COMPREHENSIVE MOCK EXAM 2

Supplemental to: Physiology Board Review 2026-2027

Rasmus Broberg

USMLE Step 1 (NBME/FSMB) — 280 single-best-answer questions, five options (A-E), physiology-focused and domain-weighted to the official Step 1 content specifications

Board-Review Questions

1. A healthy person ascends rapidly to high altitude. Within hours, hyperventilation causes respiratory alkalosis. Which change in hemoglobin most immediately promotes oxygen unloading to exercising tissues despite the fall in arterial carbon dioxide?

A. Systemic respiratory alkalosis shifts hemoglobin to the right and therefore markedly lowers oxygen affinity everywhere.

B. Local tissue increases in carbon dioxide, hydrogen ion, and temperature shift the oxygen dissociation curve to the right.

C. A fall in erythrocyte 2,3-BPG occurs within minutes and shifts hemoglobin to the right in peripheral tissues.

D. Decreased tissue temperature during exercise weakens hemoglobin oxygen binding and enhances local unloading.

E. Conversion of adult hemoglobin to fetal hemoglobin occurs within hours and lowers oxygen affinity in active muscle.

2. A hypothalamic releasing hormone is delivered continuously rather than in pulses. Which pituitary response is expected for the gonadotropin axis?

A. Continuous GnRH produces greater LH and FSH secretion than pulsatile GnRH because receptor signaling does not desensitize.

B. Continuous GnRH exposure downregulates pituitary GnRH receptors and eventually suppresses LH and FSH secretion.

C. Continuous GnRH selectively suppresses prolactin while gonadotropin secretion remains unchanged.

D. Continuous GnRH causes direct testicular testosterone release without requiring pituitary gonadotropins.

E. Continuous GnRH permanently increases hypothalamic dopamine and therefore raises gonadotropin secretion.

3. A healthy adult takes a quiet breath at rest. Which pressure change initiates inspiratory airflow into the lungs?

A. Contraction of expiratory muscles raises pleural pressure and lowers alveolar pressure below atmospheric pressure during quiet inspiration.

B. Alveolar pressure rises above atmospheric pressure as the diaphragm contracts, drawing air inward by positive pressure.

C. Contraction of inspiratory muscles makes pleural pressure more negative, expanding alveoli and lowering alveolar pressure below atmospheric pressure.

D. Pleural pressure becomes positive relative to atmosphere throughout quiet inspiration and directly pulls air into alveoli.

E. Airway resistance falls to zero before any pressure change occurs, so air enters without a pressure gradient.

4. A healthy adult receives a rapid intravenous saline bolus. Which immediate change best explains the increase in stroke volume?

A. Higher afterload reduces end-systolic volume and therefore raises stroke volume without changing preload.

B. Lower sympathetic tone increases calcium entry into ventricular myocytes and raises contractility after the bolus.

C. Reduced venous return increases end-diastolic pressure and shifts the ventricle to a more favorable sarcomere length.

D. A slower heart rate is required for any increase in stroke volume because ventricular filling cannot rise at the same rate.

E. Higher venous return raises end-diastolic fiber length, increasing force of contraction through the Frank-Starling mechanism.

5. A screening test is positive in 90 of 100 people who truly have a disease. What is the sensitivity of the test?

A. Sensitivity is 90%, because 90 of 100 affected people test positive.

B. Sensitivity is 10%, because 10 affected people had negative results.

C. Sensitivity is 50%, because positive and negative results are weighted equally regardless of disease status.

D. Sensitivity cannot be calculated without knowing how many unaffected people tested negative.

E. Sensitivity is the proportion of positive test results that represent true disease, so prevalence is required.

6. A patient has emphysema with destruction of elastic tissue. Which mechanical change is expected?

A. Lung compliance decreases and elastic recoil increases, producing low residual volume and easy forced expiration.

B. Compliance and recoil both increase because they are identical terms describing the same mechanical property.

C. Lung compliance increases and elastic recoil decreases, promoting expiratory airway collapse and air trapping.

D. Elastic recoil remains normal because only airway smooth muscle, not parenchymal tissue, determines expiratory flow.

E. Compliance falls to zero because destruction of alveolar walls prevents any increase in lung volume during inspiration.

7. A pituitary stalk is transected, interrupting hypothalamic releasing hormones and dopamine delivery. Which anterior pituitary hormone is most likely to rise?

A. TSH increases because hypothalamic TRH normally provides tonic inhibition of thyrotrophs.

B. ACTH increases because CRH normally suppresses corticotroph secretion through portal blood.

C. Prolactin increases because tonic hypothalamic dopamine normally inhibits lactotroph secretion.

D. LH rises markedly because GnRH normally inhibits gonadotrophs between pulses.

E. Growth hormone rises because somatostatin is the only hypothalamic signal and always stimulates somatotrophs.

8. A patient smells and tastes a meal before food reaches the stomach. Which neural pathway stimulates the cephalic phase of gastric secretion?

A. Sympathetic fibers release norepinephrine onto parietal cells and are the principal stimulatory pathway during the cephalic phase.

B. Vagal efferents increase gastric acid secretion directly and through stimulation of gastrin and histamine release.

C. Somatic motor neurons release acetylcholine into the gastric lumen and activate parietal cells from the apical surface.

D. Vagal stimulation suppresses gastrin and histamine so acid secretion falls until nutrients enter the duodenum.

E. Enteric neurons cannot respond until the stomach is distended, so no gastric secretion occurs before food arrival.

9. A premature infant has respiratory distress because of insufficient surfactant. Which alveolar change is most directly caused by low surfactant?

A. Surface tension rises, especially in small alveoli, increasing the pressure required to keep them open.

B. Surface tension falls, causing alveoli to overexpand at low transpulmonary pressure and eliminating elastic recoil.

C. Alveolar fluid becomes hypertonic and pulls air into the lung independently of respiratory muscle effort.

D. Pulmonary capillary oncotic pressure rises and directly prevents small alveoli from collapsing.

E. Airway smooth muscle relaxes so strongly that alveolar ventilation increases despite reduced lung compliance.

10. A patient with severe diarrhea has an arterial pH of 7.28, bicarbonate 15 mEq/L, and PCO2 31 mm Hg. Which primary acid-base disorder is most likely?

A. A primary respiratory acidosis is present because the PCO2 is below the normal range.

B. A primary metabolic acidosis with appropriate respiratory compensation is present.

C. A primary metabolic alkalosis is present because gastrointestinal fluid loss always raises bicarbonate.

D. A primary respiratory alkalosis is present because the low PCO2 fully explains the low bicarbonate.

E. No acid-base disorder is present because the fall in bicarbonate is exactly matched by a fall in PCO2.

11. A competent adult with a life-threatening condition understands the diagnosis, alternatives, risks, and likely consequences but refuses the recommended treatment. What is the most appropriate response?

A. Override the refusal because a physician may compel any treatment that is expected to prolong life.

B. Ask the family to consent in place of the patient because relatives have greater authority when the decision is high risk.

C. Declare the patient incapable solely because the patient disagrees with the medical recommendation.

D. Respect the informed refusal, document the discussion, and continue to offer care consistent with the patient's goals.

E. Discharge the patient immediately and stop all other treatment because declining one intervention ends the therapeutic relationship.

12. A breastfeeding woman has increased prolactin. Which effect helps suppress ovulation during frequent nursing?

A. Prolactin directly stimulates the LH surge and therefore increases ovulation frequency during lactation.

B. Prolactin raises ovarian progesterone continuously and makes GnRH pulses faster than during the follicular phase.

C. Prolactin inhibits hypothalamic GnRH pulsatility, reducing LH and FSH support of the ovarian cycle.

D. Prolactin acts only in the breast and has no physiologic influence on hypothalamic or gonadal function.

E. Prolactin increases dopamine release to the ovary, directly causing follicular rupture without pituitary gonadotropins.

13. A patient with delirium cannot understand a proposed nonemergency procedure. A valid health care proxy names the patient's spouse as surrogate. What should guide the decision?

A. The surrogate should choose whatever treatment the surrogate personally would want under the same circumstances.

B. The physician should ignore the proxy and make the decision alone because delirium eliminates the need for surrogate input.

C. The surrogate should use the patient's known values and prior preferences, with best interests used when those preferences are unknown.

D. The procedure should automatically be performed because inability to consent converts every intervention into an emergency.

E. The patient's adult children should vote, and the majority decision overrides the legally designated surrogate.

14. A patient with diabetic ketoacidosis has serum sodium 138 mEq/L, chloride 101 mEq/L, and bicarbonate 10 mEq/L. What is the calculated anion gap?

A. The anion gap is 10 mEq/L because bicarbonate alone determines the gap.

B. The anion gap is 27 mEq/L, indicating accumulation of unmeasured anions.

C. The anion gap is 17 mEq/L because sodium is subtracted from chloride and bicarbonate.

D. The anion gap is 37 mEq/L because chloride and bicarbonate are added to sodium.

E. The anion gap is 3 mEq/L because ketoacids lower the concentration of unmeasured anions.

15. A patient with severe iron-deficiency anemia has a hemoglobin concentration of 6 g/dL but normal lungs. Which arterial blood measurement is most likely to remain near normal?

A. Arterial oxygen content remains near normal because dissolved oxygen carries most oxygen in blood.

B. Mixed venous oxygen content rises because fewer hemoglobin molecules extract oxygen from systemic capillaries.

C. Oxygen-carrying capacity rises because each remaining hemoglobin molecule binds extra oxygen molecules.

D. Pulse oximeter saturation must fall in proportion to the decrease in total circulating hemoglobin concentration.

E. Arterial oxygen tension remains near normal because it reflects dissolved oxygen rather than hemoglobin concentration.

16. A healthy adult has an anatomic dead space of 150 mL, tidal volume of 500 mL, and respiratory rate of 12/min. What is the approximate alveolar ventilation?

A. About 1.8 L/min, calculated by multiplying dead-space volume by respiratory rate.

B. About 6.0 L/min, calculated as tidal volume multiplied by respiratory rate without subtracting dead space.

C. About 4.2 L/min, calculated as (500 minus 150) mL multiplied by 12 breaths/min.

D. About 7.8 L/min, calculated by adding dead-space ventilation to total minute ventilation.

E. About 0.35 L/min, calculated as tidal volume minus dead space without incorporating respiratory frequency.

17. A patient with chronic hypoxemia from severe lung disease develops secondary erythrocytosis. Which renal cell type is the principal physiologic source of the hormone driving this response?

A. Peritubular interstitial fibroblast-like cells in the renal cortex and outer medulla increase erythropoietin production.

B. Juxtaglomerular granular cells increase erythropoietin whenever afferent arteriolar pressure falls during hypoxemia.

C. Proximal tubular epithelial cells secrete erythropoietin directly in proportion to filtered sodium delivery.

D. Collecting-duct principal cells release erythropoietin when vasopressin increases water permeability.

E. Glomerular podocytes synthesize most circulating erythropoietin after sensing decreased capillary oxygen tension.

18. Among 200 people without a disease, 180 have a negative test result. What is the specificity?

A. Specificity is 90%, because 180 of 200 unaffected people test negative.

B. Specificity is 10%, because 20 unaffected people test positive.

C. Specificity is 180%, because true negatives are divided by false positives.

D. Specificity cannot be calculated unless disease prevalence is known.

E. Specificity is the proportion of affected people who are correctly identified by the test.

19. A patient has primary hypothyroidism. Which hormone pattern is expected if the hypothalamus and pituitary are intact?

A. Low free thyroid hormone causes TSH to fall because pituitary thyrotrophs require thyroid hormone for secretion.

B. TSH remains fixed because thyroid hormones provide feedback only to the hypothalamus and not the pituitary.

C. TSH falls while TRH falls because the hypothalamic-pituitary-thyroid axis uses positive feedback at low hormone levels.

D. Low free thyroid hormone removes negative feedback, causing TSH to rise.

E. Free thyroid hormone rises because primary thyroid failure increases pituitary TSH enough to overcome complete gland dysfunction.

20. A neuron is exposed to a drug that selectively increases membrane permeability to potassium at rest. Which change in membrane potential is most likely?

A. The membrane potential moves toward the sodium equilibrium potential and becomes more positive.

B. The membrane potential moves closer to the potassium equilibrium potential and becomes more negative.

C. The membrane potential remains fixed because resting voltage is determined only by the sodium-potassium ATPase.

D. The membrane potential becomes exactly zero because equal positive and negative charges cross the membrane.

E. The membrane potential becomes less negative because potassium entry exceeds potassium exit at normal intracellular concentrations.

21. A patient with inflammation has low serum iron despite adequate total body iron stores. Which hormone is most responsible for this pattern?

A. Erythropoietin degrades transferrin and prevents iron from circulating to developing erythroid cells.

B. Thrombopoietin closes divalent metal transporter 1 and therefore blocks iron entry into enterocytes.

C. Ceruloplasmin internalizes transferrin receptors on hepatocytes and produces systemic iron sequestration.

D. Hepcidin binds ferroportin and reduces intestinal iron export and macrophage iron release.

E. Ferritin is secreted as a circulating hormone that directly destroys ferroportin on marrow macrophages.

22. A skeletal muscle fiber is stimulated and an action potential travels down a transverse tubule. Which event most directly initiates calcium release from the sarcoplasmic reticulum?

A. Extracellular calcium binds troponin C directly and opens ryanodine receptors without a transverse-tubule signal.

B. Voltage-sensitive dihydropyridine receptors mechanically activate ryanodine receptors in the terminal cisternae.

C. Acetylcholine enters the transverse tubule and binds ryanodine receptors on the sarcoplasmic reticulum membrane.

D. Myosin ATPase hydrolyzes ATP before calcium release and sends a mechanical signal back to the terminal cisternae.

E. SERCA pumps release stored calcium into the cytosol when the muscle membrane becomes depolarized.

23. A healthy person doubles respiratory rate while tidal volume falls so that total minute ventilation remains unchanged. Why can alveolar ventilation decrease?

A. A larger fraction of each minute's ventilation is spent repeatedly filling anatomic dead space when breaths are smaller and more frequent.

B. Anatomic dead space doubles in exact proportion to respiratory rate because conducting airways lengthen with faster breathing.

C. Alveolar ventilation always equals minute ventilation, so it cannot change if total inspired volume per minute is fixed.

D. Faster breathing eliminates dead-space ventilation because inspired gas reaches alveoli before entering conducting airways.

E. Tidal volume has no effect on fresh alveolar gas delivery as long as oxygen concentration in inspired air remains constant.

24. A bronchus is completely obstructed while perfusion to the corresponding alveoli remains intact. What is the local ventilation-perfusion ratio?

A. The ratio approaches zero, producing a shunt-like region with perfusion but no ventilation.

B. The ratio approaches infinity because ventilation continues but perfusion stops distal to an airway obstruction.

C. The ratio remains near one because hypoxic vasoconstriction instantly eliminates every drop of local blood flow.

D. The ratio becomes greater than one because trapped alveolar gas continues to count as ongoing ventilation.

E. The ratio cannot be defined because V/Q concepts apply only to whole-lung averages and not to regional physiology.

25. A toxin blocks voltage-gated sodium channels in a peripheral nerve. Which phase of the neuronal action potential is most directly impaired?

A. The after-hyperpolarization is abolished because it depends exclusively on inward sodium current through blocked channels.

B. The resting membrane potential becomes strongly positive because potassium leak channels immediately close.

C. The rapid depolarizing upstroke is reduced because inward sodium current cannot develop normally.

D. Neurotransmitter synthesis in the cell body stops because sodium channels are required for ribosomal translation.

E. Myelin production ceases acutely because voltage-gated sodium channels supply the membrane lipids used by Schwann cells.

26. A parietal cell is actively secreting hydrochloric acid. Which apical transporter directly secretes hydrogen ions into the gastric lumen?

A. The Na/K-ATPase exchanges intracellular hydrogen for luminal sodium at the apical membrane.

B. A sodium-hydrogen exchanger secretes hydrogen as the final ATP-dependent step in gastric acid secretion.

C. A chloride-bicarbonate exchanger secretes hydrogen directly while moving chloride into the parietal cell.

D. The H/K-ATPase exchanges intracellular hydrogen for luminal potassium using ATP.

E. The proton channel on chief cells secretes hydrogen into the lumen and then transfers acid to adjacent parietal cells.

27. An unconscious patient arrives with a ruptured ectopic pregnancy and life-threatening hemorrhage. No surrogate can be reached in time. What is the best ethical approach?

A. Delay all treatment until a court order is obtained because consent is always required before emergency surgery.

B. Wait until a distant relative can be contacted even if the delay substantially increases the risk of death.

C. Perform only diagnostic testing because emergency consent never permits therapeutic intervention.

D. Assume refusal because the patient did not previously sign a specific consent form for this emergency.

E. Provide immediately necessary treatment under the emergency exception to informed consent.

28. A skeletal muscle fiber is exposed to enough calcium to saturate troponin C. What is the immediate effect on the thin filament?

A. Troponin C blocks the myosin-binding sites on actin and prevents cross-bridge formation during calcium elevation.

B. Calcium binds directly to myosin heads and prevents ATP binding until the muscle has fully relaxed.

C. Tropomyosin activates SERCA and removes calcium from the cytosol before any actin-myosin interaction occurs.

D. Tropomyosin moves away from myosin-binding sites on actin, permitting cross-bridge cycling.

E. Troponin I hydrolyzes ATP and pulls the thick filament toward the Z line independently of myosin.

29. A patient develops an acute increase in systemic vascular resistance while preload and contractility are initially unchanged. Which ventricular change is expected on the next beat?

A. End-systolic volume falls because higher afterload directly increases the velocity of myocardial fiber shortening.

B. End-systolic volume rises because the ventricle ejects less against the higher afterload.

C. End-diastolic volume immediately becomes zero because the aortic pressure prevents mitral-valve opening.

D. Stroke volume rises because the higher arterial pressure creates a larger gradient from aorta into the left ventricle.

E. Ejection fraction rises because afterload has no effect on ventricular emptying when contractility is unchanged.

30. A patient with salicylate toxicity has pH 7.46, PCO2 22 mm Hg, and bicarbonate 15 mEq/L. Which interpretation best fits these values?

A. A pure respiratory alkalosis is present because bicarbonate cannot fall during acute hyperventilation.

B. A pure metabolic acidosis is present because a low bicarbonate excludes a simultaneous respiratory disorder.

C. A mixed respiratory alkalosis and metabolic acidosis is present.

D. A mixed respiratory acidosis and metabolic alkalosis is present because the pH is slightly alkalemic.

E. Normal acid-base physiology is present because the opposing abnormalities cancel each other at the level of pH.

31. A patient has a TSH-secreting pituitary adenoma. Which pattern distinguishes this from primary hyperthyroidism?

A. Free thyroid hormone is elevated while TSH is inappropriately elevated or unsuppressed.

B. Free thyroid hormone is elevated with a fully suppressed TSH, which is the defining pattern of autonomous pituitary TSH secretion.

C. Free thyroid hormone is low and TSH is high because pituitary tumors cannot stimulate a normal thyroid gland.

D. Free thyroid hormone and TSH are both low because any pituitary mass abolishes all hormone secretion.

E. Free thyroid hormone is normal and TSH is undetectable because thyroid hormone secretion is independent of TSH in adults.

32. After a meal, gastric acid secretion rises. Which mediator acts directly on H2 receptors of parietal cells to raise cAMP?

A. Somatostatin from D cells activates H2 receptors and increases cAMP in parietal cells during gastric distention.

B. Secretin from the duodenum activates H2 receptors and stimulates gastric acid to neutralize pancreatic bicarbonate.

C. Cholecystokinin from I cells is the principal H2-receptor ligand that drives parietal-cell acid output.

D. Pepsin released from chief cells binds H2 receptors and directly stimulates the proton pump.

E. Histamine released from enterochromaffin-like cells activates H2 receptors and potentiates acid secretion.

33. A healthy person stands upright. Compared with the lung apex, why is perfusion much greater at the lung base?

A. Alveolar oxygen tension is always much lower at the base, causing pulmonary arteriolar dilation through systemic-type hypoxic responses.

B. Gravity raises pulmonary vascular hydrostatic pressure in dependent regions, recruiting and distending more vessels.

C. Pleural pressure is more negative at the base, compressing capillaries less and forcing blood downward by suction.

D. The right ventricle ejects blood only into lower-lobe arteries because upper-lobe vessels close during every systole.

E. Pulmonary blood flow is actively pumped by diaphragmatic contraction and therefore occurs only in dependent lung tissue.

34. A positive inotropic drug is given to a patient with otherwise unchanged preload and afterload. How does the left ventricular pressure-volume loop change?

A. The end-systolic pressure-volume relation becomes flatter, end-systolic volume rises, and stroke volume falls.

B. The end-diastolic pressure-volume relation shifts upward because contractility directly makes the ventricle less compliant in diastole.

C. End-systolic volume remains fixed because contractility affects only heart rate and not ventricular emptying.

D. Stroke volume falls because stronger contraction closes the aortic valve earlier and prevents ventricular ejection.

E. The end-systolic pressure-volume relation becomes steeper, end-systolic volume falls, and stroke volume rises.

35. A physician discovers that a medication error reached a patient and caused transient harm. What is the most appropriate communication strategy?

A. Disclose the error promptly and truthfully, explain known consequences and next steps, and report it through appropriate safety channels.

B. Conceal the error if the patient has recovered because disclosure is required only for permanent injury.

C. Alter the medical record so the event appears to have been an unavoidable disease complication.

D. Tell the patient only that an unexpected event occurred and avoid identifying the medication error to reduce distress.

E. Wait until the patient independently asks whether an error occurred before discussing the event.

36. A healthy person ascends to altitude. Which initial change in the alveolar gas equation contributes directly to lower alveolar oxygen tension?

A. The inspired oxygen fraction falls sharply below 10% because nitrogen replaces oxygen as altitude increases.

B. Water vapor pressure in the airways rises in direct proportion to altitude and displaces nearly all inspired oxygen.

C. Alveolar carbon dioxide necessarily rises because hypoxia suppresses ventilation during the first minutes at altitude.

D. Lower barometric pressure reduces inspired oxygen partial pressure even though the inspired oxygen fraction remains about 21%.

E. Respiratory quotient becomes zero at altitude, eliminating oxygen from alveolar gas independently of barometric pressure.

37. Acidic chyme enters the duodenum. Which hormone is released and what is its major pancreatic effect?

A. Gastrin stimulates pancreatic acinar bicarbonate secretion and increases gastric emptying until duodenal pH falls further.

B. Motilin stimulates pancreatic enzyme secretion only during the fed state and neutralizes acid by increasing protease output.

C. Somatostatin stimulates bicarbonate secretion while simultaneously increasing gastric acid production.

D. Ghrelin stimulates pancreatic duct cells to secrete hydrochloric acid into the duodenum.

E. Secretin stimulates pancreatic ductal bicarbonate-rich fluid secretion to neutralize luminal acid.

38. A patient with chronic hypertension develops concentric left ventricular hypertrophy. Which pressure-volume change is most consistent with reduced ventricular compliance?

A. A given end-diastolic volume is associated with a lower end-diastolic pressure because a stiff ventricle stores more elastic energy.

B. The end-diastolic pressure-volume relation becomes flatter because hypertrophy increases passive ventricular compliance.

C. A given end-diastolic volume is associated with a higher end-diastolic pressure.

D. End-diastolic pressure becomes independent of volume because chamber stiffness eliminates elastic behavior entirely.

E. Only end-systolic pressure changes because ventricular compliance affects contraction but not filling.

39. Thyroid-stimulating hormone binds its receptor on a thyroid follicular cell. Which second-messenger pathway is most important?

A. Gi activation lowers cAMP and is the principal stimulatory signal for iodide uptake and thyroglobulin synthesis.

B. Gs activation increases cAMP and stimulates multiple steps in thyroid hormone synthesis and release.

C. Gq activation is the only TSH-receptor pathway and directly opens nuclear thyroid hormone receptors at the cell surface.

D. A ligand-gated chloride channel depolarizes the follicular cell and causes exocytosis of preformed T3 from synaptic vesicles.

E. Receptor tyrosine kinase activity phosphorylates insulin receptor substrate as the exclusive TSH signaling mechanism.

40. A man has a large acute hemorrhage. During the first minutes before substantial interstitial fluid shifts occur, which change is most likely?

A. Hematocrit immediately falls sharply because red cells leave the circulation faster than plasma during whole-blood loss.

B. Hematocrit immediately rises because plasma is selectively lost while circulating erythrocytes remain intravascular.

C. Plasma volume is unchanged because capillary refill completely replaces the lost volume within the first minute.

D. Both red-cell mass and plasma volume fall proportionately, so hematocrit may initially remain near its previous value.

E. Red-cell mass is preserved because splenic contraction instantly replaces all erythrocytes lost during hemorrhage.

41. A patient with opioid-induced hypoventilation has a high arterial carbon dioxide tension. Which alveolar change is expected if metabolism is unchanged?

A. Alveolar carbon dioxide falls because less ventilation reduces delivery of carbon dioxide from blood to alveoli.

B. Alveolar carbon dioxide rises as alveolar ventilation falls, approximately following an inverse relationship.

C. Arterial carbon dioxide is independent of alveolar ventilation and depends only on inspired oxygen concentration.

D. Carbon dioxide remains fixed because respiratory quotient automatically decreases enough to offset any ventilatory change.

E. Alveolar carbon dioxide can rise only if anatomic dead space falls to zero during hypoventilation.

42. Fat and amino acids enter the duodenum. Which hormone most directly stimulates pancreatic acinar enzyme secretion and gallbladder contraction?

A. Secretin released from S cells is the principal trigger for acinar digestive enzymes and forceful gallbladder contraction after fat.

B. Gastrin released from G cells contracts the gallbladder and is the dominant regulator of pancreatic lipase secretion.

C. Cholecystokinin released from I cells coordinates pancreatic enzyme release and gallbladder emptying.

D. Motilin released during fasting produces the strongest postprandial gallbladder contraction in response to dietary fat.

E. GIP released from K cells directly contracts the gallbladder and stimulates pancreatic zymogen exocytosis more than CCK.

43. A patient in early septic shock has warm extremities, bounding pulses, and a widened pulse pressure. Which hemodynamic change most directly produces this pattern?

A. A large rise in systemic vascular resistance from diffuse arteriolar constriction produces the warm skin.

B. Complete loss of cardiac sympathetic stimulation reduces cardiac output while widening the pulse pressure.

C. A fall in venous capacitance traps blood in the central circulation and raises systemic vascular resistance.

D. An isolated increase in pulmonary vascular resistance directly causes generalized cutaneous vasodilation.

E. Marked reduction in systemic vascular resistance from widespread vasodilation increases the hyperdynamic circulation.

44. A neuron has just completed an action potential and is in the absolute refractory period. Why can a second action potential not be generated regardless of stimulus strength?

A. Most voltage-gated sodium channels are in the inactivated state and cannot reopen until the membrane repolarizes.

B. All potassium leak channels are permanently closed until the cell receives a second synaptic input.

C. The sodium-potassium ATPase has exhausted intracellular ATP and cannot restore any ion gradient during this interval.

D. The membrane has become electrically neutral, eliminating the driving force for every transmembrane ion movement.

E. Calcium channels in the axon hillock remain open and clamp the membrane at the calcium equilibrium potential.

45. A patient receives a drug that inhibits acetylcholinesterase at the neuromuscular junction. What is the immediate synaptic effect?

A. Acetylcholine release from the motor nerve terminal stops because presynaptic vesicles require acetylcholinesterase for exocytosis.

B. Nicotinic receptors become unable to bind acetylcholine because acetylcholinesterase is their obligatory receptor cofactor.

C. Calcium entry into the motor nerve terminal is eliminated because acetylcholinesterase opens presynaptic voltage-gated calcium channels.

D. Acetylcholine persists longer in the synaptic cleft and prolongs activation of nicotinic receptors on the motor end plate.

E. Acetylcholine is converted more rapidly to acetate and choline, shortening the end-plate potential below threshold.

46. A patient has severe arterial hypoxemia. Which peripheral receptor is primarily responsible for the resulting increase in ventilation?

A. Central medullary chemoreceptors directly sense low arterial oxygen because oxygen crosses the blood-brain barrier and binds their hemoglobin.

B. Aortic baroreceptors detect low oxygen content by sensing decreased arterial wall stretch independently of blood pressure.

