

COMPREHENSIVE MOCK EXAM 5

Supplemental to: Physiology Board Review 2026-2027

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*USMLE Step 1 (NBME/FSMB) — MEDREV physiology-centered simulation with
280 A-E single-best-answer questions, weighted to the approved Step 1 system
allocation*

Board-Review Questions

1. A pure tone of 500 Hz reaches the cochlea. Which property of the basilar membrane is fundamental to encoding sound frequency?
- A. Different frequencies produce maximal displacement at different longitudinal locations because stiffness varies along the cochlea
 - B. All audible frequencies maximally displace the same cochlear location and are distinguished only by sound intensity
 - C. The middle ear converts every frequency to a common mechanical frequency before cochlear transduction
 - D. The apex is stiffest and therefore always responds best to the highest-frequency sounds
 - E. Frequency is encoded only by the number of outer hair cells and not by basilar-membrane mechanics
2. TSH binds its receptor on a thyroid follicular cell in a healthy 26-year-old. Which overall response is expected?
- A. Increased iodide uptake, thyroglobulin processing, and thyroid hormone synthesis and release
 - B. Suppression of iodide uptake and inhibition of thyroglobulin endocytosis
 - C. Reduced expression of thyroid peroxidase and decreased organification of iodide
 - D. Exclusive stimulation of calcitonin secretion from parafollicular C cells
 - E. Direct conversion of circulating T3 to T4 in peripheral tissues as the only thyroid response
3. A patient with fluctuating delirium is asked to consent to a nonurgent invasive test. At the moment, the patient cannot explain the purpose or consequences of the procedure. What is the best next step?
- A. Allow any available visitor to consent because formal surrogate priority is irrelevant
 - B. Assume permanent incapacity because any episode of delirium eliminates future decision-making ability
 - C. Proceed on the basis of a nurse's signature because the test is medically indicated
 - D. Ask the patient to repeat the clinician's preferred choice and treat repetition as proof of capacity

E. Treat reversible causes and reassess decision-making capacity; if the decision cannot wait, use the legally appropriate surrogate

4. A patient with limited English proficiency needs counseling before a complex autonomic-function test. The patient's adult child offers to translate. What is the best routine approach?

A. Speak only to the interpreter and avoid eye contact with the patient so technical details are not confusing

B. Use the adult child as the default interpreter because family members are always more accurate than professionals

C. Ask the patient to sign the consent form first and arrange interpretation only if complications occur

D. Use a qualified medical interpreter and speak directly to the patient while preserving the patient's role in decision-making

E. Proceed without interpretation if the clinician uses short sentences and demonstrates the equipment

5. A healthy 70-year-old has been fasting overnight. Which hepatic effect of glucagon helps maintain plasma glucose?

A. Glucagon is the principal hormone driving GLUT4 translocation in skeletal muscle

B. Glucagon promotes hepatic glycogen synthesis and suppresses gluconeogenesis during fasting

C. Glucagon promotes glycogenolysis and gluconeogenesis while opposing hepatic glycolysis

D. Glucagon acts mainly on adipocyte insulin receptors rather than hepatic G-protein-coupled receptors

E. Glucagon suppresses lipolysis and ketogenesis whenever insulin levels are low

6. A 34-year-old develops extracellular hyperkalemia acutely. Which transcellular mechanism can move potassium into cells within minutes?

A. Aldosterone immediately moves most extracellular potassium into skeletal muscle without requiring renal excretion

- B.** Alpha-adrenergic stimulation is the principal mechanism driving potassium into cells during hyperkalemia
- C.** Metabolic acidosis from mineral acid reliably drives potassium into cells through hydrogen-potassium exchange
- D.** Hypertonicity always shifts potassium into cells and is therefore used to treat hyperkalemia
- E.** Insulin stimulates cellular potassium uptake in part by increasing Na^+/K^+ ATPase activity

7. A patient requests an unnecessary physiologic test because a relative had a serious illness. The clinician believes the test is more likely to cause harm through false positives than to help. What is the best response?

- A.** Tell the patient the concern is irrational and end the visit if the patient persists, under the physiologic conditions described
- B.** Refuse the request without discussion because explaining probabilities will only increase anxiety
- C.** Order the test but document that responsibility for all downstream harms belongs only to the patient
- D.** Order any requested test because patient autonomy requires clinicians to provide interventions regardless of net harm
- E.** Explore the patient's concern, explain the expected benefits and harms, and offer an evidence-aligned alternative plan rather than ordering the test solely to reduce anxiety

8. A febrile 38-year-old has a hypothalamic temperature set point that has been raised by inflammatory mediators. Why can the patient feel cold and shiver while core temperature is already above normal?

- A.** Sweating is the dominant response while temperature is rising toward a higher set point
- B.** Core temperature is below the newly elevated set point, so heat-conserving and heat-producing responses are activated
- C.** Peripheral thermoreceptors suppress all autonomic thermoregulation once core temperature exceeds 37 C
- D.** The hypothalamic set point is lowered during fever, making normal temperature feel excessively warm
- E.** Shivering occurs only when core temperature is below 35 C and cannot occur during fever

9. A diagnostic threshold for a continuous physiologic test is moved lower so more people are labeled positive. What tradeoff is generally expected?

- A.** Specificity is unchanged because false-positive results are independent of the cutoff
- B.** Sensitivity tends to increase while specificity tends to decrease
- C.** Sensitivity is unchanged because thresholds influence only predictive values
- D.** Sensitivity decreases while specificity increases because more tests are called positive
- E.** Sensitivity and specificity both necessarily increase because more disease is detected

10. A beta-1 agonist increases left ventricular contractility in a 50-year-old while preload and afterload are held constant. Which pressure-volume change is expected?

- A.** End-diastolic volume must increase before any change in stroke volume can occur
- B.** Stroke volume decreases because beta-1 stimulation raises calcium entry into myocytes
- C.** The end-systolic pressure-volume relation becomes flatter as inotropy increases
- D.** End-systolic volume increases because stronger contraction traps more blood in the ventricle
- E.** End-systolic volume decreases and stroke volume increases as the end-systolic pressure-volume relation becomes steeper

11. Fat and amino acids enter the duodenum of a healthy 24-year-old. Which response is most characteristic of cholecystokinin?

- A.** It relaxes the gallbladder and contracts the sphincter of Oddi to reduce bile delivery
- B.** It is released mainly by antral G cells in response to low gastric pH
- C.** It suppresses pancreatic enzyme secretion so bicarbonate can neutralize acid first
- D.** It primarily stimulates gastric acid secretion and accelerates gastric emptying of fat
- E.** It stimulates pancreatic acinar enzyme secretion and gallbladder contraction while slowing gastric emptying

12. Ionized calcium falls slightly in a healthy 36-year-old. Which integrated response is most appropriate?

- A.** Calcitonin becomes the dominant chronic regulator and raises serum calcium by increasing bone resorption
- B.** PTH rises, increasing renal calcium retention, phosphate excretion, and calcitriol production
- C.** PTH increases proximal phosphate reabsorption so calcium and phosphate rise together
- D.** PTH suppresses renal 1-alpha-hydroxylase to limit intestinal calcium absorption
- E.** PTH falls, increasing urinary calcium loss and reducing calcitriol production

13. A pure tone of 2000 Hz reaches the cochlea. Which property of the basilar membrane is fundamental to encoding sound frequency?

- A.** The middle ear converts every frequency to a common mechanical frequency before cochlear transduction
- B.** All audible frequencies maximally displace the same cochlear location and are distinguished only by sound intensity
- C.** The apex is stiffest and therefore always responds best to the highest-frequency sounds
- D.** Frequency is encoded only by the number of outer hair cells and not by basilar-membrane mechanics
- E.** Different frequencies produce maximal displacement at different longitudinal locations because stiffness varies along the cochlea

14. A 30-year-old has normal kidney function. Which property of the thick ascending limb is essential for generating the corticomedullary osmotic gradient?

- A.** It reabsorbs urea as its only major contribution to medullary hypertonicity
- B.** It secretes NaCl into the medulla and reabsorbs water to concentrate tubular fluid
- C.** It lacks active solute transport and functions only as a passive conduit to the distal nephron
- D.** It is highly permeable to water and therefore equilibrates completely with the hypertonic medulla
- E.** It actively reabsorbs NaCl while remaining relatively impermeable to water, diluting tubular fluid

- 15.** An arteriole constricts so that its radius becomes 0.7 times baseline while viscosity and length remain unchanged. According to Poiseuille behavior, resistance changes by approximately what factor?
- A.** It is unchanged because vessel radius affects velocity but not resistance
 - B.** It increases to about 1.4 times baseline because resistance varies only inversely with radius
 - C.** It increases only in direct proportion to viscosity, which was held constant here
 - D.** It increases to about 4.2 times baseline because resistance varies inversely with the fourth power of radius
 - E.** It decreases to about 0.24 times baseline because a smaller radius lowers wall shear
- 16.** A rigor-like state develops in an experimental skeletal-muscle preparation after ATP is abruptly depleted. Which step of the cross-bridge cycle fails most directly?
- A.** Calcium cannot bind troponin C because that binding requires direct ATP hydrolysis by troponin
 - B.** Myosin cannot bind actin because ATP is the structural receptor for the thin filament
 - C.** The power stroke cannot occur because phosphate release requires ATP binding to actin
 - D.** Myosin cannot detach from actin because ATP binding is required for cross-bridge release
 - E.** Tropomyosin cannot cover actin because ATP depletion forces calcium out of the cytosol immediately
- 17.** A clinician taps the patellar tendon of a relaxed 61-year-old, producing a brief muscle stretch and contraction. Which spinal circuit is the essential core of this reflex?
- A.** A sympathetic preganglionic neuron provides the efferent limb to the skeletal muscle
 - B.** A group Ia afferent makes an excitatory monosynaptic connection with the homonymous alpha motor neuron
 - C.** A C-fiber nociceptor directly excites the contralateral alpha motor neuron without interneurons
 - D.** A corticospinal neuron is required to complete the reflex arc at the spinal level
 - E.** A group Ib afferent makes a direct inhibitory monosynaptic connection with the homonymous alpha motor neuron

18. A muscle biopsy from an endurance-trained 45-year-old shows fibers adapted for prolonged submaximal activity. Which feature is most characteristic of type I skeletal-muscle fibers?

- A.** Exclusive dependence on phosphocreatine with little capacity for fatty-acid oxidation
- B.** High mitochondrial density, abundant myoglobin, and relatively fatigue-resistant oxidative metabolism
- C.** Absence of capillaries because oxygen delivery is unnecessary for slow fibers
- D.** Low mitochondrial density with predominant rapid glycolysis and very high fatigability
- E.** The largest motor neurons and highest shortening velocity of all fiber types

19. A healthy 18-year-old swallows a bolus of food. Which coordinated response allows the bolus to enter the stomach?

- A.** The lower esophageal sphincter contracts strongly throughout swallowing to prevent any gastric entry
- B.** Sympathetic activation produces the dominant peristaltic wave and relaxes all gastrointestinal sphincters
- C.** Gastrin abruptly inhibits esophageal smooth muscle and is the primary trigger for swallowing peristalsis
- D.** Primary peristalsis propels the bolus while the lower esophageal sphincter undergoes neurally mediated relaxation
- E.** The upper esophageal sphincter remains closed while gravity alone carries the bolus to the stomach

20. A healthy 70-kg adult receives 1 L of isotonic saline intravenously. After equilibration and before renal excretion, where does most of the infused volume distribute?

- A.** Equally between intracellular and extracellular compartments because saline crosses cell membranes freely
- B.** Only in plasma because isotonic saline cannot leave the vascular compartment
- C.** Within the extracellular fluid, with roughly three quarters in interstitial fluid and one quarter in plasma
- D.** Almost entirely inside cells because sodium is rapidly transported into the intracellular space

E. Primarily into total body water with a fall in extracellular sodium concentration similar to pure water

21. A resident appears intoxicated before performing an invasive test and has impaired speech and coordination. What is the immediate professional priority?

A. Protect patients by removing the impaired clinician from clinical duties and activating appropriate supervisory or institutional processes

B. Wait until objective patient harm occurs before notifying a supervisor or safety process

C. Avoid reporting the concern because collegial loyalty takes priority over patient safety

D. Confront the resident publicly in front of patients before taking any safety action

E. Allow the resident to proceed if a colleague informally watches the first few minutes of the procedure

22. In a randomized trial, an adverse physiologic outcome occurs in 20% of the control group and 10% of the treatment group. What is the number needed to treat to prevent one outcome over the study period?

A. 10, because the absolute risk reduction is 0.10 and NNT is its reciprocal

B. 5, because the control event rate alone determines NNT

C. 100, because percentages must be converted to whole numbers before taking a reciprocal

D. 20, because the treated event rate is 10% and must be doubled

E. 2, because relative risk is one half and its reciprocal gives NNT

23. A 61-year-old has isolated prolongation of prothrombin time to 16 seconds with a normal activated partial thromboplastin time. Which coagulation factor is most directly assessed by the pathway uniquely represented in the prolonged test?

A. Factor XI in the intrinsic pathway

B. Factor XII in the contact-activation pathway

C. Factor VIII as the cofactor for intrinsic factor X activation

D. Factor IX in the intrinsic tenase complex

E. Factor VII in the extrinsic pathway

24. A pregnant patient at 7 weeks has a viable intrauterine pregnancy. What is the key endocrine role of hCG early in gestation?

- A.** hCG directly closes the fetal ductus arteriosus and establishes neonatal circulation
- B.** hCG suppresses the corpus luteum so placental progesterone production must begin immediately after implantation
- C.** hCG activates LH receptors on the corpus luteum, sustaining progesterone production until placental steroidogenesis is sufficient
- D.** hCG is the dominant hormone responsible for milk ejection from the breast
- E.** hCG acts primarily on maternal FSH receptors to initiate a new wave of follicular recruitment

25. A 60-year-old has isolated prolongation of prothrombin time to 22 seconds with a normal activated partial thromboplastin time. Which coagulation factor is most directly assessed by the pathway uniquely represented in the prolonged test?

- A.** Factor IX in the intrinsic tenase complex
- B.** Factor XII in the contact-activation pathway
- C.** Factor VIII as the cofactor for intrinsic factor X activation
- D.** Factor XI in the intrinsic pathway
- E.** Factor VII in the extrinsic pathway

26. A 55-year-old has a thickened alveolar-capillary membrane. According to Fick diffusion principles, which change by itself would increase gas transfer across the membrane?

- A.** Reducing gas solubility increases diffusion because less gas remains in the membrane
- B.** Increasing surface area or the partial-pressure gradient increases diffusion rate
- C.** Increasing membrane thickness increases diffusion rate by increasing tissue contact
- D.** Reducing surface area increases diffusion because each remaining alveolus receives more ventilation

E. Decreasing the partial-pressure gradient accelerates net molecular transfer

27. A healthy 61-year-old receives exogenous cortisol for several days at a dose that raises free cortisol well above normal. What happens to the hypothalamic-pituitary-adrenal axis?

- A. CRH rises while ACTH falls because cortisol feeds back only at the pituitary
- B. The axis is unaffected because exogenous glucocorticoid cannot participate in feedback signaling
- C. ACTH rises while CRH remains unchanged because cortisol has no pituitary feedback effect
- D. CRH and ACTH fall because glucocorticoids exert negative feedback at hypothalamic and pituitary levels
- E. CRH and ACTH rise because cortisol positively feeds back to maintain adrenal stimulation

28. A fetus has normal oxygenation despite having much lower arterial PO₂ than an adult. Which property of fetal hemoglobin most directly supports oxygen transfer across the placenta?

- A. Lower oxygen affinity that promotes oxygen loading at the placenta
- B. Exclusive expression in maternal erythrocytes during late gestation
- C. Higher P₅₀ than adult hemoglobin at the same pH and temperature
- D. Greater carbon dioxide affinity that displaces oxygen from maternal hemoglobin
- E. Higher oxygen affinity caused in part by reduced binding of 2,3-BPG

29. A 41-year-old has an extracellular potassium concentration of 2.5 mEq/L after several days of gastrointestinal loss. In a neuron whose resting membrane potential is strongly influenced by potassium permeability, what immediate change is expected?

- A. The resting membrane potential becomes more negative because the potassium equilibrium potential shifts negative
- B. The membrane depolarizes because lower extracellular potassium directly opens voltage-gated sodium channels
- C. The sodium equilibrium potential becomes strongly negative and dominates the resting potential
- D. The resting membrane potential becomes less negative because potassium leaves the cell less readily

E. The resting membrane potential is unchanged because extracellular potassium does not affect excitable cells

30. A healthy 54-year-old has been fasting overnight. Which hepatic effect of glucagon helps maintain plasma glucose?

- A. Glucagon promotes hepatic glycogen synthesis and suppresses gluconeogenesis during fasting
- B. Glucagon acts mainly on adipocyte insulin receptors rather than hepatic G-protein-coupled receptors
- C. Glucagon suppresses lipolysis and ketogenesis whenever insulin levels are low
- D. Glucagon promotes glycogenolysis and gluconeogenesis while opposing hepatic glycolysis
- E. Glucagon is the principal hormone driving GLUT4 translocation in skeletal muscle

31. A healthy alveolus becomes smaller during expiration. How does surfactant help stabilize the alveolus as its radius decreases?

- A. Surfactant increases liquid cohesion so that small alveoli empty into larger neighboring alveoli
- B. Surfactant acts only in large alveoli and has little influence on small-alveolus stability
- C. Surfactant becomes more dilute at small radius and increases surface tension to prevent overexpansion
- D. Surfactant molecules become more concentrated at the interface and lower surface tension disproportionately
- E. Surfactant raises surface tension equally at every lung volume so Laplace pressure stays constant

32. A 69-year-old voluntarily contracts a skeletal muscle. Which molecular event directly exposes the myosin-binding sites on actin?

- A. ATP binds troponin T and rotates actin into an active conformation
- B. Calmodulin phosphorylates skeletal-muscle myosin light chains before actin can bind
- C. Acetylcholine binds actin and uncovers the myosin-binding sites at the Z line
- D. Calcium binds directly to tropomyosin and detaches it from the thin filament

E. Calcium binds troponin C, shifting tropomyosin away from the actin binding sites

33. A motor neuron releases acetylcholine onto skeletal muscle at the neuromuscular junction. Which event directly generates the end-plate potential in the muscle fiber?

A. Acetylcholine opens muscarinic potassium channels and hyperpolarizes the motor end plate

B. Acetylcholine inhibits sodium entry and makes the end-plate potential more negative

C. Acetylcholine activates G-protein signaling that releases calcium from the sarcoplasmic reticulum without membrane current

D. Acetylcholine directly opens skeletal-muscle voltage-gated calcium channels before any depolarization

E. Acetylcholine opens nicotinic cation channels, producing a net inward depolarizing current

34. A healthy adult moves from sea level to an altitude of approximately 3500 m. After several days, which renal response contributes most directly to increased red cell production?

A. Reduced renal oxygen sensing suppresses erythropoietin and conserves iron stores

B. The liver becomes the exclusive source of erythropoietin in healthy adults after hypoxic exposure

C. Hypoxia-inducible signaling in renal interstitial cells increases erythropoietin secretion

D. Juxtaglomerular cells release erythropoietin in direct proportion to plasma renin activity

E. Renal tubular cells increase thrombopoietin secretion, which secondarily raises erythrocyte production

35. A neuron in a 48-year-old reaches threshold at the axon initial segment. Which ionic event produces the rapid upstroke of a typical neuronal action potential?

A. Opening of voltage-gated sodium channels causes a large inward sodium current

B. Opening of voltage-gated potassium channels causes the initial rapid depolarizing current

C. Opening of ligand-gated chloride channels creates regenerative depolarization at the initial segment

D. Closing of all potassium leak channels is the sole mechanism that creates the action potential

E. Activation of the sodium-potassium ATPase directly produces the millisecond depolarizing upstroke

36. A 28-year-old receives a rapid isotonic fluid bolus that increases venous return without changing contractility or arterial pressure substantially. How does the left ventricular pressure-volume loop change?

A. End-diastolic volume and stroke volume increase through the Frank-Starling mechanism

B. End-systolic volume must rise markedly because contractility is unchanged

C. The loop becomes narrower with no change in end-diastolic volume because venous return does not affect preload

D. End-diastolic volume falls while end-systolic volume rises because preload opposes ejection

E. Stroke volume falls because increased preload directly increases afterload in the same proportion

37. A 35-year-old travels to high altitude and develops hypoxemia. Which peripheral chemoreceptor response is most important for the immediate increase in ventilation?

A. Aortic baroreceptors increase ventilation mainly by detecting low hemoglobin concentration

B. Carotid bodies increase afferent firing when arterial PO₂ falls substantially, stimulating ventilation

C. Carotid bodies reduce firing during hypoxemia so respiratory alkalosis can be avoided

D. Central chemoreceptors directly sense low arterial PO₂ and are the primary oxygen sensors

E. Pulmonary J receptors directly measure arterial PO₂ and set the hypoxic ventilatory response

38. A healthy woman ovulates at midcycle. Which acute endocrine event is most directly responsible for rupture of the dominant follicle?

A. The LH surge triggers enzymatic and cellular changes that culminate in ovulation

B. A peak in inhibin A stimulates theca cells to release the oocyte

C. A prolactin surge causes follicular smooth muscle contraction and oocyte release

D. A decline in estradiol to undetectable levels is the essential mechanical trigger for ovulation

E. A sudden fall in FSH alone ruptures the follicle by reducing granulosa-cell support

39. A pancreatic beta cell is exposed to rising plasma glucose near 110 mg/dL. Which sequence links glucose metabolism to insulin secretion?

A. ATP rises, ATP-sensitive potassium channels close, the cell depolarizes, and voltage-gated calcium channels open

B. Glucose directly opens voltage-gated calcium channels without changing potassium conductance or ATP

C. Sodium-potassium ATPase inhibition hyperpolarizes the beta cell and is the normal trigger for insulin release

D. ATP closes voltage-gated calcium channels and thereby triggers insulin granule exocytosis

E. ATP falls, ATP-sensitive potassium channels open, and calcium influx increases through hyperpolarization

40. A healthy 35-year-old swallows a bolus of food. Which coordinated response allows the bolus to enter the stomach?

A. The upper esophageal sphincter remains closed while gravity alone carries the bolus to the stomach

B. Gastrin abruptly inhibits esophageal smooth muscle and is the primary trigger for swallowing peristalsis

C. The lower esophageal sphincter contracts strongly throughout swallowing to prevent any gastric entry

D. Primary peristalsis propels the bolus while the lower esophageal sphincter undergoes neurally mediated relaxation

E. Sympathetic activation produces the dominant peristaltic wave and relaxes all gastrointestinal sphincters

41. A 59-year-old has an extracellular potassium concentration of 3.0 mEq/L after several days of gastrointestinal loss. In a neuron whose resting membrane potential is strongly influenced by potassium permeability, what immediate change is expected?

- A.** The resting membrane potential is unchanged because extracellular potassium does not affect excitable cells
- B.** The membrane depolarizes because lower extracellular potassium directly opens voltage-gated sodium channels
- C.** The resting membrane potential becomes less negative because potassium leaves the cell less readily
- D.** The resting membrane potential becomes more negative because the potassium equilibrium potential shifts negative
- E.** The sodium equilibrium potential becomes strongly negative and dominates the resting potential

42. A healthy 60-kg adult receives 1 L of isotonic saline intravenously. After equilibration and before renal excretion, where does most of the infused volume distribute?

- A.** Primarily into total body water with a fall in extracellular sodium concentration similar to pure water
- B.** Almost entirely inside cells because sodium is rapidly transported into the intracellular space
- C.** Only in plasma because isotonic saline cannot leave the vascular compartment
- D.** Equally between intracellular and extracellular compartments because saline crosses cell membranes freely
- E.** Within the extracellular fluid, with roughly three quarters in interstitial fluid and one quarter in plasma

43. A protein-rich meal enters the stomach of a healthy 44-year-old. Which stimulus most directly promotes gastrin release from antral G cells?

- A.** Luminal peptides and vagal gastrin-releasing peptide stimulate G cells
- B.** Vagal acetylcholine acts only on parietal cells and has no pathway influencing G cells
- C.** Gastric distention suppresses gastrin release so acid output remains unchanged after meals
- D.** Very low antral pH directly stimulates gastrin release through somatostatin-independent signaling
- E.** Secretin from the duodenum is the main physiologic trigger for antral gastrin secretion

- 44.** A 65-year-old with acute hemorrhage loses enough blood to lower effective arterial blood volume. Which early compensatory response is expected before substantial fluid replacement?
- A.** Sympathetic activation raises heart rate and vascular tone while renin and vasopressin promote volume conservation
 - B.** Systemic veins dilate to store additional blood in the peripheral circulation
 - C.** Baroreceptor firing rises and suppresses sympathetic tone to prevent tachycardia
 - D.** Atrial natriuretic peptide rises because atrial stretch increases despite hemorrhage
 - E.** Renin and vasopressin are suppressed so the kidneys can excrete sodium and water
- 45.** A 49-year-old has whole-body oxygen consumption of 250 mL/min. Arterial oxygen content is 200 mL/L and mixed venous oxygen content is 150 mL/L. By the Fick principle, what is the approximate cardiac output?
- A.** 1.25 L/min, using arterial oxygen content as the only denominator
 - B.** 1.67 L/min, using mixed venous oxygen content as the only denominator
 - C.** 10.0 L/min, after dividing by only half of the oxygen-content difference
 - D.** 12.5 L/min, by multiplying oxygen consumption by the oxygen-content difference
 - E.** 5.0 L/min, from 250 mL/min divided by the 50 mL/L arteriovenous O₂ difference
- 46.** A clinician taps the Achilles tendon of a relaxed 43-year-old, producing a brief muscle stretch and contraction. Which spinal circuit is the essential core of this reflex?
- A.** A corticospinal neuron is required to complete the reflex arc at the spinal level
 - B.** A group Ia afferent makes an excitatory monosynaptic connection with the homonymous alpha motor neuron
 - C.** A sympathetic preganglionic neuron provides the efferent limb to the skeletal muscle
 - D.** A group Ib afferent makes a direct inhibitory monosynaptic connection with the homonymous alpha motor neuron
 - E.** A C-fiber nociceptor directly excites the contralateral alpha motor neuron without interneurons

47. A 50-year-old has GFR 100 mL/min and renal plasma flow 500 mL/min. What is the filtration fraction?

- A.** Approximately 0.44, requiring hematocrit in the denominator even though RPF is already plasma flow
- B.** Approximately 0.60, based on the sum of the two flow rates
- C.** Approximately 0.80, representing the fraction of plasma not filtered
- D.** Approximately 0.20, because filtration fraction equals GFR divided by renal plasma flow
- E.** Approximately 5.0, because renal plasma flow divided by GFR is the filtration fraction

48. A 32-year-old mounts an antibody response to an encapsulated bacterium. Complement is activated on the microbial surface. Which complement product most directly acts as a major opsonin that enhances phagocytosis?

- A.** C3b deposited on the microbial surface, where it is recognized by complement receptors on phagocytes
- B.** C3a deposited on the microbial surface as the principal phagocytic ligand
- C.** C5a incorporated into the membrane attack complex as the major opsonin
- D.** Factor H covalently bound to bacteria to promote complement receptor recognition
- E.** C9 released into plasma as the dominant chemotactic signal for neutrophils

49. Two laboratories measure the same physiologic variable with similar standard deviations, but one study has four times as many independent participants. What happens to the standard error of the mean in the larger study, all else equal?

