidases)	Passive Intracellular resynthesis Chylomicron formation
	Intraluminal (gastric and pancreatic lipase)	
	Bile salts required for micelle formation and solubilization of lipids	
	Colipase essential for lipase hydrolysis of micellar lipids	

Fats, proteins, and carbohydrates are digested by intestinal enzymes. Bile is necessary for the digestion and absorption of fats. However, the amount of bile acids emptied into the proximal small intestine from the gallbladder is insufficient for complete fat digestion and absorption. Receptor-mediated active transport of bile acids in the terminal ileum returns the bile acids via the portal blood to the liver for secretion into the small intestine (this circulation of bile is called the *enterohepatic circulation*). Approximately 95% of the bile acid pool is recirculated from the intestine and about 5% is lost in the stool.

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

RENAL AND ACID-BASE PHYSIOLOGY

- 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. Each day, 160 to 180 L of fluid are filtered into the approximately one million nephrons in the human kidney. The glomerular filtration rate (GFR) is dependent on the Starling forces:

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

The amount of material filtered into the proximal tubule is called the *filtered load*.

Approximately 20% of the plasma flowing through the glomerulus (RPF) is filtered into the proximal tubule:

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

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

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

U_{conc} = Urinary concentration of material

P_{conc} = Plasma concentration of material

\dot{V} = Urinary flow rate

If a material is filtered but not reabsorbed or secreted, its renal clearance will be equal to the GFR. The clearances of creatinine or 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 PAH is used clinically to measure RPF:

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

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

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

- The loop of Henle is responsible for producing a dilute filtrate. It reabsorbs approximately 25% of the salt and 15% of the water filtered from the glomerulus. The filtrate flowing from the loop of Henle to the distal convoluted tubule has a Na^+ concentration of approximately 100 meq/L.
- The distal nephron is responsible for regulating salt and water balance. Na^+ balance is regulated by aldosterone and atrial natriuretic peptide (ANP). Water balance is regulated by antidiuretic hormone (ADH), which is also called arginine vasopressin (AVP). K^+ balance is regulated by aldosterone.

Aldosterone increases Na^+ reabsorption and K^+ secretion by the principle 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 principle 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-AMP-dependent process.

- The extracellular osmolarity is controlled by ADH.

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 also is secreted in response to low blood pressure. Under these conditions, reabsorption of water by the kidneys can make the extracellular fluid hypotonic.

- The extracellular volume is controlled by the salt content of the extracellular fluid. Salt content is controlled by aldosterone and 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.

Aldosterone secretion is controlled by the renin-angiotensin system. Renin is released from the juxtaglomerular cells (JG cells) in response to (1) decreased perfusion pressure within the afferent arteriole, (2) sympathetic stimulation of the JG cells, and (3) decreased Cl^- concentration in fluid bathing the macula densa. Renin catalyzes the conversion of angiotensinogen to angiotensin I. Angiotensin I is converted to angiotensin II (AII) by angiotensin-converting enzyme (ACE) located within the lung. AII stimulates aldosterone secretion from the adrenal cortex gland.

ANP release is controlled directly by stretch receptors within the right atrium.

- Extracellular K^+ is controlled by aldosterone. Increases in extracellular K^+ stimulate the secretion of aldosterone, causing K^+ secretion to increase. K^+ transport into cells is increased by epinephrine and insulin.
- 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 extracellular fluid is maintained by buffering the acid as it is formed and excreting the acid over time. CO_2 is rapidly excreted by the lungs. The kidneys require approximately 24 h to excrete the fixed acids.



When CO_2 is added to water, it forms H^+ and HCO_3^- .

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

$$pH = 6.1 + \log \frac{HCO_3^-}{0.03 \cdot P_{CO_2}}$$

The H^+ concentration of the plasma is calculated with the Henderson equation:

$$H^+ = 24 \cdot \frac{P_{CO_2}}{HCO_3^-}$$

Plasma PCO_2 is normally maintained at 40 mmHg by the central chemoreceptors. Increases in PCO_2 cause an increase in ventilation; decreases in PCO_2 cause a decrease in ventilation. The respiratory system rapidly eliminates all of the CO_2 produced by metabolism.

Plasma HCO_3^- concentration is normally maintained at 24 meq/L by the kidneys. HCO_3^- is an important buffer for fixed acids produced by metabolism.



The HCO_3^- lost during the buffering process is replaced by the distal nephron as the fixed acid (H^+ + anion $^-$) is excreted. The replaced HCO_3^- is called *new bicarbonate*.

The H^+ secreted into the urine is buffered by titratable acids (mostly phosphate) and ammonia. The following equation is used to calculate the net acid excretion:

$$\text{Net acid excretion} = ([\text{Titratable acids}] + [NH_4^+] - [HCO_3^-]) \cdot \dot{V}$$

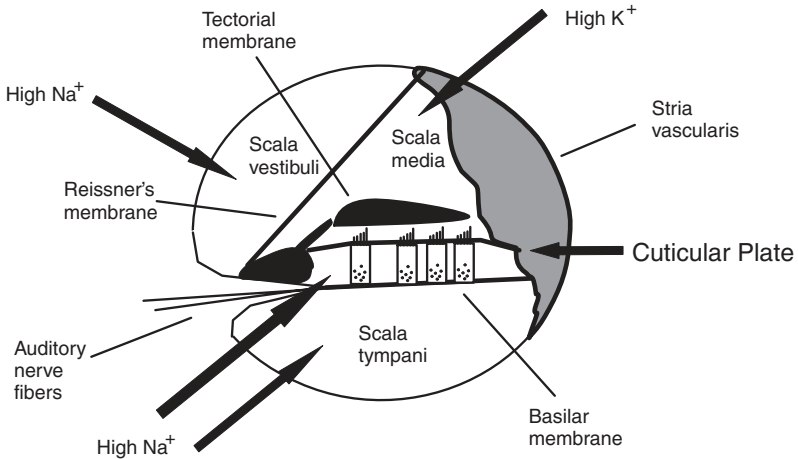
- Acid-base disorders result from failure of the respiratory system and kidneys to maintain PCO_2 and HCO_3^- at their normal levels.

Disturbance	Examples	Compensation	Blood-Gas Profile
Respiratory acidosis	Depression of the respiratory centers	Kidney produces new HCO_3^-	PaCO_2 ↑ (cause) pH ↓ (result) HCO_3^- ↑ (compensation)
	Respiratory muscle fatigue		
Respiratory alkalosis	Hypoxemia, anxiety	Kidney excretes HCO_3^-	PaCO_2 ↓ (cause) pH ↑ (result) HCO_3^- ↑ (compensation)
Metabolic acidosis	Excessive fixed-acid production, as in diabetes	Hyperventilation	HCO_3^- ↓ (cause) pH ↓ (result) PaCO_2 ↓ (compensation)
	Failure of kidney to excrete H^+ , as in renal tubular acidosis		
Metabolic alkalosis	Loss of acid, as in excessive vomiting	Hypoventilation	HCO_3^- ↑ (cause) pH ↑ (result) PaCO_2 ↑ (compensation)
	Movement of H^+ into cells, as in hypokalemia		

NEUROPHYSIOLOGY

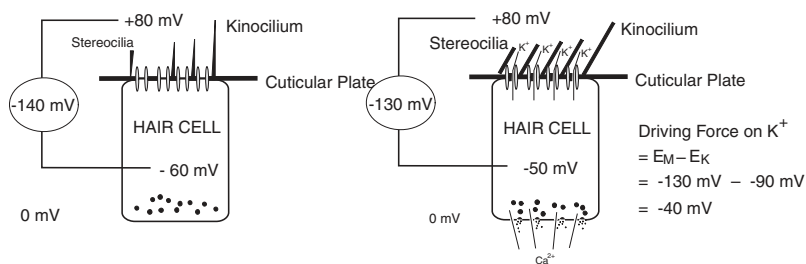
- Sensory receptors (touch, pain, temperature, smell, taste, sound, and sight) are activated by environmental stimuli. The stimulus produces a receptor potential; the magnitude of the receptor potential is proportional to the stimulus. The receptor potential produces a train of action potentials. Tonic receptors fire as long as the stimulus is present and encode intensity. Phasic receptors slow down or stop firing during the presentation of the stimulus and encode velocity.

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



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

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

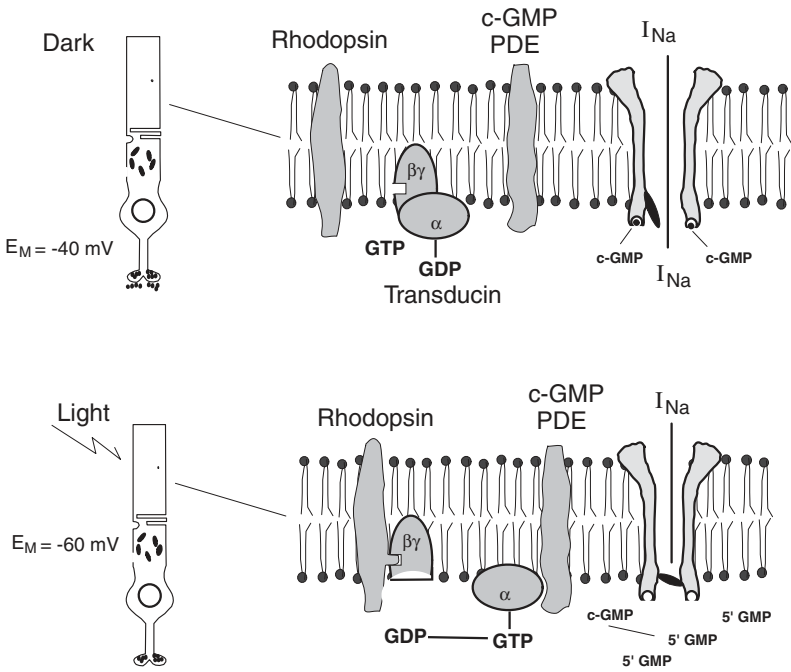


The basilar membrane is most stiff at the base of the cochlea (near the middle ear) and most compliant at the apex of the cochlea. High-frequency sounds cause a greater vibration of the stiff portion of the cochlea, and, therefore, the hair cells located near the base of the cochlea transmit information about high-frequency sounds to the auditory cortex. Similarly, low-frequency sounds are transmitted to the auditory cortex by the hair cells near the base of the cochlea, which are located on the more compliant portions of the basilar membrane.

- Light is detected by the rods and cones contained in the retina of the eye. The retina contains five types of neurons: photoreceptors (rods and cones), bipolar cells, ganglion cells, horizontal cells, and amacrine cells. Light rays from distant objects are normally focused on the photoreceptors by the cornea and the relaxed lens. When objects are brought closer to the eye, they are kept focused on the retina by the accommodation reflex, which causes the refractive power of the lens to increase. The rods and cones contain a visual pigment, called rhodopsin, which absorbs light energy. Rhodopsin contains two components: opsin, which determines the wavelength of light absorbed by rhodopsin, and retinal, which 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, which in turn activates a G protein called transducin. Activated transducin activates a cGMP esterase. Hydrolysis of cGMP causes Na⁺ channels on the rod and cone outer segments to close, which produces the membrane hyperpolarization.

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



- Spinal reflexes provide rapid control of posture and movement. Ia afferents provide proprioceptive information about muscle length and velocity of movement. The sensitivity of the intrafusal muscle fibers is modulated by γ -motoneurons. Ib afferents provide proprioceptive information about strength of muscle contraction.

Name	Stimulus	Receptors	Afferent Fiber	No. of Synapses
Withdrawal reflex	Skin damage or irritation	Pain receptors (nociceptors)	A δ and C	Polysynaptic
Stretch reflex	Muscle stretch	Intrafusal muscle fibers within muscle spindle	Ia	Monosynaptic
Lengthening reflex	Muscle contraction	Golgi tendon organ	Ib	Disynaptic

- 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 non-pyramidal system cause spasticity.
- The basal ganglia and cerebellum assist in the control of movement. Lesions to the basal ganglia produce paucity of movement or uncontrolled movements.

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

- Lesions to the cerebellum produce uncoordinated movements.
- The vestibular system provides information about the position and movement of the head, coordinates head and eye movements, and initiates reflexes that keep the head and body erect. Lesions to the vestibular system result in loss of balance and nystagmus.
- The cortex is responsible for cognition, language, emotions, and motivation.

ENDOCRINE PHYSIOLOGY

- Most of the hormones secreted by the endocrine glands are controlled by the endocrine hypothalamus and pituitary gland. The posterior pituitary gland is divided into a posterior and an anterior lobe. The pituitary gland contains the axons of neurons located within the paraventricular and supraoptic nuclei of the hypothalamus. These hypothalamic neurons synthesize oxytocin (responsible for milk ejection and uterine contraction) and ADH (increases water permeability of renal collecting ducts). The anterior hypothalamus secretes six major hormones.

The synthesis and release of these hormones are controlled by the hypothalamus. The hypothalamic releasing hormones are secreted into the median eminence from which they enter the capillary plexus that coalesces to form the anterior pituitary portal veins. These veins form another capillary plexus within the pituitary from which the releasing factors diffuse to the pituitary endocrine cells.

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

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

- Adrenocortical steroid hormones (glucocorticoids and adrenocorticoids) are synthesized from cholesterol. Glucocorticoids promote gluconeogenesis, inhibit the inflammatory immune responses, and are essential for the vasoconstrictive action of catecholamines.
- Insulin and glucagon are secreted by the pancreas. Insulin affects carbohydrate, lipid, and protein metabolism in adipose, liver, and muscle tissues. Insulin is secreted by the β cells of the islets of Langerhans. Insulin increases the entry of glucose, amino acids, and fatty acids into cells. It promotes the storage of these metabolites and inhibits their synthesis and mobilization. Glucagon is secreted by the α cells of the islets of Langerhans. Glucagon's effects oppose those of insulin.

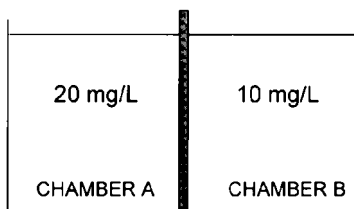
Cellular Physiology

Questions

DIRECTIONS: Each question below contains several suggested responses. Select the **one best** response to each question.

1. 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
2. A red blood cell will swell the most when it is placed in a solution containing
 - a. 100 mmol calcium chloride
 - b. 150 mmol sodium chloride
 - c. 200 mmol potassium chloride
 - d. 250 mmol urea
 - e. 300 mmol mannitol
3. If the extracellular K^+ concentration is increased from 4 meq/L to 10 meq/L,
 - a. The membrane potential will become more negative
 - b. The sodium conductance will increase
 - c. The potassium conductance will increase
 - d. The membrane will become more excitable
 - e. The Na-K pump will become inactivated
4. Inactivation of the sodium-potassium pump will cause
 - a. An increase in the intracellular volume
 - b. An increase in the intracellular potassium concentration
 - c. Hyperpolarization of the membrane potential
 - d. An increase in the excitability of nerve cells
 - e. An increase in the flow of sodium out of the cell

5. Membrane excitability will be increased by the greatest amount by
- Increasing extracellular Na^+
 - Increasing extracellular K^+
 - Decreasing extracellular Cl^{2-}
 - Decreasing extracellular Ca^{2+}
 - Decreasing extracellular H^+
6. The resting potential of a nerve membrane is primarily dependent on the concentration gradient of
- Potassium
 - Sodium
 - Calcium
 - Chloride
 - Bicarbonate
7. The diagram below illustrates the concentration of a substance in two chambers. If the concentration of the substance in chamber A doubles, the diffusion of the substance will change from 10 mg/h to



- 5 mg/h
 - 10 mg/h
 - 15 mg/h
 - 20 mg/h
 - 30 mg/h
8. Which of the following statements best characterizes a molecule whose reflection coefficient to a membrane is zero?
- It will not permeate the membrane
 - It can only cross the membrane through the lipid bilayer
 - It causes water to flow across the membrane
 - It is as diffusible through the membrane as water
 - It is transported across the membrane by a carrier

9. The characteristic of a water-insoluble substance most important in governing its diffusibility through a cell membrane is its

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

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

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

11. During the process of excitation-contraction coupling in skeletal muscle, calcium is released from the sarcoplasmic reticulum by

- a. Inositol triphosphate (IP_3)
- b. Protein kinase A
- c. An increase in intracellular calcium concentration
- d. Membrane depolarization
- e. An increase in intracellular sodium concentration

12. Which of the following words or phrases is most closely associated with an end-plate potential at the neuromuscular junction?

- a. "All-or-none response"
- b. Depolarization
- c. Hyperpolarization
- d. Action potential
- e. Electrically excitable gates

13. In a nerve, the magnitude of the action potential overshoot is normally a function of the

- a. Magnitude of the stimulus
- b. Intracellular potassium concentration
- c. Extracellular sodium concentration
- d. Resting membrane potential
- e. Diameter of the axon

14. Nicotinic receptors are responsible for

- a. Producing the skeletal muscle end-plate potential
- b. Decreasing the rate of phase-4 depolarization at the SA node
- c. Increasing the force of stomach contractions
- d. Delaying the emptying of liquids from the stomach
- e. Decreasing the excitability of sympathetic postganglionic neurons

15. Inactivation of phospholamban in cardiac muscle decreases

- a. The velocity of contraction in smooth muscle
- b. The duration of contraction
- c. The strength of contraction
- d. The depolarization required to initiate a contraction
- e. The amount of calcium released from the sarcoplasmic reticulum

16. Which of the following statements about synaptic transmission at the neuromuscular junction is true?

- a. It is enhanced by high levels of cholinesterase
- b. It is caused by an influx of potassium ions through the muscle membrane
- c. It is depressed by abnormally low levels of magnesium
- d. It is depressed by increased parasympathetic nerve activity
- e. It is produced by the release of acetylcholine from the alpha motoneuron

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

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

18. The amount of force produced by a skeletal muscle can be increased by

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

19. The velocity of nerve conduction is increased with a decrease in the

- a. Diameter of the nerve fiber
- b. Degree of myelination
- c. Space constant of the nerve fiber
- d. Capacitance of the nerve fiber membrane
- e. Resting membrane potential

20. The rate of diffusion of a particle across a membrane will increase if

- a. The area of the membrane decreases
- b. The thickness of the membrane increases
- c. The size of the particle increases
- d. The concentration gradient of the particle decreases
- e. The lipid solubility of the particle increases

21. Periodic hyperkalemic paralysis is characterized by high potassium concentration and muscle weakness. Which of the following is likely to cause muscle weakness as a result of increased extracellular potassium concentration?

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

22. The flow of calcium into the cell is an important component of the upstroke phase of action potentials in

- a. Cardiac ventricular muscle
- b. Intestinal smooth muscle
- c. Skeletal muscle fibers
- d. Nerve cell bodies
- e. Presynaptic nerve terminals

23. The membrane potential will depolarize by the greatest amount if the membrane permeability increases for

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

24. Which of the following will be less during the overshoot of an action potential than during the resting state?

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

25. Preventing the inactivation of sodium channels will decrease

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

26. Statements descriptive of both the equilibrium and steady states include which of the following?

- a. The sum of all the fluxes across the membrane is zero in both
- b. Both are maintained by the consumption of free energy
- c. The concentration gradient across the membrane is zero in both
- d. Both are maintained by homeostatic processes
- e. The membrane potential is zero in both

27. Connexin is an important component of the

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

28. An increase in sodium conductance is associated with

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

29. Electrically excitable gates are normally involved in

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

30. The sodium gradient across the nerve cell membrane is

- a. A result of the Donnan equilibrium
- b. Significantly changed during an action potential
- c. Used as a source of energy for the transport of other ions
- d. An important determinant of the resting membrane potential
- e. Maintained by a Na/Ca exchanger

31. Increasing the extracellular potassium concentration will

- a. Increase the threshold for eliciting an action potential
- b. Hyperpolarize the membrane potential
- c. Decrease potassium permeability
- d. Decrease the activity of the sodium-potassium pump
- e. Make the equilibrium potential for potassium more negative

32. Which of the following would cause an immediate reduction in the amount of potassium leaking out of a cell?

- a. Increasing the permeability of the membrane to potassium
- b. Increasing the intracellular potassium concentration
- c. Increasing (hyperpolarizing) the membrane potential
- d. Reducing the activity of the sodium-potassium pump
- e. Decreasing the potassium equilibrium potential

33. Excitation-contraction coupling in smooth muscle is initiated when calcium binds to

- a. Myosin light chains
- b. Calmodulin
- c. Troponin
- d. Tropomyosin
- e. Protein kinase A

34. Synaptic transmission between pain fibers from the skin and spinal cord neurons is mediated by

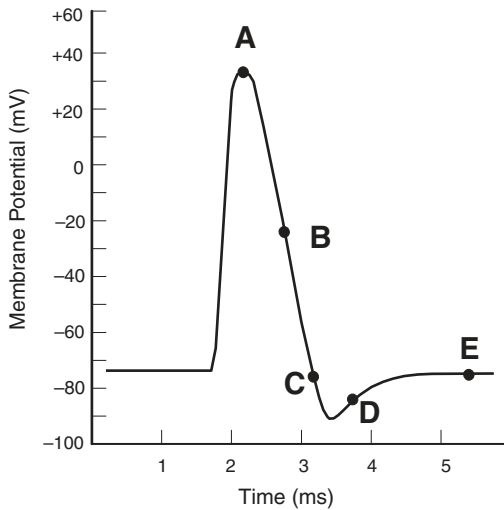
- a. Acetylcholine
- b. Substance P
- c. Endorphins
- d. Somatostatin
- e. Serotonin

35. In which one of the following transport processes is the substance moving down its electrochemical gradient?

- a. Sodium out of nerve cells
- b. Calcium into the sarcoplasmic reticulum
- c. Hydrogen into the lumen of the distal nephron
- d. Glucose into adipose tissue
- e. Potassium into striated muscle cells

Questions 36–37

Use the following diagram to answer the questions.



36. At which point on the action potential does the Na^+ current exceed the K^+ current?

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

37. At which point on the action potential is the membrane closest to the Na^+ equilibrium potential?

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

38. When skeletal muscle is in its resting state, myosin cross-bridges are prevented from binding to actin molecules by

- a. Calmodulin
- b. Troponin
- c. Tropomyosin
- d. Titin
- e. Phospholamban

39. The activity of the calcium pump on the sarcoplasmic reticulum of cardiac muscle is regulated by

- a. Inositol triphosphate
- b. Myosin light chain kinase
- c. Phospholamban
- d. Protein kinase A
- e. Phospholipase C

40. Patients who are extremely allergic to bee stings will self-administer epinephrine when stung. The activation of adrenergic beta-receptors by the injected epinephrine will decrease

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

41. Nitric oxide produces many of its physiologic effects by stimulating the synthesis of

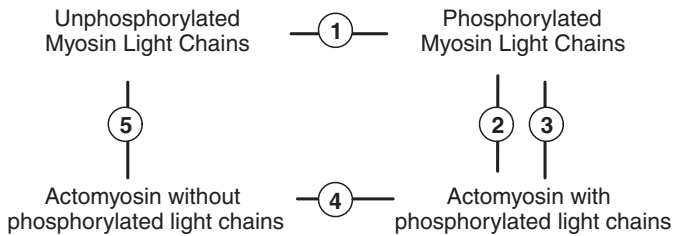
- a. Cyclic AMP
- b. Cyclic GMP
- c. Protein kinase A
- d. Protein kinase C
- e. Calmodulin

42. The NMDA receptor is activated by

- a. Glycine
- b. Acetylcholine
- c. Substance P
- d. Histamine
- e. Glutamate

Questions 43–44

Use the following diagram, which illustrates the chemical reactions that occur during cross-bridge cycling in smooth muscle, to answer the following two questions.



43. Which one of the following enzymes is responsible for step 1 in the diagram?

- Calmodulin
- Protein kinase A
- Myosin light chain kinase
- Phospholipase C
- Actomyosin ATPase

44. Which one of the steps in the diagram is responsible for the formation of latch bridges?

- Step 1
- Step 2
- Step 3
- Step 4
- Step 5

Cellular Physiology

Answers

1. The answer is c. (*Rhoades, pp 38–40.*) The conduction velocity of an action potential along an axon is proportional to the axon's diameter for both unmyelinated and myelinated axons. In myelinated axons, the conduction velocity of an action potential also increases as the distance between nodes of Ranvier increases. The resting potential and the action potential of a nerve axon 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.

2. The answer is d. (*Guyton, p 271.*) If a red blood cell is placed in a hypotonic solution, the cell will swell until its osmolarity equals the osmolarity of the extracellular fluid. The tonicity of the extracellular solution is equal to the osmolarity of those particles within the extracellular solution that are not permeable to the cell membrane. Because urea is able to permeate the cell membrane, its effective osmotic pressure is zero. Therefore, red blood cells placed in a urea solution will swell until hemolyzed. The osmolarity of the NaCl solution is approximately the same (300 mmol) as that of the red blood cell and, therefore, will not cause any change in intracellular volume.

3. The answer is c. (*Berne, 3/e, pp 31–32.*) Increasing the extracellular concentration of K^+ causes the cell to depolarize, that is, to become more positive. When the cell depolarizes, the activation gate on the K^+ channel opens, causing K^+ conductance to rise. Depolarization causes both the opening of the Na^+ activation (m) gate and the closing of the Na^+ inactivation (h) gate. As a result, Na^+ conductance remains the same. The inactivation of the Na^+ channels resulting from depolarization reduces membrane excitability. The activity of the Na-K pump will decrease if extracellular K^+ concentration is decreased.

4. The answer is a. (*Rhoades, pp 27–28.*) The sodium-potassium pump (Na^+, K^+ -ATPase) maintains a low intracellular Na^+ concentration. Decreases

ing the activity of Na^+, K^+ -ATPase leads to an accumulation of intracellular Na^+ . The osmotic activity of the increased intracellular Na^+ pulls water into the cell, causing the cell to swell. As Na^+ enters the cell and K^+ leaves the cell, the concentration gradients across the cell membrane are dissipated and the cell depolarizes. Depolarization inactivates Na^+ channels, leading to a decrease in membrane excitability.

5. The answer is d. (*Guyton, p 59.*) Membrane excitability is related to the ease with which Na^+ channels open when the cell is depolarized. The activation of Na^+ channels or the opening of the m gate is governed in part by the extracellular Ca^{2+} concentration. When extracellular Ca^{2+} is lowered, the m gate can open at more negative membrane potentials, and therefore the membrane is more easily excited. Although increasing extracellular K^+ will bring the membrane closer to threshold and thus may make it more excitable, its predominant effect is to cause the inactivation of Na^+ channels by the closing of the h gates. Inactivation of sodium channels makes the cell membrane less excitable.

6. The answer is a. (*Rhoades, p 30.*) The membrane potential is determined by the concentration gradient of the ion to which it is most permeable or for which it has the greatest conductance. In the resting state, the conductance for potassium is approximately nine times as great as the conductance for sodium. Hence, the membrane potential is dependent on the concentration gradient for potassium. The concentration gradient for chloride is not an important determinant of the membrane potential (even in those cells in which chloride conductance is high) because, unlike sodium and potassium, which are actively pumped across the membrane, chloride is passively distributed across the membrane. Therefore, its concentration gradient is a result of, rather than a cause of, the membrane potential.

7. The answer is c. (*Rhoades, pp 18–19.*) Fick's law states that diffusional flux is proportional to the concentration difference ($\text{Flux} \propto [C_1 - C_2]$). Doubling the concentration of the substance in chamber A causes the concentration difference to increase by threefold. Therefore, the flux increases from 10 mg/h to 30 mg/h.

8. The answer is d. (*Berne, 3/e, pp 12–13, 251.*) The reflection coefficient is a measure of a membrane's permeability to a substance in compar-

ison to its permeability to water. It can be calculated from the following equation:

$$\text{Reflection coefficient} = [P(\text{water}) - P(\text{substance})]/P(\text{water})$$

It is also a measure of the actual osmotic pressure developed by the substance compared with the osmotic pressure it should theoretically develop according to van't Hoff's equation. A substance with a reflection coefficient of zero would have the same diffusibility through the membrane as water and would not develop any osmotic pressure.

9. The answer is d. (*Berne, 3/e, pp 8–10.*) Materials that are not soluble in water can only cross 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.

10. The answer is d. (*Berne, 3/e, pp 70–73, 87–88, 96.*) In both smooth and striated muscle, contraction is produced by the cross-bridge cycle in which the cross-bridge on the thick filament binds to the actin molecule on the thin filament. In excitation-contraction coupling in striated muscle, calcium initiates contraction by binding to troponin. The calcium-activated troponin then acts to remove the tropomyosin-mediated inhibition of the actin-myosin interaction. In excitation-contraction coupling in smooth muscle, calcium initiates contraction by binding to calmodulin. The calcium-activated calmodulin then activates the myosin light chain protein kinase (MLCK) enzyme, which phosphorylates the myosin light chains. Actin-myosin interaction follows light-chain phosphorylation.

11. The answer is d. (*Rhoades, pp 158–160.*) Depolarization of the T tubules in skeletal muscle fibers causes the calcium channels of the sarcoplasmic reticulum (SR) to open, allowing calcium to enter the myoplasm. Depolarization moves the voltage sensor within the dihydropyridine (DHP) receptor on the T-tubular membrane. The voltage sensor is linked to the gate blocking the calcium channel (ryanodine receptor) in the SR membrane. When the voltage sensor is moved, the gate opens. In cardiac muscle,

the calcium channels on the SR membranes are opened by calcium, not by depolarization. Calcium enters the cell through a calcium channel within the DHP receptor during the plateau phase of the cardiac action potential. In smooth muscle, the SR calcium channels are opened by IP_3 .

12. The answer is b. (*Rhoades, pp 166–168.*) An end-plate potential is a depolarization caused by the opening of chemically excitable gates in response to the release of acetylcholine from the presynaptic nerve terminals of alpha motoneurons. Its magnitude is proportional to the amount of transmitter released. Although it is not propagated, it acts as a stimulus for the generation of an action potential on the muscle membrane contiguous to the end-plate region. The action potential is propagated and results in a muscle twitch.

13. The answer is c. (*Guyton, pp 55–56.*) 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. An action potential is normally an all-or-none response; that is, its magnitude is independent of the stimulus strength. The magnitude of the action potential is reduced during the relative refractory period or when the membrane is depolarized by an abnormally high extracellular potassium concentration.

14. The answer is a. (*Rhoades, pp 46–47, 166.*) Nicotinic receptors are located on the skeletal muscle end plates and on the postganglionic neurons within the autonomic nervous system. Acetylcholine excites both of these cell types. In skeletal muscle, activation of nicotinic receptors by acetylcholine produces the end-plate potential by opening channels permeable to Na^+ and K^+ . The acetylcholine receptors on the SA node and within the stomach are muscarinic receptors.

15. The answer is b. (*Berne, p 204.*) Phospholamban is a protein contained within the sarcoplasmic reticulum that inhibits the activity of the SR calcium pump. Inactivation of phospholamban results in an increase in calcium sequestration by the SR. In cardiac muscle, the rapid sequestration of calcium shortens the duration of the contraction. In smooth muscle, calcium sequestration causes the muscle to relax. Phospholamban has little effect on skeletal muscle contraction.

16. The answer is e. (*Berne, 3/e, pp 41–43.*) Synaptic transmission at the myoneural junction is produced by the release of acetylcholine from the nerve terminal of the alpha motoneuron. High levels of cholinesterase would tend to interfere with synaptic transmission, as would high (not low) levels of magnesium. The end-plate potential is produced by the flow of Na^+ through channels permeable to both Na^+ and K^+ .

17. The answer is b. (*Guyton, pp 84–86, 89–90.*) The greatest difference in excitation-contraction coupling involves the role of calcium in initiating contraction. In smooth muscle, calcium binds to and activates calmodulin, which, by activating myosin light chain kinase (MLCK), catalyzes the phosphorylation of the 20,000-Da myosin light chain (LC_{20}). Once the light chains are phosphorylated, myosin cross-bridges bind to actin on the thin filaments, which initiates contraction. In skeletal muscle, calcium binds to troponin, which removes the tropomyosin-mediated inhibition of the actin-myosin interactions. Once the inhibition is removed, cross-bridge cycling (and contraction) begins. In both smooth and skeletal muscle, force is generated by the cycling of cross-bridges. ATP provides the energy for the cycling of the cross-bridges in both muscles. In skeletal muscle, activator calcium comes exclusively from the sarcoplasmic reticulum (SR), while in smooth muscle, calcium can come from both the SR and the extracellular fluid.

18. The answer is d. (*Berne, 3/e, pp 115–116, 157–158.*) 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 μm 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.

19. The answer is d. (*Berne, 3/e, pp 34–36.*) 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

threshold. The amount of charge that must flow to produce this depolarization decreases as the capacitance decreases. Therefore, as the capacitance decreases, conduction velocity increases. The flow of charge decreases as the diameter of the nerve fiber decreases, therefore decreasing the velocity of conduction. The space constant ($\sqrt{R_m/R_{in}}$) is a measure of how far along the axon the charge will flow. The smaller the space constant, the greater the dissipation of charge through the membrane and therefore the slower the propagation velocity. Decreasing (depolarizing) the resting membrane potential inactivates sodium channels. This will decrease the flow of charge across the membrane during an action potential and thus decrease the velocity of propagation.

20. The answer is c. (*Berne, 3/e, pp 8–10.*) The rate of diffusion is described by Fick's law, which states that the flux of material across a membrane is directly proportional to the area of a membrane and the concentration difference of the particles on either side of the membrane and is inversely proportional to the thickness of the membrane. In general, if all other properties of the membrane are the same, the greater the lipid solubility of a particle, the greater its concentration in the membrane and, therefore, the greater its flux across the membrane.

21. The answer is b. (*Rhoades, p 38.*) Periodic hyperkalemic paralysis is caused by inactivation of the skeletal muscle membranes. Inactivation is produced by depolarization of the skeletal muscle membrane, which occurs when extracellular potassium concentration increases. 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.

22. The answer is b. (*Berne, 3/e, p 358.*) 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.

23. The answer is e. (*Berne, 3/e, pp 24–25.*) When the permeability of a particular ion is increased, the membrane potential moves toward the equilibrium potential for that ion. The equilibrium potentials for chloride (−80 mV) and potassium (−92 mV) are close to the resting membrane potential, so increases in their permeability have little effect on the resting membrane potential. The equilibrium potential for sodium (+60 mV) is very far from the resting membrane potential. Thus, increasing the permeability for sodium causes a large depolarization.

24. The answer is d. (*Berne, 3/e, pp 24–25, 31–33.*) During an action potential, the conductance for both sodium and potassium is higher than it is at rest. However, the conductance for sodium is higher than the conductance for potassium during the overshoot. Hence, the transference for potassium is less. Recall that transference is a measure of an ion's relative conductance:

$$T_{\text{ion}} = \frac{g_{\text{ion}}}{g_{\text{total}}}$$

where T = transference and g = conductance.

25. The answer is c. (*Rhoades, p 40.*) The repolarization phase of the action potential is produced by a decrease in Na^+ conductance, due to the inactivation of Na^+ channels, and the increase in K^+ conductance, due to the activation of K^+ channels. Preventing the inactivation of Na^+ channels will decrease the downstroke velocity of the action potential. This will slow the normal repolarization phase of the action potential and thereby prolong the duration of the action potential. The relative refractory period is prolonged because of the prolonged duration of the action potential.

26. The answer is a. (*Rhoades, pp 7–8.*) In both equilibrium and steady state conditions, there is no change in the concentration of materials inside or outside the cell. However, in a steady state condition energy must be consumed to keep the concentrations from changing. An equilibrium condition is not considered to be a homeostatic process because active physiologic mechanisms are not used to maintain it. Membrane potential and concentration differences across the membrane can be maintained in both states.

27. The answer is a. (*Berne, 3/e, pp 39–41.*) 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.

28. The answer is e. (*Berne, 3/e, pp 41–42.*) The channel opened by ACh when it binds to receptors on the end plates of skeletal muscle fibers is equally permeable to potassium and sodium. The increase in sodium permeability allows sodium to flow into the cell and produces the end-plate potential. The plateau phase of ventricular muscle action potentials and the upstroke of smooth muscle action potentials are produced by an increase in calcium conductance. An increase in potassium conductance is responsible for the downstroke of the action potential. The refractory period is caused by an increase in potassium conductance and a decrease in the number of sodium channels available to produce an action potential (i.e., sodium channel inactivation).

29. The answer is e. (*Guyton, pp 56–58.*) 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. When potassium is added to the extracellular fluid, it depolarizes the nerve cell membrane and causes the electrically excitable gates on the potassium channel to open. 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.

30. The answer is c. (*Guyton, p 49.*) 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 cal-

cium 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.

31. The answer is a. (*Berne, 3/e, pp 31–34.*) When the extracellular potassium concentration is increased, the membrane depolarizes. Depolarization causes potassium channels to open, which increases potassium permeability. Depolarization also causes sodium channels to inactivate, which reduces the number of sodium channels that are able to open in response to a stimulus. Since fewer channels can respond to the stimulus, a larger than normal stimulus is required to generate an action potential. The activity of the sodium-potassium pump may increase somewhat in response to the increase in extracellular potassium. However, the increase will be quite small because the potassium binding sites on the pump are nearly saturated at normal physiologic potassium concentrations.

32. The answer is c. (*Berne, 3/e, pp 34–37.*) The amount of potassium leaking out of the cell depends on its driving force and its membrane conductance. The driving force is the difference between the membrane potential and the equilibrium potential for potassium. Since the membrane potential is more positive than the equilibrium potential for potassium, hyperpolarizing the membrane (that is, making it more negative) would reduce the driving force. Increasing the intracellular potassium concentration increases the equilibrium potential for potassium, that is, makes it more negative and thus increases the driving force. Reducing the sodium-potassium pump activity would cause the potassium concentration gradient to fall, which, in turn, would cause a decrease in the amount of potassium leaking out of the cell. However, this would not occur immediately. In fact, because the pump is electrogenic, a small depolarization would initially follow a cessation of pump activity and this would cause an increase in the driving force for potassium.

33. The answer is b. (*Berne, 3/e, pp 170–172.*) Smooth muscle contraction is regulated by a series of reactions that begins with the binding of calcium to calmodulin. The calcium-calmodulin complex then binds to and activates a protein kinase called myosin light chain kinase (MLCK). MLCK

catalyzes the phosphorylation of the myosin light chains (LC_{20}). Once these light chains are phosphorylated, myosin and actin interaction can occur and the muscle shortens and develops tension. Although two molecules of ATP are required to initiate contraction, one for the phosphorylation of myosin light chains and one to bend the myosin cross-bridge, smooth muscle is energetically efficient because the rate of cross-bridge cycling is so slow.

34. The answer is b. (*Rhoades, p 54. Guyton, 10/e, pp 552–555.*) Substance P is an 11-amino acid polypeptide found in neurons within the hypothalamus and spinal cord. It is released from small A delta and C fibers that relay information from nociceptors to neurons within the substantia gelatinosa of the spinal cord. Endorphins and other opioid neurotransmitters may partially inhibit the perception of pain by presynaptically inhibiting the release of substance P from nociceptor afferent fibers.

35. The answer is d. (*Guyton, pp 43–44, 885–886.*) Glucose is transported into fat cells by facilitated diffusion and thus does not require the direct or indirect use of energy. Insulin increases the rate of diffusion but is not necessary for the diffusion. Sodium and potassium are transported by the Na-K pump, calcium is transported into the sarcoplasmic reticulum by a Ca pump, and hydrogen is transported by a H^+ pump. All of these transporters use ATP directly in the transport process. In the proximal tubule, hydrogen is secreted by an Na/H exchange process; this is an example of secondary active transport.

36–37. The answers are 36-d, 37-a. (*Rhoades, pp 7, 37–40. Berne, 3/e, pp 31–32.*) When the inward Na current exceeds the outward potassium current, the membrane potential depolarizes toward the Na^+ equilibrium potential. The only point on the diagram in which the membrane is depolarizing is point D. When the K^+ current exceeds the Na^+ current, the membrane potential hyperpolarizes toward the K^+ equilibrium potential. When the membrane potential is not changing, for example, at point A and E, the two currents are equal.

The Na^+ equilibrium potential is usually between +60 mV and +70 mV, depending on the ratio of the intracellular and extracellular Na^+ concentrations. During an action potential, the peak of the action potential (point A) is close, but not equal, to the Na^+ equilibrium potential. The

membrane potential doesn't reach the Na^+ equilibrium potential because the Na^+ channels start to inactivate and the K^+ channels begin to activate during the upstroke of the action potential.

38. The answer is c. (*Rhoades, pp 151–154.*) When skeletal muscle fibers are at rest, tropomyosin inhibits the interaction between actin and myosin. The inhibition is removed when Ca^{2+} binds to troponin. The binding of Ca^{2+} to troponin causes troponin to undergo a conformational change, during which tropomyosin is moved from its resting position to a position where it no longer blocks the interaction between the myosin cross-bridges and actin.

39. The answer is c. (*Berne, 3/e, pp 203–204.*) Phospholamban regulates the activity of the SR calcium pump in cardiac muscle. The inhibition is reduced when phospholamban is phosphorylated by a cAMP-dependent kinase called protein kinase A. When the ventricular muscle beta-receptors are activated by sympathetic stimulation or circulating catecholamines, they activate a G protein, which, in turn, activates adenylyl cyclase. Adenylyl cyclase catalyzes the formation of cAMP, which activates protein kinase A.

40. The answer is a. (*Guyton, p 440.*) Beta-receptor-activated G proteins activate adenylyl cyclase which catalyzes the formation of cAMP. cAMP activates protein kinase A, which phosphorylates phospholamban. Phosphorylated phospholamban releases the SR Ca^{2+} pump from inhibition. The sequestration of Ca^{2+} into the SR relaxes bronchiolar smooth muscle. In cardiac muscle, the sequestration of Ca^{2+} into the SR increases contractile strength because there is more Ca^{2+} available for release with each action potential. The depolarization of the SA node is caused by activation of the “funny” channel. This channel is activated at negative membrane potentials. The rate of its activation is increased when it is phosphorylated by protein kinase A. The transport of Ca^{2+} into skeletal muscle fibers is not affected by beta-receptors. Glycogenolysis in the liver is also increased by activated beta-receptors. In this case, the protein kinase A phosphorylates an enzyme called phosphorylase, which begins the process of glycogenolysis.

41. The answer is b. (*Berne, 3/e, pp 63–64.*) Nitric oxide (NO) produces its physiologic effects by activating guanylyl cyclase, which, in turn, catalyzes the formation of cGMP. cGMP can affect membrane function di-

rectly—for example, it keeps Na^+ channels open in rods and cones—and indirectly by activating a protein kinase. NO is the endothelial-derived relaxing factor (EDRF) that allows blood vessels to relax. NO is synthesized by nitric oxide synthase (NOS): It diffuses through cell membranes and so produces its effects within the cytoplasm of a cell, and it is degraded rapidly, so its effects are short-lived.

42. The answer is c. (*Rhoades, pp 45–51.*) The NMDA receptor channel is a large channel permeable to Ca^{2+} , K^+ , and Na^+ . It is activated by glutamate, but unlike other glutamate receptor channels, the NMDA channel is blocked by Mg^{2+} in its resting state. Depolarization of the cell membrane to approximately -40 mV removes the Mg^{2+} blockade. Therefore, the NMDA channel is only opened when the cell is depolarized by other excitatory neurotransmitters. The Ca_2 entering the cell activates a number of intracellular enzymes, some of which may be involved in memory.

43–44. The answers are 43-c, 44-d. (*Rhoades, pp 182–186. Guyton, pp 89–90.*) Cross-bridge cycling in smooth muscle cannot begin until the myosin light chains are phosphorylated (step 1). Phosphorylation is enzymatically stimulated by myosin light chain kinase (MLCK). Phospholipase C is a phosphodiesterase enzyme that catalyzes the hydrolysis of PIP_2 to IP_3 . IP_3 promotes the release of Ca^{2+} from the sarcoplasmic reticulum (SR). Ca^{2+} activates calmodulin, which, in turn, activates MLCK.

Latch bridges are unphosphorylated myosin cross-bridges that are bound to actin. These cross-bridges cycle very slowly or not at all and are responsible for the ability of smooth muscle to maintain its tone for a long time without expending energy for cross-bridge cycling. The enzyme myosin light chain phosphatase is responsible for dephosphorylating cycling cross-bridges. The smooth muscle relaxes when Ca^{2+} is removed from the myoplasm and the latch bridges detach from actin.

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Cardiac Physiology

Questions

DIRECTIONS: Each question below contains five suggested responses. Select the **one best** response to each question.

45. In a test subject, oxygen consumption was measured at 700 mL/min. Pulmonary artery oxygen content was 140 mL per liter of blood and brachial artery oxygen content was 210 mL per liter of blood. Cardiac output was which of the following?

- a. 4.2 L/min
- b. 7.0 L/min
- c. 10.0 L/min
- d. 12.6 L/min
- e. 30.0 L/min

46. Which one of the following is the best index of preload?

- a. Blood volume
- b. Central venous pressure
- c. Pulmonary capillary wedge pressure
- d. Left ventricular end-diastolic volume
- e. Left ventricular end-diastolic pressure

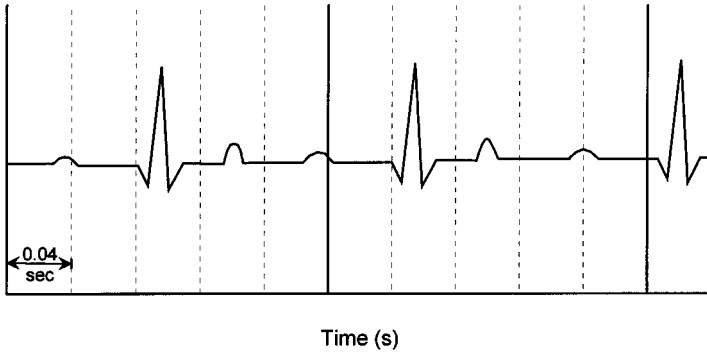
47. Which one of the following is the best index of afterload?

- a. Left ventricular end-diastolic pressure
- b. Left ventricular mean systolic pressure
- c. Pulmonary capillary wedge pressure
- d. Total peripheral resistance
- e. Mean arterial blood pressure

48. The highest blood flow per gram of left ventricular myocardium would occur

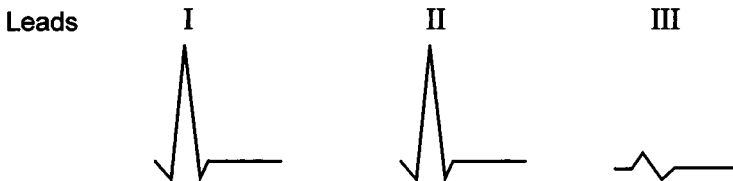
- a. When aortic pressure is highest
- b. When left ventricular pressure is highest
- c. At the beginning of isovolumic contraction
- d. When aortic blood flow is highest
- e. At the beginning of diastole

49. Which of the following is consistent with the ECG tracing shown below?



- a. Bradycardia
- b. First-degree heart block
- c. Second-degree heart block
- d. Third-degree heart block
- e. Tachycardia

50. The mean electrical axis during the ventricular depolarization recorded in the three leads shown below would be closest to



- a. 30 degrees
- b. 90 degrees
- c. 150 degrees
- d. 210 degrees
- e. 270 degrees

51. During ventricular ejection, the pressure difference smallest in magnitude is between the

- a. Pulmonary artery and left atrium
- b. Right ventricle and right atrium
- c. Left ventricle and aorta
- d. Left ventricle and left atrium
- e. Aorta and capillaries

52. Which of the following would result from a regurgitant aortic valve in a nonfailing heart?

- a. A decrease in diastolic pressure
- b. A decrease in cardiac energy consumption
- c. A systolic murmur
- d. A decrease in heart rate
- e. A decrease in systolic blood pressure

53. Stroke volume is increased by

- a. A decrease in venous compliance
- b. An increase in afterload
- c. A decrease in contractility
- d. An increase in heart rate
- e. A decrease in coronary blood flow

54. An increased preload would most likely be caused by an increase in

- a. Arteriolar tone
- b. Venous tone
- c. Myocardial contractility
- d. Heart rate
- e. Capillary permeability

55. Propagation of the action potential through the heart is fastest in the

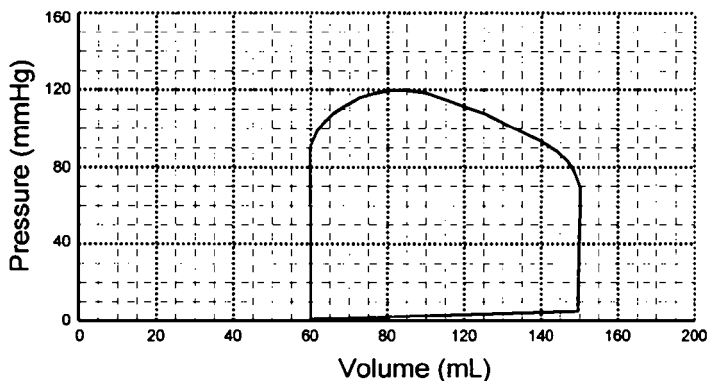
- a. SA node
- b. Atrial muscle
- c. AV node
- d. Purkinje fibers
- e. Ventricular muscle

56. A patient in heart failure improves markedly after using a drug that increases the inotropic state of her heart. Which one of the following changes is primarily responsible for the improvement in her condition?

- a. A reduction in heart rate
- b. A reduction in heart size
- c. An increase in end-diastolic pressure
- d. An increase in wall thickness
- e. An increase in cardiac excitability

Questions 57–58

Use the pressure-volume curve illustrated below to determine the ejection fraction and diastolic pressure.



57. The ejection fraction equals

- a. 0.50
- b. 0.55
- c. 0.60
- d. 0.65
- e. 0.70

58. The diastolic pressure equals

- a. 0 mmHg
- b. 5 mmHg
- c. 70 mmHg
- d. 90 mmHg
- e. 120 mmHg

59. Closure of the aortic valve occurs at the onset of which phase of the cardiac cycle?

- a. Isovolumetric contraction
- b. Rapid ejection
- c. Protodiastole
- d. Isovolumetric relaxation
- e. Rapid filling

60. If the QRS complex is positive in leads II and aVF and negative in lead III, the mean electrical axis (MEA) is between

- a. -30° and 0°
- b. 0° and $+30^\circ$
- c. $+30^\circ$ and $+60^\circ$
- d. $+60^\circ$ and $+90^\circ$
- e. $+90^\circ$ and $+120^\circ$

61. Which one of the following is most likely to be observed in a patient with untreated atrial fibrillation?

- a. An increased venous A wave
- b. An increased left atrial pressure
- c. A decreased heart rate
- d. An increased stroke volume
- e. An increased arterial blood pressure

62. Normal splitting of the second heart sound (S_2) into two components is increased during inspiration because

- a. The closing of the aortic valve is delayed
- b. The opening of the mitral valve is delayed
- c. The closing of the pulmonic valve is delayed
- d. The stroke volume of the left ventricle is increased
- e. The heart rate is decreased

63. Which of the following statements about the third heart sound (S_3) is correct?

- a. It is usually diminished in congestive heart failure
- b. It is produced by turbulence during rapid ventricular filling in early diastole
- c. It is produced by turbulence following atrial contraction
- d. It is often associated with the “floppy” mitral valve syndrome
- e. It is produced by flow through the patent foramen ovale

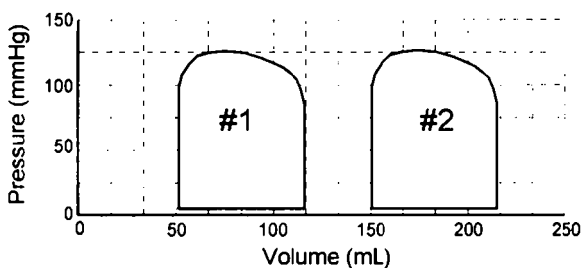
64. In a resting, healthy man, the ejection fraction is approximately?