C. Carotid bodies increase afferent firing when arterial oxygen tension falls substantially, especially below about 60 mm Hg.

D. Pulmonary J receptors are the main systemic oxygen sensors and release erythropoietin when PaO2 falls.

E. Hypothalamic osmoreceptors detect low oxygen saturation and stimulate ventilation by increasing vasopressin release.

47. A healthy person stands suddenly from a supine position. Which immediate hemodynamic change occurs before the baroreflex compensates?

A. Venous pooling in the legs reduces central venous pressure, ventricular preload, and stroke volume.

B. Venous return rises because gravity drives blood from the legs directly toward the right atrium during standing.

C. Stroke volume rises because reduced thoracic blood volume increases ventricular end-diastolic fiber stretch.

D. Systemic arterial pressure rises immediately because standing directly constricts arterioles before any reflex signaling occurs.

E. Pulmonary venous pressure increases because lower-extremity veins empty into the lungs before reaching the right heart.

48. A healthy person performs dynamic exercise. Which vascular change is expected in active skeletal muscle?

A. Alpha-adrenergic vasoconstriction completely overrides local metabolites, causing active muscle blood flow to fall below rest.

B. Capillary recruitment decreases because contracting muscle requires less oxygen extraction when metabolic rate rises.

C. Local adenosine and potassium cause vasoconstriction so blood can be redirected to inactive tissues.

D. Venous oxygen content from active muscle rises substantially because extraction falls as oxygen demand increases.

E. Local metabolites dilate resistance vessels, markedly increasing muscle blood flow despite increased sympathetic activity.

49. A healthy person fasts overnight. Which gastrointestinal motility pattern helps clear residual material from the stomach and small bowel between meals?

A. The migrating motor complex produces periodic propagated contractions during fasting and is associated with motilin.

B. Segmentation contractions stop completely during fasting, and no organized motor activity occurs until the next meal.

C. Mass movements occur continuously in the small intestine and are driven primarily by gastrin during fasting.

D. Receptive relaxation of the stomach generates a peristaltic wave that traverses the entire small bowel every minute.

E. The gastrocolic reflex is the principal fasting pattern and empties the small intestine into the colon before breakfast.

50. A diagnostic test has fixed sensitivity and specificity. The same test is moved from a low-prevalence clinic population to a much higher-prevalence referral population. Which change is expected?

A. Positive predictive value generally falls because true-positive results become less common as prevalence increases.

B. Positive predictive value generally increases because a positive result is more likely to represent true disease when prevalence is higher.

C. Sensitivity must increase because prevalence is part of the formula for the true-positive fraction.

D. Specificity must decrease because a higher prevalence automatically creates more false-positive results among unaffected people.

E. Likelihood ratios become equal to prevalence and therefore cannot be used across populations.

51. A resident enters the wrong medication dose, but a pharmacist catches it before administration and the patient is unharmed. What should the resident do?

A. Hide the event because no medication reached the patient and therefore no safety problem occurred.

B. Delete the original order from the record and avoid discussing it so the resident is not blamed.

C. Report the near miss through the safety system and participate in analysis of how the ordering process allowed the error.

D. Wait for the same error to cause patient harm before using the reporting system.

E. Report only the pharmacist for delaying medication administration rather than reviewing the ordering process.

52. A patient has interstitial pulmonary fibrosis. Which gas-exchange measurement is likely to be reduced because of increased diffusion distance?

A. Diffusing capacity increases because carbon monoxide remains longer in the alveolus when the membrane is thickened.

B. Diffusing capacity for carbon monoxide decreases because the thickened alveolar-capillary barrier impairs transfer.

C. Anatomic dead space becomes zero because fibrotic tissue converts conducting airways into gas-exchange surfaces.

D. Pulmonary blood flow necessarily doubles, making diffusion capacity independent of membrane thickness.

E. Residual volume alone determines carbon monoxide transfer, so membrane fibrosis does not affect diffusing capacity.

53. A patient has a do-not-resuscitate order but develops bacterial pneumonia that is readily treatable. Which interpretation is most appropriate?

A. A DNR order automatically means comfort-only care, so antibiotics and diagnostic testing must be withheld.

B. The DNR order should be ignored until the patient is actively dying because it has no effect on emergency decisions.

C. The DNR order limits cardiopulmonary resuscitation after arrest and does not automatically prohibit antibiotics or other indicated treatments.

D. A DNR order prevents the patient from receiving oxygen, intravenous fluids, rehabilitation, or symptom treatment.

E. The physician should convert the patient to full code before treating pneumonia because DNR status and active treatment cannot coexist.

54. A healthy person performs a sustained heavy isometric handgrip. Which hemodynamic response is most likely?

A. Sympathetic activation increases heart rate and systemic vascular resistance, raising both systolic and diastolic pressure.

B. Systemic vascular resistance falls dramatically because mechanically compressed muscle arterioles remain maximally dilated.

C. Heart rate falls through dominant vagal activation because static exercise does not engage the sympathetic nervous system.

D. Arterial pressure decreases because isometric contraction eliminates venous return to the heart throughout the body.

E. Diastolic pressure falls toward zero because all resistance vessels open fully during static muscle contraction.

55. A healthy term newborn takes the first several breaths after delivery. Pulmonary vascular resistance falls rapidly and left atrial pressure rises above right atrial pressure. Which immediate physiologic change most directly produces functional closure of the foramen ovale?

A. Higher right atrial pressure pulls the septum primum away from the septum secundum during inspiration.

B. Increased placental venous return maintains right-to-left flow across the atrial septum after birth.

C. Higher left atrial than right atrial pressure presses the septum primum against the septum secundum.

D. Rising pulmonary vascular resistance redirects blood from the left atrium toward the right atrium.

E. Constriction of the ductus venosus directly seals the interatrial communication through shared smooth muscle.

56. During the cross-bridge cycle in skeletal muscle, ATP binds to a myosin head. What occurs next?

A. Myosin binds more tightly to actin because ATP directly stabilizes the rigor state of the cross-bridge.

B. The power stroke occurs immediately because ATP binding releases inorganic phosphate from actin.

C. Calcium is pumped out of the sarcoplasmic reticulum because myosin-bound ATP activates ryanodine receptors.

D. Troponin C releases calcium because ATP binding to myosin directly lowers troponin affinity for calcium.

E. Myosin detaches from actin; subsequent ATP hydrolysis recocks the head for another cycle.

57. A motor neuron action potential reaches the presynaptic terminal at a skeletal neuromuscular junction. Which event directly triggers acetylcholine vesicle fusion?

A. Opening of postsynaptic nicotinic sodium channels raises presynaptic calcium before acetylcholine is released.

B. Opening of voltage-gated calcium channels raises terminal calcium and activates the vesicle-fusion machinery.

C. Closure of presynaptic potassium leak channels causes vesicles to fuse independently of intracellular calcium.

D. Activation of acetylcholinesterase releases stored calcium from the synaptic vesicle lumen into the terminal cytoplasm.

E. Binding of acetylcholine to presynaptic muscarinic receptors is required before the first vesicle can undergo exocytosis.

58. A patient has hereditary spherocytosis with splenic sequestration of poorly deformable red cells. Which normal red-cell property is most important for passage through splenic cords and sinusoids?

A. A rigid spectrin lattice prevents shape change and preserves the biconcave disc while crossing narrow splenic channels.

B. A low surface-area-to-volume ratio allows cells to become spherical and therefore pass more efficiently through slits.

C. Nuclear contraction provides the major mechanical adaptation that lets mature erythrocytes traverse splenic sinusoids.

D. Continuous actin polymerization propels erythrocytes actively through splenic cords against local pressure gradients.

E. A high surface-area-to-volume ratio permits marked reversible deformation without membrane rupture.

59. A bolus distends a segment of small intestine. Which enteric reflex pattern promotes forward propulsion?

A. Contraction occurs proximal to the bolus and relaxation distal to it, creating peristaltic propulsion.

B. Relaxation occurs proximal to the bolus and contraction distal to it, forcing contents backward toward the stomach.

C. Both proximal and distal segments contract equally, trapping the bolus in place without net propulsion.

D. Peristalsis requires direct sympathetic activation and cannot be generated by intrinsic enteric circuits.

E. The bolus is propelled only by gravity because circular smooth muscle does not coordinate directional contractions.

60. A thyroid follicular cell takes up iodide from blood. Which basolateral transporter performs this step?

A. Pendrin is the basolateral sodium-iodide symporter and carries iodide from blood directly into the follicular cell.

B. Thyroid peroxidase pumps iodide across the basolateral membrane using ATP before oxidizing it in the cytoplasm.

C. The Na/K-ATPase transports iodide directly in exchange for potassium at the basolateral surface.

D. The chloride-bicarbonate exchanger is the exclusive thyroid iodide transporter and is independent of sodium.

E. The sodium-iodide symporter uses the sodium gradient to concentrate iodide inside the follicular cell.

61. A cohort study finds disease in 30 of 300 exposed participants and 10 of 500 unexposed participants. What is the relative risk?

A. The relative risk is 5 because risk is 10% in the exposed group and 2% in the unexposed group.

B. The relative risk is 3 because there are three times as many cases in the exposed group without accounting for group size.

C. The relative risk is 0.2 because the unexposed risk is divided by the exposed risk.

D. The relative risk is 20 because the difference between 30 and 10 cases is used directly.

E. Relative risk cannot be calculated from a cohort study because only odds ratios are available.

62. A meal enters the stomach and the proximal stomach expands with little increase in intragastric pressure. Which mechanism permits this accommodation?

A. Sympathetic activation contracts the fundus strongly, increasing compliance by raising wall tension.

B. Gastric smooth muscle becomes electrically silent because food blocks all enteric neurotransmission during filling.

C. Pyloric contraction pulls the fundus open mechanically and is the sole cause of gastric accommodation.

D. Parietal-cell acid secretion relaxes gastric smooth muscle directly through luminal hydrogen ions.

E. Vagovagal reflexes produce receptive relaxation of the gastric fundus and proximal body.

63. A patient with a large acute myocardial infarction develops hypotension, cool extremities, pulmonary edema, and elevated jugular venous pressure. Which hemodynamic profile is most consistent with cardiogenic shock?

A. Cardiac output is increased while systemic vascular resistance and filling pressures are reduced.

B. Cardiac output is reduced while systemic vascular resistance and cardiac filling pressures are increased.

C. Cardiac output and systemic vascular resistance are both increased while filling pressures are low.

D. Cardiac output is normal because reflex tachycardia fully compensates for severe loss of contractility.

E. Systemic vascular resistance falls markedly because cardiogenic shock is primarily a distributive process.

64. A patient has increased peripheral conversion of thyroxine to the more active hormone triiodothyronine. Which enzyme class performs this reaction?

A. Thyroid peroxidase removes iodine from circulating T4 in peripheral tissues to generate active T3.

B. Aromatase converts T4 into T3 by removing a methyl group from the thyroid hormone backbone.

C. Monoamine oxidase converts T4 into T3 after uptake into adrenergic nerve terminals.

D. Carbonic anhydrase converts T4 into T3 by altering plasma pH and releasing bound iodine.

E. 5-prime deiodinases remove an outer-ring iodine from T4 to generate active T3.

65. A patient with severe anemia undergoes measurement of pulmonary diffusing capacity for carbon monoxide. How can anemia affect the result?

A. Measured diffusing capacity rises markedly because anemia creates more empty plasma space for carbon monoxide dissolution.

B. Measured diffusing capacity can be reduced because less hemoglobin is available to bind carbon monoxide in pulmonary capillary blood.

C. Anemia has no effect because carbon monoxide transfer is determined only by alveolar membrane thickness and surface area.

D. Anemia makes carbon monoxide unable to cross the alveolar membrane because red cells generate the diffusion gradient.

E. Measured diffusing capacity becomes infinite because carbon monoxide cannot bind hemoglobin and therefore never equilibrates.

66. A patient with massive pulmonary embolism is hypotensive with distended neck veins and clear lungs. Which physiologic mechanism best explains the shock?

A. Pulmonary embolism primarily lowers systemic vascular resistance through direct dilation of systemic arterioles.

B. An abrupt increase in right ventricular afterload reduces right ventricular output and consequently lowers left ventricular preload.

C. The embolus increases left ventricular preload by forcing blood rapidly through the pulmonary circulation.

D. Shock occurs because pulmonary capillary hydrostatic pressure always rises enough to cause severe left-sided pulmonary edema.

E. The main defect is isolated bradycardia from excessive carotid sinus stimulation rather than impaired forward flow.

67. A patient has severe hemorrhage. Which sympathetic effect most directly increases venous return?

A. Venoconstriction decreases venous capacitance and shifts blood from peripheral reservoirs toward the central circulation.

B. Venodilation increases venous capacitance and pushes stored blood toward the heart by lowering peripheral venous pressure.

C. Arteriolar dilation raises mean systemic filling pressure and is the principal mechanism of increased venous return.

D. Reduced skeletal-muscle tone enhances the muscle pump and empties dependent veins more efficiently.

E. Slower heart rate increases right atrial pressure enough to draw additional blood from the systemic veins.

68. A patient receives a competitive antagonist at skeletal-muscle nicotinic acetylcholine receptors. Which change occurs at the motor end plate?

A. The end-plate potential becomes larger because fewer receptors decrease local potassium permeability and prolong depolarization.

B. Motor-nerve action potentials fail to arrive because postsynaptic nicotinic receptors are required for axonal conduction.

C. Acetylcholine release increases enough to guarantee a muscle action potential regardless of antagonist concentration.

D. The end-plate potential becomes smaller, reducing the likelihood that nearby voltage-gated sodium channels reach threshold.

E. Muscle contraction becomes independent of membrane depolarization because the antagonist directly opens sarcoplasmic calcium channels.

69. A patient has a sudden decrease in carotid sinus pressure. What happens to baroreceptor firing and autonomic output?

A. Afferent firing rises, sympathetic activity falls, and parasympathetic activity rises.

B. Afferent firing falls, but both sympathetic and parasympathetic activity fall because the reflex is purely inhibitory.

C. Afferent firing falls, sympathetic activity rises, and parasympathetic activity falls.

D. Afferent firing is unchanged because carotid baroreceptors respond to oxygen tension rather than stretch.

E. Afferent firing rises and directly causes renal sodium excretion without changing cardiovascular autonomic tone.

70. A patient with autonomic neuropathy stands suddenly and has a large fall in blood pressure. Which normal reflex response is impaired?

A. Reduced carotid-sinus firing should increase sympathetic outflow and decrease parasympathetic outflow to restore arterial pressure.

B. Reduced carotid-sinus firing should decrease sympathetic outflow and increase vagal activity to slow the heart further.

C. Increased carotid-sinus firing should increase sympathetic vasoconstriction because baroreceptors are activated by low stretch.

D. Aortic arch baroreceptors should release renin directly into the bloodstream within one heartbeat of standing.

E. Vagal efferents should constrict systemic arterioles as the main mechanism for restoring total peripheral resistance.

71. A patient with terminal cancer asks for stronger analgesia despite concern that appropriately titrated opioids might unintentionally shorten life. What principle best guides care?

A. Withhold adequate analgesia whenever there is any theoretical possibility of respiratory depression, regardless of the patient's suffering.

B. Give a deliberately lethal opioid dose because terminal illness makes intent irrelevant to ethical analysis.

C. Treat pain proportionately to relieve suffering when the intention is symptom control, while titrating and monitoring appropriately.

D. Treat pain only after the patient loses consciousness so analgesia cannot affect informed decision-making.

E. Use placebo analgesia first because terminally ill patients should not be told when opioids are withheld.

72. A healthy adult has an increased glomerular filtration rate after isolated dilation of the afferent arteriole. Which glomerular change most directly causes this effect?

A. Glomerular capillary hydrostatic pressure falls because afferent dilation prevents blood from entering the capillary tuft.

B. Bowman space hydrostatic pressure rises enough to increase filtration by pushing fluid into glomerular capillaries.

C. Plasma oncotic pressure in the glomerulus rises abruptly before filtration begins and drives fluid into Bowman space.

D. Glomerular capillary hydrostatic pressure rises as resistance to inflow decreases.

E. The filtration coefficient falls to zero because afferent dilation closes endothelial fenestrations.

73. A patient dies and skeletal muscles become rigid several hours later. Which molecular event best explains rigor mortis?

A. Excess ATP locks myosin heads onto actin and prevents calcium from leaving the sarcoplasmic reticulum.

B. Loss of acetylcholine causes persistent depolarization of the motor end plate and continuous action potentials.

C. Troponin C is destroyed immediately after death, exposing actin sites that bind myosin irreversibly.

D. Potassium depletion prevents actin from polymerizing, causing thick filaments to fuse to the Z discs.

E. ATP depletion prevents myosin heads from detaching from actin after cross-bridge formation.

74. A muscle fiber shortens while lifting a constant external load. Which type of contraction is occurring?

A. An eccentric contraction occurs because the activated muscle is lengthening while resisting the load.

B. An isometric contraction occurs because muscle length remains fixed while tension increases against an immovable load.

C. A passive elastic recoil occurs because no cross-bridge cycling is required once external load is constant.

D. A concentric isotonic contraction develops enough tension to shorten the muscle while the load is moved.

E. A tetanic relaxation occurs because repeated stimuli reduce intracellular calcium and shorten the muscle.

75. A patient asks the physician not to tell family members about a new cancer diagnosis. The family later calls requesting details. What should the physician do?

A. Disclose the full diagnosis because close relatives automatically have access to an adult patient's medical information.

B. Ask the family to sign a confidentiality waiver on the patient's behalf and then release the record.

C. Postpone telling the patient about treatment options until the family agrees to the confidentiality preference.

D. Refuse to speak with the family at all, including listening to information they may wish to provide about the patient.

E. Protect the patient's confidentiality and share information with family only to the extent the patient authorizes or another recognized exception applies.

76. A skeletal muscle is stimulated at progressively higher frequencies until individual twitches merge into sustained force. What explains temporal summation?

A. Each stimulus recruits a new sarcomere within the same muscle fiber, so the fiber becomes physically longer with frequency.

B. Repeated stimulation lowers cytosolic calcium, which increases troponin sensitivity and raises force despite fewer cross-bridges.

C. Action potentials become larger with each stimulus and eventually exceed the sodium equilibrium potential.

D. Cytosolic calcium remains elevated between stimuli, allowing more cross-bridges to remain active and force to increase.

E. Motor neurons release progressively larger acetylcholine molecules that remain bound longer to each receptor.

77. Investigators begin with patients who have a rare disease and matched controls without the disease, then compare prior exposures. Which measure of association is most appropriate?

A. The incidence rate ratio is calculated directly because prospective person-time is measured from exposure to outcome.

B. The absolute risk reduction is directly available because disease risks in exposed and unexposed populations are known.

C. The prevalence ratio is required because every case-control study is a cross-sectional survey.

D. The number needed to treat is the preferred measure even though no intervention was assigned.

E. The odds ratio is the standard association measure because subjects were selected according to outcome status.

78. A patient with hyperthyroidism has a widened pulse pressure and warm skin. Which cardiovascular effect of thyroid hormone contributes?

A. Reduced beta-adrenergic responsiveness lowers cardiac output while intense cutaneous vasoconstriction lowers heat loss.

B. Increased beta-adrenergic responsiveness raises cardiac output while peripheral vasodilation lowers systemic vascular resistance.

C. Thyroid hormone directly closes cardiac calcium channels and slows heart rate despite increased metabolic demand.

D. Systemic vascular resistance rises markedly because thyroid hormone suppresses local metabolic vasodilation in active tissues.

E. Cardiac output remains unchanged because thyroid hormone affects metabolism but has no cardiovascular actions.

79. A drug blocks beta-1 adrenergic receptors. Which direct cardiac effect is expected during sympathetic stimulation?

A. Increased IP3 signaling raises sinoatrial rate because beta-1 receptors normally inhibit phospholipase C.

B. Reduced cGMP breakdown causes systemic vasoconstriction and increases myocardial calcium entry through alpha-1 receptors.

C. Increased acetylcholine release from sympathetic terminals slows the heart because beta-1 receptors normally suppress choline uptake.

D. Reduced skeletal-muscle nicotinic signaling blocks all sympathetic ganglionic transmission selectively to the heart.

E. Reduced cAMP signaling lowers sinoatrial rate and myocardial contractility compared with the unblocked state.

80. A carbohydrate meal is digested and glucose is absorbed across the small-intestinal apical membrane. Which transporter is most important for glucose uptake from the lumen?

A. GLUT2 on the apical membrane is the only normal glucose transporter and works independently of sodium at all concentrations.

B. The Na/K-ATPase directly binds luminal glucose and pumps it into enterocytes together with potassium.

C. SGLT1 cotransports glucose with sodium using the electrochemical sodium gradient.

D. CFTR transports glucose with chloride across the brush border after cAMP activation.

E. PepT1 transports intact glucose polymers with hydrogen ions and is the principal carbohydrate absorptive pathway.

81. A healthy person experiences acute stress. Which adrenal cortical zone produces cortisol?

A. The zona glomerulosa produces cortisol primarily under direct sympathetic stimulation.

B. The zona reticularis produces aldosterone as its main hormone under angiotensin II control.

C. The zona fasciculata produces glucocorticoids under ACTH stimulation.

D. The adrenal medulla produces cortisol from cholesterol under ACTH stimulation.

E. The renal cortex produces cortisol and releases it into the adrenal vein during stress.

82. A laboratory specimen is exposed to carbon monoxide. Which change in the oxygen-hemoglobin dissociation relationship is expected?

A. Oxygen content rises because carbon monoxide increases the number of available heme-binding sites for oxygen.

B. The curve shifts right because carbon monoxide lowers hemoglobin affinity for oxygen at unoccupied heme sites.

C. PaO2 falls to nearly zero because carbon monoxide prevents oxygen from dissolving normally in plasma.

D. Hemoglobin affinity is unchanged; carbon monoxide affects only dissolved oxygen and not cooperative heme binding.

E. Oxygen content falls and the remaining occupied hemoglobin sites hold oxygen more tightly, producing a left shift.

83. A healthy person gradually increases the force of a voluntary contraction. Which motor units are generally recruited first?

A. Large fast-fatigable motor units are always recruited first because their larger axons conduct action potentials more rapidly.

B. All motor units activate simultaneously at low force and force rises only by increasing action-potential amplitude.

C. Small fatigue-resistant motor units are recruited before larger high-threshold units according to the size principle.

D. Motor units are recruited randomly without regard to motor-neuron size, threshold, or metabolic phenotype.

E. Only slow motor units can be recruited voluntarily; fast motor units are reserved for spinal reflexes.

84. A marathon runner has a high proportion of type I skeletal muscle fibers. Which property is characteristic of these fibers?

A. High mitochondrial density, abundant myoglobin, and strong oxidative capacity support fatigue-resistant force production.

B. Low mitochondrial density and low capillary supply support rapid anaerobic force with exceptional fatigue resistance.

C. High myosin ATPase activity and large glycolytic stores make type I fibers the fastest and most fatigable motor units.

D. Absence of myoglobin permits efficient oxygen diffusion and gives type I fibers their pale appearance.

E. Sparse oxidative enzymes force type I fibers to rely almost entirely on phosphocreatine during prolonged exercise.

85. A healthy adult has moderate constriction of the efferent arteriole while the afferent arteriole is unchanged. What is the typical initial effect?

A. Glomerular capillary pressure and filtration fraction rise, although renal plasma flow falls.

B. Glomerular capillary pressure falls and filtration fraction decreases because resistance downstream of the glomerulus is reduced.

C. Renal plasma flow rises because efferent constriction draws blood through the glomerulus by suction.

D. GFR becomes zero because any increase in efferent resistance prevents blood from entering the glomerular capillaries.

E. Filtration fraction is independent of arteriolar tone and can change only when plasma protein concentration changes.

86. A patient with diabetic ketoacidosis has increased erythrocyte 2,3-BPG. What is the functional consequence for hemoglobin?

A. Stabilization of oxygenated hemoglobin raises oxygen affinity and reduces oxygen delivery to metabolically active tissues.

B. Stabilization of deoxygenated hemoglobin lowers oxygen affinity and facilitates unloading in peripheral tissues.

C. Binding of 2,3-BPG to heme blocks oxygen chemically and lowers arterial oxygen tension within the pulmonary capillary.

D. Increased 2,3-BPG converts hemoglobin iron from ferrous to ferric form and creates methemoglobin.

E. Binding of 2,3-BPG increases hemoglobin affinity for carbon dioxide without changing its oxygen dissociation curve.

87. A patient receives high-dose glucocorticoids for several weeks. What happens to endogenous ACTH secretion?

A. Exogenous glucocorticoids stimulate CRH and ACTH through positive feedback to maintain adrenal cortical size.

B. Exogenous glucocorticoids suppress hypothalamic CRH and pituitary ACTH through negative feedback.

C. ACTH remains unchanged because cortisol provides feedback only to the adrenal gland and not the central axis.

D. ACTH increases because glucocorticoids directly activate corticotroph CRH receptors.

E. ACTH is secreted by the adrenal cortex and therefore rises in parallel with circulating glucocorticoid concentration.

88. A patient has severe hypoalbuminemia from advanced liver disease and develops peripheral edema. Which Starling-force change most directly favors edema formation?

A. Increased plasma oncotic pressure pulls additional water out of capillaries into the interstitial space.

B. Reduced interstitial hydrostatic pressure forces protein-rich fluid from lymphatics directly into arteries.

C. Decreased capillary hydrostatic pressure is the primary force driving filtration into tissues in this setting.

D. Reduced plasma oncotic pressure decreases reabsorption of fluid from the interstitium into capillaries.

E. Higher red-cell oncotic pressure prevents plasma water from returning to the capillary circulation.

89. A patient has bilateral carotid sinus denervation. Which change is most likely in long-term mean arterial pressure under otherwise stable conditions?

A. Mean pressure can remain near normal, but short-term beat-to-beat variability increases because rapid buffering is lost.

B. Mean pressure must fall permanently to near venous pressure because baroreceptors generate all basal sympathetic tone.

C. Mean pressure must rise without limit because the kidneys cannot regulate sodium excretion without carotid afferents.

D. Blood pressure becomes completely fixed because removal of baroreceptors eliminates every source of cardiovascular variability.

E. Renal renin release stops permanently because juxtaglomerular cells require carotid sinus action potentials to function.

90. A substance is freely filtered and then completely reabsorbed with no secretion. What is its renal clearance?

A. Its clearance equals GFR because filtration alone determines clearance regardless of tubular handling.

B. Its clearance equals renal plasma flow because complete reabsorption means all plasma is processed by the tubules.

C. Its clearance exceeds renal plasma flow because reabsorption adds substance to the urine after filtration.

D. Its clearance equals urine flow rate because complete reabsorption fixes urine concentration at plasma concentration.

E. Its clearance is zero because none of the filtered substance appears in the urine.

91. A sprinter has many type IIx fast glycolytic muscle fibers. Which property best distinguishes these fibers from type I fibers?

A. They have slower myosin ATPase activity and greater mitochondrial density, producing lower power with marked fatigue resistance.

B. They contain the greatest myoglobin concentration and capillary density, which makes them dark red and primarily oxidative.

C. They generate rapid high power through fast myosin ATPase activity and glycolytic metabolism but fatigue relatively quickly.

D. They cannot use phosphocreatine or anaerobic glycolysis and therefore depend on blood oxygen for every contraction.

E. They are innervated only by small low-threshold motor neurons recruited first during fine postural activity.

92. A patient has primary adrenal insufficiency. Which hormonal pattern is expected?

A. Low cortisol causes ACTH to fall because ACTH secretion requires cortisol stimulation at the pituitary.

B. ACTH remains low while aldosterone rises markedly because primary adrenal disease spares all mineralocorticoid production.

C. Cortisol rises because the pituitary compensates fully for destruction of adrenal steroidogenic tissue.

D. Both cortisol and ACTH are high because primary adrenal insufficiency is a state of excessive adrenal steroid production.

E. Low cortisol removes negative feedback, so ACTH rises; aldosterone may also be reduced if the adrenal cortex is broadly damaged.

93. A patient receives atropine. Which change is most likely at the sinoatrial node?

A. Blocking muscarinic M3 receptors directly opens potassium channels and slows phase 4 depolarization in pacemaker cells.

B. Blocking nicotinic receptors at the motor end plate increases vagal acetylcholine release and slows the sinoatrial node.