- A.** It is four times larger because standard error rises directly with sample size
- B.** It is unchanged because standard error is identical to standard deviation
- C.** It is approximately one half as large because standard error equals standard deviation divided by the square root of sample size
- D.** It cannot change with sample size unless the population mean changes
- E.** It becomes one quarter as large because standard error is inversely proportional to sample size itself

50. During breastfeeding, an infant suckles and milk is rapidly ejected from the breast. Which hormone and target cell mediate this reflex?

- A.** Prolactin causes immediate contraction of mammary myoepithelial cells within seconds
- B.** Progesterone is released from the posterior pituitary and ejects stored milk
- C.** Oxytocin causes contraction of myoepithelial cells surrounding mammary alveoli and ducts
- D.** Estrogen contracts ductal smooth muscle and produces the milk let-down reflex
- E.** Dopamine directly contracts mammary ducts while suppressing pituitary prolactin

51. A 23-year-old receives an alpha-1 agonist that constricts systemic veins. Which immediate effect most directly increases cardiac preload?

- A.** Reduced venous capacitance shifts blood from the peripheral venous reservoir toward the heart
- B.** Venous smooth muscle has negligible influence on stressed blood volume and preload
- C.** Venoconstriction lowers mean systemic filling pressure and therefore reduces the gradient for venous return
- D.** Increased venous capacitance stores more blood peripherally and raises central venous return
- E.** Arteriolar dilation lowers capillary pressure and directly increases ventricular end-diastolic volume

52. A newborn is transitioning from placental to pulmonary gas exchange. Which event most directly causes the early fall in pulmonary vascular resistance?

- A.** Reduced pulmonary blood flow after birth lowers pulmonary arterial pressure
- B.** Removal of the placenta directly constricts pulmonary arterioles
- C.** Expansion and oxygenation of the lungs dilate the pulmonary vascular bed
- D.** Closure of the foramen ovale precedes and causes pulmonary vasodilation
- E.** A fall in alveolar oxygen tension relaxes pulmonary arteriolar smooth muscle

53. A patient asks that the result of a sensitive reproductive-physiology test not be shared with family members. The patient has capacity and there is no immediate safety exception. What should the clinician do?

- A.** Refuse to document the result in the medical record because confidentiality means information cannot be recorded
- B.** Share the result with immediate family because relatives are presumed to have automatic access to adult medical information
- C.** Post the result in a family group message so everyone receives the same explanation
- D.** Tell the family first because reproductive information has broader social implications than ordinary clinical data
- E.** Maintain confidentiality and discuss information with others only with the patient's permission or another valid legal basis

54. A seated subject is suddenly accelerated left. Which sensory structure primarily detects angular acceleration of the head?

- A.** Macular hair cells of the cochlea respond to angular acceleration through the tectorial membrane
- B.** Semicircular canals primarily encode static head position relative to gravity through otoconia
- C.** Otolith organs detect only sound frequency and do not participate in vestibular sensation
- D.** Hair cells in the cristae of the semicircular canals respond to endolymph-driven deflection of the cupula
- E.** Middle-ear ossicles directly stimulate vestibular afferents whenever the head rotates

55. A 61-year-old lowers a heavy dumbbell slowly from an elbow-flexed position as gravity extends the elbow. The elbow flexors remain active while lengthening. This is what type of contraction?

- A.** An eccentric contraction in which active muscle develops force while lengthening
- B.** A concentric contraction in which active muscle develops force while shortening
- C.** An isotonic contraction that by definition excludes any change in muscle length
- D.** An isometric contraction in which muscle length remains constant throughout the movement
- E.** A passive stretch in which no cross-bridge cycling occurs despite muscle activation

56. A pregnant patient at 10 weeks has a viable intrauterine pregnancy. What is the key endocrine role of hCG early in gestation?

- A.** hCG is the dominant hormone responsible for milk ejection from the breast
- B.** hCG acts primarily on maternal FSH receptors to initiate a new wave of follicular recruitment
- C.** hCG suppresses the corpus luteum so placental progesterone production must begin immediately after implantation
- D.** hCG directly closes the fetal ductus arteriosus and establishes neonatal circulation
- E.** hCG activates LH receptors on the corpus luteum, sustaining progesterone production until placental steroidogenesis is sufficient

57. A 71-year-old adapts to bright daylight. Which photoreceptor property is most characteristic of rods compared with cones?

- A.** Rods are more sensitive to low light but have lower spatial acuity because of greater convergence
- B.** Rods provide the highest visual acuity because each rod has a one-to-one ganglion-cell connection in the fovea
- C.** Rods depolarize in response to light because cGMP-gated sodium channels open
- D.** Rods mediate color discrimination through three wavelength-specific photopigments
- E.** Rods are concentrated in the foveal center and dominate vision in bright light

58. A 75-year-old has diffuse pulmonary fibrosis. Which change in static lung mechanics is expected?

- A.** Compliance is unchanged because fibrosis alters diffusion but not pressure-volume behavior
- B.** Lung compliance increases because fibrotic tissue removes elastic recoil
- C.** Lung compliance increases while total lung capacity falls solely from airway closure
- D.** Elastic recoil falls, causing marked air trapping as the primary mechanical defect
- E.** Lung compliance decreases because the parenchyma is stiff and elastic recoil is increased

59. Acidic chyme enters the duodenum of a 57-year-old. Which hormonal response most directly increases bicarbonate-rich pancreatic ductal secretion?

- A.** Secretin released from duodenal S cells stimulates pancreatic ductal bicarbonate secretion
- B.** Somatostatin from pancreatic delta cells selectively increases bicarbonate output into the duodenum
- C.** Motilin released during fasting is the main signal for neutralizing duodenal acid after meals
- D.** Cholecystokinin from I cells primarily stimulates a bicarbonate-rich ductal secretion without affecting enzymes
- E.** Gastrin from G cells is the dominant hormone driving pancreatic ductal bicarbonate secretion

60. A healthy adult is upright standing. Compared with the lung base, which statement about the lung apex is most accurate?

- A.** The apex has a higher V/Q ratio because perfusion falls more steeply than ventilation from base to apex
- B.** The base has negligible blood flow because pulmonary arterial pressure is lowest there
- C.** The apex behaves as a true right-to-left shunt with perfusion but no ventilation
- D.** The apex and base have identical V/Q ratios because gravity affects ventilation and perfusion equally
- E.** The apex has a lower V/Q ratio because ventilation falls more steeply than perfusion toward the apex

61. A 50-year-old has respiratory rate 18/min, tidal volume 450 mL, and anatomic dead space 150 mL. What is the approximate alveolar ventilation?

- A.** 8.1 L/min, calculated from total minute ventilation without subtracting dead space
- B.** 10.8 L/min, calculated by adding dead space to each tidal breath
- C.** 16.67 L/min, calculated by dividing effective tidal volume by respiratory rate
- D.** 5.4 L/min, calculated from respiratory rate times tidal volume minus dead-space volume
- E.** 2.7 L/min, calculated from dead-space ventilation alone

- 62.** FSH rises in a healthy male with intact testes. Which Sertoli-cell response is expected?
- A.** Conversion of all testosterone to estrogen so intratesticular androgen concentration falls
 - B.** Suppression of seminiferous-tubule function so germ cells remain quiescent
 - C.** Release of GnRH into the testicular circulation as the main feedback signal
 - D.** Direct production of most circulating testosterone from cholesterol within Sertoli cells
 - E.** Support of spermatogenesis together with increased production of androgen-binding protein and inhibin B
- 63.** During a physiology demonstration, an action potential reaches a motor-nerve terminal and acetylcholine is released onto a skeletal-muscle fiber. Which event directly generates the end-plate potential?
- A.** Acetylcholine opens nicotinic cation channels, producing a net inward depolarizing current
 - B.** Acetylcholine activates G-protein signaling that releases calcium from the sarcoplasmic reticulum without membrane current
 - C.** Acetylcholine opens muscarinic potassium channels and hyperpolarizes the motor end plate
 - D.** Acetylcholine directly opens skeletal-muscle voltage-gated calcium channels before any depolarization
 - E.** Acetylcholine inhibits sodium entry and makes the end-plate potential more negative
- 64.** A 75-year-old has a primary metabolic acidosis with serum bicarbonate 18 mEq/L and appropriate acute respiratory compensation. What physiologic change provides this compensation?
- A.** Renal bicarbonate excretion is the immediate respiratory compensation for metabolic acidosis
 - B.** Increased alveolar ventilation lowers PaCO₂ and partially raises extracellular pH toward normal
 - C.** Decreased alveolar ventilation raises PaCO₂ and consumes hydrogen ions through respiratory acid retention
 - D.** Peripheral chemoreceptors suppress ventilation so carbon dioxide can buffer the excess acid
 - E.** The lungs increase bicarbonate synthesis directly and normalize pH without changing PaCO₂

65. A 60-year-old has normal kidney function. Which property of the thick ascending limb is essential for generating the corticomedullary osmotic gradient?

- A.** It lacks active solute transport and functions only as a passive conduit to the distal nephron
- B.** It actively reabsorbs NaCl while remaining relatively impermeable to water, diluting tubular fluid
- C.** It reabsorbs urea as its only major contribution to medullary hypertonicity
- D.** It secretes NaCl into the medulla and reabsorbs water to concentrate tubular fluid
- E.** It is highly permeable to water and therefore equilibrates completely with the hypertonic medulla

66. A study fails to detect a real improvement in a physiologic endpoint. Increasing sample size is being considered. What is the expected effect of a larger sample, assuming the true effect and variability are unchanged?

- A.** Sample size affects precision but can never influence power, under the physiologic conditions described
- B.** Statistical power decreases because more observations make the null hypothesis harder to reject
- C.** Type II error necessarily rises because larger studies contain more variable participants
- D.** Statistical power generally increases because the standard error falls and the study is better able to detect the true effect
- E.** The alpha level automatically increases even if the investigators do not change it

67. A cohort study follows 1,000 exposed and 1,000 unexposed adults. During follow-up, 100 exposed and 50 unexposed participants develop the outcome. What is the relative risk?

- A.** 5.0, because the exposed event count is divided by the unexposed percentage
- B.** Cannot be calculated from a cohort design because only odds ratios are valid
- C.** 0.5, because the unexposed risk is divided by the exposed risk
- D.** 1.5, because the two risks are added rather than divided
- E.** 2.0, because the risk is 10% in the exposed group and 5% in the unexposed group

68. An arteriole constricts so that its radius becomes 0.8 times baseline while viscosity and length remain unchanged. According to Poiseuille behavior, resistance changes by approximately what factor?

- A.** It increases to about 1.2 times baseline because resistance varies only inversely with radius
- B.** It increases only in direct proportion to viscosity, which was held constant here
- C.** It decreases to about 0.41 times baseline because a smaller radius lowers wall shear
- D.** It is unchanged because vessel radius affects velocity but not resistance
- E.** It increases to about 2.4 times baseline because resistance varies inversely with the fourth power of radius

69. After ovulation in a normal cycle, basal body temperature rises slightly and cervical mucus becomes thicker. Which hormone is primarily responsible?

- A.** Inhibin B is the major steroid responsible for the rise in basal body temperature
- B.** Progesterone from the corpus luteum produces the thermogenic and mucus-thickening effects
- C.** Estradiol from the follicle produces the main sustained postovulatory thermogenic effect
- D.** LH remains at surge levels throughout the luteal phase and directly thickens cervical mucus
- E.** FSH directly increases hypothalamic temperature set point after ovulation

70. A muscle biopsy from an endurance-trained 43-year-old shows fibers adapted for prolonged submaximal activity. Which feature is most characteristic of type I skeletal-muscle fibers?

- A.** Absence of capillaries because oxygen delivery is unnecessary for slow fibers
- B.** High mitochondrial density, abundant myoglobin, and relatively fatigue-resistant oxidative metabolism
- C.** Exclusive dependence on phosphocreatine with little capacity for fatty-acid oxidation
- D.** Low mitochondrial density with predominant rapid glycolysis and very high fatigability
- E.** The largest motor neurons and highest shortening velocity of all fiber types

71. A 36-year-old performs a heavy isometric contraction that markedly increases tendon tension. Which receptor is specialized to detect this tension and signal through group Ib afferents?

- A.** The neuromuscular junction on alpha motor neurons within the tendon
- B.** The muscle spindle primary ending arranged in parallel with extrafusal fibers
- C.** A Pacinian corpuscle inside the muscle spindle capsule
- D.** The Golgi tendon organ located in series with extrafusal muscle fibers
- E.** A nociceptor whose group Ia afferent specifically measures tendon force

72. A 55-year-old performs repeated sprint exercise and skeletal-muscle lactate production rises. Which statement best describes lactate physiology during intense exercise?

- A.** Lactate is produced only when tissue oxygen tension reaches absolute zero
- B.** Lactate can be exported and used as an oxidative fuel or recycled by the liver rather than being merely a waste product
- C.** The liver cannot metabolize lactate and therefore relies exclusively on renal excretion
- D.** Lactate formation irreversibly traps all pyruvate and prevents any later oxidative metabolism
- E.** Lactate itself is the sole chemical cause of delayed-onset muscle soreness days later

73. A 68-year-old begins moderate dynamic exercise. Which integrated respiratory response occurs as oxygen consumption and carbon dioxide production rise?

- A.** Ventilation rises only after arterial PCO₂ doubles because neural and feed-forward signals are absent
- B.** Minute ventilation falls so arterial PCO₂ rises steadily during ordinary moderate exercise
- C.** Arterial PO₂ must fall markedly because diffusion cannot increase in healthy lungs during exercise
- D.** Physiologic dead space always increases enough to prevent maintenance of normal arterial gases
- E.** Minute ventilation increases to match metabolic demand, often keeping arterial PO₂ and PCO₂ near normal at moderate intensity

74. A lactating 67-year-old has increased nipple stimulation during nursing. Which hypothalamic change permits prolactin secretion to rise?

- A.** Somatostatin becomes the primary prolactin-releasing hormone during nursing
- B.** Reduced hypothalamic dopamine delivery removes tonic inhibition of pituitary lactotrophs
- C.** Nipple stimulation suppresses prolactin and acts only through oxytocin
- D.** GnRH secretion rises and acts directly on lactotrophs as the main prolactin-releasing signal
- E.** Increased hypothalamic dopamine directly stimulates lactotroph D2 receptors to release prolactin

75. A person with chronic hypoxemia develops a hematocrit of 60%. If vascular caliber and pressure gradient are unchanged, what is the most direct rheologic consequence of this marked rise in hematocrit?

- A.** Blood viscosity decreases because erythrocytes align and eliminate internal friction
- B.** Resistance becomes independent of viscosity once hematocrit exceeds the normal range
- C.** Blood viscosity increases, tending to increase resistance to flow
- D.** Plasma oncotic pressure rises in direct proportion to hematocrit and drives vasodilation
- E.** Systemic vascular resistance must fall because oxygen content has increased

76. A 20-year-old has normal pancreatic lipase secretion but impaired delivery of bile acids to the small intestine. Which absorptive step is most directly impaired?

- A.** Active uptake of amino acids through sodium-dependent brush-border transporters
- B.** Basolateral export of monosaccharides through GLUT2 in jejunal enterocytes
- C.** Hydrolysis of triglycerides by pancreatic lipase because bile acids are the lipase enzyme itself
- D.** Formation of micelles that ferry poorly water-soluble lipid digestion products to the enterocyte surface
- E.** Intrinsic factor binding to vitamin B12 in the terminal ileum

77. A case-control study compares prior exposure between patients with an uncommon outcome and matched controls. Which measure of association is most directly calculated from the sampling design?

- A.** The incidence rate ratio calculated directly from new cases per person-time in each exposure group

- B.** The prevalence ratio because all subjects are sampled without regard to outcome status
- C.** The absolute risk reduction because population event risks are measured prospectively
- D.** The number needed to treat because treatment is randomly assigned to cases and controls
- E.** The odds ratio comparing the odds of prior exposure in cases and controls

78. A 30-year-old forms a clot and then activates the endothelial thrombomodulin-protein C anticoagulant pathway. Activated protein C, with protein S as a cofactor, primarily limits coagulation by inactivating which factors?

- A.** Factors XIa and XIIa at the start of the contact pathway
- B.** Factors IIa and Xa by direct irreversible proteolysis as its principal action
- C.** Factors Va and VIIIa, under the physiologic conditions described
- D.** Factors VIIa and tissue factor at the endothelial surface
- E.** Fibrin and fibrinogen through the same mechanism as plasmin

79. A healthy 33-year-old absorbs glucose from the small-intestinal lumen after a carbohydrate-rich meal. Which transporter mediates the principal apical uptake of glucose and galactose?

- A.** SGLT1 cotransports sodium with glucose or galactose across the apical membrane
- B.** GLUT5 is the main apical transporter for both glucose and galactose
- C.** PEPT1 carries glucose together with small peptides across the apical membrane
- D.** GLUT2 cotransports sodium with glucose across the apical brush border under all conditions
- E.** The Na⁺/K⁺ ATPase directly transports luminal glucose into the enterocyte

80. A 71-year-old voluntarily contracts a skeletal muscle. Which molecular event directly exposes the myosin-binding sites on actin?

- A.** Calcium binds troponin C, shifting tropomyosin away from the actin binding sites
- B.** Calmodulin phosphorylates skeletal-muscle myosin light chains before actin can bind
- C.** ATP binds troponin T and rotates actin into an active conformation

- D.** Acetylcholine binds actin and uncovers the myosin-binding sites at the Z line
- E.** Calcium binds directly to tropomyosin and detaches it from the thin filament

81. A 95% confidence interval for a mean difference in a physiologic outcome is 2.0 to 7.0 units. The null value for the difference is 0. What is the most appropriate interpretation?

- A.** The result is not statistically significant because every confidence interval must include zero
- B.** The interval proves there is a 95% probability that the true mean difference lies between 2.0 and 7.0 for this already observed dataset
- C.** The interval establishes clinical importance regardless of the size or meaning of the physiologic effect
- D.** The interval excludes the null value, so the observed difference is statistically significant at approximately the two-sided 0.05 level
- E.** The confidence interval shows that 95% of individual patients have responses between 2.0 and 7.0 units

82. A gastric parietal cell from a 48-year-old is stimulated after a meal. Which transporter performs the final active step of hydrogen ion secretion into the gastric lumen?

- A.** The basolateral Na^+/K^+ ATPase directly pumps hydrogen ion into the gastric lumen
- B.** The apical $\text{Na}^+/\text{glucose}$ cotransporter exchanges luminal glucose for intracellular hydrogen ion
- C.** A chloride-bicarbonate exchanger on the apical membrane pumps hydrogen ion into the lumen
- D.** The apical H^+/K^+ ATPase exchanges intracellular hydrogen ion for luminal potassium
- E.** Pepsin actively transports protons across the parietal-cell membrane using ATP

83. A 27-year-old with severe distributive shock has warm skin early in the course and a high cardiac output. Which hemodynamic abnormality is most characteristic of this early pattern?

- A.** High left ventricular afterload caused by diffuse arteriolar constriction
- B.** Loss of plasma volume is the only mechanism capable of producing a high-output shock state
- C.** Markedly reduced systemic vascular resistance from widespread vasodilation

- D.** Near-zero cardiac output with compensatory skin vasodilation
- E.** Markedly increased systemic vascular resistance as the defining cause of warm extremities

84. A 44-year-old has a transient fall in ionized calcium. Parathyroid hormone rises. Which renal effect of PTH helps restore plasma calcium while limiting calcium-phosphate precipitation?

- A.** It increases proximal sodium-phosphate cotransporters and raises serum phosphate
- B.** It suppresses 1-alpha-hydroxylase and thereby reduces intestinal calcium absorption
- C.** It decreases calcium reabsorption and increases phosphate reabsorption in the proximal tubule
- D.** It causes equivalent urinary retention of calcium and phosphate without changing vitamin D metabolism
- E.** It increases distal calcium reabsorption while decreasing proximal phosphate reabsorption

85. A 59-year-old has isolated prolongation of prothrombin time to 18 seconds with a normal activated partial thromboplastin time. Which coagulation factor is most directly assessed by the pathway uniquely represented in the prolonged test?

- A.** Factor XI in the intrinsic pathway
- B.** Factor XII in the contact-activation pathway
- C.** Factor IX in the intrinsic tenase complex
- D.** Factor VIII as the cofactor for intrinsic factor X activation
- E.** Factor VII in the extrinsic pathway

86. A patient has an advance directive refusing prolonged mechanical ventilation under specified circumstances and now lacks decision-making capacity. The clinical situation clearly matches the directive. What should guide care?

- A.** Ask the surrogate to substitute the surrogate's own values rather than the patient's known preferences
- B.** Honor the patient's documented prior autonomous preferences while discussing implementation with the appropriate surrogate
- C.** Provide indefinite ventilation until every family member reaches unanimous agreement

D. Ignore the directive because current incapacity automatically transfers all authority to the treating physician

E. Treat the advance directive as advisory only when the clinician would personally choose differently

87. A demyelinating lesion affects a peripheral nerve in a 73-year-old. Why does loss of myelin slow or block action-potential propagation?

A. Loss of membrane insulation increases current leak and disrupts saltatory conduction between nodes of Ranvier

B. Demyelination increases membrane resistance and length constant, causing conduction to accelerate excessively

C. Myelin normally opens voltage-gated channels uniformly along every internodal membrane segment

D. Loss of myelin prevents neurotransmitter synthesis within the neuronal cell body

E. Myelin is required for axonal sodium-potassium ATPase expression but not for passive current spread

88. A muscle biopsy from an endurance-trained 41-year-old shows fibers adapted for prolonged submaximal activity. Which feature is most characteristic of type I skeletal-muscle fibers?

A. Low mitochondrial density with predominant rapid glycolysis and very high fatigability

B. The largest motor neurons and highest shortening velocity of all fiber types

C. High mitochondrial density, abundant myoglobin, and relatively fatigue-resistant oxidative metabolism

D. Exclusive dependence on phosphocreatine with little capacity for fatty-acid oxidation

E. Absence of capillaries because oxygen delivery is unnecessary for slow fibers

89. A patient with acute blood loss has intact kidneys and adequate iron stores. Approximately 4 days later, the bone marrow response is being assessed. Which peripheral blood finding best reflects an appropriate erythropoietin-driven marrow response?

A. A marked fall in reticulocytes because erythropoietin suppresses release of immature cells

- B.** An immediate increase in mature erythrocyte number within minutes of hemorrhage
- C.** A rise in neutrophils that directly substitutes for reduced oxygen-carrying capacity
- D.** An increased reticulocyte fraction as newly produced erythrocytes enter the circulation
- E.** An increase in platelet size that is the principal marker of erythroid marrow recovery

90. A healthy 26-year-old absorbs dietary nonheme iron. Which condition generally favors iron uptake by duodenal enterocytes?

- A.** High hepcidin concentrations that increase ferroportin-mediated export into plasma
- B.** An alkaline lumen that keeps ferric iron insoluble at the brush border
- C.** Binding of iron to intrinsic factor before transport through the terminal ileum
- D.** An acidic lumen and reduction of ferric iron to the ferrous form facilitate apical uptake
- E.** Complete oxidation of ferrous iron to ferric iron before DMT1 can transport it

91. A 37-year-old has normal pancreatic lipase secretion but impaired delivery of bile acids to the small intestine. Which absorptive step is most directly impaired?

- A.** Formation of micelles that ferry poorly water-soluble lipid digestion products to the enterocyte surface
- B.** Basolateral export of monosaccharides through GLUT2 in jejunal enterocytes
- C.** Intrinsic factor binding to vitamin B12 in the terminal ileum
- D.** Hydrolysis of triglycerides by pancreatic lipase because bile acids are the lipase enzyme itself
- E.** Active uptake of amino acids through sodium-dependent brush-border transporters

92. A 75-year-old enters a dark room and the pupils dilate. Which efferent pathway mediates contraction of the iris radial dilator muscle?

- A.** Sympathetic postganglionic fibers activate alpha-1 adrenergic receptors on the radial muscle
- B.** Sympathetic fibers activate beta-1 receptors on the sphincter pupillae to produce dilation
- C.** Parasympathetic postganglionic fibers activate M3 receptors on the radial muscle

- D.** Parasympathetic fibers inhibit alpha-1 receptors and thereby actively contract the radial muscle
- E.** Somatic motor fibers from the oculomotor nerve activate nicotinic receptors on the radial muscle

93. A febrile 44-year-old has a hypothalamic temperature set point that has been raised by inflammatory mediators. Why can the patient feel cold and shiver while core temperature is already above normal?

- A.** Shivering occurs only when core temperature is below 35 C and cannot occur during fever
- B.** Sweating is the dominant response while temperature is rising toward a higher set point
- C.** Peripheral thermoreceptors suppress all autonomic thermoregulation once core temperature exceeds 37 C
- D.** The hypothalamic set point is lowered during fever, making normal temperature feel excessively warm
- E.** Core temperature is below the newly elevated set point, so heat-conserving and heat-producing responses are activated

94. Acidic chyme enters the duodenum of a 74-year-old. Which hormonal response most directly increases bicarbonate-rich pancreatic ductal secretion?

- A.** Gastrin from G cells is the dominant hormone driving pancreatic ductal bicarbonate secretion
- B.** Cholecystokinin from I cells primarily stimulates a bicarbonate-rich ductal secretion without affecting enzymes
- C.** Secretin released from duodenal S cells stimulates pancreatic ductal bicarbonate secretion
- D.** Motilin released during fasting is the main signal for neutralizing duodenal acid after meals
- E.** Somatostatin from pancreatic delta cells selectively increases bicarbonate output into the duodenum

95. During counseling about a complex acid-base disorder, the patient repeatedly nods but gives vague answers. Which technique best checks understanding?

- A.** Ask only whether the patient understands and accept a yes-or-no answer as sufficient
- B.** Repeat the same technical explanation more rapidly so the patient hears all details again
- C.** Ask a nurse to sign that the patient appeared attentive during the discussion

D. Avoid checking understanding because doing so may embarrass the patient

E. Ask the patient to explain the diagnosis and plan back in the patient's own words using teach-back

96. A term newborn takes the first several breaths. Pulmonary vascular resistance falls sharply while systemic vascular resistance rises after cord clamping. Which immediate change most strongly promotes functional closure of the foramen ovale?

A. Right atrial pressure rises above left atrial pressure because pulmonary resistance falls

B. Left atrial pressure rises above right atrial pressure as pulmonary venous return increases

C. Placental venous return increases and maintains fetal right-to-left atrial flow

D. Pulmonary arterial pressure rises above systemic pressure after lung expansion

E. Ductus venosus flow increases and raises right atrial preload after cord clamping

97. A 18-year-old has normal pulsatile hypothalamic GnRH secretion. Why is pulsatility important for the reproductive axis?

A. Pulsatile GnRH sustains pituitary LH and FSH secretion, whereas continuous exposure causes receptor desensitization

B. Continuous GnRH is required for sustained gonadotropin secretion and pulsatile exposure suppresses the pituitary

C. GnRH pulsatility determines prolactin secretion but has little effect on LH or FSH

D. The pituitary stores no gonadotropins and therefore cannot respond to episodic hypothalamic signals

E. GnRH acts directly on gonads and does not require pituitary responsiveness

98. A patient and clinician disagree about whether to continue a burdensome treatment that is not achieving the patient's stated goals. What is the best next step?

A. Clarify the goals of care, the treatment's physiologic effects and burdens, and the patient's values before revisiting the decision together

- B.** Continue treatment indefinitely because stopping any medical intervention is ethically equivalent to causing death
- C.** Avoid discussing burdens so the patient is not influenced toward treatment limitation
- D.** Frame the disagreement as noncompliance and end discussion once the clinician has stated a recommendation
- E.** Ask the family to overrule a capacitated patient if the family prefers more treatment

99. A demyelinating lesion affects a peripheral nerve in a 33-year-old. Why does loss of myelin slow or block action-potential propagation?