- a. 0.1
- b. 0.2
- c. 0.3
- d. 0.6
- e. 0.9

65. Sustained elevation of cardiac output will occur with which of the following conditions?

- a. Hypertension
- b. Aortic regurgitation
- c. Anemia
- d. Third-degree heart block
- e. Cardiac tamponade

66. The diagram below illustrates the pressure-volume curves for two different hearts. Which of the following is greater in curve 1?



- a. Preload
- b. Work
- c. Energy consumption
- d. Efficiency
- e. Stroke volume

67. A diastolic murmur accompanied by an increased preload can be caused by

- a. Mitral stenosis
- b. Mitral regurgitation
- c. Atherosclerosis
- d. Aortic regurgitation
- e. Tachycardia

68. Increasing vagal stimulation of the heart will cause an increase in

- a. Heart rate
- b. PR interval
- c. Ventricular contractility
- d. Ejection fraction
- e. Cardiac output

69. During exercise, there is an increase in a person's

- a. Stroke volume
- b. Diastolic pressure
- c. Venous compliance
- d. Pulmonary arterial resistance
- e. Total peripheral resistance

70. Phase-4 depolarization of SA nodal cells is caused by

- a. An increase in the flow of sodium into the cell
- b. A decrease in the flow of potassium out of the cell
- c. An increase in the activity of the Na/Ca exchanger
- d. A decrease in the flow of chloride out of the cell
- e. A decrease in the activity of the Na-K pump

71. Cardiovascular changes that occur during inspiration include decreased

- a. Right ventricular filling
- b. Right ventricular output
- c. Pressure gradient from extrathoracic veins to the right atrium
- d. Systemic blood pressure
- e. Left ventricular contractility

72. Blood pressure increases and heart rate decreases in response to

- a. Exercise
- b. Increased body temperature
- c. Exposure to high altitude
- d. Increased intracranial pressure
- e. Hemorrhage

73. During exercise, cardiac output is augmented by

- a. Sympathetic stimulation of resistance vessels
- b. Dilation of venous vessels
- c. Decreased end-diastolic volume
- d. Decreased mean systemic arterial pressure
- e. Increased ventricular contractility

74. When flow through the mitral valve is restricted by mitral stenosis,

- a. Exercise can induce acute pulmonary edema
- b. Left ventricular preload increases
- c. Left atrial pressure diminishes
- d. Right ventricular end-diastolic pressure decreases
- e. Central venous pressure decreases

75. Stroke volume can be decreased by

- a. Increasing ventricular contractility
- b. Increasing heart rate
- c. Increasing central venous pressure
- d. Decreasing total peripheral resistance
- e. Decreasing systemic blood pressure

76. An ectopic extrasystole caused by a ventricular focus is characterized by

- a. Interruption of the regular SA node discharge
- b. Retrograde conduction of the action potential to the atria
- c. A skipped ventricular contraction
- d. A skipped atrial contraction
- e. A larger than normal force of contraction

77. The electrocardiogram is most effective in detecting a decrease in

- a. Ventricular contractility
- b. Mean blood pressure
- c. Total peripheral resistance
- d. Ejection fraction
- e. Coronary blood flow

78. Stroke volume can be increased by

- a. Decreasing ventricular compliance
- b. Increasing venous compliance
- c. Decreasing total peripheral resistance
- d. Increasing heart rate
- e. Decreasing atrial contractility

79. Which one of the following will be observed in a patient with a dilated failing left ventricle and a normal resting mean blood pressure?

- a. A decreased heart rate
- b. A decreased left ventricular wall stress
- c. An increased left ventricular ejection fraction
- d. A decreased left ventricular energy consumption
- e. An increased pulmonary capillary hydrostatic pressure

80. Which one of the following correctly describes an event that normally occurs during the PR interval?

- a. The ventricle is contracting
- b. The cardiac action potential passes through the AV node
- c. There is no change in the voltage tracing on the ECG
- d. The mitral and aortic valves are both closed
- e. The second heart sound is heard

81. Left ventricular wall stress will be decreased by an increase in

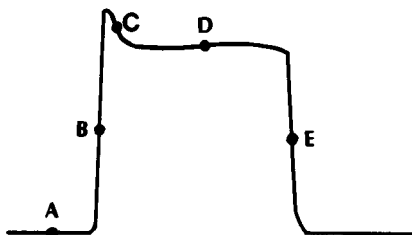
- a. The left ventricular end-diastolic volume
- b. The contractility of the left atrium
- c. The thickness of the free wall of the left ventricle
- d. The total peripheral resistance
- e. The mean arterial blood pressure

82. Which one of the following will be observed in a patient with aortic regurgitation?

- a. An increased ejection fraction
- b. An increased mean blood pressure
- c. An increased diastolic blood pressure
- d. A decreased pulse pressure
- e. A decreased left atrial end-diastolic pressure

Question 83

The phases of the ventricular muscle action potential are represented by the lettered points on the diagram.

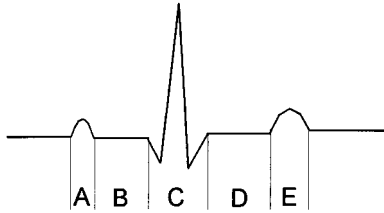


83. At which point on the above ventricular action potential is membrane potential most dependent on calcium permeability?

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

Questions 84–85

Use the following ECG to answer the next two questions.



84. During which interval on the above ECG does the aortic valve close?

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

85. During which interval on the ECG does the bundle of His depolarize?

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

86. The diagnosis of a first-degree heart block is made if

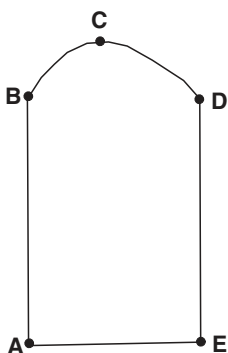
- a. The PR interval of the ECG is increased
- b. The P wave of the ECG is never followed by a QRS complex
- c. The P wave of the ECG is sometimes followed by a QRS complex
- d. The T wave of the ECG is inverted
- e. The ST segment of the ECG is elevated

87. Positive inotropic drugs such as digitalis reduce ischemic cardiac pain (angina) in a dilated failing heart by

- a. Decreasing preload
- b. Increasing diastolic filling time
- c. Decreasing total peripheral resistance
- d. Increasing heart rate
- e. Increasing coronary blood flow

Questions 88–90

Use the following pressure-volume loop to answer the questions.



88. The mitral valve opens at point

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

89. The second heart sound begins at point

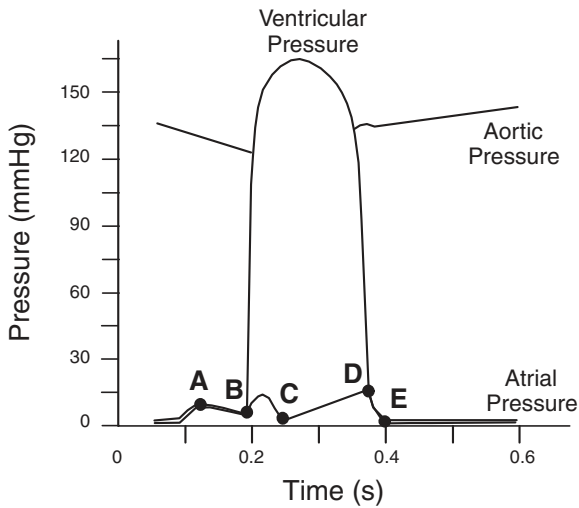
- a. A
- b. B
- c. C
- d. D
- e. E

90. Systole begins at point

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

Questions 91–92

Use the following diagram to answer the questions.



91. Ventricular filling begins at point

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

92. Closing of the mitral valve begins at point

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

93. Mitral prolapse is a common cause of mitral regurgitation in young women. Which one of the following is observed in a patient with mitral prolapse?

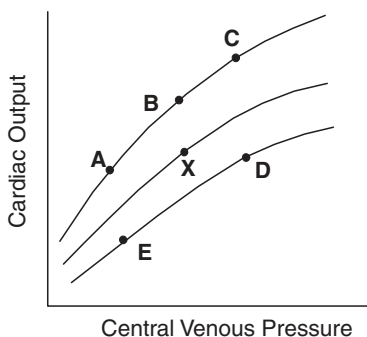
- a. A diastolic murmur
- b. A decrease in left ventricular volume
- c. A normal stroke volume
- d. An increase in the V wave
- e. A decrease in cardiac output

94. A major sign of cardiac tamponade is

- a. Hypertension
- b. Bradycardia
- c. Ventricular dilation
- d. Pulsus paradoxus
- e. Third-degree heart block

Questions 95–96

Use the following diagram of three Starling curves to answer the questions.



95. A mild hemorrhage will cause stroke volume to shift from point X to point

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

96. An increase in afterload and venous compliance can cause stroke volume to change from the point marked X to point

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

97. The upstroke of the SA nodal action potential is produced by opening a channel that is

- a. Primarily permeable to Na^+
- b. Primarily permeable to Ca^{2+}
- c. Primarily permeable to K^+
- d. Primarily permeable to Cl^-
- e. Equally permeable to Na^+ and K^+

98. The channel responsible for the initiation of phase-4 depolarization in SA nodal cells

- a. Is primarily permeable to Na^+
- b. Is opened by membrane depolarization
- c. Is opened by vagal nerve stimulation
- d. Is primarily permeable to K^+
- e. Is closed by norepinephrine

99. Sympathetic stimulation of the heart results in

- a. An increase in the activity of the SR calcium pump
- b. An increase in the duration of systole
- c. An increase in the duration of diastole
- d. A decrease in the affinity of troponin for calcium
- e. A decrease in the concentration of Ca^{2+} during systole

100. An exercise stress test to rule out ischemic heart disease is positive if

- a. The systolic blood pressure rises
- b. The ST segment of the ECG is depressed
- c. The heart rate fails to increase
- d. A diastolic murmur is heard
- e. The diastolic blood pressure decreases

Cardiac Physiology

Answers

45. The answer is c. (*Guyton, pp 220–221.*) Cardiac output can be measured by using Fick's principle, which asserts that the rate of uptake of a substance by the body (e.g., O_2 consumption in milliliters per minute) is equal to the difference between its concentrations (milliliters per liter of blood) in arterial and venous blood multiplied by the rate of blood flow (cardiac output). This principle is restricted to situations in which arterial blood is the only source of the substance measured. If oxygen consumption by the body at steady state is measured over a period of time and the difference in arterial O_2 and venous O_2 measured by sampling arterial blood and *pulmonary* arterial blood (which is fully mixed venous blood), cardiac output is obtained from the expression

$$CO = \frac{V_{O_2}}{(AO_2 - VO_2) \text{ content}}$$

$$CO = \frac{700 \text{ mL/min}}{210 \text{ mL/min} - 140 \text{ mL/min}} = 10 \text{ L/min}$$

46. The answer is d. (*Berne, 3/e, pp 202–206.*) *Preload* is defined as the sarcomere length at the end of diastole. The parameter most directly related to sarcomere length during this time period is left ventricular end-diastolic volume. Although blood volume, central venous pressure, pulmonary capillary wedge pressure, and left ventricular end-diastolic pressure can all influence preload, they all exert their influence through changes in end-diastolic volume. Each of these parameters could change without altering preload.

47. The answer is b. (*Berne, 3/e, pp 204–206.*) The *afterload* is the force that the sarcomeres must overcome in order to shorten during systole. According to the law of Laplace, this force is proportional to the pressure (P) and radius (r) of the ventricle during ejection ($\text{force} \propto P \times r$). The mean left ventricular systolic pressure would therefore be the best index of afterload. Although total peripheral resistance can influence afterload by causing

changes in mean arterial blood pressure, these factors can only influence afterload by causing a change in ventricular pressure. Pulmonary capillary wedge pressure and left ventricular end-diastolic pressure are estimates of the volume of blood in the ventricle during diastole and are indices of preload.

48. The answer is e. (*Guyton, pp 226–227.*) Blood flow through the coronary vessels of the left ventricle is determined by the ratio of perfusion pressure to vascular resistance. The perfusion pressure is directly related to the aortic pressure at the ostia of the coronaries. Myocardial vascular resistance is significantly influenced by the contractile activity of the ventricle. During systole, when the ventricle is contracting, vascular resistance increases substantially. Flow is highest just at the beginning of diastole because, during this phase of the cardiac cycle, aortic pressure is still relatively high and vascular resistance is low due to the fact that the coronary vessels are no longer being squeezed by the contracting myocardium.

49. The answer is b. (*Guyton, pp 134–136.*) The only abnormality in the ECG illustrated is a prolonged PR interval representing a delay in the propagation of the cardiac action potential from the atria to the ventricles. This is defined as a first-degree heart block. The normal PR interval is between 0.12 and 0.20 s. In a second-degree heart block, some of the P waves are not propagated into the ventricles, but every QRS complex is preceded by a P wave. In third-degree heart block, the atria and ventricles are electrically isolated and thus beat independently. The ventricular rate during a third-degree heart block is typically about 40 beats per minute. Tachycardia is a rapid heart rate above 100 beats per minute, and bradycardia is a slow heart rate below 60 beats per minute. The heart rate from which this ECG tracing was obtained was 75 beats per minute.

50. The answer is a. (*Guyton, pp 120–122.*) The mean electrical axis (MEA) represents the average direction traveled by the ventricular muscle action potentials as they propagate through the heart. The propagation path and the mass of tissue through which the action potentials travel influence the direction. The MEA is approximately perpendicular to the axis of the limb lead with the smallest QRS wave magnitude. In this case, the smallest deflection is in lead III. Therefore, the MEA lies along lead aVR. As shown in the diagram, the MEA could be either $+30^\circ$ or -150° . Since the deflection is upright in leads I and II, the MEA is $+30^\circ$.

51. The answer is c. (*Guyton, pp 99–102.*) 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. Since the tricuspid valve is closed during ventricular ejection, there is an appreciable pressure difference between the right ventricle and the left atrium, although this pressure difference is opposite in direction to the flow of blood through the circulatory system. Although pulmonary vascular resistance is relatively small compared with systemic vascular resistance, it nonetheless produces a pressure drop between the right ventricle and the left atrium. Since 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.

52. The answer is a. (*Guyton, pp 248–249.*) Blood leaks from the aorta into the left ventricle during diastole in patients with regurgitant aortic valves. The rapid flow of blood out of the aorta reduces diastolic pressure in the aorta. At the same time, the rapid flow of blood into the left ventricle causes an increase in preload, which results in a larger stroke volume. The large stroke volume injected into the aorta during systole would increase the volume in the arterial system during ejection and therefore increase systolic pressure. The increase in stroke volume would also be associated with an increase in energy consumption by the heart. Murmurs result from the turbulence of blood passing through a narrowed orifice, such as a stenotic valve or one which has not fully closed. Blood flowing from the aorta into the ventricle through the partially opened aortic valve produces the sounds responsible for the diastolic murmur associated with a regurgitant aortic valve. 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.

53. The answer is a. (*Rhoades, pp 263–269.*) Stroke volume depends on preload, afterload, and contractility. Decreasing venous compliance forces more blood into the ventricle, resulting in an increased preload and an increased stroke volume. Increasing afterload and decreasing contractility decreases stroke volume. An increase in heart rate may result in a decreased filling time and, therefore, a decrease in preload and stroke volume. A

decrease in coronary blood flow causes a decrease in ventricular contractility and stroke volume.

54. The answer is b. (*Guyton, pp 216–219.*) *Preload* is the volume of blood within the ventricles at the end of diastole. Preload can be increased directly by increasing venous volume or decreasing venous compliance. Thus, an increase in venous tone would decrease venous compliance and lead to an increase in preload. Increasing capillary permeability would decrease vascular blood volume and lead to a decrease in preload. Indirectly, reducing cardiac output can increase preload. A reduction in cardiac output leaves a larger portion of the vascular blood volume on the venous side. The increase in venous blood volume leads to a larger preload. Cardiac output is increased by an increase in myocardial contractility and heart rate and so would tend to lower preload. An increase in arteriolar tone, leading to an increase in total peripheral resistance, would tend to trap more blood on the arterial side of the circulation and therefore lower the amount of venous blood. The decrease in venous vascular blood volume would lead to a decrease in preload.

55. The answer is d. (*Guyton, pp 109–111.*) The most rapid conduction of the action potential occurs through the Purkinje fibers. The slowest conduction occurs in the AV node. The cardiac action potential is initiated normally by pacemaker cells located within the SA node. The action potential propagates from the SA node into the atrial muscle fibers. It then passes through the AV node and the His-Purkinje network to the ventricular muscle fibers. The rapid conduction of the action potential through the His-Purkinje network ensures rapid and synchronous activation of the entire ventricular muscle. The slow conduction through the AV node produces a delay between atrial and ventricular systole, allowing the ventricle to receive the blood ejected by the atria before it contracts.

56. The answer is b. (*Guyton, pp 241–243.*) The most obvious deleterious effect of a failing heart is the inability to pump enough blood to satisfy the energy requirements of all the tissues. Among the compensatory mechanisms that develop in response to heart failure is an increase in retention of fluid by the kidney. Increased retention of fluid causes the end-diastolic volume of the heart to increase, which, by the Starling mechanism, increases the strength of the heartbeat. However, two deleterious effects result from an

increase in end-diastolic volume. A larger than normal end-diastolic volume causes an increase in end-diastolic pressure, which can lead to pulmonary edema. In addition, the large end-diastolic volume increases the wall stress that must be developed by the heart with each beat, and this increases the myocardial requirement of oxygen. The increase in contractility that results from the administration of a positive inotropic drug such as digoxin will allow the heart to produce the same force at a lower volume and thus eliminate the need for an increase in volume of fluid.

57. The answer is c. (*Guyton, pp 100–103.*) The ejection fraction (EF) is equal to the stroke volume (SV) divided by the end-diastolic volume (EDV)

$$EF = \frac{SV}{EDV - ESV} = \frac{EDV - ESV}{EDV} = \frac{150 \text{ mL} - 90 \text{ mL}}{150 \text{ mL}} = 0.6$$

58. The answer is c. (*Guyton, pp 102–103.*) Diastolic pressure is the lowest pressure observed in the aorta during each cardiac cycle. It occurs at the end of isovolumic contraction, just before ejection of blood from the left ventricle begins. In this case, isovolumic contraction ends when the pressure within the ventricle rises to 70 mmHg. The term *diastolic pressure* always refers to arterial blood pressure. In the diagram, the left ventricular end-diastolic pressure equals 5 mmHg.

59. The answer is d. (*Guyton, pp 99–103.*) Closure of the semilunar valves (aortic and pulmonic valves) marks the beginning of the isovolumetric relaxation phase of the cardiac cycle. During this brief period (approximately 0.06 s), 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.

60. The answer is b. (*Guyton, pp 100–103, 125–127.*) If the QRS complex is positive in lead II, the MEA must be between -30° and $+150^\circ$. If the QRS complex is positive in aVF, the MEA must be between 0° and 180° . If the QRS complex is negative in lead III, the MEA must be between -150° and $+30^\circ$. For all three conditions to exist, the MEA must be between 0° and $+30^\circ$.

61. The answer is b. (*Guyton, pp 141–142.*) Atrial fibrillation is an arrhythmia in which the electrical activity of the atrium becomes disorganized and therefore unable to produce a coordinated atrial contraction. The absence of an atrial pulse reduces the emptying of the atria during diastole and results in an enlarged left atrium and increased left atrial pressure. The venous A wave represents atrial contraction and disappears due to the absence of an atrial beat. Decreased filling of the heart results in a decrease in stroke volume. Heart rate increases because the continuous electrical activity of the atria initiates a high rate of ventricular activity. Systemic blood pressure typically falls because of inadequate filling of the ventricles and the resulting decrease in stroke volume.

62. The answer is c. (*Rhoades, p 262.*) The second heart sound (S_2) is produced by vibrations in the arterial blood column and arterial walls as the aortic and pulmonic valves undergo tension during closure. Heard over the left sternal border, this sound normally can be resolved into two components representing closure of the aortic and pulmonic valves. Resolution is greatest during inspiration, when venous return increases on the right and prolongs right ventricular ejection. Any event that delays closure of the pulmonic valve thus enhances the splitting; delayed closure of the aortic valve or early closure of the pulmonic valve diminishes the splitting. Closure of the mitral valve and atrial systole influence the first heart sound (S_1).

63. The answer is b. (*Rhoades, p 262.*) The third heart sound (S_3) is commonly heard in children and young adults. It is usually a pathological sign when heard in adults over 40. It is produced by the sudden deceleration of blood at the end of the rapid ventricular filling phase of the cardiac cycle. It is most often caused by conditions that decrease ventricular compliance, such as increased end-systolic volumes, ischemic heart disease, or cardiac tamponade. However, it can also occur when rapid filling of the ventricle is abnormally high, for example, in anemia or mitral regurgitation.

64. The answer is d. (*Guyton, pp 99–103.*) The *ejection fraction* is the fraction of blood ejected from the ventricle during systole, which is typically between 0.6 and 0.7. Ejection fraction can be increased by an increase in contractility or a decrease in afterload. Heart failure causes a decrease in ejection fraction.

65. The answer is c. (*Guyton, pp 213–214.*) The magnitude of the cardiac output is regulated to maintain an adequate blood pressure and to deliver an adequate supply of oxygen to the tissues. In anemia, a greater cardiac output is required to supply oxygen to the tissues because the oxygen-carrying capacity of the blood is reduced. In aortic regurgitation, the stroke volume will be increased. However, a portion of the blood ejected by the heart will return to the heart during diastole. Thus, the output delivered to the tissues does not increase despite the fact that the blood ejected by the heart has increased. In hypertension, third-degree heart block, and cardiac tamponade (decreased filling of the heart due to accumulation of fluid within the pericardium), cardiac output will be normal, or, if compensation is not possible, cardiac output will be reduced.

66. The answer is d. (*Guyton, p 103.*) Efficiency is defined as work divided by energy consumption. The heart represented by pressure-volume curve 1 in the diagram has a lower end-diastolic volume and, therefore, ejects blood at a lower wall stress than the heart represented by pressure-volume curve 2. Cardiac energy consumption is directly related to wall stress. Because both hearts eject the same amount of blood (stroke volume) at the same pressure, they perform the same amount of work. Therefore, heart 1 is more efficient because it does the same work using less energy.

67. The answer is d. (*Guyton, pp 247–248.*) A diastolic murmur occurs when blood leaks back into the ventricle through an incompetent pulmonic or aortic valve during diastole or travels through a stenotic mitral or tricuspid (AV) valve during ventricular filling. Preload is increased during aortic or pulmonic regurgitation because the blood retrogradely passing through the valve will be added to the blood entering through the AV valves. Preload is reduced when the AV valves are stenotic because less blood is able to enter the ventricles during diastole. Therefore, regurgitation of blood through an incompetent pulmonic or aortic valve will cause an increase in preload and a diastolic murmur.

68. The answer is b. (*Guyton, pp 134–136.*) The vagal fibers innervating the heart stimulate intracardiac postganglionic fibers, which release acetylcholine (ACh). The postganglionic fibers innervate the SA and AV nodal fibers. ACh causes a decrease in the rate of phase-4 depolarization, thus

slowing the heart, and a decrease in conduction velocity through the AV node, thus increasing the PR interval. ACh also causes a slight decrease in contractility. Decreasing the heart rate increases the amount of time available for ventricular filling and thus increases end-diastolic volume. However, the end-systolic volume will be somewhat elevated because of the slight decrease in contractility and increase in afterload. Thus, the ejection fraction will remain the same or decrease slightly.

69. The answer is a. (*Guyton, pp 224–226.*) During exercise, increased oxygen consumption and increased venous return to the heart result in an increase in cardiac output and an increase in blood flow to both skeletal muscle and the coronary circulation, where oxygen utilization is greatest. The increase in cardiac output is due to an increase in both heart rate and stroke volume. Systemic arterial pressure also increases in response to the increase in cardiac output. However, the fall in total peripheral resistance, which is caused by dilation of the blood vessels within the exercising muscles, results in a decrease in diastolic pressure. The pulmonary vessels undergo passive dilation as more blood flows into the pulmonary circulation. As a result, pulmonary vascular resistance decreases. The decrease in venous compliance, caused by sympathetic stimulation, helps maintain ventricular filling during diastole.

70. The answer is a. (*Berne, 3/e, pp 378–381.*) Phase-4 depolarization is caused by the activation of a Na^+ channel. The channel is called the *funny channel* because it is activated when the membrane hyperpolarizes in contrast to the Na channel responsible for the action potential, which is activated when the cell depolarizes. Potassium conductance decreases during phase-4 depolarization and thus the flow of potassium out of the cell is diminished. However, this change in potassium current is not responsible for phase-4 depolarization. Chloride conductance does not change during phase 4. The Na/Ca exchanger maintains low intracellular calcium at rest and may reverse its direction and pump calcium into the cell during phase 2 of the cardiac action potential. However, neither the Na/Ca exchanger nor the Na-K pump is involved in phase-4 depolarization.

71. The answer is d. (*Guyton, pp 193, 215.*) During inspiration, blood flow into the pulmonary circulation increases. The increased volume of blood in the right ventricle pushes the intraventricular septum toward the

left ventricle, resulting in a decreased filling of the left ventricle. The decrease in left ventricular preload results in a decreased left ventricular stroke volume and a decrease in systemic blood pressure.

72. The answer is d. (*Guyton, p 192.*) Exercise increases blood pressure and heart rate. Although tissue hypoxia causes arteriolar dilatation, acute hypoxia associated with sudden exposure to high altitudes generates hypertension, as well as excitement, disorientation, and headache. Fever produces tachycardia; blood pressure changes associated with increased body temperature depend on the cause of the temperature. With exercise and increased heat production (and increased blood pressure), vessels dilate in an attempt to dissipate heat. Fever with septic shock will, of course, be associated with a blood pressure decrease owing to vasodilation by endotoxin. Hemorrhage will cause a reflex sympathetic discharge that results in tachycardia and increased total peripheral resistance. If compensation is adequate, blood pressure may not fall. If intracranial pressure is rapidly elevated, cerebral blood flow is reduced. The increase in intracranial pressure stimulates the vasomotor center and produces an increase of systemic blood pressure that may lead to a restoration of cerebral blood flow (Cushing response). A profound bradycardia is also associated with this response.

73. The answer is e. (*Guyton, pp 224–226.*) During exercise, sympathetic stimulation of the heart and circulating epinephrine cause an increase in ventricular contractility and heart rate leading to an increase in cardiac output. Sympathetic stimulation also causes constriction of the venous vessels, which tends to increase end-diastolic volume. Despite sympathetic stimulation of the resistance vessels, local metabolites produced by the exercising muscles cause small arterioles within the muscles to dilate, which produces a decrease in total peripheral resistance (TPR). However, the fall in TPR does not normally produce a drop in mean systemic blood pressure because the increase in cardiac output is sufficient to counteract the fall in resistance. The increased vascular resistance from sympathetic stimulation of the nonexercising muscles and other organs tends to increase TPR and decrease cardiac output.

74. The answer is a. (*Guyton, pp 247–249.*) In patients with mitral stenosis, the flow of blood from the left atrium to left ventricle during diastole is diminished. The left atrium progressively dilates and left atrial pressure

risers. The increase in pressure is transmitted through the pulmonary circulation and eventually leads to an increase in right ventricular pressure. When cardiac output increases during exercise, restriction to flow through the mitral valve causes a sudden increase in pulmonary blood volume, and pulmonary venous and capillary pressures rise, which leads to transudation of fluid into alveoli and pulmonary edema.

75. The answer is b. (*Rhoades, pp 268–269.*) Stroke volume is determined by preload, afterload, and contractility. Increasing heart rate decreases the time for filling during diastole and may decrease preload and therefore stroke volume. Increasing preload by increasing central venous pressure will increase stroke volume. Similarly, decreasing afterload by decreasing total peripheral resistance or systemic blood pressure will cause an increase in stroke volume. Increasing contractility will also increase stroke volume.

76. The answer is c. (*Guyton, pp 98, 136–138.*) A premature heartbeat, or ectopic extrasystole, places the myocardium in a refractory period at the time of arrival of the next normal stimulus from the SA node. Therefore, no ventricular contraction can occur. The impulse from the ectopic focus is incapable of exciting the bundle of His and thus no retrograde conduction to the atrium takes place. Inasmuch as the ectopic event does not extend to the atrium, the atrium continues to contract regularly under the influence of the SA node. The ventricular contraction is smaller because the heart has not filled to its normal end-diastolic volume when the extrasystole occurs. In addition, the extrasystole does not propagate normally through the ventricle, so the force of contraction is reduced.

77. The answer is e. (*Guyton, pp 128–130.*) Abnormalities in coronary blood flow resulting in ischemia of the ventricular muscle will lead to a current of injury, which is reflected as an upward or downward shift in the ST segment of the ECG recording. The electrical activity of the heart does not reflect changes in ventricular contractility, blood pressure, ejection fraction, or total peripheral resistance, although all of these can be altered by changes in coronary blood flow.

78. The answer is c. (*Guyton, pp 211–213, 976.*) Stroke volume is influenced by ventricular preload, afterload, and contractility. Decreasing total

peripheral resistance may result in a decrease in afterload and therefore an increase in stroke volume. Decreasing ventricular compliance (making the heart stiffer) or increasing venous compliance will decrease ventricular filling and, therefore, preload and stroke volume. Similarly, increasing heart rate and decreasing atrial contractility will decrease filling and stroke volume.

79. The answer is e. (*Guyton, pp 235–236.*) When the left ventricle fails, preload (left ventricular end-diastolic volume) is increased in an attempt to normalize stroke volume. The increase in preload increases the left ventricular end-diastolic pressure. Since the pulmonary capillaries are supplying the blood to the left ventricle, an increase in left ventricular end-diastolic pressure must be accompanied by an increase in pulmonary capillary hydrostatic pressure. The increase in radius of the dilated ventricle increases wall tension according to the Laplace relationship, $T \propto P \times r$ (where T = tension, P = systolic pressure, and r = radius). The increase in wall tension requires an increase in energy consumption. Since the end-diastolic volume is increased and the stroke volume remains the same (or is decreased), the ejection fraction (SV/EDV) will be less than normal. Heart rate will be increased by the increased sympathetic nerve activity that accompanies heart failure.

80. The answer is b. (*Berne, 3/e, pp 197–198.*) The PR interval starts at the beginning of the P wave and ends at the beginning of the QRS complex. The physiologic events that occur during this time period include atrial depolarization, which is responsible for the P wave, AV nodal depolarization, and depolarization of the bundle of His and the Purkinje fibers. SA nodal depolarization precedes the P wave. Since the mass of the SA node is so small, this event cannot be detected on the standard ECG recording. The mitral and aortic valves are closed during isovolemic contraction, which occurs after the QRS complex has begun. The second heart sound occurs at the end of systole.

81. The answer is c. (*Berne, 3/e, pp 220–221.*) The factors that influence wall stress are given by the Laplace relationship ($WS = [P \times r] \div Th$), where P equals the transmural pressure across the wall of the ventricle, r , the radius of the ventricle (determined by end-diastolic volume), and Th , the thickness of the ventricular wall. Wall stress is reduced if the wall thickness increases. Increasing the systolic pressure developed by the heart (ventricular transmural pressure) or increasing the end-diastolic volume will

increase wall stress. Wall stress will also be increased if total peripheral resistance is increased or mean arterial blood pressure is increased because, under both conditions, the heart will have to develop more pressure.

82. The answer is a. (*Guyton, pp 154, 246–247.*) In aortic regurgitation, some of the blood ejected during systole reenters the left ventricle during diastole. The retrograde flow of blood into the ventricle during diastole increases ventricular volume (preload). At the same time, the retrograde blood flow decreases the diastolic blood pressure. The low diastolic pressure allows the heart to produce a greater ejection fraction. The pulse pressure is widened because of the elevated systolic pressure (brought about by the increased stroke volume) and reduced diastolic pressure (as a consequence of backflow of blood through the incompetent aortic valve).

83. The answer is d. (*Berne, 3/e, pp 184–188.*) The plateau phase (phase 2) is the result of the influx of calcium. Although calcium channels begin to open during the upstroke (phase 0), the greatest number of calcium channels is open during the plateau. The upstroke is primarily dependent on the opening of Na channels. The initial repolarization (phase 1) is dependent on the inactivation of Na⁺ channels and the opening of a transient K⁺ channel. Repolarization (phase 3) is produced by the inactivation of Ca²⁺ channels and the activation of the delayed rectifier K⁺ channels.

84–85. The answers are 84-e, 85-b. (*Berne, 3/e, pp 206–210.*) The aortic valve closes when the pressure within the ventricle falls below the pressure within the aorta. This occurs when the ventricular muscle begins to relax. Relaxation begins at the end of the ventricular action potential, which is represented by the T wave (segment E) on the ECG recording.

The bundle of His depolarizes during the PR segment (segment E), that is, during the interval between the end of atrial depolarization and the beginning of ventricular depolarization. Segment A, the P wave, represents atrial depolarization, segment C, the QRS complex, represents ventricular depolarization, and segment D, the ST segment, represents the time interval during which all of the ventricular muscle is depolarized.

86. The answer is a. (*Guyton, p 135.*) The PR interval represents the time it takes for the cardiac action potential to propagate from the SA node to the ventricular muscle. A delay in this interval, normally produced by a

slowing in the conduction velocity through the AV node, is called a first-degree heart block. A second-degree heart block occurs when the action potential does not always propagate through the SA node. This produces an uneven heart beat. A third-degree block occurs when the action potential never reaches the ventricle. Under these conditions, pacemakers within the ventricle produce ventricular contraction but the rate is very slow. Inversion of the T wave and elevation of the ECG are indicators of membrane potential defects within the ventricular muscle.

87. The answer is a. (*Guyton, pp 237–238.*) Ischemic cardiac pain is produced when oxygen demand is greater than the oxygen that can be delivered by the coronary arteries. Positive inotropic agents reduce oxygen demand by increasing cardiac contractility. Although under normal circumstances an increase in contractility will increase oxygen demand, in a dilated heart, it actually decreases oxygen demand. The increase in contractility allows the heart to generate adequate force without increasing preload as much. As a result, the volume of the heart is reduced. Reducing volume decreases wall stress, because, according to the law of Laplace, the wall stress is proportional to the product of force and radius (which is proportional to ventricular volume).

88–90. The answers are 88-a, 89-b, 90-c. (*Berne, 3/e, pp 209–211.*) The left ventricular pressure-volume loop represents the changes in pressure and volume that occur during a cardiac cycle. 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. Point B represents the end of the ejection phase. At this point, the pressure in the left ventricle falls below the pressure in the aorta, and the aortic valve closes. The retrograde flow of blood against the closed aortic valve produces the second heart sound. Point E represents the end of the filling phase and the beginning of the isovolumic contraction phase. At this point, the pressure in the left ventricle increases above the pressure in the left atrium, causing the mitral valve to close. The retrograde flow of blood against the closed mitral valve produces the first heart sound. Systole is defined as the period between the first and second heart sounds and includes the isovolumic contraction and ejection phases. Aortic pressure continues to fall during the isovolumic contraction phase so that the rise in

aortic blood pressure (which begins at point D) lags behind the beginning of systole.

91–92. The answers are 91-d, 92-a. (*Guyton, pp 99–103.*) The graph accompanying the questions illustrates the development of pressure in the aorta, the left atrium, and the left ventricle during a single cardiac cycle. At point D, the pressure within the left ventricle is less than the pressure in the left atrium, and, therefore, the mitral valve opens and ventricular filling begins. Although the volume in the left ventricle is increasing, the pressure is falling. During this time period, the recoil of the ventricle causes its pressure to decrease as it is filling. Later in diastole, the pressure of the blood returning from the lungs causes both volume and pressure in the ventricle to increase. At point A, the ventricle begins to contract, raising its pressure above that in the atrium and closing the mitral valve. The aortic valve opens at point B and closes at point C.

93. The answer is d. (*Guyton, pp 99–100, 247–248.*) The V wave is the increase in atrial pressure that occurs during systole. Normally, it is produced by the blood returning to the left atrium from the lungs. However, in mitral regurgitation, the blood forced through the incompetent mitral valve during ventricular systole increases the magnitude of the V wave. The increase in atrial volume causes an increase in ventricular filling resulting in a larger than normal end-diastolic volume. The greater left ventricular preload produces a greater than normal stroke volume. However, the forward stroke volume, the volume entering the aorta, does not increase, so there is no increase in cardiac output. The regurgitant flow of blood through the mitral valve during systole produces a systolic murmur.

94. The answer is d. (*Guyton, pp 214, 231.*) Cardiac tamponade is a disorder of the heart in which an increase in the volume of pericardial fluid compresses the heart and reduces ventricular filling during diastole. Pulsus paradoxus is a clinical sign in which there is an abnormally large decrease (greater than 10 mmHg) in systolic pressure during inspiration. The drop in systolic pressure normally occurs during inspiration because the decreased intrathoracic pressure reduces the flow of blood from the lungs to the left ventricle. The decrease in intrathoracic pressure also increases venous return to the right ventricle. The decrease in ventricular filling during inspiration is exacerbated in cardiac tamponade because the increased

volume of blood in the right ventricle cannot push out the right ventricular wall because of the increased fluid in the pericardial space. Instead, the blood pushes against the intraventricular septum, greatly reducing the volume of blood that can enter the left ventricle.

95–96. The answers are 95-a, 96-c. (*Guyton, pp 214–220.*) Starling's law of the heart states that increasing preload increases the force of contraction. The curves shown in the diagram illustrate that relationship by plotting stroke volume as a function of end-diastolic volume. The Starling curve above the one on which the X is marked will result from an increase in contractility or a decrease in afterload. The Starling curve below the one on which the X is marked will result from a decrease in contractility or an increase in afterload. A mild hemorrhage, which causes a decrease in blood volume and pressure, will evoke the baroreceptor reflex, which produces an increase in contractility and an increase in heart rate. The increase in heart rate indicates that the new stroke volume will be on the upper curve. The low blood volume and increased heart rate causes a decrease in end-diastolic volume. Therefore, the stroke volume will be at the point marked A. An increase in afterload indicates that the new stroke volume will be on the lower curve. The increase in venous compliance results in a decrease in end-diastolic volume, and, therefore, the stroke volume will be at the point marked C.

97. The answer is a. (*Berne, 3/e, p 188.*) Opening the L-type calcium channel produces the upstroke of the SA nodal action potential. This is the same channel that is responsible for the plateau phase of the ventricular action potential. The SA nodal cells have very few of the Na^+ channels that open during the upstroke of the ventricular action potential. And because the maximum diastolic potential of the SA nodal cells is approximately -60 mV, any sodium channels that may be expressed on their cell membrane will be inactivated.

98. The answer is a. (*Berne, 3/e, pp 190–193.*) Phase-4 depolarization of the SA nodal cells is produced by the funny channel, which is permeable to Na^+ . The channel is called a *funny channel* because, unlike most Na^+ channels which open when the cell is depolarized, this channel is activated when the cell is polarized. It therefore opens at the end of the previous action potential, allowing Na^+ to flow through the cell membrane and depolarize

the cell. Vagal stimulation slows the heart rate by hyperpolarizing the SA node (by opening K^+ channels) and by slowing the rate of phase-4 depolarization (by making it more difficult for the funny channels to open. Norepinephrine increases the heart rate by increasing the rate at which the funny channels open, increasing the rate of phase-4 depolarization.

99. The answer is a. (*Berne, 3/e, p 193.*) Sympathetic stimulation of the heart activates a G protein, which, by activating adenylyl cyclase, increases the intracellular concentration of cAMP. cAMP activates protein kinase A, which phosphorylates a number of proteins, including phospholamban. Unphosphorylated phospholamban inhibits the SR Ca^{2+} pump. Inhibition of the SR Ca^{2+} pump is removed when phospholamban is phosphorylated, and, therefore, its activity is increased. The increased activity of the SR Ca^{2+} pump removes Ca^{2+} from the cytoplasm rapidly and therefore reduces the duration of systole. Sympathetic stimulation of the heart also increases heart rate. Therefore, the total duration of the cardiac cycle is decreased, resulting in a decrease in systole and diastole. Because the duration of systole is reduced disproportionately by the phosphorylation of phospholamban, the decrease in diastole isn't as great as might be predicted by the increase in heart rate, and, therefore, diastolic filling is not compromised. Sympathetic stimulation increases the amount of Ca^{2+} released from the SR during systole and decreases the affinity of troponin for Ca^{2+} . The increase in systolic Ca^{2+} concentration overcomes the decreased affinity of troponin for Ca^{2+} , resulting in an increased contractility.

100. The answer is b. (*Guyton, pp 128–130.*) A stress test is conducted by asking a patient to increase his or her exercise intensity while monitoring blood pressure and the electrical activity of the heart. Ischemia occurs if the myocardial oxygen demand brought about by the increased exercise intensity is not matched by an increase in myocardial blood flow. An ischemic episode is indicated by an ST segment depression. Systolic pressure normally rises and diastolic pressure normally falls during aerobic exercise. A failure of the heart rate to rise or the development of a diastolic murmur is a sign of pathology but is unlikely to be a sign of exercise-induced myocardial ischemia.

Vascular Physiology

Questions

DIRECTIONS: Each question below contains five suggested responses. Select the **one best** response to each question.

101. After a mild hemorrhage, compensatory responses initiated by the baroreceptor reflex keeps blood pressure at or close to its normal value. Which one of the following values is less after compensation for the hemorrhage than it was before the hemorrhage?

- a. Venous compliance
- b. Heart rate
- c. Ventricular contractility
- d. Total peripheral resistance
- e. Coronary blood flow

102. The constriction of a blood vessel to one-half of its resting diameter would increase its resistance to blood flow by a factor of

- a. 2
- b. 4
- c. 8
- d. 12
- e. 16

103. During aerobic exercise, blood flow remains relatively constant within

- a. The skin
- b. The heart
- c. The brain
- d. The skeletal muscles
- e. The kidneys

104. Which of the following conditions causes pulse pressure to increase?

- a. Tachycardia
- b. Hypertension
- c. Hemorrhage
- d. Aortic stenosis
- e. Heart failure

105. Sudden standing evokes the baroreceptor reflex. Which one of the following will be greater after a person suddenly stands up than it was before the person stood?

- a. The end-diastolic volume
- b. The renal blood flow
- c. The venous return
- d. The pulse pressure
- e. The ejection fraction

106. The enzyme ultimately responsible for the formation of fibrin monomers is

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

107. Central venous pressure is increased by

- a. Decreasing blood volume
- b. Increasing venous compliance
- c. Increasing total peripheral resistance
- d. Decreasing heart rate
- e. Decreasing plasma aldosterone concentration

108. Capillary permeability is lowest within the

- a. Kidneys
- b. Spleen
- c. Liver
- d. Brain
- e. Skin

109. Blood flow through an organ would be increased by decreasing

- a. The diameter of the arterial vessels
- b. The number of open arterial vessels
- c. The arterial pressure
- d. The diameter of the venous vessels
- e. The hematocrit

110. Net filtration from capillaries will increase following

- a. Increased contraction of the precapillary sphincter
- b. Decreased arterial pressure
- c. Increased plasma protein concentration
- d. Decreased capillary permeability
- e. Increased postcapillary resistance

111. A reduction in carotid sinus pressure would cause a decrease in

- a. Heart rate
- b. Myocardial contractility
- c. Total peripheral resistance
- d. Venous compliance
- e. Cardiac output

112. Which one of the following organs has the highest arteriovenous O_2 difference under normal resting conditions?

- a. Brain
- b. Heart
- c. Skeletal muscle
- d. Kidney
- e. Stomach

113. The percentage of the total cardiac output distributed to any single organ is most dependent on

- a. The contractile state of the heart
- b. The magnitude of mean blood pressure
- c. The magnitude of diastolic pressure
- d. The ratio of an organ's vascular resistance to total peripheral resistance (TPR)
- e. The magnitude of cardiac output

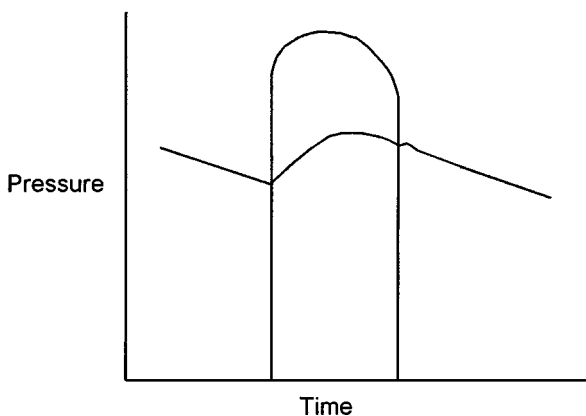
114. At which of the following sites does the blood flow lose the greatest amount of energy?

- a. Mitral valve
- b. Large arteries
- c. Arterioles
- d. Capillaries
- e. Venules

115. Which one of the following decreases during aerobic exercise?

- a. Circulating blood volume
- b. Heart rate
- c. Skin temperature
- d. Cerebral blood flow
- e. Mean blood pressure

116. Which one of the following conditions would most likely cause the aortic and ventricular pressure waves shown in the diagram?



- a. Aortic regurgitation
- b. Aortic stenosis
- c. Increased ventricular contractility
- d. Mitral stenosis
- e. Atherosclerosis

117. Based on the following values, the flow of fluid out of the capillaries will be zero if the average interstitial hydrostatic pressure is

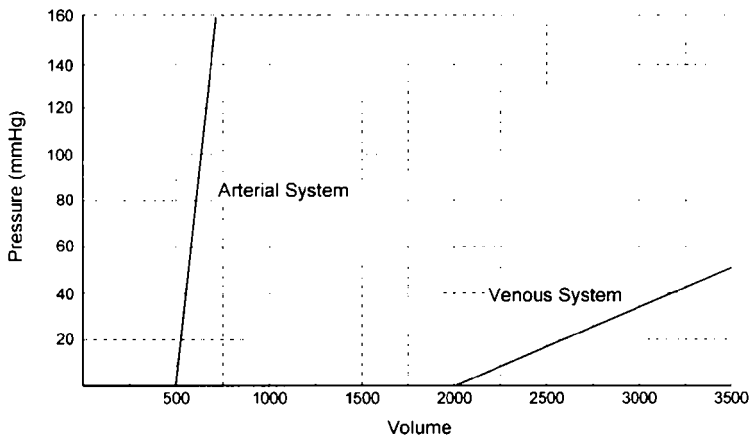
Average capillary hydrostatic pressure = 18 mmHg

Average capillary oncotic pressure = 27 mmHg

Average interstitial oncotic pressure = 7 mmHg

- 4 mmHg
- 2 mmHg
- 0 mmHg
- +1 mmHg
- +2 mmHg

118. The graph below illustrates the pressure-volume curves for the arterial and venous systems. The ratio of the arterial compliance to the venous compliance is approximately



- 15:1
- 10:1
- 1:1
- 1:10
- 1:20

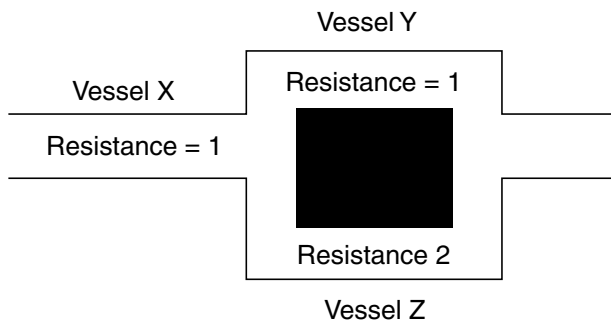
119. Which one of the following characteristics is most similar in the systemic and pulmonary circulations?

- a. Stroke work
- b. Preload
- c. Afterload
- d. Peak systolic pressure
- e. Blood volume

120. Which one of the following statements correctly describes the ductus arteriosus?

- a. It prevents the flow of blood into the lungs of the fetus
- b. It delivers oxygenated blood from the placenta to the left ventricle
- c. It allows blood to flow from the aorta to the pulmonary artery in the fetus
- d. Its resistance to blood flow decreases soon after birth
- e. It is located in the septum between the left and right atrium

121. The following diagram illustrates the relative resistance of three vessels. The ratio of the flow in vessel X to the flow in vessel Y is



- a. 1:1
- b. 3:2
- c. 2:1
- d. 3:1
- e. 4:3

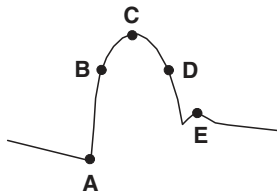
122. The data below was obtained from a patient before and after administration of a drug that increased his mean right atrial pressure.

	Before	After
Mean right atrial pressure	8 mmHg	20 mmHg
Mean aortic pressure	80 mmHg	80 mmHg
Cardiac output	4 L/min	5 L/min

The ratio of the patient's total peripheral resistance before administration of the drug to the total peripheral resistance after administration of the drug is

- 1:1
- 3:2
- 4:3
- 5:4
- 6:5

123. At which point in the following diagram of an aortic pressure wave is coronary blood flow the greatest?



- A
- B
- C
- D
- E

124. Which one of the following values is greater in the pulmonary circulation than in the systemic circulation?

- a. The mean arterial pressure
- b. The arterial resistance
- c. The vascular compliance
- d. The blood flow
- e. The sympathetic tone

125. The greatest percentage of blood volume is found in the

- a. Heart
- b. Aorta
- c. Distributing arteries and arterioles
- d. Capillaries
- e. Venules and veins

126. Warfarin (coumarin) is an anticoagulant that is often given to patients following a heart attack. However, if too much warfarin is administered, the patient can have episodes of bleeding. The bleeding produced by warfarin can be overcome by administering

- a. Aspirin
- b. Heparin
- c. t-PA (tissue plasminogen activator)
- d. Vitamin K
- e. Fibrinogen

127. Citrate is a useful anticoagulant because of its ability to

- a. Buffer basic groups of coagulation factors
- b. Bind factor XII
- c. Bind vitamin K
- d. Chelate calcium
- e. Be slowly metabolized

128. Bleeding time is determined by nicking the skin superficially with a scalpel blade and measuring the time required for hemostasis. It will be markedly abnormal (prolonged) in a person who

- a. Lacks factor VIII
- b. Cannot absorb vitamin K
- c. Has liver disease
- d. Takes large quantities of aspirin
- e. Takes coumarin derivatives

129. Lymph capillaries differ from systemic blood capillaries in that they

- a. Are less permeable
- b. Are not lined by endothelium
- c. Lack valves
- d. Are absent in the central nervous system
- e. Collapse when interstitial pressure increases

130. Correct statements about the increase in pulmonary blood flow during vigorous exercise include which of the following?

