

COMPREHENSIVE MOCK EXAM 7

Supplemental to: Physiology Board Review 2026-2027

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USMLE Step 1 (NBME/FSMB) - 280 questions, single-best-answer with A-E options in this parent-book format, domain-weighted to the current Step 1 blueprint

Board-Review Questions

1. A patient develops abrupt hydrocephalus from obstruction of cerebrospinal fluid flow at the cerebral aqueduct. Which ventricles enlarge?
 - A. Both lateral ventricles and the third ventricle
 - B. Only the fourth ventricle
 - C. All ventricles equally because the obstruction is distal to them all
 - D. The fourth ventricle and central canal only
 - E. Only the third and fourth ventricles

2. A patient acutely ascends to altitude and hyperventilates. Which change in arterial pH and PCO₂ occurs first?
 - A. pH falls and PCO₂ falls
 - B. pH rises and PCO₂ falls
 - C. Both remain unchanged until erythropoietin rises
 - D. pH rises and PCO₂ rises
 - E. pH falls and PCO₂ rises

3. A patient asks the physician not to tell family members about a new cancer diagnosis. The patient has capacity and there is no rapid threat to others. Which action best fulfills the physician's obligation?
 - A. Ask another clinician to disclose the information to avoid responsibility
 - B. Maintain confidentiality and discuss with the patient how support needs can be met
 - C. Post the diagnosis in a shared family portal without permission
 - D. Notify the employer so work duties can be modified
 - E. Disclose the diagnosis to the family because they may be emotionally affected

4. A patient has abrupt blood loss. What is the expected rapid autonomic response to reduced carotid sinus stretch?

- A.** Suppression of renin release via beta-1 blockade
- B.** Reduced sympathetic outflow and increased parasympathetic outflow
- C.** Greater sympathetic outflow and decreased parasympathetic outflow
- D.** Greater vagal activity with systemic vasodilation
- E.** Reduced heart rate with increased splanchnic blood flow

5. A patient who has metabolic alkalosis increases bicarbonate secretion from the collecting duct. Which cell type mediates this response?

- A.** Alpha-intercalated cells using apical H^+ -ATPase
- B.** Beta-intercalated cells using apical chloride-bicarbonate exchange
- C.** Podocytes using slit diaphragms
- D.** Principal cells using epithelial sodium channels
- E.** Juxtaglomerular cells using renin granules

6. A patient who has bacterial sepsis develops fever. Which endogenous mediator acts on the hypothalamus to raise the thermoregulatory set point?

- A.** Nitric oxide released by skeletal muscle to trigger shivering
- B.** Prostaglandin E₂ generated in response to pyrogenic cytokines
- C.** Histamine released in the stomach to activate brown adipose tissue
- D.** Bradykinin generated in peripheral tissues to lower the set point
- E.** Erythropoietin released by the kidney to conserve body heat

7. During evaluation, two alveoli have different radii but similar surface tension. According to the law of Laplace, which alveolus requires greater pressure to remain open?

- A.** Both require identical pressure regardless of radius
- B.** Only the alveolus with greater wall thickness
- C.** Only the alveolus with lower perfusion pressure

- D.** The larger alveolus
- E.** The smaller alveolus because pressure rises as radius falls

8. During evaluation, a patient has glucosuria despite a normal plasma glucose concentration because a proximal tubular transporter is defective. Under normal conditions, filtered glucose is reabsorbed mainly through which apical transport process?

- A.** Glucose-chloride cotransport
- B.** ATP-dependent glucose pumping directly into the lumen
- C.** Facilitated diffusion from blood into tubular fluid
- D.** Hydrogen-glucose exchange in the collecting duct
- E.** Apical sodium-glucose cotransport driven by the sodium gradient

9. A patient hears a tone. Deflection of cochlear inner hair-cell stereocilia toward the tallest stereocilia causes which rapid event?

- A.** Potassium efflux into endolymph that hyperpolarizes the hair cell
- B.** Generation of an action potential within the hair cell axon
- C.** Closure of calcium channels and reduced transmitter release
- D.** Opening of mechanically gated channels and potassium influx from endolymph
- E.** Opening of sodium channels and sodium efflux into endolymph

10. During evaluation, a patient has a tidal volume of 500 mL, an anatomic dead space of 150 mL, and a respiratory rate of 12/min. What is the alveolar ventilation?

- A.** 3.0 L/min
- B.** 6.0 L/min
- C.** 4.2 L/min
- D.** 7.8 L/min
- E.** 1.8 L/min

11. A patient who has severe iron deficiency has reduced hemoglobin concentration but normal arterial PO₂. Which of the following variables is most directly decreased?

- A.** Reduced arterial oxygen content from reduced hemoglobin concentration
- B.** The alveolar oxygen tension predicted by the alveolar gas equation
- C.** The diffusion coefficient of oxygen across the alveolar-capillary membrane
- D.** The percentage saturation of normal hemoglobin at a given PO₂
- E.** The fraction of dissolved oxygen determined by arterial PO₂

12. During evaluation, pTH stimulates renal 1- α -hydroxylase. What is the resulting hormonal product?

- A.** Cholecalciferol synthesized in skin
- B.** Calcitriol, or 1,25-dihydroxyvitamin D
- C.** Calcitonin from thyroid parafollicular cells
- D.** Aldosterone from zona glomerulosa cells
- E.** Calcidiol, or 25-hydroxyvitamin D

13. A patient who has an encapsulated bacterial infection improves after antibodies coat the organism. Which of the following processes is most directly enhanced by IgG and C3b deposition on the bacterial surface?

- A.** Phagocytosis via Fc and complement receptors
- B.** Eosinophil activation by helminth-bound IgE alone
- C.** Mast-cell degranulation via cross-linked surface IgE
- D.** Natural killer cell recognition of reduced MHC class I
- E.** Direct intracellular killing by cytotoxic T lymphocytes

14. A patient who has iron deficiency is prescribed oral iron. In which region is dietary iron absorbed most efficiently?

- A.** Duodenum and proximal jejunum
- B.** Ascending and transverse colon
- C.** Gastric body and fundus
- D.** Rectum and anal canal
- E.** Terminal ileum and cecum

15. Shortly after delivery, a term neonate begins sustained breathing and the lungs expand. Which rapid physiologic change primarily increases pulmonary blood flow?

- A.** A decrease in left atrial pressure caused by increased pulmonary venous return
- B.** A decrease in pulmonary vascular resistance caused by lung expansion and rising alveolar oxygen
- C.** An increase in right atrial pressure caused by closure of the foramen ovale
- D.** A decrease in systemic vascular resistance caused by umbilical cord clamping
- E.** An increase in pulmonary vascular resistance caused by loss of placental flow

16. During evaluation, a patient has primary hyperaldosteronism. Which principal-cell transport change is stimulated by aldosterone?

- A.** Reduced epithelial sodium channel activity and reduced potassium secretion
- B.** Inhibition of basolateral Na^+/K^+ ATPase
- C.** Insertion of aquaporin-2 independent of vasopressin
- D.** Greater epithelial sodium channel activity and Na^+/K^+ ATPase expression
- E.** Reduced ROMK activity with potassium retention

17. A patient develops severe right heart failure with elevated right atrial pressure. Which of the following effects on systemic venous return is expected if mean systemic filling pressure is unchanged?

- A.** Venous return is independent of right atrial pressure
- B.** Venous return rises only because capillary hydrostatic pressure falls

- C. Venous return increases because right atrial pressure pulls blood forward
- D. Venous return doubles because venous valves close
- E. Venous return decreases because the pressure gradient to the right atrium is reduced

18. During evaluation, a patient develops bilateral ureteral obstruction. Which Starling force at the glomerulus most directly lowers GFR?

- A. Reduced plasma oncotic pressure in glomerular capillaries
- B. Greater filtration coefficient from capillary dilation
- C. Greater hydrostatic pressure in Bowman space
- D. Greater glomerular capillary hydrostatic pressure
- E. Reduced hydrostatic pressure in Bowman space

19. During evaluation, after ovulation, which ovarian structure becomes the major source of progesterone during the luteal phase?

- A. Fimbria of the fallopian tube
- B. Luteinized corpus luteum
- C. Primordial follicle
- D. Ovarian surface epithelium
- E. Theca externa

20. A patient who has hyperkalemia initially develops increased skeletal-muscle excitability. What is the rapid membrane effect of increasing extracellular potassium?

- A. The sodium equilibrium potential becomes markedly more negative
- B. The membrane becomes impermeable to potassium via leak channels
- C. The resting membrane potential becomes less negative
- D. The resting membrane potential becomes more negative
- E. All voltage-gated sodium channels become permanently activated immediately

21. A patient who has autoimmune hemolytic anemia has IgG directed against erythrocyte surface antigens. Which hypersensitivity mechanism best describes this process?

- A.** T-cell-mediated delayed tissue injury without antibody
- B.** Superantigen-mediated polyclonal T-cell activation
- C.** Immune-complex deposition with neutrophilic vasculitis
- D.** IgE-mediated mast-cell degranulation after allergen exposure
- E.** Antibody-mediated cellular injury with opsonization and phagocytosis

22. During evaluation, a patient receives a large amount of sodium bicarbonate. Which buffer system is the main extracellular defense against the added base?

- A.** Carbonic acid-bicarbonate system linked to pulmonary CO₂ excretion
- B.** Intracellular proteins only, with no extracellular buffering
- C.** Ammonium buffer only within the renal medulla
- D.** Phosphate buffer alone with no respiratory contribution
- E.** Hemoglobin buffer only inside erythrocytes

23. During evaluation, a patient attempts to lift a load that is too heavy for a muscle to shorten. The muscle develops force while remaining the same length. What type of contraction is occurring?

- A.** Isotonic eccentric contraction
- B.** Isometric contraction with no change in muscle length
- C.** Auxotonic shortening with constant force
- D.** Isotonic concentric contraction
- E.** Passive elastic recoil without cross-bridge cycling

24. During evaluation, most filtered sodium and water are reabsorbed together in which nephron segment?

- A.** Distal convoluted tubule

- B.** Thick ascending limb
- C.** Collecting duct
- D.** Thin descending limb
- E.** Proximal convoluted tubule

25. During evaluation, an isolated skeletal muscle is stimulated at progressively greater initial lengths. At which sarcomere condition is active force maximal?

- A.** Complete overlap of thin filaments with maximal actin-actin interference
- B.** A sarcomere so shortened that thick filaments press against the Z discs
- C.** An optimal overlap of actin and myosin that permits the greatest number of cross-bridges
- D.** Any sarcomere length because active force is independent of overlap
- E.** A sarcomere stretched enough that actin and myosin no longer overlap

26. During evaluation, a sprinter performs a short all-out effort. Which skeletal-muscle fiber type is best suited for the highest power output over a brief interval?

- A.** Slow oxidative fibers with abundant mitochondria and low shortening velocity
- B.** Cardiac myocytes with intercalated discs and long refractory periods
- C.** Smooth muscle fibers with latch-state cross-bridges
- D.** Fast glycolytic fibers with high myosin ATPase activity
- E.** Type I fibers with high myoglobin and fatigue resistance

27. A patient who has heart failure develops dependent edema despite increased total body sodium. Which concept best explains why renal sodium retention can persist?

- A.** The kidneys sense total body sodium directly and therefore always excrete it
- B.** Plasma osmolality must be low whenever edema is present
- C.** Atrial stretch always completely suppresses the renin-angiotensin system
- D.** Reduced effective arterial blood volume is sensed despite expanded extracellular fluid

E. Interstitial edema directly increases renal perfusion pressure

28. An otherwise healthy person breathes 100% oxygen. Which component of arterial oxygen content changes relatively little compared with hemoglobin-bound oxygen?

- A. Dissolved oxygen increases, but it remains a small fraction of total oxygen content
- B. Hemoglobin-bound oxygen rises without an upper saturation limit
- C. Arterial oxygen content falls because high PO₂ shifts hemoglobin to the right
- D. Dissolved oxygen becomes the dominant form of oxygen transport
- E. Hemoglobin concentration doubles because oxygen stimulates erythropoiesis immediately

29. During evaluation, a patient has prolonged fasting with marked ketogenesis. Why can the liver produce but not consume ketone bodies?

- A. Hepatocytes cannot perform beta-oxidation
- B. Hepatocytes cannot synthesize acetoacetate
- C. Lack of hepatic thiophorase for ketone-body oxidation
- D. Hepatocytes lack mitochondria
- E. Hepatocytes lack acetyl-CoA

30. During evaluation, a patient has complete heart block. Which tissue normally has the fastest intrinsic pacemaker rate and therefore drives the healthy heart?

- A. Ventricular myocardium
- B. Purkinje fibers
- C. His bundle
- D. Sinoatrial node
- E. Atrioventricular node

31. An otherwise healthy young adult has an audible third heart sound during rapid ventricular filling. What produces this sound?

- A.** Ventricular vibration during rapid early diastolic filling
- B.** Opening of the atrioventricular valves
- C.** Closure of the semilunar valves
- D.** Isovolumetric contraction before ejection
- E.** Atrial contraction against a stiff ventricle

32. A patient increases oxygen extraction during exercise. Which of the following occurs to mixed venous oxygen content if arterial oxygen content is unchanged?

- A.** It decreases as tissues remove more oxygen from each unit of blood
- B.** It increases because exercising tissues return more oxygen to the veins
- C.** It becomes zero in all healthy exercise
- D.** It remains fixed because venous oxygen content is independent of extraction
- E.** It equals arterial oxygen content once cardiac output rises

33. A patient has nephrogenic diabetes insipidus. Which of the following findings distinguishes it from central diabetes insipidus?

- A.** Plasma osmolality is always low
- B.** Urine becomes markedly concentrated after desmopressin
- C.** Urine remains dilute after desmopressin administration
- D.** Collecting ducts have excessive aquaporin-2 insertion
- E.** Vasopressin secretion is absent by definition

34. An otherwise healthy person receives a small cut. Platelets adhere to exposed subendothelium at the injury site. Which interaction is essential for the initial adhesion step?

- A.** Platelet glycoprotein IIb/IIIa binding directly to exposed collagen fibers

- B.** Platelet glycoprotein Ib binding to von Willebrand factor attached to collagen
- C.** Plasmin binding to fibrin and promoting platelet attachment to the vessel wall
- D.** Thrombin binding to antithrombin and bridging platelets to fibrinogen
- E.** Tissue factor binding to platelet ADP receptors on the endothelial surface

35. A patient who has hemorrhage activates the renin-angiotensin-aldosterone system. Which factor directly stimulates aldosterone secretion most strongly?

- A.** Angiotensin II and elevated plasma potassium
- B.** ACTH alone as the dominant chronic regulator
- C.** Low extracellular potassium
- D.** Atrial natriuretic peptide
- E.** Reduced angiotensin II signaling

36. A patient who has primary hyperparathyroidism has elevated PTH. Which renal effect is expected?

- A.** Reduced calcium reabsorption with increased phosphate reabsorption
- B.** Reduced distal calcium reabsorption and reduced calcitriol synthesis
- C.** Greater phosphate reabsorption without changing calcium handling
- D.** Suppressed 1-alpha-hydroxylase activity
- E.** Greater calcium reabsorption with decreased phosphate reabsorption

37. During evaluation, acidic chyme enters the duodenum. Which hormone is released and stimulates pancreatic bicarbonate secretion?

- A.** Ghrelin
- B.** Somatostatin
- C.** Gastrin
- D.** Motilin

E. Secretin

38. During evaluation, a patient has volume depletion with increased renin release. Which intrarenal signal directly stimulates juxtaglomerular renin secretion?

- A. Greater afferent arteriolar pressure
- B. Reduced sodium chloride delivery to the macula densa
- C. Greater atrial natriuretic peptide signaling
- D. Reduced sympathetic beta-1 receptor stimulation
- E. Greater sodium chloride delivery to the macula densa

39. During evaluation, a patient has vomiting for several days and develops metabolic alkalosis. Which factor helps maintain the alkalosis after volume depletion develops?

- A. Greater proximal bicarbonate reabsorption and aldosterone-driven distal hydrogen secretion
- B. Greater chloride delivery that always forces bicarbonate retention
- C. Reduced aldosterone with reduced hydrogen secretion
- D. Suppressed bicarbonate reabsorption because extracellular volume is low
- E. Reduced renin-angiotensin activity with reduced sodium reabsorption

40. During evaluation, a patient has loss of vibration and position sense below a spinal cord lesion but preserved pain and temperature. Which ascending pathway is most likely damaged?

- A. Anterolateral spinothalamic pathway
- B. Reticulospinal motor pathway
- C. Dorsal column-medial lemniscus pathway
- D. Dorsal spinocerebellar tract only
- E. Lateral corticospinal tract

41. During evaluation, a screening test is evaluated in 1,000 people. Among 100 people with disease, 90 test positive. What is the sensitivity?

- A.** 99%
- B.** 10%
- C.** 50%
- D.** 90%
- E.** 81%

42. A patient who has schizophrenia refuses hospitalization. The patient accurately describes the diagnosis, treatment options, consequences of refusal, and gives a stable reasoned choice. Which conclusion is most appropriate?

- A.** Any diagnosis of schizophrenia automatically eliminates decision-making capacity
- B.** Capacity is determined only by whether the patient agrees with the physician
- C.** Capacity can be assessed only by a judge
- D.** A patient who refuses recommended care necessarily lacks appreciation
- E.** The patient may have decision-making capacity despite the psychiatric diagnosis

43. A patient receives a pure arterial vasoconstrictor that increases systemic vascular resistance without changing contractility. What is the rapid effect on the left ventricular pressure-volume loop?

- A.** Greater end-diastolic volume with unchanged end-systolic volume only
- B.** No change because systemic vascular resistance does not affect ventricular ejection
- C.** Reduced afterload with a wider loop and lower arterial pressure
- D.** Higher systolic pressure and elevated end-systolic volume with reduced stroke volume
- E.** Lower systolic pressure and reduced end-systolic volume with elevated stroke volume

44. A patient who has longstanding kidney disease develops a normocytic anemia. Which normal renal response to hypoxia is impaired?

- A. Peritubular interstitial cell production of erythropoietin
- B. Collecting duct synthesis of hepcidin in response to low iron
- C. Macula densa secretion of renin into the peritubular capillaries
- D. Juxtaglomerular cell release of intrinsic factor into plasma
- E. Proximal tubular secretion of thrombopoietin into the urine

45. Afferent arteriolar constriction occurs in one kidney. What is the expected rapid effect on glomerular filtration rate and renal plasma flow in that kidney?

- A. Both increase
- B. GFR remains unchanged while renal plasma flow doubles
- C. GFR decreases while renal plasma flow increases
- D. Both GFR and renal plasma flow decrease
- E. GFR increases while renal plasma flow decreases

46. During evaluation, a patient has iodine deficiency. Which step in thyroid hormone synthesis becomes substrate limited?

- A. Binding of T₃ to nuclear receptors in target cells
- B. Iodination of tyrosyl residues within thyroglobulin
- C. Endocytosis of colloid into follicular cells
- D. Peripheral conversion of T₄ to T₃ by deiodinases
- E. Proteolysis of thyroglobulin in lysosomes

47. During evaluation, a patient develops vasodilation of skin vessels during heat stress. What is the main thermoregulatory benefit?

- A. Greater renal heat excretion through glomerular filtration
- B. Reduced sweat evaporation by lowering skin blood flow
- C. Greater transfer of core heat to the skin for radiation and convection

- D.** Reduced skin temperature to minimize heat transfer to the environment
- E.** Greater metabolic heat production in skeletal muscle

48. During evaluation, in a randomized trial, 10% of the control group and 5% of the treatment group experience an adverse event. What is the absolute risk reduction?

- A.** 50 percentage points
- B.** 10 percentage points
- C.** 5 percentage points
- D.** 2 percentage points
- E.** 95 percentage points

49. A patient who has left ventricular hypertrophy has increased myocardial oxygen demand. Under normal conditions, coronary blood flow to the left ventricular myocardium is greatest during which phase?

- A.** Early systole during isovolumetric contraction
- B.** Late systole during ongoing ventricular ejection
- C.** Peak systole during maximal ventricular wall tension
- D.** Atrial systole just before ventricular contraction
- E.** Ventricular diastole during myocardial relaxation

50. During evaluation, a patient performs repeated high-intensity contractions. Creatine phosphate helps buffer ATP levels by donating phosphate to which molecule?

- A.** Pyruvate via lactate dehydrogenase
- B.** AMP via adenylate cyclase
- C.** ADP via the creatine kinase reaction
- D.** Myosin via myosin light-chain kinase
- E.** Glucose via hexokinase

51. During evaluation, a patient receives an intravenous infusion of pure free water after it is metabolically equivalent to water. How does it distribute after osmotic equilibration?

- A.** Only in interstitial fluid because intracellular osmoles repel water
- B.** Only in red cells because hemoglobin is the major osmole
- C.** Only in extracellular fluid because aquaporins exclude solute-free water
- D.** Only in plasma because water cannot cross cell membranes
- E.** Across total body water, with most entering the intracellular compartment

52. A patient loses a large volume of hypotonic sweat during prolonged exercise without drinking. Which of the following changes is expected?

- A.** ECF volume falls and ECF osmolality rises, shrinking cells
- B.** Extracellular volume increases and osmolality falls
- C.** Intracellular volume increases because water moves into cells
- D.** Both compartments expand because sodium is lost
- E.** Extracellular osmolality remains unchanged because sweat is isotonic

53. A patient who has primary adrenal insufficiency has low cortisol. Which of the following changes is expected in ACTH if the pituitary is normal?

- A.** ACTH disappears because CRH secretion stops
- B.** ACTH increases because cortisol negative feedback is reduced
- C.** ACTH remains fixed because it is regulated only by aldosterone
- D.** ACTH increases only if serum potassium is low
- E.** ACTH decreases because cortisol negative feedback is reduced

54. A patient who has fever begins shivering while the measured core temperature is already elevated. Why does shivering occur?

- A.** Core thermoreceptors cannot detect temperature during infection

- B.** Peripheral vasodilation always precedes fever
- C.** The hypothalamic set point has risen above the current body temperature
- D.** The hypothalamic set point has fallen below the current body temperature
- E.** Sweating has lowered plasma osmolality below normal

55. A patient acclimatizes to high altitude for several weeks. Which of the following changes improves long-term oxygen delivery?

- A.** Greater erythropoietin-driven red-cell mass
- B.** Reduced ventilation to restore arterial PCO₂
- C.** Reduced capillary density in skeletal muscle
- D.** Persistent suppression of erythropoietin despite hypoxemia
- E.** Reduced 2,3-BPG concentration with a strong left shift

56. During evaluation, an endurance athlete has a high proportion of type I skeletal-muscle fibers. Which feature is characteristic of these fibers?

- A.** Dependence on phosphocreatine with poor aerobic ATP production
- B.** High mitochondrial density, myoglobin content, and fatigue resistance
- C.** High myosin ATPase activity with the fastest shortening velocity
- D.** Minimal oxidative enzyme activity and very low myoglobin
- E.** Low capillary density with predominant anaerobic glycolysis

57. During evaluation, after enterocytes absorb long-chain fatty acids, they package re-esterified triglycerides into chylomicrons. Where do chylomicrons enter the circulation first?