- A.** Myelin normally opens voltage-gated channels uniformly along every internodal membrane segment
- B.** Loss of membrane insulation increases current leak and disrupts saltatory conduction between nodes of Ranvier
- C.** Myelin is required for axonal sodium-potassium ATPase expression but not for passive current spread
- D.** Demyelination increases membrane resistance and length constant, causing conduction to accelerate excessively
- E.** Loss of myelin prevents neurotransmitter synthesis within the neuronal cell body

100. During quiet expiration, a healthy alveolus decreases in radius without collapsing. Which property of pulmonary surfactant helps stabilize the alveolus at the smaller size?

- A.** Surfactant acts only in large alveoli and has little influence on small-alveolus stability
- B.** Surfactant molecules become more concentrated at the interface and lower surface tension disproportionately
- C.** Surfactant becomes more dilute at small radius and increases surface tension to prevent overexpansion
- D.** Surfactant increases liquid cohesion so that small alveoli empty into larger neighboring alveoli
- E.** Surfactant raises surface tension equally at every lung volume so Laplace pressure stays constant

101. A 65-year-old has a region of lung that remains perfused but receives essentially no ventilation because an airway is completely obstructed. What is the limiting V/Q relationship in that region?

- A.** The region has maximal oxygen transfer because low ventilation increases capillary transit time
- B.** V/Q remains one because local hypoxic vasoconstriction always perfectly matches perfusion to ventilation
- C.** V/Q approaches zero, producing shunt-like blood that cannot be fully corrected by increasing inspired oxygen
- D.** V/Q approaches infinity because perfusion is absent while ventilation persists
- E.** The region becomes pure anatomic dead space with ventilation but no blood flow

102. A healthy 26-year-old is at midcycle and the dominant ovarian follicle is about to rupture. Which acute endocrine event most directly triggers ovulation?

- A.** The LH surge triggers enzymatic and cellular changes that culminate in ovulation
- B.** A decline in estradiol to undetectable levels is the essential mechanical trigger for ovulation
- C.** A peak in inhibin A stimulates theca cells to release the oocyte
- D.** A sudden fall in FSH alone ruptures the follicle by reducing granulosa-cell support
- E.** A prolactin surge causes follicular smooth muscle contraction and oocyte release

103. A clinician discovers that an incorrect physiologic test result was previously communicated to a patient and led to an unnecessary medication change. What is the appropriate response?

- A.** Disclose the error promptly, explain known consequences and corrective steps, and address the patient's questions
- B.** Do not disclose the error unless the patient independently notices the discrepancy
- C.** Alter the record so the original result appears consistent with the later correction
- D.** Tell the patient only that the plan has changed without acknowledging the inaccurate prior information
- E.** Ask another clinician to disclose the error while avoiding any discussion of how it occurred

104. A naive CD4 T lymphocyte recognizes its specific peptide on an antigen-presenting cell. Which additional interaction provides the classic costimulatory signal required for full activation of the naive T cell?

- A.** Fas ligand on the antigen-presenting cell binds Fas and drives clonal expansion
- B.** MHC class I on the antigen-presenting cell binds CD8 on the naive CD4 T cell
- C.** PD-L1 binds PD-1 and supplies the dominant positive costimulatory signal
- D.** Secreted IgM cross-links the T-cell receptor and substitutes for cell-cell costimulation
- E.** B7 molecules on the antigen-presenting cell bind CD28 on the T cell

105. A premature infant develops respiratory distress because of inadequate surfactant. Which mechanical consequence is expected in the affected alveoli?

- A.** Higher surface tension increases the pressure required to keep small alveoli open
- B.** Lower surface tension increases the tendency of small alveoli to collapse during expiration
- C.** Lower opening pressure prevents atelectasis in the smallest alveoli
- D.** Increased lung compliance reduces the work needed to inflate fluid-lined alveoli
- E.** Increased surfactant concentration raises recoil and reduces functional residual capacity

106. A clinician is offered an expensive personal gift by a device company while choosing equipment for a physiology laboratory. What is the best response?

- A.** Ask the company to send the gift to a family member so the conflict no longer involves the clinician
- B.** Avoid accepting a gift that could create or appear to create a conflict of interest in professional judgment
- C.** Accept the gift but do not disclose it because disclosure itself creates bias
- D.** Accept the gift because professional training guarantees that financial relationships cannot influence judgment
- E.** Choose the company's equipment first and evaluate alternatives only if it performs poorly

107. A sudden rise in aortic pressure increases left ventricular afterload in a 76-year-old, with preload and contractility initially unchanged. What is the immediate beat-to-beat effect?

- A.** End-systolic volume decreases and stroke volume increases because higher aortic pressure assists ejection
- B.** End-systolic volume increases and stroke volume decreases because the ventricle ejects against a higher pressure
- C.** Stroke volume is unchanged because afterload affects only diastolic filling
- D.** End-diastolic volume instantly falls to zero while ejection fraction remains unchanged
- E.** Contractility automatically rises enough on the same beat to maintain identical end-systolic volume

108. A 63-year-old controls the downward phase of a heavy curl while the elbow flexors remain active and lengthen under load. This is what type of contraction?

- A.** A passive stretch in which no cross-bridge cycling occurs despite muscle activation
- B.** A concentric contraction in which active muscle develops force while shortening
- C.** An isotonic contraction that by definition excludes any change in muscle length
- D.** An isometric contraction in which muscle length remains constant throughout the movement
- E.** An eccentric contraction in which active muscle develops force while lengthening

109. A competent patient asks that a trusted partner be present during discussion of a sensitive endocrine diagnosis. What is the best response?

- A.** Exclude the partner automatically because sensitive diagnoses can never be discussed with anyone else
- B.** Require the partner to sign the consent form before hearing any clinical information
- C.** Direct all discussion to the partner once permission is given because the partner is now the decision-maker
- D.** Share the entire medical record with the partner because permission for one discussion is unlimited authorization

E. Confirm the patient's permission and preferences, then include the partner while continuing to address the patient directly

110. A healthy 29-year-old is several days past ovulation and notes a small sustained rise in basal body temperature with thicker cervical mucus. Which hormone is primarily responsible?

- A. LH remains at surge levels throughout the luteal phase and directly thickens cervical mucus
- B. Inhibin B is the major steroid responsible for the rise in basal body temperature
- C. Progesterone from the corpus luteum produces the thermogenic and mucus-thickening effects
- D. Estradiol from the follicle produces the main sustained postovulatory thermogenic effect
- E. FSH directly increases hypothalamic temperature set point after ovulation

111. A healthy 60-year-old hypoventilates for several minutes and PaCO₂ rises. Which sensors provide the dominant ventilatory drive from this acute rise in CO₂ under ordinary conditions?

- A. Central chemoreceptors respond to increased brain extracellular hydrogen ion generated from diffused CO₂
- B. Cortical motor neurons automatically normalize PaCO₂ without medullary chemosensory input
- C. Pulmonary stretch receptors provide the primary minute-to-minute response to arterial CO₂
- D. Carotid body chemoreceptors are completely insensitive to carbon dioxide and pH
- E. Central chemoreceptors directly sense arterial oxygen content rather than carbon dioxide-derived hydrogen ion

112. When a 39-year-old becomes mildly volume depleted, colonic sodium and water conservation increases. Which general physiologic principle best explains how water is absorbed across the intestinal epithelium?

- A. Colonic water movement is independent of electrolyte transport because the epithelium is impermeable to water
- B. Water follows net solute absorption osmotically through transcellular and paracellular pathways
- C. Water is pumped directly by an ATP-dependent water transporter against its osmotic gradient
- D. Water absorption requires secretion of sodium into the lumen to create a favorable gradient

E. Water is absorbed only in the stomach and cannot be reclaimed in the small intestine or colon

113. A new physiologic screening test is evaluated in 200 people known to have a disorder; 180 test positive. What is the sensitivity of the test?

A. 80%, because sensitivity is the proportion of all tested individuals who are true positives

B. 10%, because sensitivity is the proportion of affected individuals who test negative

C. 95%, because sensitivity is calculated from unaffected individuals who test negative

D. 90%, because sensitivity is the proportion of affected individuals who test positive

E. Cannot be determined without knowing disease prevalence in the source population

114. A mildly dehydrated 35-year-old has plasma osmolality near 300 mOsm/kg and rising vasopressin. What is the major renal action of vasopressin in the collecting duct?

A. V1-receptor signaling removes aquaporin-2 channels from principal cells and increases free-water excretion

B. Vasopressin directly closes basolateral aquaporins so water is trapped inside principal cells

C. V2-receptor signaling inserts aquaporin-2 channels into the apical membrane of principal cells

D. Vasopressin stimulates sodium-glucose cotransport in the proximal tubule as its main antidiuretic mechanism

E. Vasopressin blocks the medullary osmotic gradient and thereby produces maximally dilute urine

115. A 21-year-old with severe distributive shock has warm skin early in the course and a high cardiac output. Which hemodynamic abnormality is most characteristic of this early pattern?

A. Markedly reduced systemic vascular resistance from widespread vasodilation

B. Loss of plasma volume is the only mechanism capable of producing a high-output shock state

C. High left ventricular afterload caused by diffuse arteriolar constriction

D. Near-zero cardiac output with compensatory skin vasodilation

E. Markedly increased systemic vascular resistance as the defining cause of warm extremities

116. A healthy 2-month-old infant has circulating antibody that was acquired from the mother before birth. Which immunoglobulin class accounts for most of this passive transplacental immunity?

- A.** IgD actively transported across the placenta to seed the infant B-cell repertoire
- B.** IgM transported across the placenta because its pentameric form binds Fc receptors most avidly
- C.** IgE transferred in large amounts to provide systemic antibacterial protection
- D.** IgG transported across the placenta by neonatal Fc receptors
- E.** Secretory IgA transported from maternal plasma directly across the placenta

117. A 34-year-old has normal pulsatile hypothalamic GnRH secretion. Why is pulsatility important for the reproductive axis?

- A.** The pituitary stores no gonadotropins and therefore cannot respond to episodic hypothalamic signals
- B.** Continuous GnRH is required for sustained gonadotropin secretion and pulsatile exposure suppresses the pituitary
- C.** Pulsatile GnRH sustains pituitary LH and FSH secretion, whereas continuous exposure causes receptor desensitization
- D.** GnRH pulsatility determines prolactin secretion but has little effect on LH or FSH
- E.** GnRH acts directly on gonads and does not require pituitary responsiveness

118. A 31-year-old adapts to dim starlight. Which photoreceptor property is most characteristic of rods compared with cones?

- A.** Rods provide the highest visual acuity because each rod has a one-to-one ganglion-cell connection in the fovea
- B.** Rods are more sensitive to low light but have lower spatial acuity because of greater convergence
- C.** Rods mediate color discrimination through three wavelength-specific photopigments
- D.** Rods depolarize in response to light because cGMP-gated sodium channels open
- E.** Rods are concentrated in the foveal center and dominate vision in bright light

119. A mechanically ventilated 27-year-old has PaCO₂ acutely increased from 40 to 60 mm Hg without a major change in arterial pressure. What is the expected effect on cerebral blood flow over the next several minutes?

- A.** Cerebral blood flow is unchanged because autoregulation completely overrides CO₂ reactivity
- B.** The blood-brain barrier prevents CO₂ from influencing extracellular hydrogen ion concentration
- C.** Cerebral arterioles constrict and cerebral blood flow falls because CO₂ suppresses local metabolism
- D.** Cerebral arterioles dilate and cerebral blood flow increases because CO₂ is a potent local vasodilator
- E.** Cerebral blood flow falls only because hemoglobin releases less oxygen at higher CO₂

120. A 51-year-old with severe hypoalbuminemia develops dependent edema. Which Starling-force alteration contributes most directly?

- A.** Increased plasma oncotic pressure draws fluid into the interstitium and causes edema
- B.** Reduced plasma colloid oncotic pressure decreases the force retaining water within capillaries
- C.** Higher lymphatic drainage is the primary cause of fluid accumulation in the interstitial space
- D.** A fall in capillary filtration coefficient increases fluid movement into tissues
- E.** Reduced interstitial hydrostatic pressure always prevents filtration and eliminates edema

121. Renal perfusion pressure falls in a 40-year-old. Which combination most directly stimulates renin release from juxtaglomerular cells?

- A.** Increased afferent stretch, increased macula densa NaCl, and reduced sympathetic activity
- B.** Increased angiotensin II acting through negative feedback as a direct renin secretagogue
- C.** High distal NaCl delivery combined with alpha-1 blockade as the classic renin stimulus
- D.** Reduced afferent arteriolar stretch, reduced macula densa NaCl delivery, and beta-1 sympathetic stimulation
- E.** High atrial natriuretic peptide and increased renal perfusion pressure

122. A beta-1 agonist increases left ventricular contractility in a 27-year-old while preload and afterload are held constant. Which pressure-volume change is expected?

- A.** End-diastolic volume must increase before any change in stroke volume can occur
- B.** End-systolic volume decreases and stroke volume increases as the end-systolic pressure-volume relation becomes steeper
- C.** Stroke volume decreases because beta-1 stimulation raises calcium entry into myocytes
- D.** The end-systolic pressure-volume relation becomes flatter as inotropy increases
- E.** End-systolic volume increases because stronger contraction traps more blood in the ventricle

123. A smooth-muscle cell in the wall of a resistance artery is exposed to increased intracellular calcium. Which pathway most directly initiates contraction?

- A.** Calcium opens nicotinic receptors on smooth muscle and directly produces cross-bridge cycling
- B.** Calcium inhibits calmodulin so that actin-myosin interaction can begin
- C.** Calcium activates myosin light-chain phosphatase, causing greater myosin phosphorylation
- D.** Calcium-calmodulin activates myosin light-chain kinase, increasing myosin phosphorylation
- E.** Calcium binds troponin C and shifts tropomyosin exactly as in skeletal muscle

124. A surrogate must decide about a procedure for an incapacitated patient who previously expressed clear values but left no specific written directive. Which decision standard is preferred?

- A.** Always choose maximal life-prolonging treatment regardless of the patient's known goals
- B.** Use a population-majority vote about what most people would want in the same situation
- C.** Use substituted judgment by choosing the option the patient would likely choose based on known values and prior statements
- D.** Choose the most expensive intervention because resource use correlates with benefit
- E.** Use the surrogate's personal preference because the surrogate now becomes the patient for decision-making purposes

125. A patient participating in a physiology research study wants to withdraw after enrollment. The study intervention has already begun, but stopping is medically safe. What is the appropriate response?

- A.** Respect the participant's decision to withdraw and explain any medically relevant follow-up or data-handling issues allowed by the consent process
- B.** Require continued participation because signing research consent creates an irrevocable contract
- C.** Continue collecting all new study procedures without permission because enrollment already occurred
- D.** Threaten loss of ordinary clinical care if the participant leaves the study
- E.** Ask the investigator to decide whether the participant's reason is sufficiently important to permit withdrawal

126. A 65-year-old travels to high altitude and develops hypoxemia. Which peripheral chemoreceptor response is most important for the immediate increase in ventilation?

- A.** Carotid bodies increase afferent firing when arterial PO₂ falls substantially, stimulating ventilation
- B.** Central chemoreceptors directly sense low arterial PO₂ and are the primary oxygen sensors
- C.** Carotid bodies reduce firing during hypoxemia so respiratory alkalosis can be avoided
- D.** Aortic baroreceptors increase ventilation mainly by detecting low hemoglobin concentration
- E.** Pulmonary J receptors directly measure arterial PO₂ and set the hypoxic ventilatory response

127. A healthy adult has a transient rise in plasma potassium to 6.0 mEq/L. Which adrenal response helps restore potassium balance?

- A.** Increased cortisol secretion directly blocks ENaC and raises urinary potassium excretion
- B.** Hyperkalemia inhibits zona glomerulosa depolarization and therefore prevents aldosterone release
- C.** Direct stimulation of zona glomerulosa aldosterone secretion increases distal potassium secretion
- D.** Increased ACTH is required as the dominant minute-to-minute controller of aldosterone during hyperkalemia
- E.** Suppression of aldosterone increases collecting-duct potassium secretion

128. A 51-year-old begins progressive resistance training. Over months, bone at loaded sites adapts to repeated mechanical strain. Which cellular process best describes the physiologic remodeling response?

- A.** Osteocytes sense mechanical loading and help coordinate a shift toward bone formation at stressed sites
- B.** Bone mass changes only in response to serum calcium and is independent of local mechanical strain
- C.** Chondrocytes replace cortical bone with cartilage whenever strain increases
- D.** Mechanical loading suppresses all osteoblast signaling and reduces local bone mass
- E.** Osteoclasts permanently cease activity so that remodeling stops once training begins

129. A 22-year-old has hemoglobin 10 g/dL, arterial oxygen saturation 98%, and PaO₂ 96 mm Hg. Using an oxygen-binding capacity of 1.34 mL O₂/g hemoglobin, what is the approximate arterial oxygen content?

- A.** Approximately 13.4 mL O₂/dL of arterial blood
- B.** Approximately 0.3 mL O₂/dL, using dissolved oxygen alone
- C.** Approximately 6.7 mL O₂/dL of arterial blood
- D.** Approximately 9.8 mL O₂/dL, omitting hemoglobin binding capacity
- E.** Approximately 20.1 mL O₂/dL of arterial blood

130. A 35-year-old experiences a sudden decrease in ambient temperature. Which combination best describes the coordinated cold-defense response?

- A.** Cutaneous vasodilation conserves heat while sweating increases metabolic heat production
- B.** Vagal stimulation of skeletal muscle produces shivering while sympathetic tone is suppressed
- C.** Cutaneous vasoconstriction conserves heat while shivering and sympathetic metabolic responses increase heat production
- D.** Cold exposure lowers thyroid and catecholamine effects to minimize oxygen consumption
- E.** Sweating and reduced muscle activity are the primary responses to prevent further cooling

131. A 33-year-old is exposed to cold wind. Which response most directly reduces dry heat loss from the skin during the initial autonomic response?

- A.** Shivering lowers core heat production while blood is redirected to the skin
- B.** Cutaneous vasoconstriction reduces warm blood flow to the skin surface
- C.** Sweating increases and forms an insulating water layer over the skin
- D.** Piloerection in humans provides the dominant reduction in convective heat loss
- E.** Cutaneous vasodilation increases the insulating effect of subcutaneous tissue

132. A 24-year-old has hemoglobin 12 g/dL, arterial oxygen saturation 99%, and PaO₂ 101 mm Hg. Using an oxygen-binding capacity of 1.34 mL O₂/g hemoglobin, what is the approximate arterial oxygen content?

- A.** Approximately 8.1 mL O₂/dL of arterial blood
- B.** Approximately 16.2 mL O₂/dL of arterial blood
- C.** Approximately 11.9 mL O₂/dL, omitting hemoglobin binding capacity
- D.** Approximately 0.3 mL O₂/dL, using dissolved oxygen alone
- E.** Approximately 24.3 mL O₂/dL of arterial blood

133. A physiologic diagnostic test is applied to 300 people known not to have the target disorder; 285 test negative. What is the specificity?

- A.** 5%, because specificity is the proportion of unaffected individuals who test positive
- B.** 85%, because specificity is calculated from all positive test results
- C.** Cannot be calculated unless the positive predictive value is known first
- D.** 95%, because specificity is the proportion of unaffected individuals who test negative
- E.** 90%, because specificity is the same numerical quantity as sensitivity

134. A 72-year-old undergoes several days of fasting. Which metabolic adaptation helps spare skeletal-muscle protein as fasting continues?

- A.** Insulin rises markedly and suppresses adipose lipolysis during prolonged fasting
- B.** The brain increases use of ketone bodies, reducing its ongoing requirement for glucose derived from amino acids
- C.** Red blood cells switch completely to fatty-acid oxidation and stop producing lactate
- D.** The brain stops using ketone bodies and requires progressively more glucose from muscle protein
- E.** Hepatic ketogenesis falls to zero once glycogen stores are depleted

135. A dietary protein is being digested in the small intestine of a 63-year-old. How are many dipeptides and tripeptides taken up across the apical enterocyte membrane?

- A.** They are cotransported with hydrogen ions by PEPT1 and then hydrolyzed intracellularly
- B.** They require intrinsic factor and a terminal-ileal receptor before absorption
- C.** They are cotransported with chloride by CFTR and remain intact in portal blood
- D.** They use the same sodium-glucose cotransporter responsible for glucose uptake
- E.** They diffuse only through tight junctions because enterocytes lack peptide transporters

136. A 35-year-old with fever to 38.5 C and lactic acidosis has active skeletal muscle consuming oxygen rapidly. Which change in the hemoglobin-oxygen dissociation curve is expected in the affected tissues?

- A.** A lower P50 that increases hemoglobin affinity for oxygen in metabolically active tissue
- B.** A rightward shift that facilitates oxygen unloading at a given PO₂
- C.** A leftward shift caused by increased hydrogen ion concentration and temperature
- D.** A rightward shift that reduces oxygen unloading and preserves arterial saturation
- E.** No shift because tissue pH changes alter only dissolved oxygen, not hemoglobin affinity

137. Ionized calcium falls slightly in a healthy 20-year-old. Which integrated response is most appropriate?

- A.** PTH suppresses renal 1-alpha-hydroxylase to limit intestinal calcium absorption

- B.** Calcitonin becomes the dominant chronic regulator and raises serum calcium by increasing bone resorption
- C.** PTH rises, increasing renal calcium retention, phosphate excretion, and calcitriol production
- D.** PTH increases proximal phosphate reabsorption so calcium and phosphate rise together
- E.** PTH falls, increasing urinary calcium loss and reducing calcitriol production

138. A healthy 50-year-old stands suddenly after lying supine. Baroreceptor unloading increases sympathetic outflow. Which receptor-mediated response most directly raises heart rate?

- A.** Norepinephrine acting at nicotinic receptors directly depolarizes ventricular myocytes to set the heart rate
- B.** Norepinephrine acting at alpha-1 receptors in the sinoatrial node opens potassium channels and slows phase 4 depolarization
- C.** Epinephrine acting at beta-2 receptors is the only autonomic mechanism capable of changing heart rate
- D.** Norepinephrine acting at beta-1 receptors in the sinoatrial node increases pacemaker current and cAMP signaling
- E.** Acetylcholine acting at M2 receptors increases cAMP and accelerates sinoatrial nodal firing

139. A neuron in a 26-year-old reaches threshold at the axon initial segment. Which ionic event produces the rapid upstroke of a typical neuronal action potential?

- A.** Activation of the sodium-potassium ATPase directly produces the millisecond depolarizing upstroke
- B.** Opening of ligand-gated chloride channels creates regenerative depolarization at the initial segment
- C.** Closing of all potassium leak channels is the sole mechanism that creates the action potential
- D.** Opening of voltage-gated potassium channels causes the initial rapid depolarizing current
- E.** Opening of voltage-gated sodium channels causes a large inward sodium current

140. In a healthy male, LH rises transiently. Which gonadal cell and steroidogenic product are directly stimulated by LH?

- A.** Leydig cells increase testosterone synthesis in response to LH-receptor signaling
- B.** Spermatogonia increase testosterone synthesis independently of Leydig cells
- C.** Epididymal epithelial cells increase dihydrotestosterone secretion into plasma
- D.** Sertoli cells increase inhibin B as the primary direct LH response
- E.** Prostatic stromal cells increase FSH secretion through local steroidogenesis

141. A 34-year-old briefly contacts a pinprick and experiences sharp, well-localized pain followed by slower burning pain. Which fiber type carries the initial fast pain signal most prominently?

- A.** Thinly myelinated A-delta fibers conduct the initial sharp pain relatively rapidly
- B.** Group Ia proprioceptive fibers carry the main signal from free nerve ending nociceptors
- C.** Large A-alpha motor fibers are the principal nociceptors for fast cutaneous pain
- D.** Postganglionic sympathetic fibers transmit the conscious sensory component of fast pain
- E.** Unmyelinated C fibers conduct the earliest sharp pain faster than all myelinated fibers

142. A 36-year-old with fever to 40.0 C and lactic acidosis has active skeletal muscle consuming oxygen rapidly. Which change in the hemoglobin-oxygen dissociation curve is expected in the affected tissues?

- A.** A rightward shift that reduces oxygen unloading and preserves arterial saturation
- B.** No shift because tissue pH changes alter only dissolved oxygen, not hemoglobin affinity
- C.** A leftward shift caused by increased hydrogen ion concentration and temperature
- D.** A rightward shift that facilitates oxygen unloading at a given PO₂
- E.** A lower P₅₀ that increases hemoglobin affinity for oxygen in metabolically active tissue

143. A patient asks the clinician to keep a potentially transmissible condition secret from a spouse, but the patient has not indicated any plan to expose the spouse imminently. What should the clinician do first?

- A.** Promise that the information can never be disclosed under any circumstance, including legally mandated reporting
- B.** Immediately disclose all information to the spouse without considering applicable confidentiality or public-health rules
- C.** Counsel the patient about disclosure, prevention, and applicable public-health obligations while maintaining confidentiality within legal limits
- D.** Delete the diagnosis from the medical record to prevent any future disclosure
- E.** Refuse further care until the patient personally informs every household contact

144. A medical student is asked to perform a sensitive physical examination for teaching on an anesthetized patient when that examination is not part of the planned procedure. What is required?

- A.** The examination is acceptable without consent if a supervising physician is physically present
- B.** A student may perform the examination whenever the finding would be educationally useful
- C.** General hospital consent automatically authorizes any educational examination while the patient is anesthetized
- D.** Specific appropriate consent for the teaching examination should be obtained before anesthesia
- E.** Consent can be obtained retrospectively after the patient awakens because the examination has no therapeutic purpose

145. A gastric parietal cell from a 31-year-old is stimulated after a meal. Which transporter performs the final active step of hydrogen ion secretion into the gastric lumen?

- A.** The basolateral Na^+/K^+ ATPase directly pumps hydrogen ion into the gastric lumen
- B.** The apical $\text{Na}^+/\text{glucose}$ cotransporter exchanges luminal glucose for intracellular hydrogen ion
- C.** The apical H^+/K^+ ATPase exchanges intracellular hydrogen ion for luminal potassium
- D.** A chloride-bicarbonate exchanger on the apical membrane pumps hydrogen ion into the lumen
- E.** Pepsin actively transports protons across the parietal-cell membrane using ATP

146. Renal perfusion pressure falls in a 70-year-old. Which combination most directly stimulates renin release from juxtaglomerular cells?

- A.** Reduced afferent arteriolar stretch, reduced macula densa NaCl delivery, and beta-1 sympathetic stimulation
- B.** High atrial natriuretic peptide and increased renal perfusion pressure
- C.** Increased angiotensin II acting through negative feedback as a direct renin secretagogue
- D.** High distal NaCl delivery combined with alpha-1 blockade as the classic renin stimulus
- E.** Increased afferent stretch, increased macula densa NaCl, and reduced sympathetic activity

147. A demyelinating lesion affects a peripheral nerve in a 55-year-old. Why does loss of myelin slow or block action-potential propagation?

- A.** Loss of myelin prevents neurotransmitter synthesis within the neuronal cell body
- B.** Myelin normally opens voltage-gated channels uniformly along every internodal membrane segment
- C.** Myelin is required for axonal sodium-potassium ATPase expression but not for passive current spread
- D.** Demyelination increases membrane resistance and length constant, causing conduction to accelerate excessively
- E.** Loss of membrane insulation increases current leak and disrupts saltatory conduction between nodes of Ranvier

148. A low-dose para-aminohippurate infusion is used to estimate renal plasma flow in a healthy 45-year-old. Why can PAH clearance approximate effective renal plasma flow?