- a. The percentage of increase in flow is greater in the bases of the lungs than in the apices
- b. The increase in flow is caused by a greater-than-fivefold increase in pulmonary arterial pressure
- c. The increase in pulmonary blood flow is less than the increase in systemic blood flow
- d. The increase in pulmonary blood flow is accommodated by dilation of pulmonary arterioles and capillaries
- e. The increase in pulmonary blood flow is caused by sympathetic nerve stimulation of the pulmonary vasculature

131. Pulmonary lymph flow exceeds that in other tissues because

- a. Pulmonary capillary pressure is higher than systemic capillary pressure
- b. Pulmonary endothelial cells contain a large number of fenestrations
- c. Alveolar epithelial cells secrete a fluid that is added to the lymph formed from the blood plasma
- d. Pulmonary interstitial fluids contain more proteins than the interstitial fluid in other tissues
- e. Pulmonary capillaries have a lower oncotic pressure than systemic capillaries

132. At birth, changes that occur in the fetal circulation include

- a. Increased systemic arterial pressure
- b. Increased pulmonary vascular resistance
- c. Increased pulmonary arterial pressure
- d. Decreased left atrial pressure
- e. Decreased pulmonary blood flow

133. Turbulence is more likely to occur in a blood vessel if

- a. The velocity of blood within the vessel increases
- b. The viscosity of blood within the vessel increases
- c. The diameter of the vessel decreases
- d. The density of the blood decreases
- e. The length of the vessel increases

134. Systemic arteriolar constriction may result from an increase in the local concentration of

- a. Nitric oxide
- b. Angiotensin II
- c. Atrial natriuretic peptide
- d. Beta (β) agonists
- e. Hydrogen ion

135. Which of the following will be lower than normal in a patient with an abnormally high intracranial pressure?

- a. Ventricular contractility
- b. Heart rate
- c. Mean blood pressure
- d. Stroke volume
- e. Total peripheral resistance

136. After an episode of exercise training, the trained individual will have a

- a. Decreased density of mitochondria in the trained muscles
- b. Increased resting heart rate
- c. Decreased maximum oxygen consumption
- d. Increased stroke volume
- e. Decreased extraction of oxygen by exercising muscles

137. Which one of the following increases during aerobic exercise?

- a. Diastolic blood pressure
- b. Cerebral vascular resistance
- c. Mixed venous oxygen tension
- d. Blood flow to the kidney
- e. Circulating blood volume

138. Pulse pressure increases when

- a. Heart rate increases
- b. Stroke volume decreases
- c. Aortic compliance increases
- d. Aortic stenosis develops
- e. Mean arterial pressure increases

139. The distribution of blood among the various organs of the body is regulated by regulating the resistance of the

- a. Arteries
- b. Arterioles
- c. Precapillary sphincters
- d. Postcapillary venules
- e. Veins

140. Flow of fluid through the lymphatic vessels will be decreased if there is an increase in

- a. Capillary pressure
- b. Capillary permeability
- c. Interstitial protein concentration
- d. Capillary oncotic pressure
- e. Central venous pressure

141. Which one of the following signs is observed in a patient who has lost a significant amount of blood?

- a. Respiratory acidosis
- b. Dry skin
- c. Polyuria
- d. Bradycardia
- e. Low hematocrit

142. A patient is diagnosed with anaphylactic shock rather than hypovolumic shock because

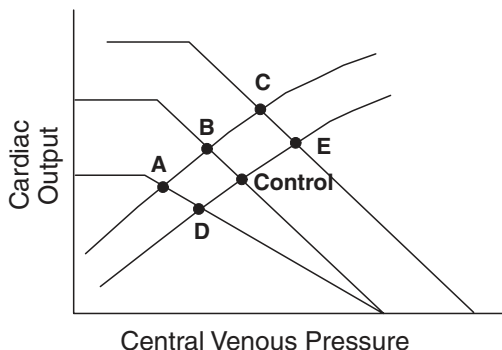
- a. Cardiac output is higher than normal
- b. Ventricular contractility is greater than normal
- c. Total peripheral resistance is greater than normal
- d. Serum creatinine is elevated
- e. Heart rate is greater than normal

143. Which one of the following will increase if massaging the neck stretches the carotid sinus baroreceptor?

- a. Total peripheral resistance
- b. Right atrial pressure
- c. Venous tone
- d. Ventricular contractility
- e. Vagal nerve activity

Questions 144–146

Use the diagram below to answer the following three questions. The point marked *control* represents the state of the cardiovascular system in the resting state.



144. An increase in total peripheral resistance and contractility is represented by a shift from the resting state to point

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

I45. Which one of the following would be consistent with a shift from the resting state (control) to point B?

- a. The person stood up suddenly
- b. The person began exercising
- c. The person was given a transfusion
- d. The person's afterload was increased
- e. The person was given a positive inotropic drug

I46. Which one of the following would be consistent with a shift from the resting state (control) to point E?

- a. The person stood up suddenly
- b. The person began exercising
- c. The person was given a transfusion
- d. The person's afterload was increased
- e. The person was given a positive inotropic drug

Vascular Physiology

Answers

101. The answer is a. (*Guyton, pp 189–190, 254–255.*) The fall in blood volume and pressure produced by hemorrhage elicits the baroreceptor reflex. The reflex increases the activity of the sympathetic nervous system and decreases the activity of the parasympathetic nerves innervating the heart. Sympathetic stimulation of the smooth muscle surrounding the venous vessels decreases their compliance, causing end-diastolic volume (EDV) to increase. However, the EDV does not increase above the levels observed prior to the hemorrhage. Heart rate, ventricular contractility, and total peripheral resistance are all increased above their prehemorrhage levels by sympathetic stimulation. The coronary blood flow increases to meet the increased energy requirements of the heart beating at a higher rate with increased contractility.

102. The answer is e. (*Berne, 3/e, pp 228–230.*) 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.

103. The answer is c. (*Berne, 3/e, pp 282, 289–283.*) Aerobic exercise causes an increase in sympathetic discharge and circulating catecholamines, which results in an increased heart rate, ventricular contractility, and cardiac output. Blood pressure rises despite the fall in TPR that results from the dilation of the blood vessels providing blood to the exercising skeletal muscle. Blood flow to the gut, the kidneys, and the nonexercising muscles is reduced by sympathetic constriction of the arterioles leading to these organs. Blood flow to the skin is increased to prevent overheating. Coronary blood flow increases to meet the increased metabolic needs of the heart. Blood flow to the brain is kept relatively constant by autoregulatory mechanisms.

104. The answer is b. (*Berne, 3/e, pp 241–243.*) Pulse pressure is proportional to the amount of blood entering the aorta during systole and inversely proportional to aortic compliance. Pulse pressure increases with

hypertension because hypertension causes aortic compliance to decrease. Whether the hypertension is a result of an increased cardiac output or an increased peripheral resistance, the higher arterial pressure is caused by an increase in arterial blood volume. The increased blood volume stretches the arterial wall, making it stiffer and decreasing its compliance. Stroke volume is decreased with tachycardia, hemorrhage, and heart failure, reducing pulse pressure in all three cases. In aortic stenosis, the ejection of blood from the ventricle is slowed and the increase in arterial blood volume during systole is less than normal.

105. The answer is c. (*Berne, 3/e, pp 258–260.*) When a person rises suddenly, blood pools in the dependent portions of the body, causing decreases in venous return, left ventricular end-diastolic volume, stroke volume, and pulse pressure. The reduced stroke volume leads to a drop in cardiac output and, therefore, a drop in blood pressure. Decreased blood pressure produces the baroreceptor reflex, leading to an increase in sympathetic activity, which increases total peripheral resistance, cardiac contractility, heart rate, and ejection fraction. These changes in the cardiovascular system return blood pressure toward normal.

106. The answer is c. (*Guyton, pp 420–421.*) 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. Plasminogen is the inactive precursor of plasmin, the proteolytic enzyme involved in clot dissolution. Heparin is an ant clotting agent that is found on endothelial cell surfaces.

107. The answer is d. (*Guyton, pp 215–220.*) Central venous pressure is the hydrostatic pressure in the great veins at their entrance to the right atrium. Increasing venous compliance would decrease pressure in the venous vessels and therefore would decrease central venous pressure. Decreasing blood volume would have the same effect. Reducing the plasma concentration of aldosterone would result in a decrease in blood volume. Increasing total peripheral resistance would tend to shift volume from the venous side of the circulation to the arterial side, resulting in a decrease in venous pressure. Increasing cardiac output tends to lower central venous

pressure, whereas lowering cardiac output tends to increase central venous pressure. A reduction in heart rate would tend to lower cardiac output and therefore increase central venous pressure.

108. The answer is d. (*Guyton, p 714.*) Capillaries within the brain are continuous capillaries; they do not contain any aqueous pores for diffusion of water-soluble materials. Unlike other continuous capillaries, such as those found in skin and muscle, the gaps between endothelial cells in brain capillaries are closed. These closed gaps make them essentially impermeable to all but fat-soluble materials. The brain's capillaries are the least permeable of all the body's capillaries. The endothelial cells within the kidney are fenestrated. They contain fenestrations, or windows, through which all substances dissolved in the plasma except proteins can diffuse. Capillaries within the spleen and liver are discontinuous. Wide gaps between adjacent capillary endothelial cells allow proteins and cellular elements to easily pass through.

109. The answer is e. (*Guyton, pp 150–151.*) Blood flow through an organ is increased by either increasing the perfusion pressure across the organ or by decreasing the vascular resistance. A decrease in the arterial pressure would decrease the perfusion pressure. Decreasing the diameter of the arterial or venous vessels or decreasing the number of open arterial vessels would contribute to increasing vascular resistance. If the hematocrit is decreased, the viscosity of the blood is decreased, resulting in a decrease in resistance and, therefore, an increase in blood flow through an organ.

110. The answer is e. (*Guyton, pp 166–170.*) Net filtration from systemic capillaries is dependent on the Starling forces and capillary permeability. The equation is

$$\text{Filtration} = k_f[(P_{\text{cap}} + \pi_{\text{interstitial}}) - (\pi_{\text{cap}} + P_{\text{interstitial}})]$$

Increasing postcapillary resistance will increase the hydrostatic pressure within the capillary (P_{cap}) and consequently increase net filtration.

111. The answer is d. (*Berne, 3/e, pp 258–261.*) A reduction in carotid sinus pressure due to a decrease in mean blood pressure would elicit a baroreceptor reflex tending to restore blood pressure to normal. The reflex

response includes an increase in sympathetic nervous system activity, which would cause an increase in heart rate and myocardial contractility, both of which would tend to increase cardiac output. Sympathetic stimulation would also cause constriction of both the arterioles and venous vessels. Arteriolar constriction would cause an increase in total peripheral resistance. Sympathetic stimulation of the venous vessels would cause a decrease in venous compliance.

112. The answer is b. (*Berne, 3/e, pp 279–282.*) The overall arteriovenous O_2 difference is determined by the oxygen consumption of a tissue and its blood flow. Because of the high rate of metabolism in the heart compared with its blood flow, it has the highest arteriovenous O_2 difference of any major organ of the body under normal conditions. The heart can extract a large amount of oxygen because of its high capillary density. Blood flow to the kidney and skin is far in excess of their metabolic needs, so little oxygen is removed from the blood as it passes through these organs; therefore, their arteriovenous O_2 differences are rather small. Under normal conditions, the arteriovenous O_2 difference in skeletal muscle is quite low. However, this value can increase substantially during vigorous exercise.

113. The answer is d. (*Berne, 3/e, pp 176–178, 250–252.*) Arterial vessels arranged in parallel supply the major organs of the body. The relative resistance of each parallel pathway determines the distribution of blood flow through a parallel network of vessels. The ratio of that resistance to the total resistance will determine the percentage of flow going through each of the parallel networks. The other factors mentioned would influence the magnitude of the cardiac output, which is the total amount of blood flowing through the entire system. However, none of these factors have any direct effect on the way blood flow is distributed to the organs of the body.

114. The answer is c. (*Berne, 3/e, pp 230–232.*) The energy imparted to the blood by ventricular systole is dissipated as the blood flows through the circulation. The greatest energy loss occurs where the resistance to blood flow is greatest. This would also be the site of the greatest pressure change. The arteriolar vessels produce the largest resistance to blood, and thus the greatest energy loss and pressure drop occur as the blood passes through them. Normal mitral valves offer almost no resistance to flow and thus

there is almost no difference between ventricular pressure and atrial pressure during diastole. This explains why left atrial pressure, as evaluated by pulmonary capillary wedge pressure, can be used as an index of left ventricular end-diastolic pressure in patients with normal mitral valves. Under normal conditions, venous vessels contribute very little to vascular resistance.

115. The answer is a. (*Berne, 3/e, pp 290–293.*) Under normal circumstances, circulating blood volume decreases during aerobic exercise. The decrease in volume is the result of increased filtration of water out of the capillaries within the exercising muscles. Increased filtration occurs because more capillaries within the exercising muscles are filled with blood and the pressure within each capillary is higher. The increased sympathetic activity accompanying the exercise causes an increase in heart rate, which in turn increases the cardiac output. The increase in cardiac output causes an increase in blood pressure, despite the decreased peripheral resistance. The skin temperature increases as more blood is diverted to the skin for the purpose of eliminating the heat generated by the exercising muscles. Brain blood flow is kept constant by autoregulation.

116. The answer is b. (*Guyton, pp 248–249.*) The ventricular pressure illustrated in the diagram is much higher than the aortic pressure. The pressure difference between the left ventricle and aorta during ejection results from a large resistance across the aortic valve as would occur with aortic stenosis. Under normal conditions, the aortic valve offers almost no resistance to flow, and, therefore, there would be virtually no pressure gradient between the left ventricle and the aorta.

117. The answer is b. (*Guyton, 9/e, pp 187, 191–193.*) The movement of fluid through capillaries is governed by hydrostatic pressures and by the capillaries' permeability to water. The hydrostatic pressures are referred to as *Starling forces* and include the oncotic pressures of the capillary and interstitial proteins and the hydrostatic pressures within the capillary and interstitium. Flow is zero when the sum of the Starling forces equals zero.

$$[(P_{\text{cap}} + \pi_{\text{interstitial}}) - (\pi_{\text{cap}} + P_{\text{interstitial}})] = 0$$
$$P_{\text{interstitial}} = 18 \text{ mmHg} + 7 \text{ mmHg} - 27 \text{ mmHg} = -2 \text{ mmHg}$$

118. The answer is e. (*Guyton, 9/e, pp 152–153.*) 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. The arterial compliance is

$$\frac{250 \text{ mL}}{160 \text{ mmHg}} = 1.56 \text{ mL/mmHg}$$

The venous compliance is

$$\frac{1500 \text{ mL}}{50 \text{ mmHg}} = 30 \text{ mL/mmHg}$$

The ratio of arterial compliance to venous compliance is $1.56:30 = 1:19.2 \approx 1:20$.

119. The answer is b. (*Rhoades, pp 372–376.*) The right and left ventricles are in series with one another so that the entire cardiac output (except for a small anatomic shunt) passes through both circulations. Since the two ventricles beat at the same rate, their stroke volumes are the same. However, the resistance of the pulmonary vasculature is much smaller than that of the systemic circulation; thus, the afterload and stroke work are greater on the left side than on the right side. Because the same cardiac output is ejected into a higher resistance, peak systolic pressure is higher on the left side than on the right side. Only about 10% of the blood volume is within the pulmonary circulation at any one time. About two-thirds of the blood volume is stored within the systemic veins and venules. Although the left and right preloads are not identical, they are very similar.

120. The answer is a. (*Guyton, pp 249–251, 960–962.*) The ductus arteriosus is a low-resistance arterial vessel of the fetus through which blood flows from the pulmonary artery to the aorta, bypassing the lungs. In fetal life, there is no need for blood to flow through the lungs because blood is oxygenated in the placenta. Soon after birth, the pulmonary vascular resistance falls, allowing blood to flow from the pulmonary artery to the lungs. The high oxygen tension in the blood of the baby causes the resistance of the ductus arteriosus to increase. When the ductus arteriosus does not close at birth, it is called a *patent ductus arteriosus*. The opening between the left and right atria in the fetus is called the *foramen ovale*. It, too, normally closes at birth.

121. The answer is b. (*Berne, 3/e, pp 230–232.*) The ratio of the blood flow through vessels Y and Z is inversely proportional to their resistance:

$$\frac{Q_Y}{Q_Z} = \frac{R_Z}{R_Y} = \frac{2}{1}$$

Therefore, the flow of blood through vessel Y is twice the flow of blood through vessel Z. 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 flow of blood through vessel X to the flow of blood through vessel Y is 3:2.

122. The answer is b. (*Guyton, pp 146–151.*) The relationship between cardiac output (CO), total peripheral resistance (TPR), and blood pressure (ΔP) is $\Delta P = CO \times TPR$. Accordingly, TPR before administration of the drug is

$$18 \text{ mmHg/L/min} = \frac{(80 \text{ mmHg} - 8 \text{ mmHg})}{4 \text{ L/min}}$$

After administration of the drug, the TPR is

$$12 \text{ mmHg/L/min} = \frac{(80 \text{ mmHg} - 20 \text{ mmHg})}{5 \text{ L/min}}$$

Therefore, the ratio of the TPR before administering the drug to the TPR after administering the drug is $18/12 = 3/2$.

123. The answer is d. (*Berne, 3/e, pp 279–281.*) Coronary blood flow depends on the pressure perfusing the coronary vessels and the compressive forces produced by the contracting ventricles. The coronary blood flow is lowest during isovolemic contraction when the aortic pressure is low and the compressive forces are high. Coronary blood flow increases during ejection, as the perfusing pressure increases. However, the flow is still limited by the compressive forces produced by the contracting ventricle. The greatest coronary blood flow occurs early in diastole, when the ventricle has relaxed and the aortic perfusing pressure is still relatively high.

124. The answer is c. (*Guyton, pp 444–446.*) The same amount of blood flows through the pulmonary and systemic circulations. However, the mean blood pressure in the pulmonary circulation is much lower (15

mmHg) compared to the mean blood pressure in the systemic circulation (90 mmHg). The pulmonary blood pressure is lower because the resistance to blood flow in the pulmonary circulation is much lower than the resistance to blood flow in the systemic circulation. In addition, the pulmonary blood vessels are more compliant than the systemic blood vessels. Therefore, although the stroke volume of the left and right ventricles is the same, the pulse pressure in the pulmonary artery (25/10) is lower than that in the aorta (120/80). The resistance of the systemic circulation is determined by the activity of the sympathetic nerves innervating the arteriolar smooth muscle. The smooth muscle surrounding the pulmonary vessels receives very little sympathetic innervation.

125. The answer is e. (*Guyton, p 160.*) The total circulating blood volume is approximately 70 mL/kg, about two-thirds of which is found in the systemic veins and venules. A significant volume of blood (15%) is found in the pulmonary circulation. The large volume of blood found on the venous side of the circulation is used to adjust circulating blood volume. For example during hemorrhage, contraction of the veins and venules of the skin increases the amount of blood available for perfusion of the heart and brain.

126. The answer is d. (*Guyton, pp 428–429.*) Warfarin is often prescribed for patients at risk for thromboembolic episodes. Vitamin K is necessary for the conversion of prothrombin to thrombin. Thrombin is an important intermediate in the coagulation cascade. It converts fibrinogen to fibrin and is a powerful activator of platelets. Warfarin interferes with the activity of vitamin K and therefore reduces the likelihood of clot formation. Administering vitamin K can restore coagulation if warfarin therapy leads to excessive bleeding. Heparin prevents clotting by inhibiting thrombin. Aspirin blocks the formation of thromboxane A_2 , which is necessary for platelet aggregation. Tissue plasminogen activator (t-PA) is a thrombolytic agent.

127. The answer is d. (*Guyton, pp 428–429.*) 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.

128. The answer is d. (*Guyton, pp 428–429.*) Hemostasis following blood vessel injury depends on (1) vascular spasm, (2) formation of a platelet plug, and (3) clot formation. When injury to a vessel produces only a small defect, the platelet plug itself can cause hemostasis. This is the basis for the bleeding time that is employed clinically to distinguish hemostatic abnormalities caused by platelet abnormalities from those caused by coagulation defects. Aspirin diminishes platelet aggregation by inhibiting cyclooxygenase, an enzyme required for generation of thromboxanes, which promote platelet aggregation. All the other situations described in the question are associated with coagulation deficiency. Persons thus affected would have a normal bleeding time but would present clinically with delayed posttraumatic bleeding caused by their inability to form an effective clot to reinforce the platelet plug.

129. The answer is d. (*Guyton, pp 170–171.*) Nearly all tissues of the body have a lymphatic circulation, one exception being the central nervous system. The lymphatic channels (or capillaries), which ultimately drain into the venous circulation, are lined by endothelial cells. These cells are attached to surrounding tissues by anchoring filaments and have large gaps between them to permit the free movement of macromolecules and particulate matter such as bacteria. Overlapping, loosely adherent cell processes, which act as valves to prevent the backflow of fluid once it enters the lumen, cover the endothelial gaps. Valves, as well, exist within the channels every few millimeters to promote unidirectional flow.

130. The answer is d. (*Guyton, pp 446–447.*) The pulmonary circulation is a low-pressure system compared with the systemic circulation. Because of this low pressure and the hydrostatic pressure gradient from the top, or apex, of the lung to the bottom, or base, of the lung, the apex of the lung is not as well perfused as the base of the lung. During vigorous exercise, there is a large (up to sixfold) increase in cardiac output. The increased flow through the systemic circulation is equal to the increase in flow through the pulmonary circulation. Total lung flow increases and flow at the base of the lung is still greater than flow at the apex. However, the flow at the apex,

since it was originally low, may increase by up to 800%, whereas flow in the base of the lung only increases by up to about 300%. The pulmonary vessels are very compliant. The increased flow causes recruitment of previously closed capillaries and dilation of pulmonary arterioles and capillaries. Because of this, pulmonary artery pressure normally does not increase or increases by only a small amount, and it rarely increases more than twofold.

131. The answer is d. (*Guyton, pp 448–450.*) The rate of lymph flow is increased by factors that favor the flow of fluid from the capillaries to the interstitial spaces. Such factors include an elevation of capillary pressure, a decrease in plasma oncotic pressure, an increase in interstitial plasma proteins, and an increase in capillary permeability. The major factor involved in the increased formation of lymph within the lungs is the large leak of plasma proteins from the capillary to the interstitial fluid. The loss of plasma proteins from the capillaries occurs by diffusion through the spaces between capillary endothelial cells and not through endothelial cell fenestrations. The pressure within the pulmonary capillaries is lower than in systemic capillaries and so acts to reduce lymph formation. However, the negative intrapleural pressure acts to increase the pressure gradient across the capillary wall and so promotes lymph formation.

132. The answer is a. (*Berne, 3/e, pp 960–962.*) At birth, two major events cause changes in the fetal circulation. First, loss of the placenta results in increased peripheral resistance and increased systemic arterial pressure. Second, expansion of the lungs allows marked pulmonary vasodilatation, which, by diminishing vascular resistance and promoting pulmonary blood flow, results in elevation of left atrial pressure.

133. The answer is a. (*Berne, 3/e, pp 232–233.*) The English physicist Osborne Reynolds described the critical factors affecting the flow of incompressible fluids in pipes late in the nineteenth century. He discovered that the point at which flow changes from laminar (smooth) to turbulent is a function of fluid density, viscosity, and velocity and of the diameter of the vessel expressed in the relationship that became known as the Reynolds number (Re):

$$\text{Re} = \frac{(\text{density} \times \text{diameter} \times \text{velocity})}{\text{viscosity}}$$

This relationship is equally valid for blood moving in the vessels of living organisms and for water moving in pipes. Increasing the length of the vessel may indirectly decrease the likelihood of turbulence by increasing vascular resistance and thus decreasing blood velocity.

134. The answer is b. (*Guyton, pp 201–204.*) Angiotensin II is a powerful vasoconstrictor that is formed when renin is released from the kidney in response to a fall in blood pressure or vascular volume. Renin converts angiotensinogen to angiotensin I. Angiotensin II is formed from angiotensin I by an angiotensin-converting enzyme localized within the vasculature of the lung. All the other listed substances cause vasodilation.

135. The answer is b. (*Guyton, p 192.*) A high intracranial pressure produces the Cushing reaction in which both sympathetic and parasympathetic input to the cardiovascular system increase. The parasympathetic stimulation of the heart causes the heart rate to decrease. The sympathetic stimulation to the blood vessels causes an extremely large increase in peripheral resistance. The sympathetic stimulation to the heart causes an increase in contractility, which, in turn, produces an increase in stroke volume. The Cushing reaction produces a rise in blood pressure, allowing the brain to be perfused despite high intracranial pressure (pressure as high as 300 to 400 mmHg).

136. The answer is d. (*Berne, 3/e, pp 289–293.*) Exercise training decreases the resting heart rate. To maintain the same cardiac output with a lower heart rate, stroke volume is increased. Exercise training increases the aerobic capacity of an individual by increasing both the density of capillaries supplying the trained muscle and the concentration of mitochondria within the muscles. These changes allow the muscles to extract more oxygen from the blood perfusing them. At the same time, they permit a higher intensity of exercise during which a greater amount of oxygen can be used. Therefore, the maximum oxygen consumption (MVO_2) of trained individuals is above average.

137. The answer is b. (*Berne, 3/e, pp 282, 289–293.*) Blood flow to the brain remains constant during exercise. To counteract the increased perfusion pressure that occurs during exercise, an autoregulatory process increases vascular resistance. The increase in mean blood pressure during

exercise occurs despite a decrease in vascular resistance, because of the large increase in cardiac output. The decreased vascular resistance allows more blood to enter the exercising muscles during diastole, resulting in a lower diastolic pressure. Blood flow to the kidney is decreased in order to shunt blood to the heart and exercising muscles. Circulating blood volume decreases during exercise because of the increased capillary pressures within the exercising muscles and the accumulation of metabolites in the interstitial spaces which produces an osmotic flow of water out of the capillaries.

138. The answer is e. (*Berne, 3/e, pp 99, 241–243.*) *Pulse pressure* is the difference between the systolic and diastolic pressure that occurs during the cardiac cycle. It is determined by the change in volume in the aorta during systole and the compliance of the aorta. A decrease in aortic compliance (that is, an increase in the stiffness of the aorta) will increase pulse pressure. When mean arterial pressure increases, the average volume of blood in the aorta is higher than normal. The increased volume decreases aortic compliance. Assuming that the stroke volume remains normal, the decreased compliance will result in an increased pulse pressure. If heart rate increases, stroke volume and therefore pulse pressure will decrease. An increase in total peripheral resistance will prevent blood from flowing out of the aorta during systole and therefore decrease pulse pressure. In aortic stenosis, the rate at which blood is ejected from the ventricle is decreased. The decreased ejection rate provides time for blood to flow from the aorta to the periphery during systole. Therefore, the increase in aortic volume during systole and the pulse pressure are decreased.

139. The answer is b. (*Berne, 3/e, pp 256–259.*) The arterioles control the flow of blood to the various organs of the body. The resistance of the arterioles is controlled by the sympathetic nervous system and metabolites released by the organs. When the organs are very active (e.g., exercising skeletal muscle), the metabolites increase blood flow, even when the sympathetic stimulation of the arterioles is high. When metabolic production is low (e.g., nonexercising muscle), the sympathetic tone controls the amount of blood flowing into the organ. The precapillary sphincters control the distribution of blood within an organ, supplying blood to cells that are more active and restricting blood flow to those that are less active. The arteries, postcapillary venules, and veins are not involved in regulation of blood flow through individual organs.

140. The answer is d. (*Berne, 3/e, pp 252–254.*) 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 increases and, again, capillary filtration increases. Lymph flow is approximately 2 to 3 L per day.

141. The answer is e. (*Berne, 3/e, pp 393–295.*) Loss of blood causes blood pressure to fall. The baroreceptor reflex response to the fall in blood pressure causes arteriolar resistance to increase, further decreasing capillary perfusing pressure. Because whole blood is lost, the concentration of circulating proteins remains normal and, therefore, the oncotic pressure remains the same. The decreased capillary pressure and normal oncotic pressure result in the transfer of fluid from the interstitium to the vascular bed, decreasing the hematocrit. The increased arteriolar constriction lowers blood flow to the kidney causing urine formation to decrease. Sympathetic stimulation causes peripheral constriction and produces sweating, resulting in the classic sign of hemorrhage: cold, damp skin. The baroreceptor reflex increases heart rate.

142. The answer is a. (*Guyton, pp 254–261.*) Anaphylactic shock is characterized by a decreased peripheral resistance and a high cardiac output. The decrease in peripheral resistance is so great that mean blood pressure falls below normal. Hypovolumic shock is caused by a decrease in circulating blood volume and pressure. In both types of shock, the baroreceptor reflex increases ventricular contractility and heart rate. Also, in both types of shock, blood is shunted away from the kidney, decreasing renal blood flow and glomerular filtration. As a result, plasma creatinine levels rise.

143. The answer is e. (*Berne, 3/e, pp 259–261.*) If the carotid sinus baroreceptors are stimulated by mechanical deformation, the reflex response will be the same as if the baroreceptors were stimulated by high blood pressure. Stimulating the carotid sinus nerve will increase vagal nerve in an attempt to slow heart rate and, therefore, cardiac output and

mean blood pressure. The baroreceptor reflex response to carotid sinus stimulation will also decrease total peripheral resistance, venous tone, and ventricular contractility. The reduction in venous tone will decrease central venous pressure and, therefore, right atrial pressure.

144–146. The answers are 144-a, 145-c, 146-c. (*Berne, 3/e, pp 265–272.*) The diagram represents the cardiac and venous function curves that are often referred to as the Guyton curves. The cardiac function curves, which are similar to the familiar Starling curves, graph cardiac output as a function of central venous pressure. The cardiac function curves are shifted up and to the left by an increase in contractility and a decrease in afterload; they are shifted down and to the right by a decrease in contractility and an increase in afterload. The vascular function curves graph central venous pressure as a function of cardiac output. The graph is somewhat unusual in that the independent variable, cardiac output, is represented on the y axis. According to the vascular function curves, an increase in cardiac output causes a fall in central venous pressure. A decrease in blood volume or venous tone shifts the vascular function curves to the left; an increase in blood volume or venous tone shifts the vascular function curves to the right. The point at which the two curves intersect represents the central venous pressure and cardiac output of the cardiovascular system. An increase in total peripheral resistance (TPR) decreases the slope; a decrease in TPR increases the slope. An increase in total peripheral resistance decreases the slope of the vascular function curve, and the increase in contractility shifts the cardiac function curve up and to the right. The new intersection of these curves is at point A. The shift from the resting state to point E represents an increase in vascular volume or venous tone without any change in TPR or ventricular contractility. This is consistent with 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. When a person suddenly stands up, contractility and TPR increase while venous compliance decreases (i.e., venous tone increases). When a person begins to exercise, contractility increases, TPR decreases, and venous compliance decreases.

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Gastrointestinal Physiology

Questions

DIRECTIONS: Each question below contains five suggested responses. Select the **one best** response to each question.

147. Chronic administration of which of the following types of drugs would lead to a sustained increase in serum gastrin levels?

- a. H₂ receptor antagonist
- b. Proton pump inhibitor
- c. Anticholinergic
- d. Antacid
- e. Beta blocker

148. Which one of the following statements about small intestinal motility is correct?

- a. Contractile frequency is constant from duodenum to terminal ileum
- b. Peristalsis is the major contractile pattern during feeding
- c. Migrating motor complexes occur during the digestive period
- d. Vagotomy abolishes contractile activity during the digestive period
- e. Contractile activity is initiated in response to bowel wall distention

149. Which one of the following statements about gastric emptying is correct?

- a. Solids empty more rapidly than liquids
- b. Vagotomy accelerates the emptying of solids
- c. Indigestible food empties during the digestive period
- d. Acidification of the antrum decreases gastric emptying
- e. Vagotomy decreases accommodation of the proximal stomach

150. Vitamin B₁₂ is absorbed primarily in the

- a. Stomach
- b. Duodenum
- c. Jejunum
- d. Ileum
- e. Colon

151. The principal paracrine secretion involved in the inhibitory feedback regulation of gastric acid secretion is

- a. Gastrin
- b. Somatostatin
- c. Histamine
- d. Enterogastrone
- e. Acetylcholine

152. Which one of the following is the putative inhibitory neurotransmitter responsible for relaxation of gastrointestinal smooth muscle?

- a. Dopamine
- b. Vasoactive intestinal peptide
- c. Somatostatin
- d. Substance P
- e. Acetylcholine

153. Cholera toxin causes diarrhea by inhibiting

- a. Neutral NaCl absorption in the small intestine
- b. Electrogenic Na absorption from the small intestine
- c. Na-glucose coupled absorption from the small intestine
- d. Na/H exchange in the small intestine
- e. Electrogenic Na absorption from the colon

154. Which one of the following statements best describes water and electrolyte absorption in the GI tract?

- a. Most water and electrolytes come from ingested fluids
- b. The small intestine and colon have similar absorptive capacities
- c. Osmotic equilibration of chyme occurs in the stomach
- d. The majority of absorption occurs in the jejunum
- e. Water absorption is independent of Na⁺ absorption

155. Hypokalemic metabolic acidosis can occur with excess fluid loss from the

- a. Stomach
- b. Ileum
- c. Colon
- d. Pancreas
- e. Liver

156. Which gastrointestinal motor activity is most affected by vagotomy?

- a. Secondary esophageal peristalsis
- b. Distention-induced intestinal segmentation
- c. Oral stomach accommodation
- d. Caudal stomach peristalsis
- e. Migrating motor complexes

157. The hormone involved in the initiation of the migrating motor complex is

- a. Gastrin
- b. Motilin
- c. Secretin
- d. Cholecystokinin
- e. Enterogastrone

158. The rate of gastric emptying increases with an increase in

- a. Intragastric volume
- b. Intraduodenal volume
- c. Fat content of duodenum
- d. Osmolality of duodenum
- e. Acidity of duodenum

159. Basal acid output is increased by

- a. Acidification of the antrum
- b. Administration of an H_2 receptor antagonist
- c. Vagotomy
- d. Alkalinization of the antrum
- e. Acidification of the duodenum

160. Which one of the following processes applies to the proximal stomach?

- a. Accommodation
- b. Peristalsis
- c. Retropulsion
- d. Segmentation
- e. Trituration

161. After secretion of trypsinogen into the duodenum, the enzyme is converted into its active form, trypsin, by

- a. Enteropeptidase
- b. Procarboxypeptidase
- c. Pancreatic lipase
- d. Previously secreted trypsin
- e. An alkaline pH

162. The major mechanism for absorption of sodium from the small intestine is

- a. $\text{Na}^+\text{-H}^+$ exchange
- b. Cotransport with potassium
- c. Electrogenic transport
- d. Neutral NaCl absorption
- e. Solvent drag

163. Pharmacological blockade of histamine H_2 receptors in the gastric mucosa

- a. Inhibits both gastrin- and acetylcholine-mediated secretion of acid
- b. Inhibits gastrin-induced but not meal-stimulated secretion of acid
- c. Has no effect on either gastrin-induced or meal-stimulated secretion of acid
- d. Prevents activation of adenyl cyclase by gastrin
- e. Causes an increase in potassium transport by gastric parietal (oxyntic) cells

164. Removal of proximal segments of the small intestine results in a decrease in

- a. Basal acid output
- b. Maximal acid output
- c. Gastric emptying of liquids
- d. Gastric emptying of solids
- e. Pancreatic enzyme secretion

165. Dietary fat, after being processed, is extruded from the mucosal cells of the gastrointestinal tract into the lymphatic ducts in the form of

- a. Monoglycerides
- b. Diglycerides
- c. Triglycerides
- d. Chylomicrons
- e. Free fatty acids

166. Acute obstruction of the common bile duct produced experimentally will incur which of the following changes in plasma and urinary levels of bilirubin?

	Unconjugated bilirubin in plasma	Conjugated bilirubin in plasma	Conjugated bilirubin in urine
a.	Increase	No change	Increase
b.	No change	Increase	Increase
c.	Decrease	Decrease	Decrease
d.	Increase	Decrease	Increase
e.	Decrease	No change	Increase

167. Gas within the colon is primarily derived from which one of the following sources?

- a. CO_2 liberated by the interaction of HCO_3^- and H^+
- b. Diffusion from the blood
- c. Fermentation of undigested oligosaccharides by bacteria
- d. Swallowed atmospheric air
- e. Air pockets within foodstuffs

168. Removal of the pyloric sphincter is associated with

- a. A decrease in gastric compliance
- b. An increase in maximal output of acid
- c. An increase in basal output of acid
- d. An increase in the rate of gastric emptying of solids
- e. An increase in the serum gastrin level

169. Removal of the terminal ileum will result in

- a. A decrease in absorption of amino acids
- b. An increase in the water content of the feces
- c. An increase in the concentration of bile acid in the enterohepatic circulation
- d. A decrease in the fat content of the feces
- e. An increase in the absorption of iron

170. Vitamins synthesized by intestinal bacteria and absorbed in significant quantities include

- a. Vitamin B₆
- b. Vitamin K
- c. Thiamine
- d. Riboflavin
- e. Folic acid

171. Which one of the following statements about the colon is correct?

- a. Absorption of Na⁺ in the colon is under hormonal (aldosterone) control
- b. Bile acids enhance absorption of water from the colon
- c. Net absorption of HCO₃⁻ occurs in the colon
- d. Net absorption of K⁺ occurs in the colon
- e. The luminal potential in the colon is positive

172. Contraction of the gallbladder is correctly described by which of the following statements?

- 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

173. Acidification of the duodenum will

- a. Decrease pancreatic secretion of bicarbonate
- b. Increase secretion of gastric acid
- c. Decrease gastric emptying
- d. Increase contraction of the gallbladder
- e. Increase contraction of the sphincter of Oddi

174. Which one of the following statements about small intestine crypt cells is correct?

- a. They evidence well-developed microvilli
- b. They are responsible for net NaCl and water absorption
- c. They contain significant quantities of brush border hydrolases
- d. They are responsible for net NaCl and water secretion
- e. They demonstrate little or no proliferative activity

175. In contrast to secondary esophageal peristalsis, primary esophageal peristalsis is characterized by which of the following statements?

- a. It does not involve relaxation of the lower esophageal sphincter
- b. It involves only contraction of esophageal smooth muscle
- c. It is not influenced by the intrinsic nervous system
- d. It has an oropharyngeal phase
- e. It involves only contraction of esophageal skeletal muscle

176. Absorption of fat-soluble vitamins requires

- a. Intrinsic factor
- b. Chymotrypsin
- c. Pancreatic lipase
- d. Pancreatic amylase
- e. Secretin

177. Which of the following sugars is absorbed from the small intestine by facilitated diffusion?

- a. Glucose
- b. Galactose
- c. Fructose
- d. Sucrose
- e. Lactose

178. Nearly all binding of cobalamin (vitamin B₁₂) to intrinsic factor occurs in the

- a. Stomach
- b. Duodenum
- c. Jejunum
- d. Ileum
- e. Colon

179. Secondary esophageal peristalsis

- a. Is preceded by an oral-pharyngeal phase of swallowing
- b. Involves activation of medullary swallowing centers
- c. Is accompanied by lower esophageal sphincter relaxation
- d. Occurs in both the skeletal and smooth muscle portions of the esophagus
- e. Is abolished by vagotomy

180. At concentrations present in the diet, which vitamin is absorbed primarily by diffusion?

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

181. As compared to long-chain fatty acids, medium-chain fatty acids

- a. Are also packaged as chylomicrons
- b. Can be used as a source of calories in patients with malabsorptive disease
- c. Are more abundant in the diet
- d. Are less water-soluble
- e. Are also returned to the circulation via the lymph

182. Severe inflammation of the ileum may be accompanied by

- a. Increased vitamin B₁₂ absorption
- b. Decreased bile acid pool size
- c. Increased colon absorption of water
- d. Decreased release of secretin
- e. Increased absorption of dietary fats

183. Which one of the following statements about the process of vitamin B₁₂ absorption is correct?

- a. In humans, intrinsic factor is secreted from chief cells of the gastric gland
- b. Vitamin B₁₂ binds preferentially to intrinsic factor in the stomach
- c. In adults, vitamin B₁₂ absorption occurs along the length of the small intestine
- d. Absorption may be reduced in a patient with pancreatic insufficiency
- e. Absorption occurs via passive diffusion into the enterocyte

184. Patients may experience nausea and a sense of early satiety following

- a. Surgical resection of the proximal small bowel
- b. A vagotomy of the distal stomach
- c. Surgical resection of the proximal stomach
- d. Surgical removal of the gastric antrum
- e. A vagotomy of the orad stomach

185. The origin of electrical slow wave activity in gastrointestinal tract smooth muscle is

- a. The interstitial cells of Cajal
- b. The smooth muscle of the circular muscle layer
- c. The smooth muscle of the longitudinal muscle layer
- d. The smooth muscle of the muscularis mucosa
- e. The myenteric plexus

186. Which one of the following statements is correct?

- a. Pepsin is inactivated at a pH of 3 and below
- b. Enterotoxynin is a small intestinal hormone inhibitory to gastric acid secretion
- c. Gastric acid secretion is greatest during the cephalic phase of digestion
- d. Somatostatin increases antral G cell gastrin release
- e. Maximal acid output may be increased in a patient with duodenal ulcer disease

187. The major factor that protects the duodenal mucosa from damage by gastric acid is

- a. Pancreatic bicarbonate secretion
- b. The endogenous mucosal barrier of the duodenum
- c. Duodenal bicarbonate secretion
- d. Hepatic bicarbonate secretion
- e. Bicarbonate contained in bile

188. Bicarbonate absorption from the upper small intestine is closely coupled with

- a. Na-glucose absorption
- b. Neutral NaCl absorption
- c. Na/H exchange
- d. Electrogenic Na absorption
- e. Na-vitamin B₁₂ absorption

189. Which one of the following statements about bile acids is correct?

- a. Conjugation with glycine enhances passive absorption of bile acids
- b. Bile acids constitute approximately 80% of the total solutes in bile
- c. Deoxycholic acid and lithocholic acid are examples of primary bile acids
- d. Bile acid synthesis is catalyzed by the microsomal enzyme 7 α -hydroxylase
- e. Bile acids are essentially water-insoluble

190. Withdrawal from chronic administration of an antisecretory compound is followed by rebound gastric acid hypersecretion. Which drug could account for the observed result?

- a. A H_1 receptor antagonist
- b. A proton pump inhibitor
- c. A cholinergic receptor antagonist
- d. An antacid
- e. A CCK_B receptor antagonist

191. The migrating motor complex in humans

- a. Occurs only in the small intestine
- b. Requires an intact intrinsic nervous system for coordinated propagation
- c. Is the result of food-mediated distension of the small intestine
- d. Mixes intestinal contents with bile and the digestive enzymes
- e. Is correlated with periodic increases in plasma gastrin levels

192. The delivery of chyme into the proximal small intestine will

- a. Increase gastric acid secretion
- b. Decrease pancreatic bicarbonate secretion
- c. Increase gastric emptying of solids
- d. Decrease circulating CCK levels
- e. Increase small intestine segmentation

193. A person is found to have increased basal and maximal acid outputs, decreased serum calcium levels, and microcytic anemia. Inflammation in which area of the gastrointestinal tract would explain these findings?

- a. Colon
- b. Jejunum
- c. Duodenum
- d. Gallbladder
- e. Stomach

194. Which one of the following statements best describes water and electrolyte absorption in the gastrointestinal tract?

- a. Most water and electrolytes derive from the oral intake of fluids
- b. The small and large intestines have similar absorptive capacities
- c. Net secretion of potassium occurs from the ileum
- d. Osmotic equilibration of chyme occurs in the duodenum
- e. Cholera toxin inhibits sodium-coupled nutrient transport

195. The paracrine secretion responsible for inhibiting gastric acid secretion is

- a. Histamine
- b. Enterogastrone
- c. Somatostatin
- d. Pepsin
- e. Enterooxynin

196. A medical student presents to the emergency room with a two-day history of severe vomiting and orthostatic hypotension. What kind of metabolic abnormalities would you expect?

- a. Hypokalemia, hypochloremia, and metabolic acidosis
- b. Hyperkalemia, hyperchloremia, and metabolic alkalosis
- c. Normal serum electrolytes and metabolic acidosis
- d. Normal serum electrolytes and metabolic alkalosis
- e. Hypokalemic, hypochloremic, metabolic alkalosis

197. The metabolic effects of insulin include

- a. Decreased glucose utilization
- b. Decreased lipolysis
- c. Increased proteolysis
- d. Increased gluconeogenesis
- e. Increased ketogenesis

198. Which one of the following statements about bile acids is correct?

- a. They are essentially water-insoluble
- b. The majority of bile acids is absorbed by passive diffusion
- c. Glycine conjugates are more soluble than taurine conjugates
- d. The amount lost in the stool each day represents the daily loss of cholesterol
- e. The bile acid dependent fraction of bile is stimulated by the hormone secretin

199. In contrast to secretory diarrhea, osmotic diarrhea

- a. Is characterized by an increase in stool osmolality
- b. Is the result of increased crypt cell secretion
- c. Is the result of decreased electroneutral sodium absorption
- d. Is caused by bacterial toxins
- e. Occurs only in the colon

200. The macrolide antibiotic erythromycin is associated with gastrointestinal disturbances related to increased motility. The antibiotic works by binding to receptors on nerves and smooth muscle that recognize the gastrointestinal hormone

- a. Gastrin
- b. Motilin
- c. Secretin
- d. Cholecystokinin
- e. Enteroglucagon

201. The transport protein responsible for entry of glucose into the intestinal enterocyte is called

- a. Glut-2
- b. Glut-5
- c. SGLT1
- d. SGLT2
- e. SGLT5

202. Short-chain fatty acid absorption occurs almost exclusively from the

- a. Stomach
- b. Duodenum
- c. Jejunum
- d. Ileum
- e. Colon

203. Which one of the following statements about medium-chain fatty acids is correct?

- a. They are more water-soluble than long-chain fatty acids
- b. Within the enterocyte, they are used for triglyceride resynthesis
- c. They are packaged into chylomicrons
- d. They are transported in the lymph
- e. They require emulsification prior to enterocyte uptake

Gastrointestinal Physiology

Answers

147. The answer is b. (*Guyton, pp 742–746.*) Gastric acid secretion by the parietal cells occurs in response to neural (acetylcholine), hormonal (gastrin), and paracrine (histamine) excitatory inputs. Secretion of HCl by the parietal cell involves H^+ - K^+ -ATPase actively pumping H^+ out of a cell in exchange for K^+ entering the cell. Inhibition of pump activity leads to a prolonged increase in gastric pH and the removal of the inhibitory effect of low pH (<3.0) on gastrin release. The hypergastrinemia that develops may actually increase the number of parietal cells as a result of the trophic effects of the hormone.

148. The answer is c. (*Guyton, pp 723–724, 733–734.*) Segmentation, the primary motility pattern of the digestive period in humans, is defined as irregular and uncoordinated contraction of the circular muscle layer. This pattern, which develops in response to intestinal wall distention, is determined by activation of preprogrammed neural circuits within the myenteric plexus. The contractile frequency of the small intestine decreases in an aboral direction. The contractions, which are caused by underlying changes in smooth muscle electrical activity called *electrical slow waves*, decrease from approximately 11 per minute in the duodenum to approximately 6 to 7 per minute in the distal ileum. Elimination of extrinsic input to the bowel wall has little functional effect on bowel motility during the digestive period. Segmentation develops immediately upon the delivery of food into the small intestine and is accompanied by abolishment of the migrating motor complexes characteristic of the inter-digestive period.

149. The answer is c. (*Guyton, pp 730–733.*) Distention of the oral stomach elicits an inhibitory vago-vagal accommodation reflex that controls intragastric pressure and the emptying of liquids. Removal of inhibitory vagal input leads to decreased gastric accommodation and increased emptying of liquid. Distention of the caudad stomach elicits an

excitatory vago-vagal reflex that results in the trituration of solid food in particles of 1 mm and smaller. Because solids must be liquefied prior to emptying from the stomach, the gastric emptying of liquids begins before the emptying of solids. The actual rate of emptying depends upon neural (enterogastric reflex) and hormonal (enterogastrone) inhibitory feedback from the proximal small bowel. Undigested food residue empties during the interdigestive period in concert with the development of migrating motor complexes.

150. The answer is d. (*Guyton, pp 386–389, 811.*) Vitamin B₁₂ (cobalamin) is absorbed primarily by the enterocytes of the distal ileum. Efficient absorption requires intrinsic factor, a glycoprotein secreted by the parietal cells of the gastric mucosa. The vitamin B₁₂-intrinsic factor complex is emptied from the stomach and propelled along the small intestine to the terminal ileum, where specific transporters located on the enterocyte microvilli bind the vitamin B₁₂-intrinsic factor complex. Binding requires calcium and is optimal at pH 6.6. Absorption is an active transport process.

151. The answer is b. (*Guyton, pp 742–746.*) Somatostatin, located within the SS cells of the gastric antral mucosa, is the principal paracrine secretion involved in the inhibitory feedback of gastric acid secretion. Somatostatin is released in response to an increase in hydrogen ions. In humans, gastric acid secretion by the parietal cell occurs in response to excitatory neural (acetylcholine), hormonal (gastrin), and paracrine (histamine) stimuli. Inhibitory feedback regulation of acid output also involves neural (enterogastric reflex), hormonal (enterogastrone), and paracrine (somatostatin) influences.

152. The answer is b. (*Berne, 4/e, pp 590–598.*) Important inhibitory neurotransmitters in the gastrointestinal tract include vasoactive intestinal peptide and nitric oxide. Relaxation of gastrointestinal smooth muscle occurs following activation of nonadrenergic, noncholinergic (NANC) enteric nerve fibers. Acetylcholine, substance P, and dopamine are excitatory neurotransmitters. Somatostatin is a paracrine secretory product with multiple effects on gastrointestinal function.

153. The answer is a. (*Berne, 3/e, pp 66, 655–658.*) Diarrhea is defined as the excretion of 200 g or more of water in the stools of an adult during a

24-h period. Although Na is absorbed from the small intestine by several mechanisms, cholera toxin specifically inhibits neutral NaCl absorption. In addition, cholera, the most severe form of diarrhea, produces its effect by increasing salt and water secretion by intestinal crypt cells.

154. The answer is d. (*Berne, 4/e, pp 654–660.*) Most water and electrolyte absorption occurs in the jejunum, with the duodenum serving primarily as the site of osmotic equilibration of chyme. Water absorption is passive and occurs as the direct result of active sodium absorption. The small intestine and colon absorb approximately 9 to 12 L of fluid per 24-h period, most of which comes from gastrointestinal secretions. In contrast to the small intestine, the colon has a limited capacity to absorb water (approximately 3 to 6 L per day).

155. The answer is c. (*Berne, 4/e, pp 654–660.*) Loss of gastric juice results in hypokalemic, metabolic alkalosis. Excessive loss of fluid from the gastrointestinal tract can lead to dehydration and, depending upon the origin of the fluid loss, electrolyte and acid-base disturbances. The hydrogen ion and potassium ion concentration of gastric juice exceeds that of the plasma. As a result, excess fluid loss leads to metabolic alkalosis accompanied by hypokalemia. Because the pancreas, liver, ileum, and colon secrete bicarbonate, excessive loss leads to metabolic acidosis. In addition, the colon secretes potassium. Thus, the acidosis is accompanied by hypokalemia.