C. Blocking beta-1 receptors reduces cAMP and decreases the funny current that drives spontaneous pacemaker depolarization.

D. Blocking muscarinic M2 receptors reduces vagal braking and increases the slope of phase 4 depolarization.

E. Blocking alpha-1 receptors decreases intracellular calcium and prevents spontaneous depolarization of sinoatrial nodal cells.

94. A patient with extensive thermal burns develops marked tissue swelling during the first hours after injury. Which change contributes most directly to this edema?

A. Increased capillary permeability allows protein and fluid to move into the interstitial space.

B. Decreased capillary permeability traps plasma proteins intravascularly and lowers interstitial oncotic pressure.

C. A generalized fall in interstitial protein concentration pulls water out of capillaries into burned tissue.

D. Immediate renal excretion of sodium and water is the dominant cause of local burn edema.

E. Loss of all lymphatic flow increases plasma oncotic pressure enough to draw water into the interstitium.

95. A patient begins warfarin therapy. Which coagulation test changes first because of the relatively short half-life of factor VII?

A. Activated partial thromboplastin time becomes prolonged first because factor VII is part of the intrinsic pathway.

B. Bleeding time becomes prolonged first because warfarin directly blocks platelet cyclooxygenase activity.

C. Thrombin time becomes prolonged first because warfarin directly inhibits conversion of fibrinogen to fibrin.

D. Platelet count falls before clotting times change because vitamin K antagonism suppresses megakaryocyte production.

E. Prothrombin time becomes prolonged before the activated partial thromboplastin time changes substantially.

96. A new screening program detects cancer several years earlier but does not delay the time of death. Measured survival from the date of diagnosis appears longer. What bias best explains this finding?

A. Recall bias makes screened patients forget the date of diagnosis and therefore extends biologic survival.

B. Lead-time bias makes survival after diagnosis appear longer solely because diagnosis occurred earlier.

C. Selection bias necessarily shortens measured survival because screened people are healthier than unscreened people.

D. Confounding by indication occurs because treatment is assigned randomly after diagnosis.

E. Observer-expectancy bias changes the date of death even when the natural history of disease is unchanged.

97. Angiotensin II stimulates aldosterone secretion. Which adrenal zone responds directly?

A. Zona glomerulosa cells increase mineralocorticoid synthesis in response to angiotensin II and elevated potassium.

B. Zona fasciculata cells release aldosterone primarily in response to ACTH and are insensitive to angiotensin II.

C. Zona reticularis cells produce aldosterone in response to gonadotropins during sodium depletion.

D. Adrenal medullary chromaffin cells synthesize aldosterone from catecholamines after sympathetic activation.

E. Posterior pituitary cells release aldosterone into adrenal capillaries when vasopressin rises.

98. A patient says, “I know you recommend surgery, but I am terrified I will not be able to care for my children afterward.” Which response best demonstrates patient-centered communication?

A. Repeat the surgical recommendation more forcefully because emotional concerns are not relevant to informed decision-making.

B. Tell the patient that fear is irrational and should not influence a medically appropriate choice.

C. End the discussion and ask a family member to decide because anxiety automatically removes decision-making capacity.

D. Acknowledge the concern and explore what postoperative limitations and support needs are most important to the patient before revisiting options.

E. Avoid discussing recovery expectations because uncertainty could make the patient less willing to consent.

99. A person begins intense exercise lasting about 6 seconds. Which energy source supplies ATP most rapidly at the start of the effort?

A. Hepatic gluconeogenesis provides most ATP directly inside skeletal muscle during the first several seconds of maximal work.

B. Beta-oxidation of long-chain fatty acids is the fastest pathway and supplies nearly all ATP during the first sprint seconds.

C. Oxidative phosphorylation reaches maximal steady-state output instantly and makes phosphocreatine unnecessary.

D. Ketone-body oxidation is the obligatory first energy source because muscle glycogen cannot be mobilized during maximal exercise.

E. Stored ATP and phosphocreatine provide immediate high-power energy before slower metabolic pathways predominate.

100. A skeletal muscle is stretched rapidly, producing reflex contraction of the same muscle. Which receptor initiates this response?

A. Golgi tendon organs detect muscle length directly and excite alpha motor neurons monosynaptically during rapid stretch.

B. Pacinian corpuscles in skin are the principal receptors controlling alpha motor neurons in the stretch reflex.

C. Muscle spindles detect changes in muscle length and rate of stretch through Ia afferent signaling.

D. Free nerve endings within muscle detect tension and provide the monosynaptic excitatory afferent of the stretch reflex.

E. Ruffini endings in joint capsules monitor sarcomere length and directly activate gamma motor neurons only.

101. A patient experiences a painful pinprick to the foot. Which fiber type normally carries the rapid, well-localized first pain sensation?

A. Thin myelinated A-delta fibers conduct the fast, sharp component of nociception.

B. Large heavily myelinated A-alpha fibers are specialized for slow burning pain after tissue injury.

C. Unmyelinated C fibers conduct the earliest sharp pain because their small diameter minimizes capacitance.

D. Preganglionic autonomic B fibers are the principal somatic nociceptors for skin and deep tissue.

E. Large A-beta touch fibers normally carry the primary nociceptive signal from free nerve endings after pinprick.

102. A heavy isometric contraction activates Golgi tendon organs. What variable do these receptors primarily monitor?

A. Tension developed in the muscle-tendon unit is sensed by Ib afferents from receptors arranged in series with muscle fibers.

B. Muscle length is sensed through Ia afferents from receptors arranged in parallel with extrafusal fibers.

C. Joint angle is sensed only by cutaneous mechanoreceptors and then relayed through autonomic efferents.

D. Intracellular calcium concentration is sensed by sensory axons that terminate directly on the sarcoplasmic reticulum.

E. Motor-neuron firing rate is sensed by tendon fibroblasts that generate action potentials during every contraction.

103. A healthy adult absorbs dietary fructose in the small intestine. Which apical transporter is most directly involved?

A. SGLT1 is the exclusive fructose transporter and requires two sodium ions for every fructose molecule absorbed.

B. GLUT5 facilitates fructose entry into enterocytes without sodium cotransport.

C. PepT1 transports fructose together with dipeptides using the hydrogen gradient.

D. CFTR conducts fructose through an anion pore after chloride secretion is activated.

E. Na/K-ATPase directly transports fructose across the brush border against its concentration gradient.

104. A patient has pancreatic exocrine insufficiency. Which digestive process is most likely to be impaired early and substantially?

A. Protein digestion stops completely because no proteolysis can occur in the stomach or intestinal brush border without pancreas.

B. Carbohydrate digestion becomes impossible because salivary amylase and brush-border enzymes have no role after food reaches the intestine.

C. Bile acid synthesis ceases because pancreatic acinar cells are the source of the bile salt pool.

D. Fat digestion falls because pancreatic lipase is a major enzyme for triglyceride hydrolysis.

E. Vitamin B12 cannot bind intrinsic factor because pancreatic enzymes produce intrinsic factor in the duodenum.

105. Cortisol circulates in blood and enters a target cell. How does it exert many of its genomic effects?

A. It binds a ligand-gated sodium channel on the plasma membrane and produces an all-or-none action potential.

B. It binds an intracellular glucocorticoid receptor that translocates to the nucleus and alters gene transcription.

C. It activates a cell-surface Gs receptor exclusively and cannot cross the lipid bilayer because it is a peptide hormone.

D. It binds a receptor tyrosine kinase and phosphorylates insulin receptor substrate as its only signaling mechanism.

E. It enters the nucleus without a receptor and directly base-pairs with DNA through its steroid ring structure.

106. A patient takes aspirin daily. Which platelet function is impaired for the remainder of the affected platelet's life span?

A. Glycoprotein Ib synthesis stops permanently, preventing platelets from binding von Willebrand factor at injured vessels.

B. ADP storage in dense granules is irreversibly depleted, preventing all P2Y12-mediated signaling after aspirin exposure.

C. Fibrinogen synthesis is blocked within platelets, preventing coagulation factors from forming a fibrin mesh.

D. Cyclooxygenase-dependent thromboxane A2 synthesis is reduced, weakening platelet activation and aggregation.

E. Thrombopoietin receptor signaling is inhibited in megakaryocytes, causing immediate loss of circulating platelet mass.

107. A patient has a left hemicord lesion at T8. Which pain and temperature deficit is expected well below the lesion?

A. Loss of pain and temperature on the right because spinothalamic fibers cross within a few spinal segments of entry.

B. Loss of pain and temperature on the left because spinothalamic fibers do not cross until reaching the medulla.

C. Bilateral loss of pain and temperature because each spinothalamic axon sends equal ascending branches on both sides.

D. No pain deficit because nociceptive fibers ascend exclusively in the dorsal columns below the thalamus.

E. Loss limited to the left dermatome at T8 because spinothalamic axons never ascend more than one segment.

108. A patient has marked tachycardia. Which part of the cardiac cycle shortens proportionally the most as heart rate rises?

A. Systole shortens to nearly zero while diastole remains fixed at its resting duration.

B. Diastole lengthens because rapid heart rates require extra filling time between contractions.

C. The isovolumetric phases disappear entirely while ejection and filling durations remain unchanged.

D. All phases shorten by exactly the same percentage because heart rate uniformly scales the entire cardiac cycle.

E. Diastole shortens more than systole, reducing the time available for ventricular filling and coronary perfusion.

109. A patient has a mutation that prevents activation of platelet glycoprotein IIb/IIIa. Which step of hemostasis is most directly impaired?

A. Fibrinogen-mediated cross-linking of activated platelets is impaired, reducing platelet aggregation.

B. Initial platelet adhesion to von Willebrand factor is impaired because GPIIb/IIIa is the principal vWF receptor.

C. Conversion of prothrombin to thrombin is impaired because GPIIb/IIIa is a vitamin K-dependent coagulation factor.

D. Vasoconstriction after injury is absent because GPIIb/IIIa is required for endothelial endothelin release.

E. Fibrin cross-linking is impaired because GPIIb/IIIa provides the transglutaminase activity of factor XIII.

110. A patient has a lesion of the left primary motor cortex affecting the hand area. Which motor deficit is most likely?

A. Weakness of the left hand with lower motor neuron features because corticospinal fibers never cross before the spinal cord.

B. Bilateral flaccid paralysis because each primary motor cortex supplies all spinal anterior horn cells equally.

C. Right-sided loss of vibration without weakness because the primary motor cortex contains only ascending sensory fibers.

D. Left-sided ataxia without weakness because corticospinal fibers project exclusively to the ipsilateral cerebellum.

E. Weakness of the right hand with upper motor neuron features because most corticospinal fibers cross in the caudal medulla.

111. Bile acids enter the intestinal lumen after a fatty meal. What is their primary digestive role?

A. They hydrolyze triglyceride ester bonds directly and replace pancreatic lipase as the major digestive enzyme.

B. They transport chylomicrons from enterocytes into portal blood by binding apolipoprotein B-48.

C. They form micelles that keep lipid digestion products soluble and facilitate delivery to the enterocyte surface.

D. They convert long-chain fatty acids into glucose within the intestinal lumen before absorption.

E. They are absorbed only in the duodenum and are completely lost in stool after each meal.

112. A screening test preferentially detects slowly progressive tumors that remain asymptomatic for long periods. Which bias can make screened cases appear to have a better prognosis?

A. Lead-time bias requires that slow tumors be missed completely and therefore cannot affect screening studies.

B. Recall bias selectively removes indolent tumors after diagnosis and leaves only aggressive cancers in the screened group.

C. Length-time bias overrepresents indolent disease because slowly progressing cases remain detectable for longer intervals.

D. Verification bias occurs because slowly growing tumors always have a negative reference-standard test.

E. Ecologic bias results because individual tumor biology is replaced by national mortality averages in every screening study.

113. A patient has denervation of a skeletal muscle. Which early electrophysiologic change is expected in the muscle membrane?

A. All nicotinic acetylcholine receptors disappear immediately because receptor expression requires continuous nerve action potentials.

B. Extrajunctional acetylcholine receptors increase, making the denervated membrane more sensitive to circulating or applied agonists.

C. The muscle membrane becomes unable to depolarize because voltage-gated sodium channels are present only at the motor end plate.

D. Ryanodine receptors are lost within minutes, preventing any calcium release even during direct electrical stimulation.

E. SERCA activity becomes permanently maximal and eliminates every spontaneous change in cytosolic calcium.

114. A febrile patient has a hypothalamic set point that has been raised by prostaglandin E2. Why does the patient initially feel cold and shiver even though core temperature is already normal?

A. The current temperature is below the new hypothalamic set point, so heat-conserving and heat-generating responses are activated.

B. Prostaglandin E2 lowers the hypothalamic set point below ambient temperature, causing reflex shivering until heat is lost.

C. Fever abolishes hypothalamic thermoregulation entirely, so shivering occurs without any set-point comparison.

D. Shivering is produced only by falling blood glucose and is unrelated to temperature regulation during fever.

E. The patient feels cold because cutaneous vasodilation rapidly transfers core heat to the skin while the set point remains unchanged.

115. A patient with severe liver failure has decreased synthesis of several clotting factors. Which factor is least affected because it is produced primarily by endothelial cells rather than hepatocytes?

A. Factor VIII production is relatively preserved compared with most vitamin K-dependent and other hepatic clotting factors.

B. Factor II production is relatively preserved because prothrombin is synthesized primarily by vascular endothelium.

C. Factor VII production is relatively preserved because it is stored in platelet dense granules rather than synthesized in liver.

D. Factor IX production is relatively preserved because it is generated by activated neutrophils during tissue injury.

E. Factor X production is relatively preserved because it is synthesized mainly by splenic macrophages and monocytes.

116. A physician is discussing prognosis with a seriously ill patient who asks, “How much time do I have?” Which approach is most appropriate?

A. Give an exact date of death because uncertainty should never be discussed in serious illness.

B. Avoid answering because prognostic uncertainty makes any discussion unethical.

C. Speak only with the family because prognosis should not be discussed directly with seriously ill patients.

D. Ask what the patient understands and wants to know, then provide a clear prognosis with uncertainty expressed in ranges or scenarios when possible.

E. Use technical survival statistics without first assessing the patient's preferences or understanding.

117. A patient with myasthenia gravis develops weakness that worsens with repeated use. Which physiologic defect best explains this fatigability?

A. Presynaptic calcium influx progressively rises with use, causing excessive acetylcholine release and depolarization block in every junction.

B. Motor axons lose myelin only during repeated firing, preventing sodium-channel recovery after a few action potentials.

C. Sarcoplasmic reticulum calcium stores are absent at rest and regenerate only after prolonged exercise.

D. Troponin C cannot bind calcium because the disease selectively replaces skeletal troponin with the cardiac isoform.

E. Reduced functional postsynaptic nicotinic receptor number lowers the safety factor for neuromuscular transmission during repeated activity.

118. During graded exercise, oxygen consumption rises as cardiac output and tissue oxygen extraction increase. Which equation expresses whole-body oxygen consumption according to the Fick principle?

A. Oxygen consumption equals systemic vascular resistance multiplied by mean arterial pressure.

B. Oxygen consumption equals minute ventilation divided by arterial carbon dioxide tension.

C. Oxygen consumption equals cardiac output multiplied by the arterial-venous oxygen content difference.

D. Oxygen consumption equals stroke volume multiplied only by arterial oxygen saturation, independent of venous oxygen content.

E. Oxygen consumption equals pulmonary vascular resistance multiplied by mixed venous oxygen tension.

119. A fetus has normal oxygen delivery despite a lower arterial oxygen tension than an adult. Which property of fetal hemoglobin is most important for supporting placental oxygen transfer?

A. Fetal hemoglobin binds 2,3-BPG weakly, giving it a higher oxygen affinity than adult hemoglobin.

B. Fetal hemoglobin binds 2,3-BPG more strongly, shifting its oxygen dissociation curve to the right.

C. Fetal hemoglobin has a lower oxygen affinity so that oxygen is released readily within the placenta.

D. Fetal hemoglobin contains more heme groups per tetramer than adult hemoglobin and therefore carries more oxygen.

E. Fetal hemoglobin cannot bind carbon dioxide, so placental carbon dioxide transfer automatically raises oxygen loading.

120. A researcher concludes that an association is statistically significant at a two-sided alpha of 0.05. What does a type I error represent?

A. A type I error is failing to reject a false null hypothesis, which is determined by one minus statistical power.

B. A type I error is obtaining a confidence interval that is narrow because the sample size is large.

C. A type I error occurs only when randomization fails and a confounder is unevenly distributed.

D. A type I error is rejecting the null hypothesis when the null hypothesis is actually true.

E. A type I error means the observed effect is clinically unimportant even though it is statistically significant.

121. A healthy person begins dynamic aerobic exercise. Which cardiovascular response is expected as workload rises?

A. Cardiac output falls because sympathetic activation constricts skeletal-muscle arterioles more than it raises heart rate.

B. Systemic vascular resistance rises sharply because all vascular beds constrict during dynamic exercise.

C. Systolic arterial pressure falls progressively because the exercising muscles extract more oxygen.

D. Venous return falls because the skeletal-muscle pump is inhibited during rhythmic contraction.

E. Cardiac output increases because both heart rate and, initially, stroke volume rise while active muscle vasodilates.

122. A patient has a mutation that reduces SERCA activity in skeletal muscle. Which change is most likely after a contraction?

A. Calcium disappears from the cytosol faster, shortening contraction because SERCA normally releases calcium from the sarcoplasmic reticulum.

B. Cytosolic calcium remains elevated longer, delaying relaxation because calcium reuptake into the sarcoplasmic reticulum is slowed.

C. Action potentials cannot propagate along the sarcolemma because SERCA is the main voltage-gated sodium channel in muscle.

D. Acetylcholine remains bound longer to nicotinic receptors because SERCA normally hydrolyzes transmitter at the motor end plate.

E. Myosin cannot detach from actin because SERCA supplies the ATP-binding site on the myosin head.

123. Insulin binds its receptor on skeletal muscle. Which receptor class mediates the signal?

A. A Gs-coupled receptor raises cAMP as the principal signal for glucose uptake into skeletal muscle.

B. A receptor tyrosine kinase autophosphorylates and recruits intracellular signaling proteins such as insulin receptor substrates.

C. A ligand-gated calcium channel opens and directly inserts GLUT4 into the membrane without phosphorylation cascades.

D. A nuclear steroid receptor binds insulin and alters transcription without any cell-surface receptor.

E. A guanylyl cyclase receptor raises cGMP and is the exclusive mediator of insulin metabolic actions.

124. A substance is filtered and strongly secreted so that nearly all substance delivered in renal plasma is excreted in one pass. Its clearance best approximates which quantity?

A. Glomerular filtration rate because secretion does not contribute to urinary excretion of the substance.

B. Renal blood flow directly because hematocrit has no effect on conversion from plasma flow to blood flow.

C. Effective renal plasma flow because extraction from plasma is nearly complete.

D. Filtration fraction because secretion makes clearance equal the ratio of GFR to plasma flow.

E. Urine flow rate because high secretion forces urine concentration to equal plasma concentration.

125. A patient has marked hyperglycemia and begins excreting glucose in the urine. Why does glucosuria appear once plasma glucose is sufficiently high?

A. Glomerular filtration of glucose stops and the collecting duct secretes glucose actively into urine instead.

B. Insulin normally transports glucose from urine to blood, so glucosuria occurs only when plasma insulin becomes exactly zero.

C. Distal tubular chloride channels become saturated and force glucose to diffuse through the loop of Henle into urine.

D. Hyperglycemia lowers GFR below zero, reversing filtration and moving glucose from peritubular capillaries into Bowman space.

E. Filtered glucose load exceeds the transport capacity of proximal tubular sodium-glucose cotransporters.

126. A healthy person eats a carbohydrate-rich meal. Which insulin effect increases glucose uptake in skeletal muscle and adipose tissue?

A. Insulin inserts SGLT1 into skeletal muscle membranes so glucose enters with sodium against its gradient.

B. Insulin promotes translocation of GLUT4 transporters to the plasma membrane.

C. Insulin removes GLUT4 from the surface and forces glucose to enter only through constitutive GLUT2 transporters.

D. Insulin opens voltage-gated glucose channels that conduct glucose as an ion into adipocytes.

E. Insulin phosphorylates extracellular glucose so the charged molecule can cross the lipid bilayer by simple diffusion.

127. A patient has isolated factor XII deficiency discovered on preoperative testing. Which laboratory and clinical pattern is expected?

A. The prothrombin time is prolonged and severe mucosal bleeding occurs because factor XII initiates the extrinsic pathway.

B. Bleeding time is prolonged because factor XII is required for platelet adhesion to exposed subendothelial collagen.

C. Both PT and aPTT are normal because factor XII participates only in fibrinolysis and not in laboratory clotting assays.

D. The thrombin time is markedly prolonged because factor XII directly catalyzes conversion of fibrinogen into fibrin.

E. The activated partial thromboplastin time is prolonged, but spontaneous clinical bleeding is typically absent.

128. A study is underpowered to detect a clinically meaningful difference. Which change generally increases statistical power?

A. Increasing the sample size reduces standard error and increases the chance of detecting a true effect of a given size.

B. Reducing the sample size increases power because fewer observations create less variability.

C. Lowering the expected effect size while keeping all other design features fixed increases power.

D. Using a more stringent alpha always increases power because false positives become less likely.

E. Adding random measurement error increases power by widening the separation between study groups.

129. Long-chain fatty acids are absorbed by an enterocyte and re-esterified to triglycerides. How do they normally reach the systemic circulation?

A. They enter portal blood directly as intact chylomicrons because intestinal capillaries freely admit large lipoprotein particles.

B. They are converted entirely to ketone bodies inside enterocytes and released directly into the hepatic portal vein.

C. They bind intrinsic factor and are transported through ileal cubilin receptors before entering systemic blood.

D. They remain stored permanently in enterocytes because dietary long-chain fat cannot cross the basolateral membrane.

E. They are packaged into chylomicrons, enter intestinal lymphatics, and then reach venous blood through the thoracic duct.

130. A fasting healthy adult has low insulin and increased glucagon. Which hepatic metabolic pathway is stimulated by glucagon?

A. Glycogenolysis and gluconeogenesis increase to support plasma glucose during fasting.

B. Glycogen synthesis and glycolysis increase so the liver stores circulating glucose during fasting.

C. Fatty acid synthesis rises because glucagon activates acetyl-CoA carboxylase through dephosphorylation.

D. Protein synthesis becomes the dominant hepatic response because glucagon suppresses amino-acid use for gluconeogenesis.

E. GLUT4 translocation increases in hepatocytes and becomes the main source of fasting hepatic glucose uptake.

131. At very high exercise intensity, blood lactate begins to rise more rapidly. Which physiologic change most directly contributes to this lactate threshold?

A. All skeletal-muscle mitochondria stop consuming oxygen abruptly at the threshold despite continued blood flow.

B. Lactate rises because beta oxidation becomes the sole source of ATP and directly releases lactate as its end product.

C. The threshold occurs when hemoglobin can no longer bind any oxygen in arterial blood despite normal ventilation.

D. Glycolytic pyruvate production increasingly exceeds mitochondrial oxidative handling, so more pyruvate is reduced to lactate.

E. Lactate accumulation reflects complete cessation of glycolysis in working muscle fibers.

132. A patient with absolute insulin deficiency develops marked hyperkalemia despite total body potassium depletion. Which insulin action normally lowers extracellular potassium?

A. Insulin opens renal potassium channels and shifts potassium from cells into plasma for urinary excretion.

B. Insulin inhibits Na/K-ATPase and therefore keeps potassium in the extracellular compartment after meals.

C. Insulin converts potassium into an intracellular organic anion that cannot cross the cell membrane.

D. Insulin stimulates Na/K-ATPase activity and shifts potassium into cells.

E. Insulin lowers plasma potassium only by increasing glomerular filtration and has no effect on transcellular distribution.

133. A traveler rapidly ascends to 3,500 meters. Within hours, hypoxemia stimulates peripheral chemoreceptors. Which immediate ventilatory response occurs?

A. Hypoventilation raises arterial PCO_2 to improve oxygen loading in the lungs.

B. Hyperventilation lowers arterial PCO_2 and produces an acute respiratory alkalosis.

C. Ventilation remains unchanged until erythropoietin increases red-cell mass several weeks later.

D. Peripheral chemoreceptors suppress ventilation when arterial oxygen tension falls below normal.

E. Hyperventilation causes a primary metabolic acidosis before any change in arterial carbon dioxide tension.

134. A premature infant has difficulty maintaining body temperature in a cool nursery. Which mechanism is normally a major source of heat production in newborns?

A. Sustained skeletal-muscle shivering is the dominant neonatal heat source because brown fat is metabolically inactive.

B. Cutaneous vasodilation raises core temperature by delivering more warm blood to the skin for heat conservation.

C. Reduced thyroid hormone secretion lowers oxygen consumption so that heat is retained within the central circulation.

D. Sympathetic stimulation of brown adipose tissue increases uncoupled mitochondrial oxidation through thermogenin.

E. Sweat-gland activation increases evaporative heat production and thereby protects the infant from environmental cooling.

135. Parathyroid hormone is released in response to falling ionized calcium. Which renal effect helps raise plasma calcium?

A. PTH increases distal tubular calcium reabsorption while reducing proximal phosphate reabsorption.

B. PTH decreases distal calcium reabsorption and increases proximal phosphate reabsorption to preserve calcium-phosphate product.

C. PTH blocks renal 1-alpha-hydroxylase, reducing calcitriol production and intestinal calcium absorption.

D. PTH causes both calcium and phosphate to be retained equally in the proximal tubule.

E. PTH acts only on bone and has no direct renal effects on calcium, phosphate, or vitamin D metabolism.

136. A patient has resection of the terminal ileum. Which nutrient-handling process is especially impaired?

A. Active bile acid reabsorption and vitamin B12-intrinsic factor uptake are reduced.

B. Iron absorption is abolished because virtually all dietary iron is absorbed only in the terminal ileum.

C. Glucose absorption stops because SGLT1 is expressed exclusively in the terminal ileum.

D. Pancreatic bicarbonate secretion stops because secretin is produced only by ileal epithelial cells.

E. Gastric acid secretion stops because gastrin is reabsorbed in the ileum and returned to the stomach through portal blood.

137. Which renal enzyme is stimulated by parathyroid hormone to increase active vitamin D production?

A. 25-hydroxylase in the collecting duct converts calcitriol back to cholecalciferol under PTH stimulation.

B. Thyroid peroxidase in the kidney hydroxylates vitamin D and couples it to calcium-binding protein.

C. Aromatase converts vitamin D to calcitriol in the glomerulus when plasma phosphate rises.

D. Carbonic anhydrase creates calcitriol from cholesterol within alpha-intercalated cells.

E. 1-alpha-hydroxylase converts 25-hydroxyvitamin D to calcitriol in the proximal kidney.

138. A patient with sepsis develops diffuse coagulation activation and secondary fibrinolysis. Which laboratory pattern best reflects consumption of fibrinogen and formation of cross-linked fibrin?

A. High fibrinogen with undetectable D-dimer indicates rapid fibrin formation without any activation of fibrinolysis.

B. Normal fibrinogen with low D-dimer is expected because disseminated coagulation is confined to platelet surfaces.

C. High fibrinogen with isolated prolonged bleeding time proves that only primary hemostasis has been activated.

D. Low fibrinogen with absent fibrin degradation products indicates enhanced hepatic synthesis rather than consumption.

E. Low fibrinogen with elevated D-dimer indicates consumption and breakdown of cross-linked fibrin.

139. A healthy adolescent boy enters puberty. Which endocrine event is the earliest driver of the normal pubertal rise in gonadal steroid production?

A. Continuous nonpulsatile GnRH secretion increases pituitary gonadotropin output throughout the day.

B. A fall in pituitary LH secretion removes inhibition of Leydig cells and permits testosterone synthesis.

C. Adrenal aldosterone secretion directly activates testicular steroidogenesis before hypothalamic maturation occurs.

D. Increased pulsatile hypothalamic GnRH secretion stimulates pituitary LH and FSH release.

E. Rising prolactin suppresses hypothalamic GnRH and thereby initiates the normal pubertal gonadal axis.

140. A neutrophil is recruited from blood into infected tissue. Which sequence best describes the normal early steps of leukocyte extravasation?