- A.** PAH is completely reabsorbed after filtration, so none appears in renal venous blood
- B.** PAH remains confined to erythrocytes and therefore measures renal blood flow directly
- C.** PAH is synthesized by the kidney in proportion to renal plasma flow
- D.** PAH clearance equals GFR because PAH is filtered but neither secreted nor reabsorbed
- E.** PAH is filtered and avidly secreted so most PAH entering the renal circulation is removed in one pass

149. A healthy 24-year-old exercises in an environment at 35 C with high radiant heat. Core temperature begins to rise. Which autonomic response is most important for increasing evaporative heat loss?

- A. Parasympathetic adrenergic stimulation of eccrine sweat glands increases sweating
- B. Sympathetic cholinergic stimulation of eccrine sweat glands increases sweating
- C. Withdrawal of all sympathetic activity is sufficient to activate eccrine gland secretion directly
- D. Sympathetic alpha-1 stimulation of cutaneous vessels is the principal mechanism of evaporation
- E. Somatic motor stimulation of apocrine glands produces most thermoregulatory sweating

150. A 75-year-old has sodium 132 mEq/L, glucose 360 mg/dL, and BUN 18 mg/dL. What is the approximate calculated plasma osmolality using the standard clinical formula?

- A. Approximately 158 mOsm/kg using sodium without the factor of two
- B. Approximately 290 mOsm/kg using $2 \times \text{Na} + \text{glucose}/18 + \text{BUN}/2.8$
- C. Approximately 642 mOsm/kg by adding concentrations without unit conversion
- D. Approximately 26 mOsm/kg by omitting sodium from the calculation
- E. Approximately 264 mOsm/kg using sodium alone and ignoring glucose and urea

151. In an isolated resistance arteriole, intracellular calcium rises in vascular smooth muscle while membrane integrity is preserved. Which signaling pathway most directly initiates contraction?

- A. Calcium activates myosin light-chain phosphatase, causing greater myosin phosphorylation
- B. Calcium opens nicotinic receptors on smooth muscle and directly produces cross-bridge cycling
- C. Calcium-calmodulin activates myosin light-chain kinase, increasing myosin phosphorylation
- D. Calcium inhibits calmodulin so that actin-myosin interaction can begin
- E. Calcium binds troponin C and shifts tropomyosin exactly as in skeletal muscle

152. A person breathing room air at sea level has PaCO_2 50 mm Hg and a respiratory quotient of 0.8. Using an inspired PO_2 of approximately 150 mm Hg, what alveolar PO_2 is predicted by the simplified alveolar gas equation?

- A. Approximately 62 mm Hg, using only the carbon dioxide term
- B. Approximately 70 mm Hg, multiplying inspired oxygen by the respiratory quotient first
- C. Approximately 212 mm Hg, adding the carbon dioxide term rather than subtracting it
- D. Approximately 100 mm Hg, subtracting PaCO₂ without accounting for respiratory quotient
- E. Approximately 88 mm Hg, from $PAO_2 = 150 - PaCO_2/0.8$

153. A naive CD4 T cell encounters its cognate peptide on an activated dendritic cell in a lymph node. Which additional receptor-ligand interaction provides the classic costimulatory signal for full T-cell activation?

- A. Fas ligand on the antigen-presenting cell binds Fas and drives clonal expansion
- B. B7 molecules on the antigen-presenting cell bind CD28 on the T cell
- C. PD-L1 binds PD-1 and supplies the dominant positive costimulatory signal
- D. MHC class I on the antigen-presenting cell binds CD8 on the naive CD4 T cell
- E. Secreted IgM cross-links the T-cell receptor and substitutes for cell-cell costimulation

154. In a healthy adult male, a physiologic pulse of LH reaches the testes. Which gonadal cell and steroidogenic product are directly stimulated by this signal?

- A. Sertoli cells increase inhibin B as the primary direct LH response
- B. Spermatogonia increase testosterone synthesis independently of Leydig cells
- C. Prostatic stromal cells increase FSH secretion through local steroidogenesis
- D. Epididymal epithelial cells increase dihydrotestosterone secretion into plasma
- E. Leydig cells increase testosterone synthesis in response to LH-receptor signaling

155. A 65-year-old receives a rapid isotonic fluid bolus that increases venous return without changing contractility or arterial pressure substantially. How does the left ventricular pressure-volume loop change?

- A. The loop becomes narrower with no change in end-diastolic volume because venous return does not affect preload

- B.** End-diastolic volume falls while end-systolic volume rises because preload opposes ejection
- C.** End-systolic volume must rise markedly because contractility is unchanged
- D.** End-diastolic volume and stroke volume increase through the Frank-Starling mechanism
- E.** Stroke volume falls because increased preload directly increases afterload in the same proportion

156. During rapid knee extension, a muscle is suddenly lengthened. Which sensory receptor and afferent fiber most directly signal the dynamic change in muscle length that initiates the stretch reflex?

- A.** Muscle spindle primary endings carried mainly by group Ia afferent fibers
- B.** Free nerve endings carried only by group IV fibers
- C.** Ruffini endings in skin carried mainly by autonomic postganglionic fibers
- D.** Pacinian corpuscles carried mainly by unmyelinated C fibers
- E.** Golgi tendon organs carried mainly by group Ib afferent fibers

157. A 54-year-old performs a heavy isometric contraction that markedly increases tendon tension. Which receptor is specialized to detect this tension and signal through group Ib afferents?

- A.** The Golgi tendon organ located in series with extrafusal muscle fibers
- B.** A Pacinian corpuscle inside the muscle spindle capsule
- C.** The muscle spindle primary ending arranged in parallel with extrafusal fibers
- D.** The neuromuscular junction on alpha motor neurons within the tendon
- E.** A nociceptor whose group Ia afferent specifically measures tendon force

158. A critically ill 58-year-old has oxygen delivery reduced below the level required for tissue demand. Which relationship best defines systemic oxygen delivery?

- A.** Oxygen delivery equals arterial PO₂ multiplied by respiratory rate alone
- B.** Oxygen delivery depends only on hemoglobin concentration and is independent of blood flow
- C.** Oxygen delivery equals cardiac output multiplied by arterial oxygen content
- D.** Oxygen delivery equals mixed venous oxygen content divided by cardiac output

E. Oxygen delivery is determined solely by alveolar ventilation once saturation exceeds 90%

159. A 52-year-old gradually increases voluntary force from light effort to about 40% of maximal contraction. What principle normally governs recruitment of motor units as force rises?

- A. The largest fast-fatigable motor units are recruited first to minimize activation delay
- B. Smaller, fatigue-resistant motor units are recruited before progressively larger units
- C. All motor units are activated simultaneously, and force changes only by firing frequency
- D. Motor-unit recruitment proceeds randomly and is independent of motor-neuron size
- E. Only slow motor units are used during voluntary contraction, regardless of required force

160. A person breathing room air at sea level has PaCO_2 40 mm Hg and a respiratory quotient of 0.8. Using an inspired PO_2 of approximately 150 mm Hg, what alveolar PO_2 is predicted by the simplified alveolar gas equation?

- A. Approximately 110 mm Hg, subtracting PaCO_2 without accounting for respiratory quotient
- B. Approximately 50 mm Hg, using only the carbon dioxide term
- C. Approximately 80 mm Hg, multiplying inspired oxygen by the respiratory quotient first
- D. Approximately 200 mm Hg, adding the carbon dioxide term rather than subtracting it
- E. Approximately 100 mm Hg, from $\text{PAO}_2 = 150 - \text{PaCO}_2/0.8$

161. A 35-year-old has a region of lung that remains perfused but receives essentially no ventilation because an airway is completely obstructed. What is the limiting V/Q relationship in that region?

- A. The region becomes pure anatomic dead space with ventilation but no blood flow
- B. V/Q approaches zero, producing shunt-like blood that cannot be fully corrected by increasing inspired oxygen
- C. V/Q approaches infinity because perfusion is absent while ventilation persists
- D. The region has maximal oxygen transfer because low ventilation increases capillary transit time
- E. V/Q remains one because local hypoxic vasoconstriction always perfectly matches perfusion to ventilation

- 162.** A 54-year-old gradually increases voluntary force from light effort to about 20% of maximal contraction. What principle normally governs recruitment of motor units as force rises?
- A.** The largest fast-fatigable motor units are recruited first to minimize activation delay
 - B.** Smaller, fatigue-resistant motor units are recruited before progressively larger units
 - C.** Motor-unit recruitment proceeds randomly and is independent of motor-neuron size
 - D.** All motor units are activated simultaneously, and force changes only by firing frequency
 - E.** Only slow motor units are used during voluntary contraction, regardless of required force
- 163.** A 61-year-old has a marked increase in left ventricular wall tension during systole. Why is coronary perfusion of the left ventricular subendocardium greatest during diastole rather than systole?
- A.** Coronary arterioles actively constrict whenever ventricular pressure rises above atrial pressure
 - B.** Left coronary blood flow is driven mainly by right atrial pressure rather than aortic pressure
 - C.** Systolic myocardial compression limits intramural coronary flow, especially in the subendocardium
 - D.** Myocardial oxygen consumption falls to zero during systole, eliminating the need for perfusion
 - E.** The aortic valve closes coronary ostia during systole and opens them only in diastole
- 164.** A healthy 4-month-old infant has circulating antibody that was acquired from the mother before birth. Which immunoglobulin class accounts for most of this passive transplacental immunity?
- A.** IgD actively transported across the placenta to seed the infant B-cell repertoire
 - B.** Secretory IgA transported from maternal plasma directly across the placenta
 - C.** IgM transported across the placenta because its pentameric form binds Fc receptors most avidly
 - D.** IgG transported across the placenta by neonatal Fc receptors
 - E.** IgE transferred in large amounts to provide systemic antibacterial protection
- 165.** During the late follicular phase of a normal menstrual cycle, estradiol remains high for a sustained period. Which pituitary response helps trigger ovulation?

- A.** Sustained high estradiol switches to positive feedback and produces the midcycle LH surge
- B.** Inhibin B directly stimulates a large FSH surge that alone triggers ovulation
- C.** Progesterone from the corpus luteum produces the initial LH surge before the follicle ruptures
- D.** Prolactin becomes the dominant gonadotropin and causes follicular rupture
- E.** High estradiol maintains only negative feedback and therefore completely suppresses LH before ovulation

166. A 76-year-old performs a heavy isometric contraction that markedly increases tendon tension. Which receptor is specialized to detect this tension and signal through group Ib afferents?

- A.** The neuromuscular junction on alpha motor neurons within the tendon
- B.** The muscle spindle primary ending arranged in parallel with extrafusal fibers
- C.** A nociceptor whose group Ia afferent specifically measures tendon force
- D.** The Golgi tendon organ located in series with extrafusal muscle fibers
- E.** A Pacinian corpuscle inside the muscle spindle capsule

167. A 42-year-old has a transient fall in ionized calcium. Parathyroid hormone rises. Which renal effect of PTH helps restore plasma calcium while limiting calcium-phosphate precipitation?

- A.** It increases distal calcium reabsorption while decreasing proximal phosphate reabsorption
- B.** It increases proximal sodium-phosphate cotransporters and raises serum phosphate
- C.** It causes equivalent urinary retention of calcium and phosphate without changing vitamin D metabolism
- D.** It suppresses 1-alpha-hydroxylase and thereby reduces intestinal calcium absorption
- E.** It decreases calcium reabsorption and increases phosphate reabsorption in the proximal tubule

168. A clinician needs to discuss prognosis after a serious physiologic deterioration. The patient asks, “Am I going to die?” Which response is most appropriate?

- A.** Tell the family privately and let them decide whether the patient should receive prognostic information

- B.** Answer the concern directly with honest uncertainty, explain what is known, and ask what information and goals matter most to the patient
- C.** Avoid the question and redirect to laboratory values because discussing death may remove hope
- D.** Give a precise survival date even when the evidence cannot support that level of certainty
- E.** Provide only optimistic possibilities and omit serious outcomes unless the family requests them

169. A person with chronic hypoxemia develops a hematocrit of 55%. If vascular caliber and pressure gradient are unchanged, what is the most direct rheologic consequence of this marked rise in hematocrit?

- A.** Blood viscosity decreases because erythrocytes align and eliminate internal friction
- B.** Resistance becomes independent of viscosity once hematocrit exceeds the normal range
- C.** Blood viscosity increases, tending to increase resistance to flow
- D.** Systemic vascular resistance must fall because oxygen content has increased
- E.** Plasma oncotic pressure rises in direct proportion to hematocrit and drives vasodilation

170. A pancreatic beta cell is exposed to rising plasma glucose near 140 mg/dL. Which sequence links glucose metabolism to insulin secretion?

- A.** ATP closes voltage-gated calcium channels and thereby triggers insulin granule exocytosis
- B.** Sodium-potassium ATPase inhibition hyperpolarizes the beta cell and is the normal trigger for insulin release
- C.** ATP falls, ATP-sensitive potassium channels open, and calcium influx increases through hyperpolarization
- D.** Glucose directly opens voltage-gated calcium channels without changing potassium conductance or ATP
- E.** ATP rises, ATP-sensitive potassium channels close, the cell depolarizes, and voltage-gated calcium channels open

171. A 78-year-old undergoes several days of fasting. Which metabolic adaptation helps spare skeletal-muscle protein as fasting continues?

- A.** Insulin rises markedly and suppresses adipose lipolysis during prolonged fasting

- B.** Red blood cells switch completely to fatty-acid oxidation and stop producing lactate
- C.** Hepatic ketogenesis falls to zero once glycogen stores are depleted
- D.** The brain stops using ketone bodies and requires progressively more glucose from muscle protein
- E.** The brain increases use of ketone bodies, reducing its ongoing requirement for glucose derived from amino acids

172. A 18-year-old voluntarily contracts a skeletal muscle. Which molecular event directly exposes the myosin-binding sites on actin?

- A.** Calmodulin phosphorylates skeletal-muscle myosin light chains before actin can bind
- B.** ATP binds troponin T and rotates actin into an active conformation
- C.** Calcium binds troponin C, shifting tropomyosin away from the actin binding sites
- D.** Acetylcholine binds actin and uncovers the myosin-binding sites at the Z line
- E.** Calcium binds directly to tropomyosin and detaches it from the thin filament

173. Fat and amino acids enter the duodenum of a healthy 70-year-old. Which response is most characteristic of cholecystokinin?

- A.** It suppresses pancreatic enzyme secretion so bicarbonate can neutralize acid first
- B.** It is released mainly by antral G cells in response to low gastric pH
- C.** It primarily stimulates gastric acid secretion and accelerates gastric emptying of fat
- D.** It relaxes the gallbladder and contracts the sphincter of Oddi to reduce bile delivery
- E.** It stimulates pancreatic acinar enzyme secretion and gallbladder contraction while slowing gastric emptying

174. In a renal physiology study, plasma inulin is 1.0 mg/mL, urine inulin is 100 mg/mL, and urine flow is 1.2 mL/min. What is the estimated GFR?

- A.** Approximately 120 mL/min from the inulin clearance calculation
- B.** Approximately 1.2 mL/min, using urine flow without urine concentration

- C. Approximately 120 mg/min, which is an excretion rate rather than a clearance
- D. Approximately 0.012 mL/min by inverting the concentration ratio
- E. Approximately 100 mL/min, ignoring urine flow in the clearance equation

175. A breastfeeding patient hears the infant cry and then suckles; milk is ejected within seconds. Which hormone and target cell mediate this rapid let-down reflex?

- A. Progesterone is released from the posterior pituitary and ejects stored milk
- B. Dopamine directly contracts mammary ducts while suppressing pituitary prolactin
- C. Estrogen contracts ductal smooth muscle and produces the milk let-down reflex
- D. Oxytocin causes contraction of myoepithelial cells surrounding mammary alveoli and ducts
- E. Prolactin causes immediate contraction of mammary myoepithelial cells within seconds

176. A 21-year-old has a heart rate of 75/min and a stroke volume of 80 mL/beat. What is the approximate cardiac output?

- A. 6.0 L/min, calculated as heart rate multiplied by stroke volume
- B. 12.0 L/min, after doubling the stroke volume contribution
- C. 1.07 L/min, calculated by dividing stroke volume by heart rate
- D. 155 L/min, calculated by adding heart rate and stroke volume numerically
- E. 3.0 L/min, after dividing the product by an additional factor of two

177. A 59-year-old has normal dietary vitamin B12 intake. Which sequence is required for efficient physiologic absorption of cobalamin?

- A. Cobalamin requires pancreatic lipase but not intrinsic factor for terminal ileal uptake
- B. Cobalamin is absorbed directly in the stomach through parietal-cell H⁺/K⁺ ATPase
- C. Cobalamin binds bile salts and is absorbed primarily through SGLT1 in the duodenum
- D. Cobalamin binds transferrin and enters jejunal enterocytes through iron transporters

E. Cobalamin binds intrinsic factor and the complex is taken up by specific receptors in the terminal ileum

178. An isolated skeletal-muscle fiber is activated and then abruptly deprived of ATP while cytosolic calcium remains elevated. Which step of the cross-bridge cycle fails most directly?

- A. Myosin cannot bind actin because ATP is the structural receptor for the thin filament
- B. The power stroke cannot occur because phosphate release requires ATP binding to actin
- C. Myosin cannot detach from actin because ATP binding is required for cross-bridge release
- D. Tropomyosin cannot cover actin because ATP depletion forces calcium out of the cytosol immediately
- E. Calcium cannot bind troponin C because that binding requires direct ATP hydrolysis by troponin

179. A mechanically ventilated 45-year-old has PaCO₂ acutely increased from 40 to 55 mm Hg without a major change in arterial pressure. What is the expected effect on cerebral blood flow over the next several minutes?

- A. Cerebral blood flow is unchanged because autoregulation completely overrides CO₂ reactivity
- B. The blood-brain barrier prevents CO₂ from influencing extracellular hydrogen ion concentration
- C. Cerebral blood flow falls only because hemoglobin releases less oxygen at higher CO₂
- D. Cerebral arterioles dilate and cerebral blood flow increases because CO₂ is a potent local vasodilator
- E. Cerebral arterioles constrict and cerebral blood flow falls because CO₂ suppresses local metabolism

180. An isolated skeletal muscle from a 36-year-old is stimulated at different starting lengths. At which sarcomere condition is active force generally greatest?

- A. At any sarcomere length because active force is independent of filament overlap
- B. At extreme shortening where thin filaments completely overlap and compression is maximal
- C. At an intermediate length with near-optimal overlap of thick and thin filaments
- D. At extreme stretch where actin and myosin no longer overlap but passive tension is absent

E. Only when the sarcomere is stretched beyond the point at which titin develops passive tension

181. A healthy 43-year-old has a nocturnal pulse of growth hormone. Which mediator carries many of the growth-promoting effects of growth hormone on bone and soft tissues?

A. Insulin suppresses IGF-1 production and is therefore necessary for growth-hormone action

B. Thyroxine completely replaces growth hormone signaling after childhood

C. Hepatic and locally produced IGF-1 mediates many anabolic and linear-growth effects

D. Prolactin is converted to IGF-1 in peripheral tissues and becomes the main growth signal

E. Cortisol mediates most linear growth by directly stimulating epiphyseal chondrocytes

182. TSH binds its receptor on a thyroid follicular cell in a healthy 42-year-old. Which overall response is expected?

A. Suppression of iodide uptake and inhibition of thyroglobulin endocytosis

B. Direct conversion of circulating T3 to T4 in peripheral tissues as the only thyroid response

C. Exclusive stimulation of calcitonin secretion from parafollicular C cells

D. Reduced expression of thyroid peroxidase and decreased organification of iodide

E. Increased iodide uptake, thyroglobulin processing, and thyroid hormone synthesis and release

183. A healthy adult moves from sea level to an altitude of approximately 5000 m. After several days, which renal response contributes most directly to increased red cell production?

A. Reduced renal oxygen sensing suppresses erythropoietin and conserves iron stores

B. Hypoxia-inducible signaling in renal interstitial cells increases erythropoietin secretion

C. Juxtaglomerular cells release erythropoietin in direct proportion to plasma renin activity

D. Renal tubular cells increase thrombopoietin secretion, which secondarily raises erythrocyte production

E. The liver becomes the exclusive source of erythropoietin in healthy adults after hypoxic exposure

184. A healthy 22-year-old begins dynamic aerobic exercise. Which cardiovascular pattern is expected as workload rises?

- A.** Cardiac output increases while systemic vascular resistance usually falls because active skeletal muscle vasodilates
- B.** Mean arterial pressure collapses because local muscle vasodilation cannot be offset by higher cardiac output
- C.** Heart rate falls because vagal tone increases in proportion to exercise intensity
- D.** Skeletal-muscle blood flow falls so that coronary and cerebral perfusion can be maintained
- E.** Cardiac output falls while systemic vascular resistance rises uniformly in every vascular bed

185. A 57-year-old enters a dark room and the pupils dilate. Which efferent pathway mediates contraction of the iris radial dilator muscle?

- A.** Parasympathetic fibers inhibit alpha-1 receptors and thereby actively contract the radial muscle
- B.** Sympathetic postganglionic fibers activate alpha-1 adrenergic receptors on the radial muscle
- C.** Sympathetic fibers activate beta-1 receptors on the sphincter pupillae to produce dilation
- D.** Somatic motor fibers from the oculomotor nerve activate nicotinic receptors on the radial muscle
- E.** Parasympathetic postganglionic fibers activate M3 receptors on the radial muscle

186. A resting 55-year-old has a blood pressure of 150/90 mm Hg with a normal heart rate. What is the best approximation of mean arterial pressure?

- A.** Approximately 90 mm Hg because flow occurs mainly during diastole
- B.** Approximately 60 mm Hg because pulse pressure equals mean pressure
- C.** Approximately 110 mm Hg using diastolic pressure plus one third of pulse pressure
- D.** Approximately 120 mm Hg by taking a simple arithmetic average
- E.** Approximately 150 mm Hg because systolic pressure dominates the cardiac cycle

187. A 20-year-old has respiratory rate 12/min, tidal volume 500 mL, and anatomic dead space 150 mL. What is the approximate alveolar ventilation?

- A.** 7.8 L/min, calculated by adding dead space to each tidal breath
- B.** 1.8 L/min, calculated from dead-space ventilation alone
- C.** 6.0 L/min, calculated from total minute ventilation without subtracting dead space
- D.** 29.17 L/min, calculated by dividing effective tidal volume by respiratory rate
- E.** 4.2 L/min, calculated from respiratory rate times tidal volume minus dead-space volume

188. A 19-year-old has an extracellular potassium concentration of 2.8 mEq/L after several days of gastrointestinal loss. In a neuron whose resting membrane potential is strongly influenced by potassium permeability, what immediate change is expected?

- A.** The resting membrane potential becomes more negative because the potassium equilibrium potential shifts negative
- B.** The resting membrane potential is unchanged because extracellular potassium does not affect excitable cells
- C.** The sodium equilibrium potential becomes strongly negative and dominates the resting potential
- D.** The resting membrane potential becomes less negative because potassium leaves the cell less readily
- E.** The membrane depolarizes because lower extracellular potassium directly opens voltage-gated sodium channels

189. A 62-year-old begins moderate dynamic exercise. Which integrated respiratory response occurs as oxygen consumption and carbon dioxide production rise?

- A.** Minute ventilation falls so arterial PCO₂ rises steadily during ordinary moderate exercise
- B.** Ventilation rises only after arterial PCO₂ doubles because neural and feed-forward signals are absent
- C.** Physiologic dead space always increases enough to prevent maintenance of normal arterial gases
- D.** Arterial PO₂ must fall markedly because diffusion cannot increase in healthy lungs during exercise
- E.** Minute ventilation increases to match metabolic demand, often keeping arterial PO₂ and PCO₂ near normal at moderate intensity

190. A 48-year-old loses 1 L of pure water through insensible losses without replacing it. Which compartment change is expected after osmotic equilibration?

- A.** Extracellular osmolality falls and water shifts into cells, expanding intracellular volume
- B.** Extracellular osmolality rises and water shifts out of cells, so both intracellular and extracellular volumes decrease
- C.** Only extracellular volume falls because water cannot cross cell membranes
- D.** Both compartments expand because sodium concentration rises after water loss
- E.** Intracellular volume rises while extracellular volume remains unchanged

191. A 20-year-old has sodium 140 mEq/L, glucose 90 mg/dL, and BUN 14 mg/dL. What is the approximate calculated plasma osmolality using the standard clinical formula?

- A.** Approximately 280 mOsm/kg using sodium alone and ignoring glucose and urea
- B.** Approximately 150 mOsm/kg using sodium without the factor of two
- C.** Approximately 10 mOsm/kg by omitting sodium from the calculation
- D.** Approximately 290 mOsm/kg using $2 \times \text{Na} + \text{glucose}/18 + \text{BUN}/2.8$
- E.** Approximately 384 mOsm/kg by adding concentrations without unit conversion

192. A muscle preparation develops persistent actin-myosin binding after cellular ATP is exhausted. Which cross-bridge step specifically requires ATP and therefore cannot proceed?

- A.** Calcium cannot bind troponin C because that binding requires direct ATP hydrolysis by troponin
- B.** The power stroke cannot occur because phosphate release requires ATP binding to actin
- C.** Myosin cannot detach from actin because ATP binding is required for cross-bridge release
- D.** Tropomyosin cannot cover actin because ATP depletion forces calcium out of the cytosol immediately
- E.** Myosin cannot bind actin because ATP is the structural receptor for the thin filament

193. A 40-year-old develops an acute pulmonary embolus that blocks perfusion to a ventilated lung region. What is the local gas-exchange consequence?

- A.** Alveolar gas rapidly equilibrates with mixed venous blood because perfusion is increased
- B.** The regional V/Q ratio rises toward infinity, increasing physiologic dead-space ventilation
- C.** Both ventilation and perfusion rise proportionally so V/Q remains unchanged
- D.** The regional V/Q ratio falls toward zero, creating a pure shunt
- E.** The affected alveoli contribute more carbon dioxide elimination because capillary blood flow rises

194. Investigators conclude that a physiologic intervention has an effect when in truth no effect exists. What statistical error has occurred?

- A.** A sampling error that by definition cannot occur in randomized research
- B.** A type II error, corresponding to a false-positive rejection of the null hypothesis
- C.** A confounding error that is numerically identical to the prespecified alpha level
- D.** A type I error, corresponding to a false-positive rejection of the null hypothesis
- E.** A power error, meaning the study correctly detected a true effect

195. A healthy 54-year-old stands abruptly. Venous pooling transiently lowers arterial pressure. Which reflex response occurs within seconds?

- A.** Increased baroreceptor firing suppresses sympathetic tone and further lowers vascular resistance
- B.** Arterial pressure is restored mainly by erythropoietin release rather than autonomic changes
- C.** Reduced baroreceptor firing increases vagal tone to the sinoatrial node and slows heart rate
- D.** The reflex immediately lowers venous tone so that peripheral blood storage increases
- E.** Reduced carotid and aortic baroreceptor firing increases sympathetic and decreases parasympathetic outflow

196. A healthy 27-year-old has a nocturnal pulse of growth hormone. Which mediator carries many of the growth-promoting effects of growth hormone on bone and soft tissues?