156. The answer is c. (*Guyton, pp 598–610.*) Orad stomach accommodation depends exclusively upon an intact vago-vagal reflex. Vagal innervation of the gastrointestinal tract extends from the esophagus to the level of the transverse colon. Preganglionic fibers from cell bodies in the medulla synapse with ganglion cells located in the enteric nervous system. Distention-induced contraction of gastrointestinal smooth muscle develops as the result of long (vago-vagal) and local (enteric nerves) reflexes. The importance of long versus local reflex pathways varies along the gut. Secondary esophageal peristalsis, intestinal segmentation, and migrating motor complexes are unaffected by vagotomy, whereas caudad stomach peristalsis is decreased but not abolished by vagotomy.

157. The answer is b. (*Guyton, p 610.*) Motilin is released during the interdigestive period and is believed to be involved in the initiation of the

migrating motor complex. The factors responsible for release are unknown. All other gastrointestinal hormones are released during the digestive period and coordinate motor and secretory activities.

158. The answer is a. (Berne, 4/e, pp 730–733.) The initial rate of emptying varies directly with the volume of the meal ingested. Gastric emptying is influenced by the intragastric volume and by the physical and chemical composition of the chyme in the small intestine. Increasing the volume, fat content, acidity, or osmolarity of the lumen of the small intestine elicits inhibitory neural (enterogastric reflex) and hormonal (enterogastrone) feedback mechanisms.

159. The answer is d. (Berne, 4/e, pp 622–624.) 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, a paracrine secretion that inhibits gastrin release. Decreased gastrin release reduces the acid output of the stomach. Acidification of the duodenum elicits inhibitory neural (enterogastric) and hormonal (enterogastrone) reflexes that also inhibit acid output. Administration of a histamine antagonist reduces acid secretion by decreasing the stimulatory effect of histamine.

160. The answer is a. (Berne, 4/e, pp 730–733.) Increases in intragastric volume normally are not associated with large increases in intragastric pressure because of distention-mediated activation of a vago-vagal inhibitory reflex, the accommodation reflex. The reflex is a property of the proximal 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 distal stomach. Segmentation is the primary contractile pattern of the small intestine during the digestive period.

161. The answer is a. (Guyton, p 746.) 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 respon-

sible for the conversion of chymotrypsinogens and other proenzymes into their active forms.

162. The answer is d. (*Berne, 4/e, pp 654–661.*) Although multiple pathways exist for the absorption of Na^+ , neutral absorption is the major mechanism. Absorption of sodium is the primary absorptive event in the small intestine. Absorption of Na^+ is necessary for absorption of water and other electrolytes. Neutral absorption may occur in two ways: Na^+ cotransported with Cl^- or in exchange for H^+ ions.

163. The answer is a. (*Berne, 4/e, pp 622–625.*) Histamine (H_2) receptor antagonists inhibit both gastrin-induced and vagal-mediated secretion of acid. Secretion of acid by gastric parietal (oxyntic) cells involves stimulation of adenyl cyclase and cyclic AMP-mediated stimulation of the active transport of chloride and potassium-hydrogen ion exchange. Neither gastrin nor vagal stimulation activates adenyl cyclase directly; both depend on concomitant release of histamine and histamine-induced activation of adenyl cyclase.

164. The answer is e. (*Guyton, pp 732–733, 745–748.*) Inflammation or removal of the upper small intestine leads to a decrease in pancreatic and hepatobiliary function. The proximal small intestine contains a number of “receptors” that monitor the physical (volume) and chemical (pH, fat content, caloric density, osmolality) composition of the chyme emptied from the stomach. Stimulation of these receptors releases hormones and activates neural reflexes that initiate pancreatic enzyme and bicarbonate secretion, stimulate gallbladder emptying, and provide feedback for inhibitory regulation of gastric function (enterogastrone, enterogastric reflex). Removal of these reflexes decreases pancreatic secretion and gallbladder emptying and increases gastric emptying and acid output.

165. The answer is d. (*Guyton, pp 756–758.*) Long-chain fatty acids are extruded from enterocytes in the form of chylomicrons into the lymphatic system. Triglycerides are hydrolyzed to monoglycerides and taken into mucosal cells. If the fatty acids are short chains (less than 10 to 12 carbon atoms), they are extruded in the form of free fatty acids into the portal blood. Chylomicrons represent triglycerides and esters of cholesterol that

have been invested in the intestinal mucosa with a coating of phospholipid, protein, and cholesterol.

166. The answer is b. (*Berne, 4/e, pp 638–641.*) Unconjugated bilirubin, which is a breakdown product of the heme ring of hemoglobin, is taken up from plasma by the liver, conjugated with glucuronic acid, and released via the bile duct into the gastrointestinal tract. Under normal conditions, some conjugated bilirubin is reabsorbed by the intestine. The kidney clears only conjugated bilirubin. Thus, acute obstruction of the bile duct does not affect the rate of hepatic conjugation of bilirubin but does result in a “backup” of conjugated bilirubin in plasma and in its eventual clearance by the kidney.

167. The answer is c. (*Guyton, pp 769–770.*) 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 (100–150 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.

168. The answer is d. (*Berne, 4/e, pp 604–606.*) Removal of the pyloric sphincter will increase the rate of gastric emptying because the resistance to flow of large particles will be removed. The distal stomach, which includes the antrum and the pyloric sphincter, is involved in the regulation of the gastric emptying of solids and in the regulation of gastric acid secretion. Antral peristaltic contractions promote the trituration of solids. The pyloric sphincter serves to limit the flow of solids out of the stomach until the particles are of a small enough size to be suspended in the liquid component of the meal. Secretion of acid will be decreased because of the loss of gas-

trin, which is normally secreted by the G cells of the antrum. Gastric compliance is a property of the proximal stomach.

169. The answer is b. (Berne, 4/e, pp 671–672.) 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.

170. The answer is e. (Berne, 4/e, pp 664–666, 672.) Folic acid is both produced in the intestine and absorbed from the intestine. In humans, several vitamins, including vitamin K, several of the B complex, and folic acid, are synthesized by intestinal bacteria. However, only folic acid is absorbed by the host. Dietary intake of the other vitamins is necessary.

171. The answer is a. (Berne, 4/e, pp 654–657, 711.) Both the absorption of Na^+ and secretion of K^+ from the colon are affected by changes in circulating levels of aldosterone. The major route of absorption of sodium in the colon is electrogenic transport. Because of the “tight” nature of the tight junctions that connect cells in the colon, a relatively large potential difference exists between the mucosal (negative) and serosal (positive) surfaces of the absorptive cells. This electrical difference favors the net secretion of K^+ into the lumen. Secretion of HCO_3^- occurs in exchange for absorption of Cl^- . No counterbalancing cation exchange pumps are present in the colon.

172. The answer is d. (Berne, 4/e, pp 641–643.) 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. Vagal stimulation, which is cholinergically mediated and blocked by atropine, also promotes gallbladder contraction.

173. The answer is c. (*Berne, 4/e, pp 628–630, 635–636.*) Acidification of the upper small intestine results in the inhibitory feedback regulation of gastric function. Secretin is released from the small intestine primarily in response to an increased delivery of hydrogen ions. Secretin is the primary stimulus for pancreatic secretion of water and bicarbonate. In addition secretin may serve as an enterogastrone, that is, a hormone involved in the inhibitory feedback regulation of gastric function. Cholecystokinin (CCK) is the hormone responsible for contraction of the gallbladder and relaxation of the sphincter of Oddi.

174. The answer is d. (*Guyton, pp 752–753.*) Intestinal crypt cells are characterized by the transport of chloride and water into the intestinal lumen. Secretion of chloride across the apical cell membrane is believed to involve the cystic fibrosis transmembrane receptor (CFTR) chloride channel. Crypt cells are the proliferative cells of the intestinal mucosa. As crypt cells migrate up the villus axis, they undergo significant morphological and biochemical differentiation. They change from short, cuboidal cells with minimal microvilli and few apical membrane transporters or brush border hydrolases into mature villus tip cells prepared for the role of nutrient, water, and electrolyte absorption.

175. The answer is d. (*Berne, 4/e, pp 598–602.*) Primary peristalsis involves not only esophageal peristalsis and relaxation of the lower esophageal sphincter (LES), but also the oral-pharyngeal phase of swallowing. The term *primary esophageal peristalsis* denotes that swallowing has been elicited as a consequence of activation of the “swallowing centers” in the medulla (nucleus ambiguus, dorsal motor X). *Secondary esophageal peristalsis* is a localized esophageal response to irritation or distention that results in a peristaltic contraction and relaxation of the LES. Both primary and secondary esophageal peristalsis require an intact intrinsic nervous system.

176. The answer is c. (*Berne, 4/e, p 672.*) Absorption of the fat-soluble vitamins (A, D, E, and K) is diminished if there is a lack of pancreatic

lipase. Lipase is required to produce monoglycerides that, in combination with bile salts, make it possible to bring the fat-soluble vitamins close to the mucosal cell surface for absorption. With the exception of vitamin B₁₂, which is absorbed bound to intrinsic factor in the ileum, vitamins are absorbed chiefly in the upper small intestine.

177. The answer is c. (*Guyton, pp 761–762.*) Facilitated diffusion is the major transport route for fructose. The duodenum and jejunum are the principal sites of carbohydrate absorption in humans. Digestion of carbohydrates is accomplished by amylase and brush border enzymes and results in a mixture of glucose, fructose, and galactose. A common sodium-dependent secondary active transporter absorbs glucose and galactose. Sucrose and lactose are disaccharides that break down into glucose and fructose, and glucose and galactose, respectively.

178. The answer is b. (*Berne, 4/e, pp 626, 665–666.*) Although intrinsic factor is secreted by the oxyntic cells of the gastric mucosa, binding to cobalamin occurs in the duodenum. Cobalamin, also known as vitamin B₁₂, is synthesized only by microorganisms and, in the human diet, is provided almost entirely from animal products. Gastric digestion of food liberates cobalamin where, at low pH, it binds primarily to the R protein-type binder, haptocorrin, derived primarily from salivary secretions. In the duodenum, pancreatic proteases release cobalamin from the haptocorrin but have no effect on intrinsic factor derived from parietal cells. Cobalamin rapidly complexes with intrinsic factor and is transported along the gut to the distal 60 cm of the ileum, where specific receptors located on the villus tip cells bind the cobalamin-intrinsic factor complex.

179. The answer is c. (*Berne, 4/e, pp 600–601.*) The term *secondary esophageal peristalsis* describes esophageal peristalsis and lower esophageal relaxation associated with distension or irritation of the smooth muscle portion of the esophageal body. The event is limited to the smooth muscle component of the esophagus and is the result of activation of enteric nerves. Initiation of secondary peristalsis does not involve extrinsic neural reflexes and, thus, is not accompanied by the oral-pharyngeal phase of swallowing.

180. The answer is c. (*Berne, 4/e, pp 664–666, 672.*) Absorption of vitamin D increases linearly as the intraluminal concentration increases, sug-

gesting 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 B₁₂, are a diverse group of organic compounds that are essential for normal growth and development. At the low concentrations present in the diet (1–100 nM), transport of the vitamins across the brush border occurs by specialized mechanisms, such as membrane carriers, active transport systems, and membrane-binding proteins and receptors, specific for a particular vitamin.

181. The answer is b. (*Berne, 4/e, pp 666–672.*) Medium-chain triglycerides (MCTs) are readily absorbed from the small intestine and can be used as a source of calories in patients with a wide variety of GI diseases resulting in malabsorption. MCTs are fatty acids of 6 to 12 carbon chain lengths that are present in small amounts in the normal diet. They are hydrolyzed by lipases more rapidly than long-chain fatty acids and are much more water-soluble than long-chain triglycerides. MCTs are not utilized for resynthesis of triglycerides and therefore are not packaged into chylomicrons. Instead, they are released directly into the portal blood.

182. The answer is b. (*Berne, 4/e, pp 608, 654–657.*) 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 (1–5 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.

183. The answer is d. (*Berne, 4/e, pp 665–666.*) Patients with pancreatic insufficiency, as well as patients with Crohn's disease, bacterial over-

growth, or who have undergone ileal resection, may exhibit vitamin B₁₂ deficiency. Cobalamin, also known as vitamin B₁₂, is an essential vitamin found in such foods as liver, fish, and dairy products. Absorption of cobalamin occurs exclusively from the ileum where specific receptors on ileal enterocytes bind a complex of cobalamin and intrinsic factor. Although intrinsic factor is secreted by gastric parietal cells, binding of the vitamin to intrinsic factor occurs primarily in the proximal small intestine. The acidic environment of the gastric lumen favors the binding of cobalamin to R protein-type binding proteins that originate from salivary and gastric secretions. Pancreatic proteases in the small intestine degrade the R proteins, and the rise in pH favors rapid and complete transfer of the vitamin to intrinsic factor.

184. The answer is b. (*Guyton, pp 732–733.*) Patients often experience a sense of fullness (early satiety), abdominal bloating, and nausea following a vagotomy of the antrum. The stomach has three important motor functions: storage, trituration, and emptying. The ability of the stomach to serve as a reservoir is characteristic of the orad stomach (gastric fundus and corpus). Upon ingestion of a mixed meal (liquids and solids) a vago-vagal mediated reflex, the accommodation reflex, limits the rise in intragastric pressure in response to an increase in intragastric volume. Sectioning of the vagus nerve or gastric resection of the orad stomach abolishes the reflex and leads to an increased intragastric pressure with a resultant increase in the gastric emptying of liquids. Trituration, the mechanical breakdown of large, solid food particles into smaller particles is essential for the gastric emptying of solids. Trituration is the result of rhythmical contractions characteristic of the gastric antrum. Normally, solids do not empty until they are smaller than 1 to 2 mm in diameter. Distension of the antrum initiates both local, enteric neural reflexes and long, vago-vagal reflexes that increase the strength of antral contractions and promote the gastric emptying of solids. The loss of vagal input to the antrum markedly impairs the emptying of solids and often leads to an early sense of fullness.

185. The answer is a. (*Berne, 4/e, pp 718–720.*) Electrical slow wave activity in the gastrointestinal tract appears to originate from specialized pacemaker cells (interstitial cells of Cajal) located between the longitudinal and circular muscle layers and within the submucosal and myenteric plexuses. These pacemaker cells input directly onto the smooth muscle

and receive input from enteric nerves. Rhythmic, phasic contractions are characteristic of the gastric antrum and the small and large intestines.

186. The answer is c. (*Guyton, pp 742–746.*) Maximal acid output may be increased in patients with duodenal ulcer disease. Gastric juice contains a number of secretions including HCl, intrinsic factor, pepsinogen, water, and electrolytes. Gastric secretion can be studied during the interdigestive (basal phase) or the digestive (cephalic, gastric, and intestinal phases of acid secretion) periods. Increased acid output is the result of neural (ACh), hormonal (gastrin), and paracrine (histamine) stimuli acting on the oxyntic cell. Feedback regulation (inhibition) of acid secretion occurs as the result of hydrogen ion–stimulated release of somatostatin from paracrine cells located near gastrin-containing antral G cells and as the result of the presence of chyme in the small intestine. The latter limits acid secretion via neural (enterogastric reflex) and hormonal (enterogastrone) pathways. Removal of intestinal inhibitory feedback leads to increased acid output. Enterotoxynin is a putative small intestinal hormone that stimulates gastric acid secretion.

187. The answer is a. (*Guyton, pp 746–748.*) 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 evidence 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.

188. The answer is c. (*Guyton, pp 759–761.*) Absorption of bicarbonate from the small intestine occurs primarily in the jejunum and is the result of bicarbonate-stimulated Na/H exchange. In the presence of luminal bicarbonate, the activity of the exchanger increases and the resultant secreted hydrogen ion combines with bicarbonate to form carbon dioxide and water, which are subsequently absorbed. In addition to the exogenous

dietary intake of bicarbonate, the ion is produced endogenously in salivary, gastric, intestinal, and hepatobiliary secretions.

189. The answer is d. (Berne, 4/e, pp 638–644.) Bile acid synthesis is catalyzed by the microsomal enzyme 7α -hydroxylase. Bile is a complex mixture of inorganic and organic substances. The predominant organic component of bile is the bile salts, which make up about 67% of the total solutes. Primary bile acids, cholic acid and chenodeoxycholic acid, are synthesized from cholesterol. The rate-limiting step is catalyzed by the microsomal enzyme 7α -hydroxylase. Secondary bile acids, deoxycholic acid and lithocholic acid, are produced by biotransformation of primary bile acids by intestinal bacteria. Prior to secretion, the bile acids are conjugated with either glycine or taurine, which greatly enhances their water solubility.

190. The answer is b. (Berne, 4/e, pp 628–630.) Withdrawal from long-term use of proton pump inhibitors prescribed for peptic ulcer disease may be associated with rebound gastric hypersecretion. Pharmacological suppression of gastric acid secretion can occur when the administered drug binds to a receptor present on the parietal cell or when it antagonizes the hydrogen-potassium-ATPase pump responsible for the active secretion of hydrogen ion into the gastric lumen. At the present time, the most effective antisecretory compounds work by blocking the histamine type-2 (H_2) receptor present on the parietal cell or by inhibition of the hydrogen pumps. The latter are the most potent and long-acting, thus increasing the probability of increasing serum gastrin.

191. The answer is b. (Berne, 4/e, p 611.) An intact enteric nervous system is essential for propagation of migrating motor complexes along the bowel. During the interdigestive period, the GI tract undergoes regular increases in peristaltic contractile activity about every 90 minutes that are termed *migrating motor complexes*. Originally recorded from the small intestine, they may begin in the smooth muscle of the esophagus or the stomach. They are commonly associated with periodic increases in the hormone motilin. Although it is still unclear, they appear to serve a “housekeeping function” by clearing the GI tract of luminal contents. They are immediately interrupted when a meal is ingested.

192. The answer is c. (*Berne, 4/e, pp 608–610.*) The delivery of food into the proximal small intestine is accompanied by the appearance of segmenting intestinal contractions. The presence of food in the small intestine initiates neural reflexes and the release of hormones that affect a variety of gastrointestinal processes. The presence of food in the proximal small intestine is inhibitory to gastric secretion and emptying (enterogastric reflex, enterogastrone), stimulates pancreatic and hepatobiliary secretions (CCK, secretin), and increases small intestine segmentation. The latter is responsible for mixing chyme with bile and the digestive enzymes.

193. The answer is c. (*Guyton, pp 758–761.*) Inflammation of the duodenum may lead to increased acid output, hypocalcemia, and microcytic anemia. Increased basal and maximal acid outputs may result from excessive stimulation of the parietal cell (e.g., hypergastrinemia) or reduced inhibitory feedback (i.e., reduced effect of enterogastrone and the enterogastric reflex). The latter may occur when the proximal small intestine is inflamed. Although calcium is absorbed along the entire length of the small intestine, it is absorbed primarily in the duodenum. Similarly, iron is absorbed primarily in the duodenum. Microcytic anemia is the result of reduced stores of iron.

194. The answer is d. (*Berne, 4/e, pp 654–664.*) Osmotic equilibration of gastric contents emptied into the small intestine occurs in the duodenum. Water and electrolyte absorption occurs in both the small intestine and colon. Unlike the small intestine, however, the colon has a relatively limited daily absorptive capacity (approximately 6 L/day). The limited capacity is the result of the highly impermeable nature of the tight junctions connecting the colonic epithelial cells. Most water and electrolytes derive from endogenous gastrointestinal secretions and may reach 6 to 8 L/day. Regional differences occur along the small bowel and between the small bowel and colon with respect to the individual transport processes. For example, although there is net absorption of nutrients and water and electrolytes in the duodenum, the leaky nature of the tight junctions leads to rapid osmotic equilibration of chyme emptied from the stomach. Also, although potassium absorption occurs in the small intestine, net secretion may occur in the colon. Cholera toxin affects electroneutral sodium transport in the small intestine.

195. The answer is c. (*Guyton, pp 628–640.*) Somatostatin is the principal paracrine secretion inhibitory to gastric acid secretion. As the free hydrogen ion concentration of the gastric lumen increases, the stimulus for continued acid secretion decreases. This negative feedback is mediated via somatostatin. Hydrogen ions release the somatostatin from antral SS cells, which in turn decreases gastrin release. Gastrin is the principal hormone released during a meal that is excitatory to gastric acid secretion. Somatostatin may also directly inhibit hydrogen ion secretion by the oxyntic cell.

196. The answer is e. (*Guyton, pp 742–744, 768–769.*) Analysis of serum electrolytes reveals low potassium (hypokalemia), low chloride (hypochloremia), and metabolic alkalosis. These abnormalities arise from two sources. First, gastric juice contains potassium and chloride in concentrations higher than found in the plasma. Loss of gastric juice through vomiting or drainage leads to depletions of these electrolytes from the plasma. Second, the metabolic abnormalities are exacerbated by the student'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.

197. The answer is b. (*Guyton, pp 884–891.*) 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.

198. The answer is d. (*Berne, 4/e, pp 637–644.*) Although only small amounts of bile acids are lost in the stool each day, the loss represents the only route of elimination of cholesterol from the body. The predominant organic component of bile is the bile salts, which make up about 67% of the total solutes. Bile salts are amphiphilic molecules, that is, they exhibit both water and lipid solubility. Primary bile acids, cholic acid and chenodeoxycholic acid, are synthesized from cholesterol. Secondary bile acids, deoxycholic acid and lithocholic acid, are produced by biotransformation of primary bile acids by intestinal bacteria. Prior to secretion, the bile acids

are conjugated with either glycine or taurine, which greatly enhances their water solubility. In general, taurine conjugates are more water-soluble than glycine conjugates.

199. The answer is a. (*Fauci, 14/e, pp 242–247.*) The two major types of diarrhea are osmotic and secretory. Osmotic diarrhea is the result of excess solute in the lumen of the small intestine (undigested nutrients) or colon (laxatives). The excess solute produces a bulk flow of water into the lumen in volumes that eventually overwhelm the absorptive capacity of the gut. In osmotic diarrhea, stool osmolarity is greater than normal. Secretory diarrhea is the result of crypt cell secretion of an isosmotic chloride solution combined with inhibition of electroneutral NaCl absorption from the small intestine. Diarrhea is defined as the excretion of 200 grams or more of water in the stool per day.

200. The answer is b. (*Fauci, 14/e, p 878.*) Motilin is the gastrointestinal peptide hormone associated with the initiation of migrating motor complexes during the interdigestive period. The hormone stimulates increased contractions by a direct action on smooth muscle and by activation of excitatory enteric nerves. Erythromycin belongs to the group of macrolide antibiotics and also shows an ability to excite motilin-like receptors on enteric nerves and smooth muscle. As a result, a common side effect of the antibiotic is abdominal cramping and diarrhea.

201. The answer is c. (*Berne, 4/e, pp 648–649.*) The transport protein responsible for the sodium-dependent glucose transport in the small intestine is termed the SGLT1. 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 occurs primarily via the sodium-dependent SGLT1 secondary active transport mechanism. Exit from the enterocyte occurs by facilitated diffusion and is mediated by the membrane transporter, Glut-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.

202. The answer is c. (*Guyton, pp 762–763.*) The colon is the major site for the generation and absorption of short-chain fatty acids. They are products of bacterial metabolism of undigested complex carbohydrates derived

from fruits and vegetables. In addition to exhibiting trophic effects on the colonic mucosa, they are believed to promote sodium absorption from the colon. The mechanism of action remains controversial.

203. The answer is a. (*Berne, 4/e, pp 666–671.*) Medium-chain triglycerides are hydrolyzed by lipases more rapidly than long-chain fatty acids and are much more water-soluble than long-chain triglycerides. Medium-chain triglycerides (MCTs) are fatty acids of 6 to 12 carbon chain lengths that are present in small amounts in the normal diet. MCTs are not utilized for resynthesis of triglycerides and therefore are not packaged into chylomicrons. Instead, they are released directly into the portal blood. Because they are readily absorbed, MCTs can be used in patients with a wide variety of GI diseases resulting in malabsorption.

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Respiratory Physiology

Questions

DIRECTIONS: Each question below contains several suggested responses. Select the **one best** response to each question.

204. The basic respiratory rhythm is generated in the

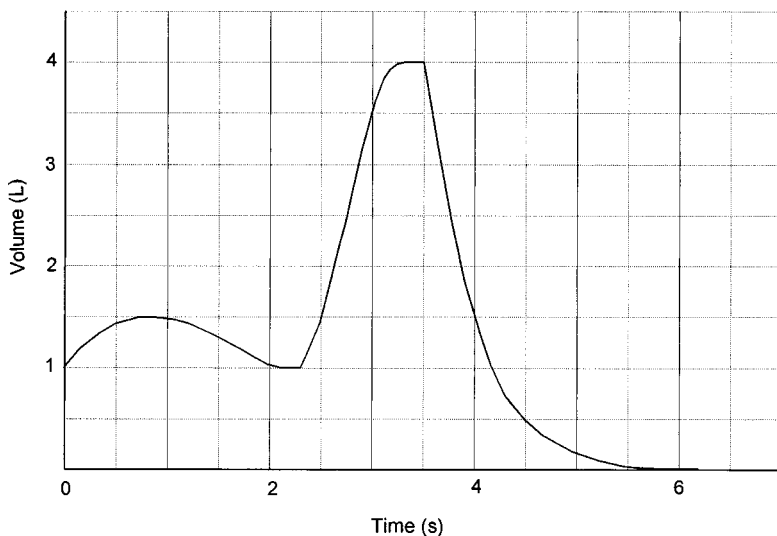
- a. Apneustic center
- b. Nucleus parabrachialis
- c. Dorsal medulla
- d. Pneumotaxic center
- e. Cerebrum

205. At the end of a quiet inspiration, intra-alveolar pressure is normally

- a. 240 cmH₂O
- b. 24 cmH₂O
- c. 0 cm H₂O
- d. 14 cmH₂O
- e. 140 cmH₂O

Questions 206–208

The diagram below represents a spirometry tracing illustrating the changes in lung volume that occurred when a subject inhaled maximally and then rapidly exhaled as much gas as possible.



206. If the patient's total lung capacity is 6 L, what is the functional residual capacity?

- a. 1 L
- b. 2 L
- c. 3 L
- d. 4 L
- e. 5 L

207. What is the FEV₁?

- a. 1.5 L
- b. 2.5 L
- c. 3.5 L
- d. 4.5 L
- e. 5.5 L

208. What is the inspiratory capacity?

- a. 1.0 L
- b. 1.5 L
- c. 2.0 L
- d. 2.5 L
- e. 3.0 L

Questions 209–211

Use the respiratory data below to answer the following questions.

Tidal volume = 400 mL
Dead space volume = 100 mL
Breathing frequency = 10 breaths/min
 P_{aCO_2} = 50 mmHg
 P_{iO_2} = 150 mmHg

209. The patient's alveolar ventilation is

- a. 3 L/min
- b. 4 L/min
- c. 5 L/min
- d. 6 L/min
- e. 7 L/min

210. The patient's alveolar oxygen tension is approximately

- a. 70 mmHg
- b. 80 mmHg
- c. 90 mmHg
- d. 100 mmHg
- e. 110 mmHg

211. If the patient doubles his tidal volume without changing his CO_2 production, his P_{aCO_2} will be

- a. 15 mmHg
- b. 20 mmHg
- c. 25 mmHg
- d. 30 mmHg
- e. 35 mmHg

Questions 212–213

212. A woman has a respiratory rate of 18, a tidal volume of 350 mL, and a dead space of 100 mL. What is her alveolar ventilation?

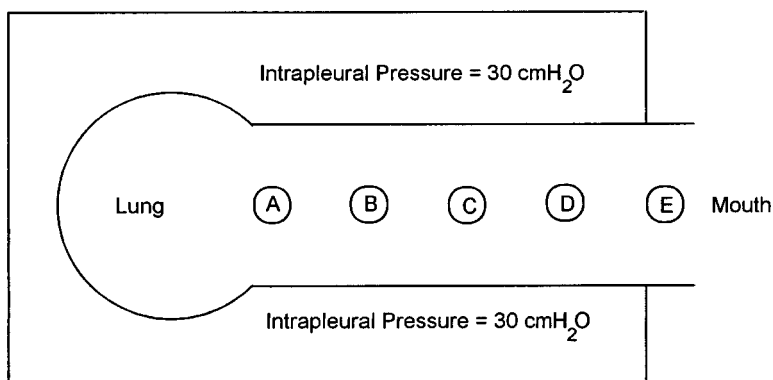
- a. 4.0 L
- b. 4.5 L
- c. 5.0 L
- d. 5.5 L
- e. 6.0 L

213. The woman in the preceding question has a normal PaCO_2 of 40 mmHg. If she increases her tidal volume by 75 mL, her PaCO_2 will become approximately

- a. 15 mmHg
- b. 20 mmHg
- c. 25 mmHg
- d. 30 mmHg
- e. 35 mmHg

Questions 214–215

The diagram below illustrates the intrapleural pressure generated by a patient who exhales forcefully after a maximal inhalation.



214. If the intrapleural pressure at the end of inspiration is 210 cmH₂O and the intrapleural pressure during expiration is 30 cmH₂O, the equal pressure point will be closest to point

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

215. The equal pressure point would be most likely to move closer to the mouth with an increase in

- a. Airway resistance
- b. Lung compliance
- c. Lung volume
- d. Expiratory effort
- e. Airway smooth muscle tone

216. Which one of the following would increase in obstructive, but not in restrictive, lung disease?

- a. Vital capacity
- b. Maximum breathing capacity
- c. FEV_1
- d. Functional residual capacity
- e. Breathing frequency

217. During the early stages of an asthmatic attack,

- a. Arterial carbon dioxide tension decreases
- b. The equal pressure point moves toward the mouth
- c. Lung compliance increases
- d. Airway resistance decreases
- e. Arterial oxygen tension increases

218. Which one of the following will decrease in a person with ventilation-perfusion (V/Q) abnormalities?

- a. Anion gap
- b. Arterial pH
- c. Arterial carbon dioxide tension
- d. Alveolar-arterial (A-a) gradient for oxygen
- e. Alveolar ventilation

219. Which one of the following is higher at the apex of the lung than at the base when a person is standing?

- a. V/Q ratio
- b. Blood flow
- c. Ventilation
- d. P_{aCO_2}
- e. Lung compliance

220. In areas of the lung with lower than normal V/Q ratios, the

- a. Capillary CO_2 tension is lower than normal
- b. Pulmonary vascular resistance is higher than normal
- c. Alveolar O_2 tension is higher than normal
- d. Water vapor pressure is higher than normal
- e. Gas exchange ratio is higher than normal

221. Very small particles are removed from the respiratory system by

- a. Bulk flow
- b. Diffusion
- c. Expectoration
- d. Phagocytosis
- e. Ciliary transport

222. Which of the following conditions causes a decrease in arterial O_2 saturation without a decrease in O_2 tension?

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

223. The bulk of CO_2 is transported in arterial blood as

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

224. The partial pressure of oxygen inhaled from a tank containing 21% O_2 by divers at a depth of 100 ft below sea level (4 atmospheres) is approximately

- a. 40 mmHg
- b. 100 mmHg
- c. 200 mmHg
- d. 600 mmHg
- e. 1200 mmHg

Questions 225–227

Use the pulmonary values below to answer the following questions.

Tidal volume = 500 mL

Expired PCO_2 = 40 mmHg

Respiratory rate = 15/min

Alveolar PCO_2 = 50 mmHg

225. The patient's physiological dead space is

- a. 80 mL
- b. 90 mL
- c. 100 mL
- d. 110 mL
- e. 120 mL

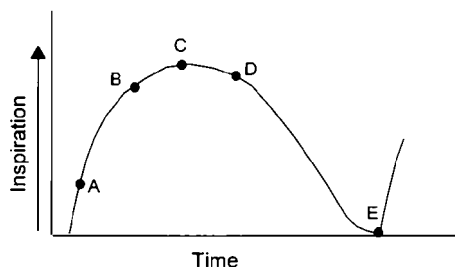
226. The patient's alveolar ventilation is

- a. 4.0 L/min
- b. 4.5 L/min
- c. 5.0 L/min
- d. 5.5 L/min
- e. 6.0 L/min

227. To return the PaCO_2 value to normal (40 mmHg), the patient would have to increase her alveolar ventilation to

- a. 6.5 L/min
- b. 7.0 L/min
- c. 7.5 L/min
- d. 8.0 L/min
- e. 8.5 L/min

228. At what point during the tidal breath illustrated below is the alveolar PCO_2 at its highest value?



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

229. Peripheral and central chemoreceptors may both contribute to the increased ventilation that occurs as a result of

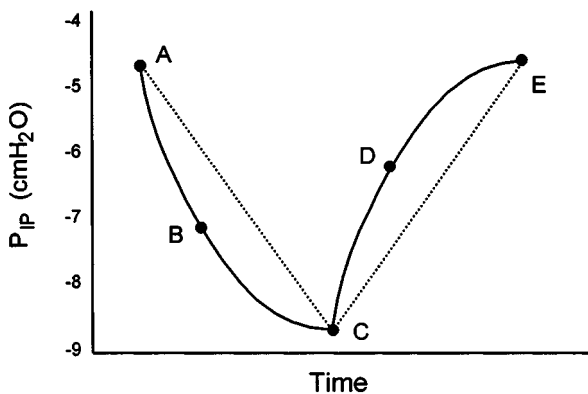
- a. A decrease in arterial oxygen content
- b. A decrease in arterial blood pressure
- c. An increase in arterial carbon dioxide tension
- d. A decrease in arterial oxygen tension
- e. An increase in arterial pH

230. Complete transection of the brainstem above the pons would

- a. Result in cessation of all breathing movements
- b. Prevent any voluntary holding of breath
- c. Prevent the central chemoreceptors from exerting any control over ventilation
- d. Prevent the peripheral chemoreceptors from exerting any control over ventilation
- e. Abolish the Hering-Breuer reflex

Questions 231–232

The diagram below illustrates the change in intrapleural pressure during a single breath.



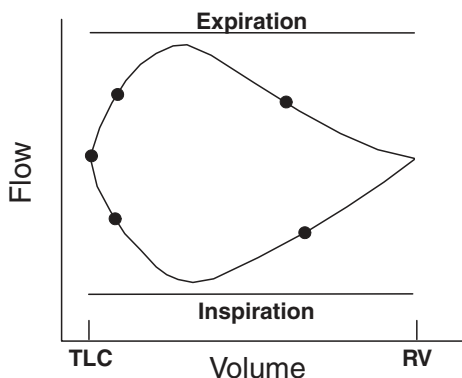
231. At which point on the diagram is inspiratory airflow the greatest?

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

232. At which point on the diagram is lung volume the greatest?

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

233. The following diagram illustrates a flow-volume loop obtained from a normal patient.



At which one of the points on the curve will airflow remain constant despite an increased respiratory effort?

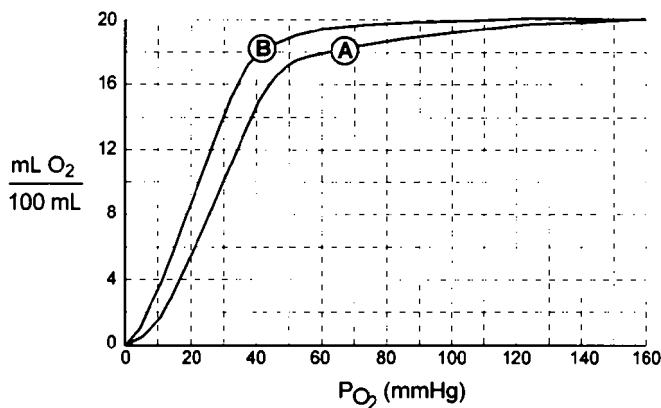
- a. A
- b. B
- c. C
- d. D
- e. E

234. A deficiency of pulmonary surfactant would

- a. Decrease surface tension in the alveoli
- b. Decrease the change in intrapleural pressure required to achieve a given tidal volume
- c. Decrease lung compliance
- d. Decrease the work of breathing
- e. Increase functional residual capacity (FRC)

Questions 235–236

Use the following diagram to answer the questions.



235. What is the P_{50} of the oxyhemoglobin curve labeled A in the diagram?

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

236. Which of the following conditions is most likely to shift the above oxyhemoglobin curve from A to B?

- a. Increased temperature
- b. Exercise
- c. Acclimatization to high altitude
- d. Hyperventilation
- e. Metabolic acidosis

237. Which one of the following is higher at total lung capacity than it is at residual volume?

- a. Anatomical dead space
- b. Maximum static inspiratory pressure
- c. Lung compliance
- d. Airway resistance
- e. Alveolar pressure

238. Which one of the following components of a pulmonary function test will be closest to normal in a patient with restrictive lung disease?

- a. FEV_1
- b. MVV
- c. FVC
- d. FEV_1/FVC
- e. TLC

239. A man breathing room air at sea level has a P_{aCO_2} of 48 mmHg. His alveolar oxygen tension (P_{aO_2}) is

- a. 150 mmHg
- b. 110 mmHg
- c. 100 mmHg
- d. 90 mmHg
- e. 60 mmHg

240. A young skier with normal pulmonary function (minute volume 4 L; pulmonary blood flow 5 L/min) who is recovering from a tibial fracture suddenly develops right-sided chest pain and tachypnea. Embolic occlusion of the right pulmonary artery is suspected. Which of the following alveolar gas measurements would immediately confirm the diagnosis?

	PO_2 (mmHg)	P_{CO_2} (mmHg)
a.	125	60
b.	125	20
c.	100	40
d.	80	20
e.	80	60

241. Measurement of the lecithin-sphingomyelin (L-S) ratio in amniotic fluid assesses

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

242. When the respiratory muscles are relaxed, the lungs are at

- a. Residual volume (RV)
- b. Expiratory reserve volume (ERV)
- c. Functional residual capacity (FRC)
- d. Inspiratory reserve volume (IRV)
- e. Total lung capacity (TLC)

243. Which one of the following is the most likely cause of a high arterial PCO_2 ?

- a. Increased metabolic activity
- b. Increased alveolar dead space
- c. Depressed medullary respiratory centers
- d. Alveolar capillary block
- e. Increased alveolar ventilation

244. Because the small airways produce a small fraction of the airway resistance, their obstruction is difficult to detect. Which one of the following changes is indicative of small rather than large airway obstruction?

- a. An increase in maximum airflow during a forced expiration
- b. A decrease in the maximum expiratory pressure that can be generated
- c. An increase in the turbulent airflow produced during inspiration
- d. A decrease in the forced vital capacity
- e. An increase in the closing volume of the lung

245. Pulmonary vascular resistance decreases if

- a. The lungs are inflated to total lung capacity
- b. Sympathetic stimulation to the pulmonary vessels is increased
- c. Alveolar oxygen tension is decreased
- d. Plasma hydrogen ion concentration is decreased
- e. Cardiac output is increased

246. Which of the following would normally be less in the fetus than in the mother?

- a. PaCO_2
- b. Pulmonary vascular resistance
- c. Affinity of hemoglobin for oxygen
- d. PaO_2
- e. Arterial hydrogen ion concentration

247. An increase in the P_{50} of an oxyhemoglobin curve would result from a decrease in

- a. Metabolism
- b. pH
- c. Temperature
- d. Oxygen
- e. 2,3-DPG

248. During moderate aerobic exercise,

- a. PaO_2 increases
- b. $PaCO_2$ decreases
- c. Arterial pH decreases
- d. Alveolar ventilation increases
- e. Blood lactate level increases

249. Reduction of functional hemoglobin associated with anemia, methemoglobinemia, or carbon monoxide poisoning does not produce hyperpnea because the

- a. Blood flow to the carotid body is decreased
- b. Total arterial oxygen content is maintained within the normal range
- c. Carotid body chemoreceptors are stimulated
- d. Central chemoreceptors are stimulated
- e. PO_2 of arterial blood is normal

250. Pulmonary alveoli are kept dry by factors that include the

- a. Phagocytic activity of alveolar macrophages
- b. Negative interstitial fluid pressure
- c. Low vapor pressure of water in inspired air
- d. Secretion of surfactant
- e. Tight junctions between the alveolar capillary endothelial cells

251. In which one of the following conditions will the diffusing capacity of the lung increase?

- a. Formation of pulmonary emboli
- b. Fibrotic lung disease
- c. Polycythemia
- d. Congestive heart failure
- e. COPD

252. The percentage of hemoglobin saturated with oxygen will increase if

- a. The arterial PCO_2 is increased
- b. The hemoglobin concentration is increased
- c. The temperature is increased
- d. The arterial PO_2 is increased
- e. The arterial pH is decreased

253. Which of the following will return toward normal during acclimatization to high altitude?

- a. Arterial hydrogen ion concentration
- b. Arterial carbon dioxide tension
- c. Arterial bicarbonate ion concentration
- d. Arterial hemoglobin concentration
- e. Alveolar ventilation

254. Which one of the following statements characterizes pulmonary compliance?

- a. It decreases with advancing age
- b. It is inversely related to the elastic recoil properties of the lung
- c. It increases in patients with pulmonary edema
- d. It is equivalent to DP/DV
- e. It increases when there is a deficiency of surfactant

255. The activity of the central chemoreceptors is stimulated by

- a. An increase in the PCO_2 of blood flowing through the brain
- b. A decrease in the PO_2 of blood flowing through the brain
- c. A decrease in the oxygen content of blood flowing through the brain
- d. A decrease in the metabolic rate of the surrounding brain tissue
- e. An increase in the pH of the CSF

256. In an acclimatized person at high altitudes, oxygen delivery to the tissues may be adequate at rest because of

- a. An increase in hemoglobin concentration
- b. The presence of an acidosis
- c. A decrease in the number of tissue capillaries
- d. The presence of a normal arterial PO_2
- e. The presence of a lower-than-normal arterial PCO_2

257. Which of the following will increase as a result of stimulating parasympathetic nerves to the bronchial smooth muscle?

- a. Lung compliance
- b. Airway diameter
- c. Elastic work of breathing
- d. Resistive work of breathing
- e. Anatomic dead space

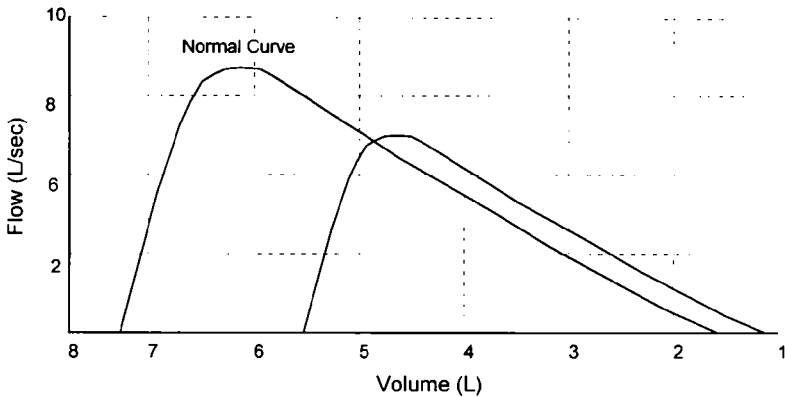
258. During a normal inspiration, more air goes to the alveoli at the base of the lung than to the alveoli at the apex of the lung because

- a. The alveoli at the base of the lung have more surfactant
- b. The alveoli at the base of the lung are more compliant
- c. The alveoli at the base of the lung have higher V/Q ratios
- d. There is a more negative intrapleural pressure at the base of the lung
- e. There is more blood flow to the base of the lung

259. A spirometer can be used to measure directly

- a. Functional residual capacity
- b. Inspiratory capacity
- c. Residual volume
- d. Total lung capacity
- e. Physiological dead space

260. Which of the following conditions is most likely to produce the change from the normal maximum flow-volume curve illustrated below?



- a. Asthma
- b. Emphysema
- c. Bronchiolitis
- d. Fibrosis
- e. Fatigue

261. The affinity of hemoglobin for oxygen is increased by

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

262. The oxygen consumption of the respiratory muscles is decreased by

- a. A decrease in lung compliance
- b. A decrease in airway resistance
- c. An increase in the rate of respiration
- d. A decrease in the production of pulmonary surfactant
- e. An increase in tidal volume

263. Which one of the following characteristics is the most similar between the pulmonary and skeletal muscle capillaries?

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

264. An increase in pulmonary blood flow during exercise

- a. Causes alveolar oxygen tension to decrease
- b. Causes the V/Q ratio at the top of the lung to increase
- c. Causes pulmonary arterial resistance to decrease
- d. Causes diffusion capacity to decrease
- e. Causes arterial oxygen saturation to decrease

265. Which one of the following will be greater than normal in a patient with a low V/Q ratio?

- a. P_{aCO_2}
- b. P_{aO_2}
- c. A-a gradient
- d. Oxygen dissolved in blood
- e. Oxygen combined with hemoglobin

266. Which one of the following contributes to the normal difference between the alveolar and arterial oxygen tension (A-a) gradient?

- a. The low PO_2 in the mixed venous blood
- b. The inability of pulmonary capillary blood to equilibrate with alveolar gas
- c. The low solubility of oxygen in blood
- d. The shape of the oxyhemoglobin saturation curve
- e. The high affinity of hemoglobin for oxygen in arterial blood

267. A patient with inadequate surfactant will have a relatively normal

- a. FEV_1
- b. FVC
- c. FEV_1/FVC
- d. MVV
- e. V/Q ratio

268. Enzymes within the lung are responsible for the activation of

- a. Angiotensin II
- b. Bradykinin
- c. Prostaglandins
- d. Serotonin
- e. Leukotrienes

269. When a person ascends to a high altitude, alveolar ventilation increases. Alveolar ventilation continues to increase over the next several days because

- a. The central chemoreceptors become more sensitive to low oxygen tensions
- b. The peripheral chemoreceptors increase their firing rate
- c. The plasma concentration of 2,3-DPG increases
- d. The pH of the cerebrospinal fluid decreases
- e. The oxygen-carrying capacity of hemoglobin increases

270. The clinical sign of cyanosis is caused by

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

271. Which one of the following gases diffuses across the alveoli-capillary membrane by a diffusion-limited transport process?

- a. Oxygen
- b. Nitrogen
- c. Carbon dioxide
- d. Carbon monoxide
- e. Nitrous oxide (N_2O)

272. Hyperventilation normally occurs during

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

273. A person ascends to the top of a mountain where the atmospheric pressure is below normal. Which one of the following blood gases was drawn from the person at the top of the mountain?

	PO_2	PCO_2
a.	50	30
b.	60	40
c.	80	50
d.	100	40
e.	120	30

274. Hyperventilation in response to a stressful situation leads to

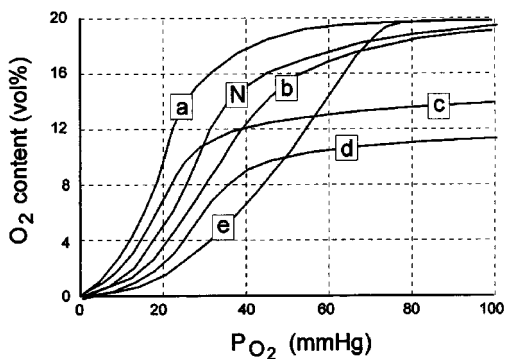
- a. A decrease in the blood flow to the brain
- b. An increase in the activity of the central chemoreceptors
- c. A decrease in pH of the arterial blood
- d. An increase in the resistance of the pulmonary blood vessels
- e. A decrease in the excitability of nerve and muscle cells

275. Patients with chronic lung disease are often divided into “blue bloaters” (those who are cyanotic) and “pink puffers” (those who are not cyanotic). The presence of cyanosis in blue bloaters but not in pink puffers results from difference in their

- a. V/Q ratios
- b. Vital capacities
- c. Airway resistances
- d. Total lung capacities
- e. Expiratory flow rates

Questions 276–277

Use the following diagram of oxyhemoglobin saturation curves to answer the next two questions.



276. Which one of the above oxyhemoglobin saturation curves was obtained from fetal blood?

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

277. Which one of the above oxyhemoglobin saturation curves was obtained from blood exposed to carbon monoxide?

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

Questions 278–279

Use the following data, obtained from a patient complaining of shortness of breath, to answer the following questions.

HR = 120 breaths/min

Blood pressure = 145/95

PaO₂ = 60 mmHg

H⁺ concentration = 25 nM

Respiratory rales

A tentative diagnosis of left heart failure is made.

278. Which one of the following values will be below normal?

- a. Left atrial pressure
- b. Pulmonary artery resistance
- c. Pulmonary artery pressure
- d. A-a gradient
- e. PaCO₂

279. Providing oxygen to this patient increased his PaO₂ to 90 mmHg. Which one of the following values will be decreased?

- a. H⁺ ion concentration
- b. Pulmonary artery resistance
- c. PaO₂
- d. PaCO₂
- e. A-a gradient

Questions 280–281

The following table shows several combinations of arterial blood-gas changes.

	pH	PaCO ₂	PaO ₂
a.	↑	↑	↑
b.	↓	↑	↑
c.	↑	↑	↓
d.	↓	↓	↑
e.	↑	↓	↓

280. Which one of the above changes in arterial blood gas values was obtained from a patient with a large intrapulmonary shunt?

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

281. Which one of the above changes in arterial blood gas values was obtained from a patient with metabolic acidosis?

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

282. A patient with reduced VC, FRC, and RV is found to have a normal pH. A tentative diagnosis of diffuse interstitial fibrosis is made. Which of the following characteristics are consistent with this disease?

- a. An increase in lung compliance
- b. A decrease in respiratory rate
- c. An increase in the V/Q ratio
- d. A decrease in PaCO₂
- e. An increase in the FEV₁/FVC ratio

283. Airway resistance is lowest

- a. During a forced expiration
- b. At the total lung capacity
- c. At the residual volume
- d. During vagal stimulation
- e. When breathing gas with low oxygen

Respiratory Physiology

Answers

204. The answer is c. (Guyton, pp 474–476.) The basic respiratory rhythm originates from spontaneous rhythmic discharge of inspiratory neurons located in the respiratory center in the dorsal medulla. This basic rhythm can be modified by many factors, including voluntary control of breathing. In the pons are the apneustic center and the pneumotaxic center (which is located in the nucleus parabrachialis). These modify and regularize the basic respiratory rhythm to produce adequate breathing.

205. The answer is c. (Guyton, pp 432–434.) During inspiration, the pressure in the alveoli becomes negative and gas is drawn into the lung by the difference in pressure between the alveoli and the atmosphere. At the peak of a normal inspiration, this pressure difference is only a few centimeters of water. At the end of inspiration, the pressure in the alveoli becomes equal to the atmospheric pressure, and flow ceases. During expiration, the intra-alveolar pressure rises above atmospheric pressure and gas is expelled from the lungs. The intra-alveolar pressure again equals atmospheric pressure at the end of expiration.

206–208. The answers are 206-c, 207-c, 208-e. (Guyton, pp 436–438.) *Functional residual capacity* (FRC) is the volume of gas in the lung at the end of a normal expiration when the muscles of inspiration and expiration are relaxed. At FRC, the elastic forces acting on the lungs are in equilibrium; that is, the tendency of the lungs to collapse is balanced by the tendency of the chest to expand. When the volume is at FRC, the spirometry trace reads 1 L. Therefore, FRC, which is 3 liters, less than total lung capacity (6 L) is 3 liters.