A. Integrin-mediated rolling is followed by selectin-mediated firm adhesion and then passive diffusion through endothelial cells.

B. Complement-mediated firm adhesion occurs first, followed by erythrocyte-dependent rolling and platelet-mediated diapedesis.

C. Immunoglobulin-mediated rolling occurs first, followed by fibrinogen-independent adhesion and lymphatic transmigration.

D. Transmigration occurs before rolling because neutrophils cross intact endothelium and then attach to selectins in tissue.

E. Selectin-mediated rolling is followed by integrin-mediated firm adhesion and then transmigration through endothelium.

141. A patient has a high serum calcium concentration. How does the calcium-sensing receptor in parathyroid cells respond?

A. Activation suppresses PTH secretion, providing negative feedback on calcium-regulating pathways.

B. Activation strongly increases PTH secretion so renal calcium reabsorption rises further.

C. The receptor is inhibited by high calcium and therefore cannot influence PTH when calcium is elevated.

D. High calcium causes the receptor to secrete calcitonin from parathyroid chief cells instead of regulating PTH.

E. The receptor acts only in bone and has no role in sensing extracellular calcium at the parathyroid gland.

142. A patient with Parkinson disease has reduced movement initiation. Which basal-ganglia change is central to the hypokinetic state?

A. Loss of nigrostriatal dopamine reduces direct-pathway facilitation and increases indirect-pathway influence on thalamocortical motor activity.

B. Excess nigrostriatal dopamine suppresses the direct pathway and causes excessive inhibition of the subthalamic nucleus.

C. Loss of cerebellar Purkinje cells removes inhibition of deep nuclei and selectively blocks basal-ganglia output to the thalamus.

D. Increased acetylcholine at the neuromuscular junction prevents cortical motor programs from reaching skeletal muscle.

E. Reduced dorsal-column input to the basal ganglia eliminates proprioception and directly causes resting tremor and bradykinesia.

143. A patient has autoimmune destruction of gastric parietal cells. Which absorption defect results most directly from loss of intrinsic factor?

A. Folate absorption in the jejunum is impaired because folate requires intrinsic factor for brush-border uptake.

B. Iron absorption in the duodenum is abolished because intrinsic factor is the apical iron transporter.

C. Vitamin B12 absorption in the terminal ileum is impaired because the intrinsic factor-B12 complex cannot undergo normal receptor-mediated uptake.

D. Calcium absorption is impaired because intrinsic factor activates vitamin D in enterocytes.

E. Bile acid absorption is lost because intrinsic factor is the ligand for the ileal bile salt transporter.

144. A medical student notices a senior physician appearing intoxicated immediately before a procedure. What is the most appropriate priority?

A. Ignore the concern because reporting a senior physician violates professional loyalty.

B. Wait until a patient is injured so there is objective proof that the physician is impaired.

C. Post the concern publicly on social media so other patients can decide whether to seek care elsewhere.

D. Protect patients by preventing unsafe practice and promptly use the appropriate supervisory or institutional pathway to address impairment.

E. Secretly alter the procedure schedule without telling anyone why, leaving the impairment unaddressed.

145. A patient has malignant hyperthermia after exposure to an anesthetic. Excessive activity of which skeletal-muscle channel directly raises cytosolic calcium?

A. Ryanodine receptor calcium-release channels in the sarcoplasmic reticulum open excessively.

B. SERCA pumps in the sarcoplasmic reticulum release calcium into the cytosol instead of transporting it inward.

C. Nicotinic acetylcholine receptors on the motor end plate release stored intracellular calcium directly from their pores.

D. Voltage-gated chloride channels in the transverse tubule secrete calcium from the extracellular space into the sarcomere.

E. Dystrophin channels in the sarcolemma open and release mitochondrial calcium stores into the cytoplasm.

146. A patient has a lesion of the cerebellar hemisphere. Which finding most directly reflects the normal role of this structure?

A. Contralateral spastic weakness occurs because cerebellar hemispheres are the origin of the lateral corticospinal tract.

B. Loss of primary pain sensation occurs because the cerebellum is the first cortical relay for spinothalamic information.

C. Aphasia occurs because the cerebellar cortex contains the dominant-language motor and sensory speech areas.

D. Complete flaccid paralysis occurs because cerebellar output directly innervates skeletal muscle without cerebral pathways.

E. Ipsilateral limb dysmetria and decomposition of movement occur because the cerebellum coordinates timing and error correction.

147. A patient has iron deficiency from poor intake. In which region is dietary iron absorbed most efficiently?

A. The terminal ileum is the exclusive site because iron must first bind intrinsic factor before uptake.

B. The colon absorbs most iron because bacterial metabolism converts all dietary iron to the readily absorbed ferrous state.

C. The stomach absorbs nearly all iron directly through parietal-cell proton pumps before chyme enters the duodenum.

D. Iron is not absorbed enterally and normally reaches blood only through breakdown of swallowed erythrocytes.

E. The duodenum and proximal jejunum are the principal sites of regulated iron absorption.

148. A patient eats a protein-rich meal. Which factor stimulates gastrin release from antral G cells?

A. Very low antral pH strongly stimulates gastrin so acid output rises as the lumen becomes increasingly acidic.

B. Peptides and amino acids in the gastric lumen, along with vagal gastrin-releasing peptide, stimulate gastrin secretion.

C. Somatostatin from D cells is the principal direct stimulant of G cells during the gastric phase.

D. Secretin from the duodenum stimulates G cells to increase acid secretion when duodenal pH is low.

E. Histamine from enterochromaffin-like cells suppresses gastrin completely during every protein-containing meal.

149. A clinician is offered an expensive personal gift by a company whose product the clinician is considering for routine prescribing. What is the main ethical concern?

A. The gift is ethically required because industry support guarantees that the clinician learns about the newest products.

B. The gift eliminates conflict if the clinician does not tell patients about it.

C. The gift can be accepted without concern because only cash payments can affect professional judgment.

D. The clinician should prescribe the company's product once to repay the gift and then return to usual practice.

E. The gift creates a conflict of interest that can bias—or appear to bias—clinical judgment and should not influence prescribing decisions.

150. A young woman is in the early follicular phase of a normal menstrual cycle. Which ovarian process is promoted by FSH?

A. FSH stimulates granulosa-cell aromatase and supports follicular growth and estrogen production.

B. FSH stimulates theca cells to produce large amounts of progesterone independently of LH.

C. FSH directly triggers ovulation by causing the midcycle rupture before any LH surge occurs.

D. FSH suppresses granulosa aromatase so androgens accumulate within the dominant follicle.

E. FSH causes corpus luteum regression and is therefore highest during the late luteal phase.

151. Why does left ventricular coronary blood flow occur predominantly during diastole?

A. The aortic valve closes during systole, preventing any blood from entering the coronary ostia until ventricular relaxation begins.

B. Coronary arterioles actively constrict during systole because myocardial oxygen consumption falls to nearly zero during contraction.

C. Aortic pressure is lowest in systole, so the coronary perfusion gradient is absent until diastolic pressure rises.

D. Systolic contraction compresses intramyocardial vessels, especially in the subendocardium, limiting flow during ejection.

E. Venous pressure exceeds aortic pressure throughout systole and reverses coronary flow through every myocardial layer.

152. After several days at high altitude, a climber can sustain greater ventilation than on the first day. Which renal adaptation facilitates this acclimatization?

A. Renal bicarbonate retention further raises plasma pH and thereby enhances central chemoreceptor stimulation.

B. Renal bicarbonate excretion lowers plasma bicarbonate and partially compensates for the respiratory alkalosis.

C. The kidneys retain hydrogen ions in the blood while secreting bicarbonate into the circulation to intensify alkalemia.

D. Renal compensation raises arterial PCO2 directly by reducing pulmonary ventilation.

E. The kidneys stop filtering bicarbonate completely, preventing any compensation for altitude-induced alkalosis.

153. Which nephron segment normally reabsorbs the largest fraction of filtered sodium and water?

A. The thin ascending limb reabsorbs most filtered sodium and water because it is highly permeable to both salt and water.

B. The distal convoluted tubule reabsorbs nearly all filtered sodium before tubular fluid reaches the collecting duct.

C. The collecting duct reabsorbs two thirds of filtered water even in the complete absence of vasopressin.

D. The proximal tubule reabsorbs roughly two thirds of filtered sodium and water in an approximately iso-osmotic fashion.

E. Bowman space actively reabsorbs sodium into glomerular capillaries before filtrate enters the proximal tubule.

154. A woman has sustained high estradiol levels late in the follicular phase. What pituitary event follows in a normal cycle?

A. Estradiol switches to positive feedback and produces the midcycle LH surge that triggers ovulation.

B. Estradiol continues to provide only negative feedback, suppressing LH to its lowest level just before ovulation.

C. Estradiol directly ruptures the follicle without any increase in pituitary gonadotropins.

D. Estradiol causes an isolated prolactin surge that replaces LH as the ovulatory hormone.

E. Estradiol suppresses GnRH permanently, initiating the luteal phase before follicular rupture.

155. A child has recurrent catalase-positive infections because of chronic granulomatous disease. Why are catalase-positive organisms particularly problematic?

A. They destroy their own hydrogen peroxide, depriving deficient phagocytes of an external source of substrate for oxidative killing.

B. They generate excessive hydrogen peroxide that irreversibly blocks residual NADPH oxidase activity in the phagocyte membrane.

C. They lack cell walls and therefore cannot be opsonized by complement or recognized by neutrophil pattern receptors.

D. They secrete catalase that directly cleaves neutrophil integrins, preventing adhesion to vascular endothelium.

E. They convert superoxide into nitric oxide, which prevents phagolysosome fusion and blocks all nonoxidative killing mechanisms.

156. After ovulation, which ovarian structure produces most progesterone during the normal luteal phase?

A. The dominant follicle remains intact after ovulation and secretes progesterone without luteinization.

B. Theca cells in atretic follicles become the sole progesterone source after the LH surge.

C. The corpus luteum secretes progesterone under LH support after the ovulated follicular cells undergo luteinization.

D. Endometrial glands synthesize circulating progesterone and then signal the ovary to form a corpus luteum.

E. The anterior pituitary secretes progesterone directly during the luteal phase under GnRH stimulation.

157. A patient has recurrent Neisseria infections. Deficiency of which immune function most strongly predisposes to this pattern?

A. C1 esterase inhibition is increased, preventing the classical complement pathway from activating at all surfaces.

B. IgE class switching is impaired, preventing mast-cell degranulation against encapsulated extracellular bacteria.

C. MHC class II expression is increased, causing excessive helper T-cell activation and complement consumption.

D. Formation of the terminal complement membrane attack complex is impaired.

E. Natural killer cell perforin release is impaired, selectively preventing lysis of gram-negative diplococci in plasma.

158. A trial reports a relative risk of 0.82 with a 95% confidence interval of 0.64 to 1.08. Which interpretation is most appropriate?

A. The result proves harm because the upper confidence limit is greater than 1.0.

B. The result proves a 18% risk reduction because the point estimate alone determines statistical significance.

C. The result is statistically significant because every value in a confidence interval differs from zero.

D. The confidence interval gives a 95% probability that this fixed calculated interval contains the true value after the data have been observed.

E. The interval includes the null value of 1.0, so the result is not statistically significant at the conventional two-sided 0.05 level.

159. A coronary artery supplying active myocardium is partially narrowed. Which local metabolite is an important mediator of increased coronary blood flow when oxygen demand rises?

A. Endothelin released from active myocytes causes coronary dilation by increasing smooth-muscle intracellular calcium.

B. Angiotensin II accumulates locally and is the principal metabolite responsible for exercise-induced coronary vasodilation.

C. Thromboxane A2 from platelets dilates coronary resistance vessels and increases flow to metabolically active tissue.

D. Norepinephrine acting on alpha-1 receptors is the dominant local dilator that matches coronary flow to myocardial oxygen use.

E. Adenosine generated during ATP breakdown contributes to arteriolar dilation and metabolic matching of flow to demand.

160. A person enters rapid eye movement sleep. Which physiologic pattern is characteristic of this stage?

A. Cortical EEG shows high-amplitude delta waves while skeletal muscle tone is higher than during wakefulness.

B. Skeletal muscle tone is preserved and sleep spindles dominate throughout the entire rapid eye movement period.

C. Cortical EEG activity is relatively desynchronized while skeletal muscle tone is markedly suppressed.

D. Autonomic activity becomes completely absent and heart rate remains fixed because brainstem output is silenced.

E. Growth hormone secretion peaks specifically because rapid eye movement sleep is the deepest slow-wave stage.

161. A randomized controlled trial assigns treatment by a concealed random sequence. What is the principal purpose of randomization?

A. Randomization guarantees that every baseline characteristic will be numerically identical between treatment groups.

B. Randomization prevents loss to follow-up after treatment begins and therefore eliminates attrition bias.

C. Randomization makes blinding unnecessary because participants cannot influence any reported outcome.

D. Randomization tends to distribute known and unknown confounders comparably between groups, reducing systematic allocation bias.

E. Randomization increases disease prevalence in the treatment arm so relative risks can be calculated directly.

162. A study estimates the proportion of a city population that has hypertension on a single date. Which epidemiologic measure is being estimated?

A. Incidence density is the proportion of all existing cases that are newly diagnosed on the specified date.

B. Cumulative incidence is the number of existing and past cases divided by person-time at risk.

C. Point prevalence is the proportion of the population with the condition at that specified time.

D. Attributable risk is the total number of cases in the population regardless of exposure status.

E. Case-fatality rate is the proportion of the entire city population with hypertension on that date.

163. A patient with recurrent pyogenic infections has C3 deficiency. Which normal C3 function is most important for defense against encapsulated bacteria?

A. C3a binds bacterial capsules and directly forms transmembrane pores that lyse encapsulated organisms.

B. C3b cross-links immunoglobulin Fc regions and converts them into high-affinity T-cell receptor ligands.

C. C3a is the major antibody-independent receptor that activates cytotoxic T cells to engulf extracellular bacteria.

D. C3b prevents neutrophil recruitment so that macrophages can clear bacteria without inflammatory tissue injury.

E. C3b coats microbial surfaces and promotes phagocytosis through complement receptors on leukocytes.

164. An osteoclast resorbs bone. Which feature is essential for dissolving the mineral component beneath the ruffled border?

A. Proton secretion acidifies the resorption lacuna, helping dissolve hydroxyapatite before proteolytic matrix degradation.

B. Bicarbonate secretion alkalinizes the resorption lacuna and precipitates hydroxyapatite away from the bone surface.

C. Osteocalcin is secreted as a strong acid that directly dissolves mineral without requiring proton pumps.

D. Alkaline phosphatase lowers local phosphate concentration and thereby acidifies the sealed resorption compartment.

E. Calcium is pumped from blood into the lacuna to create supersaturation and mechanically fracture the mineral phase.

165. A person remains at high altitude for several weeks. Which hematologic adaptation improves oxygen-carrying capacity?

A. Hypoxia suppresses renal erythropoietin so that blood viscosity falls and oxygen content rises.

B. The spleen permanently releases enough stored erythrocytes to double red-cell mass within minutes.

C. Red-cell mass rises because aldosterone directly converts plasma proteins into hemoglobin.

D. Chronic hypoxia lowers hemoglobin concentration to facilitate oxygen diffusion from alveoli into blood.

E. Hypoxia-inducible signaling increases renal erythropoietin production, raising red-cell mass over time.

166. A healthy person falls asleep and enters stage N2 non-REM sleep. Which EEG feature is most characteristic?

A. Continuous high-amplitude delta activity occupies nearly the entire epoch and defines stage N2 sleep.

B. Sleep spindles and K complexes appear against a background of relatively low-amplitude mixed-frequency activity.

C. Sawtooth waves with rapid eye movements and complete skeletal atonia define the entire N2 period.

D. An awake posterior alpha rhythm becomes stronger and remains continuous after the eyes are closed during N2.

E. Epileptiform spikes must appear because normal thalamocortical oscillations in N2 are inherently pathologic.

167. A patient has severe aortic stenosis. Which change most directly increases left ventricular wall stress according to the law of Laplace?

A. A thicker ventricular wall increases wall stress because more myocardium transmits the same intracavitary pressure.

B. A higher ventricular pressure increases wall stress when chamber radius and wall thickness are otherwise unchanged.

C. A smaller chamber radius increases wall stress because pressure is concentrated across less curvature.

D. Lower intracavitary pressure increases wall stress by reducing opposing forces within the ventricular wall.

E. Wall stress is independent of pressure and geometry and depends only on myocardial oxygen extraction.

168. A drug blocks the Na-K-2Cl cotransporter in the thick ascending limb. Which normal property of this segment is most directly lost?

A. Active salt reabsorption without water reabsorption helps dilute tubular fluid and build the medullary osmotic gradient.

B. Obligatory water reabsorption through abundant aquaporin-2 channels is blocked, preventing urine dilution.

C. Nearly all filtered glucose reabsorption is lost because the Na-K-2Cl cotransporter is also the proximal glucose transporter.

D. Urea secretion into the thin descending limb stops because NKCC2 is the only transporter capable of moving urea.

E. Hydrogen secretion by alpha-intercalated cells stops because NKCC2 directly powers the collecting-duct proton pump.

169. A patient cannot form new declarative memories after bilateral hippocampal injury. Which memory process is most directly impaired?

A. Retrieval of all remote childhood memories is abolished because every stored memory remains permanently within the hippocampus.

B. Acquisition of simple motor skills is abolished because procedural learning requires hippocampal output to the cerebellum.

C. Immediate digit span disappears because working memory can function only when hippocampal neurons are intact.

D. Consolidation of new explicit memories from short-term representations into durable long-term storage is impaired.

E. Conditioned autonomic reflexes are abolished because the hippocampus is the only structure capable of associative learning.

170. A woman tracks basal body temperature and notes a sustained rise shortly after ovulation. Which hormone causes this thermogenic effect?

A. FSH directly raises core temperature and remains maximally elevated throughout the luteal phase.

B. Estradiol from the dominant follicle causes the postovulatory temperature rise before progesterone secretion begins.

C. Inhibin B acts on the hypothalamus as the principal thermogenic hormone of the luteal phase.

D. LH remains at surge concentrations for two weeks and directly drives heat production in skeletal muscle.

E. Progesterone from the corpus luteum raises the hypothalamic temperature set point slightly during the luteal phase.

171. A healthy man has LH stimulation of the testes. Which cell responds most directly?

A. Sertoli cells increase testosterone synthesis as their principal response to LH.

B. Leydig cells increase testosterone synthesis after LH receptor stimulation activates testicular steroidogenesis.

C. Spermatids increase inhibin secretion directly in response to LH receptors on their membranes.

D. Epididymal epithelial cells synthesize testosterone and release it into seminiferous tubules after LH stimulation.

E. Prostate stromal cells produce circulating testosterone and provide negative feedback on pituitary LH.

172. A patient receives a protein vaccine and later undergoes a booster dose. Which feature best explains the faster, higher-affinity antibody response after the booster?

A. Naive B cells respond more slowly after repeat antigen exposure because prior antibodies block all antigen presentation.

B. Plasma cells revert to naive B cells between doses and then restart V(D)J recombination when the booster is given.

C. Memory T cells directly secrete high-affinity immunoglobulin and therefore bypass B-cell activation after the booster.

D. Memory B cells generated during the primary response rapidly expand and have undergone affinity maturation and class switching.

E. Somatic hypermutation occurs only in bone marrow before first antigen exposure, so booster responses cannot change affinity.

173. A patient has chronic volume overload of the left ventricle. Which structural adaptation is most consistent with the hemodynamic load?

A. Pure concentric hypertrophy without chamber enlargement is the typical adaptation to isolated chronic volume overload.

B. Ventricular wall thickness falls to zero because added volume is handled only through increased heart rate.

C. Eccentric hypertrophy with chamber dilation helps accommodate increased end-diastolic volume.

D. The chamber becomes smaller to increase end-diastolic pressure and thereby reduce venous return.

E. Myocardial mass must remain unchanged because sarcomere number cannot adapt to chronic loading conditions.

174. A patient takes a selective serotonin reuptake inhibitor. What is the immediate synaptic action of this drug class?

A. Direct activation of postsynaptic serotonin receptors eliminates the need for endogenous serotonin release from presynaptic neurons.

B. Inhibition of monoamine oxidase prevents serotonin synthesis from tryptophan and lowers vesicular serotonin content.

C. Blockade of vesicular monoamine transport prevents serotonin packaging and acutely increases stored transmitter in vesicles.

D. Blockade of the serotonin transporter reduces presynaptic reuptake and increases serotonin persistence in the synaptic cleft.

E. Stimulation of the norepinephrine transporter selectively increases serotonin clearance from serotonergic synapses.

175. A physician is recruiting patients for a study and receives payment from the sponsor for each participant enrolled. What should the physician do?

A. Conceal the payment because financial relationships are irrelevant to research consent if the protocol has scientific merit.

B. Disclose and appropriately manage the financial conflict while ensuring that research consent remains voluntary and independent of clinical pressure.

C. Tell patients that participation is required to continue receiving clinical care from the physician.

D. Enroll incapacitated patients automatically because the sponsor payment creates an obligation to meet recruitment goals.

E. Use the patient's prior consent for ordinary treatment as consent for any research conducted in the same clinic.

176. A person acclimatizing to altitude develops increased erythrocyte 2,3-BPG. What effect does this have on systemic oxygen delivery?

A. It shifts the curve to the left, preventing oxygen release to tissues at a given PO2.

B. It increases the number of heme groups in each hemoglobin molecule and thereby raises maximal saturation above 100%.

C. It shifts the hemoglobin oxygen dissociation curve to the right, facilitating oxygen unloading in peripheral tissues.

D. It eliminates the Bohr effect so tissue carbon dioxide no longer influences hemoglobin affinity.

E. It decreases tissue oxygen unloading by stabilizing the high-affinity relaxed state of adult hemoglobin.

177. During prolonged fasting, the brain gradually increases its use of ketone bodies. What is an important systemic consequence of this adaptation?

A. Ketone use increases the brain requirement for glucose and therefore accelerates skeletal-muscle proteolysis indefinitely.

B. The brain becomes completely dependent on free fatty acids crossing the blood-brain barrier as its only fuel.

C. Hepatic ketogenesis stops because insulin rises during fasting and suppresses fatty-acid oxidation.

D. Reduced cerebral glucose requirement decreases the need for gluconeogenesis from amino acids and helps conserve body protein.

E. Protein breakdown must increase because ketone bodies cannot enter neurons or contribute to ATP production.

178. A pacemaker cell in the sinoatrial node reaches threshold. Which ion current is most important for the upstroke of its action potential?

A. Fast voltage-gated sodium current produces the entire nodal phase 0 upstroke exactly as in ventricular myocytes.

B. Chloride influx produces nodal phase 0 and determines the normal positive maximum diastolic potential.

C. Potassium influx through delayed rectifier channels produces the depolarizing upstroke after threshold is reached.

D. The sodium-potassium ATPase directly generates an all-or-none phase 0 spike without opening ion channels.

E. L-type calcium current produces the phase 0 depolarization of sinoatrial nodal cells.

179. After an overnight fast, which hormonal pattern promotes release of stored fuels?

A. Higher insulin and lower glucagon favor hepatic glucose output and adipose triglyceride breakdown.

B. Both insulin and glucagon fall to zero, so stored fuels are released without hormonal regulation.

C. High insulin activates hormone-sensitive lipase in adipose tissue and increases hepatic ketogenesis.

D. High insulin suppresses glucose uptake in skeletal muscle while glucagon directly stimulates muscle glycogenolysis.

E. Lower insulin and higher glucagon favor hepatic glycogenolysis, gluconeogenesis, and adipose lipolysis.

180. A patient from a cultural background unfamiliar to the clinician declines a recommended treatment after consulting family elders. What is the best next step?

A. Assume the refusal reflects lack of capacity because cultural beliefs that differ from the clinician's values are irrational.

B. Explore the patient's values, understanding, and preferred role of family while avoiding assumptions based solely on cultural background.

C. Exclude the family from further discussion because involving relatives is incompatible with autonomous decision-making.

D. Accept the refusal without checking understanding because asking questions about values would be culturally insensitive.

E. Use a generalized description of the patient's culture to predict what decision the patient should make.

181. Light reaches the retina and activates a rod photoreceptor. What happens to the rod membrane potential?

A. Light raises cGMP, opens additional sodium channels, and depolarizes the photoreceptor, increasing glutamate release.

B. Light opens voltage-gated calcium channels directly and creates an all-or-none action potential in the rod outer segment.

C. Light blocks rhodopsin activation, allowing dark current to stop and depolarizing the photoreceptor toward zero millivolts.

D. Light lowers cGMP, closes cation channels, and hyperpolarizes the photoreceptor, reducing glutamate release.

E. Light increases chloride efflux from the rod and hyperpolarizes it without changing cGMP or synaptic transmitter release.

182. A naive B cell recognizes a protein antigen and receives helper T-cell signals in a germinal center. Which enzyme is required for both class-switch recombination and somatic hypermutation?

A. Terminal deoxynucleotidyl transferase performs class switching by inserting random nucleotides into mature heavy-chain constant regions.

B. RAG1 and RAG2 continue V(D)J recombination in germinal centers and directly generate switched immunoglobulin isotypes.

C. Activation-induced cytidine deaminase modifies immunoglobulin DNA during germinal-center diversification.

D. DNA polymerase gamma edits immunoglobulin variable regions while simultaneously replacing membrane with secreted heavy chains.

E. Myeloperoxidase oxidizes immunoglobulin DNA and thereby creates affinity maturation in activated B lymphocytes.

183. A healthy man has FSH stimulation of the testes. Which cell and function are most directly affected?

A. Leydig cells produce most inhibin B and androgen-binding protein directly in response to FSH.

B. Sertoli cells support spermatogenesis, produce androgen-binding protein, and secrete inhibin B in response to FSH.

C. Spermatogonia secrete LH into seminiferous tubules and thereby maintain local testosterone production.

D. Epididymal smooth muscle increases testosterone synthesis and drives meiotic division through FSH receptors.

E. Prostate epithelial cells produce spermatozoa when stimulated by circulating FSH.

184. A healthy person walks from bright sunlight into a dark room. Which retinal change supports dark adaptation over the following minutes?

A. Rhodopsin regenerates in rods, increasing sensitivity to low light as photopigment bleaching reverses.

B. Cone photopigment is permanently destroyed so rods receive less lateral inhibition from cone pathways.

C. Rod cGMP remains maximally depleted, keeping cation channels closed and increasing responsiveness to dim photons.

D. Pupillary constriction reduces retinal illumination and thereby increases rod sensitivity during dark adaptation.

E. Vitamin A is converted to melanin in the retina, which directly amplifies photon energy before rhodopsin activation.

185. A healthy person needs to conserve water. Which loop-of-Henle property is essential for countercurrent multiplication?

A. The thick ascending limb reabsorbs salt while remaining relatively water impermeable, creating transverse osmotic gradients that are multiplied along the loop.

B. The thick ascending limb is highly permeable to water but cannot transport salt, so water leaves and directly concentrates the medulla.

C. Both limbs have identical salt and water permeability, which allows tubular fluid and interstitium to remain in equilibrium at every level.

D. The descending limb actively pumps sodium into the medulla while preventing all water movement across its epithelium.

E. Countercurrent multiplication occurs entirely in cortical collecting ducts and does not require the loop of Henle.

186. A healthy older adult has a lower maximal heart rate during exercise than a healthy young adult despite similar resting heart rates. Which age-related physiologic change best explains this finding?

A. Increased sinoatrial-node sensitivity to catecholamines causes earlier vagal activation during strenuous exercise.

B. Aging increases maximal catecholamine-induced calcium entry into pacemaker cells and therefore lowers heart rate.

C. Higher baroreceptor sensitivity suppresses sympathetic outflow more strongly as exercise intensity rises with age.

D. Reduced beta-adrenergic responsiveness limits the chronotropic response to sympathetic stimulation.

E. Greater vagal withdrawal at peak exercise shortens diastole and directly prevents further sinoatrial acceleration.

187. A clinician is counseling a patient whose health literacy appears limited. Which communication technique best checks understanding?