- A.** Cortisol mediates most linear growth by directly stimulating epiphyseal chondrocytes

- B.** Prolactin is converted to IGF-1 in peripheral tissues and becomes the main growth signal
- C.** Hepatic and locally produced IGF-1 mediates many anabolic and linear-growth effects
- D.** Insulin suppresses IGF-1 production and is therefore necessary for growth-hormone action
- E.** Thyroxine completely replaces growth hormone signaling after childhood

197. A 45-year-old has a primary metabolic acidosis with serum bicarbonate 12 mEq/L and appropriate acute respiratory compensation. What physiologic change provides this compensation?

- A.** Decreased alveolar ventilation raises PaCO₂ and consumes hydrogen ions through respiratory acid retention
- B.** Increased alveolar ventilation lowers PaCO₂ and partially raises extracellular pH toward normal
- C.** The lungs increase bicarbonate synthesis directly and normalize pH without changing PaCO₂
- D.** Peripheral chemoreceptors suppress ventilation so carbon dioxide can buffer the excess acid
- E.** Renal bicarbonate excretion is the immediate respiratory compensation for metabolic acidosis

198. When a 22-year-old becomes mildly volume depleted, colonic sodium and water conservation increases. Which general physiologic principle best explains how water is absorbed across the intestinal epithelium?

- A.** Water is absorbed only in the stomach and cannot be reclaimed in the small intestine or colon
- B.** Water absorption requires secretion of sodium into the lumen to create a favorable gradient
- C.** Water is pumped directly by an ATP-dependent water transporter against its osmotic gradient
- D.** Water follows net solute absorption osmotically through transcellular and paracellular pathways
- E.** Colonic water movement is independent of electrolyte transport because the epithelium is impermeable to water

199. A small physiologic dataset contains one extremely high outlier. Which measure of central tendency is generally least affected by that outlier?

- A.** The standard deviation because it depends only on the sample median
- B.** The arithmetic mean because extreme values have almost no influence on it

- C. The range because it excludes the largest and smallest observations
- D. The variance because it is designed to ignore extreme observations
- E. The median because it depends primarily on rank order rather than the magnitude of extreme values

200. A 25-year-old has a thickened alveolar-capillary membrane. According to Fick diffusion principles, which change by itself would increase gas transfer across the membrane?

- A. Reducing gas solubility increases diffusion because less gas remains in the membrane
- B. Decreasing the partial-pressure gradient accelerates net molecular transfer
- C. Reducing surface area increases diffusion because each remaining alveolus receives more ventilation
- D. Increasing membrane thickness increases diffusion rate by increasing tissue contact
- E. Increasing surface area or the partial-pressure gradient increases diffusion rate

201. A 60-year-old with intact skin is acclimatizing to repeated exercise in the heat. Which adaptation typically improves thermoregulation after acclimatization?

- A. Core temperature must rise to a higher threshold before any heat-dissipating response begins
- B. Sweating begins later and becomes more concentrated with sodium to preserve plasma water
- C. Sweating begins earlier and becomes more effective, with better conservation of sodium in sweat
- D. Plasma volume contracts chronically, reducing the need for cardiovascular compensation during heat stress
- E. Cutaneous vasodilation is abolished so that central blood volume is never redistributed to skin

202. A 66-year-old has a small vascular injury with exposed subendothelial collagen. Which interaction is most important for initial platelet adhesion under high shear conditions?

- A. von Willebrand factor links exposed subendothelium to platelet glycoprotein Ib
- B. Plasmin bridges platelet receptors to collagen and initiates primary hemostasis
- C. Fibrinogen links platelet glycoprotein IIb/IIIa directly to intact endothelial cells

- D.** Thrombin binds platelet glycoprotein Ib and anchors platelets to collagen without von Willebrand factor
- E.** Protein C binds platelet glycoprotein IIb/IIIa and creates the first platelet monolayer

203. A person with chronic hypoxemia develops a hematocrit of 65%. If vascular caliber and pressure gradient are unchanged, what is the most direct rheologic consequence of this marked rise in hematocrit?

- A.** Plasma oncotic pressure rises in direct proportion to hematocrit and drives vasodilation
- B.** Blood viscosity decreases because erythrocytes align and eliminate internal friction
- C.** Resistance becomes independent of viscosity once hematocrit exceeds the normal range
- D.** Systemic vascular resistance must fall because oxygen content has increased
- E.** Blood viscosity increases, tending to increase resistance to flow

204. A 23-year-old has hemoglobin 8 g/dL, arterial oxygen saturation 97%, and PaO₂ 93 mm Hg. Using an oxygen-binding capacity of 1.34 mL O₂/g hemoglobin, what is the approximate arterial oxygen content?

- A.** Approximately 16.0 mL O₂/dL of arterial blood
- B.** Approximately 5.3 mL O₂/dL of arterial blood
- C.** Approximately 7.8 mL O₂/dL, omitting hemoglobin binding capacity
- D.** Approximately 0.3 mL O₂/dL, using dissolved oxygen alone
- E.** Approximately 10.7 mL O₂/dL of arterial blood

205. An isolated skeletal muscle from a 34-year-old is stimulated at different starting lengths. At which sarcomere condition is active force generally greatest?

- A.** At any sarcomere length because active force is independent of filament overlap
- B.** At extreme shortening where thin filaments completely overlap and compression is maximal
- C.** Only when the sarcomere is stretched beyond the point at which titin develops passive tension
- D.** At an intermediate length with near-optimal overlap of thick and thin filaments

E. At extreme stretch where actin and myosin no longer overlap but passive tension is absent

206. Circulating free T4 and T3 rise above their physiologic set point in a person with an intact hypothalamic-pituitary-thyroid axis. What feedback response is expected?

A. TRH and TSH both increase because thyroid hormone positively feeds back on pituitary thyrotrophs

B. Calcitonin rises and becomes the principal regulator of pituitary TSH secretion

C. TRH rises while TSH remains fixed because pituitary secretion is independent of thyroid hormone

D. TSH rises while TRH falls because thyroid hormone feedback acts only at the hypothalamus

E. TRH and TSH secretion decrease through negative feedback by thyroid hormone

207. A healthy fetus ejects most right ventricular output into the descending aorta rather than through the lungs. What physiologic feature is primarily responsible for this flow pattern?

A. Low fetal pulmonary vascular resistance draws most right ventricular output into the lungs

B. High left atrial pressure forces blood from the left atrium into the right atrium

C. High fetal pulmonary vascular resistance directs right ventricular output through the ductus arteriosus

D. The fetal ductus arteriosus normally carries blood from the aorta into the pulmonary artery

E. Placental vascular resistance exceeds pulmonary vascular resistance throughout gestation

208. A resting 32-year-old has a blood pressure of 120/75 mm Hg with a normal heart rate. What is the best approximation of mean arterial pressure?

A. Approximately 45 mm Hg because pulse pressure equals mean pressure

B. Approximately 120 mm Hg because systolic pressure dominates the cardiac cycle

C. Approximately 98 mm Hg by taking a simple arithmetic average

D. Approximately 90 mm Hg using diastolic pressure plus one third of pulse pressure

E. Approximately 75 mm Hg because flow occurs mainly during diastole

209. During sudden ankle dorsiflexion, a muscle is suddenly lengthened. Which sensory receptor and afferent fiber most directly signal the dynamic change in muscle length that initiates the stretch reflex?

- A.** Free nerve endings carried only by group IV fibers
- B.** Pacinian corpuscles carried mainly by unmyelinated C fibers
- C.** Golgi tendon organs carried mainly by group Ib afferent fibers
- D.** Muscle spindle primary endings carried mainly by group Ia afferent fibers
- E.** Ruffini endings in skin carried mainly by autonomic postganglionic fibers

210. A healthy 25-year-old filters a large sodium load. Which nephron segment normally reabsorbs the largest fraction of filtered sodium and water under baseline conditions?

- A.** The distal convoluted tubule normally reabsorbs two thirds of filtered sodium before the loop of Henle
- B.** The thin descending limb is the principal active sodium-reabsorbing segment of the nephron
- C.** The collecting duct reabsorbs most filtered sodium regardless of aldosterone activity
- D.** The thick ascending limb reabsorbs virtually all filtered sodium and water together
- E.** The proximal tubule reabsorbs roughly two thirds of filtered sodium and water iso-osmotically

211. A 53-year-old begins progressive resistance training. Over months, bone at loaded sites adapts to repeated mechanical strain. Which cellular process best describes the physiologic remodeling response?

- A.** Chondrocytes replace cortical bone with cartilage whenever strain increases
- B.** Osteocytes sense mechanical loading and help coordinate a shift toward bone formation at stressed sites
- C.** Mechanical loading suppresses all osteoblast signaling and reduces local bone mass
- D.** Osteoclasts permanently cease activity so that remodeling stops once training begins
- E.** Bone mass changes only in response to serum calcium and is independent of local mechanical strain

212. A 45-year-old with severe hypoalbuminemia develops dependent edema. Which Starling-force alteration contributes most directly?

- A.** A fall in capillary filtration coefficient increases fluid movement into tissues
- B.** Increased plasma oncotic pressure draws fluid into the interstitium and causes edema
- C.** Reduced plasma colloid oncotic pressure decreases the force retaining water within capillaries
- D.** Higher lymphatic drainage is the primary cause of fluid accumulation in the interstitial space
- E.** Reduced interstitial hydrostatic pressure always prevents filtration and eliminates edema

213. A 72-year-old has whole-body oxygen consumption of 300 mL/min. Arterial oxygen content is 190 mL/L and mixed venous oxygen content is 130 mL/L. By the Fick principle, what is the approximate cardiac output?

- A.** 1.58 L/min, using arterial oxygen content as the only denominator
- B.** 2.31 L/min, using mixed venous oxygen content as the only denominator
- C.** 5.0 L/min, from 300 mL/min divided by the 60 mL/L arteriovenous O₂ difference
- D.** 10.0 L/min, after dividing by only half of the oxygen-content difference
- E.** 18.0 L/min, by multiplying oxygen consumption by the oxygen-content difference

214. In a renal physiology study, plasma inulin is 1.0 mg/mL, urine inulin is 125 mg/mL, and urine flow is 1.0 mL/min. What is the estimated GFR?

- A.** Approximately 125 mL/min, ignoring urine flow in the clearance equation
- B.** Approximately 125 mL/min from the inulin clearance calculation
- C.** Approximately 1.0 mL/min, using urine flow without urine concentration
- D.** Approximately 0.008 mL/min by inverting the concentration ratio
- E.** Approximately 125 mg/min, which is an excretion rate rather than a clearance

215. A healthy 55-year-old filters a large sodium load. Which nephron segment normally reabsorbs the largest fraction of filtered sodium and water under baseline conditions?

- A.** The thin descending limb is the principal active sodium-reabsorbing segment of the nephron
- B.** The distal convoluted tubule normally reabsorbs two thirds of filtered sodium before the loop of Henle
- C.** The thick ascending limb reabsorbs virtually all filtered sodium and water together
- D.** The proximal tubule reabsorbs roughly two thirds of filtered sodium and water iso-osmotically
- E.** The collecting duct reabsorbs most filtered sodium regardless of aldosterone activity

216. A healthy ventricle is filled to an end-diastolic volume of 120 mL, greater than its prior baseline, without a change in inotropy. Which cellular mechanism contributes to the increased force of contraction?

- A.** Greater preload closes L-type calcium channels and reduces cytosolic calcium availability
- B.** Myocardial force is independent of starting fiber length within the physiologic range
- C.** Greater initial sarcomere length improves force generation over the physiologic range of the Frank-Starling relation
- D.** Increased filling immediately creates new contractile proteins before the next heartbeat
- E.** The ventricle must decrease calcium sensitivity whenever end-diastolic volume rises

217. A 54-year-old loses 1 L of pure water through insensible losses without replacing it. Which compartment change is expected after osmotic equilibration?

- A.** Both compartments expand because sodium concentration rises after water loss
- B.** Only extracellular volume falls because water cannot cross cell membranes
- C.** Intracellular volume rises while extracellular volume remains unchanged
- D.** Extracellular osmolality falls and water shifts into cells, expanding intracellular volume
- E.** Extracellular osmolality rises and water shifts out of cells, so both intracellular and extracellular volumes decrease

218. A localized inflammatory mediator increases capillary permeability in the forearm of a 71-year-old. Which Starling-force change most directly favors movement of fluid into the interstitium?

- A.** Loss of plasma proteins into the interstitium lowers the effective plasma oncotic gradient opposing filtration
- B.** Reduced hydraulic conductivity of the capillary wall directly increases transvascular water movement
- C.** A rise in plasma oncotic pressure pulls more water out of the capillary and increases edema
- D.** A fall in capillary hydrostatic pressure is the principal driver of increased filtration
- E.** A fall in interstitial oncotic pressure draws fluid from plasma into the tissue

219. A critically ill 52-year-old has oxygen delivery reduced below the level required for tissue demand. Which relationship best defines systemic oxygen delivery?

- A.** Oxygen delivery equals cardiac output multiplied by arterial oxygen content
- B.** Oxygen delivery is determined solely by alveolar ventilation once saturation exceeds 90%
- C.** Oxygen delivery depends only on hemoglobin concentration and is independent of blood flow
- D.** Oxygen delivery equals mixed venous oxygen content divided by cardiac output
- E.** Oxygen delivery equals arterial PO₂ multiplied by respiratory rate alone

220. A 24-year-old develops a primary respiratory acidosis from acute hypoventilation. Which immediate buffer response occurs before renal compensation becomes important?

- A.** The kidneys instantly generate enough new bicarbonate within seconds to normalize pH
- B.** Plasma proteins stop buffering because only bicarbonate can bind hydrogen ions
- C.** Nonbicarbonate buffers accept hydrogen ions as carbon dioxide-derived acid increases
- D.** Pulmonary excretion of fixed acid increases despite the ongoing hypoventilation
- E.** Hemoglobin releases hydrogen ions and thereby amplifies the fall in pH as the principal buffering response

221. In a person with an intact hypothalamic-pituitary-thyroid axis, free T₄ and T₃ are experimentally raised above the physiologic set point. What feedback response is expected?

- A.** TSH rises while TRH falls because thyroid hormone feedback acts only at the hypothalamus

- B.** TRH and TSH both increase because thyroid hormone positively feeds back on pituitary thyrotrophs
- C.** TRH and TSH secretion decrease through negative feedback by thyroid hormone
- D.** Calcitonin rises and becomes the principal regulator of pituitary TSH secretion
- E.** TRH rises while TSH remains fixed because pituitary secretion is independent of thyroid hormone

222. A 52-year-old briefly contacts a hot surface and experiences sharp, well-localized pain followed by slower burning pain. Which fiber type carries the initial fast pain signal most prominently?

- A.** Large A-alpha motor fibers are the principal nociceptors for fast cutaneous pain
- B.** Unmyelinated C fibers conduct the earliest sharp pain faster than all myelinated fibers
- C.** Group Ia proprioceptive fibers carry the main signal from free nerve ending nociceptors
- D.** Postganglionic sympathetic fibers transmit the conscious sensory component of fast pain
- E.** Thinly myelinated A-delta fibers conduct the initial sharp pain relatively rapidly

223. A 54-year-old develops acute bacterial pneumonia. Circulating neutrophils first slow and roll along activated venular endothelium before firm adhesion and transmigration. Which class of adhesion molecules is most important for the rolling step?

- A.** Immunoglobulins secreted into plasma tether neutrophils directly to collagen
- B.** Complement C3b provides the principal mechanical bond for leukocyte rolling on endothelium
- C.** Cadherins on erythrocytes are the dominant receptors for neutrophil rolling
- D.** Selectins mediate transient leukocyte-endothelial interactions that produce rolling
- E.** Integrins mediate the earliest weak rolling interactions before selectin expression

224. A seated subject is suddenly accelerated right. Which sensory structure primarily detects angular acceleration of the head?

- A.** Middle-ear ossicles directly stimulate vestibular afferents whenever the head rotates

- B.** Hair cells in the cristae of the semicircular canals respond to endolymph-driven deflection of the cupula
- C.** Semicircular canals primarily encode static head position relative to gravity through otoconia
- D.** Macular hair cells of the cochlea respond to angular acceleration through the tectorial membrane
- E.** Otolith organs detect only sound frequency and do not participate in vestibular sensation

225. A 79-year-old develops a primary respiratory acidosis from acute hypoventilation. Which immediate buffer response occurs before renal compensation becomes important?

- A.** The kidneys instantly generate enough new bicarbonate within seconds to normalize pH
- B.** Nonbicarbonate buffers accept hydrogen ions as carbon dioxide-derived acid increases
- C.** Pulmonary excretion of fixed acid increases despite the ongoing hypoventilation
- D.** Hemoglobin releases hydrogen ions and thereby amplifies the fall in pH as the principal buffering response
- E.** Plasma proteins stop buffering because only bicarbonate can bind hydrogen ions

226. A healthy 22-year-old receives exogenous cortisol for several days at a dose that raises free cortisol well above normal. What happens to the hypothalamic-pituitary-adrenal axis?

- A.** CRH rises while ACTH falls because cortisol feeds back only at the pituitary
- B.** CRH and ACTH rise because cortisol positively feeds back to maintain adrenal stimulation
- C.** ACTH rises while CRH remains unchanged because cortisol has no pituitary feedback effect
- D.** CRH and ACTH fall because glucocorticoids exert negative feedback at hypothalamic and pituitary levels
- E.** The axis is unaffected because exogenous glucocorticoid cannot participate in feedback signaling

227. A 60-year-old receives an alpha-1 agonist that constricts systemic veins. Which immediate effect most directly increases cardiac preload?

- A.** Reduced venous capacitance shifts blood from the peripheral venous reservoir toward the heart
- B.** Increased venous capacitance stores more blood peripherally and raises central venous return

- C.** Ven constriction lowers mean systemic filling pressure and therefore reduces the gradient for venous return
- D.** Venous smooth muscle has negligible influence on stressed blood volume and preload
- E.** Arteriolar dilation lowers capillary pressure and directly increases ventricular end-diastolic volume

228. A mildly dehydrated 65-year-old has plasma osmolality near 310 mOsm/kg and rising vasopressin. What is the major renal action of vasopressin in the collecting duct?

- A.** V1-receptor signaling removes aquaporin-2 channels from principal cells and increases free-water excretion
- B.** V2-receptor signaling inserts aquaporin-2 channels into the apical membrane of principal cells
- C.** Vasopressin stimulates sodium-glucose cotransport in the proximal tubule as its main antidiuretic mechanism
- D.** Vasopressin directly closes basolateral aquaporins so water is trapped inside principal cells
- E.** Vasopressin blocks the medullary osmotic gradient and thereby produces maximally dilute urine

229. A chronic physiologic disorder becomes more survivable because therapy extends life but does not change the rate at which new cases arise. What happens to prevalence?

- A.** Prevalence is determined only by incidence and is independent of disease duration
- B.** Incidence must increase by the same proportion as survival
- C.** Prevalence tends to increase because affected individuals remain in the population for a longer duration
- D.** Both incidence and prevalence immediately fall to zero when mortality decreases
- E.** Prevalence decreases because longer survival removes affected individuals from the denominator

230. A healthy 45-year-old begins dynamic aerobic exercise. Which cardiovascular pattern is expected as workload rises?

- A.** Cardiac output falls while systemic vascular resistance rises uniformly in every vascular bed

- B.** Mean arterial pressure collapses because local muscle vasodilation cannot be offset by higher cardiac output
- C.** Heart rate falls because vagal tone increases in proportion to exercise intensity
- D.** Cardiac output increases while systemic vascular resistance usually falls because active skeletal muscle vasodilates
- E.** Skeletal-muscle blood flow falls so that coronary and cerebral perfusion can be maintained

231. A competent adult is about to undergo an invasive physiologic study with material risks and alternatives. What is the best approach to informed consent?

- A.** Ask the family to decide even though the patient has decision-making capacity and is available
- B.** Withhold uncommon but serious material risks because discussing them could make the patient anxious
- C.** Explain the nature, benefits, material risks, alternatives, and option of no procedure, assess understanding, and obtain a voluntary decision
- D.** Obtain a signature without discussing alternatives because the written form itself establishes informed consent
- E.** Proceed once the clinician believes the study is beneficial because beneficence overrides a competent refusal

232. A 28-year-old forms a clot and then activates the endothelial thrombomodulin-protein C anticoagulant pathway. Activated protein C, with protein S as a cofactor, primarily limits coagulation by inactivating which factors?

- A.** Factors IIa and Xa by direct irreversible proteolysis as its principal action
- B.** Fibrin and fibrinogen through the same mechanism as plasmin
- C.** Factors Va and VIIIa, under the physiologic conditions described
- D.** Factors VIIa and tissue factor at the endothelial surface
- E.** Factors XIa and XIIa at the start of the contact pathway

233. A healthy 72-year-old absorbs dietary nonheme iron. Which condition generally favors iron uptake by duodenal enterocytes?

- A.** An acidic lumen and reduction of ferric iron to the ferrous form facilitate apical uptake
- B.** An alkaline lumen that keeps ferric iron insoluble at the brush border
- C.** Complete oxidation of ferrous iron to ferric iron before DMT1 can transport it
- D.** Binding of iron to intrinsic factor before transport through the terminal ileum
- E.** High hepcidin concentrations that increase ferroportin-mediated export into plasma

234. A healthy adult male receives a brief physiologic increase in FSH with otherwise intact gonadal signaling. Which Sertoli-cell response is expected?

- A.** Conversion of all testosterone to estrogen so intratesticular androgen concentration falls
- B.** Release of GnRH into the testicular circulation as the main feedback signal
- C.** Support of spermatogenesis together with increased production of androgen-binding protein and inhibin B
- D.** Suppression of seminiferous-tubule function so germ cells remain quiescent
- E.** Direct production of most circulating testosterone from cholesterol within Sertoli cells

235. A 44-year-old has a heart rate of 90/min and a stroke volume of 65 mL/beat. What is the approximate cardiac output?

- A.** 2.9 L/min, after dividing the product by an additional factor of two
- B.** 0.72 L/min, calculated by dividing stroke volume by heart rate
- C.** 155 L/min, calculated by adding heart rate and stroke volume numerically
- D.** 5.8 L/min, calculated as heart rate multiplied by stroke volume
- E.** 11.7 L/min, after doubling the stroke volume contribution

236. A patient becomes tearful after hearing that a physiologic abnormality may indicate serious disease. What communication strategy is most appropriate at that moment?

- A.** Ask a family member to take over the conversation even though the patient wants to continue
- B.** Change the subject to avoid reinforcing distress and return to the diagnosis at the next visit
- C.** Acknowledge the emotion, allow a pause, assess the patient's understanding and priorities, and then continue in manageable pieces
- D.** Reassure the patient that everything will definitely be fine before discussing uncertainty
- E.** Immediately deliver all remaining technical details without pausing so the patient receives complete information at once

237. A healthy 30-year-old hypoventilates for several minutes and PaCO_2 rises. Which sensors provide the dominant ventilatory drive from this acute rise in CO_2 under ordinary conditions?

- A.** Central chemoreceptors directly sense arterial oxygen content rather than carbon dioxide-derived hydrogen ion
- B.** Central chemoreceptors respond to increased brain extracellular hydrogen ion generated from diffused CO_2
- C.** Cortical motor neurons automatically normalize PaCO_2 without medullary chemosensory input
- D.** Carotid body chemoreceptors are completely insensitive to carbon dioxide and pH
- E.** Pulmonary stretch receptors provide the primary minute-to-minute response to arterial CO_2

238. A 41-year-old experiences a sudden decrease in ambient temperature. Which combination best describes the coordinated cold-defense response?

- A.** Cutaneous vasodilation conserves heat while sweating increases metabolic heat production
- B.** Vagal stimulation of skeletal muscle produces shivering while sympathetic tone is suppressed
- C.** Cutaneous vasoconstriction conserves heat while shivering and sympathetic metabolic responses increase heat production
- D.** Sweating and reduced muscle activity are the primary responses to prevent further cooling
- E.** Cold exposure lowers thyroid and catecholamine effects to minimize oxygen consumption

239. A 45-year-old has emphysematous destruction. Which change in static lung mechanics is expected?

- A.** Elastic recoil increases, raising expiratory driving pressure and reducing air trapping
- B.** Compliance falls while total lung capacity typically rises because recoil is stronger
- C.** Lung compliance increases because elastic recoil is reduced
- D.** Static pressure-volume behavior is unchanged because alveolar walls do not contribute to recoil
- E.** Lung compliance decreases because collagen deposition stiffens the parenchyma

240. A 76-year-old has normal dietary vitamin B12 intake. Which sequence is required for efficient physiologic absorption of cobalamin?

- A.** Cobalamin is absorbed directly in the stomach through parietal-cell H⁺/K⁺ ATPase
- B.** Cobalamin binds intrinsic factor and the complex is taken up by specific receptors in the terminal ileum
- C.** Cobalamin binds bile salts and is absorbed primarily through SGLT1 in the duodenum
- D.** Cobalamin requires pancreatic lipase but not intrinsic factor for terminal ileal uptake
- E.** Cobalamin binds transferrin and enters jejunal enterocytes through iron transporters

241. A 28-year-old develops extracellular hyperkalemia acutely. Which transcellular mechanism can move potassium into cells within minutes?

- A.** Alpha-adrenergic stimulation is the principal mechanism driving potassium into cells during hyperkalemia
- B.** Insulin stimulates cellular potassium uptake in part by increasing Na⁺/K⁺ ATPase activity
- C.** Hypertonicity always shifts potassium into cells and is therefore used to treat hyperkalemia
- D.** Aldosterone immediately moves most extracellular potassium into skeletal muscle without requiring renal excretion
- E.** Metabolic acidosis from mineral acid reliably drives potassium into cells through hydrogen-potassium exchange

242. A healthy adult has a transient rise in plasma potassium to 5.5 mEq/L. Which adrenal response helps restore potassium balance?

- A.** Increased ACTH is required as the dominant minute-to-minute controller of aldosterone during hyperkalemia
- B.** Hyperkalemia inhibits zona glomerulosa depolarization and therefore prevents aldosterone release
- C.** Increased cortisol secretion directly blocks ENaC and raises urinary potassium excretion
- D.** Suppression of aldosterone increases collecting-duct potassium secretion
- E.** Direct stimulation of zona glomerulosa aldosterone secretion increases distal potassium secretion

243. A healthy 77-year-old stands abruptly. Venous pooling transiently lowers arterial pressure. Which reflex response occurs within seconds?

- A.** Reduced baroreceptor firing increases vagal tone to the sinoatrial node and slows heart rate
- B.** Reduced carotid and aortic baroreceptor firing increases sympathetic and decreases parasympathetic outflow
- C.** Arterial pressure is restored mainly by erythropoietin release rather than autonomic changes
- D.** Increased baroreceptor firing suppresses sympathetic tone and further lowers vascular resistance
- E.** The reflex immediately lowers venous tone so that peripheral blood storage increases

244. Insulin rises after a mixed meal in a healthy 47-year-old. Which tissue response is mediated in part by translocation of GLUT4 to the cell membrane?

- A.** Increased glucose uptake in neurons through insulin-dependent GLUT3 translocation
- B.** Increased renal proximal glucose reabsorption through insertion of GLUT4 into the brush border
- C.** Increased glucose uptake in skeletal muscle and adipose tissue
- D.** Reduced glucose entry into adipocytes to preserve circulating substrate for the brain
- E.** Increased glucose uptake in hepatocytes because GLUT2 must translocate in response to insulin

245. Researchers want to determine whether a new exercise intervention causes a change in maximal oxygen uptake. Which design best minimizes measured and unmeasured baseline confounding when feasible?