- A.** Intestinal lymphatic lacteals
- B.** Gastric veins
- C.** Hepatic sinusoids directly
- D.** Portal venous capillaries directly

E. Renal lymphatics

- 58.** A patient who has inflammation has low serum iron despite adequate total body iron stores. Increased hepatic hepcidin produces this pattern by causing which change?
- A.** Greater transferrin synthesis with enhanced intestinal iron export
 - B.** Activation of divalent metal transporter 1 on the basolateral enterocyte membrane
 - C.** Reduced ferritin synthesis with rapid release of stored macrophage iron
 - D.** Internalization and degradation of ferroportin on enterocytes and macrophages
 - E.** Greater erythropoietin signaling with accelerated marrow iron uptake
- 59.** During evaluation, a patient receives an opioid analgesic. Activation of mu-opioid receptors reduces neurotransmitter release from nociceptive terminals by which mechanism?
- A.** Gi signaling that lowers cAMP, closes calcium channels, and opens potassium channels
 - B.** Gs signaling that increases cAMP and opens presynaptic calcium channels
 - C.** Direct activation of nicotinic sodium channels on pain fibers
 - D.** Gq signaling that increases IP3 and raises transmitter release
 - E.** Inhibition of potassium conductance that depolarizes nociceptive neurons
- 60.** During evaluation, a patient has terminal ileal disease and develops vitamin B12 deficiency. Which normal absorption step occurs in the terminal ileum?
- A.** Binding of vitamin B12 to intrinsic factor in the gastric lumen only
 - B.** Initial release of vitamin B12 from food by pancreatic amylase
 - C.** Synthesis of vitamin B12 by enterocytes
 - D.** Absorption of iron via DMT1 as the principal B12 pathway
 - E.** Uptake of intrinsic factor-vitamin B12 complexes by specific receptors

61. During evaluation, parathyroid hormone increases osteoclast-mediated bone resorption even though osteoclasts lack the main PTH receptor. Which intermediate signal is increased on osteoblast-lineage cells?

- A.** RANK ligand
- B.** Type II collagen
- C.** Osteoprotegerin
- D.** Calcitonin
- E.** Sclerostin

62. During evaluation, a patient has a restrictive interstitial lung disease. Which pulmonary function pattern is expected?

- A.** Reduced total lung capacity with a normal or elevated FEV1/FVC ratio
- B.** Greater total lung capacity with a reduced FEV1/FVC ratio
- C.** Reduced FEV1/FVC ratio as the defining abnormality
- D.** Greater vital capacity with reduced elastic recoil
- E.** Normal total lung capacity with isolated elevated residual volume

63. During evaluation, a study finds an association between coffee drinking and pancreatic disease, but smoking is related to both coffee use and disease risk. Smoking distorts the observed association. What is this phenomenon?

- A.** Lead-time bias from earlier disease diagnosis
- B.** Observer-expectancy effect during measurement
- C.** Selection bias from nonrepresentative sampling
- D.** Regression toward the mean after selection
- E.** Confounding by a third variable

64. A patient who has low ionized calcium has increased PTH secretion. Which receptor on parathyroid chief cells detects extracellular calcium?

- A. TSH receptor
- B. Vitamin D nuclear receptor only
- C. Insulin receptor
- D. Calcium-sensing receptor
- E. Beta-1 adrenergic receptor

65. A patient has a pulmonary embolus that blocks perfusion to a ventilated region of lung. Which of the following occurs to the local ventilation-perfusion ratio?

- A. It remains near 1 because ventilation automatically stops
- B. It becomes zero and behaves like a right-to-left shunt
- C. It becomes negative because alveolar pressure falls below pleural pressure
- D. It becomes very high and approaches dead-space behavior
- E. It becomes undefined only if both ventilation and perfusion are absent

66. During evaluation, angiotensin II increases sodium reabsorption in the proximal tubule partly by stimulating which apical transporter?

- A. Na-K-2Cl cotransporter in the thick ascending limb only
- B. Epithelial sodium channel in principal cells
- C. Aquaporin-2 in collecting-duct principal cells
- D. Sodium-chloride cotransporter in the distal tubule only
- E. Apical sodium-hydrogen exchange in the proximal tubule

67. During evaluation, investigators perform a case-control study of a rare disease. Which association measure is most appropriate?

- A. Hazard ratio from time-to-event analysis alone
- B. Odds ratio comparing prior exposure in cases and controls
- C. Attributable risk from exposed and unexposed incidence

- D. Number needed to treat from absolute risk reduction
- E. Prospective relative risk from incident disease rates

68. During evaluation, a patient at high altitude has low alveolar oxygen tension. How do small pulmonary arteries respond to regional alveolar hypoxia?

- A. They dilate via a renal erythropoietin mechanism
- B. They constrict only when systemic arterial pressure falls
- C. They remain unchanged because pulmonary vessels lack oxygen sensing
- D. They dilate to increase flow via hypoxic alveoli
- E. They constrict to divert blood toward better-ventilated alveoli

69. During evaluation, a patient moves from a dark room into bright sunlight. Which photoreceptor change occurs when light strikes a rod?

- A. Reduced cGMP closes cation channels and hyperpolarizes the photoreceptor
- B. Greater cGMP opens cation channels and depolarizes the photoreceptor
- C. Opening of voltage-gated sodium channels generates a photoreceptor action potential
- D. Greater intracellular calcium directly opens cyclic nucleotide-gated channels
- E. Greater glutamate release activates all bipolar cells equally

70. A patient has longstanding mechanical loading of bone. Osteocytes participate in adaptation primarily by performing which function?

- A. Replacing marrow stem cells during hematopoiesis
- B. Producing all circulating parathyroid hormone
- C. Sensing mechanical strain and coordinating remodeling signals
- D. Resorbing large volumes of bone with a ruffled border
- E. Synthesizing cartilage matrix at the growth plate

71. During evaluation, a skeletal muscle fiber is depolarized at the T tubule. Which interaction couples membrane depolarization to calcium release from the sarcoplasmic reticulum?

- A.** Ryanodine receptors directly open voltage-gated sodium channels
- B.** Myosin heads activate inositol trisphosphate receptors on the sarcolemma
- C.** Troponin C opens L-type calcium channels in the T tubule
- D.** Dihydropyridine receptors mechanically activate ryanodine receptors
- E.** Nicotinic receptors mechanically activate SERCA pumps

72. During evaluation, during the early follicular phase, FSH acts on granulosa cells to increase which process?

- A.** Secretion of progesterone by the corpus luteum only
- B.** Aromatization of theca-derived androgens to estrogens
- C.** Production of hCG by placental syncytiotrophoblasts
- D.** Release of GnRH from the hypothalamus
- E.** Synthesis of androgens from cholesterol under LH stimulation

73. During evaluation, a patient takes an aromatase inhibitor. Which steroid conversion is directly reduced?

- A.** Androgens to estrogens
- B.** Progesterone to aldosterone
- C.** Cortisol to cortisone only
- D.** Testosterone to dihydrotestosterone
- E.** Cholesterol to pregnenolone

74. During evaluation, a patient is breathing quietly at functional residual capacity. Which opposing forces are balanced at this volume?

- A.** Active diaphragmatic contraction and active abdominal contraction

- B.** Alveolar surface tension and arterial blood pressure
- C.** Inward recoil of both lungs and chest wall
- D.** Outward recoil of both lungs and chest wall
- E.** Inward elastic recoil of the lungs and outward recoil of the chest wall

75. During evaluation, a patient begins weight-bearing exercise that increases bone formation. Which cell directly produces osteoid?

- A.** Osteoclast
- B.** Macrophage in the marrow
- C.** Osteoblast
- D.** Osteocyte only
- E.** Chondroclast

76. A patient develops urticaria within minutes of eating peanuts. Which cellular event initiates the rapid reaction?

- A.** Binding of IgG to basement membrane antigens with complement fixation
- B.** Deposition of circulating immune complexes in postcapillary venules
- C.** Activation of cytotoxic T cells against allergen-bearing epithelial cells
- D.** Cross-linking of allergen-specific IgE bound to high-affinity receptors on mast cells
- E.** Expansion of regulatory T cells that suppress histamine release

77. A patient who has cirrhosis develops ascites and secondary hyperaldosteronism. Which physiologic signal contributes to the renal response?

- A.** Greater plasma oncotic pressure from hepatic albumin overproduction
- B.** Reduced effective arterial blood volume from splanchnic vasodilation
- C.** Reduced sympathetic activity resulting from arterial overfilling
- D.** Suppressed renin release resulting from renal vasodilation

E. Greater effective arterial blood volume from portal hypertension

78. During evaluation, a low-frequency sound enters the cochlea. Where is maximal basilar membrane displacement most likely?

- A. Near the stiff base next to the oval window
- B. Only within the semicircular canals
- C. Uniformly along the entire basilar membrane
- D. Near the flexible apex of the cochlea
- E. At the round window without traveling-wave propagation

79. During evaluation, a patient has prolonged fasting. Why does insulin concentration fall while glucagon rises?

- A. The hormonal shift prevents amino acids from entering gluconeogenesis
- B. The hormonal shift suppresses lipolysis and ketone production
- C. The hormonal shift mobilizes stored fuels and maintains plasma glucose for glucose-dependent tissues
- D. The hormonal shift increases hepatic glycogen synthesis
- E. The hormonal shift forces skeletal muscle to increase GLUT4 uptake of glucose

80. During evaluation, a patient receives a rapid isotonic saline infusion that increases venous return. If contractility and afterload are unchanged, which ventricular change is expected by the Frank-Starling mechanism?

- A. Greater end-diastolic volume followed by increased stroke volume
- B. Greater end-systolic volume with unchanged fiber stretch
- C. No change in stroke volume because venous return does not affect cardiac output
- D. Reduced preload with increased ejection fraction from sympathetic activation
- E. Reduced end-diastolic volume followed by decreased stroke volume

81. A patient who has a large full-thickness burn loses the epidermal barrier. Which rapid physiologic consequence is most likely?

- A.** Greater thermoregulatory sweating from destroyed eccrine glands
- B.** Reduced risk of infection because dermal vessels are exposed
- C.** Immediate rise in plasma oncotic pressure from albumin retention
- D.** Reduced evaporative water loss because keratin is absent
- E.** Marked increase in transepidermal water loss and risk of volume depletion

82. During evaluation, a patient has complete obstruction of a segmental bronchus while perfusion continues. What is the local ventilation-perfusion relationship?

- A.** V/Q remains normal because perfusion determines ventilation
- B.** V/Q approaches infinity and the region behaves like dead space
- C.** V/Q becomes equal to cardiac output divided by respiratory rate
- D.** V/Q approaches zero and the region behaves like a physiologic shunt
- E.** V/Q increases because alveolar PO₂ rises

83. During evaluation, a patient has impaired formation of new declarative memories after bilateral medial temporal lobe injury. Which structure is most critical?

- A.** Medulla oblongata
- B.** Primary visual cortex
- C.** Substantia nigra
- D.** Caudate nucleus
- E.** Hippocampus

84. A patient has abrupt respiratory alkalosis from anxiety-induced hyperventilation. Which rapid buffer response occurs?

- A.** The kidneys immediately generate large amounts of new bicarbonate

- B.** Renal ammonium excretion reaches chronic steady state within minutes
- C.** Bicarbonate rises sharply because carbon dioxide falls
- D.** Hydrogen ions move from intracellular buffers as bicarbonate falls slightly
- E.** Plasma proteins stop buffering hydrogen ions

85. During evaluation, a patient has recurrent pyogenic infections and very low immunoglobulin levels. Which normal function of plasma cells is absent?

- A.** High-rate secretion of antigen-specific antibody
- B.** Direct phagocytosis of encapsulated bacteria via complement receptors
- C.** Release of perforin and granzymes into infected target cells
- D.** Formation of neutrophil extracellular traps during acute inflammation
- E.** Presentation of endogenous viral peptides on MHC class I only

86. A patient who has hereditary spherocytosis has increased red-cell destruction in the spleen. Which splenic function best explains this finding?

- A.** Generation of platelets from megakaryocytes located in splenic white pulp
- B.** Production of erythropoietin by splenic sinusoidal endothelial cells
- C.** Secretion of hepcidin by the spleen to trap iron inside erythrocytes
- D.** Synthesis of hemoglobin by splenic macrophages after birth
- E.** Mechanical and macrophage filtration of poorly deformable erythrocytes in the red pulp

87. During evaluation, a local anesthetic blocks voltage-gated sodium channels in a peripheral nerve. Which phase of the action potential is most directly impaired?

- A.** Resting potassium leak that establishes baseline voltage
- B.** Slow afterhyperpolarization resulting from potassium conductance
- C.** Calcium reuptake into skeletal muscle sarcoplasmic reticulum
- D.** Neurotransmitter vesicle docking at the presynaptic terminal

E. Rapid sodium-dependent depolarizing upstroke

88. During evaluation, a patient has loss of pain and temperature sensation on the right side of the body below a left-sided brainstem lesion. Where have the affected fibers already crossed?

- A. In the cerebellar peduncles
- B. In the spinal cord near their level of entry
- C. In the posterior columns before entering the cord
- D. In the medullary pyramids
- E. In the optic chiasm

89. During evaluation, a screening program preferentially detects slowly progressive tumors because they remain asymptomatic and detectable for longer periods. Which bias is this?

- A. Interviewer bias
- B. Lead-time bias
- C. Length-time bias
- D. Attrition bias
- E. Recall bias

90. During evaluation, a patient has damage to the submucosal plexus. Which function is most likely reduced?

- A. Synthesis of pancreatic enzymes by acinar cells only
- B. Regulation of mucosal secretion and local blood flow
- C. Formation of bile salts from cholesterol
- D. Systemic sympathetic vasoconstriction
- E. Generation of skeletal-muscle swallowing movements

91. A patient who has severe insulin deficiency develops ketoacidosis. Which hormonal state drives hepatic ketone production?

- A.** Low glucagon suppresses hepatic fatty-acid oxidation
- B.** High insulin with low glucagon increases adipose lipolysis
- C.** Low catecholamines block delivery of free fatty acids to the liver
- D.** Low insulin and high glucagon drive lipolysis and hepatic fatty-acid oxidation
- E.** High insulin activates hormone-sensitive lipase

92. A patient who has a complete lower motor neuron lesion to a skeletal muscle later develops marked atrophy. Which physiologic change is expected in the denervated muscle?

- A.** Enhanced neuromuscular transmission from excess acetylcholine release
- B.** Greater motor-unit recruitment through corticospinal compensation
- C.** Selective hypertrophy of all denervated fibers from disuse
- D.** Loss of trophic neural input with reduced muscle fiber size and spontaneous fibrillation potentials
- E.** Persistent spastic contraction caused by elevated stretch reflex activity

93. A patient who has a helminth infection has eosinophilia and increased IgE. Which CD4 T-cell subset most strongly supports this response?

- A.** Th2 cells producing IL-4, IL-5, and IL-13
- B.** Cytotoxic T cells producing perforin without helper cytokines
- C.** Regulatory T cells producing IL-10 and TGF-beta only
- D.** Th1 cells producing interferon-gamma as the dominant signal
- E.** Th17 cells producing IL-17 as the dominant eosinophil signal

94. A patient who has heat stroke has a core temperature above 40 C and altered mental status. Which feature distinguishes heat stroke from a regulated fever?

- A.** The set point is not raised; heat gain or production exceeds heat loss
- B.** The condition resolves only when hypothalamic prostaglandin synthesis rises
- C.** Peripheral vasoconstriction is always the primary cause
- D.** Shivering is required to maintain the elevated set point
- E.** The set point is deliberately raised by prostaglandin E₂ as in ordinary fever

95. During evaluation, a weightlifter generates very high tendon tension. Golgi tendon organ activation produces which reflex effect on the same muscle?

- A.** Greater acetylcholine release from neuromuscular junctions independent of spinal circuits
- B.** Inhibition of alpha motor neurons via spinal interneurons
- C.** Excitation of alpha motor neurons via a direct monosynaptic pathway
- D.** Activation of gamma motor neurons without changing alpha motor output
- E.** Selective stimulation of cutaneous nociceptors around the tendon

96. A patient who has a cerebellar hemisphere lesion has dysmetria of the ipsilateral arm. Which cerebellar function is most directly impaired?

- A.** Storage of declarative memories in the hippocampus
- B.** Generation of conscious pain perception in the primary somatosensory cortex
- C.** Comparison and correction of ongoing movement using sensory feedback
- D.** Initiation of voluntary movement via lower motor neurons
- E.** Production of muscle force via neuromuscular junction transmission

97. During evaluation, histamine stimulates gastric acid secretion from parietal cells by activating which receptor and second messenger?

- A.** M₂ receptors coupled to G_i and reduced cAMP
- B.** H₂ receptors coupled to G_s and elevated cAMP
- C.** GABA-A receptors coupled to chloride conductance

- D. D2 receptors coupled to Gi and elevated proton pumping
- E. H1 receptors coupled to Gq and reduced calcium

98. An otherwise healthy person receives a small transfusion of compatible packed red blood cells. Which of the following variables increases most directly after equilibration?

- A. Hemoglobin oxygen affinity because transfused cells eliminate 2,3-BPG
- B. Plasma oncotic pressure because erythrocytes are the major plasma proteins
- C. Arterial PO₂ because additional erythrocytes dissolve more oxygen
- D. Alveolar PO₂ because hemoglobin draws oxygen from the alveoli at rest
- E. Total arterial oxygen content because hemoglobin concentration rises

99. Vagal stimulation slows the sinoatrial node. Which of the following mechanisms is principally responsible?

- A. M1 receptor activation raises IP₃ and accelerates phase 4 depolarization
- B. M2 receptor activation decreases cAMP and increases potassium conductance
- C. Beta-1 receptor activation increases cAMP and funny current
- D. Nicotinic receptor blockade increases sympathetic norepinephrine release
- E. Alpha-1 receptor activation increases calcium in pacemaker cells

100. During evaluation, a patient has a pituitary adenoma that secretes excess growth hormone. Which mediator accounts for many growth-promoting effects of GH on bone and soft tissue?

- A. Insulin-like growth factor 1 produced mainly by the liver
- B. Aldosterone produced by the zona glomerulosa
- C. Calcitonin produced by thyroid C cells
- D. Thyroxine produced by thyroid follicular cells
- E. Cortisol produced by the adrenal cortex

101. During evaluation, a drug selectively stimulates alpha-1 adrenergic receptors in vascular smooth muscle. Which intracellular pathway mediates contraction?

- A.** Gq activation with elevated IP3 and intracellular calcium
- B.** Ligand-gated sodium influx via nicotinic receptors
- C.** Gs activation with elevated cAMP and reduced calcium
- D.** Receptor tyrosine kinase activation with PI3K signaling
- E.** Gi activation with reduced cAMP in cardiac pacemaker cells

102. A patient is newly diagnosed with a serious illness and becomes silent after hearing the news. What is the most effective rapid communication strategy?

- A.** Ask rapid closed-ended questions until the patient answers
- B.** Immediately provide a long technical explanation to fill the silence
- C.** Leave the room without explaining because silence means the visit is over
- D.** Change the subject to avoid increasing distress
- E.** Allow silence, acknowledge the emotion, and invite the patient to share concerns

103. During evaluation, a beta-blocker slows conduction through the atrioventricular node. Which ECG interval is most directly prolonged?

- A.** ST segment
- B.** QRS duration
- C.** QT interval only
- D.** PR interval
- E.** T-wave amplitude

104. A patient who has prolonged immobilization develops loss of skeletal-muscle mass. Which cellular change contributes most directly to disuse atrophy?

- A.** Permanent conversion of all myofibers into adipocytes

- B.** Greater mechanical loading that activates mTOR signaling
- C.** Reduced protein synthesis with elevated proteolysis in inactive fibers
- D.** Continuous calcium elevation that increases contractile protein synthesis
- E.** Greater satellite-cell fusion causing fiber hypertrophy

105. During evaluation, which vessels contain the largest fraction of the systemic blood volume at rest?

- A.** Capillaries
- B.** Aorta and large arteries
- C.** Arterioles
- D.** Systemic veins and venules
- E.** Pulmonary arteries only

106. During evaluation, a patient drinks an oral rehydration solution containing glucose and sodium during secretory diarrhea. Why can the solution remain effective?

- A.** Sodium-glucose cotransport in enterocytes remains functional and drives water absorption
- B.** Chloride secretion stops because glucose blocks CFTR directly
- C.** Colonic potassium channels absorb glucose by active transport
- D.** Gastric acid secretion increases and pulls water into plasma
- E.** Pancreatic enzymes convert sodium into an absorbable neutral molecule

107. During evaluation, a patient has central diabetes insipidus. Which physiologic defect is present?

- A.** Excess insulin preventing collecting-duct water reabsorption
- B.** Renal resistance to vasopressin with normal or high hormone secretion
- C.** Excess atrial natriuretic peptide as the usual primary cause
- D.** Excess aldosterone causing obligatory water loss
- E.** Insufficient vasopressin secretion despite an intact renal response to the hormone

108. A patient takes exogenous thyroid hormone for several weeks. Which of the following changes is expected in the hypothalamic-pituitary-thyroid axis?

- A.** Greater prolactin as the sole feedback response
- B.** Reduced TRH and TSH secretion by negative feedback
- C.** No pituitary change because thyroid hormone lacks feedback effects
- D.** Greater TRH and TSH secretion despite elevated hormone levels
- E.** Greater TSH with reduced TRH as the normal response

109. During evaluation, a naive CD4 T cell recognizes a peptide presented by an antigen-presenting cell. Which molecule on the presenting cell carries peptides derived primarily from extracellular proteins?

- A.** MHC class I
- B.** MHC class II
- C.** CD3
- D.** B7 only
- E.** Beta-2 microglobulin alone

110. During evaluation, a patient has lactose intolerance. Why does ingestion of lactose cause watery diarrhea?

- A.** Unabsorbed lactose increases luminal osmolality and is fermented by colonic bacteria
- B.** Lactose destroys intestinal villi during every exposure
- C.** Lactose blocks pancreatic bicarbonate secretion and causes protein maldigestion
- D.** Lactose increases bile salt synthesis and accelerates fat absorption
- E.** Lactose directly stimulates chloride secretion by gastric parietal cells

111. A patient who has severe systemic inflammation has neutrophilia. Which cytokine most directly stimulates hepatic production of many acute-phase proteins?

- A.** Interleukin-2

- B. Interleukin-17**
- C. Interleukin-4**
- D. Interleukin-6**
- E. Interleukin-5**

112. During evaluation, a patient becomes hyperosmolar after water deprivation. Which hypothalamic response occurs first?

- A. Greater vasopressin release and stimulation of thirst**
- B. Greater renal free-water excretion**
- C. Suppressed collecting-duct water permeability**
- D. Suppressed vasopressin and thirst**
- E. Greater atrial natriuretic peptide release**

113. During evaluation, a child with vitamin D deficiency has impaired mineralization of newly formed osteoid. Which intestinal transport change contributes to the disorder?

- A. Reduced intestinal absorption of both calcium and phosphate**
- B. Reduced calcium absorption with markedly elevated phosphate absorption**
- C. Greater calcium absorption with reduced phosphate absorption only**
- D. Reduced iron absorption as the primary cause of defective mineralization**
- E. Greater sodium absorption that directly mineralizes osteoid**

114. During evaluation, a patient touches a hot surface and feels a fast, sharp pain followed by a slower burning pain. Which fibers carry the initial sharp sensation?

- A. Unmyelinated C fibers**
- B. Heavily myelinated Ia proprioceptive fibers**
- C. Thinly myelinated A-delta fibers**
- D. Large myelinated alpha motor fibers**

E. Preganglionic autonomic B fibers

115. A patient who has delirium cannot understand a proposed procedure. A durable power of attorney for health care is available. Who should make the decision?

- A. The designated health-care agent using the patient's known preferences and values
- B. Hospital administration using a cost-benefit calculation
- C. The oldest family member regardless of the legal designation
- D. The treating physician alone because delirium removes all patient rights
- E. Any staff member who personally agrees with the procedure

116. A patient who has severe anemia has reduced oxygen content. Which equation best describes tissue oxygen delivery?

- A. Alveolar ventilation multiplied by venous PO₂
- B. Hemoglobin concentration divided by cardiac output
- C. Cardiac output multiplied by arterial oxygen content
- D. Systemic vascular resistance multiplied by pulse pressure
- E. Arterial PO₂ multiplied by respiratory rate

117. A patient who has hypocalcemia develops muscle cramps and paresthesias. Why does low extracellular calcium increase neuromuscular excitability?