A. Ask, “Do you understand?” and accept a yes answer as proof that all key information was retained.

B. Provide a dense written handout using technical terminology so the patient can review the details independently.

C. Speak more rapidly so the clinician can repeat the same information several times within the visit.

D. Avoid asking the patient to restate information because doing so is inherently disrespectful.

E. Use plain language and ask the patient to explain the plan back in the patient's own words using teach-back.

188. A patient focuses on a nearby object. Which combination normally occurs during accommodation for near vision?

A. Ciliary muscle relaxation reduces zonular tension, flattening the lens and increasing refractive power for near objects.

B. Ciliary muscle contraction reduces zonular tension, allowing the lens to become more convex and increase refractive power.

C. Ciliary muscle contraction increases zonular tension, flattening the lens so parallel rays from nearby objects converge sooner.

D. Pupillary dilation and lens flattening occur together to increase depth of focus for near viewing.

E. Sympathetic activation contracts the sphincter pupillae and thickens the lens as the principal near-response pathway.

189. A newborn is protected against several infections by antibodies acquired before birth. Which immunoglobulin class crosses the placenta most efficiently?

A. IgM crosses efficiently because its pentameric structure creates high avidity for placental Fc receptors.

B. IgA crosses efficiently and becomes the dominant antibody in fetal serum before delivery.

C. IgE crosses efficiently because placental mast cells transport receptor-bound antibody into fetal blood.

D. IgG is transported across the placenta by neonatal Fc receptors and provides passive systemic immunity.

E. IgD crosses efficiently because its low serum concentration permits rapid diffusion through placental tight junctions.

190. A healthy person becomes hyperosmolar after water deprivation. Which renal response helps restore plasma osmolality?

A. Reduced vasopressin increases aquaporin-2 insertion, allowing more water to be reabsorbed while urine becomes dilute.

B. Increased aldosterone inserts aquaporin-2 directly and reabsorbs pure water without affecting sodium transport.

C. Atrial natriuretic peptide increases collecting-duct water permeability and is the main hormone correcting dehydration.

D. Renin directly opens luminal water channels in the proximal tubule and bypasses the need for medullary hypertonicity.

E. Increased vasopressin raises collecting-duct water permeability, allowing water reabsorption down the medullary osmotic gradient.

191. A patient receives an aldosterone infusion. Which collecting-duct principal-cell change is expected?

A. Reduced epithelial sodium channel activity promotes natriuresis while potassium reabsorption rises through the same pathway.

B. Increased apical sodium-potassium ATPase pumps sodium into urine and potassium into the cell from tubular fluid.

C. Aldosterone acts only on alpha-intercalated cells and has no effect on principal-cell sodium transport.

D. Increased epithelial sodium channel and Na/K-ATPase activity promotes sodium reabsorption and potassium secretion.

E. Aldosterone closes basolateral Na/K-ATPase and thereby prevents the electrochemical gradient needed for sodium entry.

192. A breastfed infant receives substantial mucosal immune protection from breast milk. Which antibody is most important in this role?

A. Pentameric IgM is the dominant milk antibody and enters the infant bloodstream intact to provide systemic immunity.

B. Secretory IgA resists proteolysis and helps prevent pathogen adherence to mucosal surfaces.

C. IgG is secreted into milk at the highest concentration and is the principal antibody coating the neonatal intestine.

D. IgE in milk binds intestinal mast cells and provides broad passive protection against bacterial invasion.

E. IgD is transported through epithelial cells by the polymeric immunoglobulin receptor and dominates mucosal secretions.

193. A patient develops metabolic acidosis. Which renal response increases net acid excretion?

A. Alpha-intercalated cells increase hydrogen secretion while the kidney generates and returns new bicarbonate to blood.

B. Beta-intercalated cells increase bicarbonate secretion into urine and reduce hydrogen secretion to conserve acid.

C. Principal cells stop ammonium production because ammonium excretion would worsen systemic acidosis.

D. The proximal tubule suppresses glutamine metabolism, reducing urinary ammonium and new bicarbonate generation.

E. The thick ascending limb secretes bicarbonate exclusively and becomes the only nephron site of acid-base regulation.

194. A sound wave enters the cochlea. High-frequency sound produces maximal basilar-membrane displacement at which location?

A. Near the compliant, broad apex of the cochlea close to the helicotrema.

B. Equally at every point because frequency is encoded only by auditory-nerve firing rate and not by cochlear mechanics.

C. Only within the middle ear ossicles because the basilar membrane responds exclusively to sound intensity.

D. Near the stiff, narrow base of the cochlea close to the oval window.

E. At the round window membrane because high-frequency energy bypasses the organ of Corti and exits the cochlea directly.

195. A patient begins intermittent parathyroid hormone therapy for severe osteoporosis. Why can intermittent exposure increase bone formation despite the hormone's ability to promote bone resorption?

A. Parathyroid hormone directly inhibits every osteoblast receptor when given continuously but activates only mature osteoclast receptors intermittently.

B. Brief intermittent signaling favors osteoblast survival and activity more than the sustained osteoclast-promoting effects seen with continuous elevation.

C. Intermittent parathyroid hormone prevents renal calcium reabsorption and creates chronic hypocalcemia that mineralizes bone.

D. Parathyroid hormone can stimulate bone only by suppressing vitamin D activation, thereby reducing intestinal calcium absorption.

E. Intermittent dosing permanently blocks RANKL expression, eliminating all osteoclast formation for the duration of therapy.

196. A patient has chronic metabolic acidosis. Why does renal ammonium excretion increase?

A. Ammonium is generated by glomerular podocytes and directly neutralizes plasma bicarbonate before filtration.

B. Proximal tubular glutamine metabolism generates ammonium for excretion and new bicarbonate for return to blood.

C. The kidney converts bicarbonate to ammonium in the collecting duct without using amino-acid metabolism.

D. Ammonium excretion consumes new bicarbonate and therefore helps maintain the metabolic acidosis.

E. Chronic acidosis suppresses proximal ammoniagenesis so that fewer hydrogen ions can be trapped in urine.

197. A patient develops an acute respiratory acidosis from hypoventilation. Which immediate chemical compensation occurs before the kidneys adapt?

A. The kidneys immediately excrete enough ammonium within seconds to normalize pH and bicarbonate completely.

B. Plasma bicarbonate falls sharply because carbon dioxide consumes bicarbonate without generating any carbonic acid equilibrium.

C. Hemoglobin releases no buffering groups, so extracellular pH depends only on renal transport from the first breath onward.

D. Nonbicarbonate buffers accept hydrogen ions, causing only a modest initial rise in plasma bicarbonate.

E. Respiratory acidosis cannot be buffered because carbon dioxide is volatile and does not generate hydrogen ions in body fluids.

198. A child with vitamin D deficiency has impaired mineralization of growing bone. Which intestinal change contributes most directly?

A. Reduced vitamin D signaling increases intestinal calcium absorption but blocks phosphate absorption only in the colon.

B. Reduced vitamin D signaling lowers intestinal calcium and phosphate absorption, limiting substrate available for mineralization.

C. Vitamin D deficiency raises active calcium transport enough to suppress parathyroid hormone and increase mineral deposition.

D. Vitamin D acts only on osteoclasts, so intestinal absorption of calcium and phosphate remains completely unchanged.

E. Vitamin D deficiency increases renal calcitriol production enough to fully compensate for impaired intestinal transport.

199. A severely malnourished patient is given a large carbohydrate load. Why can serum phosphate fall rapidly during refeeding?

A. Insulin blocks glucose entry into cells, causing phosphate to leave the intracellular space and accumulate in urine.

B. Carbohydrate feeding suppresses all ATP synthesis, so cells release phosphate into plasma rather than take it up.

C. Insulin stimulates cellular uptake of glucose and phosphate for phosphorylation and ATP-generating pathways.

D. Glucagon rises sharply after carbohydrate intake and drives phosphate out of skeletal muscle into extracellular fluid.

E. The phosphate decline is caused only by immediate loss of bone mineral and is unrelated to insulin-mediated cellular shifts.

200. Deflection of cochlear inner-hair-cell stereocilia toward the tallest stereocilia opens mechanically gated channels. Which ion provides much of the inward current that depolarizes the hair cell?

A. Sodium enters from perilymph through voltage-gated channels located only at the stereociliary tips.

B. Chloride enters from endolymph and depolarizes the cell because intracellular chloride concentration is higher than extracellular.

C. Potassium enters from potassium-rich endolymph because its electrochemical gradient favors entry into the hair cell.

D. Calcium leaves the hair cell through mechanosensitive channels and creates the primary depolarizing current.

E. Hydrogen ions enter from endolymph and directly trigger glutamate release without changing membrane voltage.

201. A healthy male fetus has normal internal and external genital differentiation. Which fetal cell product is required for regression of the Müllerian ducts?

A. Testosterone from Leydig cells directly causes Müllerian duct regression and is the only required fetal signal.

B. Dihydrotestosterone from the prostate causes Müllerian regression before external genital differentiation begins.

C. FSH from the fetal pituitary causes Müllerian duct apoptosis through receptors on duct epithelium.

D. Anti-Müllerian hormone from Sertoli cells causes Müllerian duct regression.

E. Inhibin B from the placenta is the principal signal for regression of female internal reproductive structures.

202. A patient has a healing long-bone fracture. Which cell type produces osteoid during new bone formation?

A. Osteoclasts synthesize osteoid while their proton pumps simultaneously dissolve hydroxyapatite beneath the same surface.

B. Osteocytes are circulating precursors that enter marrow and become the main collagen-producing cells during fracture repair.

C. Chondrocytes in articular cartilage directly secrete mature lamellar bone without an osteoblast intermediate.

D. Neutrophils synthesize type I collagen after phagocytosis of fracture debris and become embedded as osteocytes.

E. Osteoblasts synthesize type I collagen-rich osteoid that can subsequently mineralize.

203. A patient becomes angry after waiting several hours and says, “No one here cares whether I get better.” Which initial response is most appropriate?

A. Tell the patient the anger is inappropriate and end the conversation until the patient becomes calm.

B. Immediately defend the clinic workflow and explain why the delay was unavoidable before hearing the patient's concern.

C. Promise that there will never be another delay even though the clinician cannot guarantee future scheduling.

D. Acknowledge the frustration and invite the patient to describe the concern before offering explanations or solutions.

E. Ignore the emotional statement and continue asking only closed-ended medical questions.

204. A patient has chronic respiratory acidosis. Which renal adaptation is expected?

A. Renal bicarbonate excretion increases, driving plasma bicarbonate below normal to compensate for high carbon dioxide.

B. The kidneys stop acid excretion because respiratory disorders cannot be compensated by metabolic mechanisms.

C. Renal hydrogen secretion and ammonium excretion increase, raising plasma bicarbonate more than in acute respiratory acidosis.

D. Glomerular filtration ceases until arterial carbon dioxide normalizes, preventing further bicarbonate loss.

E. Collecting ducts become impermeable to hydrogen ions so that carbonic acid can be retained in urine.

205. A skin incision heals primarily by first intention. Which extracellular matrix protein provides major tensile strength to the mature scar?

A. Type IV collagen forms the bulk of the mature dermal scar because basement membrane is the strongest connective-tissue fiber.

B. Elastin replaces collagen completely by late healing and becomes the principal load-bearing protein in a mature scar.

C. Fibrin remains permanently as the dominant structural protein once the initial clot has organized.

D. Type I collagen progressively replaces earlier matrix and provides most long-term tensile strength.

E. Keratin secreted by fibroblasts forms thick extracellular bundles that provide most scar tensile strength.

206. A patient with severe anemia has normal arterial PO2 but reduced tissue oxygen delivery. Which variable is primarily reduced?

A. Arterial oxygen tension must be low because dissolved oxygen is the only form transported in blood.

B. Hemoglobin saturation must be zero whenever hemoglobin concentration falls below normal.

C. Pulmonary diffusion capacity must be absent because anemia prevents oxygen from crossing the alveolar membrane.

D. Arterial oxygen content is low because hemoglobin concentration is a major determinant of blood oxygen content.

E. Mixed venous oxygen content is necessarily higher because tissues cannot extract oxygen from anemic blood.

207. A dendritic cell ingests an extracellular bacterial protein and activates a naive helper T cell. Which antigen-presentation pathway is most directly involved?

A. Extracellular peptide is loaded exclusively onto MHC class I and recognized only by naive CD8 T cells.

B. Processed extracellular peptide is loaded onto MHC class II and recognized by the CD4 T-cell receptor complex.

C. Intact bacterial protein binds the T-cell receptor without processing and directly replaces the need for MHC molecules.

D. The dendritic cell secretes soluble MHC class II, which binds circulating antibody before contacting the helper T cell.

E. Peptide is presented on platelet glycoprotein IIb/IIIa, which functions as the principal antigen-presenting receptor in blood.

208. A patient with carbon monoxide exposure has a normal measured arterial PO2 but impaired oxygen delivery. Which mechanism contributes to tissue hypoxia?

A. Carbon monoxide lowers arterial PO2 mainly by preventing oxygen from diffusing across the alveolar-capillary membrane.

B. Carbon monoxide converts all hemoglobin to methemoglobin and therefore causes a fixed rightward shift of the dissociation curve.

C. Carbon monoxide increases the amount of oxygen physically dissolved in plasma while leaving hemoglobin function unchanged.

D. Carbon monoxide decreases hemoglobin affinity for oxygen, causing complete unloading before blood reaches peripheral tissues.

E. Carbon monoxide reduces available hemoglobin-binding sites and increases the oxygen affinity of remaining occupied hemoglobin sites.

209. A patient has low gastric pH after a meal. Which feedback pathway limits further acid secretion?

A. Acid stimulates G cells directly to release more gastrin until gastric pH falls below 1, creating positive feedback.

B. Acid suppresses somatostatin so histamine secretion rises and amplifies proton-pump activity.

C. Acid activates motilin, which directly stimulates parietal cells to increase hydrochloric acid secretion during the fed state.

D. Acid stimulates antral D cells to release somatostatin, which inhibits gastrin release and parietal-cell activity.

E. Acid activates pancreatic trypsin in the stomach, and trypsin then binds H2 receptors to stop secretion.

210. A healthy male fetus converts testosterone to dihydrotestosterone normally. Which structure depends particularly on DHT for development?

A. Wolffian ducts require DHT exclusively, while testosterone has no role in internal male reproductive development.

B. Male external genitalia and the prostate require strong DHT signaling.

C. Müllerian duct regression requires DHT rather than anti-Müllerian hormone from Sertoli cells.

D. Testicular descent is driven only by DHT and is completely independent of other hormonal and mechanical signals.

E. Sertoli-cell formation requires DHT after birth and therefore cannot occur during fetal development.

211. Early in pregnancy, which hormone maintains the corpus luteum until placental steroid production is established?

A. Human chorionic gonadotropin from trophoblasts activates LH receptors and supports luteal progesterone production.

B. Human placental lactogen activates FSH receptors and directly maintains the corpus luteum during the first trimester.

C. Prolactin from the maternal pituitary activates ovarian progesterone secretion before implantation.

D. Oxytocin from the posterior pituitary prevents luteolysis by suppressing uterine contractions after conception.

E. Maternal ACTH stimulates luteal progesterone through adrenal glucocorticoid receptors in the ovary.

212. A patient spins rapidly and then stops. Which vestibular structure detects angular acceleration of the head?

A. The utricle detects only sound frequency and has no role in sensing head movement or gravity.

B. The saccule detects angular acceleration by rotating the cochlear basilar membrane within the vestibule.

C. The organ of Corti detects angular acceleration through potassium movement in scala tympani.

D. The semicircular canals use endolymph movement to deflect the cupula and alter vestibular hair-cell firing.

E. The tympanic membrane measures angular acceleration by changing tension on middle-ear ossicles during rotation.

213. What is the main ionic basis of phase 4 spontaneous depolarization in sinoatrial nodal cells?

A. A stable high potassium conductance clamps the membrane at a fixed resting potential until a motor neuron releases acetylcholine.

B. A combination of funny inward current, declining potassium conductance, and calcium currents gradually depolarizes the membrane toward threshold.

C. Fast sodium channels repeatedly fire miniature action potentials that summate to create the pacemaker potential.

D. Chloride influx steadily depolarizes the cell because chloride equilibrium potential is strongly positive in nodal tissue.

E. The sodium-potassium ATPase reverses direction during phase 4 and pumps three sodium ions into the cell for every two potassium ions out.

214. A test threshold is lowered so that more people are classified as positive. Assuming the underlying distributions are unchanged, what tradeoff is most likely?

A. Sensitivity and specificity both increase because every lower threshold improves overall test accuracy.

B. Sensitivity decreases while specificity increases because lower thresholds create fewer positive results.

C. Sensitivity increases while specificity decreases because fewer true cases are missed but more unaffected people test positive.

D. Positive predictive value must increase regardless of disease prevalence or the amount of threshold change.

E. Likelihood ratios become independent of sensitivity and specificity once a continuous test is dichotomized.

215. A patient with severe vitamin C deficiency has poor wound healing. Which collagen-processing step is impaired?

A. Hydroxylation of selected proline and lysine residues is reduced, weakening collagen triple-helix stability.

B. Gamma-carboxylation of glutamate residues is reduced, preventing collagen from binding calcium through vitamin K-dependent sites.

C. Cleavage of procollagen terminal peptides is blocked because vitamin C is the extracellular procollagen peptidase.

D. Translation of collagen alpha chains stops because ascorbate is an obligatory ribosomal cofactor for peptide-bond formation.

E. Cross-linking by lysyl oxidase is directly abolished because vitamin C is the enzyme's required copper donor.

216. A patient receives an organ transplant and develops an acute cellular rejection episode. Which immune mechanism is central to this process?

A. Recipient erythrocytes recognize donor MHC proteins and release hemoglobin-derived cytokines that injure the graft.

B. Donor neutrophils permanently engraft in the recipient and produce antibodies against recipient vascular endothelium.

C. Recipient T lymphocytes recognize donor alloantigens and mediate cytotoxicity and inflammatory recruitment.

D. Recipient platelets undergo V(D)J recombination and generate clonally specific receptors against donor tissue.

E. Complement is activated only through IgE bound to mast cells, making T-cell recognition unnecessary for acute rejection.

217. A patient has persistent vomiting and develops metabolic alkalosis. Which primary acid-base change is expected?

A. Loss of gastric bicarbonate lowers plasma bicarbonate and produces a primary metabolic acidosis.

B. Loss of gastric sodium produces a primary respiratory alkalosis by directly lowering arterial carbon dioxide.

C. Loss of gastric hydrogen chloride raises plasma bicarbonate concentration relative to hydrogen ion.

D. Vomiting causes a primary respiratory acidosis because reduced abdominal pressure suppresses central ventilation.

E. Plasma bicarbonate remains fixed because gastric acid secretion does not influence extracellular acid-base balance.

218. A patient has increased intracranial pressure from a mass lesion. Which relationship best describes cerebral perfusion pressure?

A. Cerebral perfusion pressure is approximately intracranial pressure minus mean arterial pressure.

B. Cerebral perfusion pressure equals systolic pressure plus intracranial pressure because both forces drive arterial inflow.

C. Cerebral perfusion pressure depends only on arterial oxygen tension and is independent of hydrostatic pressures.

D. Cerebral perfusion pressure is approximately mean arterial pressure minus intracranial pressure.

E. Cerebral perfusion pressure equals central venous pressure minus mean arterial pressure in all clinical conditions.

219. A patient with a copper deficiency has fragile connective tissue partly because of reduced activity of which enzyme?

A. Prolyl hydroxylase cleaves collagen terminal peptides after secretion and requires copper as its only cofactor.

B. Collagenase creates stabilizing cross-links by digesting nonhelical collagen regions before fibril assembly.

C. Elastase polymerizes tropoelastin into elastic fibers and requires copper-dependent ATP hydrolysis.

D. Lysyl oxidase forms covalent cross-links between collagen and elastin molecules in the extracellular matrix.

E. Transglutaminase converts type I collagen into type IV collagen during maturation of dermal connective tissue.

220. A healthy pregnant woman develops progressive insulin resistance later in gestation. Which placental hormone contributes importantly?

A. Human chorionic gonadotropin is the principal late-pregnancy insulin-sensitizing hormone and drives maternal glucose uptake into muscle.

B. Human placental lactogen promotes maternal insulin resistance and lipolysis, helping preserve glucose for the fetus.

C. Oxytocin causes chronic maternal hypoglycemia by inserting GLUT4 into adipocytes throughout pregnancy.

D. Progesterone eliminates placental glucose transfer by directly blocking maternal hepatic glucose production.

E. Relaxin suppresses lipolysis and is the dominant hormone causing maternal insulin sensitivity to rise in late gestation.

221. A healthy person has an acute fall in effective arterial blood volume. Which macula densa signal favors renin release?

A. Reduced sodium chloride delivery to the macula densa increases juxtaglomerular renin secretion.

B. Increased sodium chloride delivery to the macula densa maximally stimulates renin release and afferent dilation.

C. Macula densa cells release aldosterone directly when tubular sodium chloride falls.

D. Renin secretion is controlled only by plasma osmolality and is independent of renal perfusion or tubular salt delivery.

E. Reduced sodium chloride delivery suppresses sympathetic beta-1 signaling to juxtaglomerular cells and lowers renin.

222. A patient has a vagotomy. Which gastric function is most directly reduced during the cephalic phase?

A. Bile acid synthesis stops because the vagus is the only neural input to hepatocytes that permits cholesterol conversion.

B. Intestinal glucose absorption stops because SGLT1 requires vagal acetylcholine at the brush border.

C. Pancreatic enzymes cannot be secreted in response to CCK because acinar cells have no hormone receptors.

D. Colonic sodium absorption ceases because vagal fibers directly power epithelial Na/K-ATPase throughout the colon.

E. Anticipatory acid secretion and gastric motor responses triggered by sensory and cognitive cues are diminished.

223. Sympathetic stimulation accelerates the sinoatrial node. Which cellular change contributes most directly?

A. Beta-1 signaling raises cAMP and steepens phase 4 depolarization by enhancing pacemaker and calcium currents.

B. Beta-1 signaling lowers cAMP and opens potassium channels, flattening phase 4 depolarization while increasing heart rate.

C. Alpha-2 signaling raises chloride permeability and directly produces faster L-type calcium-channel inactivation.

D. Muscarinic M2 activation raises cAMP and accelerates funny current during sympathetic stimulation.

E. Nicotinic blockade at the motor end plate is required before the sinoatrial node can respond to circulating catecholamines.

224. A patient has a type I hypersensitivity reaction to a food allergen. What happens during the immediate phase after re-exposure?

A. Allergen cross-links IgE bound to Fc epsilon receptors on mast cells, triggering release of preformed and newly synthesized mediators.

B. Allergen cross-links IgG on neutrophils, causing delayed granuloma formation as the principal immediate response.

C. Allergen activates cytotoxic T cells directly, and perforin release produces the wheal within seconds of exposure.

D. Allergen binds circulating IgM and forms complexes that deposit in tissues before mast-cell activation can occur.

E. Allergen activates complement C9 alone, which releases histamine directly from endothelial cells without mast cells.

225. A person moves from a cool dry room into a hot humid environment. Why does high humidity increase heat stress?

A. High humidity increases the vapor-pressure gradient from skin to air, causing sweat to evaporate more rapidly.

B. A high ambient water-vapor pressure reduces the gradient for sweat evaporation, limiting evaporative heat loss.

C. High humidity prevents cutaneous vasodilation by directly constricting skin arterioles through local osmotic effects.

D. High humidity lowers skin temperature enough to eliminate conductive and radiative heat transfer from the body.

E. High humidity reduces sweat production because eccrine glands require dry air to receive sympathetic cholinergic input.

226. A patient with methemoglobinemia has iron in hemoglobin oxidized from the ferrous to ferric state. What is the functional consequence?

A. Ferric heme binds oxygen with higher capacity than ferrous heme and therefore increases arterial oxygen content.

B. Methemoglobin lowers oxygen affinity of all remaining heme sites and produces a uniform rightward shift that improves unloading.

C. Ferric heme cannot bind oxygen normally, and the remaining ferrous sites hold oxygen more tightly, impairing delivery.

D. Oxidation of heme increases dissolved plasma oxygen sufficiently to compensate for loss of hemoglobin function.

E. Ferric heme causes hypoxemia solely by narrowing pulmonary arteries and has no direct effect on oxygen binding.

227. A patient develops hemolysis after receiving an incompatible ABO transfusion. Which hypersensitivity mechanism best describes the reaction?

A. Soluble immune complexes deposit in glomeruli over weeks, producing a type III reaction as the immediate cause of hemolysis.

B. Sensitized T cells release cytokines after several days, producing a type IV reaction that lyses red cells without antibody.

C. Preformed antibodies bind antigens on transfused red cells and activate complement, producing a type II cytotoxic reaction.

D. IgE bound to mast cells recognizes donor erythrocytes, producing a type I reaction as the main mechanism of intravascular lysis.

E. Natural killer cells recognize absent donor MHC class I and selectively destroy transfused erythrocytes through perforin.

228. Angiotensin II levels rise after volume depletion. Which proximal tubular effect contributes to sodium retention?

A. Angiotensin II blocks proximal sodium-hydrogen exchange and causes obligatory bicarbonaturia during volume depletion.

B. Angiotensin II closes all basolateral Na/K-ATPase pumps, preventing sodium reabsorption throughout the nephron.

C. Angiotensin II acts only on the adrenal cortex and has no direct tubular effects on sodium transport.

D. Angiotensin II decreases peritubular capillary oncotic pressure enough to oppose proximal fluid reabsorption.

E. Angiotensin II stimulates sodium-hydrogen exchange, increasing proximal sodium and bicarbonate reabsorption.

229. A patient drinks a large amount of pure water. How is the excess water distributed after equilibration?

A. All remains within plasma because pure water cannot cross capillary or cell membranes without active transport.

B. All remains extracellular because intracellular osmoles prevent any water movement into cells.

C. Most enters the interstitial space but none enters cells because sodium is the only osmotically active particle in body fluids.

D. Water distributes equally by volume among plasma, interstitial fluid, and intracellular fluid regardless of compartment size.

E. Most enters the intracellular fluid because water distributes across cell membranes according to osmotic gradients, with the remainder in extracellular fluid.

230. A patient develops serum sickness after exposure to a foreign protein. Which mechanism best accounts for tissue injury?

A. IgE-coated mast cells degranulate immediately at mucosal surfaces without formation of circulating immune complexes.

B. Cytotoxic T cells recognize foreign peptide on MHC I and directly kill vascular smooth muscle cells throughout the body.

C. Autoantibodies bind fixed basement-membrane antigens and cause a purely type II reaction without soluble complexes.

D. Circulating antigen-antibody complexes deposit in tissues and activate complement, causing inflammatory injury.

E. Neutrophils generate antibodies against the foreign protein and then phagocytose intact immune complexes in bone marrow.

231. A meal distends the stomach and soon increases colonic mass movements. Which reflex best describes this response?

A. The gastrocolic reflex increases colonic motility after gastric filling and nutrient entry.

B. The enterogastric reflex accelerates colonic mass movements by increasing gastric acid secretion only.

C. The rectoanal inhibitory reflex begins when the stomach fills and contracts the internal anal sphincter.

D. The ileogastric reflex empties the colon whenever ileal contents enter the cecum.

E. The migrating motor complex is a fed-state colonic reflex triggered specifically by gastric distention.

232. A healthy pregnant woman has increased minute ventilation. What acid-base change commonly accompanies normal pregnancy?

A. Progesterone suppresses ventilation, raising arterial carbon dioxide and producing chronic respiratory acidosis throughout pregnancy.

B. Pregnancy causes a primary metabolic acidosis because fetal bicarbonate diffuses into maternal blood and consumes hydrogen ions.

C. Arterial carbon dioxide remains identical to the nonpregnant state because pregnancy alters only oxygen consumption, not ventilation.

D. Renal bicarbonate rises markedly to create a metabolic alkalosis that secondarily suppresses maternal ventilation.

E. Progesterone stimulates ventilation, lowering arterial carbon dioxide and producing a mild chronic respiratory alkalosis with renal bicarbonate compensation.

233. Rectal distention occurs before defecation. What is the normal response of the internal anal sphincter?

A. It contracts reflexively through somatic pudendal motor neurons and is therefore under voluntary control.

B. It remains permanently contracted because only the external anal sphincter can respond to rectal distention.

C. It relaxes only when sympathetic activity rises, while parasympathetic input always contracts it.

D. It relaxes reflexively through enteric inhibitory pathways, allowing sampling of rectal contents.

E. It opens because the pelvic floor skeletal muscles secrete nitric oxide directly onto its smooth muscle.

234. A healthy infant is compared with a healthy adult during a brief period of fasting. Which feature makes the infant more vulnerable to hypoglycemia?