- A.** Random assignment to intervention and control groups with prospective outcome measurement
- B.** A case-control study that selects participants based on high or low oxygen uptake after the fact
- C.** An ecological comparison of cities with different average exercise participation rates
- D.** A cross-sectional survey measuring current exercise habits and oxygen uptake at one time point
- E.** A case series of participants who chose the intervention and improved afterward

246. During normal puberty, pulsatile hypothalamic GnRH secretion increases. Which response is expected if GnRH instead becomes continuously elevated without pulsatility?

- A.** Pituitary LH and FSH secretion rises continuously without loss of responsiveness
- B.** Hypothalamic GnRH neurons become the primary source of circulating gonadotropins
- C.** Pituitary GnRH receptors become desensitized, reducing LH and FSH secretion over time
- D.** Gonadal steroid production increases indefinitely because receptor signaling is sustained
- E.** Pituitary prolactin secretion replaces LH and FSH as the main gonadal stimulus

247. A dietary protein is being digested in the small intestine of a 46-year-old. How are many dipeptides and tripeptides taken up across the apical enterocyte membrane?

- A.** They diffuse only through tight junctions because enterocytes lack peptide transporters
- B.** They are cotransported with chloride by CFTR and remain intact in portal blood
- C.** They use the same sodium-glucose cotransporter responsible for glucose uptake
- D.** They require intrinsic factor and a terminal-ileal receptor before absorption
- E.** They are cotransported with hydrogen ions by PEPT1 and then hydrolyzed intracellularly

248. A localized inflammatory mediator increases capillary permeability in the forearm of a 34-year-old. Which Starling-force change most directly favors movement of fluid into the interstitium?

- A.** Loss of plasma proteins into the interstitium lowers the effective plasma oncotic gradient opposing filtration
- B.** A fall in capillary hydrostatic pressure is the principal driver of increased filtration

- C. A fall in interstitial oncotic pressure draws fluid from plasma into the tissue
- D. Reduced hydraulic conductivity of the capillary wall directly increases transvascular water movement
- E. A rise in plasma oncotic pressure pulls more water out of the capillary and increases edema

249. A healthy 50-year-old absorbs glucose from the small-intestinal lumen after a carbohydrate-rich meal. Which transporter mediates the principal apical uptake of glucose and galactose?

- A. SGLT1 cotransports sodium with glucose or galactose across the apical membrane
- B. GLUT2 cotransports sodium with glucose across the apical brush border under all conditions
- C. PEPT1 carries glucose together with small peptides across the apical membrane
- D. GLUT5 is the main apical transporter for both glucose and galactose
- E. The Na⁺/K⁺ ATPase directly transports luminal glucose into the enterocyte

250. A healthy 26-year-old exercises in an environment at 38 C with high radiant heat. Core temperature begins to rise. Which autonomic response is most important for increasing evaporative heat loss?

- A. Sympathetic alpha-1 stimulation of cutaneous vessels is the principal mechanism of evaporation
- B. Withdrawal of all sympathetic activity is sufficient to activate eccrine gland secretion directly
- C. Sympathetic cholinergic stimulation of eccrine sweat glands increases sweating
- D. Somatic motor stimulation of apocrine glands produces most thermoregulatory sweating
- E. Parasympathetic adrenergic stimulation of eccrine sweat glands increases sweating

251. In the late follicular phase, estradiol from a dominant follicle remains high for a sustained interval. Which pituitary response helps initiate the transition to ovulation?

- A. Progesterone from the corpus luteum produces the initial LH surge before the follicle ruptures
- B. Sustained high estradiol switches to positive feedback and produces the midcycle LH surge
- C. Inhibin B directly stimulates a large FSH surge that alone triggers ovulation

- D.** High estradiol maintains only negative feedback and therefore completely suppresses LH before ovulation
- E.** Prolactin becomes the dominant gonadotropin and causes follicular rupture

252. A sudden rise in aortic pressure increases left ventricular afterload in a 39-year-old, with preload and contractility initially unchanged. What is the immediate beat-to-beat effect?

- A.** End-systolic volume decreases and stroke volume increases because higher aortic pressure assists ejection
- B.** End-diastolic volume instantly falls to zero while ejection fraction remains unchanged
- C.** Contractility automatically rises enough on the same beat to maintain identical end-systolic volume
- D.** Stroke volume is unchanged because afterload affects only diastolic filling
- E.** End-systolic volume increases and stroke volume decreases because the ventricle ejects against a higher pressure

253. An isolated skeletal muscle from a 32-year-old is stimulated at different starting lengths. At which sarcomere condition is active force generally greatest?

- A.** At any sarcomere length because active force is independent of filament overlap
- B.** At extreme shortening where thin filaments completely overlap and compression is maximal
- C.** Only when the sarcomere is stretched beyond the point at which titin develops passive tension
- D.** At an intermediate length with near-optimal overlap of thick and thin filaments
- E.** At extreme stretch where actin and myosin no longer overlap but passive tension is absent

254. A healthy adult moves from sea level to an altitude of approximately 4200 m. After several days, which renal response contributes most directly to increased red cell production?

- A.** Reduced renal oxygen sensing suppresses erythropoietin and conserves iron stores
- B.** The liver becomes the exclusive source of erythropoietin in healthy adults after hypoxic exposure
- C.** Renal tubular cells increase thrombopoietin secretion, which secondarily raises erythrocyte production

- D.** Juxtaglomerular cells release erythropoietin in direct proportion to plasma renin activity
- E.** Hypoxia-inducible signaling in renal interstitial cells increases erythropoietin secretion

255. A 62-year-old with intact skin is acclimatizing to repeated exercise in the heat. Which adaptation typically improves thermoregulation after acclimatization?

- A.** Plasma volume contracts chronically, reducing the need for cardiovascular compensation during heat stress
- B.** Core temperature must rise to a higher threshold before any heat-dissipating response begins
- C.** Sweating begins earlier and becomes more effective, with better conservation of sodium in sweat
- D.** Cutaneous vasodilation is abolished so that central blood volume is never redistributed to skin
- E.** Sweating begins later and becomes more concentrated with sodium to preserve plasma water

256. A 38-year-old has a marked increase in left ventricular wall tension during systole. Why is coronary perfusion of the left ventricular subendocardium greatest during diastole rather than systole?

- A.** Myocardial oxygen consumption falls to zero during systole, eliminating the need for perfusion
- B.** Left coronary blood flow is driven mainly by right atrial pressure rather than aortic pressure
- C.** The aortic valve closes coronary ostia during systole and opens them only in diastole
- D.** Systolic myocardial compression limits intramural coronary flow, especially in the subendocardium
- E.** Coronary arterioles actively constrict whenever ventricular pressure rises above atrial pressure

257. A 34-year-old with fever to 39.0 C and lactic acidosis has active skeletal muscle consuming oxygen rapidly. Which change in the hemoglobin-oxygen dissociation curve is expected in the affected tissues?

- A.** A rightward shift that reduces oxygen unloading and preserves arterial saturation
- B.** A lower P50 that increases hemoglobin affinity for oxygen in metabolically active tissue
- C.** No shift because tissue pH changes alter only dissolved oxygen, not hemoglobin affinity
- D.** A leftward shift caused by increased hydrogen ion concentration and temperature

E. A rightward shift that facilitates oxygen unloading at a given PO₂

258. A 20-year-old has GFR 120 mL/min and renal plasma flow 600 mL/min. What is the filtration fraction?

- A. Approximately 0.72, based on the sum of the two flow rates
- B. Approximately 0.80, representing the fraction of plasma not filtered
- C. Approximately 0.44, requiring hematocrit in the denominator even though RPF is already plasma flow
- D. Approximately 0.20, because filtration fraction equals GFR divided by renal plasma flow
- E. Approximately 5.0, because renal plasma flow divided by GFR is the filtration fraction

259. A healthy adult is quietly seated. Compared with the lung base, which statement about the lung apex is most accurate?

- A. The apex has a lower V/Q ratio because ventilation falls more steeply than perfusion toward the apex
- B. The apex has a higher V/Q ratio because perfusion falls more steeply than ventilation from base to apex
- C. The apex behaves as a true right-to-left shunt with perfusion but no ventilation
- D. The apex and base have identical V/Q ratios because gravity affects ventilation and perfusion equally
- E. The base has negligible blood flow because pulmonary arterial pressure is lowest there

260. A protein-rich meal enters the stomach of a healthy 61-year-old. Which stimulus most directly promotes gastrin release from antral G cells?

- A. Very low antral pH directly stimulates gastrin release through somatostatin-independent signaling
- B. Secretin from the duodenum is the main physiologic trigger for antral gastrin secretion
- C. Vagal acetylcholine acts only on parietal cells and has no pathway influencing G cells
- D. Gastric distention suppresses gastrin release so acid output remains unchanged after meals

E. Luminal peptides and vagal gastrin-releasing peptide stimulate G cells

261. A 29-year-old forms a clot and then activates the endothelial thrombomodulin-protein C anticoagulant pathway. Activated protein C, with protein S as a cofactor, primarily limits coagulation by inactivating which factors?

- A. Factors VIIa and tissue factor at the endothelial surface
- B. Factors Va and VIIIa, under the physiologic conditions described
- C. Fibrin and fibrinogen through the same mechanism as plasmin
- D. Factors IIa and Xa by direct irreversible proteolysis as its principal action
- E. Factors XIa and XIIa at the start of the contact pathway

262. A 53-year-old develops acute bacterial pneumonia. Circulating neutrophils first slow and roll along activated venular endothelium before firm adhesion and transmigration. Which class of adhesion molecules is most important for the rolling step?

- A. Immunoglobulins secreted into plasma tether neutrophils directly to collagen
- B. Cadherins on erythrocytes are the dominant receptors for neutrophil rolling
- C. Complement C3b provides the principal mechanical bond for leukocyte rolling on endothelium
- D. Selectins mediate transient leukocyte-endothelial interactions that produce rolling
- E. Integrins mediate the earliest weak rolling interactions before selectin expression

263. A 71-year-old with acute hemorrhage loses enough blood to lower effective arterial blood volume. Which early compensatory response is expected before substantial fluid replacement?

- A. Renin and vasopressin are suppressed so the kidneys can excrete sodium and water
- B. Sympathetic activation raises heart rate and vascular tone while renin and vasopressin promote volume conservation
- C. Systemic veins dilate to store additional blood in the peripheral circulation
- D. Baroreceptor firing rises and suppresses sympathetic tone to prevent tachycardia
- E. Atrial natriuretic peptide rises because atrial stretch increases despite hemorrhage

264. During quick elbow extension, a muscle is suddenly lengthened. Which sensory receptor and afferent fiber most directly signal the dynamic change in muscle length that initiates the stretch reflex?

- A.** Free nerve endings carried only by group IV fibers
- B.** Pacinian corpuscles carried mainly by unmyelinated C fibers
- C.** Muscle spindle primary endings carried mainly by group Ia afferent fibers
- D.** Ruffini endings in skin carried mainly by autonomic postganglionic fibers
- E.** Golgi tendon organs carried mainly by group Ib afferent fibers

265. A lactating 28-year-old has increased nipple stimulation during nursing. Which hypothalamic change permits prolactin secretion to rise?

- A.** Nipple stimulation suppresses prolactin and acts only through oxytocin
- B.** Reduced hypothalamic dopamine delivery removes tonic inhibition of pituitary lactotrophs
- C.** GnRH secretion rises and acts directly on lactotrophs as the main prolactin-releasing signal
- D.** Somatostatin becomes the primary prolactin-releasing hormone during nursing
- E.** Increased hypothalamic dopamine directly stimulates lactotroph D2 receptors to release prolactin

266. A neuron in a 66-year-old reaches threshold at the axon initial segment. Which ionic event produces the rapid upstroke of a typical neuronal action potential?

- A.** Closing of all potassium leak channels is the sole mechanism that creates the action potential
- B.** Opening of voltage-gated potassium channels causes the initial rapid depolarizing current
- C.** Activation of the sodium-potassium ATPase directly produces the millisecond depolarizing upstroke
- D.** Opening of ligand-gated chloride channels creates regenerative depolarization at the initial segment
- E.** Opening of voltage-gated sodium channels causes a large inward sodium current

267. A lucid adult understands the risks of refusing a recommended physiologic evaluation, can explain the consequences, and consistently declines. What should the clinician do?

- A.** Declare the patient incapacitated solely because the patient disagrees with the medical recommendation
- B.** Ask a family member to consent on the patient's behalf despite intact decision-making capacity
- C.** Ask hospital security to detain the patient until the test is completed
- D.** Respect the informed refusal after addressing questions, alternatives, and reversible barriers to the decision
- E.** Override the refusal because a clinician may compel any test believed to be medically useful

268. A 35-year-old is exposed to cold wind. Which response most directly reduces dry heat loss from the skin during the initial autonomic response?

- A.** Cutaneous vasodilation increases the insulating effect of subcutaneous tissue
- B.** Sweating increases and forms an insulating water layer over the skin
- C.** Shivering lowers core heat production while blood is redirected to the skin
- D.** Piloerection in humans provides the dominant reduction in convective heat loss
- E.** Cutaneous vasoconstriction reduces warm blood flow to the skin surface

269. A patient with acute blood loss has intact kidneys and adequate iron stores. Approximately 6 days later, the bone marrow response is being assessed. Which peripheral blood finding best reflects an appropriate erythropoietin-driven marrow response?

- A.** An immediate increase in mature erythrocyte number within minutes of hemorrhage
- B.** An increased reticulocyte fraction as newly produced erythrocytes enter the circulation
- C.** A rise in neutrophils that directly substitutes for reduced oxygen-carrying capacity
- D.** An increase in platelet size that is the principal marker of erythroid marrow recovery
- E.** A marked fall in reticulocytes because erythropoietin suppresses release of immature cells

270. Insulin rises after a mixed meal in a healthy 63-year-old. Which tissue response is mediated in part by translocation of GLUT4 to the cell membrane?

- A.** Reduced glucose entry into adipocytes to preserve circulating substrate for the brain

- B.** Increased renal proximal glucose reabsorption through insertion of GLUT4 into the brush border
- C.** Increased glucose uptake in hepatocytes because GLUT2 must translocate in response to insulin
- D.** Increased glucose uptake in skeletal muscle and adipose tissue
- E.** Increased glucose uptake in neurons through insulin-dependent GLUT3 translocation

271. At a normal neuromuscular junction, acetylcholine released from a motor neuron binds the postsynaptic motor end plate. Which ionic event creates the local end-plate potential?

- A.** Acetylcholine opens muscarinic potassium channels and hyperpolarizes the motor end plate
- B.** Acetylcholine directly opens skeletal-muscle voltage-gated calcium channels before any depolarization
- C.** Acetylcholine inhibits sodium entry and makes the end-plate potential more negative
- D.** Acetylcholine activates G-protein signaling that releases calcium from the sarcoplasmic reticulum without membrane current
- E.** Acetylcholine opens nicotinic cation channels, producing a net inward depolarizing current

272. A 67-year-old has a small vascular injury with exposed subendothelial collagen. Which interaction is most important for initial platelet adhesion under high shear conditions?

- A.** Protein C binds platelet glycoprotein IIb/IIIa and creates the first platelet monolayer
- B.** von Willebrand factor links exposed subendothelium to platelet glycoprotein Ib
- C.** Fibrinogen links platelet glycoprotein IIb/IIIa directly to intact endothelial cells
- D.** Plasmin bridges platelet receptors to collagen and initiates primary hemostasis
- E.** Thrombin binds platelet glycoprotein Ib and anchors platelets to collagen without von Willebrand factor

273. A low-dose para-aminohippurate infusion is used to estimate renal plasma flow in a healthy 75-year-old. Why can PAH clearance approximate effective renal plasma flow?

- A.** PAH clearance equals GFR because PAH is filtered but neither secreted nor reabsorbed

- B.** PAH is filtered and avidly secreted so most PAH entering the renal circulation is removed in one pass
- C.** PAH remains confined to erythrocytes and therefore measures renal blood flow directly
- D.** PAH is completely reabsorbed after filtration, so none appears in renal venous blood
- E.** PAH is synthesized by the kidney in proportion to renal plasma flow

274. A highly sensitive physiologic screening test is used in a population where disease prevalence falls substantially while test characteristics remain unchanged. What generally happens to positive predictive value?

- A.** Positive predictive value increases automatically when prevalence falls
- B.** Positive predictive value remains fixed because it depends only on sensitivity
- C.** Positive predictive value becomes identical to specificity at low prevalence
- D.** Positive predictive value is unaffected by pretest probability or population selection
- E.** Positive predictive value decreases because false positives make up a larger share of positive tests when prevalence is low

275. A 68-year-old has a small vascular injury with exposed subendothelial collagen. Which interaction is most important for initial platelet adhesion under high shear conditions?

- A.** Thrombin binds platelet glycoprotein Ib and anchors platelets to collagen without von Willebrand factor
- B.** von Willebrand factor links exposed subendothelium to platelet glycoprotein Ib
- C.** Protein C binds platelet glycoprotein IIb/IIIa and creates the first platelet monolayer
- D.** Fibrinogen links platelet glycoprotein IIb/IIIa directly to intact endothelial cells
- E.** Plasmin bridges platelet receptors to collagen and initiates primary hemostasis

276. A 70-year-old develops an acute pulmonary embolus that blocks perfusion to a ventilated lung region. What is the local gas-exchange consequence?

- A.** The affected alveoli contribute more carbon dioxide elimination because capillary blood flow rises

- B.** Alveolar gas rapidly equilibrates with mixed venous blood because perfusion is increased
- C.** The regional V/Q ratio falls toward zero, creating a pure shunt
- D.** Both ventilation and perfusion rise proportionally so V/Q remains unchanged
- E.** The regional V/Q ratio rises toward infinity, increasing physiologic dead-space ventilation

277. A 61-year-old performs repeated sprint exercise and skeletal-muscle lactate production rises. Which statement best describes lactate physiology during intense exercise?

- A.** Lactate can be exported and used as an oxidative fuel or recycled by the liver rather than being merely a waste product
- B.** Lactate is produced only when tissue oxygen tension reaches absolute zero
- C.** The liver cannot metabolize lactate and therefore relies exclusively on renal excretion
- D.** Lactate formation irreversibly traps all pyruvate and prevents any later oxidative metabolism
- E.** Lactate itself is the sole chemical cause of delayed-onset muscle soreness days later

278. An adolescent requests confidential counseling about reproductive physiology and contraception. There is no sign of abuse, coercion, or immediate danger. What is the best communication approach?

- A.** Document no history so the encounter cannot later be discovered by anyone, under the physiologic conditions described
- B.** Explain the usual scope and limits of confidentiality, encourage supportive family involvement when appropriate, and provide care consistent with applicable rules
- C.** Promise absolute confidentiality under every possible circumstance before asking any safety questions
- D.** Refuse to discuss contraception because adolescents cannot participate in confidential health decisions
- E.** Disclose the visit immediately to parents without first discussing confidentiality with the adolescent

279. A 31-year-old mounts an antibody response to an encapsulated bacterium. Complement is activated on the microbial surface. Which complement product most directly acts as a major opsonin that enhances phagocytosis?

- A.** C3b deposited on the microbial surface, where it is recognized by complement receptors on phagocytes
- B.** C5a incorporated into the membrane attack complex as the major opsonin
- C.** Factor H covalently bound to bacteria to promote complement receptor recognition
- D.** C9 released into plasma as the dominant chemotactic signal for neutrophils
- E.** C3a deposited on the microbial surface as the principal phagocytic ligand

280. A healthy 68-year-old stands suddenly after lying supine. Baroreceptor unloading increases sympathetic outflow. Which receptor-mediated response most directly raises heart rate?

- A.** Epinephrine acting at beta-2 receptors is the only autonomic mechanism capable of changing heart rate
- B.** Norepinephrine acting at beta-1 receptors in the sinoatrial node increases pacemaker current and cAMP signaling
- C.** Norepinephrine acting at nicotinic receptors directly depolarizes ventricular myocytes to set the heart rate
- D.** Norepinephrine acting at alpha-1 receptors in the sinoatrial node opens potassium channels and slows phase 4 depolarization
- E.** Acetylcholine acting at M2 receptors increases cAMP and accelerates sinoatrial nodal firing

Answers

1. A. The basilar membrane is tonotopically organized: the stiff, narrow base responds best to high frequencies, whereas the wider, more compliant apex responds best to low frequencies. Place of maximal vibration therefore contributes importantly to frequency encoding.

2. A. TSH acts through a Gs-cAMP pathway on follicular cells to stimulate multiple steps in thyroid hormone production, including iodide uptake, thyroglobulin synthesis/processing, and release of T4 and T3.

- 3. E.** Capacity can fluctuate and should be assessed for the specific decision. Nonurgent decisions can often wait until reversible impairment improves; if a decision is urgent and capacity is absent, an appropriate surrogate or emergency exception is used according to the circumstances.
- 4. D.** Qualified medical interpreters improve accuracy, confidentiality, and patient participation for complex care. The clinician should address the patient directly, use clear language, and verify understanding rather than making a family member the default interpreter.
- 5. C.** Glucagon rises during fasting and signals hepatocytes through Gs-cAMP pathways to support glycogenolysis, gluconeogenesis, and ketogenesis while reducing glycolytic flux. These actions help preserve circulating glucose for glucose-dependent tissues.
- 6. E.** Insulin promotes cellular K⁺ uptake, especially in skeletal muscle, through effects including stimulation of Na⁺/K⁺ ATPase. Beta-2 adrenergic stimulation can also shift K⁺ into cells, whereas aldosterone is especially important for renal potassium excretion over a longer time scale.
- 7. E.** Autonomy does not obligate clinicians to provide interventions whose expected harms outweigh benefits. Shared decision-making starts by understanding the patient's goals and concerns, then communicating probabilities and proposing appropriate alternatives.
- 8. B.** Fever represents a regulated increase in the hypothalamic set point. Until body temperature reaches that higher target, the nervous system interprets the body as relatively cold and activates vasoconstriction, behavioral warming, and shivering.
- 9. B.** Lowering a positivity threshold usually captures more true cases, increasing sensitivity, but also labels more unaffected people positive, decreasing specificity. ROC analysis displays this threshold-dependent tradeoff.
- 10. E.** Positive inotropy raises the pressure generated at any end-systolic volume, steepening the end-systolic pressure-volume relationship. With preload and afterload unchanged, the ventricle empties more completely, decreasing ESV and increasing stroke volume.
- 11. E.** CCK is released from small-intestinal I cells in response to fats and amino acids. It stimulates pancreatic enzyme secretion and gallbladder contraction, facilitates biliary delivery, and slows gastric emptying to match delivery with digestive capacity.
- 12. B.** A fall in ionized calcium activates parathyroid chief cells to release PTH. PTH conserves calcium, promotes phosphaturia, stimulates calcitriol formation, and increases calcium mobilization from bone indirectly through osteoblast-lineage signaling.
- 13. E.** The basilar membrane is tonotopically organized: the stiff, narrow base responds best to high frequencies, whereas the wider, more compliant apex responds best to low frequencies. Place of maximal vibration therefore contributes importantly to frequency encoding.

- 14. E.** The thick ascending limb reabsorbs Na^+ , K^+ , and Cl^- through NKCC2 and is relatively water-impermeable. This separation of solute from water helps establish the medullary gradient while diluting the fluid delivered to the distal nephron.
- 15. D.** For laminar flow in a cylindrical vessel, resistance is proportional to $1/r^4$. Even a modest decrease in arteriolar radius can therefore produce a large increase in resistance and a major reduction in flow for the same pressure gradient.
- 16. D.** ATP binding to myosin lowers its affinity for actin and permits cross-bridge detachment. Without ATP, myosin remains tightly bound to actin, which is the molecular basis of rigor.
- 17. B.** The tendon tap stretches muscle spindles, increasing Ia afferent firing. Ia fibers make a direct excitatory synapse on alpha motor neurons supplying the same muscle, while reciprocal inhibition of antagonists occurs through an interneuron.
- 18. B.** Type I fibers are slow oxidative fibers with many mitochondria, rich capillary supply, and abundant myoglobin. They generate force more slowly but resist fatigue and are well suited to posture and endurance activity.
- 19. D.** Swallowing activates a coordinated motor program: the upper sphincter opens, a peristaltic wave moves down the esophagus, and inhibitory enteric/vagal pathways relax the lower esophageal sphincter ahead of the bolus.
- 20. C.** Isotonic saline adds volume to the extracellular compartment without materially changing extracellular osmolality, so there is little water shift across cell membranes. The added extracellular volume partitions between interstitial and plasma spaces according to their relative sizes.
- 21. A.** The immediate duty is to protect patients from an impaired clinician. The situation should then be addressed through appropriate supervisory, occupational health, wellness, or institutional mechanisms rather than ignored or managed solely through public confrontation.
- 22. A.** Absolute risk reduction is $0.20 - 0.10 = 0.10$. The number needed to treat is $1/0.10 = 10$ over the specified follow-up period.
- 23. E.** PT is especially sensitive to the extrinsic pathway, whose unique upstream factor is factor VII, while both PT and aPTT also depend on the common pathway. Isolated PT prolongation therefore points toward factor VII deficiency or impaired vitamin K-dependent factor activity before broader common-pathway defects appear.
- 24. C.** Syncytiotrophoblast-derived hCG has LH-like activity and rescues the corpus luteum from regression. Luteal progesterone supports the endometrium until the placenta becomes capable of adequate steroid production.
- 25. E.** PT is especially sensitive to the extrinsic pathway, whose unique upstream factor is factor VII, while both PT and aPTT also depend on the common pathway. Isolated PT prolongation therefore points

toward factor VII deficiency or impaired vitamin K-dependent factor activity before broader common-pathway defects appear.

26. B. Gas diffusion across a membrane is proportional to surface area, diffusion coefficient, and partial-pressure gradient, and inversely proportional to thickness. Thickening impairs diffusion; a larger area or pressure gradient can increase transfer when other variables are fixed.

27. D. Glucocorticoids suppress both hypothalamic CRH and pituitary ACTH. Sustained exogenous exposure can therefore reduce endogenous adrenal stimulation and, over time, cause adrenal cortical atrophy.

28. E. Fetal hemoglobin binds 2,3-BPG less avidly than adult hemoglobin, shifting the oxygen dissociation curve to the left. Its lower P50 and higher oxygen affinity facilitate transfer of oxygen from maternal to fetal blood across the placenta.

29. A. Lower extracellular K^+ makes the potassium equilibrium potential more negative. Because resting neuronal membranes are highly permeable to K^+ , the resting membrane potential generally hyperpolarizes, reducing excitability until compensatory changes occur.

30. D. Glucagon rises during fasting and signals hepatocytes through Gs-cAMP pathways to support glycogenolysis, gluconeogenesis, and ketogenesis while reducing glycolytic flux. These actions help preserve circulating glucose for glucose-dependent tissues.

31. D. As alveolar surface area decreases, surfactant becomes more concentrated and reduces surface tension. This limits the rise in collapsing pressure predicted by Laplace law and helps prevent small alveoli from emptying into larger ones.

32. E. Excitation-contraction coupling releases Ca^{2+} from the sarcoplasmic reticulum. Ca^{2+} binds troponin C, changing the troponin-tropomyosin complex so that myosin can interact cyclically with actin.

33. E. Nicotinic acetylcholine receptors are ligand-gated cation channels. At the resting potential, their opening causes a net inward current dominated by Na^+ influx, producing the end-plate potential that can trigger nearby voltage-gated Na^+ channels.

34. C. Reduced renal tissue oxygen tension stabilizes hypoxia-inducible factors in peritubular interstitial cells, increasing erythropoietin synthesis. Erythropoietin stimulates erythroid progenitors in bone marrow and increases reticulocyte production.