- A. It lowers the threshold for opening voltage-gated sodium channels
- B. It raises the threshold by stabilizing sodium channels in the closed state
- C. It reduces sodium permeability during the action-potential upstroke
- D. It blocks acetylcholine release by increasing presynaptic calcium influx
- E. It hyperpolarizes skeletal muscle by opening chloride channels

118. A patient has isolated systolic hypertension due to stiff large arteries. Which of the following changes contributes most directly to a widened pulse pressure?

- A.** Greater venous compliance only
- B.** Reduced arterial compliance
- C.** Reduced stroke volume with unchanged arterial stiffness
- D.** Greater capillary filtration coefficient
- E.** Reduced aortic pulse-wave velocity

119. A patient who has serum sickness develops fever, arthralgias, and proteinuria after exposure to a foreign protein. Which of the following mechanisms drives the tissue injury?

- A.** Loss of central tolerance resulting from absent thymic selection alone
- B.** CD8 T-cell killing of target cells displaying viral peptides
- C.** Antibody binding directly to a fixed cell-surface receptor
- D.** Deposition of circulating antigen-antibody complexes with complement activation
- E.** IgE cross-linking on mast cells with immediate histamine release

120. During evaluation, a food bolus distends a segment of small intestine. Which local enteric reflex pattern propels it aborally?

- A.** Relaxation oral to the bolus with contraction distal to it
- B.** Contraction only after a cortical motor command
- C.** Contraction oral to the bolus with relaxation distal to it
- D.** Complete inhibition of circular muscle throughout the intestine
- E.** Simultaneous contraction on both sides without relaxation

121. During evaluation, thyroid-stimulating hormone binds receptors on thyroid follicular cells. Which intracellular signaling pathway is most strongly activated?

- A.** Gq-mediated decrease in IP3

- B.** Gs-mediated increase in cAMP
- C.** Intracellular steroid receptor binding
- D.** Gi-mediated decrease in cAMP
- E.** Receptor guanylyl cyclase activation only

122. During evaluation, after several days of fasting, which metabolic adaptation reduces skeletal-muscle use of ketone bodies so that more ketones are available to the brain?

- A.** Adipose tissue stops lipolysis
- B.** Skeletal muscle increasingly oxidizes free fatty acids
- C.** Skeletal muscle switches back to exclusive glucose oxidation
- D.** The liver begins oxidizing the ketone bodies it produces
- E.** Red blood cells begin using ketone bodies instead of glucose

123. A patient who has metabolic acidosis increases renal net acid excretion. Which cell type directly secretes hydrogen ions into the collecting duct?

- A.** Mesangial cells
- B.** Principal cells only
- C.** Macula densa cells
- D.** Alpha-intercalated cells
- E.** Beta-intercalated cells

124. During evaluation, atrial natriuretic peptide is released during atrial stretch. Which renal effect promotes natriuresis?

- A.** Greater GFR with reduced renin and aldosterone activity
- B.** Greater sympathetic renal vasoconstrictor tone
- C.** Greater aldosterone secretion from the adrenal cortex
- D.** Greater sodium reabsorption in collecting-duct principal cells

E. Reduced GFR with elevated renin release

125. During evaluation, a fasting patient has increased glucagon. Which hepatic process is stimulated?

- A. Glycogenolysis and gluconeogenesis
- B. GLUT4 translocation in hepatocytes
- C. Glycogen synthesis and glycolysis
- D. Fatty-acid synthesis with malonyl-CoA accumulation
- E. Protein synthesis with suppression of amino-acid uptake

126. A randomized trial has a p value of 0.03 for the primary outcome using an alpha of 0.05. Which of the following statements is correct?

- A. There is a 97% probability that the treatment is clinically important
- B. The result guarantees replication in 97% of future studies
- C. Under the null model, results this extreme or more occur with probability 0.03
- D. There is a 3% probability that the null hypothesis is true
- E. The result proves the study has no bias or confounding

127. During evaluation, a fatty meal enters the duodenum. Which hormone most strongly stimulates gallbladder contraction and pancreatic enzyme secretion?

- A. Motilin released from small-intestinal M cells
- B. Secretin released from duodenal S cells
- C. Ghrelin released from gastric endocrine cells
- D. Cholecystokinin released from duodenal I cells
- E. Gastrin released from antral G cells

128. A person enters rapid eye movement sleep. Which of the following findings is most characteristic of this stage?

- A. Sleep spindles and K complexes with no dreaming
- B. Persistent sympathetic silence with absent autonomic variability
- C. High-amplitude delta waves with preserved postural muscle tone
- D. Uniform alpha waves with closed eyes and full muscle tone
- E. Low-amplitude mixed-frequency EEG activity with skeletal muscle atonia

129. During evaluation, a patient is exposed to an oxidizing drug and develops methemoglobinemia. What chemical change has occurred in hemoglobin?

- A. Oxidation of heme iron from Fe^{2+} to Fe^{3+}
- B. Replacement of heme iron by copper within beta chains
- C. Reduction of heme iron from Fe^{3+} to Fe^{2+}
- D. Covalent binding of carbon monoxide to globin amino groups
- E. Greater 2,3-BPG occupancy of all four heme pockets

130. A patient who has sepsis initially has warm extremities and a low systemic vascular resistance. Which mediator contributes to distributive vasodilation?

- A. Greater endothelin as the sole dominant mechanism
- B. Excess nitric oxide production in the vasculature
- C. Greater blood viscosity from rapid erythrocytosis
- D. Reduced nitric oxide with diffuse alpha-1 vasoconstriction
- E. Reduced inflammatory signaling with increased arterial tone

131. During evaluation, a patient has damage to the myenteric plexus. Which function is most directly impaired?

- A. Transport of chylomicrons via lymphatics only
- B. Synthesis of bile acids in hepatocytes
- C. Absorption of vitamin B12 by intrinsic factor

- D.** Secretion from intestinal crypts only
- E.** Coordination of gastrointestinal smooth-muscle motility

132. During evaluation, a patient hypoventilates after receiving an opioid. If carbon dioxide production is unchanged, what happens to arterial PCO₂?

- A.** It falls only if arterial oxygen content falls
- B.** It becomes independent of metabolism during hypoventilation
- C.** It falls in direct proportion to reduced alveolar ventilation
- D.** It remains unchanged because CO₂ diffuses rapidly
- E.** It rises inversely as alveolar ventilation falls

133. During evaluation, a 95% confidence interval for a risk ratio is 0.80 to 1.20. What can be concluded at the conventional two-sided 0.05 level?

- A.** The true risk ratio has a 95% probability of lying in this specific interval
- B.** The result is not statistically significant because the interval includes 1.0
- C.** The treatment definitely has no effect
- D.** The study has 95% power by definition
- E.** The result is statistically significant because the interval includes values below 1.0

134. During evaluation, a patient develops local myocardial hypoxia during exercise. Which metabolite is an important coronary vasodilator?

- A.** Adenosine released during local ATP breakdown
- B.** Angiotensin II generated by renin-angiotensin signaling
- C.** Endothelin released by vascular endothelial cells
- D.** Vasopressin acting at vascular V₁ receptors
- E.** Norepinephrine acting at vascular alpha-1 receptors

135. A patient who has severe anemia has increased resting cardiac output. Which of the following mechanisms contributes to this response?

- A.** Higher arterial oxygen content suppresses sympathetic activity
- B.** Lower blood viscosity plus hypoxia-driven sympathetic activation
- C.** Greater plasma oncotic pressure directly raises myocardial contractility
- D.** Reduced tissue metabolism lowers the need for blood flow
- E.** Greater blood viscosity raises venous return and stroke volume

136. During evaluation, late in pregnancy, which organ becomes the major source of progesterone supporting uterine quiescence?

- A.** Fetal thyroid gland
- B.** Anterior pituitary gland
- C.** Placenta after the luteal shift
- D.** Posterior pituitary gland
- E.** Maternal adrenal medulla

137. During evaluation, a woman in the follicular phase has rising estradiol from the dominant follicle. For most of the cycle, estradiol exerts what effect on gonadotropin secretion?

- A.** No feedback on the hypothalamus or pituitary
- B.** Continuous strong positive feedback throughout the entire cycle
- C.** Selective positive feedback on FSH with suppression of LH
- D.** Direct inhibition of ovarian aromatase by the pituitary
- E.** Negative feedback on GnRH, LH, and FSH

138. During evaluation, a patient has a mean arterial pressure of 90 mm Hg and a cardiac output of 5 L/min. If central venous pressure is negligible, which relation best describes systemic vascular resistance?

- A. Approximately mean arterial pressure divided by cardiac output
- B. Approximately systolic pressure minus diastolic pressure only
- C. Approximately pulse pressure multiplied by heart rate
- D. Approximately cardiac output divided by mean arterial pressure
- E. Approximately stroke volume divided by venous compliance

139. During evaluation, a patient has a cardiac output of 5 L/min and a heart rate of 100/min. What is the stroke volume?

- A. 50 mL per beat
- B. 20 mL per beat
- C. 75 mL per beat
- D. 500 mL per beat
- E. 100 mL per beat

140. A pregnant woman at 30 weeks is given antenatal betamethasone because preterm delivery is likely. The treatment most directly improves neonatal lung function by increasing which process?

- A. Proliferation of type I pneumocytes to increase diffusion distance
- B. Closure of the ductus arteriosus before delivery to redirect flow
- C. Production of fetal hemoglobin to increase placental oxygen extraction
- D. Synthesis and release of surfactant by type II pneumocytes
- E. Constriction of fetal pulmonary arterioles to preserve right-to-left shunting

141. A patient who has Lambert-Eaton myasthenic syndrome has antibodies against presynaptic voltage-gated calcium channels. Why can muscle strength transiently improve with repeated activation?

- A. Acetylcholinesterase activity falls because the enzyme is depleted
- B. Postsynaptic nicotinic receptors rapidly increase in number within seconds
- C. Motor neurons switch from acetylcholine to glutamate release

- D.** Muscle sodium channels remain permanently open after repeated impulses
- E.** Residual presynaptic calcium accumulates and increases acetylcholine release

142. A patient develops metabolic acidosis with a plasma bicarbonate of 12 mEq/L. What is the expected rapid respiratory compensation?

- A.** No change in ventilation until several days have passed
- B.** Hypoventilation that raises arterial PCO₂
- C.** Suppression of peripheral chemoreceptors by low pH
- D.** Renal bicarbonate excretion before any respiratory change
- E.** Hyperventilation that lowers arterial PCO₂

143. During evaluation, a patient stands suddenly from a supine position. Which initial hemodynamic change activates the arterial baroreflex?

- A.** Greater carotid sinus stretch directly lowers sympathetic tone
- B.** Immediate renal sodium retention raises plasma volume before pressure changes
- C.** Greater venous return raises stroke volume and arterial pressure
- D.** Reduced venous return lowers stroke volume and arterial pressure
- E.** Greater intracranial pressure stimulates the Cushing response

144. A patient who has longstanding hypertension develops a fourth heart sound. Which mechanical event generates S₄?

- A.** Closure of the semilunar valves during early diastole
- B.** Closure of the atrioventricular valves during early systole
- C.** Rapid passive filling of a highly compliant ventricle
- D.** Atrial contraction forcing blood into a stiff, noncompliant ventricle
- E.** Turbulent ejection via a normal aortic valve

145. During evaluation, a preterm infant lacks adequate surfactant. Which mechanical consequence is expected?

- A.** Greater alveolar surface tension with reduced lung compliance
- B.** Reduced tendency of small alveoli to collapse
- C.** Loss of the normal pressure difference across the pleura only
- D.** Greater functional residual capacity from easier inflation
- E.** Reduced alveolar surface tension with increased lung compliance

146. During evaluation, a diagnostic test is negative in 855 of 900 people who do not have the disease. What is the specificity?

- A.** 45%
- B.** 95%
- C.** 5%
- D.** 90%
- E.** 85%

147. A patient who has limited English proficiency needs informed consent for a complex procedure. A bilingual adolescent child offers to interpret. Which of the following is the best approach?

- A.** Obtain consent from the child instead of the patient
- B.** Use a qualified medical interpreter and speak directly to the patient
- C.** Avoid discussing risks because interpretation may be imperfect
- D.** Provide only an English consent form and assume understanding
- E.** Use the child because family members are always preferred interpreters

148. A patient who has Duchenne muscular dystrophy has progressive skeletal-muscle weakness. Dystrophin normally helps transmit contractile force by linking which structures?

- A.** Troponin C to collagen fibers in the extracellular matrix

- B.** Myosin thick filaments directly to calcium channels in the sarcoplasmic reticulum
- C.** The intracellular actin cytoskeleton to the sarcolemmal protein complex and extracellular matrix
- D.** Actin thin filaments to mitochondrial oxidative enzymes
- E.** The Z disc directly to acetylcholine receptors at the motor end plate

149. During evaluation, a disease becomes much more prevalent in the population, but a test's sensitivity and specificity do not change. Which test characteristic generally increases?

- A.** False-negative rate necessarily becomes zero
- B.** Positive predictive value
- C.** Negative likelihood ratio becomes exactly zero
- D.** Specificity
- E.** Sensitivity

150. A patient develops abrupt hypernatremia after water deprivation. What is the rapid effect on cell volume?

- A.** Cells swell as water moves into a hypo-osmotic extracellular compartment
- B.** Cells swell only in skeletal muscle but shrink in brain
- C.** Cells shrink as water moves into the hyperosmotic extracellular compartment
- D.** Cells gain sodium rapidly enough to prevent water movement
- E.** Cell volume remains fixed because aquaporins close

151. During evaluation, during the first day of fasting, which hepatic process is the major source of circulating glucose?

- A.** Protein synthesis
- B.** Ketone-body oxidation
- C.** Glycogenolysis
- D.** Cholesterol esterification

E. De novo fatty-acid synthesis

152. During evaluation, a patient exercises until skeletal-muscle oxygen delivery becomes limiting. Which metabolic change allows ATP production to continue transiently?

- A. Direct phosphorylation of ADP by molecular oxygen
- B. Conversion of lactate to pyruvate without consuming NADH
- C. Suppression of glycolysis to preserve glucose
- D. Complete oxidation of fatty acids without mitochondrial oxygen
- E. Conversion of pyruvate to lactate to regenerate cytosolic NAD⁺

153. A patient who has severe hemorrhage has cool clammy skin and tachycardia. Which compensatory mechanism produces the skin finding?

- A. Local adenosine accumulation in skin causing hyperemia
- B. Reduced catecholamine release from the adrenal medulla
- C. Parasympathetic muscarinic vasodilation of skin arterioles
- D. Sympathetic alpha-1 mediated cutaneous vasoconstriction
- E. Suppressed baroreflex activity despite hypotension

154. During evaluation, a hospitalized patient repeatedly receives medications late because unit handoffs are inconsistent. Which intervention best targets the system cause?

- A. Ask each clinician to create an individual handoff style
- B. Discipline the most recent nurse without examining the workflow
- C. Increase medication doses to compensate for unpredictable timing
- D. Stop reporting late medications so performance appears better
- E. Standardize the handoff process and measure whether medication timing improves

155. During evaluation, a patient becomes hypercapnic during hypoventilation. How does this change cerebral blood flow?

- A.** It decreases only because systemic blood pressure always falls
- B.** It decreases because CO₂ directly constricts cerebral arterioles
- C.** It remains fixed because cerebral flow lacks metabolic autoregulation
- D.** It increases only after renal bicarbonate excretion over several days
- E.** It increases because elevated CO₂ causes cerebral vasodilation

156. During evaluation, a loop diuretic inhibits the Na-K-2Cl cotransporter in the thick ascending limb. Which medullary function is reduced?

- A.** Urea synthesis in hepatocytes
- B.** Hydrogen secretion by alpha-intercalated cells
- C.** Water reabsorption via aquaporin-1 in the descending limb
- D.** Generation of the corticomedullary osmotic gradient
- E.** Glucose reabsorption in the proximal tubule

157. A neonate exposed to a cool environment increases heat production without shivering. Which cellular mechanism is most responsible?

- A.** Reduced lipolysis in brown adipocytes to conserve triglyceride stores
- B.** Suppression of sympathetic activity to reduce cutaneous vasoconstriction
- C.** Uncoupling of oxidative phosphorylation in brown adipose tissue via UCP1
- D.** Activation of skeletal muscle nicotinic receptors causing sustained tetanic contraction
- E.** Inhibition of mitochondrial proton leak to maximize ATP production

158. A patient who has myasthenia gravis has antibodies against postsynaptic nicotinic acetylcholine receptors. Which electrophysiologic change occurs at the neuromuscular junction?

- A.** Greater end-plate potential amplitude due to receptor upregulation

- B.** Prolonged muscle action potentials resulting from potassium-channel blockade
- C.** Failure of presynaptic calcium entry with absent acetylcholine release
- D.** Greater acetylcholine synthesis that fully restores the safety factor
- E.** Reduced end-plate potential amplitude with preserved presynaptic acetylcholine release

159. A patient who has carbon monoxide poisoning has a normal arterial PO₂ but profound tissue hypoxia. Which hemoglobin change contributes to impaired oxygen delivery?

- A.** Reduced oxygen-carrying capacity plus a left shift of the remaining oxyhemoglobin curve
- B.** Greater 2,3-BPG binding that immediately restores oxygen unloading
- C.** Conversion of hemoglobin iron to the ferric state as the defining mechanism
- D.** Greater oxygen-carrying capacity plus a right shift of the curve
- E.** Normal oxygen-carrying capacity with isolated reduction in dissolved oxygen

160. During evaluation, a patient receives a proton-pump inhibitor. Which parietal-cell transporter is directly inhibited?

- A.** Sodium-glucose cotransporter in the brush border
- B.** H⁺/K⁺ ATPase on the apical membrane
- C.** CFTR chloride channel in pancreatic ducts
- D.** Na⁺/K⁺ ATPase on the basolateral membrane
- E.** Cl⁻/HCO₃⁻ exchanger on the apical membrane

161. During evaluation, LH acts on ovarian theca interna cells. Which steroidogenic product is supplied to granulosa cells?

- A.** Aldosterone produced locally to support follicular sodium balance
- B.** Cortisol synthesized from cholesterol under LH stimulation
- C.** Estradiol synthesized directly by theca interna cells
- D.** Androgens that granulosa-cell aromatase converts to estrogens

E. Progesterone supplied as the final follicular estrogen precursor

162. A patient who has septic shock has elevated lactate despite adequate arterial oxygen saturation. Which of the following mechanisms can contribute?

- A. Hemoglobin saturation above 95% prevents all lactate formation
- B. Regional hypoperfusion and impaired oxygen use increase anaerobic glycolysis
- C. Lactate can rise only when arterial PO₂ is zero
- D. Insulin always suppresses lactate production during stress
- E. Renal bicarbonate reabsorption directly converts bicarbonate to lactate

163. During evaluation, a patient enrolled in a clinical trial decides to withdraw after randomization. What should the research team do?

- A. Withhold routine medical care as a consequence of withdrawal
- B. Permit withdrawal without penalty and arrange safe transition of care
- C. Ask the employer to pressure the patient to remain enrolled
- D. Charge a penalty to prevent loss to follow-up
- E. Require participation until the study ends because randomization is binding

164. During evaluation, a patient's systolic pressure is 120 mm Hg and diastolic pressure is 75 mm Hg at a normal heart rate. What is the approximate mean arterial pressure?

- A. 90 mm Hg
- B. 82 mm Hg
- C. 75 mm Hg
- D. 120 mm Hg
- E. 105 mm Hg

165. During evaluation, a patient has obstruction of the common bile duct. Which intestinal process is most impaired?

- A.** Secretion of hydrochloric acid by parietal cells
- B.** Absorption of iron in the duodenum
- C.** Micelle formation and absorption of long-chain dietary lipids
- D.** Activation of pepsin in the stomach
- E.** Absorption of glucose by sodium-glucose cotransport

166. A child receives a booster vaccine and rapidly produces high-affinity IgG. Which of the following processes during the primary response created the cells responsible for this faster secondary response?

- A.** Germinal-center selection with class switching and memory B-cell formation
- B.** Somatic recombination of immunoglobulin genes in activated neutrophils
- C.** Positive selection of immature T cells in the thymic cortex
- D.** Complement-mediated lysis of naive B cells lacking antigen receptors
- E.** Deletion of all antigen-specific plasma cells after the initial exposure

167. During evaluation, a neuron is at rest. Which ion movement contributes most to the resting membrane potential in a typical neuron?

- A.** Chloride efflux via ligand-gated GABA receptors
- B.** Calcium influx via voltage-gated L-type channels
- C.** Potassium influx via nicotinic acetylcholine receptors
- D.** Sodium influx via voltage-gated sodium channels
- E.** Potassium efflux via resting leak channels

168. During evaluation, a positive inotropic drug increases left ventricular contractility while preload and afterload remain constant. Which pressure-volume change is expected?

- A.** Greater end-systolic volume and reduced stroke volume

- B. Greater end-diastolic pressure caused by impaired relaxation only
- C. Reduced end-systolic volume and elevated stroke volume
- D. Reduced end-diastolic volume with unchanged end-systolic volume
- E. A parallel rightward shift of the end-systolic pressure-volume relation

169. During evaluation, a patient develops a pulmonary embolus and then activates endogenous fibrinolysis. Tissue plasminogen activator promotes clot breakdown by generating which enzyme?

- A. Plasmin from plasminogen
- B. Protein C from activated protein S
- C. Thrombin from prothrombin
- D. Kallikrein from high-molecular-weight kininogen
- E. Factor Xa from factor X

170. During evaluation, during dynamic exercise, blood flow to active skeletal muscle rises markedly despite increased sympathetic activity. Which local factor contributes to this vasodilation?

- A. Reduced nitric oxide formation from vascular endothelium
- B. Greater alpha-1 receptor sensitivity that overwhelms metabolites
- C. Accumulation of metabolites such as adenosine, K^+ , CO_2 , and H^+
- D. Greater endothelin release as the dominant local response
- E. Reduced tissue metabolism with lower interstitial potassium

171. A climber makes a rapid ascent to high altitude and remains there for several days. Which erythrocyte adaptation helps improve oxygen unloading to peripheral tissues?

- A. Reduced 2,3-BPG concentration with a left shift of the oxygen dissociation curve
- B. Greater 2,3-BPG concentration with a right shift of the oxygen dissociation curve
- C. Greater fetal hemoglobin synthesis with reduced 2,3-BPG binding
- D. Reduced erythropoietin release caused by renal hypoxemia

E. Greater hemoglobin affinity caused by reduced glycolytic activity

172. During evaluation, a patient eats a protein-rich meal. Which hormone released from gastric G cells stimulates acid secretion and mucosal growth?

A. Secretin

B. Gastrin

C. Somatostatin

D. Cholecystokinin

E. Motilin

173. During evaluation, insulin promotes glucose uptake in skeletal muscle and adipose tissue by increasing membrane insertion of which transporter?

A. GLUT2

B. GLUT1

C. SGLT1

D. GLUT5

E. GLUT4

174. During evaluation, suckling also increases prolactin secretion. Which hypothalamic change is responsible?

A. Greater dopamine release into the hypophyseal portal circulation

B. Suppressed portal blood flow to the anterior pituitary

C. Greater somatostatin release as the dominant prolactin stimulus

D. Reduced oxytocin release from the posterior pituitary

E. Reduced dopamine release into the hypophyseal portal circulation

175. During evaluation, a patient has a meal rich in carbohydrates. Which transporter moves glucose and galactose from the intestinal lumen into enterocytes?