A. A lower brain-to-body mass ratio sharply reduces cerebral glucose use and therefore speeds glycogen depletion.

B. A higher glucose requirement relative to body mass is supported by smaller absolute glycogen reserves.

C. Infants cannot perform hepatic glycogenolysis, so all fasting glucose must come from intestinal absorption.

D. Neonatal glucagon secretion is absent after birth, preventing any increase in hepatic glucose production during fasting.

E. Infants have much larger hepatic glycogen stores per kilogram, but insulin prevents those stores from being mobilized.

235. Near term, uterine contractions progressively intensify during labor. Which positive-feedback loop supports this process?

A. Cervical stretch suppresses oxytocin, which weakens contractions and thereby increases cervical stretch further.

B. Cervical stretch increases oxytocin release, which strengthens uterine contractions and causes additional cervical stretch.

C. Progesterone rises sharply with each contraction and directly relaxes myometrium to produce stronger subsequent contractions.

D. Prolactin released by cervical stretch contracts the uterus and stimulates additional prolactin through a closed endocrine loop.

E. FSH release from the posterior pituitary increases uterine calcium entry and drives the Ferguson reflex.

236. A postpartum woman begins nursing. Why do circulating prolactin levels rise after suckling?

A. Suckling increases hypothalamic dopamine, which directly stimulates prolactin release through D2 receptors on lactotrophs.

B. Suckling causes posterior pituitary prolactin release from stored vesicles without involving the anterior pituitary.

C. Suckling raises somatostatin, the principal prolactin-releasing hormone, and thereby increases milk synthesis.

D. Suckling raises GnRH, which directly stimulates prolactin secretion while simultaneously suppressing LH and FSH.

E. Suckling reduces hypothalamic dopamine delivery to lactotrophs, removing tonic inhibition of prolactin secretion.

237. A patient has a positive tuberculin skin test 48 hours after intradermal antigen placement. Which immune process produces the induration?

A. Preformed IgE on mast cells causes maximal edema within minutes and remains the dominant mechanism at 48 hours.

B. Circulating immune complexes deposit at the injection site and activate complement as the principal delayed mechanism.

C. IgM binds antigen on dermal fibroblasts and activates complement-mediated cytotoxicity throughout the epidermis.

D. Previously sensitized T cells release cytokines that recruit and activate macrophages in a delayed type IV response.

E. Natural killer cells recognize absent self MHC on keratinocytes and create a delayed reaction independent of T cells.

238. Vagal stimulation slows atrioventricular nodal conduction. Which mechanism is most important?

A. Muscarinic M2 signaling lowers cAMP and increases potassium conductance, slowing nodal depolarization and conduction.

B. Muscarinic signaling increases L-type calcium current and accelerates the nodal upstroke while prolonging conduction time.

C. Vagal acetylcholine activates skeletal nicotinic receptors on ventricular myocytes and blocks gap junctions directly.

D. Vagal stimulation raises norepinephrine release from sympathetic terminals, which selectively suppresses AV nodal conduction.

E. M2 receptors activate phospholipase C strongly and produce vasoconstriction that mechanically compresses the AV node.

239. A patient has acromegaly from excess growth hormone. Which mediator accounts for many growth-promoting effects of growth hormone?

A. Cortisol from the adrenal cortex mediates all growth effects by stimulating epiphyseal cartilage proliferation.

B. Aldosterone from the zona glomerulosa acts on bone growth plates and is the principal downstream hormone of growth hormone.

C. T3 produced exclusively in pituitary somatotrophs mediates growth hormone effects without involvement of liver.

D. Prolactin from the posterior pituitary is converted to IGF-1 within skeletal muscle after growth hormone stimulation.

E. Insulin-like growth factor 1 produced mainly by the liver mediates many somatic growth effects.

240. A patient receives isotonic saline. Which fluid-compartment change is expected after equilibration?

A. Extracellular fluid volume expands with little change in intracellular volume or plasma osmolality.

B. Intracellular fluid expands markedly because isotonic saline creates a large osmotic gradient into cells.

C. Both intracellular and extracellular osmolality rise sharply because saline is hypertonic to normal plasma.

D. Only intracellular volume expands because sodium crosses cell membranes freely and draws water with it.

E. Total body water is unchanged because isotonic saline remains entirely within the vascular plasma compartment.

241. A patient with marked neutropenia has a bacterial skin infection. Which leukocyte function is most directly lost when neutrophils are absent?

A. Long-term high-affinity antibody production is abolished because neutrophils are the precursors of memory B cells.

B. MHC class I presentation by all nucleated cells is lost because neutrophils supply the required beta-2 microglobulin.

C. Platelet aggregation fails because neutrophils provide most circulating fibrinogen for glycoprotein IIb/IIIa binding.

D. Rapid phagocytosis and killing of extracellular bacteria at acute inflammatory sites are substantially reduced.

E. Natural killer cytotoxicity disappears because neutrophils are the sole source of perforin and granzyme proteins.

242. A healthy person becomes acutely hypercapnic. What is the expected effect on cerebral blood flow?

A. Cerebral arterioles constrict, reducing flow because carbon dioxide directly blocks vascular smooth-muscle relaxation.

B. Cerebral arterioles dilate, increasing cerebral blood flow as local hydrogen ion concentration rises.

C. Cerebral blood flow remains fixed because autoregulation prevents carbon dioxide from influencing resistance vessels.

D. Cerebral veins constrict selectively while arterioles remain unchanged, reducing intracranial blood volume without changing flow.

E. Cerebral flow falls only because hemoglobin releases less oxygen during hypercapnia despite unchanged vascular resistance.

243. A patient hyperventilates for several minutes. Which change in cerebral circulation is expected?

A. Reduced arterial carbon dioxide causes cerebral vasodilation and raises flow because alkalosis relaxes cerebral arterioles.

B. Reduced arterial carbon dioxide causes cerebral vasoconstriction and lowers cerebral blood flow.

C. Cerebral blood flow does not change because carbon dioxide cannot cross the blood-brain barrier.

D. Reduced arterial oxygen content from hyperventilation is the dominant cause of increased cerebral perfusion in a healthy person.

E. Venous pressure rises enough to offset any arteriolar response, leaving intracranial blood volume unchanged.

244. A patient with severe hyponatremia develops cerebral edema. Which osmotic principle explains the initial cell swelling?

A. Low extracellular sodium raises extracellular effective osmolality and draws water out of neurons.

B. Water leaves cells because intracellular proteins become osmotically inactive when plasma sodium falls.

C. Low extracellular effective osmolality drives water into brain cells until transmembrane osmotic gradients diminish.

D. Sodium rapidly enters neurons until concentrations equalize, preventing any change in cell water.

E. Brain-cell volume is independent of extracellular osmolality because the blood-brain barrier blocks water movement.

245. A patient receives a benzodiazepine. Which effect on the GABA-A receptor best describes its action?

A. The drug increases the duration of glutamate-gated sodium-channel opening, enhancing excitatory neurotransmission.

B. The drug blocks GABA binding and directly opens voltage-gated calcium channels on cortical pyramidal neurons.

C. The drug increases the frequency of GABA-mediated chloride-channel opening, enhancing inhibitory neurotransmission.

D. The drug irreversibly inhibits GABA transaminase and therefore prevents all GABA metabolism for the life of the neuron.

E. The drug activates GABA-B receptors to open chloride channels directly without requiring endogenous GABA.

246. A patient receives an opioid agonist for severe pain. Which cellular action is typical of mu-opioid receptor activation?

A. Gi-coupled signaling lowers cAMP, opens potassium channels, and reduces presynaptic calcium entry, decreasing transmitter release.

B. Gs-coupled signaling raises cAMP and increases presynaptic calcium entry, enhancing release of substance P and glutamate.

C. Gq-coupled signaling increases IP3 and directly activates skeletal nicotinic receptors throughout the dorsal horn.

D. Ligand-gated sodium channels open on nociceptive neurons and depolarize them, reducing pain by conduction block.

E. Tyrosine kinase activation increases glutamate vesicle fusion and accelerates ascending spinothalamic transmission.

247. A patient has prerenal hypoperfusion with intact tubular function. Which renal response helps conserve sodium?

A. Enhanced proximal and distal sodium reabsorption lowers the fractional excretion of sodium.

B. Tubular injury prevents sodium reabsorption and raises fractional sodium excretion as the defining prerenal response.

C. Atrial natriuretic peptide rises sharply and blocks sodium reabsorption despite low effective arterial volume.

D. Renin and sympathetic activity fall, promoting sodium loss and restoring renal perfusion by lowering blood volume.

E. Proximal sodium reabsorption stops so more sodium reaches the macula densa and suppresses renin.

248. A patient with chronic hypoxemia develops secondary polycythemia. Which change can eventually limit the benefit of the increased red-cell mass?

A. Higher hematocrit always lowers blood viscosity, allowing unlimited increases in oxygen delivery.

B. Additional red cells decrease arterial oxygen content because hemoglobin molecules compete for dissolved oxygen.

C. Polycythemia abolishes erythrocyte deformability at any hematocrit above normal and immediately stops capillary flow.

D. Excessive hematocrit increases blood viscosity and can raise resistance to flow.

E. Increased red-cell mass directly lowers systemic vascular resistance by reducing friction within small vessels.

249. Investigators want to estimate the effect of an exposure on a rare outcome but follow-up of a large disease-free cohort would be inefficient. Which design is particularly efficient?

A. A cross-sectional study guarantees direct measurement of disease incidence by following all participants prospectively.

B. A case series without controls provides an unbiased relative risk because every participant has the outcome.

C. A case-control study samples people with the outcome and controls without it, then compares prior exposure histories.

D. An ecologic study of national averages eliminates confounding because individual-level data are not collected.

E. A randomized trial assigning a harmful suspected exposure is required before any association can be estimated.

250. A patient has damage to the posterior hypothalamus and has difficulty conserving heat in a cold environment. Which normal response would be impaired?

A. Sweating and cutaneous vasodilation, which are the principal posterior-hypothalamic mechanisms for dissipating excess heat.

B. Salivary secretion and gastric motility, which are the main physiologic mechanisms for generating core heat in adults.

C. Renal bicarbonate excretion, which normally increases body temperature by accelerating systemic metabolic acidosis.

D. Sympathetic vasoconstriction and heat-generating responses that reduce heat loss and increase thermogenesis.

E. Pulmonary surfactant secretion, which is the dominant hypothalamic mechanism for preventing conductive heat loss.

251. A child has normal growth hormone secretion but severe hepatic inability to produce IGF-1. Which growth pattern is expected?

A. Linear growth is accelerated because absence of IGF-1 removes all inhibitory effects of growth hormone on the growth plate.

B. Growth is normal because IGF-1 is used only for glucose regulation and has no role in skeletal development.

C. Linear growth is impaired because many growth-promoting effects of growth hormone require IGF-1.

D. Growth is impaired only after epiphyseal closure because IGF-1 has no effect on childhood cartilage.

E. Growth hormone levels must be low because loss of IGF-1 increases negative feedback on pituitary somatotrophs.

252. A patient has eosinophilia during a helminth infection. Which effector mechanism is especially associated with eosinophils?

A. Eosinophils become plasma cells and secrete high-affinity IgG that penetrates the parasite cuticle directly.

B. Eosinophils form the membrane attack complex from intracellular stores of C5 through C9 without complement activation.

C. Eosinophils kill helminths primarily by engulfing the entire organism into a single phagolysosome.

D. Eosinophils suppress type 2 helper T-cell responses by degrading all local interleukin-5 before degranulation begins.

E. Fc receptor-mediated degranulation releases toxic granule proteins against antibody-coated parasites too large for phagocytosis.

253. A patient develops hyperkalemia. Which early effect on the resting membrane potential of ventricular myocytes is expected?

A. The resting membrane potential becomes less negative because the potassium equilibrium potential shifts in the positive direction.

B. The resting membrane potential becomes more negative because extracellular potassium increases the gradient for potassium efflux.

C. Resting membrane potential is unchanged because ventricular cells are impermeable to potassium between action potentials.

D. The resting membrane becomes exactly equal to the sodium equilibrium potential because potassium no longer contributes to voltage.

E. Hyperkalemia lowers intracellular potassium immediately to zero, eliminating all electrical activity without a voltage shift.

254. A person develops goosebumps when cold. Which autonomic pathway causes piloerection?

A. Sympathetic adrenergic activation contracts arrector pili smooth muscle attached to hair follicles.

B. Parasympathetic cholinergic activation contracts arrector pili because all cutaneous smooth muscle is vagally innervated.

C. Somatic alpha motor neurons release acetylcholine onto arrector pili through nicotinic receptors.

D. Sympathetic cholinergic fibers acting on muscarinic receptors are the exclusive pathway to arrector pili.

E. Sensory C fibers directly contract arrector pili by releasing glutamate into the dermis without autonomic neurons.

255. A patient is exposed to cold for several hours. Which physiologic response reduces heat loss from the skin?

A. Cutaneous vasodilation lowers the skin-to-environment temperature gradient and therefore conserves core heat.

B. Sweating increases evaporative heat conservation by trapping a layer of water over the skin.

C. Cutaneous sympathetic vasoconstriction lowers skin blood flow and reduces transfer of core heat to the environment.

D. Sympathetic withdrawal increases skin perfusion and directs warm blood away from the body surface.

E. Cold exposure suppresses all vascular reflexes so heat conservation depends only on voluntary muscle contraction.

256. A patient is immobilized for several weeks. Which skeletal response is expected from reduced mechanical loading?

A. Osteoblast activity always exceeds osteoclast activity because bone automatically strengthens when mechanical loading falls.

B. Bone resorption can exceed formation because reduced strain shifts remodeling toward loss of bone mass.

C. Bone remodeling stops completely because osteocytes cannot sense the absence of strain in mineralized tissue.

D. Reduced loading causes immediate conversion of trabecular bone into cartilage without altering mineral content.

E. Osteoclasts disappear during immobilization, so serum calcium falls from excessive skeletal mineral deposition.

257. A patient lacks normal enteric ganglion cells in a distal bowel segment. Why can the affected segment remain tonically contracted?

A. Loss of excitatory enteric neurons causes maximal smooth-muscle contraction because acetylcholine normally relaxes the bowel.

B. The segment cannot contract at all, so obstruction occurs only because the bowel becomes excessively compliant and dilated distally.

C. Sympathetic denervation causes sustained contraction because norepinephrine is the main inhibitory transmitter in intestinal smooth muscle.

D. Loss of inhibitory enteric neurons prevents normal relaxation, creating functional obstruction despite intact smooth muscle.

E. Absence of mucosal epithelial cells eliminates sodium absorption and directly locks the muscularis into a tetanic contraction.

258. A patient has an acute decrease in plasma calcium concentration. Which cardiac action-potential change is most likely?

A. The ventricular action potential shortens markedly because low calcium maximally accelerates L-type calcium-channel inactivation.

B. The QRS complex disappears because plasma calcium is the only ion responsible for ventricular phase 0 depolarization.

C. The ventricular action potential can be prolonged, contributing to QT-interval prolongation.

D. The resting membrane potential becomes strongly positive because low calcium reverses the potassium equilibrium potential.

E. The sinoatrial node stops because low calcium selectively blocks funny current while leaving every other channel normal.

259. During a prolonged febrile illness, a patient loses weight despite adequate oxygen availability. Which stress-hormone pattern promotes catabolism?

A. Suppression of cortisol and catecholamines is required for hepatic glucose output during systemic stress.

B. High insulin with absent counterregulatory hormones is the main driver of stress-related proteolysis and lipolysis.

C. Aldosterone alone directly breaks down skeletal-muscle protein to provide amino acids for gluconeogenesis.

D. Increased cortisol and catecholamines promote substrate mobilization, including proteolysis, lipolysis, and hepatic glucose production.

E. Stress lowers all hepatic glucose production because glycogenolysis and gluconeogenesis are inhibited by sympathetic activation.

260. Which hypothalamic factor directly inhibits growth hormone secretion from anterior pituitary somatotrophs?

A. Somatostatin inhibits growth hormone release, opposing stimulatory growth hormone-releasing hormone.

B. Dopamine is the only inhibitor of growth hormone and has no major role in prolactin regulation.

C. GnRH inhibits growth hormone during each reproductive pulse and is the dominant regulator of somatotrophs.

D. CRH suppresses growth hormone while simultaneously stimulating thyroid hormone secretion.

E. Oxytocin from the posterior pituitary provides tonic inhibition of somatotrophs through portal blood.

261. A patient with a viral infection has early cytotoxic activity before a large antigen-specific T-cell response develops. Which feature enables natural killer cells to target some infected cells?

A. Reduced expression of self MHC class I removes inhibitory signaling and favors natural killer cell activation.

B. Increased expression of self MHC class I removes inhibitory signaling and is the strongest trigger for natural killer killing.

C. Natural killer cells require prior V(D)J recombination to make a unique antigen receptor for each viral peptide.

D. Natural killer cells recognize only peptide presented by MHC class II and therefore require professional antigen-presenting cells.

E. Natural killer cells cannot kill host cells directly and act only by secreting antibody into the extracellular space.

262. A patient asks whether a serious diagnosis is certain. The available evidence supports several possibilities and additional testing is pending. What is the best communication approach?

A. Name the most dangerous diagnosis as certain so the patient will take the evaluation seriously.

B. Avoid discussing any diagnosis until uncertainty has been eliminated completely.

C. List every theoretical disease without explaining relative likelihood because uncertainty should never be prioritized.

D. State what is known, explain the meaningful uncertainty, and describe how the next tests or observations will narrow the possibilities.

E. Reassure the patient that nothing serious is possible because definitive proof has not yet been obtained.

263. A patient has high sodium chloride delivery to the macula densa. Which tubuloglomerular feedback response is expected?

A. Afferent dilation and increased renin release raise single-nephron GFR further despite already high distal salt delivery.

B. Afferent arteriolar constriction and reduced renin release help lower single-nephron GFR.

C. Efferent dilation is the only response, and afferent tone remains completely unaffected by macula densa signals.

D. Macula densa cells release aldosterone directly into the afferent arteriole, increasing filtration fraction.

E. High sodium chloride causes vasopressin release from the macula densa and increases collecting-duct water reabsorption.

264. A patient has hypokalemia. Which renal adaptation helps conserve potassium?

A. Principal-cell potassium secretion rises because low plasma potassium directly opens apical ROMK channels maximally.

B. Aldosterone necessarily rises and forces continued potassium loss until plasma concentration returns to normal.

C. The proximal tubule begins secreting most filtered potassium rather than reabsorbing it during potassium depletion.

D. Potassium secretion by principal cells falls, and alpha-intercalated H/K-ATPase activity can favor potassium reabsorption.

E. Collecting ducts become impermeable to hydrogen ions so all electrochemical driving force is redirected toward potassium secretion.

265. A person starts resistance training and gains strength substantially during the first two weeks before major muscle hypertrophy develops. Which adaptation is most responsible?

A. Rapid formation of entirely new muscle fibers doubles cross-sectional area before neural adaptation has time to occur.

B. A large increase in capillary density is the main early mechanism because resistance strength is limited primarily by oxygen diffusion.

C. Improved motor-unit recruitment, firing coordination, and neural drive increase force before large structural growth occurs.

D. Tendon collagen disappears transiently, lowering series elasticity and allowing every sarcomere to shorten farther.

E. Mitochondrial volume increases several-fold within days and is the major determinant of maximal one-repetition strength.

266. A capillary bed experiences an acute rise in capillary hydrostatic pressure with other Starling forces unchanged. What happens to transcapillary fluid movement?

A. Net absorption into the capillary increases because hydrostatic pressure pulls interstitial water inward.

B. Fluid movement stops because hydrostatic pressure is not part of the forces governing capillary exchange.

C. Net filtration from capillary to interstitium increases because the outward capillary hydrostatic force is greater.

D. Plasma oncotic pressure immediately rises by the same amount, guaranteeing no change in net filtration.

E. Lymphatic flow must fall because greater filtration decreases interstitial fluid formation.

267. A patient has a lesion of the suprachiasmatic nucleus. Which physiologic function is most directly disrupted?

A. Generation of spinal stretch reflexes is impaired because the suprachiasmatic nucleus contains alpha motor neurons.

B. Entrainment of circadian rhythms to the light-dark cycle is impaired.

C. Primary auditory frequency discrimination is impaired because the nucleus receives direct cochlear hair-cell input.

D. Cerebellar error correction is impaired because the nucleus is the major source of climbing fibers to Purkinje cells.

E. Voluntary saccades are abolished because the nucleus is the cortical eye field that initiates conjugate gaze.

268. Two clinicians disagree about whether a patient has decision-making capacity. Which assessment best addresses capacity?

A. Evaluate whether the patient can understand relevant information, appreciate its application, reason about options, and communicate a choice.

B. Determine whether the patient chooses the option preferred by the medical team, because disagreement demonstrates incapacity.

C. Use age alone, with all adults older than 80 presumed unable to make complex medical decisions.

D. Rely exclusively on a psychiatric diagnosis, because any mental illness automatically removes capacity for medical decisions.

E. Ask whether the patient can remember every technical detail of the consent form word for word.

269. A patient who previously expressed clear wishes in an advance directive now lacks capacity. The family asks for treatment that directly conflicts with those documented wishes. What should guide the team?

A. Honor the patient's applicable prior autonomous wishes and explain to the family that the surrogate role is to represent the patient rather than replace the patient's values.

B. Follow the family request automatically because current relatives always override an advance directive once the patient loses capacity.

C. Ignore both the directive and the family and choose treatment solely according to the physician's personal values.

D. Treat the advance directive as invalid because it was written before the present illness developed.

E. Ask the family to decide by majority vote even when the patient's prior preferences are clear and applicable.

270. A patient has a complete tendon rupture. Which mechanical role of tendon is lost?

A. Generation of action potentials in muscle fibers is lost because tendon is the source of voltage-gated sodium channels.

B. Storage of intracellular calcium is lost because tendon collagen forms the terminal cisternae of the sarcoplasmic reticulum.

C. Synthesis of acetylcholine is lost because tenocytes supply choline acetyltransferase to motor nerve terminals.

D. Activation of alpha motor neurons is lost because tendon fibroblasts are the principal spinal interneurons for voluntary movement.

E. Transmission of muscle-generated force to bone is interrupted, preventing normal joint torque despite intact muscle contraction.

271. A patient has nephrogenic diabetes insipidus. Which response to desmopressin is expected?

A. Urine concentrating ability changes little because the kidney is resistant to vasopressin signaling.

B. Urine osmolality rises dramatically because nephrogenic diabetes insipidus is caused by absent vasopressin secretion.

C. Urine flow stops completely because desmopressin directly closes glomerular filtration pores in the nephron.

D. Plasma osmolality falls immediately below normal because desmopressin causes obligatory sodium loss independent of water.

E. Urine becomes more dilute because desmopressin removes aquaporin-2 from collecting-duct apical membranes.

272. A ventricular myocyte is in phase 2 of its action potential. What creates the plateau?

A. Fast sodium channels remain fully open throughout phase 2 and exactly balance inward chloride current.

B. The sodium-potassium ATPase stops during phase 2, so membrane voltage is held constant without any channel currents.

C. Potassium influx through inward rectifier channels balances calcium efflux from the cell during the plateau.

D. Inward calcium current through L-type channels is balanced by outward potassium currents for a prolonged interval.

E. Chloride channels alone clamp the membrane near zero and are the only conductance active during phase 2.

273. A patient has a lesion of Broca area in the dominant frontal lobe. Which language pattern is most likely?

A. Speech is fluent but nonsensical, with severely impaired comprehension and poor awareness of errors.

B. Speech and comprehension are intact, but the patient cannot recognize familiar faces because language cortex is spared.

C. Only repetition is impaired while spontaneous speech and comprehension remain fully normal, defining an isolated motor aphasia.

D. Speech is nonfluent and effortful, with relatively preserved comprehension compared with verbal output.

E. Language is normal but contralateral pain and temperature sensation is lost because Broca area is a primary sensory relay.

274. A patient has a lesion of Wernicke area in the dominant posterior temporal region. Which pattern is most likely?

A. Speech remains fluent but lacks meaningful content, and comprehension is substantially impaired.

B. Speech is sparse and effortful while comprehension remains relatively preserved, reflecting a frontal expressive-language lesion.

C. Only writing is affected because spoken language comprehension and production bypass posterior temporal cortex entirely.

D. Speech is normal but voluntary eye movements cannot be initiated because Wernicke area is the frontal eye field.

E. Comprehension is preserved and repetition is enhanced because posterior temporal lesions increase auditory working memory.

275. A patient has syndrome of inappropriate antidiuretic hormone secretion. Which renal effect is central to the resulting hyponatremia?

A. Persistent vasopressin causes massive renal sodium secretion without any change in water permeability.

B. Vasopressin prevents water reabsorption, causing free-water loss and dilutional hyponatremia.

C. SIADH raises plasma sodium because aquaporin-2 removes water from the circulation into urine.

D. The syndrome is caused by aldosterone excess, which retains sodium but not water and therefore lowers sodium concentration.

E. Persistent collecting-duct water reabsorption retains water out of proportion to sodium and lowers plasma osmolality.

276. A patient with lymphatic obstruction develops chronic limb edema. Why does the edema become protein rich?

A. Capillary endothelium becomes completely impermeable to protein, so plasma proteins accumulate outside vessels by osmosis alone.

B. Lymphatic obstruction increases renal albumin synthesis, and the excess albumin is secreted directly into the affected limb.

C. Venous valves pump plasma proteins across capillary walls when lymph flow stops, producing selective tissue protein accumulation.

D. Proteins that normally enter interstitial fluid cannot be returned efficiently to the circulation through lymphatic drainage.

E. Blocked lymphatics convert interstitial sodium into protein through fibroblast metabolism, raising local oncotic pressure.

277. A healthy person has an increase in mean arterial pressure within the autoregulatory range of many tissues. How can local blood flow remain relatively stable?

A. Resistance arterioles dilate in proportion to pressure so that flow remains unchanged despite a larger pressure gradient.

B. Resistance arterioles constrict in response to increased transmural pressure, offsetting the higher perfusion pressure.

C. Veins constrict until arterial inflow stops completely, and then reopen when pressure returns to baseline.

D. Capillary hydrostatic pressure falls to zero because autoregulation occurs by closing all precapillary sphincters simultaneously.

E. Blood viscosity instantly doubles whenever arterial pressure rises, providing the only mechanism of autoregulation.

278. A clinician must deliver unexpected bad news. Which communication sequence is most appropriate?

A. Give all technical details rapidly at the start so the patient receives the entire message before becoming emotional.

B. Begin with reassurance that everything will be fine, even when the prognosis is uncertain or poor.

C. Avoid pauses after giving the diagnosis because silence may encourage emotional reactions.

D. Arrange privacy, assess what the patient understands and wants to know, give information clearly in small portions, respond to emotion, and discuss next steps.

E. Discuss treatment logistics only and avoid acknowledging emotion because empathy can reduce objectivity.

279. A healthy person has an acute increase in plasma protein concentration. What happens to glomerular filtration if all other variables are initially unchanged?

A. Higher plasma oncotic pressure increases filtration by pulling water from Bowman space into glomerular capillaries and then through the filter.

B. GFR rises because plasma proteins cross the filtration barrier and create a strong oncotic force within Bowman space.

C. Higher glomerular capillary oncotic pressure opposes filtration and tends to decrease GFR.

D. GFR remains unchanged because oncotic pressure has no role in the glomerular Starling forces.

E. Filtration becomes independent of capillary pressure because concentrated plasma closes podocyte slit diaphragms.

280. A patient has a lesion of the right parietal association cortex and ignores the left side of space. Which principle best explains the severity of this neglect?

A. The left hemisphere attends equally to both sides, so right-sided lesions are compensated more completely than left-sided lesions.

B. Each parietal lobe attends only to the ipsilateral side, so a right lesion should produce isolated right-sided neglect.

C. Neglect is caused by primary visual loss because parietal association cortex is the only source of retinal input to the occipital lobe.

D. The right hemisphere attends to both sides of extrapersonal space, whereas the left hemisphere attends predominantly to the right.