The FEV_1 is the amount of gas that can be expelled from the lungs in 1 s during a forced expiration from total lung capacity (TLC). Based on the spirometry tracing, FEV_1 equals 3.5 L. The FEV_1 is normally about 85% of VC, so the patient has a normal FEV_1 . The FEV_1 can be decreased by an obstructive disease such as asthma or emphysema. In a restrictive disease, the FEV_1 is also lower than normal, but the ratio of FEV_1 to VC is normal or slightly higher than normal.

The *inspiratory capacity* (IC) is the maximum amount of gas that can be inhaled when the subject starts from functional residual capacity (FRC). In this subject, the IC is 3 L. The maximum amount of gas that can be inhaled when the subject starts at the end of a normal inspiration is called the *inspiratory reserve volume* (IRV). In this subject, the IRV equals 2.5 L. The *expiratory reserve volume* (ERV) is the maximum amount of gas that can be exhaled when the subject starts from FRC. In this subject, the ERV equals 1 L.

209–211. The answers are 209-a, 210-c, 211-b. (*Rhoades, pp 350–356, 353–354.*) Alveolar ventilation V_A is equal to the fresh air entering the lung with each breath. The fresh air volume equals the tidal volume V_T minus the dead space volume V_D times the frequency of breathing f .

$$V_A = (V_T - V_D) \cdot f = (400 \text{ mL} - 10 \text{ mL}) \cdot 10 \text{ breaths/min} = 3 \text{ L/min}$$

The alveolar oxygen tension can be calculated from the simplified alveolar gas equation:

$$PaO_2 = PiO_2 - PCO_2/0.8 = 150 \text{ mmHg} - 48 \text{ mmHg}/0.08 = 90 \text{ mmHg}$$

$Paco_2$ is inversely proportional to alveolar ventilation:

$$Paco_2 \propto 1/V_A$$

If the patient in the question doubles his tidal volume, his alveolar ventilation ($V_T - V_D$) will increase from 3 L/min (see question 209) to

$$[(800 \text{ mL} - 100 \text{ mL}) \cdot 10 \text{ breaths/min}] = 7 \text{ L/min}$$

Therefore, his $Paco_2$ will decrease from 50 mmHg to 21 mmHg:

$$\begin{aligned} Paco_2 \cdot V_A &= \text{constant} \\ 50 \text{ mmHg} \cdot 3 \text{ L/min} &= Paco_2 \cdot 7 \text{ L/min} \\ Paco_2 &= 21 \text{ mmHg} \end{aligned}$$

212–213. The answers are 212-b, 213-d. (*Berne, 3/e, pp 311–312.*) Alveolar ventilation V_A is the amount of gas per minute that enters the res-

piratory exchange areas of the lung and is equal to the minute ventilation V_{\min} minus the dead space ventilation V_D :

$$V_A = V_{\min} - V_D$$
$$V_A \times (18 \cdot 350) - (18 \cdot 100) = 4500 \text{ mL} = 4.5 \text{ L}$$

Because all of the CO_2 eliminated ($\dot{V}\text{CO}_2$) enters the alveolar gas, the concentration of CO_2 in the alveoli (FACO_2) is equal to $\dot{V}\text{CO}_2/\dot{V}_A$. Assuming that the amount of CO_2 produced each minute does not change with changes in ventilation, then

$$\dot{V}\text{CO}_2 = \text{FACO}_2 \cdot V_A = 5\text{FACO}_2 \cdot V_A$$

or since PACO_2 is proportional to FACO_2

$$\text{PCO}_2 \cdot V_A = \text{PACO}_2 \cdot V_A$$

If her tidal volume increases from 350 mL to 425 mL, then her alveolar ventilation becomes $18 \cdot (425 - 100)$, or 5850 mL/min, and her VACO_2 decreases from a normal value of 40 mmHg to $\text{PACO}_2 (40 \cdot 4500) \div 850 = 30.8 \text{ mmHg}$.

214–215. The answers are 214-b, 215-c. (*Rhoades, pp 364–367.*) The *equal pressure point* is the point at which the pressure inside the airways equals the intrapleural pressure. If the equal pressure point occurs where the bronchioles can collapse, the airway will narrow and the maximum expiratory flow rate will be limited. The intra-airway pressure at the beginning of the airways (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). Therefore, the intra-airway pressure at the alveoli equals 40 cmH₂O (10 cmH₂O + 30 cmH₂O). Assuming that the intra-airway pressure is zero at the mouth and drops linearly from the alveoli to the mouth, the intra-airway pressure will be 30 cmH₂O one-fourth of the way down the airway, 20 cmH₂O one-half of the way down the airway, and 10 cmH₂O three-fourths of the way down the airway. Since the intrapleural pressure is 30 cmH₂O, the equal pressure point will be approximately one-fourth of the way down the airway (point B). 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 and makes their recoil force greater. This moves the equal pressure point toward the mouth. If airway resistance increases, for example, by increasing airway smooth muscle tone, then a greater expiratory effort and consequently a greater intrapleural pressure will be necessary to expel the gas from the lungs.

216. The answer is d. (*Rhoades, pp 356–359, 362–366.*) An increased resistance to airflow, which makes it more difficult to expel gas from the lung during expiration, characterizes obstructive lung disease. As a result, the amount of gas in the lung at the end of each expiration, the functional residual capacity (FRC), increases. The increased airway resistance limits the rate at which gas can be expired, and so maximum breathing capacity, FEV_1 , and breathing frequency all decrease. Vital capacity usually decreases because of gas trapping. In restrictive disease, the decreased lung compliance causes vital capacity (VC) and FRC to decrease. The decreased compliance also reduces the amount of air that can be inhaled with each breath, so maximum breathing capacity decreases. Because less air is in the lungs, the amount of air that can be expelled in 1 s decreases and, therefore, FEV_1 decreases. At the same time, breathing frequency has to increase to compensate for the decreased tidal volume.

217. The answer is a. (*Berne, 3/e, pp 317–321.*) During the early stages of an asthmatic attack, the increased airway resistance makes it difficult to inhale and exhale rapidly, and therefore each breath is slower and deeper. However, the accompanying dyspnea usually increases alveolar ventilation, and, as a result, P_{aCO_2} decreases. Arterial oxygen tension usually decreases, despite normal alveolar oxygen levels, because of the increased V/Q mismatch that accompanies asthma. This hypoxia may also cause alveolar ventilation to increase. The equal pressure point moves toward the lung because of the increased respiratory effort. Acute asthmatic attacks do not produce any direct change in lung compliance. However, air trapping will cause functional residual capacity (FRC) to increase, and the larger lung volumes will lead to a decrease in lung compliance.

218. The answer is c. (*Guyton, pp 460–461.*) V/Q mismatches will cause arterial oxygen levels (P_{aO_2}) to decrease. Decreased P_{aO_2} will stimulate the peripheral chemoreceptors, which, in turn, will increase alveolar ventila-

tion and decrease PaCO_2 . The decreased PaCO_2 will cause a respiratory alkalosis (increasing pH). Hypoxemia will also cause lactate levels to rise, increasing the anion gap (and blunting the rise in pH). The fall in PaO_2 causes the A-a gradient to rise.

219. The answer is a. (*Rhoades, pp 379–383.*) 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 PaO_2 higher at the apex than they are at the base.

220. The answer is b. (*Rhoades, pp 379–383, 395–398.*) Proper gas exchange requires an appropriate matching of ventilation and blood flow referred to as the \dot{V}/\dot{Q} ratio. If perfusion (\dot{Q}) exceeds ventilation (\dot{V}), the amount of oxygen diffusing into the capillary blood and the amount of carbon dioxide diffusing out of the capillary blood are reduced. The result is a lower than normal PO_2 and a higher than normal CO_2 . The lower PO_2 will cause vascular resistance to rise above normal.

221. The answer is d. (*Guyton, pp 440–442.*) The lung has a variety of mechanisms to remove particulate matter from the inspired gas. Large particles become deposited in the mucus layer that lies within the bronchi. The mucus is swept up and out of the bronchioles by the ciliated epithelial cells that line the bronchioles. Smaller particles remain suspended in the inspired gas and reach the alveoli. Alveolar macrophages remove these particles by phagocytosis. The macrophages are usually removed from the lung through the lymphatic or blood circulation. Cigarette smoking can prevent cilia from beating, reduce macrophage migration, and thus impair the ability of the lungs to remove potentially harmful particles inhaled from the atmosphere.

222. The answer is b. (*Rhoades, pp 391–398.*) A rise or fall in the oxygen saturation of hemoglobin is caused by a decrease in the arterial O_2 tension, which can result from a low \dot{V}/\dot{Q} ratio, hypoventilation, or an anatomical

right-to-left shunt. Because carbon monoxide (CO) competes with O₂ on the hemoglobin molecule, CO poisoning can cause a decrease in hemoglobin's saturation even when the PO₂ is normal. In anemia, oxygen saturation is unchanged but the concentration of hemoglobin is less than normal, reducing the oxygen content.

223. The answer is d. (*Guyton, pp 470–472.*) CO₂ is transported in arterial blood in three forms: as physically dissolved CO₂ (about 5%), in combination with the amino groups of hemoglobin as carbaminohemoglobin (about 5%), and as bicarbonate ion HCO₃[−] (about 90%). The amount of CO₂ actually carried as carbonic acid, H₂CO₃, is negligible. Carboxyhemoglobin refers to the combination of carbon monoxide (CO) and hemoglobin.

224. The answer is c. (*Guyton, p 452.*) The partial pressure of a gas mixture is proportional to its concentration in the mixture, and the sum of the partial pressures is equal to the total pressure of the gas. Because the inhaled gas is saturated with water by the respiratory system and oxygen is 21% of dry gas, the partial pressure of oxygen is

$$0.21 \times [(4 \times 760) - 47] = 629 \text{ mmHg}$$

The water vapor pressure is 47 mmHg at body temperature regardless of the ambient barometric pressure.

225–227. The answers are 225-c, 226-e, 227-c. (*Rhoades, pp 350–355.*) The physiological dead space can be calculated using the Bohr equation:

$$\begin{aligned} V_D &= V_T \cdot [\text{PaCO}_2 - \text{Peco}_2] \div \text{PaCO}_2 \\ &= 500 \text{ mL} \times [50 \text{ mmHg} - 40 \text{ mmHg}] \div 50 \text{ mmHg} = 100 \text{ mL} \end{aligned}$$

The physiological dead space includes the anatomical dead space (the conducting airways) and the areas of the lung that are ventilated but not perfused or poorly perfused, that is, the areas of the lung with a high V/Q ratio. Typically, the areas of the lung with a high V/Q ratio are balanced by areas of the lung with a low V/Q ratio, and, consequently, the physiological and

anatomical dead spaces are equal. The alveolar ventilation is the fresh gas entering the lung each minute:

$$(V_T - V_D) \times f = (500 \text{ mL} - 100 \text{ mL}) \times 15 \text{ breaths/min} = 6000 \text{ mL/min}$$

PaCO_2 is inversely proportional to alveolar ventilation:

$$\text{PaCO}_2 \propto 1/V_A$$

Therefore, the PaCO_2 can be decreased from the current value of 50 mmHg to the normal value of 40 mmHg by increasing the alveolar ventilation. The alveolar ventilation required to return the PaCO_2 to normal can be calculated by setting the current value of $\text{PaCO}_2 \times V_A$ ($40 \text{ mmHg} \times 6 \text{ L/min}$) equal to the desired value of $\text{PaCO}_2 \times V_A$ ($50 \text{ mmHg} \times V_A$) and solving for V_A .

$$(40 \text{ mmHg} \times 6 \text{ L/min}) \div 40 \text{ mmHg} = 7.5 \text{ L/min}$$

228. The answer is a. (*Rhoades, pp 350–353.*) The alveolar PCO_2 rises and falls with each breath. As CO_2 diffuses into the alveoli from the blood, the alveolar PCO_2 rises. The PCO_2 falls when fresh air is added to the alveolar gas. The highest PCO_2 occurs just before fresh air is inhaled. The first gas entering the alveoli during inspiration is actually alveolar gas because the conducting airways are filled with alveolar gas at the end of expiration. Fresh air doesn't enter the alveoli until the alveolar gas has been emptied from the dead space. In normal tidal breathing, dead space volume is approximately 30% of tidal volume. Therefore, the alveolar PCO_2 continues to rise for the first one-third of each breath and reaches its highest value at the point labeled A.

229. The answer is c. (*Rhoades, pp 406–411.*) The central chemoreceptors located on or near the ventral surface of the medulla cause an increase in ventilation in response to an increase in PaCO_2 and to a lesser extent to a decrease in arterial pH because the blood-brain barrier is relatively impermeable to hydrogen ions. The peripheral chemoreceptors in the carotid bodies cause an increase in ventilation in response to an increase in PaCO_2 , a decrease in arterial pH, and a decrease in PaO_2 . Neither the central chemoreceptors nor the carotid bodies are stimulated by a decrease in arterial blood pressure or O_2 content.

230. The answer is b. (*Guyton, pp 475–476.*) Transection of the brainstem above the pons would prevent any voluntary changes in ventilation by cutting the pathways from the higher centers. Breathing would continue because the pontine-medullary centers that control rhythmic ventilation would be intact. Inputs to the brainstem from the central and peripheral chemoreceptors that stimulate ventilation and from lung stretch receptors that inhibit inspiration (Hering-Breuer reflex) would also be intact and these reflexes would be maintained.

231–232. The answers are 231-b, 232-c. (*Rhoades, pp 367–368.*) During inspiration (curve ABC), the respiratory muscles pull the chest wall out and diaphragm down and intrapleural pressure (P_{IP}) becomes more negative. The muscles must overcome the elastic recoil forces of the lungs and the resistance of the airways to airflow. The P_{IP} necessary to overcome the elastic forces of the lung is depicted by dashed line AC. The P_{IP} necessary to overcome the airway resistance is the difference between dashed line AC and curve ABC. The maximum airflow occurs at point B, where the difference between the two is the greatest. Lung volume is the greatest at point C, where P_{IP} is the most negative.

233. The answer is c. (*Berne, 3/e, pp 319–320.*) The initial expiratory flow is effort-dependent. That is, increasing expiratory effort will increase expiratory flow. The remainder of the expiratory flow is effort-independent; once maximum flow rates are achieved, increasing effort will not produce an increased flow rate. The inability to increase flow rates is caused by airway compression. The pressure within the airways decreases from the lungs to the mouth. The pressure outside the airways, at any given lung volume, is the same throughout the thoracic cavity. Somewhere along the airways, an equal pressure point is reached at which the pressure inside and outside the airways is the same. If this point occurs at a region of the airways where compression can occur, it will limit the maximum flow. Increasing effort increases compression so that increased airway resistance counteracts the increased effort and no increase in flow occurs. This limitation of flow due to compression is referred to as the *effort-independent* portion of the flow-volume curve. It characterizes all but the initial portion of expiration. No effort limitation occurs during inspiration because increased expiratory efforts make the intrathoracic cavity more negative, which expands the airways, lowering their resistance.

234. The answer is c. (*Rhoades, pp 479–481.*) Because of the inherent elasticity of the lung, the alveoli tend to collapse during expiration. This tendency is explained by Laplace's law, which relates the radius (r) and surface tension (T) of an elastic bubble to the pressure (P) required to distend it ($P = 2T/r$). If T is constant, the pressure required to distend alveoli would increase markedly during expiration as the radius decreased. This does not occur in normal lungs because the unique properties of surfactant cause surface tension to decrease as lung volume decreases. Thus, surfactant prevents alveolar collapse at end-expiratory intra-alveolar pressures that otherwise would lead to atelectasis. A deficiency of surfactant would increase surface tension, tending to collapse the lungs and decrease FRC. It would be more difficult to expand the lungs. Lung compliance would decrease, and thus a greater change in intrapleural pressure and greater work to maintain ventilation would be required.

235–236. The answers are 235-b, 236-d. (*Rhoades, pp 391–394.*) The P_{50} of the oxyhemoglobin curve is the oxygen tension at which half of the hemoglobin is saturated with oxygen. When fully saturated, the hemoglobin represented by curve A has an oxygen content of 20 mL/dL. Therefore, the P_{50} is the PO_2 at which the hemoglobin contains one-half of 20 mL/dL (10 mL/dL), which is 30 mmHg.

The oxyhemoglobin curve shifts to the left when pH is increased. Hyperventilation will decrease PCO_2 and cause an increase in pH. Increased temperature, decreased pH, and increased concentration of 2,3-DPG can shift the oxyhemoglobin dissociation curve to the right. Exercise will cause the temperature of the working muscles to increase and right-shift the oxyhemoglobin dissociation curve of the blood flowing through the working muscles. When a person remains at altitude for several days, the 2,3-DPG concentrations increase as part of the acclimatization process.

237. The answer is a. (*Berne, 3/e, pp 315–321.*) Expanding the lungs lowers the intrathoracic pressure, which causes the airways to expand. Expanding the airways increases their volume and, therefore, the volume of the anatomical dead space. Expanding the airways also causes a decrease in airway resistance. Maximum static inspiratory pressure is maximal at function residual volume and decreases as lung volume is increased. Lung compliance is decreased; that is, the lungs are stiffer at high lung volumes. Alveolar pressure is atmospheric at residual volume and at total lung capacity.

238. The answer is b. (*Rhoades, pp 352–355.*) The volume of the physiologic dead space (V_D) can be calculated using the Bohr equation:

$$V_D = [(F_{aCO_2} - F_{eCO_2})/F_{aCO_2}] \cdot V_T$$

V_T is tidal volume, F_{aCO_2} is the fraction of CO_2 in alveolar gas, and F_{eCO_2} is the fraction of CO_2 in mixed expired gas. F_{aCO_2} can be approximated using the F_{CO_2} from a sample of end-expiratory gas or by sampling P_{aCO_2} . In normal lungs, physiologic dead space equals anatomic dead space. In diseased lungs, physiologic dead space often exceeds anatomic dead space because of abnormalities of ventilation and blood flow.

239. The answer is d. (*Rhoades, pp 355–356.*) In patients, it is useful to calculate the alveolar oxygen tension (P_{aO_2}) in order to assess the alveolar-arterial oxygen gradient. P_{aO_2} can be calculated using the alveolar gas equation:

$$P_{aO_2} = P_{iO_2} - P_{aCO_2} [F_{iO_2} + (1 - F_{iO_2})/R]$$

This equation can be greatly simplified without sacrificing a great deal of accuracy. The modified alveolar gas equation is

$$P_{aO_2} = P_{iO_2} - (P_{aCO_2}/R)$$

P_{aCO_2} is equivalent to P_{aCO_2} , R is the respiratory exchange ratio (V_{CO_2}/V_{O_2}), which depends on the diet and is normally 0.8. P_{iO_2} equals the fraction of oxygen in room air (0.21) times the barometric pressure at sea level (760 mmHg) minus the water vapor pressure (47 mmHg) of saturated tracheal gas at body temperature (37°C).

$$\begin{aligned} P_{aO_2} &= 0.21 (760 \text{ mmHg} - 47 \text{ mmHg}) - (48 \text{ mmHg}/0.8) \\ &= 150 \text{ mmHg} - 60 \text{ mmHg} \\ &= 90 \text{ mmHg} \end{aligned}$$

240. The answer is b. (*Rhoades, pp 380–383, 395–398.*) Under normal conditions, the V/Q ratio in both lungs is the same, so that mixed alveolar gas in both lungs has the same PO_2 and PCO_2 . The gas from the normal lung

will be approximately normal ($PO_2 = 100$ mmHg, $PCO_2 = 40$ mmHg). While the gas from the occluded lung, which now represents alveolar dead space, will resemble tracheal gas ($PO_2 = 150$ mmHg, $PCO_2 = 0$ mmHg). When the gas from the two lungs mixes, the average alveolar O_2 becomes 125 mmHg and the average PCO_2 becomes 20 mmHg.

241. The answer is e. (*Rhoades, pp 359–362.*) Lecithin (phosphatidylcholine) and sphingomyelin are choline phospholipids found in a variety of tissues. Lecithin is a major component of surfactant and its synthesis increases as the fetus matures and the lungs are prepared for expansion. Surfactant, a lipoprotein mixture, prevents alveolar collapse by permitting the surface tension of the alveolar lining to vary during inspiration and expiration. Thus, measurement of the lecithin-sphingomyelin (L-S) ratio in amniotic fluid provides an index of fetal lung maturity.

242. The answer is c. (*Guyton, pp 436–438.*) The lungs tend to recoil inward, whereas the chest wall tends to recoil outward. When the respiratory muscles are all relaxed, these two opposing forces are balanced. The volume of gas in the lungs at this point is the relaxation volume, or functional residual capacity (FRC).

243. The answer is c. (*Guyton, pp 476–479.*) A high arterial PCO_2 is most likely caused by depressed medullary respiratory centers. Depression of these centers decreases alveolar ventilation and results in hypoventilation with an increased $Paco_2$ and decreased PaO_2 . This depression can be caused by drugs such as barbiturates or narcotics. Slight depression also occurs during sleep. If metabolic activity increases, as during mild exercise, alveolar ventilation increases in parallel and $Paco_2$ does not change. Retention of CO_2 could result from alveolar capillary block, but it would have to be extremely severe because CO_2 is so soluble in tissue.

244. The answer is e. (*Rhoades, pp 342–343, 362–364.*) Although it may seem paradoxical, about 80% of the total resistance to airflow occurs in the large- and medium-sized airways. Turbulent flow, which increases the pressure necessary to cause gas to flow, is more likely to occur in larger airways. In patients, an increased resistance to airflow usually indicates the presence of disease of the large airways.

245. The answer is e. (*Rhoades, pp 374–376.*) Pulmonary vascular resistance is affected by cardiac output, pulmonary artery pressure, lung volume, and O_2 tension. Increasing cardiac output or pulmonary artery pressure causes the pulmonary vasculature to expand, thereby decreasing PVR. At high lung volumes, intrapulmonary blood vessels are stretched and compressed, increasing PVR. At low lung volumes, extrapulmonary blood vessels are compressed, increasing PVR. The lowest PVR occurs near FRC. Decreasing PO_2 or increasing PCO_2 or H^+ concentration causes PVR to rise. The sympathetic nervous system has little direct effect on PVR.

246. The answer is d. (*Guyton, pp 946–947.*) Because fetal hemoglobin (hemoglobin F) is chemically different from adult hemoglobin in that it has two α and two γ chains instead of two α and two β chains, it has a greater affinity for oxygen. This is advantageous in the placental exchange of O_2 from maternal blood ($PaO_2 = 100$ mmHg) to fetal blood ($PaO_2 = 25$ mmHg). $Paco_2$ is about 2 to 3 mmHg higher in the fetus than in the mother. Arterial H^+ concentration is about the same in both. Pulmonary vascular resistance is high in the fetus, shunting blood away from the lungs. It decreases at birth and remains low.

247. The answer is b. (*Rhoades, pp 391–394.*) The P_{50} indicates the affinity of hemoglobin for O_2 . A decrease in affinity results in an increase in the P_{50} . Hemoglobin's affinity for O_2 is decreased by a decrease in pH (an increase in H^+ concentration), an increase in temperature, and an increase in 2,3-DPG concentrations.

248. The answer is d. (*Berne, 3/e, pp 289–293.*) During moderate aerobic exercise, oxygen consumption and CO_2 production increase, but alveolar ventilation increases in parallel. Thus, PaO_2 and $Paco_2$ do not change. Arterial pH does not decrease and blood lactate concentration does not increase during moderate aerobic exercise, but arterial pH does decrease and blood lactate concentration does increase during anaerobic exercise because of increased production of lactic acid.

249. The answer is e. (*Rhoades, pp 409–411.*) The reduction in functional hemoglobin that occurs in anemia, methemoglobinemia, or carboxyhemoglobinemia lessens the total oxygen content (dissolved O_2 +

Hb O₂) in the blood but not the oxygen tension (PO₂). The chemoreceptors of the carotid body are sensitive to the PO₂ of arterial blood, not to its content. Central chemoreceptors are stimulated by decreases in the pH of brain extracellular fluid. They do not respond to changes in PO₂.

250. The answer is b. (*Rhoades, pp 376–379.*) The forces tending to remove fluid from the alveoli are the negative interstitial fluid pressure and the osmotic pressure exerted at the alveolar membrane by ions and crystalloid molecules in the interstitial fluid. Fluid movement into pulmonary capillaries, however, is a function of plasma oncotic pressure. The pulmonary capillaries are actually more permeable than those in the systemic circulation; that is, they have a higher hydraulic conductivity. Alveolar phagocytes do not take up significant amounts of water, and very little water from the alveoli goes into inspired air because the air is well humidified by the upper airways. Surfactant lowers the surface tension in the alveoli but does not affect fluid movement.

251. The answer is c. (*Guyton, pp 458–460.*) In the tissues, the diffusing capacity is the volume of gas transported across the lung per minute per mmHg partial pressure difference. It is determined by the surface area and the thickness of the alveolar-capillary interface. Increases in the diffusing capacity can be produced by opening pulmonary capillaries, expanding the surface area of the pulmonary capillaries, optimizing the V/Q ratio within the lung, or by increasing the concentration of hemoglobin within the blood (polycythemia). It can be decreased by mismatching of ventilation and perfusion, pulmonary edema, or pulmonary emboli, all of which interfere with gas diffusion.

252. The answer is d. (*Guyton, pp 466–469.*) The percentage of hemoglobin saturated with oxygen depends on the level of PO₂ in the blood and on other factors that affect the position of the oxyhemoglobin dissociation curve. Factors that shift the curve to the left, such as a decrease in PCO₂, an increase in pH, or a decrease in temperature, would increase the percentage of hemoglobin saturated with oxygen as would an increase in PO₂, provided that the percentage of saturation was not already at 100%. At a given PO₂, increasing the concentration of hemoglobin would not affect the percentage of saturation but would increase the oxygen content of the blood.

253. The answer is a. (*Guyton, pp 497–501.*) At high altitude, the barometric pressure is reduced, resulting in a decrease in P_{iO_2} , which decreases both alveolar and arterial PO_2 . If PaO_2 is less than 60 mmHg, the carotid bodies are stimulated and cause hyperventilation, which increases alveolar ventilation and decreases $Paco_2$ with a resultant respiratory alkalosis. During acclimatization, PaO_2 remains low, ventilation remains high, and therefore $Paco_2$ remains low. The kidneys act to lower plasma bicarbonate and return arterial pH toward normal. The oxygen content of arterial blood increases owing to an increase in hematocrit stimulated by the increased production of erythropoietin in the kidney.

254. The answer is b. (*Rhoades, pp 356–362.*) *Pulmonary compliance*, defined as the ratio of change of lung volume to the change in pressure required to inflate the lung ($\Delta V/\Delta P$), is an index of lung distensibility. It decreases in patients with pulmonary edema and interstitial fibrosis and increases in patients with emphysema and in persons of advancing years. The stiffer the lung, the lower the pulmonary compliance. Surfactant lowers the surface tension in the alveoli and makes the lung more distensible.

255. The answer is a. (*Guyton, pp 476–479.*) The central chemoreceptors are located at or near the ventral surface of the medulla. They are stimulated to increase ventilation by a decrease in the pH of their extracellular fluid (ECF). The pH of this ECF is affected by the PCO_2 of the blood supply to the medullary chemoreceptor area as well as by the CO_2 and lactic acid production of the surrounding brain tissue. The central chemoreceptors are not stimulated by decreases in PaO_2 or blood oxygen content but rather can be depressed by long-term or severe decreases in oxygen supply.

256. The answer is a. (*Guyton, pp 497–501.*) At a high altitude, arterial PO_2 is low because of the low barometric pressure. Ventilation increases owing to stimulation of the carotid body chemoreceptors, and PaO_2 increases somewhat, although it does not return to a normal, sea-level value. Hyperventilation causes a decrease in $Paco_2$, resulting in a respiratory alkalosis that may become fully compensated with time via renal mechanisms. A lower-than-normal $Paco_2$ would shift the oxyhemoglobin dissociation curve to the left, thereby increasing the affinity of hemoglobin for oxygen. Chronic hypoxia at high altitudes or in disease states stimulates the increased release of erythropoietin from the kidneys, which increases

the hematocrit and thereby increases the hemoglobin concentration of the blood. Thus, at the same lowered P_{aO_2} , the oxygen content of blood and oxygen delivery to tissues increase. Chronic hypoxia also stimulates increased capillary growth in tissues.

257. The answer is d. (*Guyton, pp 440–441.*) The tone of bronchial smooth muscle is under autonomic control. Stimulation of sympathetic nerves causes bronchodilation, whereas parasympathetic stimulation via the vagus nerve causes bronchoconstriction. Bronchoconstriction reduces the radius of the airways and thereby decreases anatomic dead space and increases airway resistance, which consequently increases the resistive work of breathing. Bronchoconstriction has no significant effect on the elastic properties of the lung.

258. The answer is b. (*Rhoades, pp 379–383.*) There is a negative, or sub-atmospheric, intrapleural pressure (P_{IP}) between the lungs and the chest wall due to the tendency of the chest wall to pull outward and the tendency of the lungs to collapse. Because the lungs are essentially “hanging” in the chest, the force of gravity on the lungs causes the P_{IP} to be more negative at the top of the lung. This also causes the alveoli at the apex (top) of the lung to be larger than those at the base (bottom) of the lung. Larger alveoli are already more inflated and are less compliant than smaller alveoli. During inspiration, when all alveoli are subjected to essentially the same alveolar pressure, more air will go to the more compliant alveoli. Because of the effect of gravity on blood, more blood flow will go to the base of the lung. This does not appreciably affect lung compliance. Ventilation is about three times greater at the base of the lung, but flow is about 10 times greater at the base than at the apex of the lung. Therefore, the \dot{V}/\dot{Q} ratio is lower at the base than at the apex in a normal lung.

259. The answer is b. (*Rhoades, pp 349–353.*) A *spirometer* is an instrument that records the volume of air moved into and out of the lungs during respiration and therefore can only be used to measure changes in lung volumes. It cannot be used to measure absolute lung volumes. The *inspiratory capacity* is the maximal amount of gas that can be inhaled when the lung volume is at its functional residual capacity (FRC). Therefore, changes in lung volume can be measured by spirometry, as can tidal volume, expiratory reserve volume, and vital capacity. The absolute lung volumes, residual volume, functional residual capacity, and total lung capacity cannot be

measured directly by spirometry. Although the anatomical dead space can be estimated directly from spirometry if the subject breathes in a breath of pure oxygen, the physiological dead space, which is the combination of anatomical and alveolar dead spaces, can only be measured indirectly using a spirometer.

260. The answer is d. (*Rhoades, pp 364–367. Berne, 3/e, pp 319–320.*)

The maximum flow-volume curve represents the greatest flow that can be produced at each volume during expiration. Muscular effort, lung recoil, and airway resistance affect the expiratory flow rate. Lung compliance decreases in fibrosis. The low lung compliance increases the recoil force at any given lung volume, and, therefore, the maximum flow rate at any given lung volume is higher than normal. Maximum flows are decreased in asthma and bronchiolitis because airway resistance has increased, in emphysema and bronchiolitis because lung recoil force has decreased, and in fatigue because muscular effort has decreased.

261. The answer is e. (*Rhoades, pp 391–394.*)

Hemoglobin's O_2 affinity is increased by carbon monoxide. In carbon monoxide poisoning, carbon monoxide not only displaces O_2 from hemoglobin, it also makes it more difficult for the O_2 that is bound to hemoglobin (Hb) to dissociate from it in the tissues. Increasing H^+ ion concentration (decreasing pH) by metabolic acidosis or respiratory acidosis (decreased alveolar ventilation) decreases the affinity of hemoglobin for O_2 . Exercise decreases the affinity of Hb for O_2 by increasing the temperature of the exercising muscles. Anemia has no direct effect on Hb affinity for oxygen, but if it results in tissue hypoxemia, it will cause an increase in 2,3-DPG, which decreases the affinity of Hb for O_2 .

262. The answer is b. (*Rhoades, pp 367–368.*)

Respiratory muscles consume oxygen in proportion to the work of breathing, which can be divided into resistance work and elastic work. Resistance work includes work to overcome tissue as well as airway resistance. A decrease in the amount of pulmonary surfactant would decrease lung compliance and increase the elastic work of breathing. An increase in respiratory rate increases the work of breathing.

263. The answer is c. (*Guyton, pp 166–170, 448–450.*)

Blood flows in series through the systemic and pulmonary circulations, and, therefore, blood perfusing the skeletal muscles has the same oncotic pressure as the

blood flowing through the pulmonary circulation. However, the blood pressure is much lower in the pulmonary circulation than in the systemic circulation, and because the thoracic cavity has a negative pressure, the interstitial fluid pressure is more negative in the pulmonary circulation than in the systemic circulation. The pulmonary capillaries are more permeable to proteins than the skeletal muscle capillaries, and, therefore, the interstitial concentration of protein is greater in the pulmonary circulation.

264. The answer is c. (*Guyton, pp 446–448.*) The increase in blood flow through the pulmonary circulation during exercise increases the diameter of the pulmonary vessels and therefore decreases their resistance. The decrease in resistance can occur because the pulmonary vessels are very compliant and are large enough to prevent an increase in pulmonary artery blood pressure when cardiac output increases. The increased blood flow to the lung evens out the V/Q ratio, decreasing it at the top of the lung and increasing it at the bottom. Making the V/Q ratio more similar throughout the lung may decrease some of the shunting effect that normally occurs at the base of the lung where the V/Q ratio is quite low and may actually increase the oxygen saturation of arterial blood. The increased blood flow will also increase the surface area for respiratory exchange and therefore increase the diffusing capacity.

265. The answer is c. (*Rhoades, pp 380–383, 395–398.*) Capillary blood draining from areas of the lung with low V/Q ratios has low oxygen saturations. Capillary blood draining from areas of the lung with high V/Q ratios does not have oxygen saturations higher than normal because, under normal circumstances, the blood is fully saturated. When blood from areas of low V/Q ratios (with less than normal saturations) combines with blood from high V/Q ratios (with no more than normal saturations), the saturation of the combined blood is less than normal. The low saturation of the blood causes the PO_2 of the arterial blood to be lower than normal. In the lungs, the alveolar oxygen tension is higher in areas of high V/Q ratio and lower in areas of low V/Q ratio. When the air from the two regions combines, it produces a normal PO_2 . Because the alveolar PO_2 is normal and the arterial PO_2 is less than normal, the A-a gradient is greater than normal.

266. The answer is d. (*Rhoades, pp 379–383.*) In a normal person, there is an A-a gradient for O_2 of about 4 to 10 mmHg. The V/Q ratios at the apices of the lungs are greater than at the bases of the lungs; this results in end-pulmonary capillary blood coming from the apices with higher PO_2

and from the bases with lower PO_2 than normal. The PO_2 of the mixed blood from these areas must be determined by the average of their O_2 contents. Because of the nonlinearity of the oxyhemoglobin dissociation curve, the resultant PaO_2 is not the average of the end-pulmonary capillary PO_2 values. In addition, about 2 to 5% of the blood returning to the left heart—that is, blood from the bronchial veins and from the thebesian veins draining the left ventricle—is venous blood that has not been oxygenated and constitutes a right-to-left absolute shunt. Normally, levels of alveolar and end-pulmonary capillary blood PO_2 do come into equilibrium. If they do not, as in some disease states, this alveolar-capillary block would contribute to the A-a gradient for O_2 .

267. The answer is c. (*Rhoades, pp 359–362.*) Surfactant acts to diminish the surface tension of the lung. In the absence of surfactant, the lungs are more difficult to expand. Patients with a restrictive lung disease cannot expand their lungs as easily as normal, and, therefore, their total lung capacity is lower than normal. Because they have a lower total lung volume, the amount of gas they can exhale in 1 s (the FEV_1) is less than normal. Similarly, their forced vital capacity (FVC) is lower than normal. However, because they have a greater than normal recoil force, they can exhale a normal or even fraction of their TLC in 1 s. Therefore, their FEV_1/FVC is normal or even slightly higher than normal. The greater recoil reduces the amount of gas they can inhale with each breath so their maximum voluntary ventilation (MVV) is less than normal.

268. The answer is a. (*Rhoades, pp 359–361, 372.*) The lung has many metabolic functions, including synthesis of surfactant and prostaglandins and withdrawal of prostaglandins and bradykinin from the circulation. Other metabolic functions include activation of angiotensin I to angiotensin II, release of histamine, and inactivation of serotonin. Prostaglandins E and F both are synthesized and removed from the circulation by the lungs.

269. The answer is d. (*Guyton, pp 496–500.*) Hyperventilation occurs as soon as a person is exposed to low atmospheric pressures at high altitudes. The rise in pH attenuates the chemoreceptor response to low oxygen tensions. When the pH of the cerebrospinal fluid returns to normal, the chemoreceptors are restored to their normal responsiveness, and they are able to produce an even greater increase in ventilation. The plasma con-

centration of 2,3-DPG and, therefore, the oxygen-carrying capacity of hemoglobin increase with prolonged exposure to high altitudes. These changes increase the ability of the cardiovascular system to deliver oxygen to the tissues.

270. The answer is e. (*Guyton, pp 390–391, 491.*) Cyanosis is the blue color of the skin produced by desaturated hemoglobin. Cyanosis appears when 5 g of hemoglobin per 100 mL of blood are desaturated. For a person with a normal hemoglobin concentration of 15 g/100 mL, cyanosis appears when one-third of the blood is desaturated. For a person with polycythemia (a higher than normal concentration of hemoglobin), cyanosis may appear when only one-fourth of the hemoglobin is desaturated. This individual may not be hypoxic because of the high concentration of saturated hemoglobin. On the other hand, a person with anemia (a lower than normal concentration of hemoglobin) may have a significant portion of the hemoglobin desaturated without displaying cyanosis. This individual will not appear cyanotic but may be hypoxic.

271. The answer is d. (*Rhoades, pp 387–390.*) A diffusion-limited transport process is one in which the alveolar gas does not reach equilibrium with the end-pulmonary capillary blood. When diffusional equilibrium does not occur, the amount of gas transferred is proportional to the concentration gradient and the permeability of the gas to the alveolar-capillary interface. Carbon monoxide (CO) is transported by a diffusion-limited process because it is avidly bound to hemoglobin. So much CO binds to hemoglobin that the partial pressure of CO in the capillary blood remains near zero. As a result, the concentration gradient from alveolar gas to capillary blood remains constant and the amount of CO diffusing across the alveolar capillary interface depends only on the permeability of the gas. In contrast, all of the other gases reach equilibrium with the capillary blood, and, therefore, the amount of those gases that diffuses across the alveolar capillary membrane is dependent on the amount of blood passing through the pulmonary capillaries. This type of transport process is described as *perfusion-limited*.

272. The answer is a. (*Berne, 3/e, p 312.*) Hyperventilation occurs when the rate of alveolar ventilation reduces the arterial PCO_2 below 40 mmHg. Pregnancy produces hyperventilation because progesterone stimulates the

brain stem respiratory centers to increase alveolar ventilation above that required to maintain arterial PCO_2 at 40 mmHg. Sleep and morphine depress the respiratory centers and, therefore, produce hypoventilation (an arterial PCO_2 below 40 mmHg). During exercise, ventilation increases in parallel with carbon dioxide production so that the arterial PCO_2 remains at 40 mmHg. Metabolic alkalosis causes a small decrease in alveolar ventilation, producing a compensatory respiratory acidosis.

273. The answer is a. (*Guyton, pp 496–500.*) Breathing air with a low partial pressure of oxygen will stimulate the peripheral chemoreceptors which, in turn, will stimulate respiration. The increased alveolar ventilation will decrease the arterial PCO_2 to a value below normal (less than 40 mmHg). Although the increased ventilation will increase the arterial PO_2 , the resulting value will remain below normal for as long as the individual is breathing air with a low partial pressure of oxygen. A lower than normal arterial O_2 tension and a normal or greater than normal arterial CO_2 tension is usually a sign of a depressed respiratory center. A greater than normal arterial O_2 tension and a lower than normal arterial CO_2 tension can only occur if the person is breathing air with a greater than normal concentration of oxygen.

274. The answer is a. (*Berne, 3/e, pp 382–383.*) Hyperventilation, by definition, reduces the arterial PCO_2 below normal, that is, to a value less than 40 mmHg. Low arterial PCO_2 in the blood perfusing the brain causes vasoconstriction of the cerebral vasculature, leading to a lowering of blood flow to the brain. The low arterial CO_2 will increase the pH of the arterial blood (i.e., produce a respiratory alkalosis) and decrease the activity of the central chemoreceptors. Pulmonary vasculature, unlike the systemic vasculature, is dilated by low PCO_2 and high PO_2 and constricted by high PCO_2 and low PO_2 . The respiratory alkalosis will cause Ca^{2+} to bind to plasma proteins, lowering the concentration of ionized Ca^{2+} . Low concentrations of ionized Ca^{2+} increase the excitability of nerve and muscle membranes, causing them to contract spontaneously or with minimal stimulation. The increased contractile activity of skeletal muscle produced by low concentration of ionized Ca^{2+} is called *tetany*.

275. The answer is a. (*Rhoades, p 355.*) Patients with chronic lung disease typically have difficulty maintaining a normal arterial oxygen tension due to an increase in lung compliance and V/Q abnormalities. Blue bloaters

are patients with cyanosis and peripheral edema. These patients have extensive areas of lung tissue with lower than normal V/Q ratios; therefore, they are not able to fully oxygenate their blood and then develop cyanosis. The low oxygen tension leads to increased pulmonary arterial resistance and enlarged right ventricles (cor pulmonale). The resulting increased central venous pressure causes peripheral edema (bloating). Pink puffers are able to maintain normal arterial PO_2 levels. All patients with chronic lung disease will have decreased vital capacity and expiratory flow rates and increased airway resistance.

276–277. The answers are 276-a, 277-c. (*Rhoades, pp 391–394.*) The oxyhemoglobin saturation (Hb O_2) curve represents the relationship between the partial pressure of oxygen and the amount of oxygen bound to hemoglobin (Hb). Normal Hb is 50% saturated with a PO_2 of approximately 27 mmHg (the P_{50}), 75% saturated with a PO_2 of 40 mmHg (the normal PO_2 of mixed venous blood), and almost 100% saturated at a PO_2 of 100 mmHg (the normal arterial PO_2). Increasing the affinity of Hb for O_2 shifts the Hb O_2 saturation curve to the left and decreases the P_{50} ; decreasing the affinity of Hb for O_2 shifts the Hb O_2 saturation curve to the right and increases the P_{50} . Fetal blood has a higher than normal oxygen affinity and therefore is represented by the curve labeled A. Carbon monoxide (CO) competitively inhibits the binding of oxygen to hemoglobin, so the total amount of oxygen that can bind to Hb at any PO_2 is less than normal. However, somewhat paradoxically, CO increases the affinity of Hb for O_2 so the Hb O_2 curve is shifted to the left. The Hb O_2 curve for blood exposed to CO is represented by the curve labeled C, which is shifted to the left but is unable to bind as much O_2 as normal at a PO_2 of 100 mmHg.

278–279. The answers are 278-e, 279-b. (*Berne, 3/e, pp 326–328.*) The tentative diagnosis of left heart failure is based on the shortness of breath and the accompanying respiratory rales. The low PaO_2 most likely results from the pulmonary edema accompanying the left heart failure, which interferes with gas exchange. The low PaO_2 stimulates the chemoreceptors, which, in turn, stimulate ventilation. The increased ventilation reduces PaCO_2 to below normal. The presence of hyperventilation is confirmed by the low H^+ ion concentration. The heart failure is responsible for the increased left atrial pressure, and the low PO_2 is responsible for the increased pulmonary artery resistance and pressure. Providing oxygen will overcome the diffusional bar-

rier and increase arterial PO_2 . The high PO_2 will reduce pulmonary artery resistance. In order to restore PaO_2 toward normal, the alveolar PO_2 must be raised more than the arterial PO_2 will increase, and, therefore, the A-a gradient will be increased. Restoring the arterial PO_2 toward normal will decrease the chemoreceptor respiratory drive, and, therefore, both the PCO_2 and the H^+ ion concentration will increase toward normal.

280–281. The answers are 280-e, 281-d. (*Berne, 3/e, pp 326, 339, 476–477.*) A large intrapulmonary shunt will cause arterial oxygen tension to decrease. This will increase respiratory drive causing a respiratory alkalosis, which will result in a low PCO_2 and a high pH. The low oxygen tension may also produce a lactic acidosis, which may attenuate the rise in pH produced by hyperventilation. A patient with metabolic acidosis will have a lower than normal pH, which will stimulate the chemical and peripheral chemoreceptors. The ensuing rise in alveolar ventilation will lower PCO_2 and slightly increase PO_2 .

282. The answer is e. (*Rhoades, pp 364–368.*) Interstitial lung disease is a restrictive-type lung disease in which all the lung volumes, including VC, FRC, and RV, are reduced. The decrease in lung volumes is caused by a decrease in lung compliance. The low compliance produces a high recoil force so that a higher than normal fraction of the forced vital capacity (FEV_1/FVC) can be exhaled during expiration. The normal pH is consistent with a normal alveolar ventilation. Because lung compliance is reduced, the normal alveolar ventilation is maintained with a breathing pattern consisting of a high rate and a low volume.

283. The answer is b. (*Rhoades, pp 362–365.*) Most of the airway is within the thoracic cavity, and, therefore, the intrathoracic pressure affects airway diameter and resistance. The intrathoracic pressure is most negative at the total lung capacity. The negative thoracic pressure increases airway diameter and decreases airway resistance. During a forced expiration or at the residual volume, the intrathoracic pressure is positive, compressing the airways and increasing their resistance. The vagus nerve constricts airway smooth muscle. Low oxygen will have little effect on airway tone.

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Renal and Acid-Base Physiology

Questions

DIRECTIONS: Each question below contains several suggested responses. Select the **one best** response to each question.

284. The consumption of oxygen by the kidney

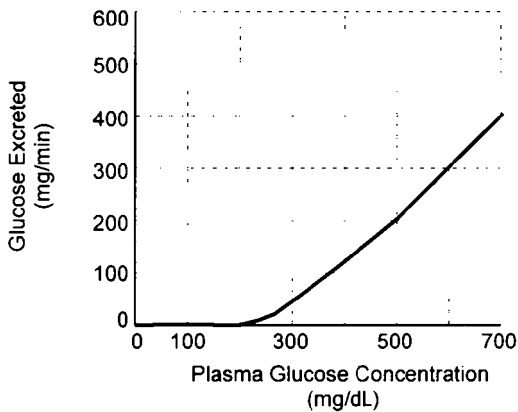
- a. Decreases as blood flow increases
- b. Is regulated by erythropoietin
- c. Remains constant as blood flow increases
- d. Directly reflects the level of sodium transport
- e. Is greatest in the medulla

285. The anion gap will increase with an increase in the plasma concentration of

- a. Sodium
- b. Potassium
- c. Chloride
- d. Bicarbonate
- e. Lactate

Questions 286–287

286. The graph below illustrates the relationship between plasma glucose concentration and glucose reabsorption by the kidney. The GFR is 100 mL/min. The renal threshold for glucose is



- a. 50 mg/dL
- b. 100 mg/dL
- c. 150 mg/dL
- d. 200 mg/dL
- e. 500 mg/dL

287. The T_{\max} for glucose is

- a. 100 mg/min
- b. 200 mg/min
- c. 300 mg/min
- d. 400 mg/min
- e. 500 mg/min

288. In the presence of ADH, the filtrate will be isotonic to plasma in the

- a. Descending limb of the loop of Henle
- b. Ascending limb of the loop of Henle
- c. Cortical collecting tubule
- d. Medullary collecting tubule
- e. Renal pelvis

289. Sodium reabsorption from the distal tubule will be increased if there is an increase in

- a. Plasma potassium concentration
- b. Plasma volume
- c. Mean arterial pressure
- d. Urine flow rate
- e. Plasma osmolality

290. ADH will be released from the posterior pituitary when there is a decrease in

- a. Plasma Na^+ concentration
- b. Plasma volume
- c. Plasma K^+ concentration
- d. Plasma pH
- e. Plasma Ca^{2+} concentration

291. If 600 mL of water is ingested rapidly, plasma volume will increase by approximately

- a. 400 mL
- b. 200 mL
- c. 100 mL
- d. 50 mL
- e. 25 mL

292. Use the data below to calculate the net amount of substance X secreted by the kidney.

Clearance of inulin = 120 mL/min

Plasma concentration of X = 10 mg/dL

Urine concentration of X = 10 mg/mL

Urinary flow rate = 1.5 mL/min

- a. 1 mg/min
- b. 2 mg/min
- c. 3 mg/min
- d. 4 mg/min
- e. 5 mg/min

293. Renin secretion by the kidney is increased by

- a. Increasing mean blood pressure
- b. Increasing glomerular filtration rate
- c. Increasing sympathetic nerve activity
- d. Increasing angiotensin II synthesis
- e. Increasing atrial natriuretic hormone secretion

294. Na^+ is reabsorbed from the basolateral surface of the renal epithelial cells by

- a. Na/H exchange
- b. Na -glucose cotransport
- c. Na -K pump
- d. Facilitated diffusion
- e. Solvent drag

295. Which of the following is most likely to cause an increase in the glomerular filtration rate?

- a. Contraction of mesangial cells
- b. Blockage of the ureter
- c. Release of renin from the juxtaglomerular apparatus
- d. Dilation of the afferent arterioles
- e. Volume depletion

296. The daily production of hydrogen ion from CO_2 is primarily buffered by

- a. Extracellular bicarbonate
- b. Red blood cell bicarbonate
- c. Red blood cell hemoglobin
- d. Plasma proteins
- e. Plasma phosphate

297. Glomerular filtration rate would be decreased by

- a. Constriction of the efferent arteriole
- b. An increase in afferent arteriolar pressure
- c. Compression of the renal capsule
- d. A decrease in the concentration of plasma protein
- e. An increase in renal blood flow

298. Use the following clinical laboratory data obtained from a patient with diabetes mellitus to calculate the anion gap.

Plasma $[\text{Na}^+] = 140 \text{ meq/L}$

Plasma $[\text{HCO}_3^-] = 6 \text{ meq/L}$

Plasma $[\text{K}^+] = 7.0 \text{ meq/L}$

Arterial $[\text{H}^+] = 80 \text{ meq/L}$

Plasma $[\text{Cl}^-] = 105 \text{ meq/L}$

Plasma $[\text{glucose}] = 600 \text{ mg/dL}$

The anion gap is

- a. 12 meq/L
- b. 22 meq/L
- c. 29 meq/L
- d. 36 meq/L
- e. 42 meq/L

299. The secretion of H^+ in the proximal tubule is primarily associated with

- a. Excretion of potassium ion
- b. Excretion of hydrogen ion
- c. Reabsorption of calcium ion
- d. Reabsorption of bicarbonate ion
- e. Reabsorption of phosphate ion

Questions 300–301

Use the following laboratory values to answer the next two questions.

PAH clearance = 750 mL/min

Urinary flow = 2 mL/min

Plasma creatinine

Plasma glucose

concentration = 0.8 mg/dL

concentration = 120 mg/dL

Urinary creatinine concentration = 66 mg/dL

300. What is the patient's filtration fraction?

- a. 0.18
- b. 0.20
- c. 0.22
- d. 0.24
- e. 0.26

301. Approximately how much glucose is reabsorbed by this patient's kidneys?

- a. 0 mg/min
- b. 120 mg/min
- c. 165 mg/min
- d. 200 mg/min
- e. 320 mg/min

Questions 302–304

Use the following laboratory values to answer the questions.