- A.** Na⁺/K⁺ ATPase on the apical brush border
- B.** CFTR coupled to chloride
- C.** SGLT1 coupled to sodium
- D.** GLUT2 on the apical membrane as the main fasting pathway
- E.** GLUT5 coupled to sodium

176. During evaluation, a patient has a lesion of the right optic tract. Which visual field deficit is expected?

- A.** Bitemporal hemianopia
- B.** Left homonymous hemianopia
- C.** Right monocular blindness
- D.** Right nasal hemianopia only
- E.** Left central scotoma only

177. During evaluation, a patient has pulmonary fibrosis with thickening of the alveolar-capillary barrier. Which gas-exchange property is reduced according to Fick's law?

- A.** Diffusion rate because the partial-pressure gradient is increased
- B.** Diffusion rate because gas solubility is increased
- C.** Diffusion rate because membrane thickness is decreased
- D.** Diffusion rate because membrane surface area is increased
- E.** Diffusion rate because membrane thickness is increased

178. During evaluation, a patient has an obstructive pulmonary disorder. Which spirometric pattern is most characteristic?

- A.** A normal FEV1/FVC ratio with no air trapping

- B.** A low total lung capacity with preserved expiratory flow
- C.** A disproportionate reduction in FEV1 causing a low FEV1/FVC ratio
- D.** A proportional reduction in FEV1 and FVC with a normal or high ratio
- E.** An isolated increase in FEV1 with unchanged FVC

179. A patient who has elevated catecholamines has increased metabolic fuel availability. Which receptor mechanism in adipose tissue promotes lipolysis?

- A.** Insulin receptor signaling directly activates hormone-sensitive lipase
- B.** Alpha-2 Gi signaling increases cAMP and protein kinase A activity
- C.** Beta-adrenergic Gs signaling increases cAMP and protein kinase A activity
- D.** Nuclear thyroid receptors acutely open lipase channels within seconds
- E.** Muscarinic M2 signaling increases cAMP in adipocytes

180. During evaluation, a cohort study reports a relative risk of 2.0 for an exposure and disease. What does this mean?

- A.** Exposed participants had twice the risk of disease as unexposed participants
- B.** The disease occurred in 2% of exposed participants
- C.** The exposure caused disease in exactly half of exposed participants
- D.** The exposure reduced risk by 50%
- E.** The odds of exposure among cases was necessarily 2.0

181. A patient develops abrupt hyponatremia from excessive water intake. Which of the following occurs to brain-cell volume before adaptation occurs?

- A.** Cells shrink because water leaves the intracellular space
- B.** Cells dehydrate because extracellular osmolality rises
- C.** Cells lose potassium immediately enough to prevent all swelling
- D.** Cell volume remains unchanged because sodium cannot cross the blood-brain barrier

E. Cells swell because water moves into the relatively hyperosmotic intracellular space

182. A patient who has portal hypertension develops esophageal varices. Which normal vascular arrangement exposes the liver to absorbed intestinal nutrients before they reach the systemic circulation?

- A. Renal venous flow carrying nutrients from the colon to the liver
- B. Pulmonary venous flow from the intestine to the left atrium
- C. Portal venous flow from gastrointestinal capillaries to hepatic sinusoids
- D. Lymphatic flow from lacteals directly into hepatic portal veins
- E. Direct arterial flow from the mesenteric arteries to the inferior vena cava

183. An otherwise healthy person is awake with eyes closed and relaxed. Which EEG pattern is most likely?

- A. Alpha rhythm
- B. Delta rhythm
- C. Sleep spindles
- D. Burst suppression
- E. Generalized spike-and-wave activity

184. During evaluation, a growing child has longitudinal bone growth at the epiphyseal plate. Which zone contains actively dividing chondrocytes arranged in columns?

- A. Calcification zone
- B. Primary ossification center
- C. Resting zone
- D. Hypertrophic zone
- E. Proliferative zone

185. During evaluation, a fasting patient develops periodic waves of stomach and small-intestinal motility between meals. Which hormone is most associated with this migrating motor complex?

- A. Insulin
- B. Calcitonin
- C. Motilin
- D. Gastrin
- E. Secretin

186. During evaluation, a drug stimulates beta-1 adrenergic receptors in the sinoatrial node. Which intracellular change increases heart rate?

- A. Gi-mediated fall in cAMP that reduces funny current
- B. Gs-mediated rise in cAMP that increases pacemaker currents and calcium entry
- C. Opening of ligand-gated chloride channels that hyperpolarize pacemaker cells
- D. Gq-mediated fall in IP3 that slows spontaneous depolarization
- E. Blockade of HCN channels with a flatter phase 4 depolarization

187. During evaluation, a patient has a positive tuberculin skin test 48 hours after intradermal antigen injection. Which immune response is responsible for the induration?

- A. Natural killer cell activation without antigen-specific T cells
- B. Circulating immune-complex deposition in dermal vessels
- C. IgG-mediated complement lysis of antigen-bearing erythrocytes
- D. Th1-cell cytokine release with macrophage recruitment and activation
- E. Preformed IgE-mediated mast-cell degranulation within minutes

188. During evaluation, at a chemical synapse, an action potential reaches the presynaptic terminal. Which event directly triggers neurotransmitter vesicle fusion?

- A. Sodium efflux via voltage-gated sodium channels

- B.** Calcium influx via voltage-gated calcium channels
- C.** ATP-dependent calcium export before depolarization occurs
- D.** Potassium influx via inward-rectifier channels
- E.** Chloride influx via postsynaptic GABA-A receptors

189. A skeletal muscle relaxes after a brief contraction. Which of the following processes most directly lowers cytosolic calcium?

- A.** ATP-dependent uptake of calcium into the sarcoplasmic reticulum by SERCA
- B.** Binding of calcium to troponin C until all cross-bridges detach
- C.** Passive calcium diffusion from the sarcoplasmic reticulum into the cytosol
- D.** Opening of ryanodine receptors during membrane repolarization
- E.** Sodium influx via nicotinic acetylcholine receptors at the end plate

190. A patient who has severe hypoalbuminemia develops generalized edema. Which of the following changes in Starling forces is the dominant cause?

- A.** Greater lymphatic return raises interstitial fluid volume
- B.** Reduced plasma colloid oncotic pressure increases net capillary filtration
- C.** Greater plasma oncotic pressure draws fluid into the interstitium
- D.** Reduced interstitial oncotic pressure prevents reabsorption into capillaries
- E.** Reduced capillary hydrostatic pressure increases net filtration

191. During evaluation, para-aminohippurate is filtered and strongly secreted so that most PAH entering the kidney is excreted in one pass at low plasma concentrations. Its clearance approximates which quantity?

- A.** Effective renal plasma flow
- B.** Filtration fraction
- C.** Plasma oncotic pressure

D. Renal blood flow without hematocrit correction

E. Glomerular filtration rate

192. A patient asks for a nonindicated antibiotic for a viral upper respiratory infection. Which of the following responses best supports shared decision-making?

A. Tell the patient antibiotics are forbidden in all respiratory illnesses

B. Explain why antibiotics will not help, address the concern, and offer symptomatic care

C. Order an invasive test solely to justify refusing the prescription

D. Prescribe the antibiotic to preserve satisfaction despite lack of benefit

E. Dismiss the request without exploring the patient's concern

193. During evaluation, a patient steps on a sharp object and withdraws the foot before consciously perceiving pain. Which neural circuit permits this rapid response?

A. A cerebellar long-loop reflex requiring visual input

B. A corticospinal loop requiring cortical motor planning

C. A spinal polysynaptic withdrawal reflex using interneurons

D. A monosynaptic stretch reflex from muscle spindle Ia afferents

E. A vestibulo-ocular reflex driven by semicircular canals

194. During evaluation, a child with recurrent *Neisseria* infections is found to have a terminal complement deficiency. Which complement function is most impaired?

A. Opsonization of bacteria by C3b

B. Generation of the anaphylatoxin C3a

C. Cleavage of C4 during the classical pathway

D. Binding of C1q to antibody-coated antigen

E. Formation of the C5b-9 membrane attack complex

195. A patient who has severe hypophosphatemia develops muscle weakness. Which energetic process is most directly compromised?

- A.** Collagen hydroxylation in the endoplasmic reticulum
- B.** Passive diffusion of potassium via resting channels
- C.** ATP generation and phosphorylation-dependent cellular work
- D.** Formation of acetylcholine from choline and acetate only
- E.** Oxygen binding to heme iron in circulating hemoglobin

196. During evaluation, a screening program appears to improve survival time from diagnosis even though patients die at the same age they would have without screening. Which bias explains this appearance?

- A.** Detection bias from differential test sensitivity only
- B.** Recall bias
- C.** Lead-time bias
- D.** Publication bias
- E.** Berkson bias

197. A patient who has diabetic ketoacidosis has fever and increased tissue carbon dioxide production. Which of the following changes promotes oxygen unloading from hemoglobin in metabolically active tissues?

- A.** No change in hemoglobin affinity because PO_2 alone determines unloading
- B.** A rightward shift caused by reduced 2,3-BPG concentration
- C.** A leftward shift caused by elevated H^+ and increased temperature
- D.** A rightward shift of the oxygen dissociation curve due to elevated H^+ , CO_2 , and temperature
- E.** A leftward shift caused by elevated carbon dioxide and reduced pH

198. During evaluation, during a single skeletal-muscle twitch, cytosolic calcium rises rapidly. Which protein binds calcium to initiate cross-bridge cycling?

- A. Myosin light-chain kinase
- B. Dystrophin
- C. Troponin C
- D. Tropomyosin
- E. Troponin I

199. During evaluation, during moderate dynamic exercise in a healthy adult, how does mean arterial pressure usually change?

- A. It remains absolutely fixed because the baroreflex prevents any change
- B. It doubles because all vascular beds constrict
- C. MAP rises modestly as higher cardiac output outweighs the fall in resistance
- D. It falls profoundly because systemic vascular resistance always reaches zero
- E. It falls because cardiac output decreases

200. During evaluation, a virus-infected nucleated cell presents viral peptides to cytotoxic T lymphocytes. Which interaction is required for recognition?

- A. IgE binding to Fc receptors on the infected cell
- B. CD8 binding to MHC class I on the infected cell
- C. CD40 binding to CD40 ligand on a neutrophil
- D. C3b binding directly to the T-cell receptor
- E. CD4 binding to MHC class II on the infected cell

201. During evaluation, a patient rapidly turns the head to the left. The vestibulo-ocular reflex keeps the eyes fixed on a stationary target. Which initial eye movement occurs?

- A. Both eyes move to the right
- B. The right eye moves right while the left eye moves left
- C. Both eyes move to the left

- D. No eye movement occurs until visual cortex processing
- E. Both eyes move upward

202. During evaluation, which hormone acts on Sertoli cells to support spermatogenesis and increase androgen-binding protein production?

- A. Adrenal aldosterone
- B. Pituitary luteinizing hormone
- C. Thyroid-stimulating hormone
- D. Pituitary follicle-stimulating hormone
- E. Adrenocorticotrophic hormone

203. A patient who has a brain mass has increased intracranial pressure. According to the Monro-Kellie principle, early compensation occurs through reduction of which intracranial component?

- A. Skull volume via acute expansion of cranial sutures in adults
- B. Arterial blood volume via complete cessation of cerebral flow
- C. White matter myelin content via enzymatic degradation
- D. Brain tissue volume via rapid neuronal dehydration only
- E. Cerebrospinal fluid and venous blood volume

204. A competent adult with severe anemia refuses a blood transfusion after demonstrating understanding of the risks, benefits, and alternatives. Which of the following is the best next step?

- A. Declare the patient incompetent because the choice carries substantial risk
- B. Respect the refusal and continue to offer acceptable alternative treatments
- C. Administer the transfusion because preventing death overrides an informed refusal
- D. Seek a court order solely because the clinician disagrees
- E. Ask the family to overrule the patient's decision

205. During evaluation, a patient eats a carbohydrate-rich meal. Which pancreatic beta-cell event triggers insulin granule exocytosis?

- A.** ATP-sensitive potassium channel opening followed by hyperpolarization
- B.** Suppression of ATP production in the beta cell
- C.** Direct opening of chloride channels by glucose
- D.** Voltage-gated calcium channel closure after glucose entry
- E.** ATP-sensitive potassium channel closure followed by depolarization and calcium influx

206. During evaluation, during clot formation, thrombin amplifies coagulation and converts a soluble plasma protein into an insoluble clot framework. Which substrate is directly cleaved?

- A.** von Willebrand factor
- B.** Fibrinogen
- C.** Plasminogen
- D.** Antithrombin
- E.** Protein C

207. During evaluation, a patient smells and tastes food before eating. Which phase of gastric secretion is activated predominantly through vagal pathways?

- A.** Colonic mass-movement phase
- B.** Gastric phase
- C.** Cephalic phase
- D.** Migrating motor complex phase
- E.** Intestinal phase

208. A patient who has an upper motor neuron lesion develops spasticity and hyperreflexia below the lesion. Which of the following changes contributes to these findings?

- A.** Loss of muscle spindle afferent fibers from peripheral neuropathy

- B.** Destruction of neuromuscular junction acetylcholine receptors
- C.** Blockade of voltage-gated calcium channels at motor nerve terminals
- D.** Loss of descending inhibitory modulation of spinal reflex circuits
- E.** Selective degeneration of anterior horn alpha motor neurons

209. During evaluation, a patient has impaired defense against intracellular mycobacteria because macrophage activation is deficient. Which cytokine from Th1 cells is most important for classical macrophage activation?

- A.** Interleukin-10
- B.** Interferon-gamma
- C.** Transforming growth factor-beta
- D.** Interleukin-4
- E.** Interleukin-5

210. A normally developing adolescent enters puberty. Which of the following changes in hypothalamic-pituitary-gonadal physiology initiates the rise in gonadal steroid production?

- A.** Greater prolactin secretion that directly stimulates gonadal steroidogenesis
- B.** Continuous nonpulsatile GnRH release that maximally stimulates gonadotropes
- C.** Suppression of kisspeptin signaling with reduced hypothalamic activation
- D.** Reduced pituitary responsiveness to GnRH with lower LH and FSH secretion
- E.** Greater pulsatile secretion of hypothalamic GnRH

211. A clinician makes a medication error that reaches the patient but causes no apparent injury. Which of the following is the best communication with the patient?

- A.** Alter the chart so the error cannot be identified
- B.** Wait for the patient to discover the error before discussing it
- C.** Disclose the error, explain consequences and next steps, and apologize appropriately

- D.** Do not disclose because no injury is currently apparent
- E.** Tell the family but intentionally withhold the information from the patient

212. During evaluation, a drug blocks L-type calcium channels in the sinoatrial and atrioventricular nodes. Which action-potential phase is directly slowed in these tissues?

- A.** The ventricular sodium-dependent upstroke only
- B.** Phase 2 plateau
- C.** Phase 0 depolarization
- D.** Phase 1 early repolarization
- E.** Phase 3 potassium-mediated repolarization

213. During evaluation, immediately before ovulation, sustained high estradiol causes which endocrine event?

- A.** A sudden fall in GnRH pulsatility to zero
- B.** Positive feedback that produces the LH surge
- C.** Negative feedback that completely suppresses LH
- D.** An aldosterone surge that triggers oocyte release
- E.** A prolactin surge that directly ruptures the follicle

214. During evaluation, a patient taking aspirin has impaired primary hemostasis. Which platelet mediator is reduced because cyclooxygenase is irreversibly inhibited?

- A.** Prostacyclin generated by intact vascular endothelium
- B.** von Willebrand factor released from endothelial Weibel-Palade bodies
- C.** Tissue factor expressed by subendothelial and activated cells
- D.** Reduced platelet thromboxane A₂ synthesis and signaling
- E.** Adenosine diphosphate released from platelet dense granules

215. During evaluation, a patient takes a drug that blocks 5-alpha-reductase. Which conversion is reduced?

- A.** DHEA to androstenedione
- B.** Testosterone to dihydrotestosterone
- C.** Cholesterol to pregnenolone
- D.** Testosterone to estradiol
- E.** Androstenedione to testosterone

216. During evaluation, which segment of the loop of Henle is highly permeable to water but has relatively low permeability to sodium chloride?

- A.** Macula densa
- B.** Early distal convoluted tubule
- C.** Thin descending limb
- D.** Thick ascending limb
- E.** Cortical collecting duct without vasopressin

217. During evaluation, a tendon tap briefly stretches a muscle and produces contraction of that same muscle. Which receptor detects the initial stretch?

- A.** Muscle spindle primary afferents
- B.** Pacinian corpuscles in the overlying skin
- C.** Free nerve endings carrying slow pain
- D.** Golgi tendon organ Ib afferents
- E.** Vestibular hair cells in the semicircular canals

218. During evaluation, a patient receives 1 L of isotonic saline intravenously. After equilibration, where does the infused fluid distribute?

- A.** Only in plasma because chloride prevents capillary filtration

- B.** Almost entirely inside cells because sodium enters rapidly
- C.** Only in interstitial fluid because plasma proteins exclude sodium
- D.** Equally between intracellular and extracellular fluid
- E.** Extracellular fluid, distributed between plasma and interstitial spaces

219. A patient acclimatizes to repeated exercise in a hot climate. Which of the following changes in sweat is expected under aldosterone influence?

- A.** Lower water content because eccrine glands switch to lipid secretion
- B.** Complete absence of sweating due to reduced cholinergic signaling
- C.** Higher protein concentration because albumin is actively secreted
- D.** Higher sodium chloride concentration because ductal reabsorption is inhibited
- E.** Lower sodium chloride concentration with preserved or elevated sweat volume

220. During evaluation, a patient begins a maximal voluntary skeletal-muscle contraction. How does the nervous system normally increase whole-muscle force?

- A.** Recruitment of additional motor units and elevated firing frequency
- B.** Suppression of alpha motor neurons while activating only gamma motor neurons
- C.** Conversion of slow fibers into smooth muscle during the contraction
- D.** Reduction of motor-unit number with larger action potentials in each fiber
- E.** Reduced calcium release from recruited fibers to conserve ATP

221. Within several hours after birth, a healthy neonate undergoes functional closure of the ductus arteriosus. Which of the following changes is the principal physiologic trigger?

- A.** Greater right ventricular pressure caused by rising pulmonary resistance
- B.** Greater placental prostaglandin delivery after cord clamping
- C.** Greater arterial oxygen tension with reduced prostaglandin-mediated ductal relaxation
- D.** Reduced arterial oxygen tension with increased adenosine release

E. Reduced systemic vascular resistance caused by loss of the placenta

222. An otherwise healthy fetus extracts oxygen from maternal blood across the placenta even though fetal arterial PO₂ is relatively low. Which of the following properties most strongly facilitates this transfer?

- A. Placental blood flow eliminates the need for a hemoglobin affinity difference
- B. Fetal hemoglobin has a higher oxygen affinity than adult hemoglobin at a given PO₂
- C. Fetal hemoglobin contains more 2,3-BPG than adult hemoglobin
- D. Fetal carbon dioxide retention shifts fetal hemoglobin to the right
- E. Maternal hemoglobin becomes permanently left shifted during pregnancy

223. An otherwise healthy person receives exogenous insulin. Which enzyme activity in adipose tissue is stimulated, favoring triglyceride storage?

- A. Adipose adenylate cyclase via glucagon receptors
- B. Lipoprotein lipase on capillary endothelium
- C. Hepatic glycogen phosphorylase
- D. Carnitine palmitoyltransferase I via malonyl-CoA depletion
- E. Hormone-sensitive lipase within adipocytes

224. A patient tells a clinician of a specific plan to seriously harm an identifiable person. Which of the following responses is most appropriate?

- A. Tell only the patient's coworkers and take no other action
- B. Ignore the statement unless physical harm has already occurred
- C. Discharge the patient immediately without further risk assessment
- D. Keep the threat completely confidential because confidentiality has no exceptions
- E. Initiate a safety response consistent with applicable duty-to-protect requirements

225. A pregnant woman at 8 weeks has ongoing progesterone secretion from the corpus luteum. Which hormone maintains it during early pregnancy?

- A.** Oxytocin
- B.** Chorionic gonadotropin
- C.** Human placental lactogen
- D.** Prolactin
- E.** Follicle-stimulating hormone

226. An otherwise healthy adult is exposed to cold. Which cutaneous response reduces heat loss most effectively?

- A.** Sympathetic vasoconstriction of skin arterioles and arteriovenous shunts
- B.** Sweat gland activation with evaporative cooling
- C.** Active cutaneous vasodilation with elevated skin blood flow
- D.** Reduced sympathetic tone to superficial venous plexuses
- E.** Greater nitric oxide release in acral skin vessels

227. A patient who has extensive ileal resection develops increased colonic secretion because bile acids reach the colon. Which normal enterohepatic process has been disrupted?

- A.** Synthesis of bile salts in the pancreatic acinar cells
- B.** Secretion of bile salts by colonic crypt cells
- C.** Absorption of bile salts in the stomach by proton pumps
- D.** Active reabsorption of bile salts in the terminal ileum
- E.** Conversion of bile salts to chylomicrons in lymphatic lacteals

228. During evaluation, a patient develops hyperkalemia that slows ventricular conduction. Which cardiac cell phase relies mainly on rapid sodium influx and can be impaired by sodium-channel inactivation?

- A. Phase 0 of sinoatrial nodal cells
- B. Phase 4 of sinoatrial nodal cells
- C. Phase 2 of ventricular myocytes
- D. Phase 0 of ventricular myocytes
- E. Phase 3 of ventricular myocytes

229. During evaluation, a highly sensitive test is used as an initial screen for a dangerous disease. A patient has a negative result. Why is the result useful?

- A. A negative result on a highly sensitive test makes the disease less likely
- B. A positive result on a highly sensitive test always proves disease
- C. High sensitivity eliminates all false-positive results
- D. Sensitivity determines positive predictive value without prevalence
- E. A negative result on a highly specific test always proves disease

230. During evaluation, a patient receives a benzodiazepine that enhances GABA-A receptor action. Which postsynaptic ionic change most directly mediates inhibitory signaling?

- A. Reduced chloride conductance that removes inhibitory current
- B. Greater chloride conductance that stabilizes or hyperpolarizes the membrane
- C. Greater sodium conductance that depolarizes the membrane
- D. Greater calcium conductance that triggers an action potential
- E. Reduced potassium conductance that raises membrane resistance

231. A near miss occurs when a nurse catches a tenfold medication-dose error before the drug reaches the patient. Which of the following is the best institutional response?

- A. Punish the reporting nurse to discourage unnecessary reports
- B. Wait for a similar error to cause harm before investigating
- C. Ignore the event because no patient was harmed

- D.** Report and analyze the near miss because it can reveal hazards before harm occurs
- E.** Delete the order history to protect the prescriber

232. A patient has abrupt stress and elevated ACTH. Which adrenal cortical zone responds by increasing cortisol secretion?

- A.** Renal juxtaglomerular apparatus
- B.** Adrenal medulla
- C.** Zona reticularis only
- D.** Zona fasciculata
- E.** Zona glomerulosa

233. During evaluation, a hospital team maps every step from medication ordering to administration to identify where delays and errors arise. What quality-improvement activity is this?

- A.** Intention-to-treat analysis of a randomized trial
- B.** Blinding to reduce observer bias
- C.** Process mapping to identify failure points in the care pathway
- D.** Case-control sampling to estimate disease odds
- E.** Meta-analysis of published medication studies

234. During evaluation, a patient undergoes vagotomy. Which gastric function is most directly reduced?

- A.** Nutrient absorption by intestinal villi ceases
- B.** Cephalic-phase acid secretion and receptive relaxation
- C.** Bile salt synthesis in the liver stops
- D.** Intrinsic enteric peristalsis is completely abolished
- E.** Pancreatic bicarbonate secretion becomes impossible

235. During a clinical discussion, a patient says, 'I am terrified that this surgery will leave me disabled.' Which physician response best demonstrates empathy?