E. The right parietal lobe controls language only, so spatial neglect reflects secondary aphasia rather than attention dysfunction.

Answers

1. B. Active tissues generate carbon dioxide, hydrogen ions, and heat, producing a local rightward shift of the oxygen dissociation curve through the Bohr effect. Acute systemic alkalosis tends to shift the curve left, not right. Increased 2,3-BPG develops over days and also favors unloading but is not the immediate mechanism described.

2. B. Pituitary gonadotrophs require pulsatile GnRH stimulation to sustain LH and FSH secretion. Continuous exposure causes receptor desensitization and downregulation after an initial stimulatory phase, suppressing the axis. This principle is used therapeutically with long-acting GnRH agonists.

3. C. Quiet inspiration is an active process. Diaphragmatic and external intercostal contraction expands the thorax, makes intrapleural pressure more negative, and lowers alveolar pressure slightly below atmospheric pressure so air flows inward. Quiet expiration is largely passive elastic recoil.

4. E. A saline bolus increases intravascular volume and venous return, raising end-diastolic volume. Greater sarcomere stretch within the physiologic range increases force generation and stroke volume through Frank-Starling behavior. This is a preload effect and does not require a primary increase in contractility.

5. A. Sensitivity is the true-positive fraction among people who have the disease: TP/(TP + FN). Here, 90/(90 + 10) = 0.90, or 90%. Specificity instead describes true negatives among people without disease.

6. C. Emphysema destroys elastic parenchymal support, increasing compliance but reducing recoil. During forced expiration, lower recoil and reduced radial traction favor dynamic airway compression, causing air trapping and increased residual volume. Compliance and recoil are inversely related properties rather than synonyms.

7. C. Unlike most anterior pituitary hormones, prolactin is under dominant tonic inhibition by hypothalamic dopamine. Stalk disruption reduces dopamine delivery and can therefore increase prolactin, while other pituitary hormones tend to fall because their releasing hormones are lost. Growth hormone is regulated by both GHRH stimulation and somatostatin inhibition.

8. B. The cephalic phase is driven largely by vagal activity triggered by sight, smell, taste, and thought of food. Vagal signaling stimulates parietal cells and promotes gastrin and histamine release, amplifying acid secretion. Sympathetic input generally inhibits gastrointestinal activity rather than serving as the main cephalic stimulant.

9. A. Surfactant reduces surface tension at the air-liquid interface and is especially important for stabilizing small alveoli. Deficiency increases collapsing pressure, lowers compliance, and promotes atelectasis. The Laplace relationship explains why a small radius combined with high surface tension is particularly unstable.

10. B. Diarrhea causes loss of bicarbonate and therefore a metabolic acidosis. Winter formula predicts an expected PCO2 of about $1.5 \times 15 + 8 = 30.5 \pm 2$ mm Hg, so the measured PCO2 of 31 mm Hg represents appropriate respiratory compensation rather than a second primary disorder.

11. D. Decision-making capacity does not require agreement with the clinician. A capable adult may refuse even beneficial or life-saving treatment after an informed discussion. The clinician should ensure understanding, address reversible barriers, document the decision, and continue appropriate care.

12. C. High prolactin can suppress the reproductive axis by reducing pulsatile GnRH secretion, leading to lower LH and FSH and anovulation. This contributes to lactational amenorrhea, although it is not a reliable contraceptive outside specific conditions. Prolactin also supports milk production in the breast.

13. C. When a patient lacks capacity, an authorized surrogate should generally apply substituted judgment based on the patient's values and prior expressed wishes. If those are unknown, decisions should be based on the patient's best interests rather than the surrogate's personal preferences.

14. B. Using the common formula, anion gap = $Na - (Cl + HCO3-) = 138 - (101 + 10) = 27$ mEq/L. Ketoacids contribute unmeasured anions, producing a high-anion-gap metabolic acidosis.

15. E. PaO2 reflects oxygen dissolved in plasma and can be normal in anemia when pulmonary gas exchange is intact. Total arterial oxygen content is reduced because most oxygen is carried on hemoglobin. Oxygen saturation can also remain normal because it describes the fraction of available heme sites occupied, not the number of heme sites present.

16. C. Alveolar ventilation equals the volume of fresh gas reaching gas-exchanging regions per breath times respiratory rate. Here, (500 - 150) x 12 = 4200 mL/min, or 4.2 L/min. Minute ventilation would be 6.0 L/min, but that includes dead-space ventilation.

17. A. Renal peritubular interstitial cells sense reduced oxygen availability through hypoxia-inducible factor pathways and increase erythropoietin secretion. Erythropoietin stimulates erythroid progenitors in bone marrow. Juxtaglomerular cells primarily secrete renin rather than erythropoietin.

18. A. Specificity is TN/(TN + FP). With 180 true negatives among 200 people without disease, specificity is 180/200 = 90%. It does not require disease prevalence for its calculation.

19. D. Thyroid hormone normally exerts negative feedback on both pituitary TSH and hypothalamic TRH. Primary thyroid failure lowers circulating free T4/T3, removing feedback and raising TSH when the pituitary is functional. Central hypothyroidism instead has an inappropriately low or normal TSH.

20. B. Resting membrane potential is dominated by potassium permeability, and the potassium equilibrium potential is more negative than the usual resting voltage. Increasing potassium conductance therefore hyperpolarizes the cell toward EK. The sodium-potassium ATPase maintains ion gradients but is not the sole determinant of instantaneous membrane voltage.

21. D. Inflammatory cytokines, especially IL-6, increase hepatic hepcidin. Hepcidin causes internalization and degradation of ferroportin, reducing iron transfer from enterocytes and macrophages into plasma. This produces low serum iron despite preserved or increased storage iron.

22. B. In skeletal muscle, transverse-tubule depolarization activates dihydropyridine receptors that are mechanically coupled to ryanodine receptors on the sarcoplasmic reticulum. Ryanodine receptors then release calcium into the cytosol. SERCA performs the opposite task by pumping calcium back into the sarcoplasmic reticulum during relaxation.

23. A. Each breath must first fill the conducting-airway dead space. With rapid shallow breathing, a greater proportion of the same minute ventilation is devoted to dead space and less reaches alveoli. Thus identical minute ventilation can produce very different effective alveolar ventilation.

24. A. Complete airway obstruction eliminates fresh ventilation to that region while blood flow may continue, so V/Q approaches zero. Hypoxic pulmonary vasoconstriction can reduce perfusion and partially limit mismatch but usually does not make flow exactly zero. This is shunt-like physiology.

25. C. Opening of voltage-gated sodium channels generates the rapid inward current responsible for the action-potential upstroke. Blocking those channels prevents normal propagation in excitable membranes. Repolarization and after-hyperpolarization depend mainly on potassium conductances rather than sodium entry.

26. D. Parietal-cell acid secretion depends on the apical H/K-ATPase, which exchanges H+ for K+. Chloride exits through apical channels and combines with hydrogen in the lumen, while basolateral chloride-bicarbonate exchange produces the postprandial alkaline tide. Proton-pump inhibitors target the H/K-ATPase.

27. E. When a patient lacks capacity, delay would threaten life or serious health, and no surrogate is available, clinicians may provide treatment reasonably necessary to address the emergency. The presumption is that a reasonable person would consent to urgent life-preserving care.

28. D. Calcium binding to troponin C changes the troponin complex and shifts tropomyosin away from actin sites that interact with myosin. This allows cross-bridge formation and force generation. Calcium does not activate contraction by binding directly to the myosin head in skeletal muscle.

29. B. A sudden rise in afterload makes ventricular ejection more difficult, so less blood is ejected and end-systolic volume increases. Stroke volume and ejection fraction therefore fall on that beat. Subsequent compensatory changes in preload or contractility can modify the response, but the immediate mechanical effect is reduced emptying.

30. C. Salicylates can stimulate medullary respiratory centers, causing respiratory alkalosis, while also generating organic acids and impairing metabolism, causing metabolic acidosis. The combination of a markedly low PCO2 and low bicarbonate with near-normal or alkalemic pH is characteristic of a mixed disorder.

31. A. In primary hyperthyroidism, elevated thyroid hormone suppresses TSH. A TSH-secreting pituitary tumor produces thyroid hormone excess with TSH that is not appropriately suppressed and may be elevated. The key is loss of normal negative-feedback behavior.

32. E. Histamine from enterochromaffin-like cells acts on parietal-cell H2 receptors through Gs-cAMP signaling. Gastrin and vagal acetylcholine also stimulate acid secretion through complementary pathways. Somatostatin is inhibitory, whereas secretin generally reduces gastric acid and promotes pancreatic bicarbonate.

33. B. Gravity creates a vertical hydrostatic gradient in the pulmonary circulation. Vascular pressures are higher in dependent regions, so more vessels are open and distended at the bases. Ventilation also increases toward the bases, but perfusion increases even more, producing lower V/Q ratios there.

34. E. Increased contractility raises the slope of the end-systolic pressure-volume relation and allows the ventricle to eject to a lower end-systolic volume at a given loading condition. Stroke volume and ejection fraction rise. Diastolic compliance is described by a different relation and is not the primary change.

35. A. Patients should be informed about errors that affect their care. Disclosure should be timely, factual, and compassionate, including what is known, the clinical implications, and the plan to reduce further harm. Institutional safety reporting supports systems improvement.

36. D. The fraction of oxygen in ambient air remains essentially constant, but total barometric pressure decreases with altitude. Therefore inspired PO2 and alveolar PO2 fall. Hypoxic ventilatory stimulation subsequently lowers PaCO2, partially raising alveolar PO2 relative to what it would otherwise be.

37. E. Duodenal S cells respond to acid by releasing secretin. Secretin promotes bicarbonate-rich secretion from pancreatic and biliary ductal epithelium, helping neutralize gastric acid and optimize intestinal enzyme function. Cholecystokinin is more closely associated with pancreatic enzyme secretion and gallbladder contraction.

38. C. Reduced ventricular compliance means the chamber is stiffer, so more pressure is required to achieve a given diastolic volume. The end-diastolic pressure-volume relation shifts upward and becomes steeper. This can raise filling pressures even when ejection fraction is preserved.

39. B. The TSH receptor is primarily Gs coupled, increasing cAMP and stimulating thyroid growth, iodide handling, thyroglobulin processing, and hormone release. Other signaling can contribute, but cAMP is the classic dominant pathway. Thyroid hormone itself acts mainly through intracellular nuclear receptors.

40. D. Acute hemorrhage removes whole blood, so plasma and red-cell volume are initially lost in roughly the same proportion. Hematocrit therefore may not fall immediately. It decreases later as interstitial fluid enters the vascular space and as crystalloid resuscitation dilutes the remaining red cells.

41. B. At steady carbon dioxide production, $PaCO_2$ varies approximately inversely with alveolar ventilation. Hypoventilation therefore causes hypercapnia, whereas hyperventilation lowers $PaCO_2$. This relationship is fundamental to ventilatory control and acid-base physiology.

42. C. CCK is released from duodenal and jejunal I cells in response to fats and amino acids. It stimulates pancreatic acinar enzyme secretion, contracts the gallbladder, and helps relax the sphincter of Oddi while slowing gastric emptying. Secretin primarily promotes bicarbonate-rich ductal secretion.

43. E. Early distributive septic shock is characterized by systemic vasodilation and low systemic vascular resistance. Cardiac output may be high because of sympathetic stimulation and reduced afterload, producing warm skin and bounding pulses despite impaired effective tissue perfusion.

44. A. During the absolute refractory period, many voltage-gated sodium channels are inactivated and cannot return to the closed, activatable state until repolarization occurs. Therefore, even a very strong stimulus cannot trigger another full action potential. The relative refractory period follows when some channels have recovered but potassium conductance remains elevated.

45. D. Acetylcholinesterase normally terminates signaling by rapidly hydrolyzing acetylcholine in the synaptic cleft. Inhibition increases acetylcholine concentration and duration of receptor activation. Excessive exposure can eventually produce depolarization block, but the immediate effect is prolonged cholinergic signaling.

46. C. Peripheral chemoreceptors in the carotid and aortic bodies respond to low PaO_2, with carotid bodies providing the dominant ventilatory signal in humans. Their response becomes especially strong as PaO_2 falls below roughly 60 mm Hg. Central chemoreceptors primarily respond to carbon dioxide-related pH changes rather than oxygen directly.

47. A. Standing shifts blood toward dependent veins, transiently reducing central blood volume, preload, and stroke volume. Arterial pressure can fall until baroreflex-mediated sympathetic activation raises heart rate, contractility, venous tone, and arteriolar resistance. The initial event is therefore reduced venous return.

48. E. Active muscle releases vasodilating metabolites such as adenosine, potassium, carbon dioxide, hydrogen ions, and others. Local metabolic control can blunt sympathetic vasoconstriction and greatly increase flow, while oxygen extraction also rises. This matching of perfusion to metabolism is a central feature of exercise physiology.

49. A. The migrating motor complex is a cyclic interdigestive motility pattern that sweeps through the stomach and small intestine during fasting. Motilin is associated with this activity. Feeding interrupts the pattern and replaces it with postprandial mixing and propulsive contractions.

50. B. Predictive values depend on pretest probability or prevalence. As disease becomes more common, a positive result is more likely to be a true positive and PPV rises; NPV generally falls. Sensitivity and specificity can remain unchanged when test performance itself is stable.

51. C. Near misses reveal system vulnerabilities before injury occurs. Reporting them supports analysis of order design, workflow, communication, and verification. A just-culture approach seeks to reduce recurrence rather than conceal the event.

52. B. DLCO reflects gas transfer across the alveolar-capillary interface and is reduced by conditions that thicken the membrane or reduce surface area, including fibrosis and emphysema. The measurement is also influenced by pulmonary capillary blood volume and hemoglobin concentration. A thick barrier therefore lowers diffusion capacity rather than raising it.

53. C. DNR addresses whether CPR should be attempted in cardiopulmonary arrest. Other treatments depend on the patient's goals and preferences and can include antibiotics, hospitalization, rehabilitation, or other interventions. Orders should be interpreted according to their actual scope.

54. A. Sustained isometric exercise raises sympathetic outflow and can compress vessels within contracting muscle. Heart rate, cardiac output, and systemic vascular resistance increase, causing substantial rises in systolic and diastolic pressure. This differs from the larger fall in peripheral resistance typical of dynamic exercise.

55. C. With lung expansion, pulmonary vascular resistance falls and pulmonary blood flow increases, raising left atrial pressure. At the same time, removal of the placenta reduces venous return to the right atrium. The resulting left-to-right atrial pressure gradient apposes the septum primum to the septum secundum and functionally closes the foramen ovale.

56. E. ATP binding reduces myosin affinity for actin and causes detachment. Hydrolysis to ADP and phosphate then energizes the myosin head, and release of phosphate after actin rebinding is linked to the power stroke. Without ATP, cross-bridges remain attached, as occurs in rigor mortis.

57. B. Depolarization of the nerve terminal opens voltage-gated calcium channels. The resulting calcium influx binds synaptic proteins and triggers vesicle fusion and acetylcholine exocytosis. Postsynaptic nicotinic receptor activation occurs after transmitter release, not before it.

58. E. Normal erythrocytes are highly deformable because their biconcave shape provides excess membrane surface area relative to cell volume and because the membrane skeleton is flexible. Spherocytes lose membrane surface area, become less deformable, and are trapped in the spleen. Mature erythrocytes lack nuclei and do not crawl by actin-based motility.

59. A. The peristaltic reflex involves ascending excitation behind a bolus and descending inhibition ahead of it. This coordinated pattern propels luminal contents forward. The enteric nervous system can generate much of this reflex intrinsically, although extrinsic autonomic input modulates it.

60. E. The sodium-iodide symporter on the basolateral membrane uses the inward sodium gradient to concentrate iodide within follicular cells. Iodide then moves apically toward the colloid, with pendrin contributing to apical transport. Thyroid peroxidase oxidizes and organifies iodide at the apical-colloid interface.

61. A. Risk among exposed participants is 30/300 = 0.10. Risk among unexposed participants is 10/500 = 0.02. Relative risk = 0.10/0.02 = 5.

62. E. The proximal stomach accommodates a meal through receptive relaxation and adaptive relaxation, mediated importantly by vagovagal and enteric pathways including inhibitory transmitters such as nitric oxide. This allows volume to increase with relatively small pressure change. Failure of accommodation can cause early satiety.

63. B. Pump failure lowers cardiac output. Reflex sympathetic vasoconstriction raises systemic vascular resistance, and blood backs up behind the failing ventricle, increasing filling pressures and often causing pulmonary edema when the left ventricle is involved.

64. E. Peripheral deiodinases regulate conversion of T4 to active T3 or inactive reverse T3. Outer-ring deiodination can generate T3, while other deiodination pathways inactivate thyroid hormone. Thyroid peroxidase acts within the thyroid gland rather than serving as the main peripheral converter.

65. B. DLCO depends partly on uptake of carbon monoxide by hemoglobin. Lower hemoglobin concentration reduces the blood's capacity to take up CO and can lower the measured value, which is why correction for hemoglobin is often considered. The alveolar membrane may be structurally normal in isolated anemia.

66. B. A large pulmonary embolus acutely raises pulmonary vascular resistance and right ventricular afterload. Right ventricular dilation and failure reduce forward flow through the lungs, lowering left ventricular filling and cardiac output. This is obstructive shock.

67. A. Sympathetic constriction of capacitance veins mobilizes blood toward the central circulation and raises mean systemic filling pressure, helping sustain venous return during volume loss. Arteriolar constriction supports arterial pressure but can also affect flow distribution. Venodilation would increase peripheral storage rather than central filling.

68. D. Nicotinic receptor activation produces a local end-plate depolarization that must bring adjacent muscle membrane to threshold. Competitive antagonism reduces this depolarization and can prevent a propagated muscle action potential. The motor axon can still conduct normally because its voltage-gated channels are upstream of the blocked receptor.

69. C. Carotid sinus baroreceptors are stretch-sensitive. Reduced arterial pressure decreases their firing to the medulla, which increases sympathetic and reduces parasympathetic output. The resulting tachycardia, increased contractility, arteriolar constriction, and venoconstriction help restore pressure.

70. A. Standing transiently reduces venous return and arterial pressure, decreasing stretch and firing of high-pressure baroreceptors. The medullary response is increased sympathetic and reduced parasympathetic output, raising heart rate, contractility, and vascular tone. Autonomic failure blunts these compensatory changes and produces orthostatic hypotension.

71. C. Clinicians should relieve pain and other distress with proportionate therapy. The ethical intention is symptom relief, not causing death, and medications should be titrated to clinical need. Fear of an unintended secondary effect does not justify undertreating severe symptoms.

72. D. Afferent arteriolar dilation increases renal blood flow and raises glomerular capillary hydrostatic pressure, favoring filtration. In contrast, afferent constriction tends to lower both renal blood flow and GFR. Net filtration is opposed by Bowman space hydrostatic pressure and glomerular capillary oncotic pressure.

73. E. ATP is required for myosin to detach from actin. After death, ATP production stops and calcium leaks from intracellular stores, allowing cross-bridges to form but not release. The resulting persistent actin-myosin attachment produces rigor until proteins begin to degrade.

74. D. In a concentric contraction, active muscle shortens while generating force against a load. Eccentric contraction describes active lengthening, and isometric contraction develops tension with little or no change in muscle length. All active forms require cross-bridge cycling.

75. E. Competent adults generally control disclosure of their health information. Clinicians may listen to family concerns without revealing protected information and can encourage communication, but should respect the patient's stated confidentiality preferences absent a specific exception.

76. D. At higher stimulation frequencies, calcium released by one action potential is not fully resequestered before the next release. Cytosolic calcium therefore accumulates and more cross-bridges cycle simultaneously, producing summation and eventually tetanus. Individual action potentials themselves remain all-or-none.

77. E. In a case-control study, participants are sampled according to outcome status, so population disease incidence cannot usually be calculated directly. The odds of prior exposure in cases and controls are compared using an odds ratio, which can approximate relative risk when disease is rare.

78. B. Thyroid hormone increases metabolic demand and enhances catecholamine responsiveness, increasing heart rate and contractility. Peripheral vasodilation supports heat dissipation and lowers systemic vascular resistance, while increased stroke volume and systolic pressure can widen pulse pressure. These changes help deliver oxygen to tissues with increased metabolism.

79. E. Cardiac beta-1 receptors are Gs coupled and increase cAMP, enhancing pacemaker currents and calcium handling. Blocking them reduces chronotropy and inotropy during sympathetic activation. Alpha-1 receptors use Gq signaling and are not the principal mechanism of this direct cardiac response.

80. C. SGLT1 uses the sodium gradient established by the basolateral Na/K-ATPase to cotransport glucose and galactose into enterocytes. Glucose then exits basolaterally mainly through GLUT2. Fructose uses a different facilitated-diffusion pathway, primarily GLUT5 apically.

81. C. The adrenal cortex is functionally organized into zona glomerulosa for mineralocorticoids, fasciculata for glucocorticoids, and reticularis for adrenal androgens. ACTH is a major regulator of cortisol synthesis in the fasciculata. Aldosterone is governed mainly by angiotensin II and potassium.

82. E. Carbon monoxide occupies heme with very high affinity, reducing the number of sites available for oxygen and lowering oxygen content. It also increases the oxygen affinity of remaining sites, shifting the curve left and impairing tissue unloading. PaO2 can remain normal because dissolved oxygen is not directly reduced by hemoglobin binding.

83. C. The size principle describes orderly recruitment from smaller, lower-threshold motor neurons to progressively larger, higher-threshold units as force demand rises. This strategy supports fine control and fatigue resistance at low forces while reserving powerful fast units for greater demands. Force also increases through rate coding within active units.

84. A. Type I fibers are slow oxidative fibers with many mitochondria, rich capillary supply, and abundant myoglobin. They generate lower peak power than fast fibers but resist fatigue and are well suited to prolonged endurance activity. Fast glycolytic fibers have higher shortening velocity and fatigue more rapidly.

85. A. Moderate efferent constriction raises pressure within glomerular capillaries and can preserve or increase GFR while reducing renal plasma flow, thereby increasing filtration fraction. Severe constriction can eventually lower GFR because renal flow falls substantially and glomerular oncotic pressure rises. The effect therefore depends on degree.

86. B. 2,3-BPG binds preferentially to deoxygenated hemoglobin and stabilizes the tense state, shifting the oxygen dissociation curve to the right. This promotes oxygen unloading at a given tissue PO2. It does not oxidize heme iron or directly lower alveolar or arterial PO2.

87. B. Glucocorticoids exert negative feedback on both hypothalamic CRH and pituitary ACTH. Prolonged exogenous exposure suppresses ACTH and can cause adrenal cortical atrophy, making abrupt withdrawal dangerous. Recovery of the hypothalamic-pituitary-adrenal axis can take time.

88. D. Albumin is the major contributor to plasma colloid oncotic pressure. When albumin falls, the inward oncotic force opposing filtration is reduced, favoring movement of fluid into the interstitium. Sodium retention and altered portal hemodynamics can further worsen edema in liver disease.

89. A. Arterial baroreceptors are especially important for rapid buffering of acute pressure changes. Longer-term pressure is strongly influenced by renal-body fluid mechanisms, so average pressure can recover toward normal after baroreceptor loss while variability increases. Baroreceptors are therefore not the sole long-term pressure controller.

90. E. Clearance describes the virtual volume of plasma from which a substance is completely removed into urine per unit time. If a freely filtered solute is completely reabsorbed and not secreted, urinary excretion is zero and so is its clearance. Glucose under normal plasma concentrations is an approximate example.

91. C. Fast glycolytic fibers have rapid cross-bridge cycling, large glycolytic capacity, and high power output, but limited fatigue resistance compared with type I fibers. They are commonly associated with larger high-threshold motor units. Their mitochondrial and myoglobin content is generally lower than that of slow oxidative fibers.

92. E. Primary adrenal insufficiency reduces adrenal cortisol output, removing negative feedback and raising ACTH. If the zona glomerulosa is affected, aldosterone can also fall, causing salt wasting and hyperkalemia. Secondary adrenal insufficiency instead has low or inappropriately normal ACTH and usually relatively preserved aldosterone.

93. D. Vagal acetylcholine activates M2 receptors in the sinoatrial node, lowering cAMP and increasing potassium conductance, which slows phase 4 depolarization. Atropine blocks this influence, allowing heart rate to rise. The relevant receptor is muscarinic M2, not a skeletal nicotinic receptor.

94. A. Inflammatory mediators released after major burns increase microvascular permeability. Plasma proteins escape into the interstitium, raising interstitial oncotic pressure while intravascular oncotic pressure falls, so water follows into tissues and effective circulating volume declines.

95. E. Factor VII is vitamin K dependent and has a short half-life, so inhibition of new functional factor synthesis is reflected early in the extrinsic-pathway PT/INR. The aPTT can also be affected at greater anticoagulant intensity but is not the primary monitoring test. Warfarin does not directly inhibit platelets or thrombin enzymatic activity.

96. B. Lead-time bias occurs when screening advances the date of diagnosis without changing the date of death. Survival measured from diagnosis therefore appears longer even though the patient does not live longer.

97. A. The zona glomerulosa produces aldosterone and responds strongly to angiotensin II and plasma potassium. ACTH can transiently influence aldosterone but is not the dominant regulator. The fasciculata and reticularis produce cortisol and adrenal androgens, respectively.

98. D. Effective communication includes eliciting the patient's goals, fears, and practical constraints. Acknowledging the concern and clarifying likely recovery, supports, and alternatives allows shared decision-making without coercion.

99. E. The phosphagen system uses intramuscular ATP and phosphocreatine to regenerate ATP at very high rates for the first seconds of intense work. Anaerobic glycolysis then becomes increasingly important, followed by oxidative metabolism as duration increases. Fat oxidation is too slow to dominate the immediate high-power phase.

100. C. Muscle spindles lie in parallel with extrafusal fibers and sense muscle length and velocity of stretch. Ia afferents monosynaptically excite alpha motor neurons supplying the stretched muscle, producing the stretch reflex. Golgi tendon organs lie in series and respond mainly to tension.

101. A. Fast, sharp, well-localized pain is carried mainly by thin myelinated A-delta fibers. Slower burning or aching pain is transmitted predominantly by unmyelinated C fibers. Large A-beta fibers carry touch and pressure and can modulate pain transmission but are not the usual first-pain afferents.

102. A. Golgi tendon organs are located at the musculotendinous junction and are arranged in series with muscle fibers, making them sensitive to force or tension. Their Ib afferents participate in spinal reflex circuits that can inhibit the same muscle under high force. Muscle spindles instead monitor length and stretch velocity.

103. B. Fructose is absorbed across the apical membrane mainly through GLUT5 by facilitated diffusion. Glucose and galactose use sodium-coupled SGLT1. Basolateral GLUT2 then allows monosaccharides to leave enterocytes toward portal blood.

104. D. Pancreatic lipase is central to fat digestion, so pancreatic insufficiency commonly produces steatorrhea and fat-soluble vitamin deficiency. Protein and carbohydrate digestion are also impaired but have additional gastric and brush-border contributions. Bile acids are synthesized in the liver, and intrinsic factor is produced by gastric parietal cells.

105. B. Cortisol is a steroid hormone and diffuses across cell membranes. It binds an intracellular receptor, and the hormone-receptor complex regulates transcription through glucocorticoid response elements and interactions with other transcription factors. Genomic effects therefore develop more slowly than typical membrane second-messenger signals.

106. D. Aspirin irreversibly acetylates platelet cyclooxygenase-1, reducing thromboxane A2 formation. Because platelets lack nuclei, they cannot synthesize new cyclooxygenase, so the effect persists for the platelet life span. Aspirin does not directly eliminate GPIb, P2Y12, or circulating platelets.

107. A. Pain and temperature afferents synapse in the dorsal horn and second-order neurons cross through the anterior white commissure, usually within a few segments. A left hemicord lesion therefore interrupts already-crossed spinothalamic fibers from the right side below the lesion. This contrasts with dorsal-column modalities, which remain ipsilateral in the cord.

108. E. With increasing heart rate, diastolic duration decreases disproportionately. Very rapid rates can therefore impair ventricular filling and reduce time for left coronary perfusion, which occurs predominantly during diastole. Systole shortens less dramatically.

109. A. Activated GPIIb/IIIa binds fibrinogen, which bridges adjacent platelets and produces aggregation. Platelet adhesion to vWF is mediated chiefly by GPIb. The coagulation cascade and factor XIII function are distinct from this platelet receptor.