35. A. Threshold opens voltage-gated Na^+ channels, and the resulting inward Na^+ current rapidly depolarizes the membrane. Delayed opening of voltage-gated K^+ channels and Na^+ channel inactivation contribute to repolarization rather than the upstroke.

- 36. A.** Increased venous return raises ventricular end-diastolic volume and myocardial fiber stretch. At unchanged afterload and contractility, the Frank-Starling mechanism increases force of contraction and stroke volume, so the loop widens mainly through a rightward shift of end-diastolic volume.
- 37. B.** Peripheral chemoreceptors, especially the carotid bodies, respond strongly when arterial PO₂ falls below roughly the range where hemoglobin saturation declines steeply. Their afferent input increases ventilation rapidly at altitude.
- 38. A.** The midcycle LH surge initiates resumption of oocyte meiosis, luteinization, prostaglandin/protease activity, and follicular rupture. FSH rises more modestly and supports follicular processes but is not the principal trigger.
- 39. A.** Glucose metabolism increases the ATP/ADP ratio, closing KATP channels and depolarizing the beta-cell membrane. Voltage-gated Ca²⁺ channels then open, and the rise in intracellular Ca²⁺ triggers insulin-granule exocytosis.
- 40. D.** Swallowing activates a coordinated motor program: the upper sphincter opens, a peristaltic wave moves down the esophagus, and inhibitory enteric/vagal pathways relax the lower esophageal sphincter ahead of the bolus.
- 41. D.** Lower extracellular K⁺ makes the potassium equilibrium potential more negative. Because resting neuronal membranes are highly permeable to K⁺, the resting membrane potential generally hyperpolarizes, reducing excitability until compensatory changes occur.
- 42. E.** Isotonic saline adds volume to the extracellular compartment without materially changing extracellular osmolality, so there is little water shift across cell membranes. The added extracellular volume partitions between interstitial and plasma spaces according to their relative sizes.
- 43. A.** Gastrin secretion rises with peptides/amino acids, gastric distention, and vagal stimulation mediated importantly by gastrin-releasing peptide. Falling antral pH increases somatostatin release from D cells, which inhibits gastrin as a negative-feedback mechanism.
- 44. A.** Hemorrhage unloads arterial and cardiopulmonary stretch receptors, increasing sympathetic output and reducing vagal activity. Renin-angiotensin-aldosterone and vasopressin responses help preserve sodium, water, vascular tone, and perfusion pressure.
- 45. E.** The Fick principle states $VO_2 = \text{cardiac output} \times (\text{arterial O}_2 \text{ content} - \text{mixed venous O}_2 \text{ content})$. Because oxygen consumption is in mL/min and the oxygen-content difference is in mL/L, direct division gives cardiac output in L/min; here the result is 5.0 L/min.
- 46. B.** The tendon tap stretches muscle spindles, increasing Ia afferent firing. Ia fibers make a direct excitatory synapse on alpha motor neurons supplying the same muscle, while reciprocal inhibition of antagonists occurs through an interneuron.

- 47. D.** Filtration fraction is the fraction of renal plasma flow filtered at the glomerulus: $FF = GFR/RPF$. It is distinct from renal blood flow, which would additionally require correction for hematocrit.
- 48. A.** C3b covalently coats microbial surfaces and is recognized by complement receptors on phagocytes, making it a major opsonin. C3a and C5a are anaphylatoxins, C5a is strongly chemotactic, and C5b-9 forms the membrane attack complex.
- 49. C.** $SEM = SD/\sqrt{n}$. Increasing sample size fourfold doubles $\sqrt{n}$, so the standard error is halved if the underlying standard deviation remains similar.
- 50. C.** Suckling activates hypothalamic neurons whose axons release oxytocin from the posterior pituitary. Oxytocin contracts mammary myoepithelial cells, producing milk let-down; prolactin primarily supports milk production.
- 51. A.** Veins are highly compliant capacitance vessels. Sympathetic venoconstriction reduces capacitance and increases stressed volume and mean systemic filling pressure, shifting blood centrally and increasing the pressure gradient for venous return.
- 52. C.** Aeration of the lungs and the rise in alveolar oxygen tension reverse fetal hypoxic pulmonary vasoconstriction. Pulmonary vascular resistance falls rapidly, pulmonary blood flow increases, and this contributes to the normal pressure changes that close fetal shunts.
- 53. E.** Confidentiality is a core clinical obligation. For a competent adult, family involvement generally requires the patient's permission unless a recognized exception applies; confidentiality does not mean omitting accurate information from the medical record.
- 54. D.** The semicircular canals are specialized for angular acceleration. Head rotation causes relative endolymph movement and cupular deflection at the cristae; the utricle and saccule are more important for linear acceleration and head position relative to gravity.
- 55. A.** During eccentric contraction, active muscle generates tension while lengthening under an external load. Eccentric actions can produce high force at relatively low metabolic cost compared with concentric shortening.
- 56. E.** Syncytiotrophoblast-derived hCG has LH-like activity and rescues the corpus luteum from regression. Luteal progesterone supports the endometrium until the placenta becomes capable of adequate steroid production.
- 57. A.** Rods are highly light-sensitive and support scotopic vision, but convergence of many rods onto downstream neurons reduces spatial resolution. Cones dominate high-acuity and color vision, especially in the fovea, and photoreceptors hyperpolarize rather than depolarize in light.
- 58. E.** Fibrosis stiffens the lung, decreasing compliance and increasing elastic recoil. More pressure is required to achieve a given change in volume, and static lung volumes are often reduced.

- 59. A.** Duodenal acid stimulates S cells to release secretin. Secretin promotes bicarbonate-rich pancreatic and biliary secretions that neutralize gastric acid and create a more favorable pH for pancreatic enzymes.
- 60. A.** Both ventilation and perfusion are greater at the bases, but perfusion changes more steeply with gravity. Thus V/Q is relatively high at the apex and low at the base, contributing to regional differences in alveolar PO₂ and PCO₂.
- 61. D.** Alveolar ventilation is respiratory rate multiplied by the portion of each tidal breath that reaches gas-exchanging alveoli: $VA = RR \times (VT - VD)$. Total minute ventilation overestimates effective ventilation because part of each breath remains in dead space.
- 62. E.** FSH acts on Sertoli cells to support germ-cell development, promote androgen-binding protein, and increase inhibin B. High intratesticular testosterone generated by LH-stimulated Leydig cells is also essential for normal spermatogenesis.
- 63. A.** Nicotinic acetylcholine receptors are ligand-gated cation channels. At the resting potential, their opening causes a net inward current dominated by Na⁺ influx, producing the end-plate potential that can trigger nearby voltage-gated Na⁺ channels.
- 64. B.** Metabolic acidosis stimulates ventilation, lowering PaCO₂ and reducing the carbonic-acid component of the bicarbonate buffer system. Respiratory compensation cannot fully normalize pH and does not correct the underlying metabolic process.
- 65. B.** The thick ascending limb reabsorbs Na⁺, K⁺, and Cl⁻ through NKCC2 and is relatively water-impermeable. This separation of solute from water helps establish the medullary gradient while diluting the fluid delivered to the distal nephron.
- 66. D.** Larger samples reduce standard error and usually increase power to detect a specified true effect at a fixed alpha level. Higher power corresponds to a lower probability of type II error under the assumed alternative.
- 67. E.** Relative risk is incidence proportion in the exposed group divided by incidence proportion in the unexposed group. The risks are 0.10 and 0.05, giving an RR of 2.0.
- 68. E.** For laminar flow in a cylindrical vessel, resistance is proportional to $1/r^4$. Even a modest decrease in arteriolar radius can therefore produce a large increase in resistance and a major reduction in flow for the same pressure gradient.
- 69. B.** Progesterone dominates the luteal phase, raises basal body temperature modestly, and makes cervical mucus thicker and less penetrable. Estradiol predominates before ovulation and produces thinner, more stretchable cervical mucus.

- 70. B.** Type I fibers are slow oxidative fibers with many mitochondria, rich capillary supply, and abundant myoglobin. They generate force more slowly but resist fatigue and are well suited to posture and endurance activity.
- 71. D.** Golgi tendon organs are arranged in series with muscle fibers and respond strongly to active tension. Their group Ib afferents participate in spinal circuits that regulate force and can inhibit homonymous motor output when tension is excessive.
- 72. B.** Lactate formation regenerates cytosolic NAD^+ and supports high glycolytic flux. Lactate is shuttled among tissues, oxidized by muscle and heart, or converted back to glucose in the liver through the Cori cycle.
- 73. E.** Ventilation increases rapidly with exercise through central command, sensory feedback, and chemical control. In healthy people at moderate workloads, the rise in alveolar ventilation closely tracks CO_2 production, so arterial PCO_2 and PO_2 remain near resting values.
- 74. B.** Dopamine tonically inhibits prolactin secretion through D_2 receptors on lactotrophs. Suckling reduces dopaminergic inhibition, allowing prolactin to rise and support milk synthesis; suckling also triggers oxytocin for milk ejection.
- 75. C.** A high hematocrit increases whole-blood viscosity. In Poiseuille terms, higher viscosity increases resistance for a given vessel geometry, so severe erythrocytosis can impair flow despite increased oxygen-carrying capacity.
- 76. D.** Bile acids emulsify dietary lipid and form mixed micelles containing fatty acids, monoglycerides, cholesterol, and fat-soluble vitamins. Micelles permit these hydrophobic products to traverse the unstirred water layer to the enterocyte membrane.
- 77. E.** Case-control studies sample on outcome status, so population risks and incidence usually cannot be calculated directly. The odds ratio compares exposure odds in cases versus controls and approximates relative risk when the outcome is uncommon under appropriate conditions.
- 78. C.** Thrombin bound to thrombomodulin activates protein C. Activated protein C with protein S proteolytically inactivates factors Va and VIIIa, reducing amplification of thrombin generation and helping localize clotting.
- 79. A.** SGLT1 uses the inward sodium gradient, maintained by basolateral Na^+/K^+ ATPase, to absorb glucose and galactose. Fructose uses GLUT5 apically, and monosaccharides generally leave enterocytes through basolateral GLUT2.
- 80. A.** Excitation-contraction coupling releases Ca^{2+} from the sarcoplasmic reticulum. Ca^{2+} binds troponin C, changing the troponin-tropomyosin complex so that myosin can interact cyclically with actin.

- 81. D.** For a conventional two-sided analysis, a 95% CI for a difference that excludes zero corresponds to statistical significance near alpha 0.05. The interval describes uncertainty in the estimated population effect, not the distribution of individual responses or guaranteed clinical importance.
- 82. D.** Parietal-cell acid secretion is completed by the apical H^+/K^+ ATPase. Intracellular carbonic anhydrase supplies H^+ and bicarbonate; bicarbonate exits basolaterally in exchange for chloride, producing the postprandial alkaline tide.
- 83. C.** Early distributive shock often features profound vasodilation and reduced systemic vascular resistance. Cardiac output may be normal or high initially, yet maldistribution of flow and cellular dysfunction can still impair effective tissue oxygen use.
- 84. E.** PTH increases renal calcium reabsorption, especially distally, while reducing proximal phosphate reabsorption by downregulating sodium-phosphate cotransporters. It also stimulates renal 1-alpha-hydroxylase, increasing calcitriol and intestinal calcium absorption.
- 85. E.** PT is especially sensitive to the extrinsic pathway, whose unique upstream factor is factor VII, while both PT and aPTT also depend on the common pathway. Isolated PT prolongation therefore points toward factor VII deficiency or impaired vitamin K-dependent factor activity before broader common-pathway defects appear.
- 86. B.** Advance directives preserve patient autonomy when capacity is lost. Surrogates and clinicians should follow clearly applicable prior wishes; when preferences are unknown, substituted judgment and then best-interest standards guide decisions.
- 87. A.** Myelin raises membrane resistance and lowers effective capacitance across internodes, allowing depolarizing current to spread rapidly to the next node. Demyelination increases leak and capacitance, reducing safety factor and slowing or blocking conduction.
- 88. C.** Type I fibers are slow oxidative fibers with many mitochondria, rich capillary supply, and abundant myoglobin. They generate force more slowly but resist fatigue and are well suited to posture and endurance activity.
- 89. D.** Renal hypoxia after significant anemia increases erythropoietin, which stimulates erythroid progenitors. After the marrow production and maturation delay, reticulocytes rise in peripheral blood and provide evidence of an appropriate regenerative response.
- 90. D.** Nonheme iron absorption is favored by gastric acidity and reduction of Fe^{3+} to Fe^{2+} , which can enter enterocytes through DMT1. Ferroportin exports iron basolaterally, while hepcidin reduces iron release by promoting ferroportin internalization.
- 91. A.** Bile acids emulsify dietary lipid and form mixed micelles containing fatty acids, monoglycerides, cholesterol, and fat-soluble vitamins. Micelles permit these hydrophobic products to traverse the unstirred water layer to the enterocyte membrane.

- 92. A.** Pupillary dilation is produced by sympathetic contraction of the iris radial muscle through alpha-1 receptors. Parasympathetic fibers from the Edinger-Westphal pathway constrict the pupil by activating M3 receptors on the sphincter pupillae.
- 93. E.** Fever represents a regulated increase in the hypothalamic set point. Until body temperature reaches that higher target, the nervous system interprets the body as relatively cold and activates vasoconstriction, behavioral warming, and shivering.
- 94. C.** Duodenal acid stimulates S cells to release secretin. Secretin promotes bicarbonate-rich pancreatic and biliary secretions that neutralize gastric acid and create a more favorable pH for pancreatic enzymes.
- 95. E.** Teach-back assesses communication effectiveness by asking the patient to explain key information in their own words. It identifies misunderstandings without framing the patient as being tested and allows the clinician to clarify as needed.
- 96. B.** Lung expansion lowers pulmonary vascular resistance, increasing pulmonary blood flow and pulmonary venous return to the left atrium. Cord clamping removes the low-resistance placenta and reduces right-sided venous return, so left atrial pressure exceeds right atrial pressure and the septum primum is pressed against the septum secundum.
- 97. A.** Gonadotrophs respond physiologically to pulsatile GnRH. Continuous GnRH stimulation downregulates receptor signaling and suppresses LH and FSH, a property used therapeutically after an initial agonist flare.
- 98. A.** Many treatment disagreements reflect differences in goals, values, or understanding rather than simple refusal. Explicitly connecting the intervention's physiologic effects and burdens to the patient's goals can support a shared, ethically coherent decision.
- 99. B.** Myelin raises membrane resistance and lowers effective capacitance across internodes, allowing depolarizing current to spread rapidly to the next node. Demyelination increases leak and capacitance, reducing safety factor and slowing or blocking conduction.
- 100. B.** As alveolar surface area decreases, surfactant becomes more concentrated and reduces surface tension. This limits the rise in collapsing pressure predicted by Laplace law and helps prevent small alveoli from emptying into larger ones.
- 101. C.** Perfusion without ventilation makes V/Q approach zero. Blood exiting such units resembles mixed venous blood; true shunt physiology is relatively resistant to supplemental oxygen because some blood never contacts ventilated alveoli.
- 102. A.** The midcycle LH surge initiates resumption of oocyte meiosis, luteinization, prostaglandin/protease activity, and follicular rupture. FSH rises more modestly and supports follicular processes but is not the principal trigger.

- 103. A.** Clinicians should communicate significant errors transparently, including what is known, potential effects, and what will be done to reduce harm. Documentation should remain accurate rather than being altered to conceal the event.
- 104. E.** Naive T-cell activation requires antigen-specific TCR signaling plus costimulation. B7 (CD80/CD86) on activated antigen-presenting cells binds CD28 on T cells; absent costimulation can produce anergy rather than productive activation.
- 105. A.** Surfactant lowers surface tension, especially at low lung volumes. When surfactant is deficient, surface tension rises; by the law of Laplace, small alveoli require greater distending pressure and are more prone to collapse, reducing compliance and increasing work of breathing.
- 106. B.** Financial relationships can influence or appear to influence professional decisions. Avoiding substantial personal gifts and following institutional conflict-of-interest policies helps protect independent judgment and patient/public trust.
- 107. B.** An acute increase in afterload makes ventricular ejection more difficult. With contractility and preload initially fixed, less blood is ejected, end-systolic volume rises, and stroke volume and ejection fraction fall on that beat.
- 108. E.** During eccentric contraction, active muscle generates tension while lengthening under an external load. Eccentric actions can produce high force at relatively low metabolic cost compared with concentric shortening.
- 109. E.** A capacitated patient may invite others into clinical discussions. The clinician should clarify the scope of permission, preserve the patient's role as decision-maker, and avoid treating limited permission as blanket authorization for unrelated disclosure.
- 110. C.** Progesterone dominates the luteal phase, raises basal body temperature modestly, and makes cervical mucus thicker and less penetrable. Estradiol predominates before ovulation and produces thinner, more stretchable cervical mucus.
- 111. A.** CO₂ readily crosses the blood-brain barrier and generates H⁺ in cerebrospinal fluid and brain extracellular fluid. Central chemoreceptors respond strongly to this pH change and provide a major acute ventilatory stimulus, while peripheral chemoreceptors also respond to CO₂, H⁺, and marked hypoxemia.
- 112. B.** Net intestinal water movement is passive and follows osmotic gradients created largely by solute transport. Sodium absorption is therefore central to water reclamation, and secretory processes that add electrolytes to the lumen can draw water in the opposite direction.
- 113. D.** Sensitivity is true positives divided by all people who truly have the condition. Here, 180 of 200 affected individuals test positive, so sensitivity is 90%; prevalence is not required for this calculation.

- 114. C.** Vasopressin binds V2 receptors on collecting-duct principal cells, increases cAMP, and promotes apical insertion of aquaporin-2. Water then enters from the tubular lumen and exits basolaterally through constitutive aquaporins, concentrating urine when a medullary gradient is present.
- 115. A.** Early distributive shock often features profound vasodilation and reduced systemic vascular resistance. Cardiac output may be normal or high initially, yet maldistribution of flow and cellular dysfunction can still impair effective tissue oxygen use.
- 116. D.** Maternal IgG crosses the placenta through Fc receptor-mediated transport and provides systemic passive immunity early in life. IgA is important in breast milk and mucosal protection, while IgM is too large for significant placental transfer.
- 117. C.** Gonadotrophs respond physiologically to pulsatile GnRH. Continuous GnRH stimulation downregulates receptor signaling and suppresses LH and FSH, a property used therapeutically after an initial agonist flare.
- 118. B.** Rods are highly light-sensitive and support scotopic vision, but convergence of many rods onto downstream neurons reduces spatial resolution. Cones dominate high-acuity and color vision, especially in the fovea, and photoreceptors hyperpolarize rather than depolarize in light.
- 119. D.** Acute hypercapnia increases brain extracellular H^+ after CO_2 diffuses across the blood-brain barrier, producing cerebral vasodilation and increased cerebral blood flow. This CO_2 reactivity is clinically important because hypercapnia can increase intracranial blood volume.
- 120. B.** Albumin contributes importantly to plasma oncotic pressure. When albumin concentration falls substantially, the oncotic force opposing filtration decreases, favoring net transcapillary fluid movement into the interstitial space.
- 121. D.** Renin secretion rises when renal perfusion pressure is low, macula densa NaCl delivery is reduced, or renal sympathetic beta-1 signaling increases. Angiotensin II feeds back to suppress renin, helping regulate the system.
- 122. B.** Positive inotropy raises the pressure generated at any end-systolic volume, steepening the end-systolic pressure-volume relationship. With preload and afterload unchanged, the ventricle empties more completely, decreasing ESV and increasing stroke volume.
- 123. D.** Smooth muscle lacks the troponin-based regulatory system of skeletal muscle. Ca^{2+} -calmodulin activates myosin light-chain kinase, which phosphorylates myosin and permits productive interaction with actin; myosin light-chain phosphatase promotes relaxation.
- 124. C.** When a patient's values and likely preferences are known, substituted judgment asks the surrogate to represent the patient's perspective. A best-interest standard is used when the patient's preferences cannot reasonably be inferred.

- 125. A.** Research participation is voluntary, and participants generally may withdraw. Investigators should explain consequences, appropriate clinical follow-up, and what may happen to already collected data according to the consent and applicable research rules, without coercion.
- 126. A.** Peripheral chemoreceptors, especially the carotid bodies, respond strongly when arterial PO₂ falls below roughly the range where hemoglobin saturation declines steeply. Their afferent input increases ventilation rapidly at altitude.
- 127. C.** Elevated extracellular K⁺ directly depolarizes zona glomerulosa cells and increases aldosterone secretion. Aldosterone enhances distal sodium reabsorption and promotes potassium secretion through principal-cell transport mechanisms.
- 128. A.** Osteocytes act as mechanosensors and regulate osteoblast and osteoclast activity in response to loading. Repeated appropriate strain can favor local bone formation and improve structural adaptation, while unloading shifts remodeling toward bone loss.
- 129. A.** Arterial oxygen content is dominated by hemoglobin-bound oxygen: $CaO_2 = 1.34 \times \text{hemoglobin} \times \text{saturation} + 0.003 \times PaO_2$. The dissolved component is very small, so anemia can markedly lower oxygen content despite a normal PaO₂ and saturation.
- 130. C.** Cold defense combines reduced heat loss with increased heat generation. Sympathetic cutaneous vasoconstriction reduces dry heat transfer, while shivering and longer-term metabolic/endocrine responses can increase thermogenesis.
- 131. B.** Sympathetic vasoconstriction reduces cutaneous blood flow and lowers skin temperature, decreasing radiative and convective heat transfer. Shivering increases heat production, while sweating would increase evaporative heat loss rather than conserve heat.
- 132. B.** Arterial oxygen content is dominated by hemoglobin-bound oxygen: $CaO_2 = 1.34 \times \text{hemoglobin} \times \text{saturation} + 0.003 \times PaO_2$. The dissolved component is very small, so anemia can markedly lower oxygen content despite a normal PaO₂ and saturation.
- 133. D.** Specificity is true negatives divided by all people without the disease. With 285 true negatives among 300 unaffected individuals, specificity is 95%.
- 134. B.** As fasting continues, low insulin and higher counterregulatory hormones promote lipolysis and hepatic ketogenesis. The brain increasingly oxidizes ketone bodies, reducing glucose demand and therefore decreasing the need for amino-acid-derived gluconeogenesis.
- 135. A.** PEPT1 uses a proton gradient to transport many di- and tripeptides into enterocytes, where cytosolic peptidases often convert them to amino acids. Amino acids also have several distinct apical transport systems.

- 136. B.** Increased temperature, increased CO₂, increased H⁺, and increased 2,3-BPG shift the dissociation curve to the right. The higher P₅₀ reflects lower hemoglobin affinity and promotes oxygen unloading where metabolism is high.
- 137. C.** A fall in ionized calcium activates parathyroid chief cells to release PTH. PTH conserves calcium, promotes phosphaturia, stimulates calcitriol formation, and increases calcium mobilization from bone indirectly through osteoblast-lineage signaling.
- 138. D.** Sympathetic fibers release norepinephrine onto beta-1 receptors in the SA node, increasing cAMP-dependent pacemaker currents and calcium entry, steepening phase 4 depolarization. Parasympathetic M2 signaling has the opposite chronotropic effect.
- 139. E.** Threshold opens voltage-gated Na⁺ channels, and the resulting inward Na⁺ current rapidly depolarizes the membrane. Delayed opening of voltage-gated K⁺ channels and Na⁺ channel inactivation contribute to repolarization rather than the upstroke.
- 140. A.** LH acts on Leydig cells to stimulate testosterone production. FSH acts mainly on Sertoli cells, supporting spermatogenesis and promoting inhibin B secretion, which feeds back preferentially on FSH.
- 141. A.** Fast, sharp pain is carried mainly by thinly myelinated A-delta nociceptors. Slower, diffuse burning pain is carried largely by unmyelinated C fibers, which conduct impulses much more slowly.
- 142. D.** Increased temperature, increased CO₂, increased H⁺, and increased 2,3-BPG shift the dissociation curve to the right. The higher P₅₀ reflects lower hemoglobin affinity and promotes oxygen unloading where metabolism is high.
- 143. C.** The clinician should first counsel the patient and follow applicable reporting and confidentiality requirements. Some infections have mandatory public-health processes, but the precise legal route can vary; indiscriminate disclosure to third parties is not the default.
- 144. D.** Nontherapeutic sensitive examinations for teaching require appropriate patient authorization rather than being assumed from general procedural consent. Respect for autonomy is especially important when the patient is unable to object during anesthesia.
- 145. C.** Parietal-cell acid secretion is completed by the apical H⁺/K⁺ ATPase. Intracellular carbonic anhydrase supplies H⁺ and bicarbonate; bicarbonate exits basolaterally in exchange for chloride, producing the postprandial alkaline tide.
- 146. A.** Renin secretion rises when renal perfusion pressure is low, macula densa NaCl delivery is reduced, or renal sympathetic beta-1 signaling increases. Angiotensin II feeds back to suppress renin, helping regulate the system.
- 147. E.** Myelin raises membrane resistance and lowers effective capacitance across internodes, allowing depolarizing current to spread rapidly to the next node. Demyelination increases leak and capacitance, reducing safety factor and slowing or blocking conduction.

- 148. E.** At low plasma concentrations, PAH is filtered and efficiently secreted by proximal tubules, so the renal venous concentration is low. Its clearance therefore approximates effective renal plasma flow, although extraction is not literally 100%.
- 149. B.** Thermoregulatory sweating is mediated mainly by sympathetic postganglionic fibers that release acetylcholine onto muscarinic receptors of eccrine glands. Evaporation becomes especially important when ambient temperature approaches or exceeds skin temperature.
- 150. B.** A commonly used calculated osmolality is $2 \times [\text{Na}^+] + \text{glucose}/18 + \text{BUN}/2.8$ when glucose and BUN are in mg/dL. Sodium and its accompanying anions account for most extracellular osmolality, with glucose and urea contributing additional osmoles.
- 151. C.** Smooth muscle lacks the troponin-based regulatory system of skeletal muscle. Ca^{2+} -calmodulin activates myosin light-chain kinase, which phosphorylates myosin and permits productive interaction with actin; myosin light-chain phosphatase promotes relaxation.
- 152. E.** The simplified alveolar gas equation on room air is $\text{PAO}_2 \approx 150 - \text{PaCO}_2/R$. A rise in PaCO_2 therefore lowers predicted alveolar oxygen tension when inspired oxygen and respiratory quotient are unchanged.
- 153. B.** Naive T-cell activation requires antigen-specific TCR signaling plus costimulation. B7 (CD80/CD86) on activated antigen-presenting cells binds CD28 on T cells; absent costimulation can produce anergy rather than productive activation.
- 154. E.** LH acts on Leydig cells to stimulate testosterone production. FSH acts mainly on Sertoli cells, supporting spermatogenesis and promoting inhibin B secretion, which feeds back preferentially on FSH.
- 155. D.** Increased venous return raises ventricular end-diastolic volume and myocardial fiber stretch. At unchanged afterload and contractility, the Frank-Starling mechanism increases force of contraction and stroke volume, so the loop widens mainly through a rightward shift of end-diastolic volume.
- 156. A.** Muscle spindles lie in parallel with extrafusal fibers and detect muscle length and rate of stretch. Their primary group Ia afferents strongly excite homonymous alpha motor neurons in the monosynaptic stretch reflex; Golgi tendon organs instead sense tension via Ib afferents.
- 157. A.** Golgi tendon organs are arranged in series with muscle fibers and respond strongly to active tension. Their group Ib afferents participate in spinal circuits that regulate force and can inhibit homonymous motor output when tension is excessive.
- 158. C.** Systemic oxygen delivery is $\text{DO}_2 = \text{cardiac output} \times \text{arterial oxygen content}$. Thus tissue oxygen supply can fail because of inadequate flow, low hemoglobin, reduced saturation, or combinations of these even when PaO_2 itself is not dramatically abnormal.