- A.** Review the operation's favorable outcome statistics first, then return to the patient's concerns if anxiety persists
- B.** Explain that the surgeon has an excellent record and ask whether that information reduces the patient's fear
- C.** It sounds like losing your independence is one of your biggest fears; tell me more about that
- D.** Clarify the technical risks of disability in detail before asking the patient to describe the emotional concern
- E.** Offer to have the surgical team revisit the consent form so the patient can focus on objective probabilities

236. An unconscious patient arrives with life-threatening internal bleeding and no surrogate or advance directive can be identified. Immediate surgery is required to prevent death. Which approach is most appropriate?

- A.** Provide immediately necessary emergency treatment under the doctrine of presumed consent
- B.** Seek expedited judicial authorization before proceeding, even though the bleeding is immediately life-threatening
- C.** Provide only temporizing resuscitation until a legally authorized surrogate can be located
- D.** Request consent from an available witness who is not related to the patient but observed the emergency
- E.** Proceed with diagnostic stabilization but postpone definitive surgery until formal consent becomes possible

237. A patient has a murmur that begins promptly after the first heart sound. Which valve event normally produces S1?

- A.** Closure of the mitral and tricuspid valves
- B.** Opening of the mitral and tricuspid valves
- C.** Rapid passive filling of the ventricles
- D.** Closure of the aortic and pulmonic valves

E. Opening of the aortic and pulmonic valves

238. During evaluation, a person slowly lowers a heavy weight while the elbow flexors remain active. Which mechanical state best describes the biceps during this movement?

- A. Concentric contraction in which active muscle shortens against the load
- B. Eccentric contraction in which active muscle lengthens while generating force
- C. Tetanic contraction with no change in joint angle
- D. Isometric contraction in which muscle length remains exactly fixed
- E. Complete relaxation with passive tendon recoil only

239. During evaluation, during exercise in a hot environment, eccrine sweat secretion increases. Which neurotransmitter primarily stimulates these glands?

- A. Serotonin released from sympathetic preganglionic fibers
- B. Acetylcholine released from sympathetic postganglionic fibers
- C. Epinephrine released directly from cutaneous sensory fibers
- D. Dopamine released from somatic motor neurons
- E. Norepinephrine released from parasympathetic postganglionic fibers

240. A patient who has abrupt bacterial pneumonia has neutrophils migrating from blood into infected lung tissue. Which endothelial-leukocyte interaction mediates firm adhesion before transmigration?

- A. Platelet glycoprotein Ib binding to endothelial von Willebrand factor
- B. Endothelial selectins binding permanently to collagen in the basement membrane
- C. Leukocyte integrins binding to endothelial ICAM-1 and related adhesion molecules
- D. Neutrophil Fc receptors binding directly to endothelial prostacyclin
- E. Complement C3b binding to erythrocyte CR1 during capillary transit

241. A patient who has pulmonary fibrosis has stiff lungs. Which of the following changes is expected on the pressure-volume curve?

- A.** A right shift resulting from destruction of alveolar septa
- B.** No change in compliance because fibrosis affects only diffusion
- C.** Reduced compliance so a larger pressure change produces a smaller volume change
- D.** Greater residual volume caused by loss of elastic recoil
- E.** Greater compliance so a small pressure change produces a large volume change

242. A patient who has longstanding respiratory acidosis has renal compensation. Which of the following changes is expected after several days?

- A.** Suppressed ammoniagenesis despite persistent hypercapnia
- B.** Complete normalization of PCO_2 by the kidneys
- C.** Reduced hydrogen secretion by alpha-intercalated cells
- D.** Reduced bicarbonate reabsorption with bicarbonaturia
- E.** Greater bicarbonate reabsorption and ammonium-mediated net acid excretion

243. A patient receives a drug that selectively constricts systemic veins. Which rapid cardiac effect is expected?

- A.** Reduced right atrial filling because venous compliance increases
- B.** Reduced mean systemic filling pressure and venous return
- C.** Greater mean systemic filling pressure and venous return
- D.** No change in cardiac filling because veins do not store blood
- E.** Reduced preload because blood is trapped in peripheral veins

244. During evaluation, a man has normal testosterone production. Which pituitary hormone primarily stimulates Leydig cells?

- A.** Luteinizing hormone

- B.** Prolactin
- C.** Follicle-stimulating hormone
- D.** Growth hormone
- E.** Thyroid-stimulating hormone

245. A clinician notices that patients from one neighborhood have much poorer follow-up because transportation is unreliable. Which of the following responses best addresses this health disparity?

- A.** Exclude the neighborhood from outcome comparisons
- B.** Assume the patients are nonadherent and end outreach efforts
- C.** Provide the same appointment schedule without examining access barriers
- D.** Address the transportation barrier with more accessible follow-up options
- E.** Require cash deposits before rescheduling missed visits

246. A patient who has Parkinson disease has reduced movement initiation. Loss of dopamine from the substantia nigra pars compacta changes basal ganglia output in which direction?

- A.** Selective inhibition of lower motor neurons in the anterior horn
- B.** Reduced direct-pathway facilitation and elevated indirect-pathway inhibition of thalamocortical activity
- C.** Greater direct-pathway facilitation with decreased inhibitory output from the globus pallidus interna
- D.** Complete loss of cerebellar output to the motor cortex
- E.** Greater hippocampal glutamate release that suppresses the motor cortex

247. During evaluation, a patient has severe hyperkalemia. Which direct adrenal response helps restore potassium balance?

- A.** Greater cortisol with no aldosterone change
- B.** Greater aldosterone secretion

- C. Reduced aldosterone secretion
- D. Greater calcitonin secretion
- E. Suppressed distal nephron potassium secretion

248. A patient has loss of lymphatic drainage from one leg after pelvic surgery and develops longstanding swelling. Which Starling force consequence best explains the edema?

- A. An increase in plasma oncotic pressure increases filtration from capillaries
- B. A decrease in interstitial oncotic pressure pulls fluid out of the vasculature
- C. Accumulation of interstitial protein raises interstitial oncotic pressure and retains fluid
- D. An increase in lymphatic pumping immediately lowers interstitial protein concentration
- E. A decrease in capillary hydrostatic pressure forces additional fluid into the interstitium

249. During evaluation, a patient drinks a very large volume of water quickly. Which renal response helps restore plasma osmolality toward normal?

- A. Greater proximal water reabsorption above the filtered load
- B. Suppression of vasopressin with excretion of a large volume of dilute urine
- C. Greater aldosterone as the primary response to low osmolality
- D. Greater vasopressin with insertion of collecting-duct aquaporins
- E. Maximal urea recycling to concentrate the urine

250. During evaluation, a breastfeeding infant suckles at the nipple. Which maternal hormone directly causes milk ejection from mammary myoepithelial cells?

- A. Anterior-pituitary prolactin
- B. Ovarian estrogen secretion
- C. Ovarian progesterone secretion
- D. Pituitary follicle-stimulating hormone
- E. Posterior-pituitary oxytocin

251. During evaluation, a patient has a large arteriovenous fistula. Which hemodynamic change is expected soon after the fistula opens?

- A.** Greater systemic vascular resistance with reduced venous return
- B.** No change in cardiac output because arterial and venous pressures equilibrate locally
- C.** Reduced venous return because blood bypasses capillaries
- D.** Reduced systemic vascular resistance with increased venous return and cardiac output
- E.** Greater afterload with a fall in stroke volume as the primary effect

252. A patient has longstanding metabolic acidosis. Renal ammonium production increases primarily from metabolism of which amino acid in proximal tubular cells?

- A.** Leucine
- B.** Phenylalanine
- C.** Tryptophan
- D.** Glutamine
- E.** Tyrosine

253. During evaluation, a surrogate is deciding for an incapacitated patient whose prior wishes about the current treatment are well documented. Which decision standard should guide the surrogate?

- A.** Substituted judgment based on what the patient would have chosen
- B.** A population-level utility calculation rather than the patient's wishes
- C.** The physician's preference because it is medically informed
- D.** The surrogate's personal preference regardless of the patient's values
- E.** The least expensive option regardless of likely benefit

254. A patient who has vitamin A deficiency has difficulty seeing in dim light. Which photochemical step is impaired?

- A.** Regeneration of retinal for rhodopsin in rod photoreceptors

- B.** Opening of cochlear potassium channels during sound transduction
- C.** Synthesis of melanin in the retinal pigment epithelium
- D.** Activation of cone opsins by ultraviolet light only
- E.** Formation of aqueous humor by the ciliary epithelium

255. During evaluation, a patient has pancreatic insufficiency and poor fat digestion. Which pancreatic enzyme directly hydrolyzes dietary triglycerides?

- A.** Carboxypeptidase, a pancreatic peptide-digesting enzyme
- B.** Pancreatic lipase, a triglyceride-digesting enzyme
- C.** Trypsin, a pancreatic protein-digesting enzyme
- D.** Elastase, a pancreatic protein-digesting enzyme
- E.** Amylase, a pancreatic starch-digesting enzyme

256. During evaluation, a patient receives a large intravenous infusion of isotonic saline. Which renal change tends to increase sodium excretion?

- A.** Greater proximal reabsorption caused by higher peritubular oncotic pressure
- B.** Greater vasopressin secretion caused by hyperosmolality
- C.** Reduced proximal sodium reabsorption and pressure natriuresis from extracellular volume expansion
- D.** Greater sympathetic renal nerve activity causing avid sodium retention
- E.** Greater renin and aldosterone secretion due to reduced effective volume

257. A patient says cost may prevent filling a newly prescribed medication. Which of the following is the best physician response?

- A.** Discuss affordability and choose a lower-cost effective treatment when possible
- B.** Choose the clinically preferred drug first and ask the pharmacy to address affordability after the prescription is sent

- C.** Keep the original regimen because changing therapy for cost reasons may reduce adherence to evidence-based care
- D.** Ask the patient to try purchasing the medication once before considering less expensive therapeutic alternatives
- E.** Document the financial barrier and defer treatment changes until the next visit so efficacy can be reassessed

258. During evaluation, a patient has primary hypothyroidism. Which pituitary response is expected if the hypothalamic-pituitary axis is intact?

- A.** Reduced TSH secretion due to reduced negative feedback
- B.** Loss of TSH pulsatility with normal mean secretion
- C.** Greater TSH secretion due to reduced negative feedback
- D.** Suppressed TRH secretion despite low thyroid hormone
- E.** Greater cortisol secretion as the only pituitary response

259. During evaluation, a patient has an end-diastolic volume of 120 mL and an end-systolic volume of 48 mL. What is the ejection fraction?

- A.** 72%
- B.** 50%
- C.** 60%
- D.** 40%
- E.** 150%

260. An otherwise healthy adult has a glomerular filtration rate of 120 mL/min and a renal plasma flow of 600 mL/min. What is the filtration fraction?

- A.** 30%
- B.** 20%
- C.** 10%

D. 50%

E. 15%

261. A patient is severely dehydrated and has high circulating vasopressin. Which of the following changes occurs in collecting-duct principal cells?

- A.** Inhibition of basolateral aquaporin-3 and aquaporin-4
- B.** Insertion of NKCC2 into the apical membrane
- C.** Removal of aquaporin-2 channels from the apical membrane
- D.** Insertion of aquaporin-2 channels into the apical membrane
- E.** Activation of pendrin in alpha-intercalated cells

262. A toxin delays closure of voltage-gated potassium channels after a neuronal action potential. Which of the following changes is most likely?

- A.** Loss of the sodium concentration gradient within one action potential
- B.** A more positive resting potential resulting from reduced potassium permeability
- C.** A prolonged afterhyperpolarization and delayed return toward threshold
- D.** Immediate depletion of synaptic vesicles independent of firing
- E.** A faster depolarizing upstroke due to greater sodium entry

263. During evaluation, a patient begins prolonged endurance exercise. Which cardiovascular change helps increase oxygen delivery to active muscle?

- A.** Reduced venous return because the muscle pump is inactive
- B.** Marked reduction in systolic pressure from suppressed sympathetic tone
- C.** Complete cessation of splanchnic vasoconstriction
- D.** Greater cardiac output with redistribution of flow toward exercising skeletal muscle
- E.** Reduced cardiac output with generalized vasoconstriction in active muscle

264. A patient who has hemophilia A has prolonged activated partial thromboplastin time with a normal prothrombin time. Which coagulation factor is deficient?

- A.** Factor V, a cofactor in the common-pathway prothrombinase complex
- B.** Factor XIII, which cross-links fibrin after thrombin generation
- C.** Factor VIII, a cofactor in the intrinsic tenase complex
- D.** Tissue factor, the membrane protein that activates factor VII
- E.** Factor VII, the major initiator of the extrinsic pathway

265. Moderate constriction of the efferent arteriole occurs while systemic pressure is stable. Which of the following changes is most likely initially?

- A.** Reduced renal plasma flow with increased glomerular capillary pressure and filtration fraction
- B.** Greater renal plasma flow with reduced filtration fraction
- C.** Greater renal plasma flow with increased Bowman-space pressure
- D.** Reduced glomerular pressure with increased renal plasma flow
- E.** No change in filtration fraction because GFR and plasma flow always change equally

266. A patient at high altitude has longstanding respiratory alkalosis from sustained hyperventilation. Which renal adaptation permits ventilation to remain high?

- A.** Greater bicarbonate reabsorption that further raises pH
- B.** Greater ammonium production that generates more bicarbonate
- C.** Complete retention of filtered bicarbonate
- D.** Greater bicarbonate excretion lowers plasma bicarbonate and reduces alkalemia
- E.** Suppressed hydrogen secretion with no bicarbonate loss

267. During evaluation, a substance is freely filtered and neither secreted nor reabsorbed. Its renal clearance is therefore equal to which physiologic quantity?

- A.** Renal blood flow

- B.** Renal plasma flow
- C.** Glomerular filtration rate
- D.** Filtration fraction
- E.** Urine flow rate

268. During evaluation, a person exercises in a hot environment. Which combination most effectively increases heat loss?

- A.** Cutaneous vasodilation plus eccrine sweating
- B.** Reduced skin blood flow plus brown-fat thermogenesis
- C.** Cutaneous vasoconstriction plus shivering
- D.** Splanchnic vasodilation plus skeletal-muscle tremor
- E.** Piloerection plus reduced sweat production

269. A patient who has emphysema has destruction of alveolar walls. Which pulmonary function change is most directly caused by loss of elastic recoil?

- A.** Greater radial traction that prevents airway collapse
- B.** Reduced residual volume from complete emptying
- C.** Greater lung compliance and impaired passive expiration
- D.** Reduced lung compliance and enhanced expiratory recoil
- E.** Greater diffusing surface area

270. During evaluation, a patient receives calcitonin during treatment of severe hypercalcemia. Which skeletal effect is expected?

- A.** Greater renal calcium reabsorption with enhanced PTH secretion
- B.** Greater osteoclast differentiation through RANK ligand
- C.** Greater intestinal calcium absorption through calcitriol synthesis
- D.** Direct activation of osteoblast PTH receptors causing phosphate release

E. Reduced osteoclast activity and reduced bone resorption

271. During evaluation, a highly specific confirmatory test is positive. Why can this strongly support the diagnosis?

- A. Specificity rises automatically when disease prevalence rises
- B. A highly specific test has few false positives, so a positive result helps rule in disease
- C. High specificity makes sensitivity mathematically equal to 100%
- D. A highly specific test has no false negatives by definition
- E. A negative highly specific test always confirms disease

272. A patient undergoing prolonged fasting has low insulin. Which adipocyte enzyme becomes more active and mobilizes stored triglyceride?

- A. Adipocyte hormone-sensitive lipase
- B. Pyruvate dehydrogenase under insulin stimulation
- C. Glycogen synthase
- D. Acetyl-CoA carboxylase under high malonyl-CoA conditions
- E. Lipoprotein lipase as the sole intracellular lipase

273. During evaluation, using the same trial in which event risk falls from 10% to 5%, what is the number needed to treat?

- A. 100
- B. 10
- C. 5
- D. 20
- E. 50

274. During evaluation, a toxin prevents ATP binding to skeletal-muscle myosin. Which step of the cross-bridge cycle fails?

- A.** ATP-dependent detachment of myosin from actin
- B.** Hydrolysis of acetylcholine in the synaptic cleft
- C.** Exposure of actin binding sites by calcium-bound troponin
- D.** Release of calcium from the sarcoplasmic reticulum
- E.** Propagation of the action potential along the sarcolemma

275. During evaluation, a patient absorbs fructose from the small-intestinal lumen. Which apical transporter is primarily responsible?

- A.** ENaC
- B.** NKCC2
- C.** GLUT4
- D.** SGLT1
- E.** GLUT5

276. During evaluation, two subthreshold excitatory postsynaptic potentials arrive at the same dendrite in rapid succession and together trigger an action potential. What phenomenon is illustrated?

- A.** Temporal summation
- B.** Refractory-period blockade
- C.** Presynaptic inhibition
- D.** Saltatory conduction
- E.** Spatial summation

277. During evaluation, a researcher plans a clinical trial involving human participants. Which ethical requirement is most fundamental before enrollment begins?

- A.** Payment large enough that no participant will refuse

- B.** Guaranteed personal benefit for every participant
- C.** Exclusion of all participants with chronic disease
- D.** Independent protocol review and valid consent unless an approved exception applies
- E.** Permission from the treating physician instead of participant consent

278. A patient who has severe pneumonia is given supplemental oxygen but a large intrapulmonary shunt persists. Why can hypoxemia be relatively resistant to oxygen therapy?

- A.** Shunted blood bypasses ventilated alveoli and cannot contact the added oxygen
- B.** Pulmonary blood flow stops when oxygen is administered
- C.** Hemoglobin becomes unable to bind oxygen at high inspired concentrations
- D.** Alveolar oxygen tension always falls when inspired oxygen rises
- E.** Oxygen cannot diffuse across any normal alveolus when FiO_2 rises

279. A patient receives high-dose glucocorticoids for several months and then abruptly stops them. Why can abrupt adrenal insufficiency occur?

- A.** Aldosterone secretion stops because ACTH is its only regulator
- B.** Cortisol receptors become unable to bind endogenous hormone
- C.** Glucocorticoids directly destroy the adrenal medulla
- D.** Chronic negative feedback suppresses CRH and ACTH, causing adrenal cortical atrophy
- E.** Chronic therapy permanently increases ACTH and exhausts the pituitary

280. A patient asks the physician to make the treatment choice because the patient feels overwhelmed. Which of the following is the best response?

- A.** Tell the family to decide even though the patient has capacity
- B.** Delay all care until the patient independently selects an option
- C.** Clarify goals and desired involvement, then offer a recommendation aligned with those values
- D.** Choose the treatment without discussing values or alternatives

E. Refuse to offer any recommendation because physicians must remain completely neutral

Answers

1. **A.** The cerebral aqueduct connects the third ventricle to the fourth. Obstruction causes enlargement of the ventricles upstream of the block: both lateral ventricles and the third ventricle. The fourth ventricle remains downstream and does not enlarge from the aqueduct obstruction itself.
2. **B.** Hypoxemia stimulates peripheral chemoreceptors and increases ventilation. Carbon dioxide falls, producing an acute respiratory alkalosis with increased pH. Over several days the kidneys excrete bicarbonate, reducing the alkalemia and allowing sustained ventilatory acclimatization.
3. **B.** Confidentiality protects a competent patient's health information. Unless a recognized exception applies, the physician should not disclose the diagnosis to family without permission. The clinician can explore the patient's reasons, encourage support when helpful, and clarify who may receive information.
4. **C.** Reduced arterial pressure decreases firing of high-pressure baroreceptors. Medullary integration increases sympathetic output and reduces vagal output, producing tachycardia, increased contractility, arteriolar vasoconstriction, and venoconstriction. These responses support arterial pressure during acute volume loss.
5. **B.** Beta-intercalated cells secrete bicarbonate into the tubular lumen through apical pendrin, a chloride-bicarbonate exchanger. This helps correct alkalosis when appropriate. Alpha-intercalated cells instead secrete H^+ and reclaim bicarbonate during acidosis.
6. **B.** IL-1, TNF, and IL-6 promote prostaglandin E_2 production in the hypothalamic region, raising the temperature set point. The body then behaves as if it is cold, producing vasoconstriction and shivering until the new set point is reached. Antipyretic cyclooxygenase inhibitors lower fever by reducing prostaglandin synthesis.
7. **E.** For a spherical structure, pressure is proportional to surface tension and inversely proportional to radius. Without surfactant, smaller alveoli would require higher distending pressure and would tend to empty into larger alveoli. Surfactant reduces this instability by lowering surface tension, especially in smaller alveoli.
8. **E.** Glucose enters proximal tubular cells from the lumen through sodium-glucose cotransporters driven by the sodium gradient created by basolateral Na^+/K^+ ATPase. It then exits basolaterally by facilitated diffusion. When transport capacity is exceeded or defective, glucose remains in the tubular fluid and appears in urine.
9. **D.** Endolymph has a high potassium concentration and a positive electrical potential. Deflection toward the tallest stereocilia opens mechanically gated channels, allowing potassium to enter and

depolarize the hair cell. Depolarization then opens calcium channels and increases neurotransmitter release onto auditory nerve fibers.

10. C. Alveolar ventilation equals respiratory rate times tidal volume minus dead-space volume. Here, $12 \times (500 - 150) \text{ mL} = 4,200 \text{ mL/min}$, or 4.2 L/min . Minute ventilation would be 6 L/min , but some of that ventilation remains in conducting airways and does not participate in gas exchange.

11. A. Most oxygen content is carried bound to hemoglobin, so a reduction in hemoglobin lowers arterial oxygen content even when PO_2 and saturation are normal. Dissolved oxygen contributes only a small fraction of total content. The alveolar gas equation and membrane diffusion properties are not directly altered by iron deficiency anemia.

12. B. Renal 1-alpha-hydroxylase converts 25-hydroxyvitamin D to 1,25-dihydroxyvitamin D, the active hormone calcitriol. PTH stimulates this enzyme when calcium is low. Calcitriol then increases intestinal calcium and phosphate absorption and participates in bone and mineral homeostasis.

13. A. IgG and C3b are major opsonins. Phagocytes bind them through Fc gamma and complement receptors, greatly improving ingestion of encapsulated organisms that otherwise resist direct phagocytosis. Cytotoxic T cells and natural killer cells target infected host cells rather than extracellular encapsulated bacteria.

14. A. Iron absorption occurs mainly in the duodenum and proximal jejunum. Non-heme ferric iron is reduced and transported into enterocytes, and iron exits through ferroportin when systemic regulation permits. Hepcidin controls how much absorbed iron reaches the plasma by regulating ferroportin.

15. B. Lung expansion and increased alveolar oxygen dilate the pulmonary circulation, sharply lowering pulmonary vascular resistance and increasing pulmonary blood flow. The resulting increase in pulmonary venous return raises left atrial pressure and helps functionally close the foramen ovale. Cord clamping instead raises systemic vascular resistance and removes the low-resistance placental circuit.

16. D. Aldosterone acts on principal cells to increase ENaC activity, basolateral Na^+/K^+ ATPase, and potassium secretory pathways such as ROMK. Sodium reabsorption creates a lumen-negative potential that favors potassium secretion. Vasopressin, rather than aldosterone, is the primary regulator of aquaporin-2 insertion.

17. E. Systemic venous return is driven by the difference between mean systemic filling pressure and right atrial pressure. Raising right atrial pressure reduces that gradient and therefore reduces venous return. This relationship helps explain venous congestion in right-sided heart failure.