Urinary volume = 1.5 L/day

Urinary $[\text{NH}_4^+] = 20 \text{ meq/L}$

Urinary $[\text{HCO}_3^-] = 4 \text{ meq/L}$

Urine pH = 6.5

Urinary titratable

Plasma pH = 7.3

acids = 10 meq/L urine

302. What is the daily net acid excretion for this patient?

- a. 51 meq/day
- b. 39 meq/day
- c. 34 meq/day
- d. 30 meq/day
- e. 26 meq/day

303. How much new bicarbonate is being formed per day in this patient?

- a. 51 meq/day
- b. 39 meq/day
- c. 34 meq/day
- d. 30 meq/day
- e. 26 meq/day

304. Assuming production of a normal fixed acid load, what is this patient's acid-base status?

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

305. The major source of the total daily acid load produced by the body is

- a. Anaerobic metabolism
- b. Aerobic metabolism
- c. Phospholipid catabolism
- d. Protein catabolism
- e. Triglyceride catabolism

306. Use the following laboratory data to calculate the renal blood flow.

Renal artery para-aminohippuric acid concentration	= 0.05 mg/mL
Renal vein PAH concentration	= 0.005 mg/mL
Urinary PAH concentration	= 20 mg/mL
Urinary flow rate	= 2 mL/min

Renal plasma flow is approximately

- a. 500 mL/min
- b. 600 mL/min
- c. 700 mL/min
- d. 800 mL/min
- e. 900 mL/min

307. If a substance appears in the renal artery but not in the renal vein,

- a. Its clearance is equal to the glomerular filtration rate
- b. It must be reabsorbed by the kidney
- c. Its urinary concentration must be higher than its plasma concentration
- d. Its clearance is equal to the renal plasma flow
- e. It must be filtered by the kidney

308. A freely filterable substance that is neither reabsorbed nor secreted has a renal artery concentration of 12 mg/mL and a renal vein concentration of 9 mg/mL. Calculate the filtration fraction (GFR/RPF).

- a. 0.05
- b. 0.15
- c. 0.25
- d. 0.35
- e. 0.45

309. Destruction of the supraoptic nuclei of the brain will produce which of the following changes in urinary volume and concentration? (Assume that fluid intake equals fluid loss.)

- a. An increased urinary volume and a very dilute urine
- b. An increased urinary volume and concentrated urine
- c. A normal urinary volume and concentration
- d. Decreased urinary volume and a very dilute urine
- e. Decreased urinary volume and a concentrated urine

310. Which one of the following returns closest to normal during chronic respiratory acidosis?

- a. Alveolar ventilation
- b. Arterial PCO_2
- c. Arterial PO_2
- d. Plasma concentration of bicarbonate
- e. Arterial concentration of hydrogen ion

311. The pH of the tubular fluid in the distal nephron can be lower than that in the proximal tubule because

- a. A greater sodium gradient can be established across the wall of the distal nephron than across the wall of the proximal tubule
- b. More buffer is present in the tubular fluid of the distal nephron than in the proximal tubule
- c. More hydrogen ion is secreted into the distal nephron than into the proximal tubule
- d. The brush border of the distal nephron contains more carbonic anhydrase than that of the proximal tubule
- e. The tight junctions of the distal nephron are less leaky to solute than those of the proximal tubule

312. Which of the following statements about renin is true?

- a. It is secreted by cells of the proximal tubule
- b. Its secretion leads to loss of sodium and water from plasma
- c. Its secretion is stimulated by increased mean renal arterial pressure
- d. It converts angiotensinogen to angiotensin I
- e. It converts angiotensin I to angiotensin II

313. Use the following laboratory data to determine the GFR.

Urine creatinine concentration = 196 mg/mL

Plasma creatinine concentration = 1.4 mg/mL

Urine flow = 1 mL/min

The creatinine clearance is approximately

- a. 75 mL/min
- b. 98 mL/min
- c. 125 mL/min
- d. 140 mL/min
- e. 196 mL/min

314. Renal correction of hyperkalemia will result in

- a. Alkalosis
- b. Acidosis
- c. Increased secretion of HCO_3^-
- d. Increased secretion of H^+
- e. Increased excretion of Na^+

315. The effective renal plasma flow, which equals the clearance of PAH, is less than the true renal plasma flow because

- a. The fraction of PAH filtered is less than the filtration fraction
- b. The plasma entering the renal vein contains a small amount of PAH
- c. The cortical and medullary collecting ducts are able to reabsorb some PAH
- d. The calculated clearance of PAH depends on the urinary flow rate
- e. The measured value of the plasma PAH concentration is less than the actual PAH concentration

316. Most of the glucose that is filtered through the glomerulus undergoes reabsorption in the

- 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

317. Which of the following structural features distinguishes the epithelial cells of the proximal tubule from those of the distal tubule?

- a. The distal tubule has a thicker basement membrane
- b. The proximal tubule has a thicker basement membrane
- c. The proximal tubule has a more extensive brush border
- d. The proximal tubule forms the juxtaglomerular apparatus
- e. The distal tubule has fewer tight intercellular junctions

318. Which of the following statements concerning the 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

319. Glomerular filtration rate (GFR) and renal blood flow (RBF) will both be increased if

- a. The efferent and afferent arterioles are both dilated
- b. The efferent and afferent arterioles are both constricted
- c. Only the afferent arteriole is constricted
- d. Only the efferent arteriole is constricted
- e. The afferent arteriole is constricted and the efferent arteriole is dilated

320. A man drinks 2 L of water to replenish the fluids lost by sweating during a period of exercise. Compared with the situation prior to the period of sweating,

- a. His intracellular fluid will be hypertonic
- b. His extracellular fluid will be hypertonic
- c. His intracellular fluid volume will be greater
- d. His extracellular fluid volume will be greater
- e. His intracellular and extracellular fluid volumes will be unchanged

321. Which one of the following statements about ammonia (NH_3) is correct?

- a. It is impermeable to the epithelial cells of the proximal tubule
- b. It is classified as a titratable acid
- c. It is produced by epithelial cells in the distal nephron
- d. It reduces the concentration of bicarbonate in the plasma
- e. Its synthesis is increased in respiratory acidosis

322. The amount of potassium excreted by the kidney will decrease if

- a. Distal tubular flow increases
- b. Circulating aldosterone levels increase
- c. Dietary intake of potassium increases
- d. Na^+ reabsorption by the distal nephron decreases
- e. The excretion of organic ions decreases

323. A respiratory acidosis that results in an increase in the concentration of hydrogen ion in arterial blood from 40 meq/L (pH 7.4) to 50 meq/L (pH 7.3) would

- a. Stimulate the peripheral chemoreceptors
- b. Decrease the amount of ammonium excreted in the urine
- c. Inhibit the central chemoreceptors
- d. Increase the pH of the urine
- e. Decrease the concentration of HCO_3^- in arterial blood

324. Which of the following substances will be more concentrated at the end of the proximal tubule than at the beginning of the proximal tubule?

- a. Glucose
- b. Creatinine
- c. Sodium
- d. Bicarbonate
- e. Phosphate

325. When a person is dehydrated, hypotonic fluid will be found in the

- a. Glomerular filtrate
- b. Proximal tubule
- c. Loop of Henle
- d. Cortical collecting tubule
- e. Distal collecting duct

326. The electrically neutral active transport of sodium from the lumen of the kidney occurs in the

- a. Proximal tubule
- b. Descending limb of the loop of Henle
- c. Ascending limb of the loop of Henle
- d. Cortical collecting duct
- e. Medullary collecting duct

327. In metabolic acidosis caused by diabetic ketoacidosis, which of the following would be greater than normal?

- a. Concentration of plasma HCO_3^-
- b. Anion gap
- c. Arterial PCO_2
- d. Plasma pH
- e. Blood volume

328. Decreasing the resistance of the afferent arteriole in the glomerulus of the kidney will decrease

- a. The renal plasma flow
- b. The filtration fraction
- c. The oncotic pressure of the peritubular capillary blood
- d. The glomerular filtration rate
- e. None of the above

329. If GFR increases, proximal tubular reabsorption of salt and water will increase by a process called *glomerulotubular balance*. Contributions to this process include

- a. An increase in peritubular capillary hydrostatic pressure
- b. A decrease in peritubular sodium concentration
- c. An increase in peritubular oncotic pressure
- d. An increase in proximal tubular flow
- e. An increase in peritubular capillary flow

330. Renin release from the juxtaglomerular apparatus is inhibited by

- a. Beta-adrenergic agonists
- b. Prostaglandins
- c. Aldosterone
- d. Stimulation of the macula densa
- e. Increased pressure within the afferent arterioles

331. Patients with renal insufficiency develop very high plasma concentrations of urea (uremia) because of

- a. An increased synthesis of urea by the liver
- b. An increased reabsorption of urea by the proximal tubules
- c. A decreased secretion of urea by the distal tubules
- d. A decreased glomerular filtration rate
- e. An increased renal blood flow

332. Which one of the following statements about aldosterone is correct?

- a. It produces its effect by activating cAMP
- b. It produces its effect by increasing distal tubular permeability to sodium
- c. It causes an increased reabsorption of hydrogen ion
- d. It has its main effect on the proximal tubule
- e. It is secreted in response to an increase in blood pressure

333. The effect of antidiuretic hormone (ADH) on the kidney is to

- a. Increase the permeability of the distal nephron to water
- b. Increase the glomerular filtration rate
- c. Increase the excretion of Na^+
- d. Increase the excretion of water
- e. Increase the diameter of the renal artery

334. Hypokalemia can result from

- a. Metabolic acidosis
- b. Diarrhea
- c. Adrenal insufficiency
- d. Hypovolemia
- e. Hyperosmotic extracellular fluid

335. The ability of the kidney to excrete a concentrated urine will increase if

- a. The reabsorption of Na^+ by the proximal tubule decreases
- b. The flow of filtrate through the loop of Henle increases
- c. The glomerular capillary pressure increases
- d. The activity of the Na-K pump in the loop of Henle decreases
- e. The permeability of the collecting duct to water increases

336. The glomerular filtration rate will increase if

- a. Sympathetic nerve activity to the kidney increases
- b. The afferent arteriolar resistance increases
- c. The efferent arteriolar resistance decreases
- d. The plasma protein concentration decreases
- e. Urine flow through the urethra is blocked

337. Metabolic alkalosis will be observed in a patient with

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

338. The syndrome of inappropriate antidiuretic hormone secretion (SIADH) is caused by the excess release of ADH. SIADH will cause an increase in

- a. Concentration of plasma sodium
- b. Intracellular volume
- c. Urinary flow
- d. Plasma oncotic pressure
- e. Plasma osmolarity

339. Which one of the following comparisons between the distal nephron and the proximal tubule is correct?

- a. The distal nephron is more permeable to hydrogen ion than the proximal tubule
- b. The distal nephron is less responsive to aldosterone than the proximal tubule
- c. The distal nephron has a more negative intraluminal potential than the proximal tubule
- d. The distal nephron secretes less potassium than does the proximal tubule
- e. The distal nephron secretes more hydrogen ion than does the proximal tubule

340. An increase in the concentration of NaCl in the intraluminal fluid with the ascending limb of the loop of Henle causes the macula densa to release

- a. ADH
- b. Aldosterone
- c. Adenosine
- d. Renin
- e. Angiotensinogen

341. Metabolic acidosis is caused by

- a. Hypoaldosteronism
- b. Hyperventilation
- c. Hypokalemia
- d. Hypovolemia
- e. Hypercalcemia

342. Aldosterone secretion is increased when there is an increase in the plasma concentration of

- a. ACTH
- b. Chloride
- c. Sodium
- d. Hydrogen
- e. Potassium

343. In which one of the following situations is urinary flow less than normal?

- a. Diabetes insipidus
- b. Diabetes mellitus
- c. Sympathetic stimulation
- d. Increased renal arterial pressure
- e. Infusion of mannitol

344. Most of the volatile acid entering the blood is buffered by

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

345. Potassium-sparing diuretics inhibit Na^+ reabsorption in the

- a. Proximal tubule
- b. Thin descending limb of Henle's loop
- c. Thick descending limb of Henle's loop
- d. Distal convoluted tubule
- e. Cortical collecting duct

346. Which one of the following values will be above normal in a diabetic patient with a blood glucose concentration of 600 meq/L?

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

347. Which one of the following will be increased in a patient suffering from persistent diarrhea?

- a. The filtered load of HCO_3^-
- b. The production of ammonia by the proximal tubule
- c. H^+ secretion by the distal nephron
- d. The anion gap
- e. The production of new bicarbonate by the distal nephron

348. In addition to increasing the permeability of the collecting duct to water, ADH increases the permeability of the collecting duct to

- a. Hydrogen
- b. Ammonium
- c. Potassium
- d. Sodium
- e. Urea

349. The filtration fraction is increased by

- a. Increasing renal blood flow
- b. Increasing afferent arteriolar resistance
- c. Increasing efferent arteriolar resistance
- d. Increasing plasma oncotic pressure
- e. Increasing the pressure within Bowman's capsule

350. Which one of the following conditions causes a higher than normal plasma bicarbonate concentration?

- a. Volume depletion
- b. Renal failure
- c. Hypoxemia
- d. Diarrhea
- e. Hypoaldosteronism

351. Which one of the following substances causes renal blood flow to decrease?

- a. Nitric oxide
- b. Bradykinin
- c. Prostaglandins
- d. Adenosine
- e. Dopamine

352. Diuretics, such as acetazolamide, which produce their effect by inhibiting carbonic anhydrase, inhibit the reabsorption of sodium in

- a. The proximal tubule
- b. The thick ascending limb of Henle's loop
- c. The distal convoluted tubule
- d. The cortical collecting duct
- e. The outer medullary collecting duct

353. The extracellular potassium of a hyperkalemic patient can be decreased by administering

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

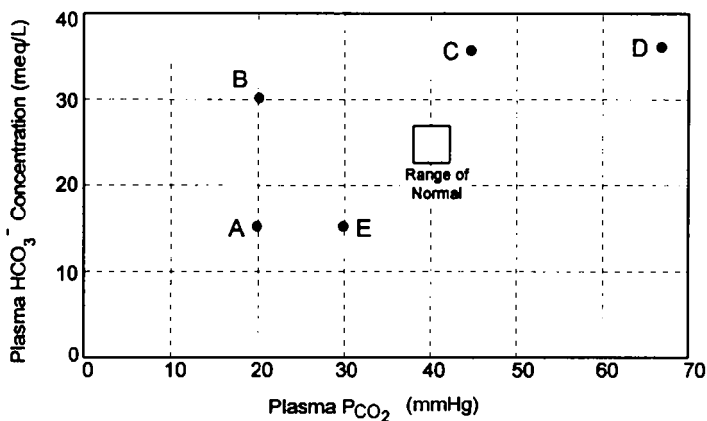
354. Which one of the following blood-gas values is consistent with metabolic acidosis?

	PaCO_2 (mmHg)	HCO_3^- (mM)	pH
a.	25	30	7.7
b.	35	20	7.3
c.	40	25	7.4
d.	50	30	7.1
e.	60	20	7.1

355. Hyperkalemia may be observed in patients with

- Volume depletion
- Diuretic therapy
- Administration of insulin
- Metabolic alkalosis
- Stimulation of adrenal medulla

356. Which point on the graph represents the blood-gas values obtained from a patient who has ascended to high altitude?



- A
- B
- C
- D
- E

357. Which one of the following substances is less concentrated at the end of the proximal tubule than at the beginning of the proximal tubule?

- a. Creatinine
- b. Hydrogen
- c. Chloride
- d. Phosphate
- e. Sodium

358. What percentage of the filtered load of sodium is reabsorbed by the proximal tubule?

- a. 15%
- b. 25%
- c. 45%
- d. 65%
- e. 95%

359. ANP (atrial natriuretic hormone) decreases Na reabsorption within

- a. The proximal tubule
- b. The thick ascending limb of Henle's loop
- c. The distal convoluted tubule
- d. The cortical collecting duct
- e. The inner medullary collecting duct

360. Free water clearance by the kidney is increased by

- a. Heart failure
- b. Renal failure
- c. Diuretic therapy
- d. Diabetes mellitus
- e. Diabetes insipidus

361. The renal clearance of phosphate is increased by

- a. Aldosterone
- b. Parathyroid hormone
- c. Norepinephrine
- d. Vasopressin
- e. Angiotensin

362. Hyponatremia will result from an excess secretion of

- a. Vasopressin
- b. Atrial natriuretic hormone
- c. Norepinephrine
- d. Insulin
- e. Aldosterone

363. Which one of the following will produce the greatest increase in potassium secretion?

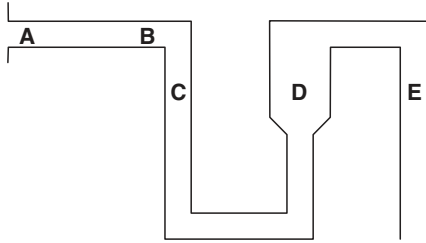
- a. A decrease in urinary flow rates
- b. An increase in distal nephron sodium concentration
- c. A decrease in circulating blood volume
- d. An increase in sympathetic nerve activity
- e. A decrease in renal blood flow

364. A decrease in the concentration of NaCl in the intraluminal fluid causes the juxtaglomerular apparatus to release

- a. ADH
- b. Aldosterone
- c. Adenosine
- d. Renin
- e. Angiotensinogen

Questions 365–367

Use the following diagram of a nephron to answer the questions.



365. In the presence of ADH, the luminal Na^+ concentration is lowest at point

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

366. New bicarbonate is produced by the secretion of H^+ at point

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

367. Active transport is not required for the reabsorption of sodium at point

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

368. Which one of the following will be observed in a patient with chronic renal failure?

- a. A decrease in the fractional excretion of sodium
- b. An increase in the free water clearance
- c. An increase in the anion gap
- d. A decrease in the excretion of creatinine
- e. An increase in the net acid excretion

369. The extracellular fluid volume of a normal individual is approximately

- 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

370. Which one of the following signs of renal failure is caused by the loss of a hormone produced by the kidney?

- a. Edema
- b. Hypertension
- c. Anemia
- d. Uremia
- e. Acidosis

371. A patient takes excessive amounts of bicarbonates to treat his heart-burn. Which one of the following blood-gas values will be observed in this patient?

- | | Paco₂
(mM) | pH |
|----|---------------------------------|-----------|
| a. | 25 | 7.7 |
| b. | 35 | 7.6 |
| c. | 45 | 7.5 |
| d. | 55 | 7.4 |
| e. | 65 | 7.3 |

Renal and Acid-Base Physiology

Answers

284. The answer is d. (*Guyton, p 369.*) In the kidney, oxygen is used primarily to support active transport of solutes, especially sodium, out of the tubules. In fact, oxygen consumption by the kidney is directly proportional to the amount of sodium reabsorbed and is greatest in the cortex, where most tubular reabsorption of sodium occurs. An increase in renal blood flow will raise the glomerular filtration rate and increase the quantity of solute to be transported, so that oxygen consumption increases as blood flow increases and the arteriovenous oxygen difference remains constant. This is in contrast to the situation in other organs where increases in blood flow are accompanied by a decrease in arteriovenous oxygen difference. Erythropoietin is released in response to renal hypoxia and acts to increase erythrocyte production.

285. The answer is e. (*Guyton, pp 361–363.*) The anion gap is the difference between the concentration of Na^+ and the concentration of the major plasma anions, Cl^- and HCO_3^- . The minor ions, lactate, phosphate, sulfate, comprise the anion gap. Increases in lactate, as in lactic acidosis, will cause an increase in the anion gap because the lactic acid reduces the plasma bicarbonate concentration. Increases in sodium normally are associated with an increase in Cl^- and therefore do not increase the anion gap. Similarly, increases in bicarbonate typically are associated with a corresponding decrease in Cl^- and do not increase the anion gap.

286–287. The answers are 286-d, 287-c. (*Guyton, pp 298–299.*) 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 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, in the situation represented by the graph, it is only 300 mg/min. At plasma concentrations above 500 mg%, the rate of excretion increases linearly with an increase in filtration, indicating that the maximum rate of reabsorption has been achieved. The maximum rate is the difference between filtration and excretion at any plasma concentration above 300 mg%. For example, at a plasma concentration of 600 mg/dL, the filtered load (FL) is 600 mg/min ($P_{\text{glucose}} \cdot \text{GFR}$). The amount excreted is 300 mg/min. Therefore, the amount reabsorbed, the difference between the filtered load and the amount excreted, is 300 mg/min.

288. The answer is c. (Berne, 3/e, pp 762–770.) In the absence of antidiuretic hormone (ADH, vasopressin), the cortical and medullary collecting tubules and ducts are impermeable to water. ADH increases the water permeability of these nephron segments and allows the filtrate to reach osmotic equilibrium with the interstitial fluid surrounding the nephron. The interstitial fluid in the cortex of the kidney is isotonic to plasma, and, therefore, the filtrate can become isotonic to plasma in the cortical collecting tubule. The interstitial fluid is hypertonic to plasma in the medullary collecting tubule, and so the filtrate becomes hypertonic to plasma in this region of the nephron and remains hypertonic as it passes through the renal pelvis. ADH has no effect on the water permeability of the loop of Henle. The filtrate is hypertonic to plasma in the descending limb and becomes hypotonic to plasma by the time it reaches the end of the ascending limb of the loop of Henle.

289. The answer is a. (Guyton, pp 369, 340–341, 872–873.) Sodium (Na^+) reabsorption in the distal nephron is controlled primarily by aldosterone. Increases in plasma aldosterone concentration increase Na^+ reabsorption. Aldosterone secretion is increased when plasma concentrations of angiotensin II or potassium (K^+) are increased. Increases in plasma volume or mean arterial pressure will lead to a decrease in angiotensin II secretion. Increases in plasma osmolality will cause an increase in ADH. ADH will decrease water excretion but have only a minimal effect on sodium reab-

sorption. An increase in urinary flow rate may cause a slight decrease in sodium reabsorption.

290. The answer is b. (*Berne, 3/e, pp 438–439.*) Large amounts of anti-diuretic hormone (ADH, vasopressin) are released from the posterior pituitary gland in response to a decrease in plasma volume or mean blood pressure. The increase in ADH helps to restore blood pressure by directly stimulating vascular smooth muscle and therefore increasing total peripheral resistance (TPR); it also helps to restore blood volume by decreasing the amount of water excreted by the kidneys. Osmoreceptors in the hypothalamus respond to a decrease in plasma osmolality by decreasing the amount of ADH secreted by the posterior pituitary gland.

291. The answer is d. (*Guyton, pp 272–273.*) When water is ingested from the intestine, it enters the plasma and rapidly achieves osmotic equilibrium with the interstitial and intracellular compartments. Since the plasma volume is approximately 8% ($\frac{1}{12}$) of the total body water volume, only 8% of the ingested water will remain in the plasma. Therefore, of the 600 mL of water ingested, approximately 50 mL remains in the plasma, 150 mL enters the interstitium, and 400 mL enters the intracellular space.

292. The answer is c. (*Rhoades, pp 422–425.*) The net secretion is the difference between the filtered load and the excretion of a substance.

$$\text{Filtered Load} = \text{GFR} \cdot P_x = 120 \text{ mL/min} \cdot 10 \text{ mg/mL} = 12 \text{ mg/min}$$

$$\text{Excretion} = U_x \cdot \dot{V} = 10 \text{ mg/mL} \cdot 1.5 \text{ mL/min} = 15 \text{ mg/min}$$

$$\text{Secretion} = 15 \text{ mg/min} - 12 \text{ mg/min} = 3 \text{ mg/min}$$

293. The answer is c. (*Rhoades, pp 421–422, 453–455, 697–699.*) Renin secretion is stimulated by the sympathetic nerves innervating the juxtaglomerular apparatus. Increasing mean blood pressure decreases sympathetic activity. Changes in GFR are detected by the macula densa. Decreases in GFR lead to an increase in renin release and the secretion of a mediator, perhaps adenosine, that contracts the afferent arteriole. ANF and angiotensin II will decrease renin release.

294. The answer is c. (*Rhoades, pp 434–436.*) The intracellular Na^+ concentration of renal epithelial cells is pumped out of renal epithelial cells by Na-K pumps located on the basolateral surface of the epithelial cells. The Na/H exchanger and the Na-glucose transporter are located on the apical surface of the epithelial cells. Na^+ is transported from the peritubular spaces to the capillaries by solvent drag.

295. The answer is d. (*Rhoades, pp 428–432. Guyton, 10/e, pp 286–290.*) The GFR is proportional to the glomerular capillary hydrostatic pressure, the renal plasma flow, and the surface area and hydraulic conductivity of the diffusion barrier between the glomerular capillary and Bowman's space. Dilating the afferent arteriole causes an increase in glomerular capillary pressure and, therefore, an increase in GFR. Volume depletion causes a release of renin from the juxtaglomerular cells, leading to an increase in angiotensin II (AII) that causes constriction of the glomerular capillaries and contraction of the mesangial cells. Contraction of the mesangial cells causes a decrease in the surface area of the diffusion barrier between the glomerular capillary and Bowman's space. Blockage of the ureter causes an increase in tubular pressure that retards the filtration of water from the capillary to the nephron.

296. The answer is c. (*Berne, 3/e, pp 475–476.*) Aerobic metabolism produces 13,000 to 24,000 mmol CO_2 per day. This yields close to that amount of H^+ ions produced per day via the reaction $\text{CO}_2 + \text{H}_2\text{O} \leftrightarrow \text{H}_2\text{CO}_3 \leftrightarrow \text{H}^+ + \text{HCO}_3^-$. At the tissues, CO_2 diffuses into the red blood cells, where the enzyme carbonic anhydrase accelerates the above reaction. The H^+ produced is buffered mainly by the large amount of hemoglobin in the red blood cells. Bicarbonate is not an effective buffer of volatile acid (from CO_2).

297. The answer is c. (*Guyton, pp 286–288.*) Glomerular filtration rate (GFR) will decrease if there is a decrease in the net glomerular capillary pressure or the flow of fluid through the glomerulus. The net glomerular capillary pressure (for Starling forces) is equal to the glomerular capillary pressure minus the sum of the plasma oncotic pressure and intrarenal pressure. Compression of the renal capsule increases the intrarenal pressure and therefore decreases the net capillary filtration pressure. Constriction of the efferent arteriole increases glomerular capillary pressure. Decreasing

the concentration of plasma protein will decrease the plasma oncotic pressure and lead to an increase in GFR.

298. The answer is c. (*Guyton, pp 362–363.*) The anion gap is equal to the difference between the plasma concentration of sodium, the major cation in the plasma, and the sum of the concentrations of plasma chloride and bicarbonate, the major measured anions in the plasma.

$$\begin{aligned}\text{Anion gap} &= [\text{Na}^+] - ([\text{Cl}^-] + [\text{HCO}_3^-]) \\ &= 140 \text{ meq/L} - (105 \text{ meq/L} + 6 \text{ meq/L}) \\ &= 29 \text{ meq/L}\end{aligned}$$

The normal plasma concentrations of Na^+ , Cl^- , and HCO_3^- are 140 meq/L, 105 meq/L, and 24 meq/L, respectively. The normal anion gap is from 9 to 14 meq/L. The anion gap is elevated when the concentration of unmeasured anions in the plasma increases, for example, in cases of metabolic acidosis such as diabetic ketoacidosis and lactic acidosis. It is not elevated in metabolic acidosis caused by diarrhea.

299. The answer is d. (*Guyton, pp 353–354.*) In the proximal tubule, a large amount of H^+ ion is secreted into the tubule lumen via an Na^+ - H^+ antiporter (exchanger). Most of this H^+ combines with bicarbonate ion in the tubular fluid to form CO_2 and water. The CO_2 diffuses into the proximal tubular cells, where the opposite reaction takes place to form H^+ and HCO_3^- . The HCO_3^- exits the cells on the basolateral side and enters the blood as reabsorbed bicarbonate. Carbonic anhydrase is located on the luminal surface of the cells as well as inside the cells to facilitate the above reactions.

300–301. The answers are 300-c, 301-d. (*Guyton, pp 309–312.*) The *filtration fraction* is the fraction of plasma filtered from the plasma flowing through the kidney, or GFR/RPF . Renal plasma flow is equal to the clearance of PAH; GFR is equal to the clearance of creatinine. Clearance of creatinine can be calculated using the following formula:

$$\begin{aligned}C_{\text{cr}} &= [U_{\text{cr}} \times \dot{V}] \div P_{\text{cr}} \\ &= [66 \times 2] \div 0.8 \\ &= 165 \text{ mL/min}\end{aligned}$$

Thus, the filtration fraction is $165/750 = 0.22$. At glucose concentrations below 150 to 200 mg/dL, the kidneys will reabsorb all the glucose passing through the kidney. The filtered load of glucose is $P_{\text{glu}} \times \text{GFR} = 120 \text{ mg/dL} \times 165 \text{ mL/min} = 198 \text{ mg/min}$. Since all of this will be reabsorbed, the kidneys reabsorb approximately 200 mg of glucose per minute.

302–304. The answers are 302-b, 303-b, 304-c. (*Guyton, pp 355–363.*) Net acid excretion is equal to the sum of the amount of titratable acids plus the amount of the ammonium ions minus the amount of bicarbonate ions contained in the volume of urine produced per day.

$$\begin{aligned} \text{Net acid excretion} &= ([\text{titratable acids}] + [\text{NH}_4^+] - 2 [\text{HCO}_3^-]) \\ &\quad \times \text{urine volume per day} \\ &= (10 \text{ meq/L} + 20 \text{ meq/L} - 4 \text{ meq/L}) \times 1.5 \text{ L/day} \\ &= 39 \text{ meq/day} \end{aligned}$$

Acid is excreted in urine bound to titratable acids, principally phosphates, and bound to ammonia as NH_4^+ . If bicarbonate is present in urine, its amount must be subtracted because a bicarbonate ion excreted in the urine means that a hydrogen ion was left behind in the body. Conversely, a net hydrogen ion excreted means that a bicarbonate ion was left behind in the body. Thus, net acid excretion is equal to new bicarbonate formation.

The normal fixed acid production is 70 to 100 meq/day. This is eliminated by the kidneys. This patient excreted only 39 meq H^+ per day and is therefore retaining hydrogen ions. The low plasma pH (normal = 7.4) suggests an acidosis. In respiratory acidosis, renal H^+ excretion exceeds daily acid production. As a result, urine HCO_3^- is negligible and urinary pH is below 5. The low acid excretion combined with a high urinary pH suggests the presence of renal tubular acidosis (in which the kidney is unable to reabsorb HCO_3^- or secrete H^+).

305. The answer is b. (*Berne, 3/e, pp 469–470.*) Acid is produced in the body as volatile acid and nonvolatile, or fixed, acid. Volatile acid is from the CO_2 produced by aerobic metabolism in the mitochondria. This amounts to 13,000 to 24,000 mmol CO_2 and, consequently, H^+ per day. $\text{CO}_2 + \text{H}_2\text{O} \leftrightarrow \text{H}_2\text{CO}_3 \leftrightarrow \text{H}^+ + \text{HCO}_3^-$. In the lungs, this CO_2 is blown off, thus eliminating the bulk of acid produced in the body. The fixed acids

produced from other reactions in the body such as anaerobic metabolism and phospholipid and protein catabolism amount to 70 to 100 mmol per day and are excreted by the kidneys.

306. The answer is e. (*Guyton, pp 309–310.*) The clearance of PAH is a good estimate of renal plasma flow (RPF) because, under normal circumstances, almost all (more than 90%) of the PAH passing through the kidney is excreted. However, less than 90% of the PAH might be reabsorbed in a diseased kidney. An accurate measure of RPF can be obtained from the formula

$$\begin{aligned}\text{RPF} &= (U_{\text{PAH}} \times V) / (A_{\text{PAH}} - V_{\text{PAH}}) \\ &= (20 \text{ mg/mL} \times 2 \text{ mL/min}) / (0.05 - 0.005) = 88.9 \text{ mL/day}\end{aligned}$$

307. The answer is d. (*Guyton, p 309.*) If a substance disappears from the circulation during its passage through the kidney, it usually indicates that it has been totally secreted into the nephron. In this case, its clearance will be equal to the RPF. If the substance is bound to plasma proteins, it can be secreted without being filtered. Even if it is entirely secreted by the kidney, its urinary concentration may be less than its plasma concentration if the urinary flow rate is very high.

308. The answer is c. (*Guyton, pp 309–312.*) Since 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 in concentration must be due to the loss of solute. Since the material is neither reabsorbed nor secreted, its removal from the plasma must have been by glomerular filtration. Given that the filtered solute was 3 mg/mL and the renal artery concentration was 12 mg/mL, the fraction of solute filtered (and thus the fraction of solvent filtered) was $\frac{1}{4}$ or 0.25.

309. The answer is a. (*Guyton, p 322.*) Destruction of the supraoptic nuclei eliminates antidiuretic hormone (ADH) production. In the absence of ADH, the collecting ducts of the kidney are impermeable to water and therefore all of the fluid passing through the distal convoluted tubule, about 10 to 20 L of hypotonic fluid per day, is excreted in the urine.

310. The answer is e. (*Guyton, pp 358–363.*) Respiratory acidosis is caused by hypoventilation, that is, a decrease in alveolar ventilation. When

alveolar ventilation initially decreases (acute respiratory acidosis), arterial PO_2 increases, arterial pH decreases (plasma $[\text{H}^+]$ increases), and arterial PO_2 decreases. If the hypoventilation persists, the kidneys act to increase the concentration of plasma bicarbonate and excrete H^+ ions to bring the arterial concentration of hydrogen ion (pH) back toward or to normal. Alveolar ventilation, arterial PCO_2 , and arterial PO_2 remain abnormal.

311. The answer is e. (*Guyton, pp 353–355.*) The pH of the tubular fluid in the distal nephron can be lower than that in the proximal tubule because the tight junctions between the cells in the distal nephron are “tighter,” or less leaky, than those in the proximal tubule. A H^+ ion gradient of only 10 to 1 (i.e., a minimum luminal pH of about 6.4) can be established in the proximal tubule, whereas a H^+ ion gradient of 1000 to 1 (i.e., a minimum luminal pH of 4.4) can be established in the distal nephron. Because of the tighter junctions, the distal nephron can also establish a greater sodium gradient. Even though the distal nephron can maintain a lower luminal pH, a lesser volume of H^+ ions is actually secreted than in the proximal tubule. The distal nephron, unlike the proximal tubule, does not have a true brush border, and there is no carbonic anhydrase on the luminal surface of the cells as in the proximal tubule.

312. The answer is d. (*Guyton, pp 201–206.*) Renin is secreted by the juxtaglomerular cells (near the afferent arterioles) in response to decreased renal arterial pressure. It acts on angiotensinogen to form angiotensin I. Angiotensin I is then converted to angiotensin II, a highly potent pressor agent that, despite a short half-life in humans, has numerous regulatory functions, including the control of aldosterone secretion and sodium and water conservation.

313. The answer is d. (*Guyton, pp 310–311.*) The clearance of a substance by the kidney represents the volume of plasma from which the substance is completely removed, or cleared, per unit time. For creatinine,

$$\begin{aligned}\text{Creatinine clearance} &= (\text{Urine creatinine concentration} \times \text{urine flow}) \\ &\quad \div \text{Plasma creatinine concentration} \\ &= (196 \text{ mg/mL} \times 1 \text{ mL/min}) \div 1.4 \text{ mg/mL} \\ &= 140 \text{ mL/min}\end{aligned}$$

314. The answer is b. (*Guyton, pp 338–342.*) Hyperkalemia produces an increase in aldosterone secretion by the adrenal cortex. Aldosterone acts on the distal tubule to increase sodium reabsorption and enhance potassium secretion. When potassium excretion in the distal tubule is enhanced, hydrogen ion secretion, which also occurs in exchange for sodium resorption, is diminished. As hydrogen ion secretion diminishes, hydrogen ion is retained and acidosis occurs.

315. The answer is b. (*Guyton, p 311.*) The clearance of PAH equals the true renal plasma flow only if the kidney reabsorbs all of the filtered PAH, that is, no PAH appears in the renal vein. Because the kidney is only able to reabsorb approximately 85 to 90% of the filtered PAH, some PAH appears in the renal vein and the PAH clearance is less than the true renal plasma flow.

316. The answer is a. (*Guyton, pp 298–299.*) Glucose reabsorption employs an active transport mechanism located in the proximal tubule. The same mechanism also transports fructose, galactose, and xylose. Essentially all filtered glucose is reabsorbed, inasmuch as the transport maximum (T_{\max}) for glucose (320 mg/min) is not exceeded in normal persons. In diabetes mellitus, hyperglycemia results in a tubular filtration load that exceeds the T_{\max} , and glycosuria ensues.

317. The answer is c. (*Guyton, pp 300–305.*) The major structural differences between epithelial cells of the proximal and distal tubules account for the fact that 65% of glomerular filtrate is reabsorbed in the proximal tubule and that the proximal tubule is more permeable to water. The proximal tubule has an extensive brush border composed of numerous microvilli, which markedly increase the surface area for reabsorption, and the tubule also has an extensive network of intracellular channels. The distal tubule has many more tight junctions between cells, which makes it less permeable to water. No significant difference in basement membrane thickness is observed between the proximal and distal tubules. The juxtaglomerular apparatus is formed by cells of the distal tubule lying adjacent to the afferent arteriole.

318. The answer is c. (*Berne, 3/e, pp 426–427.*) Approximately two-thirds of the 40 to 150 mg of protein excreted per day by the kidney is

derived from plasma proteins. The remainder is derived from the tubular secretion of a mucoprotein, the Tamm-Horsfall protein, that is present in tubular casts appearing in urinary sediment. Not all plasma proteins are filtered equally because glomerular permeability is related to molecular size and charge. The larger and negatively charged proteins are poorly filtered. Most of the filtered protein is reabsorbed in the proximal tubule unless the filtered load exceeds the tubular capacity. Such overload would occur following damage to the glomerular basement membrane and breakdown of normal barriers, or following an increase in the plasma concentration of a small protein, such as myoglobin. Protein excretion is also increased by sympathetic stimulation, such as that occurring during exercise. In this situation, renal vasoconstriction reduces the glomerular filtration rate, which, by increasing the transit time of glomerular filtrate, favors diffusion of proteins across the basement membrane.

319. The answer is a. (*Berne, 3/e, pp 419–421.*) Renal blood flow is determined by the renal artery pressure and the resistance of the renal vascular bed. Decreasing the resistance of either the afferent or efferent arterioles could increase RBF. Alternatively, if the resistance of one of these vessels decreased more than the resistance of the other one increased, RBF would also increase. Glomerular filtration rate will increase if glomerular capillary pressure increases. This can occur if the afferent arteriolar resistance decreases or if the efferent arteriolar resistance increases.

320. The answer is c. (*Guyton, pp 269–273.*) Sweat normally contains about 40 to 60 meq of sodium per liter of fluid. Thus, approximately 100 meq of sodium will be lost from the extracellular fluid during the exercise period, and when the lost water is replenished, the extracellular fluid will become hypotonic. The hypotonic extracellular fluid will equilibrate with the intracellular fluid and make it hypotonic as well. Because the extracellular fluid volume is dependent on the amount of sodium, the loss of sodium will result in a decreased extracellular fluid volume and an increased intracellular fluid volume after water is replaced.

321. The answer is c. (*Berne, 3/e, pp 473–475.*) Ammonia (NH_3) is produced from amino acids in the cells of the renal tubules (mainly the proximal tubules), and its rate of production increases during acidosis. This is important in acidosis because it increases the total amount of H^+ ion that

can be excreted in a given volume of urine. The NH_3 freely diffuses into the tubular lumen, and because of the high pK_a (9.2) of the reaction, essentially all of it combines with H^+ to form NH_4^+ . This maintains the driving force for more NH_3 to passively diffuse into the lumen. The NH_4^+ that is formed gets “trapped” in the tubules and excreted because the tubules are impermeable to this cation.

322. The answer is d. (*Berne, 3/e, pp 458–460.*) 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 secretion by maintaining a low potassium concentration within the filtrate and thus increasing the electrochemical gradient for potassium. The presence of nonreabsorbable organic anions will increase the electrochemical gradient for K^+ and therefore increase K^+ excretion.

323. The answer is a. (*Guyton, pp 351–352.*) An increase in arterial concentration of hydrogen ion from a normal value of 40 meq/L (pH 7.4) to 50 meq/L (pH 7.3) would constitute an acidosis. Acidosis in arterial blood rapidly stimulates the peripheral chemoreceptors in the carotid and aortic bodies. If the acidosis is a respiratory acidosis (elevated PaCO_2), the central chemoreceptors would be stimulated, but since the defect (hypoventilation) would be in the respiratory system, no respiratory compensation could occur. When PaCO_2 is increased, plasma concentration of HCO_3^- is increased. Renal compensation for the acidosis causes a further increase in plasma concentration of HCO_3^- . If the acidosis is a metabolic acidosis, it takes time for the concentration of hydrogen ion in the brain's extracellular fluid to rise because of the presence of the blood-brain barrier. Therefore, the central chemoreceptors are stimulated only in chronic metabolic acidosis. Acidosis increases the formation of NH_3 in the kidney and increases the

excretion of H^+ ions as ammonium (NH_4^+) ions. As more H^+ is excreted, the pH of the urine is decreased.

324. The answer is b. (*Guyton, pp 300–302.*) Sodium is isosmotically reabsorbed from the proximal tubule; that is, when sodium is reabsorbed, water flows out of the proximal tubule to maintain a constant osmolarity. Thus, the concentration of sodium does not normally change as the filtrate flows through the proximal tubule. Since creatinine cannot be reabsorbed from the tubule, its concentration rises as water is reabsorbed. The concentrations of glucose, bicarbonate, and phosphate are all less at the end of the proximal tubule than at the beginning.

325. The answer is c. (*Guyton, pp 314–315.*) When a person is dehydrated, ADH secretion increases. In the presence of ADH, the cortical and medullary collecting tubules become permeable to water and the filtrate within these portions of the nephron reaches osmotic equilibrium with the interstitial fluid surrounding them. The ascending limb of the loop of Henle is not affected by ADH and so remains impermeable to water. As sodium and other electrolytes are reabsorbed from the ascending limb, its filtrate becomes hypotonic. The glomerular filtrate and proximal tubular fluid remain isotonic to plasma, which in the case of dehydration is higher than normal.

326. The answer is c. (*Guyton, pp 302–303.*) In the ascending limb of the loop of Henle, sodium is actively transported by a transporter that has one binding site for sodium, one binding site for potassium, and two binding sites for chloride. Thus, the transport of sodium is electrically neutral. Electrically neutral sodium transport also occurs in the distal convoluted tubule and connecting segment by a carrier that binds both sodium and chloride. In all other segments of the nephron, however, sodium transport is electrogenic; that is, sodium is transported unaccompanied by a negatively charged chloride ion.

327. The answer is b. (*Guyton, pp 362–363.*) 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 consump-

tion 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 $\text{plasma } [\text{Na}^+] - (\text{plasma } [\text{HCO}_3^-] + \text{plasma } [\text{Cl}^-])$, and is normally about 12 to 15 meq/L. The acidosis would stimulate the carotid body chemoreceptors (and eventually the central 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.

328. The answer is e. (*Berne, 3/e, pp 419–421.*) Renal plasma flow, filtration fraction, the oncotic pressure, and the filtration rate all increase when the afferent arteriolar resistance is decreased. The renal blood flow increases because total renal resistance is less. Decreasing renal resistance also increases the glomerular capillary pressure, which results in an increase in filtration fraction. Because more fluid is filtered out of the glomerular capillaries and no plasma protein is removed, the oncotic pressure rises. The glomerular filtration rate (GFR) is proportional to the glomerular capillary pressure and the renal plasma flow (RPF). Since both of these increase, so does the GFR.

329. The answer is c. (*Berne, 3/e, pp 430–432.*) When water is filtered across the glomerulus, the protein concentration (the oncotic pressure) within the capillaries increases, which in turn increases the efficiency by which water reabsorbed from the proximal tubule is returned to the circulatory system. If GFR increases, it results in a larger increase in oncotic pressure. This in turn increases the amount of water reabsorbed from the proximal tubule.

330. The answer is e. (*Berne, 3/e, pp 772–774. Guyton, pp 200–202, 290–292.*) Juxtaglomerular (JG) cells are sensitive to changes in afferent arterial intraluminal pressure. Increased pressure within the afferent arteriole leads to a decrease in renin release, while decreased pressure tends to increase renin release. Angiotensin appears to inhibit renin release by initiating the flow of calcium into the JG cells. Renin release is increased in response to increased activity in the sympathetic neurons innervating the kidney. Prostaglandins, particularly 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.

331. The answer is d. (*Guyton, pp 373–376.*) Most urea is synthesized in the liver. Its excretion is dependent on its concentration in plasma and the glomerular filtration rate (GFR) in the kidney. Approximately 50 to 60% of filtered plasma urea is passively reabsorbed in the proximal tubule at normal GFR. In renal insufficiency, in which GFR is decreased, less urea is filtered and therefore less urea is excreted. The decreased excretion of urea results in an increase in its plasma concentration.

332. The answer is b. (*Berne, 3/e, pp 569–570.*) Aldosterone binds to an intracellular receptor that causes an increased synthesis of a variety of proteins, including K^+ and Na^+ ion channels and Na^+-K^+ -ATPase, which together act to increase Na^+ reabsorption and K^+ secretion by the tubular cells of the distal nephron. H^+ secretion is also enhanced by aldosterone. Aldosterone secretion is stimulated by a decrease in blood volume (through the renin-angiotensin system) and by increased plasma K^+ concentrations. High blood pressure, if it has any effect on aldosterone, will cause a decrease in its secretion.

333. The answer is a. (*Berne, 3/e, pp 438–440, 539.*) The principal physiologic action of antidiuretic hormone (ADH) is to increase water retention by the kidney. The hormone acts on the distal nephron to increase its permeability so that water more readily enters the hypertonic interstitium of the renal pyramids. Thus, the concentration of solutes in the urine is increased. ADH increases Na^+ reabsorption so that the actual amount of Na^+ excreted is decreased. It also acts as a vasoconstrictor; hence, it is called *arginine vasopressin* (AVP). ADH has no effect on glomerular filtration rate, and because it increases water reabsorption, it would decrease urine formation.

334. The answer is b. (*Berne, 3/e, p 394.*) K^+ is present in gastrointestinal fluids. Excessive loss of these fluids, as in diarrhea, will lead to hypokalemia. Hyperosmotic extracellular fluid pulls K^+ from the intracellular fluid by solvent drag. Because the concentration of K^+ in the intracellular fluid is greater than that in the extracellular fluid, the transfer of fluid from the intracellular to the extracellular fluid causes hyperkalemia. In

metabolic acidosis, H^+ is transported from the extracellular fluid to the intracellular fluid in exchange for K^+ , leading to an increase in extracellular K^+ . Aldosterone is necessary for normal K^+ excretion. When the adrenal gland fails to produce adequate amounts of aldosterone, K^+ accumulates in the extracellular fluid.

335. The answer is b. (*Guyton, pp 319–320.*) The countercurrent multiplier enables the kidney to excrete concentrated urine by increasing the tonicity of the medullary interstitium. If the water permeability of the collecting ducts is increased, the fluid flowing through the collecting ducts reaches osmotic equilibrium with the high tonicity of the medullary interstitium resulting in the excretion of concentrated urine. Anything that reduces the ability of the countercurrent multiplier to increase the tonicity of the medullary interstitium, such as increasing the flow of fluid through the loop of Henle or decreasing the activity of the Na-K pump in the thick ascending limb, will decrease the ability of the kidney to excrete a concentrated urine. Increasing the glomerular capillary pressure increases the GFR and makes it more difficult for the kidney to excrete concentrated urine.

336. The answer is d. (*Guyton, pp 286–288.*) The amount of fluid filtered by the glomerulus (the GFR) will increase if filtration pressure rises or plasma oncotic pressure decreases. Decreasing the plasma protein concentration decreases the capillary oncotic pressure, which leads to an increase in GFR. If the afferent arteriolar resistance increases without an increase in perfusion pressure, the pressure within the glomerulus will decrease, causing a decrease in GFR. A similar result will occur if the efferent arteriolar resistance falls. Increasing sympathetic nerve activity to the kidney decreases renal blood flow and increases Na^+ and water reabsorption from the proximal tube, making it easier for the kidney to excrete concentrated urine.

337. The answer is a. (*Guyton, pp 360, 873.*) Metabolic alkalosis is caused by the loss of nonvolatile, or fixed, acid from the body. An increased aldosterone secretion will cause an increase in H^+ secretion from the distal nephron, resulting in metabolic alkalosis. 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 accu-

mulation of keto acids. Hyperventilation results in a respiratory alkalosis, which is compensated for by a decreased excretion of acid by the kidneys, resulting in a metabolic acidosis.

338. The answer is b. (*Berne, 3/e, p 439.*) The increased secretion of antidiuretic hormone (ADH) increases the permeability of the distal nephron to water and therefore increases the reabsorption of water from the kidney. The excessive reabsorption of water dilutes the extracellular fluid, producing a decrease in plasma sodium, osmolarity, and oncotic pressure. The decreased extracellular osmolarity causes water to flow from the extracellular fluid compartment into the intracellular fluid compartment, increasing intracellular volume. Because more water is being reabsorbed, less is excreted and urinary flow is decreased.

339. The answer is c. (*Berne, 3/e, pp 423–425, 428–429.*) 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^- .

340. The answer is c. (*Berne, 3/e, pp 417–419.*) The macula densa senses the chloride concentration of the fluid flowing from the ascending limb of Henle's loop into the distal convoluted tubule. An increase in NaCl concentration occurs when the amount of fluid flowing through the ascending limb increases because there is less time available for the reabsorption of NaCl . The resulting increase in Cl^- concentration results in the release of adenosine from the macula densa. Adenosine constricts the afferent arteriole resulting in a decrease in filtration and a return of the flow rate within

the nephron toward normal. This response is referred to as *tubuloglomerular feedback*. If NaCl concentration decreases, for example, when circulating blood volume decreases, the decreased Cl^- concentration results in the release of renin from granular cells of the juxtaglomerular apparatus.

341. The answer is a. (Guyton, pp 360–361, 872–874.) Hypoadosteronism (Addison's disease) results in a decrease in H^+ secretion, which leads to the production of a metabolic acidosis. Hyperventilation produces a respiratory acidosis, which is compensated for by an increase in bicarbonate reabsorption, yielding a metabolic alkalosis. Hypokalemia causes an increase in K^+ reabsorption and an increase in H^+ secretion, resulting in a metabolic alkalosis. Hypovolemia results in an increase in aldosterone secretion, which can lead to an increase in H^+ secretion and a metabolic alkalosis.

342. The answer is e. (Guyton, pp 340–341.) The synthesis and secretion of aldosterone are dependent primarily upon the renin-angiotensin system. Increased potassium concentration directly stimulates aldosterone secretion. Increased circulating blood volume leads to a decrease in renin secretion and therefore a decrease in aldosterone secretion. The role of adrenocorticotrophic hormone (ACTH) in aldosterone synthesis and secretion is negligible.