- 159. B.** The size principle recruits small alpha motor neurons and their fatigue-resistant motor units first, then larger units as force demand increases. Rate coding also contributes, but orderly recruitment helps produce smooth graded force and delays fatigue.
- 160. E.** The simplified alveolar gas equation on room air is $PAO_2 \approx 150 - PaCO_2/R$. A rise in $PaCO_2$ therefore lowers predicted alveolar oxygen tension when inspired oxygen and respiratory quotient are unchanged.
- 161. B.** Perfusion without ventilation makes V/Q approach zero. Blood exiting such units resembles mixed venous blood; true shunt physiology is relatively resistant to supplemental oxygen because some blood never contacts ventilated alveoli.
- 162. B.** The size principle recruits small alpha motor neurons and their fatigue-resistant motor units first, then larger units as force demand increases. Rate coding also contributes, but orderly recruitment helps produce smooth graded force and delays fatigue.
- 163. C.** Contraction of the left ventricular myocardium compresses intramural vessels during systole, particularly in the vulnerable subendocardium. When the ventricle relaxes in diastole, compression falls and the aorta-to-coronary pressure gradient supports greater flow.
- 164. D.** Maternal IgG crosses the placenta through Fc receptor-mediated transport and provides systemic passive immunity early in life. IgA is important in breast milk and mucosal protection, while IgM is too large for significant placental transfer.
- 165. A.** For most of the cycle, estradiol exerts negative feedback, but sustained high levels from the dominant follicle produce positive feedback on the hypothalamic-pituitary axis. The resulting LH surge triggers ovulation and luteinization.
- 166. D.** Golgi tendon organs are arranged in series with muscle fibers and respond strongly to active tension. Their group Ib afferents participate in spinal circuits that regulate force and can inhibit homonymous motor output when tension is excessive.
- 167. A.** PTH increases renal calcium reabsorption, especially distally, while reducing proximal phosphate reabsorption by downregulating sodium-phosphate cotransporters. It also stimulates renal 1-alpha-hydroxylase, increasing calcitriol and intestinal calcium absorption.
- 168. B.** Serious-illness communication should be truthful, patient-centered, and calibrated to uncertainty. Directly addressing the question while exploring the patient's information preferences and goals supports informed decisions without false precision or false reassurance.
- 169. C.** A high hematocrit increases whole-blood viscosity. In Poiseuille terms, higher viscosity increases resistance for a given vessel geometry, so severe erythrocytosis can impair flow despite increased oxygen-carrying capacity.

- 170. E.** Glucose metabolism increases the ATP/ADP ratio, closing KATP channels and depolarizing the beta-cell membrane. Voltage-gated Ca^{2+} channels then open, and the rise in intracellular Ca^{2+} triggers insulin-granule exocytosis.
- 171. E.** As fasting continues, low insulin and higher counterregulatory hormones promote lipolysis and hepatic ketogenesis. The brain increasingly oxidizes ketone bodies, reducing glucose demand and therefore decreasing the need for amino-acid-derived gluconeogenesis.
- 172. C.** Excitation-contraction coupling releases Ca^{2+} from the sarcoplasmic reticulum. Ca^{2+} binds troponin C, changing the troponin-tropomyosin complex so that myosin can interact cyclically with actin.
- 173. E.** CCK is released from small-intestinal I cells in response to fats and amino acids. It stimulates pancreatic enzyme secretion and gallbladder contraction, facilitates biliary delivery, and slows gastric emptying to match delivery with digestive capacity.
- 174. A.** Clearance equals urine concentration $\times$ urine flow divided by plasma concentration. Inulin is freely filtered and neither secreted nor reabsorbed, so its clearance estimates GFR.
- 175. D.** Suckling activates hypothalamic neurons whose axons release oxytocin from the posterior pituitary. Oxytocin contracts mammary myoepithelial cells, producing milk let-down; prolactin primarily supports milk production.
- 176. A.** Cardiac output equals heart rate multiplied by stroke volume. Converting milliliters to liters gives the stated value; no additional correction factor is required.
- 177. E.** After release from food and transfer from salivary binding proteins, vitamin B12 binds intrinsic factor. The intrinsic factor-B12 complex is recognized by receptors in the terminal ileum, enabling efficient absorption before transport in blood on transcobalamin.
- 178. C.** ATP binding to myosin lowers its affinity for actin and permits cross-bridge detachment. Without ATP, myosin remains tightly bound to actin, which is the molecular basis of rigor.
- 179. D.** Acute hypercapnia increases brain extracellular H^{+} after CO_2 diffuses across the blood-brain barrier, producing cerebral vasodilation and increased cerebral blood flow. This CO_2 reactivity is clinically important because hypercapnia can increase intracranial blood volume.
- 180. C.** Active force depends on the number of actin-myosin cross-bridges that can form. It is maximal near optimal overlap and falls with excessive shortening or stretching, whereas passive tension rises at longer lengths because of elastic elements such as titin.
- 181. C.** Growth hormone stimulates production of IGF-1, especially in the liver and also locally in tissues. IGF-1 mediates many effects on cartilage, bone, and tissue growth, while growth hormone also has direct metabolic actions such as promoting lipolysis.

- 182. E.** TSH acts through a Gs-cAMP pathway on follicular cells to stimulate multiple steps in thyroid hormone production, including iodide uptake, thyroglobulin synthesis/processing, and release of T4 and T3.
- 183. B.** Reduced renal tissue oxygen tension stabilizes hypoxia-inducible factors in peritubular interstitial cells, increasing erythropoietin synthesis. Erythropoietin stimulates erythroid progenitors in bone marrow and increases reticulocyte production.
- 184. A.** Dynamic exercise increases heart rate, stroke volume, and cardiac output. Metabolic vasodilation in active muscle lowers total systemic vascular resistance, while sympathetic vasoconstriction redistributes flow from less active beds and mean pressure is maintained or rises modestly.
- 185. B.** Pupillary dilation is produced by sympathetic contraction of the iris radial muscle through alpha-1 receptors. Parasympathetic fibers from the Edinger-Westphal pathway constrict the pupil by activating M3 receptors on the sphincter pupillae.
- 186. C.** At normal resting rates, MAP is approximated as DBP + one third of pulse pressure because diastole occupies more of the cardiac cycle than systole. A simple average of systolic and diastolic pressures therefore overestimates MAP.
- 187. E.** Alveolar ventilation is respiratory rate multiplied by the portion of each tidal breath that reaches gas-exchanging alveoli: $VA = RR \times (VT - VD)$. Total minute ventilation overestimates effective ventilation because part of each breath remains in dead space.
- 188. A.** Lower extracellular K⁺ makes the potassium equilibrium potential more negative. Because resting neuronal membranes are highly permeable to K⁺, the resting membrane potential generally hyperpolarizes, reducing excitability until compensatory changes occur.
- 189. E.** Ventilation increases rapidly with exercise through central command, sensory feedback, and chemical control. In healthy people at moderate workloads, the rise in alveolar ventilation closely tracks CO₂ production, so arterial PCO₂ and PO₂ remain near resting values.
- 190. B.** Loss of hypotonic fluid or pure water raises extracellular osmolality. Water then leaves cells until osmolality is equal across membranes, producing contraction of both intracellular and extracellular compartments with hyperosmolarity.
- 191. D.** A commonly used calculated osmolality is $2 \times [Na^+] + \text{glucose}/18 + \text{BUN}/2.8$ when glucose and BUN are in mg/dL. Sodium and its accompanying anions account for most extracellular osmolality, with glucose and urea contributing additional osmoles.
- 192. C.** ATP binding to myosin lowers its affinity for actin and permits cross-bridge detachment. Without ATP, myosin remains tightly bound to actin, which is the molecular basis of rigor.

- 193. B.** Ventilation of unperfused alveoli is wasted ventilation. With Q approaching zero while V remains present, V/Q tends toward infinity, increasing physiologic dead space and potentially increasing the ventilatory requirement for CO_2 elimination.
- 194. D.** A type I error is rejecting a true null hypothesis, or a false-positive conclusion. Its long-run probability is controlled by the chosen alpha level under the statistical model and testing procedure.
- 195. E.** A fall in arterial stretch reduces baroreceptor firing to the medulla. The reflex response increases sympathetic tone and decreases parasympathetic tone, raising heart rate, contractility, arteriolar resistance, and venous tone to support pressure and venous return.
- 196. C.** Growth hormone stimulates production of IGF-1, especially in the liver and also locally in tissues. IGF-1 mediates many effects on cartilage, bone, and tissue growth, while growth hormone also has direct metabolic actions such as promoting lipolysis.
- 197. B.** Metabolic acidosis stimulates ventilation, lowering PaCO_2 and reducing the carbonic-acid component of the bicarbonate buffer system. Respiratory compensation cannot fully normalize pH and does not correct the underlying metabolic process.
- 198. D.** Net intestinal water movement is passive and follows osmotic gradients created largely by solute transport. Sodium absorption is therefore central to water reclamation, and secretory processes that add electrolytes to the lumen can draw water in the opposite direction.
- 199. E.** The median is robust to extreme values because it is the middle ranked observation. The mean, variance, standard deviation, and range can all be strongly influenced by outliers.
- 200. E.** Gas diffusion across a membrane is proportional to surface area, diffusion coefficient, and partial-pressure gradient, and inversely proportional to thickness. Thickening impairs diffusion; a larger area or pressure gradient can increase transfer when other variables are fixed.
- 201. C.** Heat acclimatization expands plasma volume and improves sweating responses, including earlier onset and greater capacity. Aldosterone-mediated sodium conservation makes sweat more dilute, helping preserve extracellular volume during repeated heat exposure.
- 202. A.** At sites of endothelial disruption, vWF binds exposed subendothelial structures and platelet GPIb, supporting adhesion particularly under high shear. Activated GPIIb/IIIa then binds fibrinogen to aggregate platelets with one another.
- 203. E.** A high hematocrit increases whole-blood viscosity. In Poiseuille terms, higher viscosity increases resistance for a given vessel geometry, so severe erythrocytosis can impair flow despite increased oxygen-carrying capacity.
- 204. E.** Arterial oxygen content is dominated by hemoglobin-bound oxygen: $\text{CaO}_2 = 1.34 \times \text{hemoglobin} \times \text{saturation} + 0.003 \times \text{PaO}_2$. The dissolved component is very small, so anemia can markedly lower oxygen content despite a normal PaO_2 and saturation.

- 205. D.** Active force depends on the number of actin-myosin cross-bridges that can form. It is maximal near optimal overlap and falls with excessive shortening or stretching, whereas passive tension rises at longer lengths because of elastic elements such as titin.
- 206. E.** Free thyroid hormone exerts negative feedback at both hypothalamus and anterior pituitary, reducing TRH and TSH. This feedback stabilizes circulating thyroid hormone around a physiologic set point.
- 207. C.** Fluid-filled lungs and relative hypoxic pulmonary vasoconstriction keep fetal pulmonary vascular resistance high. Consequently, much of right ventricular output bypasses the lungs through the ductus arteriosus into the descending aorta and placental circulation.
- 208. D.** At normal resting rates, MAP is approximated as DBP + one third of pulse pressure because diastole occupies more of the cardiac cycle than systole. A simple average of systolic and diastolic pressures therefore overestimates MAP.
- 209. D.** Muscle spindles lie in parallel with extrafusal fibers and detect muscle length and rate of stretch. Their primary group Ia afferents strongly excite homonymous alpha motor neurons in the monosynaptic stretch reflex; Golgi tendon organs instead sense tension via Ib afferents.
- 210. E.** The proximal tubule performs bulk iso-osmotic reabsorption of sodium, water, bicarbonate, glucose, amino acids, and other solutes. Downstream segments make smaller but highly regulated adjustments important for final urinary composition.
- 211. B.** Osteocytes act as mechanosensors and regulate osteoblast and osteoclast activity in response to loading. Repeated appropriate strain can favor local bone formation and improve structural adaptation, while unloading shifts remodeling toward bone loss.
- 212. C.** Albumin contributes importantly to plasma oncotic pressure. When albumin concentration falls substantially, the oncotic force opposing filtration decreases, favoring net transcapillary fluid movement into the interstitial space.
- 213. C.** The Fick principle states $VO_2 = \text{cardiac output} \times (\text{arterial } O_2 \text{ content} - \text{mixed venous } O_2 \text{ content})$. Because oxygen consumption is in mL/min and the oxygen-content difference is in mL/L, direct division gives cardiac output in L/min; here the result is 5.0 L/min.
- 214. B.** Clearance equals urine concentration $\times$ urine flow divided by plasma concentration. Inulin is freely filtered and neither secreted nor reabsorbed, so its clearance estimates GFR.
- 215. D.** The proximal tubule performs bulk iso-osmotic reabsorption of sodium, water, bicarbonate, glucose, amino acids, and other solutes. Downstream segments make smaller but highly regulated adjustments important for final urinary composition.

- 216. C.** Within the physiologic range, increased ventricular filling stretches cardiac sarcomeres toward a length that improves force generation and calcium sensitivity. This intrinsic Frank-Starling response helps match output of the two ventricles and adapts stroke volume to venous return.
- 217. E.** Loss of hypotonic fluid or pure water raises extracellular osmolality. Water then leaves cells until osmolality is equal across membranes, producing contraction of both intracellular and extracellular compartments with hyperosmolarity.
- 218. A.** Increased permeability allows protein to leave the vascular space, reducing plasma oncotic retention and increasing interstitial oncotic attraction. Along with increased filtration coefficient, these changes favor edema formation.
- 219. A.** Systemic oxygen delivery is $DO_2 = \text{cardiac output} \times \text{arterial oxygen content}$. Thus tissue oxygen supply can fail because of inadequate flow, low hemoglobin, reduced saturation, or combinations of these even when PaO_2 itself is not dramatically abnormal.
- 220. C.** Acute CO_2 retention increases carbonic acid and H^+ . Intracellular proteins, hemoglobin, phosphate, and other nonbicarbonate buffers blunt the pH change immediately; renal increases in bicarbonate reabsorption and acid excretion develop over hours to days.
- 221. C.** Free thyroid hormone exerts negative feedback at both hypothalamus and anterior pituitary, reducing TRH and TSH. This feedback stabilizes circulating thyroid hormone around a physiologic set point.
- 222. E.** Fast, sharp pain is carried mainly by thinly myelinated A-delta nociceptors. Slower, diffuse burning pain is carried largely by unmyelinated C fibers, which conduct impulses much more slowly.
- 223. D.** Endothelial selectins and their carbohydrate ligands mediate weak, rapidly forming and breaking interactions that produce rolling. Chemokine activation then increases leukocyte integrin affinity, allowing firm adhesion to ICAM-family molecules before diapedesis.
- 224. B.** The semicircular canals are specialized for angular acceleration. Head rotation causes relative endolymph movement and cupular deflection at the cristae; the utricle and saccule are more important for linear acceleration and head position relative to gravity.
- 225. B.** Acute CO_2 retention increases carbonic acid and H^+ . Intracellular proteins, hemoglobin, phosphate, and other nonbicarbonate buffers blunt the pH change immediately; renal increases in bicarbonate reabsorption and acid excretion develop over hours to days.
- 226. D.** Glucocorticoids suppress both hypothalamic CRH and pituitary ACTH. Sustained exogenous exposure can therefore reduce endogenous adrenal stimulation and, over time, cause adrenal cortical atrophy.

227. A. Veins are highly compliant capacitance vessels. Sympathetic venoconstriction reduces capacitance and increases stressed volume and mean systemic filling pressure, shifting blood centrally and increasing the pressure gradient for venous return.

228. B. Vasopressin binds V2 receptors on collecting-duct principal cells, increases cAMP, and promotes apical insertion of aquaporin-2. Water then enters from the tubular lumen and exits basolaterally through constitutive aquaporins, concentrating urine when a medullary gradient is present.

229. C. For a relatively stable condition, prevalence reflects both incidence and average duration. Extending survival increases duration of disease and therefore tends to increase prevalence even if incidence is unchanged.

230. D. Dynamic exercise increases heart rate, stroke volume, and cardiac output. Metabolic vasodilation in active muscle lowers total systemic vascular resistance, while sympathetic vasoconstriction redistributes flow from less active beds and mean pressure is maintained or rises modestly.

231. C. Valid informed consent is a communication process, not merely a signature. A patient with capacity should receive understandable information about the proposed intervention, material risks and benefits, reasonable alternatives, and the option to decline, then decide voluntarily.

232. C. Thrombin bound to thrombomodulin activates protein C. Activated protein C with protein S proteolytically inactivates factors Va and VIIIa, reducing amplification of thrombin generation and helping localize clotting.

233. A. Nonheme iron absorption is favored by gastric acidity and reduction of Fe^{3+} to Fe^{2+} , which can enter enterocytes through DMT1. Ferroportin exports iron basolaterally, while hepcidin reduces iron release by promoting ferroportin internalization.

234. C. FSH acts on Sertoli cells to support germ-cell development, promote androgen-binding protein, and increase inhibin B. High intratesticular testosterone generated by LH-stimulated Leydig cells is also essential for normal spermatogenesis.

235. D. Cardiac output equals heart rate multiplied by stroke volume. Converting milliliters to liters gives the stated value; no additional correction factor is required.

236. C. Responding explicitly to emotion helps maintain trust and improves communication. Pausing, acknowledging distress, checking understanding, and giving information in manageable chunks is preferable to false reassurance or overwhelming the patient with uninterrupted technical detail.

237. B. CO_2 readily crosses the blood-brain barrier and generates H^+ in cerebrospinal fluid and brain extracellular fluid. Central chemoreceptors respond strongly to this pH change and provide a major acute ventilatory stimulus, while peripheral chemoreceptors also respond to CO_2 , H^+ , and marked hypoxemia.

- 238. C.** Cold defense combines reduced heat loss with increased heat generation. Sympathetic cutaneous vasoconstriction reduces dry heat transfer, while shivering and longer-term metabolic/endocrine responses can increase thermogenesis.
- 239. C.** Emphysema destroys elastic tissue, increasing compliance and reducing elastic recoil. The lungs inflate easily but empty poorly, favoring air trapping and increased resting lung volumes.
- 240. B.** After release from food and transfer from salivary binding proteins, vitamin B12 binds intrinsic factor. The intrinsic factor-B12 complex is recognized by receptors in the terminal ileum, enabling efficient absorption before transport in blood on transcobalamin.
- 241. B.** Insulin promotes cellular K^+ uptake, especially in skeletal muscle, through effects including stimulation of Na^+/K^+ ATPase. Beta-2 adrenergic stimulation can also shift K^+ into cells, whereas aldosterone is especially important for renal potassium excretion over a longer time scale.
- 242. E.** Elevated extracellular K^+ directly depolarizes zona glomerulosa cells and increases aldosterone secretion. Aldosterone enhances distal sodium reabsorption and promotes potassium secretion through principal-cell transport mechanisms.
- 243. B.** A fall in arterial stretch reduces baroreceptor firing to the medulla. The reflex response increases sympathetic tone and decreases parasympathetic tone, raising heart rate, contractility, arteriolar resistance, and venous tone to support pressure and venous return.
- 244. C.** Insulin promotes GLUT4 translocation in skeletal muscle and adipose tissue, increasing glucose uptake. The brain relies mainly on insulin-independent glucose transporters, and hepatocyte GLUT2 transport is not controlled by GLUT4 translocation.
- 245. A.** Randomization balances known and unknown confounders on average and supports causal inference when adherence, follow-up, and outcome ascertainment are adequate. Observational designs can be valuable but generally require stronger assumptions about confounding.
- 246. C.** The gonadotroph requires pulsatile GnRH stimulation for sustained LH and FSH secretion. Continuous GnRH exposure downregulates/desensitizes pituitary GnRH receptors, eventually suppressing gonadotropin and gonadal steroid production.
- 247. E.** PEPT1 uses a proton gradient to transport many di- and tripeptides into enterocytes, where cytosolic peptidases often convert them to amino acids. Amino acids also have several distinct apical transport systems.
- 248. A.** Increased permeability allows protein to leave the vascular space, reducing plasma oncotic retention and increasing interstitial oncotic attraction. Along with increased filtration coefficient, these changes favor edema formation.

- 249. A.** SGLT1 uses the inward sodium gradient, maintained by basolateral Na^+/K^+ ATPase, to absorb glucose and galactose. Fructose uses GLUT5 apically, and monosaccharides generally leave enterocytes through basolateral GLUT2.
- 250. C.** Thermoregulatory sweating is mediated mainly by sympathetic postganglionic fibers that release acetylcholine onto muscarinic receptors of eccrine glands. Evaporation becomes especially important when ambient temperature approaches or exceeds skin temperature.
- 251. B.** For most of the cycle, estradiol exerts negative feedback, but sustained high levels from the dominant follicle produce positive feedback on the hypothalamic-pituitary axis. The resulting LH surge triggers ovulation and luteinization.
- 252. E.** An acute increase in afterload makes ventricular ejection more difficult. With contractility and preload initially fixed, less blood is ejected, end-systolic volume rises, and stroke volume and ejection fraction fall on that beat.
- 253. D.** Active force depends on the number of actin-myosin cross-bridges that can form. It is maximal near optimal overlap and falls with excessive shortening or stretching, whereas passive tension rises at longer lengths because of elastic elements such as titin.
- 254. E.** Reduced renal tissue oxygen tension stabilizes hypoxia-inducible factors in peritubular interstitial cells, increasing erythropoietin synthesis. Erythropoietin stimulates erythroid progenitors in bone marrow and increases reticulocyte production.
- 255. C.** Heat acclimatization expands plasma volume and improves sweating responses, including earlier onset and greater capacity. Aldosterone-mediated sodium conservation makes sweat more dilute, helping preserve extracellular volume during repeated heat exposure.
- 256. D.** Contraction of the left ventricular myocardium compresses intramural vessels during systole, particularly in the vulnerable subendocardium. When the ventricle relaxes in diastole, compression falls and the aorta-to-coronary pressure gradient supports greater flow.
- 257. E.** Increased temperature, increased CO_2 , increased H^+ , and increased 2,3-BPG shift the dissociation curve to the right. The higher P_{50} reflects lower hemoglobin affinity and promotes oxygen unloading where metabolism is high.
- 258. D.** Filtration fraction is the fraction of renal plasma flow filtered at the glomerulus: $\text{FF} = \text{GFR}/\text{RPF}$. It is distinct from renal blood flow, which would additionally require correction for hematocrit.
- 259. B.** Both ventilation and perfusion are greater at the bases, but perfusion changes more steeply with gravity. Thus V/Q is relatively high at the apex and low at the base, contributing to regional differences in alveolar PO_2 and PCO_2 .

- 260. E.** Gastrin secretion rises with peptides/amino acids, gastric distention, and vagal stimulation mediated importantly by gastrin-releasing peptide. Falling antral pH increases somatostatin release from D cells, which inhibits gastrin as a negative-feedback mechanism.
- 261. B.** Thrombin bound to thrombomodulin activates protein C. Activated protein C with protein S proteolytically inactivates factors Va and VIIIa, reducing amplification of thrombin generation and helping localize clotting.
- 262. D.** Endothelial selectins and their carbohydrate ligands mediate weak, rapidly forming and breaking interactions that produce rolling. Chemokine activation then increases leukocyte integrin affinity, allowing firm adhesion to ICAM-family molecules before diapedesis.
- 263. B.** Hemorrhage unloads arterial and cardiopulmonary stretch receptors, increasing sympathetic output and reducing vagal activity. Renin-angiotensin-aldosterone and vasopressin responses help preserve sodium, water, vascular tone, and perfusion pressure.
- 264. C.** Muscle spindles lie in parallel with extrafusal fibers and detect muscle length and rate of stretch. Their primary group Ia afferents strongly excite homonymous alpha motor neurons in the monosynaptic stretch reflex; Golgi tendon organs instead sense tension via Ib afferents.
- 265. B.** Dopamine tonically inhibits prolactin secretion through D2 receptors on lactotrophs. Suckling reduces dopaminergic inhibition, allowing prolactin to rise and support milk synthesis; suckling also triggers oxytocin for milk ejection.
- 266. E.** Threshold opens voltage-gated Na⁺ channels, and the resulting inward Na⁺ current rapidly depolarizes the membrane. Delayed opening of voltage-gated K⁺ channels and Na⁺ channel inactivation contribute to repolarization rather than the upstroke.
- 267. D.** Decision-making capacity is task-specific and depends on understanding, appreciation, reasoning, and ability to communicate a choice, not on agreement with the clinician. A capacitated adult may refuse even beneficial care after appropriate counseling.
- 268. E.** Sympathetic vasoconstriction reduces cutaneous blood flow and lowers skin temperature, decreasing radiative and convective heat transfer. Shivering increases heat production, while sweating would increase evaporative heat loss rather than conserve heat.
- 269. B.** Renal hypoxia after significant anemia increases erythropoietin, which stimulates erythroid progenitors. After the marrow production and maturation delay, reticulocytes rise in peripheral blood and provide evidence of an appropriate regenerative response.
- 270. D.** Insulin promotes GLUT4 translocation in skeletal muscle and adipose tissue, increasing glucose uptake. The brain relies mainly on insulin-independent glucose transporters, and hepatocyte GLUT2 transport is not controlled by GLUT4 translocation.

- 271. E.** Nicotinic acetylcholine receptors are ligand-gated cation channels. At the resting potential, their opening causes a net inward current dominated by Na^+ influx, producing the end-plate potential that can trigger nearby voltage-gated Na^+ channels.
- 272. B.** At sites of endothelial disruption, vWF binds exposed subendothelial structures and platelet GPIb, supporting adhesion particularly under high shear. Activated GPIIb/IIIa then binds fibrinogen to aggregate platelets with one another.
- 273. B.** At low plasma concentrations, PAH is filtered and efficiently secreted by proximal tubules, so the renal venous concentration is low. Its clearance therefore approximates effective renal plasma flow, although extraction is not literally 100%.
- 274. E.** Predictive values depend on disease prevalence or pretest probability. When prevalence is low, false positives make up a larger proportion of all positive results, so PPV generally falls even if sensitivity and specificity are unchanged.
- 275. B.** At sites of endothelial disruption, vWF binds exposed subendothelial structures and platelet GPIb, supporting adhesion particularly under high shear. Activated GPIIb/IIIa then binds fibrinogen to aggregate platelets with one another.
- 276. E.** Ventilation of unperfused alveoli is wasted ventilation. With Q approaching zero while V remains present, V/Q tends toward infinity, increasing physiologic dead space and potentially increasing the ventilatory requirement for CO_2 elimination.
- 277. A.** Lactate formation regenerates cytosolic NAD^+ and supports high glycolytic flux. Lactate is shuttled among tissues, oxidized by muscle and heart, or converted back to glucose in the liver through the Cori cycle.
- 278. B.** Adolescent confidentiality supports access to sensitive care, but clinicians should explain its limits, including safety and mandatory-reporting exceptions where applicable. Encouraging trusted adult support can be helpful without automatically breaching confidentiality.
- 279. A.** C3b covalently coats microbial surfaces and is recognized by complement receptors on phagocytes, making it a major opsonin. C3a and C5a are anaphylatoxins, C5a is strongly chemotactic, and C5b-9 forms the membrane attack complex.
- 280. B.** Sympathetic fibers release norepinephrine onto beta-1 receptors in the SA node, increasing cAMP-dependent pacemaker currents and calcium entry, steepening phase 4 depolarization. Parasympathetic M2 signaling has the opposite chronotropic effect.