18. C. Urinary tract obstruction raises hydrostatic pressure upstream in the tubules and Bowman space. This pressure opposes filtration across the glomerular capillary and lowers net filtration pressure. If prolonged, obstruction can also produce additional changes in renal blood flow and parenchymal function.

- 19. B.** The ruptured follicle luteinizes to form the corpus luteum, which secretes progesterone and estrogen under LH support. Progesterone prepares and maintains a secretory endometrium. Without pregnancy, the corpus luteum regresses and steroid levels fall, contributing to menstruation.
- 20. C.** Raising extracellular potassium reduces the potassium concentration gradient, making the potassium equilibrium potential and resting membrane potential less negative. Mild depolarization can initially increase excitability. With severe or sustained hyperkalemia, however, sodium-channel inactivation can impair action-potential generation and cause weakness.
- 21. E.** Autoimmune hemolytic anemia is a type II hypersensitivity process in which antibodies bind cell-surface antigens. Opsonized erythrocytes are removed by phagocytes, especially in the spleen, and complement may contribute. Type I, III, and IV reactions use different effector pathways.
- 22. A.** The bicarbonate buffer system is the major extracellular buffer and is uniquely linked to both lungs and kidneys. Added base consumes carbonic acid and can alter PCO₂ through ventilatory responses, while the kidneys adjust bicarbonate excretion over time. Other buffers contribute but do not replace this integrated system.
- 23. B.** During an isometric contraction, muscle tension rises but overall muscle length does not change because the load cannot be moved. Cross-bridges still cycle and consume ATP. In concentric isotonic contraction, the muscle shortens; in eccentric contraction, an activated muscle lengthens while resisting a load.
- 24. E.** The proximal tubule reabsorbs roughly two thirds of filtered sodium and water under normal conditions, along with most filtered bicarbonate, glucose, and amino acids. Water follows solute so tubular fluid remains approximately iso-osmotic. Later nephron segments fine-tune electrolyte and water balance.
- 25. C.** Active skeletal-muscle tension depends on the number of actin-myosin cross-bridges that can form. Maximal force occurs at an intermediate sarcomere length with optimal filament overlap. Excessive shortening causes filament interference, whereas excessive stretch reduces overlap and therefore decreases active tension.
- 26. D.** Fast glycolytic fibers have large diameter, high myosin ATPase activity, and rapid shortening velocity, supporting high power over short periods. They rely heavily on anaerobic glycolysis and fatigue relatively quickly. Slow oxidative fibers are optimized for endurance and sustained low-force activity.
- 27. D.** In heart failure, impaired cardiac output and altered arterial filling can reduce effective arterial blood volume even while total extracellular volume is expanded. Baroreceptor and renal signals then activate sympathetic tone, renin-angiotensin-aldosterone, and vasopressin, promoting further retention. This explains the coexistence of edema and sodium-avid kidneys.

- 28. A.** Raising inspired oxygen greatly increases arterial PO₂ and therefore dissolved oxygen, but dissolved oxygen is still small compared with hemoglobin-bound oxygen under ordinary hyperoxic conditions. Hemoglobin is already near fully saturated in a healthy person breathing room air. Thus oxygen content rises modestly relative to the large increase in PO₂.
- 29. C.** The liver generates ketone bodies from acetyl-CoA during fasting but lacks thiophorase, the enzyme required to activate acetoacetate for oxidation in the TCA cycle. Ketones are exported for use by extrahepatic tissues. This prevents the liver from consuming the fuel it is producing for the rest of the body.
- 30. D.** The sinoatrial node has the steepest spontaneous phase 4 depolarization and the highest intrinsic firing rate among normal cardiac pacemakers. It suppresses slower latent pacemakers through overdrive. If conduction from the atria is lost, junctional or ventricular escape rhythms can emerge at lower intrinsic rates.
- 31. A.** S3 occurs shortly after S2 during rapid passive filling and reflects vibration of the ventricular walls and blood column. It can be physiologic in children, young adults, and pregnancy, but in older adults may suggest volume overload or systolic dysfunction. S4 occurs later in diastole with atrial contraction against a noncompliant ventricle.
- 32. A.** When tissues extract a greater fraction of delivered oxygen, less oxygen remains in venous blood, so mixed venous oxygen content and saturation fall. Cardiac output also rises during exercise, limiting how far venous oxygen declines. The Fick principle relates oxygen consumption to cardiac output and the arterial-venous oxygen content difference.
- 33. C.** In nephrogenic diabetes insipidus, the kidney is resistant to vasopressin, so exogenous desmopressin produces little or no increase in urine osmolality. Central diabetes insipidus generally responds because the renal V2-aquaporin pathway is intact. Both disorders can cause polyuria and hypernatremia if water intake is inadequate.
- 34. B.** Initial platelet adhesion is mediated by platelet glycoprotein Ib binding to von Willebrand factor, which is anchored to exposed subendothelial collagen. After activation, glycoprotein IIb/IIIa binds fibrinogen and mediates platelet aggregation. The coagulation and fibrinolytic proteins listed in the other choices do not replace this adhesion mechanism.
- 35. A.** Aldosterone secretion from zona glomerulosa cells is regulated primarily by angiotensin II and plasma potassium. Both raise intracellular calcium and stimulate steroid synthesis. ACTH has a modest permissive or transient effect but is not the dominant chronic regulator.
- 36. E.** PTH increases renal calcium reabsorption, especially in the distal nephron, while reducing proximal phosphate reabsorption and causing phosphaturia. It also stimulates renal 1- α -hydroxylase, increasing calcitriol production. These effects help raise extracellular calcium while limiting calcium-phosphate precipitation.

- 37. E.** Duodenal S cells release secretin in response to acid. Secretin stimulates pancreatic ductal bicarbonate secretion and helps neutralize gastric acid in the small intestine. Cholecystokinin is more strongly linked to pancreatic enzyme secretion and gallbladder contraction in response to fats and amino acids.
- 38. B.** Juxtaglomerular cells release renin when renal perfusion pressure falls, sympathetic beta-1 stimulation rises, or macula densa NaCl delivery falls. Renin initiates angiotensin II formation, promoting vasoconstriction and sodium retention. High macula densa NaCl delivery suppresses rather than stimulates renin.
- 39. A.** Vomiting removes hydrogen chloride and can generate alkalosis. Volume and chloride depletion activate sodium-retaining pathways, enhance proximal bicarbonate reabsorption, and increase aldosterone-driven distal H⁺ secretion, helping maintain the alkalosis. Restoring chloride and volume often allows the kidney to excrete the excess bicarbonate.
- 40. C.** Fine touch, vibration, and conscious proprioception ascend in the dorsal columns and then cross in the medulla as internal arcuate fibers. Pain and temperature ascend mainly in the anterolateral system and cross near the spinal level of entry. This dissociation localizes the sensory deficit to the dorsal column-medial lemniscus system.
- 41. D.** Sensitivity is the proportion of people with disease who test positive. Here, 90 of 100 diseased individuals are true positives, so sensitivity is 90%. Sensitivity is calculated only within the diseased group and is distinct from positive predictive value.
- 42. E.** Decision-making capacity is task specific and depends on the ability to communicate a choice, understand relevant information, appreciate consequences, and reason about options. Psychiatric illness does not automatically remove capacity. A clinician can assess capacity, while legal competence is a court determination.
- 43. D.** Increasing arterial resistance raises left ventricular afterload. The ventricle must generate higher pressure before and during ejection and ejects less blood at the same contractility, leaving a larger end-systolic volume and reducing stroke volume. The pressure-volume loop therefore becomes taller and narrower.
- 44. A.** Erythropoietin is produced primarily by renal peritubular interstitial fibroblast-like cells in response to reduced oxygen delivery. It stimulates erythroid progenitors in the bone marrow. Chronic kidney disease reduces this endocrine response, producing a typical normocytic, normochromic anemia.
- 45. D.** Constriction of the afferent arteriole reduces blood flow into the glomerulus and lowers glomerular capillary hydrostatic pressure. Renal plasma flow and GFR therefore both decrease. The effect differs from moderate efferent constriction, which can initially raise glomerular pressure despite reducing renal plasma flow.

- 46. B.** Iodide is oxidized and attached to tyrosyl residues on thyroglobulin by thyroid peroxidase, creating monoiodotyrosine and diiodotyrosine. Iodine deficiency limits this organification step and reduces thyroid hormone synthesis. Compensatory TSH elevation can produce thyroid enlargement.
- 47. C.** Increasing cutaneous blood flow transports warm blood from the body core to the skin, enhancing dry heat loss by radiation and convection when ambient conditions permit. Sweating adds evaporative heat loss. Vasoconstriction would conserve heat rather than dissipate it.
- 48. C.** Absolute risk reduction is control event rate minus treatment event rate. Here, $10\% - 5\% = 5$ percentage points. Relative risk reduction would be 50%, but it describes the proportional rather than absolute decrease.
- 49. E.** Left ventricular intramyocardial vessels are compressed during systole, especially in the subendocardium. Most left coronary flow therefore occurs during diastole, when ventricular pressure falls and the perfusion gradient from the aorta to the myocardium is greatest. Tachycardia can reduce coronary perfusion by shortening diastole.
- 50. C.** Creatine kinase rapidly transfers a high-energy phosphate from phosphocreatine to ADP, regenerating ATP during brief bursts of high demand. The phosphocreatine pool is small but responds more quickly than many metabolic pathways. It is therefore especially important during the first seconds of intense muscular work.
- 51. E.** Free water crosses cell membranes readily and distributes according to total body water. Because intracellular fluid is the larger compartment, roughly two thirds of an added free-water load enters cells and one third remains extracellular. This differs from isotonic saline, which remains extracellular.
- 52. A.** Sweat is generally hypotonic relative to plasma, especially after heat acclimatization. Losing hypotonic fluid removes proportionally more water than solute, decreasing extracellular volume and increasing extracellular osmolality. Water then shifts from intracellular to extracellular fluid, so intracellular volume also falls.
- 53. B.** Cortisol inhibits both hypothalamic CRH and pituitary ACTH. Primary adrenal failure removes this negative feedback, leading to elevated ACTH. In secondary adrenal insufficiency from pituitary disease, ACTH is low and hyperpigmentation is absent.
- 54. C.** Pyrogen-induced prostaglandin E₂ raises the hypothalamic temperature set point. Until core temperature reaches the new set point, the body perceives itself as relatively cold and activates heat-conserving and heat-producing responses such as vasoconstriction and shivering. When the set point later falls, sweating and vasodilation promote heat loss.
- 55. A.** Chronic hypoxemia stimulates renal erythropoietin and increases red-cell mass, raising oxygen-carrying capacity. Ventilatory acclimatization and increased 2,3-BPG also contribute. Excessive erythrocytosis can eventually increase viscosity, but a moderate increase is an important adaptation.

- 56. B.** Type I fibers are slow oxidative fibers rich in mitochondria, myoglobin, oxidative enzymes, and capillaries. These properties support sustained aerobic ATP production and fatigue resistance. Fast glycolytic fibers have greater peak power and glycolytic capacity but fatigue more rapidly.
- 57. A.** Chylomicrons are too large to enter intestinal blood capillaries efficiently, so they enter lacteals and travel through lymph to the thoracic duct before reaching the systemic circulation. Short- and medium-chain fatty acids can enter portal blood more directly. This distinction is important for lipid transport physiology.
- 58. D.** Hepcidin binds ferroportin and causes its internalization and degradation. Iron then becomes trapped in enterocytes and macrophages, reducing intestinal absorption and plasma iron availability. This mechanism contributes to the anemia of chronic inflammation despite preserved or increased iron stores.
- 59. A.** Mu-opioid receptors are G_i coupled. They reduce adenylyl cyclase activity, inhibit presynaptic voltage-gated calcium channels, and increase postsynaptic potassium conductance, thereby reducing excitability and transmitter release. These effects suppress nociceptive signaling at several levels of the nervous system.
- 60. E.** Vitamin B12 binds intrinsic factor after pancreatic enzymes release it from R proteins in the small intestine. The intrinsic factor-B12 complex is then absorbed through receptor-mediated uptake in the terminal ileum. Disease or resection of this segment can therefore cause B12 malabsorption.
- 61. A.** PTH acts on osteoblast-lineage cells to increase RANK ligand expression and reduce the balance of osteoprotegerin signaling. RANK ligand binds RANK on osteoclast precursors, promoting osteoclast differentiation and activity. Thus PTH increases resorption indirectly rather than by binding directly to mature osteoclasts.
- 62. A.** Restrictive disease reduces lung volumes, including total lung capacity and often vital capacity. Because FEV1 and FVC decline together, the FEV1/FVC ratio is usually normal or increased. This contrasts with obstructive disease, in which expiratory flow is disproportionately reduced.
- 63. E.** A confounder is associated with both the exposure and the outcome and is not simply an intermediate step in the causal pathway. Smoking could therefore create or distort an apparent association between coffee and disease. Randomization, restriction, matching, stratification, and multivariable adjustment can help control confounding.
- 64. D.** Parathyroid chief cells express a G-protein-coupled calcium-sensing receptor. High extracellular calcium activates this receptor and suppresses PTH release, whereas low calcium reduces receptor signaling and permits PTH secretion. This provides rapid feedback control of ionized calcium.
- 65. D.** A pulmonary embolus can leave alveoli ventilated but underperfused, producing a high V/Q ratio and physiologic dead space. In the limit of no perfusion, V/Q approaches infinity. A V/Q ratio near zero occurs when perfusion persists but ventilation is absent, as in an airway obstruction.

- 66. E.** Angiotensin II enhances proximal sodium and bicarbonate reabsorption, in part by stimulating the apical sodium-hydrogen exchanger and basolateral transport. This supports extracellular volume during low-perfusion states. ENaC and aquaporin-2 are regulated mainly by aldosterone and vasopressin, respectively.
- 67. B.** Case-control studies begin with disease status and compare prior exposure between cases and controls. Because incidence in exposed and unexposed populations is not directly measured, the odds ratio is the standard association measure. For rare diseases, the odds ratio can approximate the relative risk.
- 68. E.** Pulmonary arterioles constrict in response to low local alveolar PO₂, a response opposite to most systemic vascular beds. Regional hypoxic vasoconstriction improves V/Q matching by diverting blood from poorly ventilated areas. Diffuse hypoxia, however, can raise pulmonary arterial pressure and contribute to pulmonary hypertension.
- 69. A.** Light activates rhodopsin and transducin, which activates phosphodiesterase and lowers cGMP. Cyclic nucleotide-gated cation channels close, hyperpolarizing the rod and reducing glutamate release. Photoreceptors signal through graded potentials rather than conventional all-or-none action potentials.
- 70. C.** Osteocytes are mature bone cells embedded within the mineralized matrix. Their interconnected processes sense mechanical loading and help regulate osteoblast and osteoclast activity through signals such as sclerostin. They are therefore important mechanosensors and coordinators of bone remodeling.
- 71. D.** In skeletal muscle, the T-tubular dihydropyridine receptor acts as a voltage sensor and is mechanically coupled to ryanodine receptor type 1 on the sarcoplasmic reticulum. Depolarization therefore triggers rapid calcium release without requiring substantial extracellular calcium influx. SERCA later returns calcium to the sarcoplasmic reticulum during relaxation.
- 72. B.** FSH stimulates granulosa-cell aromatase, converting androgens supplied by theca cells into estrogens. LH stimulates theca cells to produce those androgens. This two-cell, two-gonadotropin arrangement supports follicular estrogen production.
- 73. A.** Aromatase converts androgen substrates such as testosterone and androstenedione to estrogens. Inhibition lowers estrogen production in gonads and peripheral tissues. The testosterone-to-DHT conversion is mediated by 5- α -reductase.
- 74. E.** Functional residual capacity is the resting lung volume at the end of a normal passive expiration. At this point, inward elastic recoil of the lungs is balanced by outward recoil of the chest wall, so respiratory muscles can be relatively relaxed. Changes in compliance of either component can shift FRC.
- 75. C.** Osteoblasts synthesize osteoid, including type I collagen and other matrix proteins, and support mineralization. Some osteoblasts become embedded in bone as osteocytes. Osteoclasts are multinucleated cells specialized for bone resorption rather than matrix synthesis.

- 76. D.** Type I hypersensitivity begins when an allergen cross-links IgE already bound to Fc epsilon RI receptors on mast cells. Degranulation releases histamine and other mediators, producing rapid vasodilation, edema, and bronchoconstriction. The other mechanisms correspond to different hypersensitivity patterns or to immune suppression.
- 77. B.** Cirrhosis causes marked splanchnic vasodilation and can reduce effective arterial blood volume. The kidney responds as though the circulation is underfilled, activating sympathetic tone and the renin-angiotensin-aldosterone system. Sodium retention and low albumin can then worsen ascites and edema.
- 78. D.** The basilar membrane is narrow and stiff at the base and wider and more compliant toward the apex. High frequencies peak near the base, whereas low frequencies travel farther and peak near the apex. This tonotopic organization is preserved throughout the auditory pathway.
- 79. C.** Low insulin and high glucagon shift metabolism from storage to mobilization. Hepatic glycogenolysis and gluconeogenesis maintain glucose, while adipose lipolysis supplies fatty acids and the liver produces ketone bodies during longer fasting. This reduces reliance on glucose in tissues able to use alternative fuels.
- 80. A.** Increased venous return raises end-diastolic volume and myocardial fiber stretch. Within the physiologic range, this improves actin-myosin interaction and increases force of contraction, so stroke volume rises without requiring a primary change in contractility. This intrinsic response helps match cardiac output to venous return.
- 81. E.** The intact epidermis limits water loss and blocks entry of microbes. Full-thickness burns destroy this barrier, increasing evaporative fluid losses and susceptibility to infection while impairing thermoregulation. Capillary leak and systemic inflammatory responses can further worsen intravascular volume depletion in major burns.
- 82. D.** With no ventilation but ongoing perfusion, V/Q approaches zero. Blood leaving the region remains poorly oxygenated, creating a shunt-like effect. By contrast, ventilated but unperfused lung behaves as dead space with a very high V/Q ratio.
- 83. E.** The hippocampal formation is essential for consolidation of new declarative memories. Bilateral damage can cause profound anterograde amnesia while leaving many procedural learning abilities relatively intact. Basal ganglia circuits contribute more strongly to habit and procedural learning.
- 84. D.** Acute respiratory alkalosis lowers PCO₂ and raises pH. Nonbicarbonate buffers release hydrogen ions, producing a small fall in plasma bicarbonate within minutes. More substantial bicarbonate loss occurs later through renal compensation if hypocapnia persists.
- 85. A.** Plasma cells are terminally differentiated B cells specialized for high-rate antibody secretion. Antibodies neutralize toxins and viruses, opsonize microbes, and activate complement. Plasma cells are not professional phagocytes or cytotoxic effector cells.

- 86. E.** Erythrocytes must deform to traverse narrow splenic cords and sinusoidal slits. Spherocytes are less deformable and are retained and phagocytosed by red-pulp macrophages, causing extravascular hemolysis. The spleen is not the major adult source of erythropoietin, hemoglobin synthesis, or platelet production.
- 87. E.** The rapid upstroke of an axonal action potential depends on opening of voltage-gated sodium channels and inward sodium current. Blocking these channels prevents regenerative depolarization and propagation. Potassium conductance is more important for repolarization and afterhyperpolarization.
- 88. B.** Second-order spinothalamic neurons cross in the anterior white commissure within a few spinal segments of entry. They then ascend contralaterally through the brainstem. Therefore a left brainstem lesion can impair right-sided body pain and temperature sensation.
- 89. C.** Length-time bias arises because slowly progressing disease has a longer detectable preclinical phase and is therefore overrepresented among screen-detected cases. These tumors may have a better prognosis independent of screening. This can make screened cases appear to fare better even without a true mortality benefit.
- 90. B.** The submucosal, or Meissner, plexus helps regulate secretion, absorption, and local mucosal blood flow. The myenteric plexus is more strongly associated with smooth-muscle motility. Enteric circuits can operate independently while remaining modulated by autonomic input.
- 91. D.** Insulin deficiency with elevated glucagon and catecholamines activates adipose lipolysis, delivering free fatty acids to the liver. Hepatic beta-oxidation generates acetyl-CoA, while low insulin and high glucagon favor conversion of acetyl-CoA to ketone bodies. Accumulation of acetoacetate and beta-hydroxybutyrate produces metabolic acidosis.
- 92. D.** Denervation removes both motor activation and trophic influences on skeletal muscle, producing rapid neurogenic atrophy. Denervated fibers can develop spontaneous electrical activity seen as fibrillation potentials. Spasticity and hyperreflexia are more characteristic of upper motor neuron lesions in which the peripheral motor unit remains intact.
- 93. A.** Th2 responses are specialized for defense against helminths and for allergic inflammation. IL-4 promotes IgE class switching, IL-5 promotes eosinophil growth and activation, and IL-13 contributes to mucus production and related responses. Th1 and Th17 cells are more closely associated with intracellular pathogens and extracellular bacteria or fungi, respectively.
- 94. A.** Heat stroke represents failure of heat balance and thermoregulation rather than a controlled increase in the hypothalamic set point. Core temperature rises because heat gain and production exceed the body's ability to dissipate heat. Rapid external cooling is therefore essential, unlike fever in which the body actively defends a higher set point.

- 95. B.** Golgi tendon organ Ib afferents signal muscle tension and activate inhibitory interneurons that reduce alpha motor-neuron activity to the same muscle. This autogenic inhibition can limit excessive force. Muscle spindles, in contrast, tend to excite alpha motor neurons when the muscle is stretched.
- 96. C.** The cerebellum compares intended movement with sensory feedback and helps adjust timing, force, and coordination. Lesions commonly cause ipsilateral limb ataxia, dysmetria, and intention tremor. The cerebellum refines rather than directly initiates voluntary movement.
- 97. B.** Histamine released by enterochromaffin-like cells binds H₂ receptors on parietal cells. These G_s-coupled receptors increase cAMP and stimulate acid secretion. Acetylcholine and gastrin use mainly calcium-dependent signaling, creating synergistic stimulation with histamine.
- 98. E.** Increasing red-cell mass raises hemoglobin concentration and therefore the blood's oxygen-carrying capacity. Arterial PO₂ reflects dissolved oxygen and is not increased simply by adding erythrocytes. Plasma oncotic pressure is determined mainly by plasma proteins, especially albumin, not by the number of circulating red cells.
- 99. B.** Cardiac M₂ muscarinic receptors couple to G_i, lowering cAMP and decreasing pacemaker currents. Their beta-gamma subunits also increase potassium conductance, hyperpolarizing nodal cells. Together these effects flatten phase 4 depolarization and slow spontaneous firing.
- 100. A.** Growth hormone stimulates production of IGF-1, especially in the liver and also in peripheral tissues. IGF-1 mediates many anabolic and growth effects, including cartilage and bone growth. GH also has direct metabolic effects such as increased lipolysis and reduced insulin sensitivity.
- 101. A.** Alpha-1 receptors couple to G_q, which activates phospholipase C and generates IP₃ and DAG. IP₃ increases cytosolic calcium, promoting smooth-muscle contraction and vasoconstriction. Beta-2 receptors instead couple to G_s and generally relax vascular smooth muscle through cAMP-dependent mechanisms.
- 102. E.** After difficult news, a brief pause allows the patient to process information. Naming or acknowledging emotion and asking an open invitation can help the patient express what matters most. Dense information is often poorly retained when strong emotion is present, so communication should proceed at a pace the patient can absorb.
- 103. D.** The PR interval includes atrial depolarization and conduction through the AV node and His-Purkinje system. AV nodal slowing therefore prolongs the PR interval. QRS duration primarily reflects ventricular depolarization through the His-Purkinje network and ventricular myocardium.
- 104. C.** Reduced mechanical loading decreases anabolic signaling and promotes proteolytic pathways, causing loss of contractile proteins and fiber cross-sectional area. The process can be partly reversed with reloading and rehabilitation. It is not primarily a transformation of myocytes into adipocytes.