343. The answer is c. (Guyton, pp 332–333.) The rate of fluid volume excretion is influenced by the glomerular filtration rate (GFR) and the rate of tubular reabsorption. Increased renal arterial pressure increases urinary volume by increasing GFR, whereas sympathetic stimulation, by causing vasoconstriction, decreases both GFR and urinary volume. An increase in the filtered load of an osmotically active solute that is not reabsorbed, such as the nonmetabolized carbohydrate mannitol, or that is filtered in excess of the tubular capacity, such as glucose in diabetes mellitus, will decrease water resorption in parallel, and an osmotic diuresis will ensue. In diabetes insipidus, ADH secretion is markedly reduced or absent and water passes through the relatively impermeable collecting ducts without being reabsorbed.

344. The answer is c. (Rhoades, pp 467–469.) A large amount of volatile acid (carbon dioxide) is produced by aerobic metabolism. The lungs excrete almost all of the CO_2 as it is formed. Nonbicarbonate buffers, pri-

marily hemoglobin, buffer any CO_2 that accumulates in the blood. Phosphate, lactate, and plasma proteins are also nonbicarbonate buffers, but they buffer only a small portion of the volatile acid dissolving in the blood.

345. The answer is d. (*Guyton, pp 367–368.*) Diuretics produce an increase in water excretion primarily by blocking Na^+ reabsorption. If Na^+ reabsorption is blocked in the proximal portions of the nephron, then the amount of Na^+ in the filtrate flowing through the distal nephron increases. The increased Na^+ load in the distal nephron results in an increased Na^+ reabsorption and, as a result, an increased K^+ secretion. If Na^+ reabsorption in the distal nephron is blocked, then a diuresis can be produced without an excess loss of K^+ . These diuretics, some of which block the aldosterone receptor, others of which block the Na channels on the apical surface of the distal nephron tubular cells, are called *potassium-sparing diuretics*.

346. The answer is a. (*Guyton, pp 367–368.*) The increase in blood glucose concentration will result in a filtered load of glucose in excess of what the proximal tubule is able to absorb. As a result, glucose will remain in the filtrate, where it will act as an osmotic diuretic increasing urinary flow. The excess blood glucose will cause water to shift from the intracellular compartment to the extracellular compartment causing a decrease in intracellular volume and, by dilution, a decrease in plasma sodium concentration. The accompanying increase in ketoacid production will result in a metabolic acidosis (low pH) and a compensatory increase in alveolar ventilation, lowering alveolar PCO_2 .

347. The answer is c. (*Guyton, pp 358–360.*) Persistent diarrhea will result in a metabolic acidosis, due to the loss of the bicarbonate-rich secretions from the pancreas and gallbladder. The ensuing metabolic acidosis will decrease the plasma concentration of 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.

348. The answer is e. (*Guyton, p 319.*) ADH increases the permeability of the distal nephron to urea as well as to water. The increased urea per-

meability 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.

349. The answer is c. (*Guyton, pp 284–287.*) The filtration fraction is directly proportional to the glomerular capillary pressure. Increasing the resistance of the efferent arteriole increases the glomerular capillary pressure and, therefore, the filtration fraction. Increasing renal blood flow will not have any direct effect on the filtration fraction but may cause the filtration fraction to decrease if the excess flow rate through the glomerulus limits the amount of filtration that can occur. Increasing the afferent arteriolar resistance will decrease glomerular capillary pressure and, therefore, the filtration fraction. Increasing the plasma oncotic pressure or the hydrostatic pressure within Bowman's capsule will decrease the filtration fraction because both of these Starling forces oppose filtration.

350. The answer is a. (*Berne, 3/e, pp 470–472.*) Under normal circumstances, the kidney reabsorbs enough bicarbonate to keep the plasma concentration at 24 meq/L and excretes the rest. Therefore, bicarbonate concentrations cannot be increased very much by infusing HCO_3^- . An increase in plasma bicarbonate concentration requires a deficit in the normal excretory function or, what amounts to the same thing, an increase in bicarbonate reabsorptive capacity. 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. Renal failure, hypoxemia, and diarrhea all produce metabolic acidosis accompanied by a decreased plasma bicarbonate concentration.

351. The answer is d. (*Berne, 3/e, pp 417–418.*) Blood flow through the kidney is controlled by a myriad of humoral agents. Adenosine acts via A_2 receptors to increase afferent arteriolar resistance and thereby decrease renal blood flow. Nitric oxide dilates the afferent arteriole and constricts the efferent arteriole, producing a rise in glomerular capillary pressure (and glomerular filtration) without having much of an effect on renal blood flow.

Prostaglandins, bradykinin, and dopamine all increase renal blood flow. Cyclooxygenase inhibitors, such as aspirin, that decrease prostaglandin synthesis may impair renal blood flow sufficiently to exacerbate the effects of renal failure.

352. The answer is a. (*Guyton, pp 367–369.*) 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 prevent the formation of CO_2 and therefore block the reabsorption of bicarbonate (and Na^+), resulting in a diuresis. Since 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.

353. The answer is b. (*Rhoades, pp 455–456.*) 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 K^+ concentration.

354. The answer is b. (*Guyton, pp 357–360.*) The analysis of blood gases can suggest the presence of an acid-base disturbance, but an exact diagnosis requires a knowledge of the complete clinical condition. A metabolic acidosis is characterized by a lower than normal pH (acidemia) accompanied by a decrease in bicarbonate and a decrease in arterial PCO_2 . The lower than normal bicarbonate concentration (less than 24 meq/L) is produced by the buffering of fixed acids by bicarbonate, and the lower than normal arterial PCO_2 (less than 40 mmHg) is produced by respiratory compensation for the acidemia. If the acidemia is accompanied by a higher than normal arterial PCO_2 and a higher than normal bicarbonate concentration, respiratory acidosis is the most likely cause.

355. The answer is a. (*Guyton, pp 336–342.*) Hyperkalemia can be caused by increased consumption or decreased excretion. Pathophysiologically, chronic hyperkalemia is almost always due to decreased excretion. Decreased excretion most commonly occurs in renal failure of volume

depletion. The amount of potassium excreted each day depends primarily on the amount of potassium secreted by the distal nephron. Secretion will decrease in renal failure because there are less functional nephrons (although the functioning nephrons secrete a greater amount of potassium). Hypokalemia can result from an increase in excretion, as may occur when diuretics are administered. Hypokalemia can also result from sequestration of extracellular potassium into cells, as may occur in metabolic alkalosis, elevated epinephrine concentration, or administration of insulin.

356. The answer is a. (*Guyton, pp 359–363, 496–498.*) When a person ascends to high altitudes, the low oxygen produces hypoxemia which can produce a respiratory alkalosis (low PCO_2) and a metabolic (lactic) acidosis. Both the compensation for the respiratory alkalosis and the lactic acidosis will lower the plasma bicarbonate concentration. The only set of blood gases with low PCO_2 and low bicarbonate is located at point A on the graph.

357. The answer is d. (*Guyton, pp 300–302.*) The proximal tubule reabsorbs approximately two-thirds of the filtered water and two-thirds of the filtered Na^+ , Cl^- , and K^+ . Therefore, the concentration of these substances is the same at the beginning and end of the proximal tubule. Because creatinine is not reabsorbed, its concentration increases from the proximal to distal ends of the proximal tubule. Phosphate, however, is almost completely reabsorbed in the proximal tubule, so its concentration decreases along the length of the tubule.

358. The answer is d. (*Guyton, pp 300–302.*) About two-thirds of the filtered load of sodium is reabsorbed by the proximal tubule. This percentage is maintained when there are spontaneous changes in the filtered load by a process called *glomerular tubular balance*. However, the percentage of reabsorption can be changed when necessary to maintain homeostasis. For example, the production of angiotensin II during volume depletion can result in the reabsorption of as much as 75% of the filtered load of Na^+ .

359. The answer is e. (*Berne, 3/e, pp 436–439.*) ANP increases Na^+ excretion by decreasing the amount of Na^+ reabsorbed from the inner medullary collecting duct by decreasing the permeability of the apical membrane of

the collecting duct epithelial cells. Less Na^+ is able to enter the epithelial cells and therefore, less Na is reabsorbed. ANP also increases Na^+ excretion by increasing the filtered load of Na^+ .

360. The answer is c. (Guyton, pp 321–322.) 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 $C_{\text{H}_2\text{O}} = V \times [1 - (U_{\text{Na}} + U_{\text{K}})/P_{\text{Na}}]$. Free water clearance is positive when the urine is dilute (more than a sufficient amount of water is excreted), and free water clearance is negative when the urine is concentrated (not enough water is excreted to make the urine isotonic to plasma). An increase in free water clearance can lead to hypernatremia; a decrease in free water clearance can lead to hyponatremia. In diabetes insipidus, very little water is reabsorbed in the distal nephron, and, therefore, the free water clearance is very high. In heart failure or renal failure, very little free water can be generated even if the urine is dilute because the glomerular filtration rate is decreased. With diuretic therapy, Na^+ excretion is increased. Therefore, the increased water excretion is accompanied by an increased Na^+ excretion and the amount of free water generated is limited. Although the water loss is proportionally greater than the solute loss in diabetes mellitus, the amount of water excreted is much less and the solute concentration significantly higher than in diabetes insipidus, so the free water clearance is much less in diabetes mellitus than in diabetes insipidus.

361. The answer is b. (Guyton, pp 900–901, 907–910.) Between 85 and 90% of the filtered phosphate is reabsorbed in the proximal tubule by a sodium-dependent secondary active transport system. The transporter is electrically neutral, requiring 2 Na^+ molecules for every HPO_4^{2-} molecule that it transports. The transporter is inhibited by parathyroid hormone (PTH). The decreased reabsorption of phosphate results in an increased clearance from the plasma. PTH is released from the parathyroid gland in response to lowered plasma Ca^{2+} concentrations. In addition to inhibiting the reabsorption of phosphate from the proximal tubule, PTH increases the reabsorption of Ca^{2+} from the loop of Henle.

362. The answer is a. (Berne, 3/e, p 439.) Vasopressin (AVP or ADH) increases water reabsorption from the cortical and medullary collecting ducts in the kidney. ADH is normally released in response to a rise in

plasma Na^+ concentration and therefore the increased water reabsorption appropriately restores extracellular osmolarity toward normal. When excess ADH is excreted, the water reabsorption dilutes the extracellular fluid, producing hyponatremia. This condition is called the *syndrome of inappropriate ADH secretion* (SIADH) and can be life-threatening.

363. The answer is b. (*Berne, 3/e, pp 460–461.*) Potassium is secreted from the principle 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 principle cells. Increasing Na^+ concentration within the distal nephron increases Na^+ reabsorption, which, in turn, increases the negativity of the luminal electrical potential. The increased negativity drives K^+ into the lumen at a greater rate. Decreasing the distal flow rate, which occurs when circulating blood volume or renal blood 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.

364. The answer is d. (*Berne, 3/e, pp 417–418, 446–449.*) The juxtaglomerular apparatus (JGA) is responsible for releasing renin when the effective circulating blood volume is decreased. The JGA releases renin when the Cl^- concentration in the luminal fluid bathing the macula densa is decreased. The decrease in Cl^- (and Na^+) concentration occurs when the flow rate within the nephron decreases and ample time is available for the loop of Henle to remove NaCl from the lumen. Adenosine is released from the macula densa cells when the luminal Cl^- concentration increases in response to an increase in luminal flow rate. Adenosine decreases flow rate by constricting the afferent arteriole and, therefore, the blood flow through the glomerular capillary.

365–367. The answers are 365-d, 366-e, 367-b. (*Guyton, pp 313–315, 353–355. Berne, 3/e, pp 423–425.*) The ascending limb dilutes the fluid within the nephron by reabsorbing Na^+ without water. In the presence of ADH, the distal nephron becomes permeable to water. Water is reabsorbed along the length of the distal nephron, making the luminal fluid isotonic in the cortical collecting ducts and hypertonic in the medullary

collecting ducts. In the absence of ADH, Na is reabsorbed without water, making the luminal fluid even more dilute than it was at the top of the loop of Henle.

Each H^+ ion excreted by the kidney results in the addition of one “new bicarbonate” ion to the plasma. The H^+ secreted by the intercalated cells that line the cortical and medullary collecting ducts is buffered by ammonia and titratable acids and excreted in the urine. The H^+ secreted by the proximal tubule is reabsorbed in association with bicarbonate and does not result in the production of new bicarbonate ions.

At the end of the proximal tubule, the Cl^- concentration in the lumen is higher than the Cl^- concentration in the surrounding interstitium. The high Cl^- concentration at the end of the proximal tubule develops because Cl^- is not reabsorbed at the beginning of the proximal tubule, where bicarbonate is reabsorbed with Na^+ . As a result of the high Cl^- concentration, Cl^- can diffuse through the tight junctions between the epithelial cells lining the proximal tubule. The passive diffusion of Cl^- from the lumen to the interstitium creates a positive potential within the lumen that drives Na^+ out of the lumen and into the interstitium. Na^+ is also reabsorbed passively from the thin ascending limb of Henle’s loop.

368. The answer is d. (*Guyton, pp 371–376.*) The excretion of creatinine, which is neither reabsorbed nor secreted in any significant amount, is dependent on filtration, which is in turn dependent on renal plasma flow. The decrease in renal plasma flow that accompanies chronic renal failure results in a decrease in creatinine excretion and an increase in plasma creatinine concentration. The increase in plasma creatinine concentration is used to assess the percentage of nonfunctioning nephrons in renal failure. Interestingly, the remaining nephrons adapt to renal failure. To maintain Na^+ balance, less Na^+ is reabsorbed, so the fractional excretion (the fraction of filtered Na^+ that is excreted) goes up. Although the remaining nephrons are able to excrete a larger than normal amount of H^+ , secretion cannot fully compensate for the reduced number of nephrons because there is a limit to the amount of NH_4^+ that can be synthesized by the proximal tubules. Therefore, despite the overall increase in net acid excretion, H^+ accumulation leads to a metabolic acidosis. Even creatinine secretion can be increased so the plasma creatinine concentration does not increase proportionally to the amount of renal damage. The anion gap increases because of the reduced excretion of phosphate and other anions that are

included in the anion gap. Free water clearance decreases because there is a decreased filtration. Therefore, to prevent overhydration in patients with renal failure, water intake must be limited.

369. The answer is c. (*Guyton, pp 264–266.*) 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 (three-quarters of extracellular fluid, or 15% of body mass) and plasma water (one-fourth 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. Seventy-three percent of the lean body mass (mass excluding fat) is water. The distribution of extracellular and intracellular water is a function of the extracellular osmolarity. If the osmolarity of the extracellular fluid is above normal, the proportion of water in the extracellular fluid, in comparison to that in the intracellular water, increases; hypotonicity of the extracellular water decreases the proportion of water in the extracellular fluid.

370. The answer is c. (*Gutyon, pp 375–376, 385–386.*) The kidney produces a number of important hormones including vitamin D and erythropoietin. Erythropoietin is necessary for the normal production of red blood cells. The anemia associated with renal failure results from the decrease in the synthesis of erythropoietin. Often, the first clinical sign of renal failure is the fatigue produced by anemia.

371. The answer is c. (*Gutyon, pp 360–363.*) Increasing bicarbonate concentration in the plasma results in a metabolic alkalosis. To compensate for the alkalosis, the respiratory system decreases alveolar ventilation. Therefore, an increase in plasma bicarbonate and arteriolar PCO_2 is characteristic of metabolic alkalosis. The respiratory system will not allow arteriolar PCO_2 to increase much above 50 mmHg, so respiratory compensation for a metabolic alkalosis is limited. A similar limitation is not present when metabolic acidosis occurs, so respiratory compensation can reduce arteriolar PCO_2 to below 10 mmHg. Although NaHCO_3^- ingestion does not typically cause metabolic alkalosis, its use is not recommended because alkalosis may occur and because it may result in Na^+ retention.

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Endocrine Physiology

Questions

DIRECTIONS: Each question below contains five suggested responses. Select the **one best** response to each question.

372. The supraoptic nucleus of the hypothalamus is believed to control secretion of which of the following hormones?

- a. Antidiuretic hormone (arginine vasopressin)
- b. Oxytocin
- c. Growth hormone
- d. Adrenocorticotrophic hormone
- e. Follicle-stimulating hormone

373. Parathyroid hormone (PTH) is accurately described by which of the following statements?

- a. It is secreted in response to an increase in plasma Ca^{2+} concentration
- b. It acts directly on bone cells to increase Ca^{2+} deposition
- c. It acts directly on intestinal cells to increase Ca^{2+} absorption
- d. It causes a decrease in cAMP concentration within renal proximal tubular cells
- e. It is essential for life

374. When a person is in the fasting state,

- a. Liver glycogen levels are increased
- b. The excretion of urea in the urine decreases
- c. Basal metabolic rate (BMR) decreases
- d. Glucose is the only fuel used by the central nervous system
- e. Gluconeogenesis is inhibited

375. True statements regarding atrial natriuretic hormone (ANH) include that it

- a. Is synthesized from cholesterol
- b. Is secreted in response to hypovolemia
- c. Increases total peripheral resistance
- d. Decreases glomerular filtration rate
- e. Inhibits aldosterone secretion

376. Which one of the following statements about spermatogenesis is correct?

- a. Production and release of spermatozoa is cyclical
- b. Sertoli cells are required for mitotic and meiotic activity of germ cells
- c. Spermatogenesis requires continuous release of gonadotropin-releasing hormone (GRH)
- d. Leydig cell secretion of testosterone requires follicle-stimulating hormone (FSH)
- e. Luteinizing hormone (LH) acts directly on Sertoli cells to promote cell division

377. The secretion of growth hormone is increased by

- a. Hyperglycemia
- b. Exercise
- c. Somatostatin
- d. Hypothermia
- e. Free fatty acid

378. The source of estrogen and progesterone during the last seven months of pregnancy is the

- a. Ovary
- b. Placenta
- c. Corpus luteum
- d. Anterior pituitary
- e. Posterior pituitary

379. The source of estrogen and progesterone during the first two months of pregnancy is the

- a. Ovary
- b. Placenta
- c. Corpus luteum
- d. Anterior pituitary
- e. Posterior pituitary

380. Which one of the following hormones is secreted by the posterior pituitary gland?

- a. Adrenocorticotrophic hormone (ACTH)
- b. Oxytocin
- c. Thyroid-stimulating hormone (TSH)
- d. Growth hormone (GH)
- e. Prolactin

381. Which one of the following statements about prolactin is correct?

- a. Prolactin initiates ovulation
- b. Prolactin causes milk ejection during suckling
- c. Prolactin inhibits the growth of breast tissue
- d. Prolactin secretion is tonically inhibited by the hypothalamus
- e. Prolactin secretion is increased by dopamine

382. The principal steroid secreted by the fetal adrenal cortex is

- a. Cortisol
- b. Corticosterone
- c. Dehydroepiandrosterone
- d. Progesterone
- e. Pregnenolone

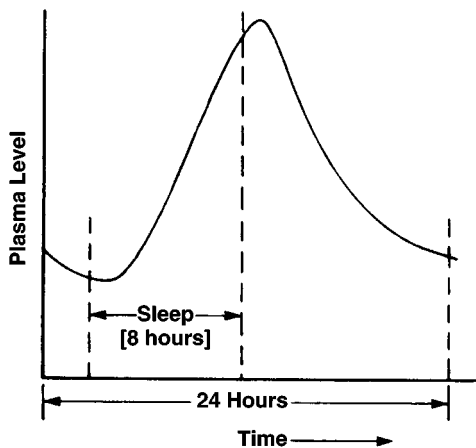
383. The effect of insulin on glucose transport is to

- a. Permit transport against a concentration gradient
- b. Enhance transport into adipocytes
- c. Enhance transport across the tubular epithelium of the kidney
- d. Enhance transport into the brain
- e. Enhance transport through the intestinal mucosa

384. Compared with the resting state, during prolonged exercise, the caloric needs of skeletal muscle are met by

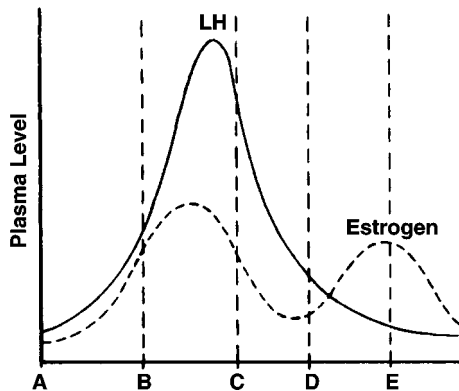
- a. Release of free fatty acids from adipose tissue
- b. An increase in hepatic glycogenolysis
- c. An increase in gluconeogenesis in muscle
- d. Increased intestinal uptake of glucose and amino acids
- e. Increased chylomicron formation

385. The graph below demonstrates diurnal variation in the plasma level of



- a. Thyroxine
- b. Insulin
- c. Parathyroid hormone
- d. Cortisol
- e. Estrogen

386. 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?

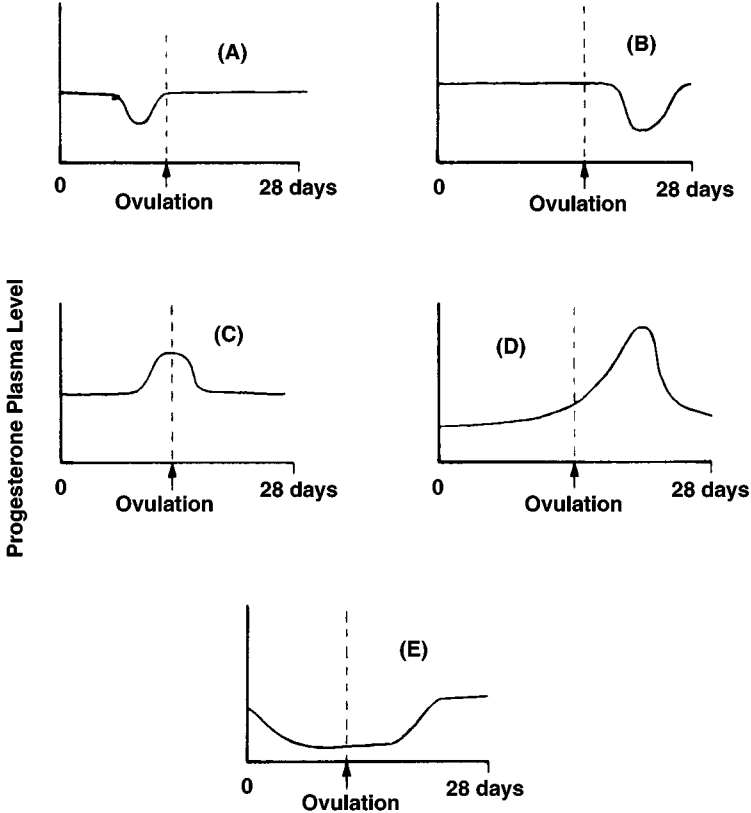


- a. A
- b. B
- c. C
- d. D
- e. E

387. Iodides are stored in the thyroid follicles mainly in the form of

- a. Thyroxine
- b. Thyroglobulin
- c. Monoiodotyrosine
- d. Diiodotyrosine
- e. 3,5,3'-triiodothyronine

388. The normal pattern of progesterone secretion during the menstrual cycle is exhibited by which of the curves shown below?



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

389. Almost all of the active thyroid hormone entering the circulation is in the form of

- a. Triiodothyronine
- b. Thyroxine
- c. Thyroglobulin
- d. Thyrotropin
- e. Long-acting thyroid stimulator (LATS)

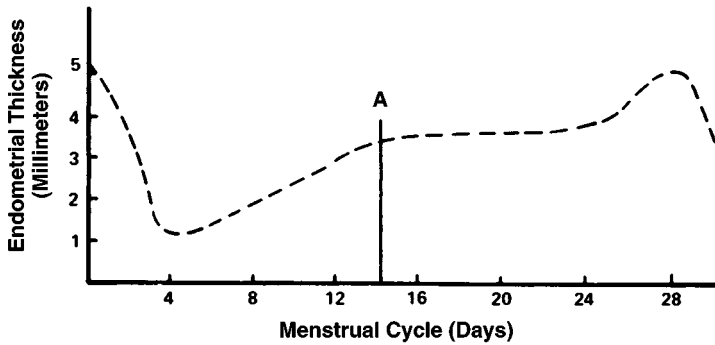
390. Physiologically active thyroxine exists in which of the following forms?

- a. Bound to albumin
- b. Bound to prealbumin
- c. Bound to globulin
- d. As a glucuronide
- e. Unbound

391. Ovulation is caused by a sudden increase in the secretion of

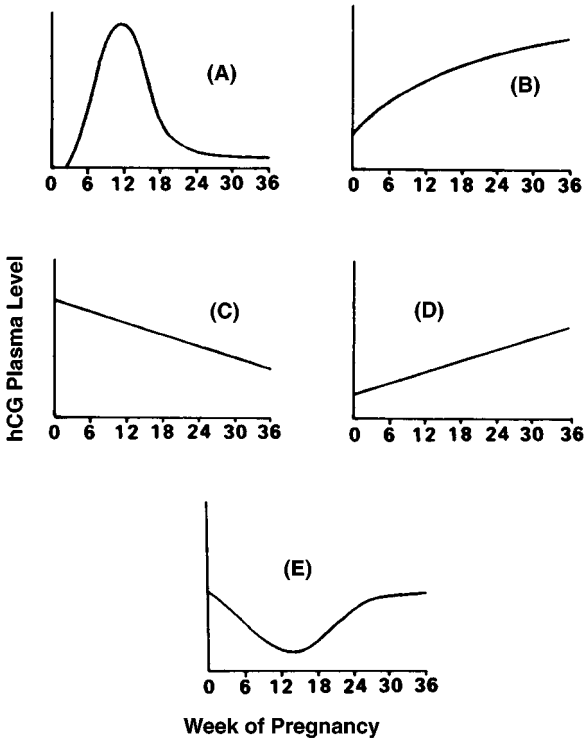
- a. Estrogen
- b. Progesterone
- c. LH
- d. FSH
- e. Prolactin

392. In the following graph of changes in endometrial thickness during a normal 28-day menstrual cycle, the event designated “A” corresponds most closely to



- a. The menstrual phase
- b. The maturation of the corpus luteum
- c. The early proliferative phase
- d. The secretory phase
- e. Ovulation

393. In a normal pregnancy, human chorionic gonadotropin (hCG) prevents the involution of the corpus luteum that normally occurs at the end of the menstrual cycle. Which of the curves shown below approximates the level of this hormone during pregnancy?



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

394. Activation of hormone-sensitive lipase in adipocytes

- a. Causes increased hydrolysis of cholesterol esters
- b. Is mediated by a cyclic AMP-dependent protein kinase
- c. Is prevented by cortisol
- d. Is stimulated by insulin
- e. Results in accumulation of monoglycerides and diglycerides in adipocytes

395. Which of the following is a correct statement about the production of human sperm?

- a. Spermatogonia undergo meiosis
- b. Spermatogenesis occurs in the epididymis
- c. Normally, 10 to 20 million sperm are produced daily
- d. FSH is required
- e. Complete maturation of spermatozoa occurs in about 1 month

396. Functions of the Sertoli cells in the seminiferous tubules include

- a. Secretion of FSH into the tubular lumen
- b. Secretion of testosterone into the tubular lumen
- c. Maintenance of the blood-testis barrier
- d. Synthesis of estrogen after puberty
- e. Expression of surface LH receptors

397. An indication that ovulation has taken place is

- a. An increase in serum FSH levels
- b. A drop in body temperature
- c. An increase in serum LH levels
- d. An increase in serum progesterone levels
- e. An increase in serum estrogen levels

398. The hormone involved in the ejection of milk from a lactating mammary gland is

- a. Prolactin
- b. FSH
- c. LH
- d. Growth hormone
- e. Oxytocin

399. Plasma levels of calcium can be increased most rapidly by the direct action of parathyroid hormone on the

- a. Kidney
- b. Intestine
- c. Thyroid gland
- d. Bones
- e. Skeletal musculature

400. Correct statements about human growth hormone include which of the following?

- a. It is synthesized in the hypothalamus
- b. It stimulates production of somatomedins by the liver
- c. Its release is stimulated by somatostatin
- d. It causes a decrease in lipolysis
- e. It is deficient in acromegaly

401. The basic effects of growth hormone on body metabolism include

- a. Decreasing the rate of protein synthesis
- b. Increasing the rate of use of carbohydrate
- c. Decreasing the mobilization of fats
- d. Increasing the use of fats for energy
- e. Inhibition of insulin-like growth factor 1

402. Which of the following is true about the actions of glucagon?

- a. It stimulates glycogenolysis in muscle
- b. It inhibits insulin secretion
- c. It stimulates gluconeogenesis in the liver
- d. It inhibits adenyl cyclase
- e. It inhibits phospholipase C

403. The actions of insulin include

- a. Converting glycogen to glucose
- b. Stimulating gluconeogenesis
- c. Increasing plasma amino acid concentration
- d. Enhancing potassium entry into cells
- e. Reducing urine formation

404. The secretion of ACTH is correctly described in which of the following statements?

- a. It shows circadian rhythm in humans
- b. It is decreased during periods of stress
- c. It is inhibited by aldosterone
- d. It is stimulated by glucocorticoids
- e. It is stimulated by epinephrine

405. Injection of thyroid hormone into a human subject will

- a. Decrease the rate of oxygen consumption
- b. Increase muscle protein synthesis
- c. Decrease the need for vitamins
- d. Increase the plasma concentration of cholesterol
- e. Decrease the rate of lipolysis

406. The effects of primary hyperaldosteronism (Conn's syndrome) include

- a. Hypertension
- b. Hyperkalemia
- c. Decreased extracellular fluid volume
- d. Increased concentrating ability of the kidney
- e. Increased hematocrit

407. Hyperparathyroidism decreases the plasma levels of

- a. Phosphate
- b. Sodium
- c. Calcium
- d. Potassium
- e. Calcitonin

408. Adrenalectomy is associated with

- a. Hyperglycemia with decreased insulin sensitivity
- b. Increased mobilization and utilization of fatty tissues
- c. Augmented water excretion by the kidneys and sodium loss in the urine
- d. Improved resistance to infection or shock
- e. Euphoria

409. Hyperthyroidism is characterized by

- a. Anorexia
- b. Increased basal metabolic rate
- c. Bradycardia
- d. Increased weight gain
- e. Decreased sweating

410. Insulin-independent glucose uptake occurs in

- a. Adipose tissue
- b. Cardiac muscle
- c. Skeletal muscle
- d. The brain
- e. The uterus

411. Which one of the following statements is correct?

- a. About 100 mg of iron is absorbed per day
- b. Iron is absorbed rapidly from the small intestine
- c. Iron is transported in the blood bound to transferrin
- d. In general, iron must be oxidized from the ferrous to the ferric state for efficient absorption
- e. Iron absorption is a passive process regulated by plasma iron levels

412. The actions of angiotensin II include

- a. Vasodilation of peripheral arterioles
- b. Promotion of salt excretion by renal tubules
- c. Decreased aldosterone secretion
- d. Increased renin secretion
- e. Initiation of thirst

413. A person with hypothyroidism would exhibit

- a. Tachycardia
- b. Increased metabolic rate
- c. Heat intolerance
- d. Sleepiness
- e. Decreased body mass index

414. Assuming a regular menstrual cycle of 28 to 30 days, ovulation would be expected to occur between

- a. Days 6 and 8
- b. Days 10 and 12
- c. Days 14 and 16
- d. Days 18 and 20
- e. Days 22 and 24

415. Secretion of growth hormone is stimulated by

- a. Increased plasma glucose levels
- b. Deep sleep
- c. Free fatty acids
- d. Somatostatin
- e. Hyperglycemia

416. Interaction of insulin with its membrane receptor

- a. Affects transmembrane ion transport
- b. Inhibits tyrosine phosphorylation of the receptor molecule
- c. Reduces cellular glucose uptake
- d. Enhances binding of additional glucose molecules
- e. Stimulates synthesis of additional receptor molecules

417. The uptake of triglycerides into adipose tissue from plasma lipoproteins

- a. Is regulated by the activity of lipoprotein lipase
- b. Is increased by catecholamines
- c. Is decreased by glucose
- d. Is decreased by insulin
- e. Requires receptor-mediated endocytosis

418. Implantation of the zygote in the uterine wall

- a. Precedes formation of the zona pellucida
- b. Involves infiltration of the endometrium by the syncytiotrophoblast
- c. Occurs 3 to 5 days after fertilization
- d. Occurs when the embryo consists of approximately 128 cells
- e. Is inhibited by secretion of progesterone from the corpus luteum

419. Biological actions of estrogens include

- a. Inhibition of follicular growth
- b. Delayed bone loss at menopause
- c. Increased glucose tolerance
- d. Decreased serum LDL cholesterol
- e. Decreased progesterone receptors

420. The hormone primarily responsible for development of ovarian follicles prior to ovulation is

- a. Chorionic gonadotropin
- b. Estradiol
- c. Follicle-stimulating hormone
- d. Luteinizing hormone
- e. Progesterone

421. Thyroid hormones

- a. Are short-acting hormones
- b. Have no effect on basal metabolic activity
- c. Are stored in extracellular sites
- d. Exist in the plasma primarily as free hormones
- e. Increase the metabolic activity of the brain

422. Melatonin

- a. Is synthesized in the anterior pituitary gland
- b. Regulates skin pigmentation in humans
- c. Secretion is increased by darkness
- d. Secretion is inhibited by norepinephrine from the sympathetic nervous system
- e. Is synthesized from the amino acid L-arginine

423. Insulin deficiency leads to

- a. Increased cellular uptake of glucose
- b. Decreased intracellular α -glycerophosphate in liver and fat cells
- c. Enhanced glucose uptake and use except by brain tissue
- d. Decreased fatty acid release from adipose tissue
- e. Indirect depression of use of glucose by excess fatty acids in the blood

424. The islets of Langerhans

- a. Are found primarily in the head of the pancreas
- b. Constitute approximately 30% of the pancreatic weight
- c. Contain six distinct endocrine cell types
- d. Have a meager blood supply
- e. Secrete insulin and glucagon

425. Progesterone

- a. Is secreted by the corpus luteum
- b. Secretion by the placenta increases at week 6 of gestation
- c. Plasma levels increase during the menses
- d. Plasma levels remain constant after implantation
- e. Plasma levels decrease subsequent to ovulation

426. The anti-inflammatory effect of cortisol treatment is thought to be due to

- a. Increased capillary membrane permeability
- b. Increased formation of leukotrienes
- c. Increased release of pyrogen from granulocytes
- d. Activation of phospholipase A₂
- e. Stabilization of cellular lysosomal membranes

427. Administration of estrogens in women will

- a. Limit the growth of ovarian follicles
- b. Produce cyclic changes in the vagina and endometrium
- c. Cause cervical mucus to become thicker and more acidic
- d. Retard ductal proliferation in the breast
- e. Produce glandular proliferation in the breast

428. The gastrointestinal hormone involved in initiation of migrating motor complexes is

- a. Gastrin
- b. Enterooxyntin
- c. Somatostatin
- d. Motilin
- e. Secretin

429. The principal androgen responsible for transforming undifferentiated fetal external genitalia into male external genitalia is

- a. Müllerian-inhibiting substance
- b. Androstenedione
- c. Dihydrotestosterone
- d. Testosterone
- e. Androsterone

430. Which one of the following statements about growth and development is correct?

- a. Thyroid hormones are essential for normal growth during puberty
- b. Linear growth ceases earlier in boys than in girls
- c. Serum IGF-1 levels decrease throughout childhood
- d. Growth hormone is essential for prenatal linear growth
- e. Prepubertal growth rates are constant throughout the year

431. The hormone most structurally related to gastrin is

- a. Secretin
- b. Cholecystokinin
- c. Motilin
- d. Vasoactive intestinal polypeptide
- e. Glucagon

432. Zollinger-Ellison syndrome patients experience severe, intractable peptic ulcer disease due to gastric acid hypersecretion. The cause of the increased acid output is increased plasma levels of

- a. Secretin
- b. Somatostatin
- c. Gastrin
- d. VIP
- e. Motilin

433. Which one of the following hormones initiates a biological effect by activation of cell membrane receptors?

- a. Progesterone
- b. Estrogens
- c. Cortisol
- d. Epinephrine
- e. Thyroxine

434. Which one of the following hormones interacts with a cytoplasmic receptor, then localizes in the nucleus and directs protein and nucleotide synthesis?

- a. Thyrotropin-releasing hormone
- b. Epinephrine
- c. Luteinizing hormone
- d. Cortisol
- e. Insulin

435. The hormone responsible for stimulating milk letdown is

- a. Oxytocin
- b. Progesterone
- c. Estradiol
- d. Insulin
- e. Prolactin

436. A patient with chronic asthma is started on glucocorticoid therapy. The treatment may result in bone loss because glucocorticoids

- a. Inhibit bone formation
- b. Increase calcium absorption from the GI tract
- c. Increase osteoblast growth
- d. Inhibit bone resorption
- e. Suppress vitamin D activation

437. Hormone replacement therapy is being considered for a 55-year-old woman undergoing menopause. Which one of the following is a benefit of the therapy?

- a. A return to normal menstrual cycle pattern
- b. Hot flashes
- c. A reduced risk of stroke
- d. Increased risk of osteoporosis
- e. Increased levels of low-density cholesterol (LDL)

438. Insulin regulates glucose transport into muscle and fat cells via which glucose transporter?

- a. GLUT-1
- b. GLUT-2
- c. GLUT-3
- d. GLUT-4
- e. GLUT-5

439. A patient with hypercalcemia would be expected to experience

- a. Diarrhea
- b. Polyuria
- c. Metabolic alkalosis
- d. Euphoria
- e. Hyperphagia

440. The hallmark of pheochromocytoma is

- a. Hypertension
- b. Hypoglycemia
- c. Dry skin
- d. Lethargy
- e. Bradycardia

441. Plasma catecholamine levels will increase when

- a. Blood pressure increases
- b. Anxiety increases
- c. Blood volume increases
- d. Blood glucose increases
- e. Moving from a standing to a supine position

442. Cortisol administration to a patient with adrenal insufficiency will

- a. Increase insulin sensitivity in muscle
- b. Enhance wound healing
- c. Increase corticotropin-releasing hormone secretion
- d. Increase ACTH secretion
- e. Increase gluconeogenesis

443. The signs and symptoms of a patient with primary adrenal insufficiency include

- a. Pallor
- b. Low ACTH levels
- c. High cortisol levels
- d. Hyperkalemia
- e. Hypertension

444. Which one of the following statements about semen is correct?

- a. The bulk of semen volume is contributed by the prostate gland
- b. It prevents sperm capacitation
- c. It buffers vaginal acidity
- d. It activates sperm motility in the male tract
- e. Sperm counts have increased over the last 20 years

445. Which one of the following statements about atrial natriuretic factor is correct?

- a. Secretion increases when central venous pressure increases
- b. It constricts afferent renal arterioles
- c. It acts only on the distal nephron to increase urine flow
- d. It enhances ADH secretion
- e. Secretion is stimulated by hyponatremia

446. A patient is diagnosed with acromegaly. Patients with this disease typically have

- a. Decreased gluconeogenesis
- b. Hypoglycemia
- c. Insulin resistance
- d. Decreased protein synthesis
- e. Decreased lipolysis

447. Prolactin secretion is tonically suppressed in nonpregnant women by

- a. Estrogens
- b. Progesterone
- c. Dopamine
- d. FSH
- e. LH

448. A woman tests positive for pregnancy. In order for the pregnancy to proceed uneventfully, which of the following must occur?

- 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

449. Symptoms of hypoglycemia develop when the plasma glucose concentration fall to between 45 and 50 mg% and may include

- a. Dry skin
- b. Bradycardia
- c. Insomnia
- d. Loss of fine motor skills
- e. Satiety

450. Radiation treatment for a pituitary tumor in an 8-year-old boy resulted in the complete loss of pituitary function. As a result, the child is likely to experience

- a. Hypothyroidism and goiter
- b. Increased ACTH
- c. Absent sexual maturation
- d. Accelerated growth spurts
- e. Increased TSH levels

451. Which one of the following statements is correct?

- a. Thyroid hormones are highly soluble in water
- b. Secretion of TSH is regulated primarily by the pituitary level of T_3
- c. TSH is secreted from the posterior pituitary
- d. TSH initiates thyroid hormone secretion via activation of nuclear receptors in thyroid gland cells
- e. T_4 is the physiologically active hormone

452. Aldosterone secretion by the adrenal gland is stimulated by

- a. Hypokalemia
- b. Angiotensin I
- c. Decreased renal afferent arteriole pressure
- d. Increased parasympathetic nerve activity
- e. Decreased sodium delivery to the distal convoluted tubule

453. Maternal physiology changes dramatically throughout pregnancy. Which one of the following changes would be expected?

- a. Reduced circulating gonadotrophin levels
- b. Increased conversion of glucose to glycogen
- c. Hypercapnia
- d. Increased hematocrit
- e. Decreased plasma cortisol levels

454. Glucagon secretion is increased by

- a. Hyperglycemia
- b. Arginine
- c. Vagal stimulation of the pancreas
- d. Insulin
- e. Somatostatin

455. Which one of the following conditions experienced by pregnant women may be due to the effects of pregnancy?

- a. Increased incidence of heartburn
- b. Decreased facial acne
- c. Increased gastric emptying leading to intestinal cramping and diarrhea
- d. Decreased afterload
- e. Increased cardiac output

456. Which one of the following is associated with prolonged fasting (3 or more days)?

- a. Decreased lipolysis
- b. Increased urinary excretion of nitrogen
- c. Decreased gluconeogenesis
- d. Increased glucose utilization by the brain
- e. Increased secretion of insulin

457. An abnormal decrease in the circulating levels of which placental hormone is indicative of a nonviable pregnancy?

- a. Human placental lactogen
- b. Estrogen
- c. Corticotropin-releasing hormone
- d. Human chorionic gonadotropin
- e. Progesterone

Endocrine Physiology

Answers

372. The answer is a. (*Guyton, pp 846–849.*) It is thought that the secretion of antidiuretic hormone (ADH)—also called arginine vasopressin (AVP)—and oxytocin by the neurohypophysis is regulated in the hypothalamic supraoptic and paraventricular nuclei, respectively. This hypothalamic control of secretion of pituitary hormone (inhibitory as well as releasing) in the case of the neurohypophysis is by direct neural connection, and, in the case of the adenohypophysis, by humoral factors conveyed by a microcirculation known as the *hypothalamic-hypophyseal portal system*.

373. The answer is e. (*Guyton, pp 906–908.*) PTH, secreted by the chief cells of the parathyroid gland, is essential for life. The secretion of PTH is inversely related to the circulating levels of ionized calcium. PTH has a direct effect on bone, involving cAMP changes in osteoblast and osteocyte permeability. It also increases calcium absorption from the gut, although that effect is the result of PTH-mediated increases in renal 1,2,5-dihydroxycholecalciferol.

374. The answer is c. (*Guyton, pp 809–811.*) Fasting persons are characterized by decreases in endogenous stores of carbohydrates, fats, and proteins and are said to be in a state of catabolism. As an adaptation, BMR decreases to limit the drain on energy stores. Catabolism of muscle protein is reflected in a rising excretion of nitrogen in the urine. Although glucose is an essential fuel for the central nervous system, with prolonged fasting, two-thirds of the energy needs are met by ketoacids. As long as sufficient fluids are ingested, a healthy person can survive up to 60 days.

375. The answer is e. (*Berne, 4/e, pp 711, 730–734.*) Atrial natriuretic hormone (ANH), a polypeptide hormone produced in the atria from preatriopeptigen, inhibits aldosterone secretion. The resultant effect is increased salt and water excretion by the kidneys. ANH is secreted in response to a variety of stimuli including atrial distention due to hypervolemia. Vasodilation of the afferent and efferent arterioles of the glomeru-

lus increases GFR. This effect combined with inhibition of aldosterone and renin secretion promotes natriuresis and diuresis.

376. The answer is b. (*Berne, 4/e, pp 976–980.*) Sertoli cells are required for germ cell mitotic and meiotic activity. Throughout the reproductive life of the human male, 100 to 200 million sperm are produced daily. Of critical importance to the hormonal regulation of spermatogenesis are the pulsatile release of GRH and the subsequent involvement of FSH and LH at their target cells. FSH acts directly on the Sertoli cells of the seminiferous tubules to initiate mitotic and meiotic activity of germ cells. LH effects are thought to be mediated via stimulation of testosterone secretion by the Leydig cells.

377. The answer is b. (*Berne, 4/e, pp 1002–1005.*) Numerous factors serve as a stimulus for growth hormone (GH) release, including hypoglycemia (e.g., insulin administration); moderate to severe exercise; stress due to emotional disturbances, illness, and fever; and dopamine agonists such as bromocriptine. GH, also known as somatotropin, is among a group of tropic hormones, including prolactin, ACTH, TSH, LH, and FSH, that are synthesized, stored, and secreted by the endocrine cells of the anterior pituitary. Its release is stimulated by growth hormone–releasing hormone and inhibited by somatostatin.

378–379. The answers are 378-b, 379-c. (*Guyton, pp 946–950.*) During the first two 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.

380. The answer is b. (*Berne, 4/e, pp 901–907.*) Oxytocin is secreted by the posterior pituitary and is involved in lactation and parturition. The

pituitary gland (the hypophysis) is located just beneath the hypothalamus and is connected to the hypothalamus by the infundibulum. It is a compound gland consisting of an anterior lobe (adenohypophysis) and a neural, or posterior, lobe. The anterior pituitary secretes six physiologically important hormones that govern the function of the thyroid (TSH) and adrenal glands (ACTH), the mammary glands (prolactin), and the gonads (FSH, LH) as well as regulate growth (GH).

381. The answer is d. (*Berne, 4/e, pp 897–901.*) Unique among the pituitary hormones, prolactin secretion is tonically inhibited by the hypothalamus. Prolactin is a single-chain protein secreted by the anterior pituitary whose principal physiologic effects involve breast development and milk production. Consistent with its role in lactogenesis, prolactin secretion increases during pregnancy. Dopamine has many characteristics of the hypothalamic inhibitory factor, although it is not found in the hypothalamus.

382. The answer is c. (*Guyton, pp 869–872.*) Because it lacks 3β -hydroxysteroid dehydrogenase, the enzyme that converts pregnenolone to progesterone (the initial step in both glucocorticoid and mineralocorticoid synthesis), the fetal cortex synthesizes primarily dehydroepiandrosterone. This steroid is released as its sulfate and is metabolized further to estrogen and androgen by the placenta. During fetal life, the adrenal cortex consists of a thin subcapsular rim, which eventually gives rise to the adult cortex, and a thick inner fetal cortex, which constitutes 80% of the gland. This zone undergoes rapid involution after birth.

383. The answer is b. (*Guyton, pp 886–890.*) Insulin increases glucose uptake by adipocytes. Transport of glucose into cells is by facilitated diffusion. Insulin increases the number of transporters available for glucose uptake in many cells, including adipocytes, skeletal and cardiac muscle, and some smooth muscle. Insulin does not enhance glucose transport into brain cells, intestinal mucosal cells, or renal tubular epithelial cells.

384. The answer is b. (*Guyton, pp 972–973.*) During prolonged exercise, skeletal muscle becomes relatively anaerobic when compared with its resting state and relies heavily upon glycolysis for ATP production. The increase in glucose required is met primarily by glycogenolysis and gluconeogenesis in the liver. Gluconeogenesis does not occur in skeletal muscle.

Thus, long-distance runners “carbohydrate load” before a race to increase hepatic glycogen stores. Intestinal uptake of glucose is influenced primarily by dietary intake, which would not ordinarily increase during exercise. At rest, the caloric needs of skeletal muscle are met primarily by mitochondrial oxidation of free fatty acids derived from adipose tissue. Glucose is used primarily by the brain and erythrocytes.

385. The answer is d. (*Guyton, pp 878, 879.*) Cortisol is the only hormone that has a diurnal variation, as shown in the graph accompanying the question. Plasma cortisol levels rise sharply during sleep, peaking soon after awakening, and sinking to a low level approximately 12 h 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.

386. The answer is c. (*Guyton, pp 929–933.*) Ovulation takes place just after the peak of the luteinizing hormone (LH) and estrogen curves, which occurs on approximately the fourteenth day of the menstrual cycle. Although FSH is primarily responsible for follicular maturation within the ovary, LH is necessary for final follicular maturation; without it, ovulation cannot take place. Both estrogen, following a sharp preovulatory rise in plasma concentration, and progesterone are secreted in abundance by the postovulatory corpus luteum.

387. The answer is b. (*Guyton, pp 858–864.*) The thyroid gland stores iodide primarily as thyroglobulin. The thyroid gland has a specialized active transport system that very efficiently traps iodide from circulating blood and can accumulate iodide against a large concentration gradient. Within the thyroid, the iodide rapidly undergoes organification by which it is oxidized and covalently linked to tyrosine residues in thyroglobulin. The iodinated tyrosine residues gradually become coupled to form thyroxine, the major secretion product of the thyroid.

388. The answer is d. (*Guyton, pp 929–933.*) There is a marked increase in progesterone secretion following ovulation. Almost all the progesterone secreted in nonpregnant women is secreted by the corpus luteum. Secretion of both progesterone and estrogen is controlled by luteinizing hormone (LH) released by the adenohypophysis, and LH release itself is under the direction of a hypothalamic releasing factor.

389. The answer is b. (*Guyton, pp 858–864.*) Thyroxine is the main thyroid hormone entering the circulation and constitutes approximately 95% of active plasma thyroid hormone; the percentage remaining is almost entirely triiodothyronine, which, although more potent than thyroxine, has a more transient presence. Thyroglobulin is the principal storage form of thyroid hormone within the gland and very little is released into the blood. Thyrotropin (TSH) and long-acting thyroid stimulator (LATS) both stimulate thyroid hormone production and growth of the thyroid gland.

390. The answer is e. (*Guyton, pp 858–860.*) Only the free unbound form of thyroxine is physiologically active. Circulating thyroxine can be bound to albumin, thyroxine-binding prealbumin (TBPA), or thyroxine-binding globulin (TBG). Most thyroxine is bound, and, despite the large available pool of albumin, most of it is bound to TBG. This reflects the relatively greater affinity of TBG for thyroxine.

391. The answer is c. (*Berne, 4/e, pp 987–990.*) 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.

392. The answer is e. (*Berne, 4/e, pp 990–996.*) Ovulation occurs at point A on the graph. In response to estrogen secretion by the ovary, the endometrial lining of the uterus undergoes proliferation of both glandular epithelium and supporting stroma during the first 10 to 14 days of the menstrual cycle. Following ovulation, the glands begin to secrete mucus and the stroma undergoes pseudodecidual reaction in preparation for potential pregnancy. When ovulation is not followed by implantation of a fertilized ovum, progesterone secretion declines as the corpus luteum involutes, and the endometrial lining is almost completely shed during menses.

393. The answer is a. (*Guyton, pp 948–950.*) Human chorionic gonadotropin (hCG) begins to appear in the maternal blood approxi-

mately 6 to 8 days following ovulation, upon implantation of the fertilized ovum in the endometrium. The secretion of hCG is essential to prevent involution of the corpus luteum and to stimulate secretion of progesterone and estrogens, which continues until the placenta becomes large enough to secrete sufficient quantities of those hormones. Following a peak at 7 to 9 weeks, hCG secretion gradually declines to a low level by 20 weeks gestation.