- 105. D.** Systemic veins and venules are highly compliant capacitance vessels and contain most of the circulating blood volume at rest. Sympathetic venoconstriction can mobilize part of this reservoir toward the heart. Arterioles are the major resistance vessels but contain a much smaller fraction of total blood volume.
- 106. A.** The apical sodium-glucose cotransporter in small-intestinal enterocytes remains functional in many secretory diarrheas, including cholera. Coupled sodium and glucose uptake promotes net solute absorption, and water follows osmotically. This is the physiologic basis of oral rehydration therapy.
- 107. E.** Central diabetes insipidus results from deficient synthesis or release of vasopressin. The kidney can still respond, so desmopressin markedly increases urine concentration. Nephrogenic diabetes insipidus instead reflects impaired renal responsiveness to vasopressin.
- 108. B.** Circulating T3 and T4 exert negative feedback on both the hypothalamus and pituitary. Exogenous thyroid hormone therefore suppresses TRH and TSH when doses are sufficient. This feedback principle is central to interpreting thyroid function tests.
- 109. B.** Professional antigen-presenting cells process many extracellular proteins in endosomal compartments and present resulting peptides on MHC class II to CD4 T cells. MHC class I generally presents cytosolic peptides to CD8 T cells. B7 provides costimulation but does not serve as the peptide-presenting groove.
- 110. A.** Lactase deficiency leaves lactose in the intestinal lumen, where it exerts an osmotic effect that retains water. Colonic bacteria ferment the carbohydrate, producing gas and organic acids that contribute to bloating and discomfort. The disorder does not require mucosal destruction.
- 111. D.** IL-6 is a major driver of the hepatic acute-phase response, increasing synthesis of proteins such as C-reactive protein and fibrinogen. Other cytokines have important immune roles but are not the principal signal for broad acute-phase protein production. The rise in fibrinogen can also increase the erythrocyte sedimentation rate.
- 112. A.** Hypothalamic osmoreceptors respond to small increases in effective plasma osmolality by increasing vasopressin release and thirst. Vasopressin increases renal water reabsorption, while drinking replaces lost water. Together these responses lower osmolality toward normal.
- 113. A.** Calcitriol increases intestinal absorption of both calcium and phosphate. Deficiency reduces the availability of these minerals for hydroxyapatite formation, impairing mineralization in growing bone. Secondary hyperparathyroidism can further lower serum phosphate through renal phosphate wasting.
- 114. C.** Fast, well-localized pain is carried mainly by thinly myelinated A-delta fibers. Slower, diffuse burning pain is carried by unmyelinated C fibers. Larger myelinated sensory fibers conduct proprioceptive or touch information rather than the initial nociceptive signal.

- 115. A.** When a patient lacks capacity, an authorized surrogate should guide decisions. The surrogate should use substituted judgment based on the patient's known wishes and values when possible, and otherwise use the patient's best interests. A valid designated health-care agent generally takes priority over informal family preference.
- 116. C.** Global oxygen delivery equals cardiac output times arterial oxygen content. Because oxygen content depends strongly on hemoglobin concentration and saturation, anemia can reduce delivery despite normal arterial PO₂. The body can compensate partly by increasing cardiac output and tissue oxygen extraction.
- 117. A.** Extracellular calcium stabilizes excitable membranes by influencing voltage-gated sodium-channel activation. When extracellular calcium falls, sodium channels open at more negative membrane potentials, lowering threshold and increasing spontaneous firing. Severe hypocalcemia can therefore cause tetany despite reduced total calcium availability.
- 118. B.** Pulse pressure rises when a given stroke volume is ejected into a less compliant arterial system. Aging and arteriosclerosis increase arterial stiffness, producing higher systolic pressure and often lower or unchanged diastolic pressure. Reduced compliance also increases pulse-wave velocity rather than decreasing it.
- 119. D.** Serum sickness is a type III hypersensitivity reaction. Soluble antigen-antibody complexes deposit in tissues, activate complement, and recruit inflammatory cells, producing systemic manifestations such as fever, arthralgias, and glomerular injury. The other mechanisms describe type I, type II, or type IV reactions.
- 120. C.** The peristaltic reflex produces contraction behind the bolus and relaxation ahead of it, moving contents in the aboral direction. This pattern can be coordinated by intrinsic enteric circuits. Extrinsic autonomic input modulates but is not required for every local peristaltic event.
- 121. B.** The TSH receptor is primarily G_s coupled, increasing cAMP and stimulating thyroid hormone synthesis, secretion, and gland growth. Persistent receptor stimulation, as in Graves disease, can produce diffuse thyroid enlargement. Thyroid hormones themselves act through intracellular nuclear receptors rather than through the TSH receptor pathway.
- 122. B.** During prolonged fasting, skeletal muscle relies increasingly on free fatty acids, conserving ketone bodies for the brain. The liver cannot use the ketone bodies it produces because it lacks thiophorase. Red blood cells cannot use ketones because they lack mitochondria and remain dependent on glycolysis.
- 123. D.** Alpha-intercalated cells secrete H⁺ through apical H⁺-ATPase and H⁺/K⁺ ATPase while returning bicarbonate to blood. This physiologic response is enhanced during acidosis. Beta-intercalated cells perform the opposite net function by secreting bicarbonate during alkalosis.

- 124. A.** ANP is released in response to atrial stretch and promotes sodium and water excretion. It can increase GFR through favorable arteriolar effects while suppressing renin, aldosterone, and tubular sodium reabsorption. These actions oppose volume-expanding signals such as the renin-angiotensin-aldosterone system.
- 125. A.** Glucagon maintains plasma glucose during fasting by stimulating hepatic glycogenolysis and gluconeogenesis and by favoring fatty-acid oxidation and ketogenesis. It opposes many actions of insulin. Hepatocytes use GLUT2 rather than insulin-responsive GLUT4.
- 126. C.** A p value is the probability, assuming the null hypothesis and statistical model are true, of observing data at least as extreme as the data obtained. It is not the posterior probability that the null hypothesis is true and does not measure clinical importance. Statistical significance also does not eliminate bias or guarantee reproducibility.
- 127. D.** Cholecystikinin is released from I cells in response to fatty acids and amino acids. It contracts the gallbladder, relaxes the sphincter of Oddi, and stimulates pancreatic acinar enzyme secretion. Secretin primarily promotes bicarbonate-rich ductal secretion.
- 128. E.** REM sleep has an activated, low-amplitude mixed-frequency EEG resembling wakefulness, vivid dreaming, rapid eye movements, and marked skeletal muscle atonia. Autonomic activity can be variable. Slow-wave delta activity is characteristic of deep non-REM sleep rather than REM.
- 129. A.** Methemoglobin contains ferric iron, Fe^{3+} , which cannot bind oxygen normally. Oxidation also alters the oxygen affinity of remaining ferrous heme groups and can impair tissue delivery. Normal cytochrome b5 reductase systems keep methemoglobin levels low by reducing iron back to Fe^{2+} .
- 130. B.** Sepsis can induce widespread nitric oxide production and other vasodilatory inflammatory pathways, lowering systemic vascular resistance. Early distributive shock may therefore feature warm skin despite hypotension. Cardiac output may initially be preserved or elevated, although myocardial depression and other changes can occur later.
- 131. E.** The myenteric, or Auerbach, plexus lies between muscle layers and primarily regulates gastrointestinal motility, including tone and coordinated contractions. The submucosal plexus is more involved in secretion, local blood flow, and mucosal function. Both are components of the enteric nervous system.
- 132. E.** At steady state, arterial PCO_2 is approximately proportional to CO_2 production divided by alveolar ventilation. If CO_2 production is unchanged and alveolar ventilation falls, PCO_2 rises. This is the physiologic basis of respiratory acidosis from hypoventilation.
- 133. B.** For a ratio measure such as relative risk, the null value is 1.0. Because the 95% confidence interval includes 1.0, the corresponding conventional two-sided test would not reject the null at alpha 0.05. The interval also shows the range of effect sizes reasonably compatible with the data and model, not proof of no effect.

134. A. Myocardial metabolism generates local vasodilators, including adenosine, that reduce coronary resistance when oxygen demand rises. This metabolic control helps match coronary flow to cardiac work. Potent circulating vasoconstrictors can influence the vessels, but local metabolic regulation is dominant in active myocardium.

135. B. Anemia lowers oxygen content and also reduces blood viscosity. Lower viscosity decreases resistance, while tissue hypoxia promotes vasodilation and sympathetic activation, increasing cardiac output. These compensations help maintain oxygen delivery despite a reduced oxygen content per unit blood volume.

136. C. After the luteal-placental shift, the placenta produces large amounts of progesterone and becomes the major source maintaining pregnancy. Progesterone supports the endometrium and reduces uterine contractility. The early corpus luteum becomes less essential once placental production is established.

137. E. At low to moderate concentrations, estradiol exerts negative feedback on the hypothalamus and pituitary, helping regulate LH and FSH secretion. Near midcycle, sustained high estradiol reverses to positive feedback and triggers the LH surge. The feedback pattern therefore depends on concentration and timing.

138. A. For the systemic circulation, flow equals pressure gradient divided by resistance. Rearranging gives systemic vascular resistance approximately equal to (mean arterial pressure - right atrial pressure) divided by cardiac output. Because right atrial pressure is small compared with mean arterial pressure, MAP/CO is often a useful approximation.

139. A. Cardiac output equals heart rate multiplied by stroke volume. Dividing 5,000 mL/min by 100 beats/min gives a stroke volume of 50 mL/beat. This relation is useful for interpreting changes in cardiac output caused by heart rate or ventricular ejection.

140. D. Glucocorticoids accelerate type II pneumocyte maturation and surfactant production. Surfactant lowers alveolar surface tension and reduces the tendency of small alveoli to collapse, improving compliance after birth. The other choices do not explain the established benefit of antenatal corticosteroids in threatened preterm delivery.

141. E. Repeated depolarization allows calcium to accumulate in the presynaptic terminal despite reduced calcium-channel function. The higher residual calcium concentration increases acetylcholine vesicle release, producing facilitation. The rapid improvement is not due to synthesis of new postsynaptic receptors or a change in neurotransmitter identity.

142. E. Metabolic acidosis stimulates chemoreceptors and increases ventilation, lowering PCO₂ and thereby reducing the carbonic acid component of the buffer system. This respiratory compensation begins quickly. It does not fully normalize pH because the primary metabolic disturbance persists.

143. D. Standing causes gravitational pooling in dependent veins, transiently reducing central venous volume, ventricular filling, stroke volume, and arterial pressure. Reduced carotid sinus and aortic arch stretch decreases baroreceptor firing, increasing sympathetic and reducing parasympathetic output. This rapidly restores heart rate, contractility, and vascular tone.

144. D. S4 is a late-diastolic sound produced when atrial contraction forces blood into a stiff ventricle. It is associated with reduced ventricular compliance, such as from hypertrophy or ischemia. Because it depends on atrial contraction, S4 is absent in atrial fibrillation.

145. A. Surfactant lowers surface tension at the air-liquid interface. Deficiency raises the pressure required to keep small alveoli open, reduces compliance, and promotes atelectasis. The infant must therefore perform more work to inflate the lungs.

146. B. Specificity is the proportion of people without disease who test negative. Here, $855/900 = 0.95$, or 95%. High specificity means relatively few false-positive results among people who are disease free.

147. B. Professional interpreters improve accuracy, confidentiality, and informed decision-making, especially for complex or high-stakes discussions. The clinician should address the patient directly and use the interpreter as a communication bridge. Reliance on children can introduce errors, role conflicts, and inappropriate burdens.

148. C. Dystrophin is part of a structural complex that connects cortical actin to transmembrane proteins and the extracellular matrix. This linkage stabilizes the sarcolemma during contraction. Loss of dystrophin makes muscle fibers vulnerable to membrane injury and progressive degeneration.

149. B. When prevalence rises, a positive test result is more likely to represent true disease, so positive predictive value increases. Negative predictive value generally falls. Sensitivity and specificity are intrinsic test-performance characteristics that do not directly change simply because prevalence changes.

150. C. Hypernatremia generally reflects a relative water deficit and raises extracellular osmolality. Water leaves cells until osmotic equilibrium is re-established, causing cellular shrinkage. Brain cells can adapt over time by generating or accumulating intracellular osmolytes.

151. C. In early fasting, hepatic glycogenolysis provides much of the glucose needed to maintain blood concentration. As hepatic glycogen stores become depleted, gluconeogenesis from lactate, glycerol, and amino acids becomes increasingly important. Prolonged fasting also increases ketone production to spare glucose.

152. E. When oxidative phosphorylation cannot match ATP demand, glycolysis continues only if NAD⁺ is regenerated. Lactate dehydrogenase reduces pyruvate to lactate while oxidizing NADH to NAD⁺, sustaining glycolytic ATP production. This pathway has limited capacity and contributes to lactate accumulation during intense exercise.

153. D. Acute hemorrhage activates the sympathetic nervous system through the baroreflex. Alpha-1 mediated vasoconstriction reduces blood flow to skin and other less immediately essential beds, producing cool, pale, clammy skin while helping preserve pressure for heart and brain. Tachycardia and venoconstriction are parallel sympathetic responses.

154. E. A recurring handoff-related failure suggests a process problem. Standardized communication, clear responsibility, and measurement of outcomes can reduce variation and reveal whether the intervention works. Focusing only on individual blame can miss the system conditions that permit repeated errors.

155. E. Carbon dioxide readily influences extracellular and cerebrospinal fluid pH and is a potent cerebral vasodilator. Acute hypercapnia therefore increases cerebral blood flow and can raise intracranial pressure. Hypocapnia has the opposite effect and can transiently reduce cerebral blood volume.

156. D. The thick ascending limb actively reabsorbs NaCl while remaining relatively impermeable to water. This dilutes tubular fluid and helps create the hyperosmotic medullary interstitium through countercurrent multiplication. Blocking NKCC2 weakens the medullary gradient and limits the kidney's ability to concentrate urine.

157. C. Newborns rely heavily on nonshivering thermogenesis in brown fat. Sympathetic stimulation promotes lipolysis, and UCP1 allows the mitochondrial proton gradient to generate heat rather than ATP. Skeletal muscle shivering is less developed in neonates, and suppressing sympathetic tone would increase rather than prevent heat loss.

158. E. Loss of functional nicotinic receptors reduces the end-plate potential generated by each quantum of acetylcholine. Presynaptic acetylcholine release is initially normal, but the reduced postsynaptic safety factor can fail to reach threshold during repeated activity. This differs from Lambert-Eaton syndrome, which impairs presynaptic calcium-channel function and transmitter release.

159. A. Carbon monoxide binds hemoglobin with very high affinity, reducing available oxygen-binding sites. It also increases the affinity of remaining sites for oxygen, shifting the dissociation curve left and impairing unloading. Arterial PO₂ measures dissolved oxygen and may therefore remain normal despite severely reduced oxygen content.

160. B. Parietal cells secrete hydrogen into the gastric lumen using the apical H⁺/K⁺ ATPase. Proton-pump inhibitors irreversibly inhibit active pumps and markedly reduce gastric acid secretion. Basolateral chloride-bicarbonate exchange produces the postprandial alkaline tide but is not the drug's direct target.

161. D. LH stimulates theca interna cells to synthesize androgens from cholesterol. The androgens diffuse to granulosa cells, where FSH-induced aromatase converts them to estrogens. This cooperation is central to ovarian follicular steroidogenesis.

162. B. Serum lactate can rise when oxygen delivery is inadequate in some tissues or when cellular metabolism and adrenergic stimulation increase glycolytic flux. A normal arterial oxygen saturation does not guarantee adequate microcirculatory delivery or utilization. Lactate therefore reflects integrated perfusion and metabolic processes rather than arterial saturation alone.

163. B. Research participation is voluntary, and participants may withdraw consent. The team should explain any safety implications of stopping an intervention, arrange appropriate clinical care, and clarify what data may still be used under the consent and protocol. Withdrawal should not trigger punishment or loss of entitled care.

164. A. At a normal heart rate, mean arterial pressure can be approximated as diastolic pressure plus one third of pulse pressure. Pulse pressure is 45 mm Hg, so MAP is about $75 + 15 = 90$ mm Hg. The approximation changes somewhat at extreme heart rates because systole and diastole occupy different fractions of the cardiac cycle.

165. C. Bile salts are amphipathic molecules that emulsify dietary fat and form micelles containing fatty acids, monoglycerides, cholesterol, and fat-soluble vitamins. Loss of bile delivery therefore impairs absorption of long-chain lipids and vitamins A, D, E, and K. Carbohydrate and iron absorption use different mechanisms.

166. A. Activated B cells in germinal centers undergo somatic hypermutation, affinity-based selection, and class switching with T-cell help. Some become long-lived plasma cells or memory B cells, enabling a rapid, high-affinity IgG response on re-exposure. Thymic selection concerns T cells rather than the antibody memory described.

167. E. At rest, neuronal membranes are much more permeable to potassium than to sodium because of potassium leak channels. Potassium efflux leaves the cell interior relatively negative, bringing membrane voltage near the potassium equilibrium potential. The Na^+/K^+ ATPase maintains the concentration gradients but is not the dominant instantaneous conductance.

168. C. Greater contractility increases the pressure generated at a given ventricular volume and shifts the end-systolic pressure-volume relation upward and leftward. The ventricle ejects more completely, reducing end-systolic volume and increasing stroke volume and ejection fraction. Preload need not change for this immediate effect.

169. A. Tissue plasminogen activator converts plasminogen to plasmin on the fibrin surface. Plasmin cleaves fibrin and generates fibrin degradation products, including D-dimer from cross-linked fibrin. Thrombin and factor Xa favor clot formation rather than fibrinolysis.

170. C. Active muscle releases vasodilatory metabolites and endothelial signals that markedly reduce local arteriolar resistance. This functional hyperemia can override sympathetic vasoconstriction in exercising muscle while sympathetic tone preserves pressure in less active beds. The result is redistribution of cardiac output toward tissues with high metabolic demand.

171. B. Tissue hypoxia increases erythrocyte 2,3-BPG, which stabilizes deoxyhemoglobin and shifts the oxygen dissociation curve to the right. This lowers hemoglobin oxygen affinity and facilitates unloading in tissues. Erythropoietin also rises with sustained hypoxemia, but it increases red cell mass rather than producing the immediate affinity change described.

172. B. Gastrin is released from antral G cells in response to peptides, amino acids, distension, and vagal stimulation. It promotes acid secretion largely by stimulating enterochromaffin-like cell histamine release and also has trophic effects on gastric mucosa. Somatostatin inhibits gastrin and acid secretion.

173. E. Insulin signaling causes intracellular vesicles containing GLUT4 to fuse with the plasma membrane in skeletal muscle and adipocytes. This increases facilitated diffusion of glucose into those tissues. GLUT2 is important in hepatocytes and pancreatic beta cells and is not insulin dependent in the same way.

174. E. Dopamine from the hypothalamus tonically inhibits prolactin secretion. Suckling reduces dopaminergic inhibition, allowing prolactin to rise and support milk production. This is an unusual pituitary axis because the dominant hypothalamic control is inhibitory rather than stimulatory.

175. C. SGLT1 uses the sodium electrochemical gradient to absorb glucose and galactose across the apical membrane. Fructose is absorbed mainly by GLUT5. Monosaccharides exit the basolateral side largely through GLUT2.

176. B. Each optic tract carries information from the contralateral visual hemifield: ipsilateral temporal retina plus contralateral nasal retina. A right optic tract lesion therefore removes the left visual field from both eyes, producing a left homonymous hemianopia. Bitemporal loss localizes more typically to the optic chiasm.

177. E. Fick's law states that diffusion is proportional to surface area, diffusion coefficient, and partial-pressure gradient, and inversely proportional to membrane thickness. Fibrosis increases diffusion distance and therefore reduces gas transfer. Oxygen is often affected clinically before carbon dioxide because CO₂ is more soluble and diffuses more readily.

178. C. Airflow obstruction reduces the amount of air that can be forcibly exhaled in the first second more than it reduces forced vital capacity. The FEV₁/FVC ratio therefore falls. Restrictive disorders generally reduce both FEV₁ and FVC while preserving or increasing the ratio.

179. C. Beta-adrenergic receptor activation raises cAMP and activates protein kinase A, which promotes lipolytic signaling including activation of hormone-sensitive lipase and perilipin phosphorylation. Insulin opposes this process. Alpha-2 adrenergic signaling is G_i coupled and tends to inhibit cAMP formation.

180. A. A relative risk of 2.0 means the incidence proportion in the exposed group was twice that in the unexposed group during the observed period. It does not by itself establish causation or specify the absolute risk. Relative risk is directly estimable in cohort studies when incidence can be measured.

- 181. E.** Acute hypotonic hyponatremia lowers extracellular osmolality, causing water to move into cells. Brain swelling can increase intracranial pressure and cause neurologic symptoms. Over time, brain cells adapt by losing electrolytes and organic osmolytes, but rapid severe hyponatremia can be dangerous before adaptation develops.
- 182. C.** Most water-soluble nutrients absorbed from the gastrointestinal tract enter portal venous blood and pass through hepatic sinusoids before reaching the systemic circulation. This allows the liver to regulate nutrient storage, metabolism, and detoxification. Long-chain dietary lipids are a notable exception because chylomicrons initially enter lymphatics.
- 183. A.** Relaxed wakefulness with closed eyes is associated with posterior alpha activity. Opening the eyes or focusing attention suppresses alpha and produces lower-amplitude beta activity. Delta waves are most prominent in deep non-REM sleep.
- 184. E.** In the proliferative zone, chondrocytes undergo mitosis and form organized columns that contribute to longitudinal growth. They later hypertrophy, the matrix calcifies, and bone replaces the cartilage scaffold. The resting zone contains relatively quiescent chondrocytes.
- 185. C.** Motilin helps initiate the migrating motor complex during fasting. These cyclic contractions sweep residual material through the stomach and small intestine between meals. Feeding interrupts the fasting pattern and replaces it with meal-related motility.
- 186. B.** Beta-1 receptors are Gs coupled. Increased cAMP directly enhances HCN funny current and also promotes calcium-channel activity, steepening phase 4 depolarization in nodal cells. Gi-coupled muscarinic M2 signaling has the opposite effect and slows the heart rate.
- 187. D.** The tuberculin reaction is a delayed type IV hypersensitivity response. Previously sensitized Th1 cells recognize antigen and release cytokines that recruit and activate macrophages, producing induration over 48 to 72 hours. Immediate IgE reactions occur much sooner and use mast cells rather than a delayed T-cell response.
- 188. B.** Presynaptic depolarization opens voltage-gated calcium channels. Calcium enters the terminal and binds vesicle-associated release machinery, triggering exocytosis into the synaptic cleft. Sodium and potassium currents propagate the action potential, but calcium is the immediate trigger for transmitter release.
- 189. A.** SERCA pumps use ATP to transport calcium from the cytosol back into the sarcoplasmic reticulum. As cytosolic calcium falls, calcium dissociates from troponin C and tropomyosin again blocks actin-myosin interaction. Ryanodine receptor closure limits further calcium release but does not itself perform the active reuptake step.
- 190. B.** Albumin is the major contributor to plasma colloid oncotic pressure. When albumin falls substantially, the force retaining water within capillaries is reduced, increasing net filtration into the

interstitium. Lymphatic drainage can compensate only to a point, after which clinically apparent edema develops.

191. A. Because PAH is both filtered and avidly secreted, nearly all PAH delivered in the renal plasma is removed during a single pass when transporters are not saturated. PAH clearance therefore approximates effective renal plasma flow. Renal blood flow can then be estimated by correcting plasma flow for hematocrit.

192. B. Shared decision-making combines patient goals and concerns with accurate evidence about benefits and harms. The clinician should explain why antibiotics are not indicated, address the reason for the request, and offer a concrete alternative plan. Prescribing ineffective therapy exposes the patient and community to avoidable harms.

193. C. The flexor withdrawal reflex is organized within the spinal cord and uses interneurons to activate ipsilateral flexors while inhibiting extensors. It can occur before ascending nociceptive signals reach conscious perception. The stretch reflex is monosynaptic and serves different mechanical functions.

194. E. Terminal complement components C5b through C9 assemble the membrane attack complex, which is particularly important for killing *Neisseria* species. C3b-mediated opsonization and upstream classical-pathway functions can remain intact. The characteristic susceptibility therefore reflects defective terminal lytic activity.

195. C. Phosphate is required for ATP, creatine phosphate, and many phosphorylated metabolic intermediates. Severe depletion can impair cellular energy transfer, producing skeletal-muscle weakness and other systemic manifestations. The defect is energetic rather than a direct loss of hemoglobin oxygen binding.

196. C. Lead-time bias occurs when earlier diagnosis increases the measured interval from diagnosis to death without changing the time of death. Screening therefore seems to prolong survival even when mortality is unchanged. Disease-specific mortality rather than postdiagnosis survival is often more informative when evaluating screening benefit.

197. D. Higher H^+ , CO_2 , and temperature reduce hemoglobin oxygen affinity through the Bohr effect and related allosteric changes. The curve shifts right, allowing more oxygen to be released at a given tissue PO_2 . A left shift would impede unloading and is produced by the opposite acid-base and temperature changes.

198. C. Calcium released from the sarcoplasmic reticulum binds troponin C. This shifts the troponin-tropomyosin complex away from myosin-binding sites on actin, permitting cross-bridge formation. Myosin light-chain kinase is central to smooth-muscle contraction rather than the troponin-based skeletal-muscle mechanism.

- 199. C.** Exercise raises cardiac output substantially while local vasodilation lowers total systemic vascular resistance. The net effect is usually a modest increase in mean arterial pressure, with a larger rise in systolic pressure and relatively little change or a slight fall in diastolic pressure. The arterial baroreflex is reset rather than simply switched off.
- 200. B.** Nearly all nucleated cells express MHC class I and can present intracellular peptides to CD8 cytotoxic T cells. CD8 stabilizes the interaction between the T-cell receptor and MHC class I. MHC class II is mainly used by professional antigen-presenting cells to activate CD4 T cells.
- 201. A.** The vestibulo-ocular reflex drives the eyes opposite the direction of head rotation to stabilize the retinal image. A leftward head turn therefore produces a compensatory rightward slow eye movement. The reflex is rapid and does not require conscious visual processing.
- 202. D.** FSH acts on Sertoli cells, promoting functions that support developing germ cells, including production of androgen-binding protein and inhibin B. LH acts on Leydig cells to generate testosterone. High intratesticular testosterone plus Sertoli-cell support are both required for normal spermatogenesis.
- 203. E.** In adults the skull is essentially rigid, so the total intracranial volume of brain, blood, and cerebrospinal fluid is constrained. Early compensation for an expanding mass includes displacement of cerebrospinal fluid and venous blood. Once compensatory reserve is exhausted, small additional volume increases can cause a steep rise in intracranial pressure.
- 204. B.** A decisionally capable adult may refuse even potentially life-saving treatment. The clinician should confirm capacity and informed understanding, document the discussion, and respect the refusal while continuing to provide alternatives and supportive care. A risky or unconventional choice does not by itself demonstrate incapacity.
- 205. E.** Glucose metabolism raises the beta-cell ATP/ADP ratio, closing ATP-sensitive potassium channels. Membrane depolarization opens voltage-gated calcium channels, and calcium triggers insulin granule exocytosis. This coupling links nutrient metabolism to hormone secretion.
- 206. B.** Thrombin cleaves fibrinogen to fibrin monomers, which polymerize and are later cross-linked by factor XIIIa. Thrombin also activates platelets and several upstream coagulation factors. Plasminogen participates in fibrinolysis, whereas antithrombin and protein C are anticoagulant regulators.
- 207. C.** The cephalic phase is triggered by sight, smell, taste, and thought of food and is mediated largely by vagal input. Vagal signaling stimulates parietal cells directly and promotes gastrin and histamine release. The gastric phase begins when food enters and distends the stomach.
- 208. D.** Upper motor neuron lesions remove descending control that normally modulates spinal reflex excitability. Over time this produces increased stretch reflexes, spasticity, and pathologic reflexes such as Babinski signs. Lower motor neuron or neuromuscular junction lesions instead tend to cause weakness with reduced tone and reflexes.

209. B. Interferon-gamma is the major Th1 cytokine that drives classical macrophage activation and enhances killing of intracellular microbes. IL-4 and IL-5 favor Th2 responses, whereas IL-10 and TGF-beta generally restrain inflammatory immune activation. Deficient interferon-gamma signaling therefore compromises control of organisms such as mycobacteria.

210. E. Puberty is initiated by reactivation of pulsatile GnRH secretion, initially with prominent nocturnal pulses. Pulsatile GnRH stimulates pituitary LH and FSH, which drive gonadal steroidogenesis and gametogenesis. Continuous GnRH instead downregulates pituitary GnRH receptors after an initial stimulatory phase.

211. C. Patients should be informed of clinically significant errors that affect their care, even when harm is not yet apparent. Disclosure should be factual, timely, and include what is known, what will be done to monitor or mitigate harm, and appropriate acknowledgment or apology. Concealment undermines trust and patient autonomy.

212. C. Nodal cells lack the fast sodium-dependent phase 0 seen in ventricular myocytes. Their depolarizing upstroke depends mainly on L-type calcium influx, so calcium-channel blockade slows nodal conduction. This is especially important in the AV node and explains the use of non-dihydropyridine calcium-channel blockers for some supraventricular tachyarrhythmias.

213. B. Sustained high estradiol from the mature dominant follicle produces positive feedback on the hypothalamic-pituitary axis. This generates the midcycle LH surge, which triggers ovulation and luteinization. Most of the rest of the cycle, estradiol participates in negative rather than positive feedback.

214. D. Aspirin irreversibly acetylates platelet cyclooxygenase, reducing thromboxane A2 synthesis for the life of the platelet. Thromboxane A2 promotes platelet activation, aggregation, and vasoconstriction. ADP and von Willebrand factor remain available through separate pathways, while endothelial cells can resynthesize cyclooxygenase and continue making prostacyclin.

215. B. 5-alpha-reductase converts testosterone to dihydrotestosterone, a more potent androgen in several target tissues. DHT is important for development and maintenance of the prostate and external male genital structures. Aromatase, not 5-alpha-reductase, converts testosterone to estradiol.

216. C. The thin descending limb is highly water permeable, so tubular fluid becomes concentrated as it descends into the hyperosmotic medulla. The thick ascending limb reabsorbs NaCl but is essentially impermeable to water, which helps dilute tubular fluid and build the medullary gradient.

217. A. Muscle spindles lie in parallel with extrafusal fibers and detect muscle length and rate of change in length. Ia afferents make a monosynaptic excitatory connection with alpha motor neurons supplying the same muscle. Golgi tendon organs lie in series with muscle and primarily monitor tension.

218. E. Isotonic saline remains mainly in the extracellular compartment because sodium and chloride do not freely cross cell membranes. Within extracellular fluid, distribution follows the approximate plasma-

to-interstitial volume ratio, so about one quarter remains intravascular and three quarters enters interstitial fluid. Intracellular volume changes little because extracellular osmolality is essentially unchanged.

219. E. Heat acclimatization increases the capacity to sweat while improving sodium conservation. Aldosterone increases sodium reabsorption in sweat ducts, so acclimatized sweat becomes more dilute in sodium chloride. This reduces salt loss during sustained heat exposure.

220. A. Whole-muscle force is graded by motor-unit recruitment and by the firing rate of active motor neurons. Increasing stimulus frequency allows temporal summation and can produce tetanic force. Gamma motor neurons adjust spindle sensitivity but do not substitute for alpha motor-unit recruitment in producing force.

221. C. After birth, arterial oxygen tension rises and placental prostaglandin delivery falls, promoting ductal smooth muscle constriction. Functional closure generally occurs within hours in healthy term infants. Persistently low oxygen tension and high prostaglandin activity favor ductal patency rather than closure.

222. B. Hemoglobin F binds 2,3-BPG less avidly than adult hemoglobin, giving it a higher oxygen affinity and a left-shifted oxygen dissociation curve. This allows fetal blood to load oxygen efficiently at the relatively low PO₂ of placental blood. Carbon dioxide transfer from fetus to mother also supports oxygen transfer but does not replace the affinity advantage of hemoglobin F.

223. B. Insulin promotes fat storage by stimulating adipose lipoprotein lipase, which releases fatty acids from circulating triglyceride-rich lipoproteins for uptake. It simultaneously inhibits hormone-sensitive lipase, reducing mobilization of stored triglyceride. These actions favor energy storage in the fed state.

224. E. Confidentiality can be limited when there is a credible, serious threat to an identifiable person, although exact legal duties vary by jurisdiction. The clinician should perform a careful risk assessment and use appropriate protective and emergency resources. The goal is safety while limiting disclosure to what is necessary.

225. B. Syncytiotrophoblasts secrete hCG, which acts through the LH receptor to rescue and maintain the corpus luteum in early pregnancy. The corpus luteum continues progesterone production until placental steroidogenesis is sufficient. hCG therefore supports the endometrium during the early weeks of gestation.

226. A. Cold activates sympathetic vasoconstrictor pathways that reduce skin blood flow, limiting heat transfer from the body core to the environment. Arteriovenous anastomoses in acral skin are particularly important for thermoregulation. Sweating and active vasodilation are heat-dissipating responses used during heat stress.

227. D. Most bile salts are actively reabsorbed in the terminal ileum and returned to the liver through the portal circulation. Ileal resection increases fecal bile-salt loss and can allow bile acids to enter the colon,

where they stimulate secretion and diarrhea. Larger losses can also reduce the bile-salt pool enough to impair fat absorption.

228. D. The rapid upstroke of ventricular and Purkinje action potentials is phase 0 and depends on fast voltage-gated sodium channels. Significant depolarization from hyperkalemia can inactivate these channels and slow conduction. Nodal phase 0 depends mainly on calcium influx rather than fast sodium current.

229. A. A highly sensitive test has few false negatives, so a negative result can help rule out disease when applied appropriately. This is the basis of the SnNout mnemonic. Confirmation of a positive screening result may require a more specific test depending on the clinical context.

230. B. GABA-A receptors are ligand-gated chloride channels. Increasing their activity raises chloride conductance, which tends to hyperpolarize or shunt excitatory currents and makes action-potential generation less likely. Benzodiazepines increase the frequency of channel opening in the presence of GABA.

231. D. Near misses provide valuable information about latent system hazards and weak safeguards. Reporting and analyzing them can identify opportunities to redesign processes before a patient is injured. A strong safety culture encourages reporting and distinguishes human error from reckless behavior.

232. D. The zona fasciculata produces glucocorticoids, primarily cortisol, under ACTH regulation. The zona glomerulosa produces aldosterone and is regulated mainly by angiotensin II and potassium. The adrenal medulla produces catecholamines rather than steroid hormones.

233. C. Process mapping visually describes the sequence of work and can reveal bottlenecks, duplications, unclear ownership, and risky handoffs. It is a common starting point for quality-improvement interventions. It differs from epidemiologic or trial-analysis methods designed primarily to estimate associations or treatment effects.

234. B. Vagal signaling contributes strongly to cephalic-phase gastric secretion and receptive relaxation of the proximal stomach. The enteric nervous system can still generate many local reflexes and motility patterns without vagal input. Pancreatic, biliary, and absorptive functions are influenced by multiple hormonal and local mechanisms.

235. C. An empathic response recognizes the emotion and its meaning without dismissing or prematurely reassuring. Inviting the patient to elaborate helps clarify values and concerns that may affect decisions. False reassurance or comparison with other patients can shut down communication.

236. A. When a patient lacks capacity and delay would threaten life or major function, clinicians may provide emergency treatment under the presumption that a reasonable person would consent to necessary care. Efforts to identify preferences and surrogates should continue, but urgent treatment should not be withheld solely because formal consent is unavailable.

- 237. A.** S1 occurs when ventricular pressure rises above atrial pressure at the onset of systole, closing the atrioventricular valves. S2 is produced by closure of the semilunar valves at the end of systole. Rapid ventricular filling can generate an S3 under some physiologic or pathologic conditions.
- 238. B.** An eccentric contraction occurs when an activated muscle is lengthened by an external load, as during controlled lowering of a weight. Eccentric contractions can generate high force with relatively low energy cost. Concentric contractions shorten the active muscle, whereas isometric contractions generate force without overall length change.
- 239. B.** Eccrine sweat glands are unusual sympathetic effectors because their postganglionic fibers release acetylcholine onto muscarinic receptors. Sweating supports evaporative heat loss. Most other sympathetic postganglionic fibers release norepinephrine rather than acetylcholine.
- 240. C.** Chemokine signaling increases the affinity of leukocyte integrins, allowing firm binding to ICAM-1 and related endothelial ligands. Selectins mediate the earlier rolling step, not firm adhesion. The platelet and complement interactions listed are important in other physiologic contexts but do not drive neutrophil arrest on endothelium.
- 241. C.** Fibrosis increases elastic stiffness and decreases lung compliance. Greater transpulmonary pressure is required to achieve a given lung volume, and vital capacity is often reduced. This contrasts with emphysema, in which compliance is increased because elastic recoil is lost.
- 242. E.** Chronic hypercapnia stimulates the kidneys to increase H^+ secretion, bicarbonate reclamation and generation, and ammonium excretion. Plasma bicarbonate rises and pH moves toward normal, although the primary elevation in PCO_2 persists. Renal compensation does not directly normalize ventilation or arterial PCO_2 .
- 243. C.** Venoconstriction decreases venous capacitance and shifts blood from the unstressed to the stressed volume. Mean systemic filling pressure rises, increasing the pressure gradient for venous return at a given right atrial pressure. The resulting increase in preload can raise stroke volume through the Frank-Starling mechanism.
- 244. A.** LH binds receptors on Leydig cells and stimulates testosterone synthesis. FSH acts mainly on Sertoli cells to support spermatogenesis and produce inhibin B. Testosterone then exerts negative feedback at the hypothalamus and pituitary.
- 245. D.** Health outcomes can be shaped by structural and social barriers such as transportation, work schedules, language, and access to services. Recognizing and addressing the specific barrier can improve equitable access while preserving the same clinical standards. Labeling the problem as simple nonadherence misses a modifiable determinant of care.
- 246. B.** Nigrostriatal dopamine normally promotes movement by stimulating D1 receptors in the direct pathway and inhibiting D2 receptors in the indirect pathway. Dopamine loss therefore reduces

thalamocortical excitation and makes movement initiation more difficult. The deficit reflects altered basal ganglia gating, not direct destruction of lower motor neurons.

247. B. Elevated extracellular potassium directly depolarizes zona glomerulosa cells and increases aldosterone release. Aldosterone enhances distal sodium reabsorption and potassium secretion, promoting renal potassium excretion. This feedback helps defend extracellular potassium concentration.

248. C. Lymphatics return filtered fluid and interstitial proteins to the circulation. When lymphatic drainage is obstructed, protein accumulates in the interstitial space, raising interstitial oncotic pressure and favoring persistent edema. This differs from edema caused primarily by increased capillary hydrostatic pressure or reduced plasma oncotic pressure.

249. B. Acute water loading lowers plasma osmolality and suppresses hypothalamic vasopressin release. Collecting ducts become less water permeable, allowing excretion of free water in a dilute urine. Thirst is also suppressed, helping restore osmotic balance.

250. E. Suckling activates a neuroendocrine reflex that releases oxytocin from the posterior pituitary. Oxytocin contracts mammary myoepithelial cells and ejects milk. Prolactin from the anterior pituitary primarily supports milk synthesis rather than the immediate let-down response.

251. D. An arteriovenous fistula provides a low-resistance pathway from artery to vein, lowering total systemic vascular resistance. Venous return increases, and cardiac output rises through increased preload and reflex sympathetic effects. Large chronic shunts can eventually produce high-output heart failure.

252. D. Proximal tubular cells metabolize glutamine to generate ammonium and new bicarbonate. Ammonium is excreted in urine, allowing net acid excretion, while bicarbonate is returned to blood. This pathway is strongly upregulated during chronic metabolic acidosis.

253. A. When a patient's preferences are known, the surrogate should apply substituted judgment and choose as the patient would have chosen. Best-interest reasoning is used when the patient's values and preferences cannot be reasonably inferred. The surrogate's own values should not replace those of the patient.

254. A. Vitamin A is required to form 11-cis-retinal, the chromophore used in rhodopsin and other visual pigments. Deficiency most prominently impairs rod function and dark adaptation, causing night blindness. The defect is in photopigment regeneration rather than ocular fluid production or auditory transduction.

255. B. Pancreatic lipase hydrolyzes triglycerides, producing free fatty acids and monoglycerides that can be incorporated into micelles. Trypsin, elastase, and carboxypeptidase digest proteins, while amylase digests starch. Bile salts assist lipid digestion by emulsification and micelle formation but are not digestive enzymes.

256. C. Extracellular volume expansion suppresses renin-angiotensin-aldosterone and renal sympathetic activity and favors pressure natriuresis. Peritubular Starling forces also become less favorable for proximal reabsorption. The net effect is increased renal sodium and water excretion until volume returns toward baseline.

257. A. Medication cost directly affects whether a treatment plan is feasible. Clinicians should invite discussion of affordability, consider equally effective lower-cost options, simplify regimens when possible, and connect patients with assistance resources. Incorporating cost into shared decision-making improves the chance that an evidence-based plan can actually be followed.

258. C. Low circulating thyroid hormone removes negative feedback at the pituitary and hypothalamus, increasing TSH and TRH. In primary hypothyroidism, TSH is therefore typically elevated. In secondary hypothyroidism due to pituitary disease, TSH is low or inappropriately normal.

259. C. Stroke volume is $120 - 48 = 72$ mL. Ejection fraction equals stroke volume divided by end-diastolic volume, so $72/120 = 0.60$, or 60%. Ejection fraction reflects the fraction of end-diastolic volume ejected per beat, not the absolute stroke volume alone.

260. B. Filtration fraction equals GFR divided by renal plasma flow. Here, $120/600 = 0.20$, or 20%. It represents the fraction of plasma entering the kidneys that is filtered across the glomerular capillaries.

261. D. Vasopressin binds V2 receptors on principal cells, activates Gs and cAMP signaling, and promotes insertion of aquaporin-2 water channels into the apical membrane. Water then moves down the medullary osmotic gradient and exits through basolateral aquaporins. This concentrates urine and conserves body water.

262. C. Persistently open voltage-gated potassium channels maintain outward potassium current after repolarization, producing a deeper or longer afterhyperpolarization. This keeps membrane voltage farther from threshold and can reduce short-term excitability. The depolarizing upstroke still depends primarily on sodium current.

263. D. Dynamic exercise increases sympathetic activity, heart rate, contractility, venous return, and cardiac output. Local metabolic vasodilation directs a large fraction of flow to active muscle, while vasoconstriction in some other vascular beds helps maintain pressure. The skeletal-muscle pump also supports venous return.

264. C. Hemophilia A is caused by factor VIII deficiency. Factor VIIIa serves as a cofactor for factor IXa in the intrinsic tenase complex, which activates factor X. Because the defect is in the intrinsic pathway, the aPTT is prolonged while the PT is typically normal.

265. A. Moderate efferent constriction raises resistance to outflow from the glomerulus, increasing glomerular capillary hydrostatic pressure while reducing renal plasma flow. GFR may be maintained or increased, so filtration fraction rises. Severe constriction can eventually lower GFR because renal flow falls markedly and glomerular oncotic pressure rises.

266. D. Persistent hyperventilation lowers PCO₂ and raises pH. The kidneys compensate by reducing bicarbonate reabsorption and increasing bicarbonate excretion, bringing pH closer to normal. This reduces inhibitory alkalemic effects on ventilation and supports ongoing acclimatization.

267. C. For a freely filtered substance that undergoes no tubular reabsorption or secretion, the amount excreted equals the amount filtered. Its clearance therefore equals GFR. Inulin approximates this ideal behavior and is the classic reference marker for measuring filtration rate.

268. A. Heat stress activates skin vasodilation and sweating. Increased cutaneous blood flow transfers core heat to the skin, while evaporation of sweat can remove large amounts of heat even when ambient temperature approaches body temperature. Vasoconstriction and shivering are cold-defense mechanisms.

269. C. Emphysema destroys elastic tissue, making the lungs more compliant but reducing elastic recoil. Small airways are less supported and can collapse during expiration, causing air trapping and increased residual volume. Alveolar wall destruction also reduces gas-exchange surface area.

270. E. Calcitonin binds receptors on osteoclasts and acutely inhibits bone resorption. Its role in long-term human calcium homeostasis is limited compared with PTH and vitamin D, but pharmacologic doses can lower calcium partly through this antiresorptive effect. It does not stimulate PTH or RANK ligand.

271. B. Specificity measures the ability to correctly identify people without disease. A highly specific test generates few false positives, so a positive result can strongly support the diagnosis in the right setting. This is the basis of the SpPin mnemonic.

272. A. Low insulin and counterregulatory hormones increase hormone-sensitive lipase activity in adipocytes, releasing free fatty acids and glycerol. Fatty acids provide fuel to many tissues and support hepatic ketogenesis. Insulin normally suppresses this mobilization pathway.

273. D. Number needed to treat is the reciprocal of the absolute risk reduction expressed as a proportion. An absolute reduction of 0.05 gives $1/0.05 = 20$. Thus 20 patients would need treatment, on average, to prevent one additional adverse event over the study period.

274. A. ATP binding to myosin reduces its affinity for actin and permits cross-bridge detachment. Without ATP, actin-myosin complexes remain locked, as occurs after death in rigor mortis. ATP hydrolysis subsequently re-cocks the myosin head for another power stroke.

275. E. Fructose enters enterocytes through facilitated diffusion mediated mainly by GLUT5. Unlike glucose and galactose uptake through SGLT1, this process is not directly sodium coupled. Fructose then exits across the basolateral membrane through transporters including GLUT2.

276. A. Temporal summation occurs when postsynaptic potentials from the same input arrive closely enough in time that they overlap and add. Spatial summation involves simultaneous inputs from

different synapses. The resulting membrane depolarization can reach threshold at the axon initial segment.

277. D. Human-subject research generally requires independent ethical review to assess risks, benefits, scientific validity, and participant protections. Participants also require valid informed consent unless a narrowly defined and approved exception applies. Research may involve uncertainty and does not guarantee direct personal benefit.

278. A. In a true right-to-left shunt, part of the cardiac output reaches systemic blood without contacting ventilated alveoli. Raising inspired oxygen improves oxygenation of ventilated units but cannot directly oxygenate the shunted fraction. This makes shunt hypoxemia less responsive to supplemental oxygen than many V/Q mismatches.

279. D. Prolonged exogenous glucocorticoids suppress CRH and ACTH. Reduced trophic ACTH causes atrophy of the cortisol-producing adrenal cortex, so abrupt withdrawal can leave endogenous cortisol production inadequate. Gradual tapering allows the hypothalamic-pituitary-adrenal axis time to recover.

280. C. Shared decision-making does not require every patient to make choices without guidance. Some patients want a clear clinician recommendation, which can be ethically appropriate when based on the patient's goals and informed preferences. The clinician should still explain reasonable options and preserve the patient's authority to accept or reject the recommendation.