394. The answer is b. (*Guyton, pp 786–787.*) Hormone-sensitive lipase is a cytoplasmic enzyme in adipocytes that catalyzes the complete hydrolysis of triglyceride to fatty acids and glycerol. It is activated by a cyclic AMP-dependent protein kinase that phosphorylates the enzyme, converting it to its active form. Since no accumulation of monoglycerides or diglycerides is detected in adipocytes following the action of hormone-sensitive lipase, it is the initial hydrolysis of triglyceride to fatty acid and diglyceride that is the rate-limiting step. Hormone-sensitive lipase is sensitive to several hormones in vitro, but it appears to be regulated in vivo primarily by epinephrine and glucagon, which activate it by increasing cyclic AMP, and insulin, which inhibits it by preventing cyclic AMP-dependent phosphorylation. Cortisol enhances lipolysis indirectly by promoting increased enzyme synthesis.

395. The answer is d. (*Berne, 4/e, pp 976–982.*) Complete maturation of spermatozoa within the seminiferous tubules requires approximately 70 days in man. Spermatogenesis occurs within the seminiferous tubules of the testis and requires secretion of both FSH and LH. FSH acts directly on the seminiferous tubules while the effects of LH are thought to be due to its stimulation of secretion of testosterone by the Leydig cells. Spermatogonia are the stem cells, which divide several times by mitosis to produce more stem cells and type B spermatogonia. The type B spermatogonia give rise to primary spermatocytes, which undergo meiosis. Normally, 100 to 200 million sperm are produced per day.

396. The answer is c. (*Berne, 4/e, pp 979–982.*) 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.

397. The answer is d. (*Berne, 4/e, pp 990–996.*) Progesterone production by the corpus luteum increases significantly at the time of ovulation. 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. Progesterone affects the set point for thermoregulation and increases body temperature approximately 0.5°F.

398. The answer is c. (*Guyton, pp 954–956.*) A combined neurogenic and hormonal reflex involving oxytocin, a posterior pituitary hormone, causes the actual ejection (“let-down”) of milk from breast tissue. Although estrogen and progesterone are essential for the physical development of breast tissue during pregnancy, both hormones inhibit milk secretion. Milk secretion is regulated by prolactin, a pituitary hormone secreted throughout pregnancy and after parturition. Adequate amounts of growth hormone are required to provide the nutrients that are essential for milk production by breast tissue. Suckling on breast tissue is the stimulus that leads to milk secretion.

399. The answer is d. (*Guyton, pp 906–909.*) PTH increases plasma calcium levels primarily by mobilizing bone calcium. The main function of the parathyroid gland is to maintain a constant ionized calcium level in the extracellular fluid. To do this, parathyroid hormone stimulates increased plasma calcium levels, chiefly by mobilizing calcium from bones. Although parathyroid hormone can also increase renal tubular reabsorption of calcium and intestinal absorption of calcium, these effects depend on adequate dietary ingestion of calcium and thus occur more slowly.

400. The answer is b. (*Berne, 4/e, pp 891–897.*) GH increases the production and release of somatomedins from the liver. These peptides have a multitude of effects on the body and promote growth of organs, bones, and lean body mass. Human growth hormone (GH) is a peptide that is synthesized and released from the anterior pituitary. Its release is stimulated by growth hormone–releasing hormone (GHRH) and inhibited by somatostatin. Both of these peptides are synthesized and released by the hypothalamus and their releases are regulated by multiple feedback loops. GH has the direct effect on adipose tissue of decreasing glucose uptake and increasing lipolysis.

401. The answer is d. (*Guyton, pp 846–848.*) Growth hormone (GH) promotes the utilization of fats as an energy source. GH hormone exerts a wide variety of effects on body metabolism, including increased protein synthesis, decreased use of carbohydrate, and increased use of fat. The net effect is the accumulation of protein and conservation of carbohydrate at the expense of fat stores. In addition, GH promotes growth by stimulating synthesis of cartilage and bone via the actions of somatomedin C (insulin-like growth factor 1 [IGF-1]).

402. The answer is c. (*Guyton, pp 891–893.*) The primary action of glucagon is to increase blood glucose concentration, which it accomplishes by promoting gluconeogenesis and glycogenolysis in the liver but not in muscle. These effects are mediated by cyclic AMP, which is produced by hepatic adenyl 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.

403. The answer is d. (*Guyton, pp 884–893.*) One of insulin's major effects is the stimulation of the Na-K pump, which increases potassium entry into cells. Insulin given along with glucose, to prevent hypoglycemia, is often used as a treatment for hyperkalemia. Insulin's major effect on metabolism is the synthesis of proteins and lipids and the storage of glucose as glycogen. Insulin stimulates the uptake of amino acids and glucose by most cells of the body and decreases the rate of gluconeogenesis. Insulin has

no effect on urine formation, but in diabetes, when glucose levels increase to a level at which the kidney can no longer reabsorb the filtered glucose, glucose acts as an osmotic diuretic and increases the formation of urine.

404. The answer is a. (*Guyton, pp 878–880.*) The secretion of ACTH occurs in several irregular bursts during the day; the peak occurs early in the morning prior to awakening and thus is not due to the stress of arising. This circadian rhythm—maximum secretion in early morning, minimum in the evening—is regulated by the hypothalamus through the secretion of corticotropin-releasing hormone (CRH) into the hypothalamic-hypophyseal portal capillary system. In addition to the basal rhythm, physical or mental stress will lead to increased ACTH secretion within minutes. ACTH is also regulated as a result of feedback inhibition by the hormones whose synthesis it stimulates, such as glucocorticoids. Aldosterone is a mineralocorticoid and is not controlled by ACTH. Epinephrine does not appear to have any effect on ACTH secretion.

405. The answer is b. (*Berne, 4/e, pp 923–927.*) Thyroid hormone affects all aspects of metabolism; it increases calorogenesis in every tissue in the body. The hormone stimulates protein synthesis, which may be directly responsible for a portion of its calorogenic effect. Thyroid hormone affects both synthesis and degradation of lipids; the net effect is a decrease in lipid stores. By increasing the mechanisms by which cholesterol is eliminated from the body, thyroid hormone decreases plasma cholesterol levels. Because of its stimulatory effect on metabolic processes, thyroid hormone increases the demand for coenzymes and vitamins.

406. The answer is b. (*Guyton, p 882.*) 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.

407. The answer is a. (*Guyton, pp 910–911.*) Hyperparathyroidism decreases plasma phosphate levels. Parathyroid hormone (PTH) is essential

for maintaining plasma calcium and phosphate levels. It is released in response to decreased plasma calcium and acts to increase calcium reabsorption and phosphate excretion.

408. The answer is a. (*Guyton, pp 880–882.*) Adrenalectomy leads to diuresis and natriuresis. Removal of the adrenal glands produces the clinical picture known as Addison's disease, a disorder associated with deprivation of adrenocortical hormones. Thus, a lack of glucocorticoids diminishes the body's ability to synthesize glucose by gluconeogenesis. Severe mineralocorticoid deprivation produces grave fluid and electrolyte disturbances as an ultimate consequence of impaired sodium reabsorption, excessive potassium plasma levels, and acidosis.

409. The answer is b. (*Guyton, pp 861–864.*) Hyperthyroidism can increase the basal metabolic rate 60 to 100% above normal. Thyroid hormone causes nuclear transcription of large numbers of genes in virtually all cells of the body. The result is a generalized increase in functional cell activity and metabolism. The increased metabolic activity of patients with hyperthyroidism is accompanied by increased food intake. Nevertheless, their body weight decreases. The generalized increase in cellular activity results in increased sweat production and increased heart rate. The latter sign is often used by physicians to determine whether a patient has increased thyroid hormone production.

410. The answer is d. (*Guyton, pp 886–891.*) 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.

411. The answer is c. (*Guyton, pp 387–388.*) Iron is transported in the blood bound to the beta 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.

412. The answer is e. (*Guyton, pp 201–206.*) Angiotensin II (AII) stimulates thirst. AII is an octapeptide produced in response to hypovolemia by the combined action of renin, released from the juxtaglomerular apparatus, and angiotensin-converting enzyme in the lung. It has a number of actions, all of which are directed toward increasing arterial pressure. The actions include (1) direct vasoconstriction of peripheral arterioles; (2) stimulation of aldosterone secretion by the adrenal cortex, resulting in increased sodium tubular resorption; and (3) stimulation of the subfornical organ of the diencephalon, which activates neural areas concerned with thirst. The latter two actions, by increasing blood volume, play a role in long-term regulation of blood pressure. AII also exerts negative feedback on its own production by inhibiting renin secretion. It does not act directly on renal tubules to influence salt excretion.

413. The answer is d. (*Berne, 4/e, pp 926–927.*) 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.

414. The answer is c. (*Guyton, pp 929–933.*) 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.

415. The answer is b. (*Berne, 4/e, pp 891–897.*) Deep sleep induces the greatest daily peak in the secretion of growth hormone. 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 growth hormone–releasing hormone (GHRH) and somatostatin (SS) from the hypothalamus. Insulin-induced hypoglycemia is a major stimulus for release of growth hormone. Amino acids are also potent stimuli for release of growth hormone, while fatty acids are inhibitory. Thyroxine acts directly on pituitary cells to enhance synthesis of growth hormone and is required for the normal responsiveness of the pituitary and hypothalamus to physiologic stimuli.

416. The answer is a. (*Guyton, pp 884–886.*) One of insulin's major effects is stimulation of cell membrane sodium-potassium pumps, leading to increased potassium uptake by cells. The binding of insulin to specific membrane receptors is associated with autophosphorylation of tyrosine residues in the receptor molecule and leads to negative cooperativity, that is, reduced affinity of insulin receptors for insulin.

417. The answer is a. (*Guyton, pp 886–890.*) Triglyceride uptake into adipocytes is regulated by lipoprotein lipase. The uptake of triglycerides into adipose tissue and other tissues from plasma lipoproteins requires hydrolysis of triglyceride to fatty acids and glycerol by an enzyme bound to the endothelial surface, lipoprotein lipase. The activity of this enzyme varies in reciprocal fashion with that of cytoplasmic hormone-sensitive lipase; that is, its activity is enhanced by insulin and glucose and decreased by catecholamines. Lipoprotein lipase is present in nearly every tissue and acts at the capillary surface as it does in adipose tissue. Receptor-mediated endocytosis is important in the turnover of the protein portion of plasma lipoproteins.

418. The answer is b. (*Guyton, pp 944–946.*) 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.

419. The answer is b. (*Guyton, pp 912, 933–937.*) Some estrogen receptors are found on osteoblasts and estrogen treatment delays age-related bone loss at menopause. At puberty, estrogens stimulate the growth and development of the female reproductive tract and increase the number of progesterone receptors. The metabolic effects of estrogens include antagonizing the actions of insulin on peripheral tissues and decreasing glucose tolerance. Estrogens also decrease serum cholesterol levels.

420. The answer is c. (*Guyton, pp 937–939.*) Preparation of primordial ovarian follicles for ovulation is the primary function of FSH. FSH stimulates development of the theca and granulosa cells of the follicles and promotes the synthesis of estrogens, including estradiol. LH promotes luteinization of the postovulatory follicle and stimulates progesterone secretion by the corpus luteum. During pregnancy, hCG is secreted by the placenta and continues progesterone production.

421. The answer is c. (*Guyton, pp 858–864.*) Thyroglobulin, the storage form of thyroid hormones, is stored extracellularly in follicles lined by thyroid epithelium. Only about 0.02% of the thyroxine and about 0.2% of the triiodothyronine are normally present in plasma in the free form; the rest is bound to thyroxine-binding globulin, thyroxine-binding prealbumin, and albumin. Following injection of thyroxine into a human, the effect on the metabolic rate is not noticeable for 2 to 3 days; then the rate begins to increase progressively and reaches a maximum in 10 to 12 days. Some of the activity persists for up to 2 months. The principal effect of the thyroid hormones is an increase in the metabolic rate of most tissues in the body, with a few exceptions such as brain, retina, testes, spleen, and lungs.

422. The answer is c. (*Guyton, pp 926–928.*) Synthesis and secretion of melatonin are increased in the dark via input from norepinephrine secreted by postganglionic sympathetic neurons. Melatonin is synthesized in the pineal gland from the amino acid tryptophan. Pinealomas (tumors of the pineal gland) that destroy the pineal gland and reduce secretion of melatonin and cause hypothalamic damage may cause precocious puberty by removing the inhibitory effect of melatonin on the pituitary response to gonadotropin-releasing hormone. Melatonin causes amphibian skin to become lighter in color but has no role in the regulation of skin color in humans.

423. The answer is b. (*Guyton, pp 884–891.*) 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 use of glucose by excess fatty acids is a result, and not a contributing cause, of increased use of fat.

424. The answer is c. (*Guyton, p 884.*) 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. Most islet cells are located in the head or body of the pancreas, and each is well vascularized.

425. The answer is a. (*Berne, 4/e, pp 891, 997–1000.*) Progesterone is secreted by the corpus luteum. The plasma level of progesterone is low during the menses and remains low until just prior to ovulation. It rises substantially after ovulation, owing to secretion by the corpus luteum. If fertilization occurs, the corpus luteum continues to secrete progesterone until the placenta develops and begins to produce large amounts of the hormone. The plasma level of progesterone rises steadily throughout pregnancy after the placenta takes over production at about 12 weeks of gestation.

426. The answer is e. (*Berne, 4/e, pp 945–948.*) The anti-inflammatory effects of exogenous cortisol are due to its ability to decrease capillary membrane permeability and probably also to its ability to stabilize lysosomal membranes and decrease the formation of bradykinin. Glucocorticoids inhibit the enzyme phospholipase A₂. This decreases the release of arachidonic acid and the variety of substances produced from it, such as leukotrienes, prostaglandins, thromboxanes, and prostacyclin. Cortisol owes its fever-reducing action to the hormone's ability to decrease the release of pyrogen (interleukin 1) from granulocytes. However, only in massive doses will the hormone achieve the effects described. Endogenous cortisol does not exert significant anti-inflammatory action.

427. The answer is b. (*Guyton, pp 934–936.*) Estrogens cause the mucus secreted by the cervix to become thinner and more alkaline and to exhibit a fernlike pattern upon drying. The epithelium of the vagina is so sensitive to estrogen action that vaginal smear examination is used for a bioassay of the hormone. Estrogens can stimulate growth of ovarian follicles even in hypophysectomized women and also stimulate growth of the glandular epithelium of the endometrium, the smooth muscle of the uterus, and the uterine vascular system. Growth of the glandular elements of the breast is stimulated by progesterone; growth of the ductal elements is stimulated by estrogen.

428. The answer is d. (*Berne, 4/e, pp 609–610.*) Motilin, a gastrointestinal hormone released from the small intestine during the interdigestive period, is believed to be responsible for initiating and maintaining migrating motor complexes in humans. Factors responsible for release of the hormone remain unsettled. All other gut hormones are released during the digestive period and facilitate motility and secretion.

429. The answer is c. (*Guyton, pp 922–926.*) Androgens, particularly dihydrotestosterone, are essential for regulation of the external genitalia in males. The fetus develops with multipotential internal and external genitalia. The development of male internal genitalia depends upon the presence of two hormones produced by the fetal testis—progesterone and Müllerian-inhibiting substance. The former stimulates growth and development of Wolffian ducts; the latter stimulates Müllerian duct regression.

DHT-regulated development of external sex characteristics occurs between 9 and 12 weeks of gestation.

430. The answer is a. (*Guyton, pp 850–851.*) 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. IGF-1 secretions increase throughout childhood and stimulate cell proliferation and growth in many different cell types, including chondrocytes within growth plates. Linear growth ends earlier in girls than in boys. Growth hormone does not play a significant role in prenatal linear growth. Prepubertal growth evidences seasonal variations, with most growth occurring in the spring and summer.

431. The answer is b. (*Guyton, pp 722–723.*) Gastrointestinal hormones may be divided into families based on similarities in primary protein structure. Gastrin and cholecystokinin share an identical C-terminal tetrapeptide sequence, which is the biologically active portion of both peptides. Secretin, VIP, and glucagon are all members of the secretin family.

432. The answer is c. (*Fauci, 14/e, pp 1613–1615.*) In Zollinger-Ellison (ZE) syndrome, larger than normal amounts of gastrin are produced continuously from pancreatic tumors consisting primarily of islet delta cells. As much as 10 L per day of gastric juice may be secreted. The continuous flow of acid into the small intestine produces ulcers and unremitting diarrhea with excess loss of potassium.

433. The answer is d. (*Guyton, pp 840–843.*) Due to their relatively low solubility within the lipid portions of the cell membrane, peptide hormones and catecholamines (epinephrine) must interact with receptors located on the cell membrane. Activation of the receptor is followed by the generation of intracellular second messengers that ultimately mediate the biological response to the hormone. Steroid hormones and thyroid hormones readily pass through the cell surface membrane and interact with intracellular receptors to produce their effects by regulating gene expression within the nucleus.

434. The answer is d. (*Berne, 4/e, pp 939–942.*) Cortisol, like other steroid hormones, diffuses into target cells and interacts with intracellular

receptors. The steroid-receptor complex has a high affinity for the steroid-responsive element of DNA. Once bound to DNA, the hormone-receptor complex acts as a transcription factor to regulate gene expression and formation of specific messenger RNAs.

435. The answer is a. (*Guyton, pp 855–856, 956.*) Oxytocin is a posterior pituitary peptide that promotes contraction of the myoepithelial cells surrounding breast ducts and causes expulsion of milk from lobular alveoli. Secretion of oxytocin is promoted by tactile stimulation of the breast by the nursing infant. It can also be elicited by psychic factors alone, such as the anticipation of nursing brought on by hearing the cry of the hungry infant. This anticipatory secretion of oxytocin may be experienced by the mother as a sensation of milk letdown in which milk appears at the nipple and may be forcibly ejected.

436. The answer is a. (*Fauci, 15/e, pp 1461, 2088.*) Glucocorticoid therapy enhances bone loss by inhibiting bone formation. It also increases bone resorption. Glucocorticoids are produced by the adrenal glands and have a broad spectrum of action, particularly as it relates to fuel metabolism, response to injury, and general cell function.

437. The answer is c. (*Berne, 4/e, pp 1001–1002.*) Estrogen replacement therapy decreases a patient's risk of stroke. Hot flashes, osteoporosis, and increased LDL cholesterol are consequences of estrogen deficiency. Estrogen therapy does not restore a woman's ability to have children.

438. The answer is d. (*Berne, 4/e, pp 18, 648, 649, 807, 834.*) Following insulin binding on muscle and adipocytes, the glucose transporter GLUT-4 is translocated to the cell membrane where it promotes glucose uptake by facilitated diffusion. GLUT-1 transporters are found virtually everywhere, as are GLUT-3 transporters. GLUT-2 transporters are found in liver, kidney, and intestinal cells. GLUT-5 transporters promote glucose absorption from the jejunum.

439. The answer is b. (*Guyton, pp 342–343, 900–901.*) Hypercalcemia impairs renal function and leads to polyuria and polydipsia. Hypercalcemia results from excessive bone resorption or increased calcium absorption from the small intestine and is accompanied by inadequate renal excretion

of calcium. The disease also is associated with metabolic acidosis, constipation, lethargy, and anorexia.

440. The answer is a. (*Guyton, pp 872–873.*) 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.

441. The answer is b. (*Guyton, pp 703–705.*) Emotional stress increases circulating catecholamine levels. 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.

442. The answer is c. (*Berne, 4/e, pp 938–948.*) Cortisol is defined as a glucocorticoid because it promotes the conversion of amino acids to glucose (gluconeogenesis). It also decreases glucose uptake by muscle and adipocytes by decreasing the sensitivity of the cells to insulin. The net result is to provide more glucose to non-insulin-requiring cells. Cortisol retards wound healing. It also decreases CRH and ACTH secretion by feedback inhibition.

443. The answer is d. (*Berne, 4/e, p 953.*) Patients with primary adrenal insufficiency (Addison's disease) are hyperkalemic due to a deficiency of aldosterone. This is accompanied by hyponatremia and hypotension. Hyperpigmentation occurs due to an increased production of melanin. Lack of cortisol leads to high levels of ACTH.

444. The answer is b. (*Berne, 4/e, pp 976–979.*) Sperm contains chemicals that prevent sperm capacitation, thereby prolonging the viability of the sperm. In addition, the high potassium content of the secretion inhibits sperm motility, further adding to the viability. Sperm is secreted primarily by the seminiferous tubules and the alkaline nature of the secretion buffers the acidity of the vagina. In recent years, the average sperm count has decreased from approximately 100 million/mL of semen to 60–70 million/mL of semen.

445. The answer is a. (Berne, 4/e, pp 383, 696, 731–734, 904.) Atrial natriuretic peptide (ANP) is synthesized, stored, and secreted by cardiac atrial muscle, the latter in response to increased central venous pressure or increased plasma sodium concentrations. ANP increases glomerular filtration by simultaneous dilation of afferent and constriction of efferent renal arterioles. It decreases salt and water reabsorption along the entire length of the kidney. The excretion of water is enhanced by inhibition of ADH.

446. The answer is c. (Berne, 4/e, pp 792, 891–896.) Patients with acromegaly have insulin resistance. In addition, they evidence 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.

447. The answer is c. (Guyton, pp 848–849, 954–956.) In nonpregnant women, the secretion of prolactin is kept tonically suppressed by secretion of dopamine from the hypothalamus. Prolactin is the main hormone of lactation. Hormone levels increase early in pregnancy due to the influence of estrogens. However, lactation does not occur early in pregnancy because estrogens and progesterone inhibit the interaction of prolactin with receptors located on the alveolar cell membranes. At term, estrogen and progesterone levels decrease and milk production begins usually within three days of delivery.

448. The answer is a. (Guyton, pp 948–949.) Continuous secretion of progesterone by the corpus luteum is essential for development of the fetus. During the first trimester, placental production of hCG sustains the corpus luteum and ensures continued progesterone secretion. By the second trimester, progesterone production by the placenta increases to levels sufficient to sustain fetal growth and development.

449. The answer is d. (Guyton, p 897.) 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.

450. The answer is c. (*Guyton, pp 846–853.*) Radiation treatment likely produced panhypopituitarism in the young child. Sexual maturation and growth during development will not occur because of low levels of GH, FSH, LH, ILGF1, TSH and thyroid hormones, and gonadal hormones. The cortisol response to stress is decreased due to low ACTH levels. A goiter cannot develop in the absence of TH.

451. The answer is b. (*Berne, 4/e, pp 910–918.*) Secretion of TSH is regulated primarily by the pituitary levels of T_3 . As plasma thyroid hormone levels increase, pituitary T_3 levels rise and lead to inhibition of TSH synthesis and secretion. TSH stimulates thyroid gland function by binding to specific cell membrane receptors and increasing the intracellular levels of cAMP. The thyroid gland secretes thyroxine (T_4) and triiodothyronine (T_3); the latter is the physiologically active hormone. The majority of T_3 is formed in the peripheral tissues by deiodination of T_4 .

452. The answer is c. (*Berne, 4/e, pp 949–951.*) Decreased renal afferent arteriole stretch (due to decreased pressure) stimulates renin release from the macula densa and ultimately the adrenal gland secretion of aldosterone. Aldosterone secretion is primarily under the control of the renin-angiotensin system. Aldosterone secretion is increased by hyperkalemia, increased sodium delivery to the distal nephron, angiotensin II, and increased sympathetic nerve activity.

453. The answer is a. (*Guyton, pp 950–952.*) During pregnancy, the maternal hypothalamic-pituitary axis is suppressed due to high circulating levels of sex hormones. This leads to reduced gonadotrophin 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.

454. The answer is b. (*Berne, 4/e, pp 841–843.*) Glucagon secretion from pancreatic alpha cells is increased by increased plasma arginine levels. Glucagon opposes the actions of insulin and increases blood glucose by

increasing gluconeogenesis and glycogenolysis. Secretion is also stimulated by hypoglycemia. Insulin and somatostatin decrease glucagon secretion.

455. The answer is a. (*Guyton, pp 950–951.*) Progesterone-mediated relaxation of lower esophageal sphincter smooth muscle is believed to increase the frequency of esophageal reflux and, thus, the sensation of heartburn. Progesterone may also relax gastric and colonic smooth muscle resulting in gastroparesis and constipation, respectively. Estrogens cause marked peripheral vasodilation. The resultant decrease in afterload leads to a compensatory increase in cardiac output.

456. The answer is c. (*Berne, 4/e, pp 807, 814–815, 942.*) With prolonged fasting of 3 days or more, gluconeogenesis is decreased partly due to increased ketogenesis and lipolysis. The increased availability of ketones and fatty acids as a source of fuel for brain cells decreases the demand by the brain for glucose. The decreased gluconeogenesis is reflected in a nitrogen excretion level at or below normal values. Insulin levels decrease beginning as early as 24 h after a meal.

457. The answer is d. (*Guyton, pp 838, 948–950.*) An abnormal rise in hCG early in gestation is indicative of a nonviable pregnancy. hCG is a polypeptide hormone made entirely within the placenta. Under the influence of hCG, the corpus luteum doubles its size within a month. The continued production of estrogen and progesterone by the corpus luteum maintains the decidual nature of the endometrium, which is necessary for early fetal development.

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Neurophysiology

Questions

DIRECTIONS: Each question below contains several suggested responses. Select the **one best** response to each question.

458. An increase in refractive power is produced by contraction of the

- a. Iris
- b. Ciliary body
- c. Suspensory ligaments
- d. Extraocular muscles
- e. Pupil

459. The primary function of the bones of the middle ear is to

- a. Amplify the sound stimulus
- b. Filter high-frequency sounds from the sound stimulus
- c. Enable the direction of a sound stimulus to be detected
- d. Enhance the ability to distinguish different sound frequencies
- e. Protect the ear from damage

460. During a voluntary movement, the Golgi tendon organ provides the central nervous system with information about

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

461. Repetitive stimulation of a skeletal muscle fiber will cause an increase in contractile strength because repetitive stimulation causes an increase in

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

462. Free nerve endings contain receptors that encode the sensation of

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

463. An aphasia is most likely to be associated with a lesion of

- a. The hippocampus
- b. The temporal lobe
- c. The parietal lobe
- d. The limbic system
- e. The reticular activating system

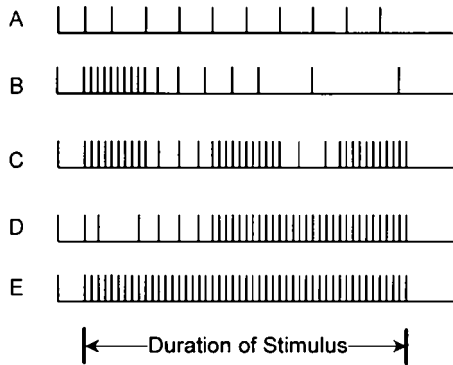
464. Depolarization of the hair cells in the cochlea is caused primarily by the flow of

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

465. The most important role of the gamma motoneurons is to

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

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



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

467. Which of the following receptors is responsible for measuring the intensity of a steady pressure on the skin surface?

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

468. The middle cerebellar peduncle contains afferent fibers conveyed in which of the following tracts?

- a. Dorsal spinocerebellar
- b. Ventral spinocerebellar
- c. Tectocerebellar
- d. Pontocerebellar
- e. Vestibulocerebellar

469. The precentral gyrus and corticospinal tract are essential for

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

470. A patient who presents with an intention tremor, “past-pointing,” and a “drunken” gait might be expected to have a lesion involving the

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

471. The otolith organs (utricle and saccule) are responsible for

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

472. Which one of the reactions in the retinal rods is caused directly by the absorption of light energy?

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

473. Which of the following statements about the cerebrospinal fluid (CSF) is true?

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

474. When a person slowly rotates toward the right,

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

475. During a normal voluntary movement

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

476. Correct statements regarding rapid eye movement (REM) sleep include which of the following?

- a. It is the first state of sleep entered when a person falls asleep
- b. It is accompanied by loss of skeletal muscle tone
- c. It is characterized by a slow but steady heart rate
- d. It occurs more often in adults than in children
- e. It lasts longer than periods of slow-wave sleep

477. When emmetropic persons become presbyopic, their

- a. Visual acuity increases
- b. Near point increases
- c. Far point decreases
- d. Total refractive power increases
- e. Ability to see distant objects decreases

478. When light strikes the eye there is an increase in

- a. The activity of the 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

479. Spasticity can be caused by sectioning

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

480. Activation of transducin by light activates an enzyme which

- a. Hydrolyzes cGMP
- b. Increases the dark current
- c. Activates adenylyl cyclase
- d. Releases calcium from intracellular stores
- e. Depolarizes the membrane

481. If nystagmus is a prominent symptom of a cerebellar lesion, the lesion is within

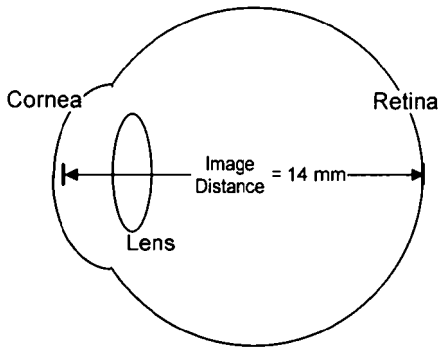
- a. The dentate nucleus
- b. The flocculonodular lobe
- c. The lateral cerebellum
- d. The cerebrocerebellar cortex
- e. The superior cerebellar peduncle

482. The alpha rhythm appearing on an electroencephalogram has which of the following characteristics?

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

Questions 483–484

The image distance of a normal relaxed eye is indicated in the diagram below.



483. The focal length of the eye is

- a. 14 mm
- b. 15 mm
- c. 17 mm
- d. 19 mm
- e. 21 mm

484. If an object is placed 25 cm away from the eye, the image will be focused on the retina if the refractive power of the eye is increased to

- a. 64 diopters
- b. 68 diopters
- c. 70 diopters
- d. 72 diopters
- e. 75 diopters

485. Tapping the patella tendon elicits a reflex contraction of the quadriceps muscle. During the contraction of the quadriceps muscle,

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

486. Increased activity of the sympathetic nervous system causes

- a. Penile erection
- b. Pupillary constriction
- c. Accommodation for near vision
- d. Bronchiolar dilation
- e. Gallbladder emptying

487. Norepinephrine will cause contraction of the smooth muscle in the

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

488. If the threshold for hearing increases 1000 times, the hearing loss is

- a. 20 decibels
- b. 30 decibels
- c. 40 decibels
- d. 50 decibels
- e. 60 decibels

489. If a patient is unable to hear high-frequency sounds, the damage to the basilar membrane is closest to the

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

490. An abnormal Babinski reflex indicates damage to the

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

491. Which of the following hypothalamic nuclei is responsible for controlling the normal circadian rhythm?

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

492. Presynaptic inhibition in the central nervous system affects the firing rate of alpha motoneurons by

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

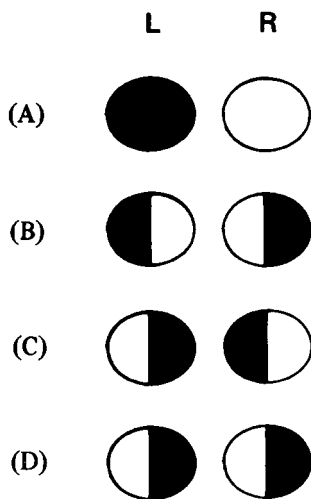
493. Which one of the following events accompanies the rapid voluntary flexion of the arm?

- a. An increase in the activity of the Ia afferent fibers from the biceps (the agonist)
- b. A decrease in the activity of the Ib afferent fibers from the biceps (the agonist)
- c. An increase in the activity of the Ia afferent fibers from the triceps (the antagonist)
- d. A decrease in the activity of the Ib afferent fibers from the triceps (the antagonist)
- e. An increase in the activity of the alpha motoneurons to the triceps (the antagonist)

494. The sympathetic response in a “fight or flight” reaction causes a decrease in

- a. The arterial blood pressure
- b. The diameter of the pupil
- c. The resistance of the airways
- d. The blood glucose concentration
- e. The heart rate

495. Which one of the optic field defects listed in the following diagram is produced by a pituitary gland tumor?



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

496. Which one of the following visual lesions will produce extensive loss of peripheral vision in the left visual fields of both eyes?

- a. A lesion of the left lateral geniculate
- b. Section of the left optic nerve
- c. A lesion of the right visual cortex
- d. Removal of the right lens
- e. Section of the left optic tract

497. The pain produced by ischemia is poorly localized and throbbing while pain from a needle stick is well localized and sharp. Which of the following comparisons of ischemic and needle stick pain is correct?

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

498. Which one of the following hypothalamic nuclei is responsible for the detection of the core body temperature?

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

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

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

500. The Klüver-Bucy syndrome is characterized by decreased emotional expression, loss of fear, excessive oral behavior, and increase in sexual activity. These characteristics of the Klüver-Bucy syndrome are produced by bilateral lesions of the

- a. Hippocampus
- b. Amygdala
- c. Ventral hypothalamus
- d. Corpus callosum
- e. Cingulate gyrus

Neurophysiology

Answers

458. The answer is b. (*Rhoades, pp 72–73. Guyton, p 570.*) Contracting the ciliary body increases the refractive power of the eye for near vision. The ciliary body is a smooth muscle located at the sclerocorneal junction where the suspensory ligaments surrounding the lens are attached. The suspensory ligaments are normally taut, keeping the eye flat. When the ciliary muscle contracts, the suspensory ligaments are pulled toward the cornea. They become slack and permit the elastic lens fibers to recoil. Recoiling of the lens causes the lens surface to bulge, increasing its refractive power. The muscles of the iris control the size of the pupils, and the extraocular muscles control the position of the eye in the socket.

459. The answer is a. (*Berne, 3/e, pp 103–105.*) 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 potentially 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. Most of the amplification results from the much larger surface area of the tympanic membrane compared with that of the oval window (or from the larger area of the malleus compared with that of the stapes). The reduction in area focuses the sound stimulus onto a smaller area, thus increasing the sound pressure. Audiologists refer to this amplification phenomenon as *impedance matching*.

460. The answer is d. (*Berne, 3/e, pp 118–121.*) The Golgi tendon organ (GTO) is located in the tendon of skeletal muscles and therefore is in series with the muscle. Each time the muscle contracts, the tension developed by the muscle causes the GTO to be stretched. The Ib afferent fibers, which innervate the GTO, fire in proportion to the amount of GTO stretch, and therefore their firing rate provides the CNS with information about the amount of tension developed by the muscle. The muscle length and speed of shortening are sent to the CNS by Ia afferents that innervate the intrafusal fibers within muscle spindles.

461. The answer is a. (*Berne, 3/e, pp 155–158.*) Each time a skeletal muscle fiber is stimulated by an alpha motoneuron, enough Ca^{2+} is released from its sarcoplasmic reticulum (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 (or bone or measuring device) 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. This occurs because each time the muscle is activated, the Ca^{2+} released from the SR replaces the Ca^{2+} that has been resequestered since the last stimulus. 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.

462. The answer is d. (*Guyton, pp 561–563.*) Free nerve endings contain receptors for temperature, pain, and touch. However, fine touch, pressure, and vibration are detected by nerve endings contained within specialized capsules that transmit the stimulus to the sensory receptors. Muscle length is encoded by the primary nerve endings of Ia fibers which are located on intrafusal fibers within the muscle spindle.

463. The answer is b. (*Guyton, pp 669–671.*) Aphasia is a language disorder in which a person is unable to properly express or understand certain aspects of written or spoken language. It is caused by lesions to the language centers of the brain, which, for the majority of persons, are located within the left hemisphere in the portions of the temporal and frontal lobes known as Wernicke's and Broca's areas, respectively. Language disorders caused by memory loss, which could be the result of a hippocampal lesion, are not classified as aphasias.

464. The answer is a. (*Rhoades, p 80.*) 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.

465. The answer is b. (*Berne, 3/e, pp 117–118.*) The gamma motoneurons innervate the intrafusal fibers of the muscle spindles. When a skeletal muscle contracts, the intrafusal muscle fiber becomes slack and the Ia afferents stop firing. By stimulating the intrafusal muscle fibers during a contraction, the gamma motoneurons prevent the intrafusal muscle fibers from becoming slack and thus maintain Ia firing during the contraction.

466. The answer is b. (*Rhoades, pp 62–69.*) A phasic receptor, illustrated by figure B, produces a high-frequency burst of action potentials when stimulated. The frequency of discharge slows down or stops even though the stimulus is maintained. The frequency of the burst discharge is proportional to the rate at which the stimulus is applied. In contrast, a tonic receptor, illustrated in A and C, continues to fire at a frequency proportional to the magnitude of the stimulus for as long as the stimulus is applied.

467. The answer is b. (*Rhoades, pp 69–70.*) 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. It 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.

468. The answer is d. (*Guyton, pp 648–650.*) The middle cerebellar peduncle contains afferent fibers conveyed in the pontocerebellar tract, which carries impulses from the motor area as well as other parts of the cerebellar cortex except the flocculonodular lobe. The dorsal spinocerebellar and vestibulocerebellar afferent tracts enter the cerebellum via the inferior peduncle. The ventral spinocerebellar and tectocerebellar tracts enter via the superior cerebellar peduncle.

469. The answer is e. (*Guyton, pp 638–640.*) The precentral gyrus is the motor area of the cortex and the corticospinal tract is the pyramidal tract proper. These two structures are essential for voluntary movement. A supplementary motor area, whose function is still unknown, exists on the medial side of the hemisphere.

470. The answer is a. (*Guyton, pp 655–656.*) 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 external and internal rotation of the foot. These symptoms all result from destruction of the normal feedback mechanisms that are coordinated in the cerebellum.

471. The answer is b. (*Rhoades, pp 83–85.*) 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.

472. The answer is c. (*Guyton, pp 579–581.*) 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 decomposition of retinal is not necessary for the activation of rhodopsin. However, rhodopsin cannot absorb another photon of light until it is enzymatically isomerized back to its 11-cis conformation.

473. The answer is d. (*Guyton, pp 711–714.*) Cerebrospinal fluid (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 between the dura mater and pia mater and is absorbed into the circulation by the arachnoid villi. The epidural space, which lies outside the dura mater, may be used

clinically for instillation of anesthetics. CSF protein and glucose concentrations are much lower than those of plasma. Changes in those concentrations in the CSF are helpful in detecting pathologic processes, such as tumor or infection, in which the blood-brain barrier is disrupted.

474. The answer is b. (*Guyton, pp 674–676.*) When the head rotates in one direction, the hair cells mounted on the cristae rotate along with the head. However, the flow of endolymph is delayed and as a result the cupula is moved in a direction opposite to the movement of the head. When the head moves to the right, the cupula moves toward the left; this bends the stereocilia on the hair cells in the right horizontal canal toward the kinocilium and bends the stereocilia on the hair cells in the left horizontal canal toward the kinocilium. As a result, the hair cells in the right horizontal canal depolarize and those in the left horizontal canal hyperpolarize. The depolarization of the hair cells in the right horizontal canal stimulates the right vestibular nerve, which in turn causes the eyes to deviate toward the left. The movement of the eyes toward the left as the head deviates toward the right keeps the image on the retina in focus.

475. The answer is c. (*Guyton, pp 74–78.*) During normal reflex or voluntary movements, small spinal motoneurons are recruited before large motoneurons. Small spinal motoneurons innervate small, weak, slow, fatigue-resistant muscle fibers. Large spinal motoneurons innervate large, fast, strong, easily fatigable muscle fibers. The fatigue-resistant muscle fibers have a dense capillary network for perfusion and use mitochondrial oxidative metabolism to produce ATP.

476. The answer is b. (*Guyton, pp 689–691.*) In a normal sleep cycle, a person passes through the four stages of slow-wave sleep before entering REM sleep. In narcolepsy, a person may pass directly from the waking state to REM sleep. REM sleep is characterized by irregular heart beats and respiration and by periods of atonia (loss of muscle tone). It is also the state of sleep in which dreaming occurs.

477. The answer is b. (*Guyton, p 570.*) In presbyopia, the ability of the lens to accommodate for near vision decreases. Thus, the total refractive power of the eye decreases and the ability of the eye to form a focused image of objects placed close to it decreases. The near point is the closest

point to which an object can be brought and still remain in focus. This increases when the accommodative power of the eye is decreased. There is no effect on the far point or visual acuity; these remain normal.

478. The answer is a. (*Guyton, pp 581–582.*) When light strikes the eye and is absorbed by rhodopsin, a photoisomerization of 11-cis retinal to all-trans retinal occurs. As a consequence of this photoisomerization, rhodopsin is activated. The rhodopsin then activates transducin, which in turn activates a phosphodiesterase, which hydrolyzes cGMP. When cGMP concentrations within the rods or cones decrease, sodium channels close, sodium conductance decreases, and the cell membrane potential increases (hyperpolarizes). Hyperpolarization of the cell causes a decrease in the release of neurotransmitter. Eventually the all-trans retinal dissociates from opsin and reduces the concentration of rhodopsin in the cell.

479. The answer is d. (*Guyton, pp 639–640.*) Spasticity results from overactivity of the alpha motoneurons innervating the skeletal musculature. Under normal circumstances, these alpha motoneurons are tonically stimulated by reticulospinal and vestibulospinal fibers originating in the brainstem. These brainstem fibers are normally inhibited by fibers originating in the cortex. Cutting the cortical fibers releases the brainstem fibers from inhibition and results in spasticity. Cutting the fibers from the reticular formation, vestibular nuclei, or the Ia afferents will reduce the spasticity.

480. The answer is a. (*Rhoades, pp 73–76.*) Transducin is the G protein that mediates the response to light by rods and cones in the eye. When transducin is activated, it activates an enzyme that hydrolyzes cyclic GMP (cGMP). In the dark, cGMP binds to Na^+ channels, keeping them open. The flow of Na^+ through these channels keeps the rods and cones depolarized. The activation of transducin by light and the subsequent hydrolysis of cGMP cause the Na^+ channels to close and the membrane to hyperpolarize. Hyperpolarization of the membrane prevents the release of an inhibitory transmitter by the rods and cones, which ultimately results in stimulation of optic nerve fibers and the awareness of a visual image.

481. The answer is b. (*Guyton, p 655.*) The flocculonodular lobe is known as the *archeocerebellum* because it is, phylogenetically, the oldest portion of the cerebellum. It is connected to the vestibular nuclei and par-

ticipates in the control of eye movements. Lesions to the flocculonodular lobe will cause nystagmus. Lesions to the other regions of the cortex, the deep nuclei of the spinocerebellar tracts, cause a variety of abnormalities in motor coordination referred to as ataxia.

482. The answer is b. (*Guyton, pp 691–692.*) In a totally relaxed adult with eyes closed, the major component of the electroencephalogram (EEG) will be a regular pattern of 8 to 12 waves per second, called the alpha rhythm. The alpha rhythm disappears when the eyes are opened. It is most prominent in the parieto-occipital region. In deep sleep, the alpha rhythm is replaced by larger, slower waves called delta waves. In REM sleep, the EEG will show fast, irregular activity.

483–484. The answers are 483-a, 484-e. (*Rhoades, pp 70–73. Guyton, pp 570–575.*) The focal length of an ideal refractive surface is equal to the distance between the refractive surface and the image formed by a distant object. In a normal eye, the image of a distant object is formed on the retina. Therefore, the focal length is 14 mm. If the image formed in front of the retina, the eye would be myopic (near-sighted); if the image formed behind the retina, the eye would be hyperopic (far-sighted).

When an image is placed close to the eye (in ophthalmology, *close* means less than 20 ft or 6 m), the eye must accommodate (increase its refractive power) for near vision. The refractive power of a lens system in diopters is equal to the reciprocal of the focal length ($1/f$) in meters. The relationship between the refractive power P , or focal distance, the image distance, and the object distance is given by the lens formula

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

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

485. The answer is a. (*Guyton, pp 625–626, 628.*) 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 alpha 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. However, the Ib activity is increased during contraction because of the tension placed on the Golgi tendon organs.

486. The answer is d. (*Rhoades, pp 118–120.*) Activation of the sympathetic nervous system produces relaxation of the smooth muscles surrounding the bronchioles, leading to bronchiolar dilation. The parasympathetic nerves are responsible for penile erection, pupillary constriction, contraction of the ciliary muscle during accommodation for near vision, and gallbladder emptying. Sympathetic stimulation causes ejaculation and pupillary dilation but does not affect the activity of the ciliary muscle or the gallbladder.

487. The answer is d. (*Guyton, pp 701–703.*) The catecholamines norepinephrine and epinephrine will activate both α - and β -adrenergic receptors. When the α_1 -adrenergic receptors are stimulated, they activate a G protein, which in turn activates phospholipase C that 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. The bronchiolar, pupillary, and ciliary smooth muscles all contain beta receptors, which cause smooth muscle relaxation. The intestinal smooth muscle relaxation is initiated by an α_2 -adrenergic receptor.

488. The answer is c. (*Rhoades, pp 76–78.*) A *decibel* is a measure of the ratio between two sound stimuli. The decibel level of a sound stimulus is referenced to the lowest sound that a normal human can hear and is calculated using the formula: Intensity (in decibels) = $20 \times \log(\text{sound}/\text{threshold})$. Therefore, the intensity of a sound that is 1000 times threshold is 60 decibels. If the threshold for hearing increases by 1000 times, that is, if the sound intensity must be increased 1000 times for the person with the hearing loss to detect its presence, then the hearing loss is 60 decibels.

489. The answer is a. (*Rhoades, pp 79–83.*) 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.

490. The answer is e. (*Rhoades, pp 104–107.*) The Babinski reflex causes the toes to dorsiflex in response to stroking the plantar or lateral portion of the foot. It is an abnormal reflex caused by damage to the corticospinal (pyramidal) tract that travels from the cortical motor cortex through the pyramids to the spinal cord. Other signs of pyramidal tract lesions include loss of the hopping and placing reaction, the cremasteric reflex, and the abdominal scratch reflex. Damage confined to the pyramidal tract results in distal muscular weakness and loss of fine motor control. Damage to other areas of the cortical motor control system is referred to as *upper motor neuron disease* and produces spasticity. Damage to the basal ganglia produces a variety of signs including dystonia (striatum), ballism (subthalamic nucleus), and tremor (substantia nigra). Damage to the cerebellum results in uncoordinated movements (dysmetria).

491. The answer is e. (*Rhoades, pp 130–132.*) A variety of physiological functions, such as alertness (the sleep-wake cycle), body temperature, and secretion of hormones, exhibits cyclic activity that varies over a 24-h period of time. These variations in activity are called *circadian rhythms* and are controlled by the suprachiasmatic nucleus of the hypothalamus. The paraventricular nucleus secretes oxytocin and vasopressin, the ventromedial and lateral nuclei control food intake, and the arcuate nucleus secretes gonadotropin-releasing hormone.

492. The answer is a. (*Guyton, p 516–517, 523.*) Presynaptic inhibition is caused by interneurons that secrete a transmitter which increases the Cl^- conductance of the presynaptic nerve ending. The increase in Cl^- conduc-

tance causes a partial depolarization of the presynaptic nerve ending and a decrease in the magnitude of the action potential in the presynaptic nerve ending. Because the amount of mediator released at the synapse is related to the magnitude of the action potential, less transmitter is released and the firing rate of the postsynaptic alpha motoneuron is decreased. Presynaptic inhibition does not change the membrane potential of the alpha motoneuron, and therefore the membrane potential of the alpha motoneuron is not affected.

493. The answer is c. (*Guyton, pp 624–628.*) The firing of the alpha motoneurons to the biceps muscle produces rapid flexion of the arm. Because the arm is rapidly flexed, the Ia afferent neurons innervating the muscle spindles in the biceps, which detect muscle length, will reduce their firing rate. The Ib afferents, innervating the Golgi tendon organs (GTO) from the biceps, will detect the contractile activity of the biceps and increase their firing rate. The triceps are stretched during the arm flexion and so their Ia afferents will increase their firing rate. Ib afferents do not respond when muscles are passively stretched, so their firing rate will not change.

494. The answer is c. (*Guyton, 9/e, pp 705–707.*) The entire sympathetic nervous system is activated when a person is frightened, preparing the individual for flight or to fight. As part of this preparation, the smooth muscle of the airways is relaxed, increasing the airway diameter, making it easier for the person to breathe. At the same time, heart rate and cardiac output are increased, causing a rise in blood pressure, and blood glucose concentrations are increased, making fuel available for whatever choice is made.

495. The answer is b. (*Guyton, pp 592, 595–596.*) The pituitary gland is situated near the optic chiasm. A pituitary gland tumor will therefore impinge on the portion of the optic nerve fibers conveying information from the nasal portions of both retinas and produce a temporal visual field defect in both eyes. This defect is referred to as a *bitemporal hemianopsia*.

496. The answer is c. (*Guyton, pp 592, 595–596.*) Lesions of the right visual cortex will produce visual field defects on the left side of both eyes (called *contralateral hemianopsia*). However, even extensive lesions of the

visual cortex will not affect the center of the visual field, which is conveyed to the cortex by nerve fibers projecting from the macula. This is called *macula sparing*. A lesion of the left optic tract will produce a complete contralateral hemianopsia (the visual field defect labeled D in the diagram of question 495).

497. The answer is e. (Guyton, pp 552–555.) Activating nociceptors on the free nerve endings of C fibers produces ischemic pain. The C fibers synapse on interneurons located within the substantia gelatinosa (laminae II and III) of the dorsal horn of the spinal cord. The pathway conveying ischemic pain to the brain is called the *paleospinothalamic system*. In contrast, well-localized pain sensations are carried within the neospinothalamic tract. Ischemic pain does not adapt to prolonged stimulation. Pain is produced by specific nociceptors and not by intense stimulation of other mechanical, thermal, or chemical receptors.

498. The answer is e. (Guyton, pp 826–830.) The hypothalamus regulates body temperature. Core body temperature, the temperature of the deep tissues of the body, is detected by thermoreceptors located within the preoptic area and the anterior hypothalamic nuclei. The preoptic area 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 head maintenance reflexes, such as vasoconstriction, are initiated by neurons located within the posterior hypothalamus.

499. The answer is a. (Guyton, pp 581–582.) The visual receptor cells, the rods and cones, are depolarized in their nonstimulated state. When exposed to light, they hyperpolarize. Light causes the rods and cones to hyperpolarize by activating a G protein called transducin, which leads to the closing of Na^+ channels. Auditory receptors are depolarized by the flow of K^+ into the hair cells. Touch receptors are activated by opening channels through which both Na^+ and K^+ can flow. Depolarization is caused by the inward flow of Na^+ . Smell and taste receptors are activated by G-protein-mediated mechanisms, some of which cause the receptor cell to depolarize; other G proteins cause the release of synaptic transmitter without any change in membrane potential.

500. The answer is b. (*Guyton, pp 686–687.*) The Klüver-Bucy syndrome is produced in animals by removal of the amygdala from both temporal lobes. The syndrome is characterized by a tendency to examine objects orally and excessive sexual behavior. The full syndrome is rarely encountered in humans but many of its characteristics are observed in patients with bilateral temporal lobe lesions produced by encephalitis or traumatic injury.

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