110. E. Most corticospinal fibers decussate at the pyramids in the caudal medulla. A cortical lesion therefore produces contralateral weakness, generally with upper motor neuron findings such as hyperreflexia and increased tone after the acute phase. Lower motor neuron signs point instead to anterior horn, root, plexus, or peripheral nerve injury.

111. C. Bile acids are amphipathic molecules that emulsify dietary fat and form mixed micelles containing fatty acids, monoglycerides, cholesterol, and fat-soluble vitamins. Micelles deliver these lipids to the brush border for absorption. Bile acids are then efficiently reabsorbed, mainly in the terminal ileum, and recycled enterohepatically.

112. C. Slowly progressive disease spends more time in a preclinical detectable phase, so periodic screening is more likely to identify it. This length-time bias can make screened cases appear to have better outcomes even without a treatment benefit.

113. B. Denervation leads to upregulation and spread of nicotinic acetylcholine receptors beyond the normal end-plate region. This creates increased sensitivity to agonists and contributes to characteristic responses to some neuromuscular drugs. The muscle membrane retains voltage-gated channels and can still respond to direct stimulation early on.

114. A. In fever, pyrogen-driven prostaglandin E2 raises the hypothalamic temperature set point. Until body temperature rises to that new target, the body responds as if it were cold by vasoconstricting and shivering. When the set point later falls, vasodilation and sweating promote heat loss.

115. A. Most coagulation factors are synthesized in the liver, including factors II, VII, IX, and X. Factor VIII is produced substantially by endothelial cells and may remain normal or even increase in liver disease. This distinction helps explain why liver failure creates complex hemostatic changes rather than a simple deficiency of every factor.

116. D. Good prognostic communication begins by assessing understanding and information preferences. Clinicians should be clear but acknowledge uncertainty, often using ranges or best-case/worst-case/most-likely scenarios, and then connect the information to goals and decisions.

117. E. Myasthenia gravis reduces the number or function of postsynaptic acetylcholine receptors or associated proteins, decreasing the end-plate potential and safety margin. With repeated activation, modest physiologic decline in acetylcholine release can make transmission fail at more junctions, producing fatigability. The primary defect is postsynaptic rather than demyelinating or contractile-protein disease.

118. C. The Fick principle states that uptake of a substance by an organ equals blood flow multiplied by the arterial-venous concentration difference. Applied to the entire body, VO_2 = cardiac output × (arterial O_2 content − mixed venous O_2 content).

119. A. Gamma chains in fetal hemoglobin bind 2,3-BPG less avidly than beta chains in adult hemoglobin. This shifts the fetal oxygen dissociation curve to the left and allows fetal blood to extract oxygen from maternal blood across the placenta. The advantage is affinity, not a greater number of heme groups.

120. D. Type I error is a false-positive inferential conclusion: rejecting a true null hypothesis. Its probability is controlled by alpha. Type II error is failing to reject a false null hypothesis, and power equals 1 − beta.

121. E. Dynamic exercise increases sympathetic drive, heart rate, contractility, venous return, and cardiac output. Local metabolites dilate arterioles in active skeletal muscle, so total systemic vascular resistance often falls despite vasoconstriction in nonessential beds. Systolic pressure rises while diastolic pressure changes little or may fall slightly.

122. B. SERCA uses ATP to pump cytosolic calcium back into the sarcoplasmic reticulum. Reduced activity prolongs cytosolic calcium elevation and therefore delays dissociation of calcium from troponin and muscle relaxation. SERCA does not mediate action-potential propagation or acetylcholine breakdown.

123. B. The insulin receptor is a transmembrane receptor tyrosine kinase. Ligand binding activates intrinsic kinase activity, leading to phosphorylation of insulin receptor substrates and downstream pathways controlling glucose uptake, metabolism, growth, and gene expression. It is not a GPCR.

124. C. A substance such as para-aminohippurate at low concentrations is filtered and avidly secreted, allowing most of the amount entering the kidney in plasma to be excreted. Its clearance therefore approximates effective renal plasma flow. Renal blood flow can then be estimated by accounting for hematocrit.

125. E. Glucose is freely filtered and normally reabsorbed in the proximal tubule. As plasma concentration rises, filtered load increases until transporters approach their maximal reabsorptive capacity; nephron heterogeneity creates the characteristic splay before the overall transport maximum. Excess filtered glucose remains in tubular fluid and is excreted.

126. B. Insulin signaling causes intracellular GLUT4-containing vesicles to translocate to the surface of skeletal muscle and adipose cells, increasing facilitated glucose uptake. Exercise can also increase muscle GLUT4 translocation through insulin-independent signaling. Hepatocytes and pancreatic beta cells use different glucose transporters.

127. E. Factor XII participates in contact activation measured by the intrinsic-pathway aPTT, so deficiency can markedly prolong aPTT. Paradoxically, factor XII deficiency generally does not cause a bleeding tendency in vivo. It is therefore an important example of a laboratory abnormality that does not predict clinical hemorrhage.

128. A. Power rises with larger sample size, larger true effect size, lower variability, and—other things equal—a less stringent significance threshold. A larger sample reduces the standard error and makes a true difference easier to distinguish from sampling noise.

129. E. Long-chain fatty acids are reassembled into triglycerides and packaged with apolipoproteins into chylomicrons. Chylomicrons are too large for ordinary intestinal capillaries and enter lacteals, traveling through lymph to the thoracic duct and systemic venous circulation. Short- and medium-chain fatty acids can enter portal blood more directly.

130. A. Glucagon acts mainly on the liver to raise cAMP and promote glucose production through glycogenolysis and gluconeogenesis. It also favors fatty acid oxidation and ketogenesis during fasting. Insulin has opposing effects, promoting glycogen, lipid, and protein storage after feeding.

131. D. As exercise intensity increases, glycolytic flux can exceed the rate at which pyruvate enters and is oxidized by mitochondria. Regeneration of NAD+ through lactate dehydrogenase allows glycolysis to continue, and lactate production and appearance in blood rise.

132. D. Insulin promotes cellular potassium uptake by stimulating Na/K-ATPase, especially in skeletal muscle. In insulin deficiency, hyperosmolality, acidosis, and lack of this uptake can raise plasma potassium even when urinary losses have depleted total body stores. Insulin is therefore used acutely to shift potassium into cells in hyperkalemia.

133. B. Low inspired oxygen tension at altitude lowers arterial PO_2, stimulating carotid bodies and increasing ventilation. The resulting decrease in PCO_2 causes respiratory alkalosis. This alkalosis initially restrains further hyperventilation until renal compensation develops.

134. D. Newborns rely heavily on nonshivering thermogenesis in brown adipose tissue. Norepinephrine stimulates lipolysis and uncoupling protein 1, allowing the proton gradient to generate heat rather than ATP. Premature infants are vulnerable because brown-fat stores and thermal insulation are limited.

135. A. PTH raises serum calcium while lowering serum phosphate. It increases renal calcium reabsorption in distal nephron segments, decreases proximal phosphate reabsorption, and stimulates 1-alpha-hydroxylase to increase calcitriol. These actions complement its effects on bone.

136. A. The terminal ileum is the major site of active bile acid reclamation and absorption of vitamin B12 bound to intrinsic factor. Resection can therefore cause bile acid depletion, fat malabsorption, and B12 deficiency. Iron is absorbed mainly in the duodenum and proximal small bowel.

137. E. The kidney converts 25-hydroxyvitamin D to active 1,25-dihydroxyvitamin D through 1-alpha-hydroxylase, primarily in proximal tubular cells. PTH stimulates this enzyme, whereas high phosphate and FGF23 tend to suppress calcitriol production. Calcitriol then increases intestinal calcium and phosphate absorption.

138. E. Disseminated intravascular coagulation consumes platelets and clotting factors, including fibrinogen. Plasmin then degrades cross-linked fibrin, generating D-dimer. Thus low fibrinogen and elevated D-dimer fit simultaneous coagulation activation and secondary fibrinolysis.

139. D. Puberty reflects reactivation of pulsatile GnRH secretion, initially often during sleep and later throughout the day. Pulsatility is essential because continuous GnRH downregulates pituitary receptors. LH then stimulates Leydig cells and FSH supports Sertoli-cell function and spermatogenesis.

140. E. Endothelial selectins interact with leukocyte carbohydrate ligands to produce rolling. Chemokines activate leukocyte integrins, which bind endothelial ICAM-family molecules for firm adhesion, followed by diapedesis through endothelial junctions. Reversing selectins and integrins gives the wrong sequence and function.

141. A. The calcium-sensing receptor detects extracellular ionized calcium. High calcium activates the receptor and suppresses PTH secretion, whereas low calcium relieves this inhibition and stimulates PTH. This feedback loop helps stabilize extracellular calcium concentration.

142. A. Dopamine from the substantia nigra pars compacta normally promotes movement by stimulating D1 direct-pathway neurons and inhibiting D2 indirect-pathway neurons. Dopamine loss therefore increases inhibitory basal-ganglia output to the thalamus and reduces cortical motor drive. The core problem is circuit modulation, not neuromuscular transmission.

143. C. Intrinsic factor from parietal cells binds vitamin B12 after pancreatic enzymes free B12 from other binding proteins. The complex is absorbed in the terminal ileum through receptor-mediated uptake. Loss of intrinsic factor therefore causes B12 malabsorption and can lead to pernicious anemia.

144. D. Patient safety takes priority when a clinician appears impaired. The concern should be escalated through appropriate supervisory, institutional, or physician-health mechanisms rather than ignored, concealed, or publicized inappropriately.

145. A. Malignant hyperthermia commonly involves abnormal ryanodine receptor function, causing uncontrolled calcium release from the sarcoplasmic reticulum. Sustained contraction and ATP consumption then generate heat, carbon dioxide, acidosis, and muscle injury. Dantrolene reduces calcium release through this pathway.

146. E. The cerebellum compares intended and actual movement and helps coordinate timing, scaling, and error correction. Cerebellar hemispheric lesions commonly produce ipsilateral appendicular ataxia, dysmetria, and intention tremor because cerebellar pathways effectively influence the ipsilateral body. They do not directly produce primary weakness or loss of pain sensation.

147. E. Dietary iron absorption occurs mainly in the duodenum and proximal small intestine, with uptake regulated by body iron status and hepcidin-ferroportin signaling. Gastric acidity can help maintain soluble iron forms but is not the main absorptive site. Intrinsic factor is specific for vitamin B12 rather than iron.

148. B. Gastrin release is stimulated by peptides, amino acids, gastric distention, and vagal input mediated largely by gastrin-releasing peptide. Gastric acidity promotes somatostatin release, which inhibits gastrin as negative feedback. Gastrin then stimulates acid secretion directly and indirectly through histamine.

149. E. Financial and personal benefits from industry can create real or perceived conflicts between professional obligations and outside interests. Clinical decisions should be based on patient welfare and evidence, with conflicts avoided or managed transparently according to professional and institutional standards.

150. A. FSH promotes granulosa-cell proliferation and aromatase activity, allowing conversion of theca-derived androgens into estrogens. LH stimulates theca androgen production. Sustained high estradiol late in the follicular phase contributes to the LH surge that triggers ovulation.

151. D. Left ventricular contraction generates high intramural pressure that compresses coronary microvessels, particularly in the vulnerable subendocardium. When the ventricle relaxes in diastole, vessel compression falls while aortic pressure remains sufficient to drive flow. The coronary ostia remain open during systole; mechanical compression is the key factor.

152. B. Sustained hyperventilation causes respiratory alkalosis. Over days, the kidneys excrete bicarbonate, bringing pH closer to normal. Reduced alkalemic inhibition of ventilation permits continued hyperventilation and improves alveolar oxygen tension.

153. D. The proximal tubule performs bulk reabsorption of sodium, water, bicarbonate, glucose, amino acids, and other solutes. Water follows solute readily, so tubular fluid remains approximately iso-osmotic. Later segments provide more regulated fine-tuning of salt and water balance.

154. A. Most of the cycle is governed by negative feedback, but sustained high estradiol from the dominant follicle produces positive feedback on hypothalamic-pituitary signaling. The resulting LH surge triggers ovulation and luteinization. FSH also rises, but the LH surge is the dominant ovulatory signal.

155. A. In chronic granulomatous disease, phagocytes cannot generate a normal respiratory burst. Some organisms produce hydrogen peroxide that can partly support killing, but catalase-positive microbes

degrade their own hydrogen peroxide and remove that potential substrate. The vulnerability is therefore linked to oxidative killing rather than loss of opsonization or adhesion.

156. C. The ruptured follicle luteinizes to form the corpus luteum, which secretes progesterone and estrogen under LH support. Progesterone transforms the endometrium into a secretory state and raises basal body temperature. Without pregnancy, luteal regression causes progesterone to fall and menstruation to occur.

157. D. Deficiency of terminal complement components C5 through C9 impairs membrane attack complex formation and strongly predisposes to recurrent Neisseria infection. Complement-mediated lysis is especially important for these organisms. IgE, NK-cell cytotoxicity, and increased MHC II expression do not produce this characteristic susceptibility.

158. E. For a relative risk, the null value is 1.0. Because the 95% confidence interval crosses 1.0, the result does not meet the conventional two-sided 0.05 significance threshold. The point estimate may still be clinically interesting, but the estimate is imprecise.

159. E. Coronary flow is tightly coupled to myocardial metabolism. Adenosine and several other local signals promote vasodilation when oxygen use rises or supply falls. Sympathetic stimulation can increase coronary flow indirectly by increasing metabolism, but alpha-1 signaling itself is vasoconstrictive.

160. C. REM sleep has a low-amplitude, mixed-frequency EEG that resembles wakefulness, vivid dreaming, rapid eye movements, and skeletal-muscle atonia. Autonomic activity can be variable rather than absent. The largest slow-wave delta activity and much growth-hormone secretion are associated with N3 non-REM sleep.

161. D. Random assignment breaks the systematic link between participant characteristics and treatment allocation. With adequate sample size, it tends to balance both measured and unmeasured confounders, supporting causal inference. It does not guarantee perfect balance or prevent other sources of bias.

162. C. Prevalence describes existing disease at a point or over a period. Incidence describes new cases arising among people at risk over time. A one-date cross-sectional estimate is point prevalence.

163. E. C3b is a major opsonin; phagocytes recognize deposited C3b through complement receptors and ingest coated microbes more efficiently. C3a is an anaphylatoxin rather than a membrane pore. The membrane attack complex is formed by terminal complement components, not C3a alone.

164. A. Osteoclasts create a sealed resorption lacuna and use proton pumps to acidify it, dissolving hydroxyapatite. Proteases then degrade the exposed organic matrix. Osteoblasts, in contrast, synthesize osteoid and express alkaline phosphatase in support of mineralization.

165. E. Reduced renal oxygen delivery stabilizes hypoxia-inducible factors, increasing erythropoietin synthesis. Erythropoietin stimulates erythroid progenitors in bone marrow, increasing hemoglobin concentration and oxygen-carrying capacity over days to weeks.

166. B. Stage N2 is identified by sleep spindles and K complexes. N3 is characterized by prominent delta slow waves, whereas REM has rapid eye movements, muscle atonia, and a wake-like EEG. Spindles reflect thalamocortical network activity and are normal.

167. B. For a ventricular wall, wall stress increases with intracavitary pressure and chamber radius and decreases with wall thickness. Pressure overload therefore raises stress, while concentric hypertrophy can partly normalize stress by increasing wall thickness. This adaptation carries its own diastolic and metabolic costs.

168. A. The thick ascending limb actively reabsorbs NaCl through NKCC2 but is relatively impermeable to water. It therefore dilutes tubular fluid and contributes to the corticomedullary osmotic gradient used to concentrate urine. Blocking NKCC2 impairs both functions.

169. D. The hippocampal formation is critical for consolidation of new declarative memories. Bilateral injury can produce profound anterograde amnesia while leaving working memory, many remote memories, and procedural learning relatively preserved. Procedural learning depends more heavily on basal ganglia, cerebellar, and related circuits.

170. E. Progesterone has a thermogenic effect and raises basal body temperature after ovulation, providing a retrospective marker of luteal activity. The LH surge is brief, and FSH is not the main thermogenic hormone. Estradiol does not account for the sustained postovulatory temperature rise.

171. B. LH binds receptors on Leydig cells and stimulates testosterone synthesis. FSH acts primarily on Sertoli cells, supporting spermatogenesis and inhibin B production. High intratesticular testosterone, maintained by LH-driven Leydig function, is also essential for normal sperm production.

172. D. The primary response generates memory B cells after germinal-center reactions that include somatic hypermutation, affinity selection, and class switching. On re-exposure, these memory cells respond rapidly and produce high-affinity antibody, often IgG or another switched isotype. T cells provide help but do not themselves secrete immunoglobulin.

173. C. Chronic volume overload tends to produce eccentric hypertrophy, characterized by increased chamber size and addition of sarcomeres in series. Chronic pressure overload more commonly produces concentric hypertrophy with increased wall thickness. These patterns are adaptive but can eventually contribute to dysfunction.

174. D. SSRIs inhibit the serotonin transporter, reducing reuptake into the presynaptic neuron and increasing extracellular serotonin. Clinical effects are delayed because receptor and network adaptations take time even though transporter inhibition is immediate. SSRIs are not direct serotonin-receptor agonists and do not inhibit monoamine oxidase.

175. B. Research recruitment creates potential conflicts when investigators have financial incentives. These interests should be disclosed and managed, and consent must remain informed and voluntary. Clinical care should not be conditioned on participation in unrelated research.

176. C. 2,3-BPG binds deoxygenated adult hemoglobin and stabilizes the low-affinity tense state. Increased 2,3-BPG shifts the dissociation curve to the right, helping unload oxygen at tissues, although it can modestly reduce loading at a given pulmonary PO2.

177. D. Early fasting requires substantial gluconeogenesis, including amino-acid substrates. As hepatic ketone production rises, the brain uses more ketones and less glucose. This protein-sparing adaptation reduces the rate of muscle proteolysis during prolonged starvation.

178. E. SA nodal cells have relatively little contribution from fast sodium channels to phase 0. Once threshold is reached, L-type calcium channels open and generate the nodal upstroke. Potassium currents then contribute to repolarization.

179. E. Fasting lowers the insulin-to-glucagon ratio. This promotes hepatic glucose production and relieves insulin-mediated suppression of adipose lipolysis. Catecholamines and other counterregulatory hormones can reinforce these effects, particularly with longer fasting or stress.

180. B. Cultural humility means eliciting an individual patient's beliefs and preferences rather than stereotyping. Autonomy can include family involvement if the patient wants it. The clinician should ensure informed understanding while respectfully exploring how values shape the decision.

181. D. Phototransduction activates transducin and phosphodiesterase, which lowers cGMP and closes cGMP-gated cation channels. The rod hyperpolarizes and releases less glutamate. Photoreceptors signal with graded membrane potentials rather than conventional all-or-none action potentials.

182. C. Activation-induced cytidine deaminase is essential for somatic hypermutation and class-switch recombination after B-cell activation. RAG proteins and TdT act mainly during initial antigen-receptor gene rearrangement in developing lymphocytes. Failure of AID therefore impairs both affinity maturation and isotype switching.

183. B. FSH acts on Sertoli cells, which create the environment for spermatogenesis, produce androgen-binding protein, and release inhibin B. LH acts on Leydig cells to produce testosterone. Inhibin B feeds back preferentially on pituitary FSH secretion.

184. A. Bright light bleaches photopigment. In darkness, rhodopsin regenerates and rod sensitivity progressively increases, allowing vision at lower luminance. Pupillary dilation contributes to increased retinal illumination, but photopigment regeneration is a major slower component of dark adaptation.

185. A. Countercurrent multiplication depends on differing transport properties of the loop segments. The thick ascending limb reabsorbs NaCl but is water impermeable, while the descending limb is

relatively water permeable. Repeated flow and transport multiply a modest transverse gradient into a large corticomedullary osmotic gradient.

186. D. Maximal heart rate declines with age largely because cardiac responsiveness to beta-adrenergic stimulation decreases. Older adults can still raise cardiac output through stroke-volume mechanisms, but chronotropic reserve is reduced. This is not caused by enhanced baroreceptor sensitivity, which generally declines with age.

187. E. Teach-back asks patients to describe key information in their own words and helps identify communication gaps without testing or blaming the patient. Plain language, focused information, and opportunities for questions also improve understanding.

188. B. Near accommodation requires increased lens curvature. Parasympathetic activation contracts the ciliary muscle, reducing tension on zonular fibers so the elastic lens becomes rounder and more powerful. The near triad also includes convergence and pupillary constriction.

189. D. Maternal IgG is actively transported across the placenta through Fc receptor-mediated mechanisms, providing passive systemic immunity to the fetus and newborn. IgM is too large to cross efficiently, so fetal or neonatal IgM generally reflects the infant's own production. Secretory IgA is instead important in breast milk and mucosal protection.

190. E. Hyperosmolality stimulates hypothalamic osmoreceptors and vasopressin release. Vasopressin increases collecting-duct water permeability so water can move into the hypertonic medullary interstitium, producing concentrated urine. Aldosterone primarily regulates sodium reabsorption and potassium secretion rather than acting as the main water-channel hormone.

191. D. Aldosterone increases sodium reabsorption in principal cells by increasing ENaC activity at the apical membrane and Na/K-ATPase activity basolaterally. The resulting lumen-negative potential and higher intracellular potassium support potassium secretion. Aldosterone also influences acid-base handling through intercalated cells.

192. B. Secretory IgA is the major immunoglobulin in breast milk and many other mucosal secretions. Its secretory component helps protect it from proteolysis, and it can neutralize pathogens and block epithelial adherence without provoking intense inflammation. Maternal IgG is more important for transplacental systemic passive immunity.

193. A. During acidosis, the kidney increases hydrogen secretion and net acid excretion as titratable acid and ammonium. Alpha-intercalated cells secrete H+ and return bicarbonate to blood, while proximal glutamine metabolism increases ammoniagenesis and generation of new bicarbonate. Beta-intercalated cells instead favor bicarbonate secretion during alkalosis.

194. D. The basilar membrane is tonotopically organized: its base is narrow and stiff and responds best to high frequencies, while the apex is wider and more compliant and responds best to low frequencies.

Hair cells transduce the local traveling-wave peak into neural activity. Frequency coding therefore begins with cochlear mechanics.

195. B. PTH has exposure-pattern-dependent skeletal effects. Chronic elevation promotes RANKL-mediated osteoclastogenesis indirectly through osteoblast-lineage cells, whereas intermittent dosing has a net anabolic effect by enhancing osteoblast number and activity. It does not eliminate osteoclasts permanently or act through chronic hypocalcemia.

196. B. Renal ammoniagenesis from glutamine is strongly upregulated during chronic acidosis. NH_4^+ can be excreted while newly generated bicarbonate enters the blood, increasing net acid elimination. This adaptive pathway is crucial because free urine hydrogen concentration alone cannot account for the required acid excretion.

197. D. Acute carbon dioxide retention shifts the carbonic acid equilibrium toward hydrogen ion and bicarbonate. Intracellular and extracellular nonbicarbonate buffers, including hemoglobin and proteins, limit the fall in pH and produce a small increase in bicarbonate. Renal bicarbonate generation and ammonium excretion provide slower compensation over days.

198. B. Calcitriol promotes intestinal absorption of calcium and phosphate. Deficiency reduces mineral availability and can trigger secondary hyperparathyroidism, which further disturbs skeletal mineralization. In children the result is rickets, whereas adults develop osteomalacia.

199. C. A carbohydrate load after prolonged undernutrition raises insulin. Cells take up glucose along with phosphate, potassium, and magnesium, and phosphate is consumed in phosphorylated intermediates and ATP production. If total-body stores are depleted, serum phosphate can fall substantially.

200. C. Endolymph has a high potassium concentration and a positive endocochlear potential. Opening mechanically gated channels therefore permits potassium entry into hair cells, causing depolarization. Basolateral calcium influx then helps trigger neurotransmitter release onto auditory afferents.

201. D. Fetal Sertoli cells secrete anti-Müllerian hormone, causing Müllerian duct regression. Leydig-cell testosterone supports Wolffian duct development, while DHT is critical for male external genitalia and prostate development. These pathways are distinct and explain patterns seen in disorders of sexual development.

202. E. Osteoblasts derive from mesenchymal lineage cells and synthesize osteoid, especially type I collagen and associated matrix proteins. Some become osteocytes when embedded within mineralized bone. Osteoclasts are multinucleated resorptive cells from the monocyte-macrophage lineage.

203. D. De-escalation begins with calm acknowledgment, active listening, and clarification of the concern. Once the patient feels heard, the clinician can explain what happened, apologize when appropriate, and work toward feasible next steps without making unrealistic promises.

204. C. With sustained hypercapnia, the kidneys increase bicarbonate reabsorption and generation and enhance net acid excretion, including ammonium. This raises plasma bicarbonate and partially restores pH toward normal. The renal response takes time and is therefore larger in chronic than acute respiratory acidosis.

205. D. Fibroblasts initially deposit matrix that includes type III collagen, and remodeling later favors stronger type I collagen. Tensile strength rises over months but generally does not return fully to that of uninjured skin. Basement-membrane type IV collagen and fibrin are not the main load-bearing proteins of a mature dermal scar.

206. D. Most oxygen in blood is carried bound to hemoglobin, so arterial oxygen content depends strongly on hemoglobin concentration and saturation. A patient can therefore have normal PO2 and saturation but reduced oxygen content and delivery when hemoglobin is low.

207. B. Exogenous proteins taken up by professional antigen-presenting cells are generally processed in endosomal compartments and loaded onto MHC class II. CD4 helper T cells recognize peptide-MHC II with appropriate costimulation. MHC class I predominantly presents endogenous peptides, although dendritic cells can cross-present in selected settings.

208. E. Carbon monoxide binds hemoglobin with high affinity, reducing oxygen-carrying capacity. It also shifts the remaining oxyhemoglobin dissociation relationship to the left, impairing oxygen unloading. Dissolved oxygen and therefore arterial PO2 may remain normal.

209. D. Low antral pH promotes somatostatin release from D cells. Somatostatin inhibits G-cell gastrin secretion and also suppresses acid-secretory pathways, providing negative feedback. This prevents unrestrained acid production as the gastric lumen becomes highly acidic.

210. B. DHT is a potent androgen formed from testosterone by 5-alpha-reductase and is especially important for development of male external genitalia and prostate. Testosterone itself supports Wolffian duct derivatives. Müllerian regression depends on anti-Müllerian hormone rather than DHT.

211. A. hCG is produced by syncytiotrophoblasts and acts on LH receptors to rescue and maintain the corpus luteum early in pregnancy. Luteal progesterone supports the endometrium until the placenta can produce sufficient steroid hormone. hCG therefore peaks early and declines as placental steroidogenesis takes over.

212. D. The semicircular canals are oriented in three planes and detect angular acceleration through inertia of endolymph and cupular deflection. The utricle and saccule instead sense linear acceleration and head position relative to gravity using otoliths. The organ of Corti is auditory rather than vestibular.

213. B. Pacemaker cells lack a stable resting membrane potential. Hyperpolarization-activated funny current, reduced outward potassium current, and later calcium currents contribute to the gradual phase 4 depolarization. Autonomic input changes its slope and therefore alters heart rate.

214. C. Lowering a positivity threshold generally captures more diseased individuals, increasing sensitivity, but it also labels more unaffected individuals as positive, reducing specificity. ROC curves display this sensitivity-specificity tradeoff across thresholds.

215. A. Vitamin C is required for hydroxylation of proline and lysine residues during collagen synthesis. Hydroxy residues help stabilize the triple helix and support later processing, so deficiency weakens connective tissue and impairs wound healing. Lysyl oxidase is copper dependent rather than directly vitamin C dependent.

216. C. Acute cellular rejection is driven largely by recipient T-cell responses to donor alloantigens, with CD8 cytotoxicity and CD4-mediated inflammation. Antibody-mediated mechanisms can also contribute to graft injury but represent a distinct pathway. Erythrocytes and platelets do not generate adaptive antigen receptors.

217. C. Gastric parietal cells secrete hydrogen chloride into the lumen while bicarbonate enters blood. Loss of gastric acid through vomiting therefore removes hydrogen from the body and produces metabolic alkalosis. Volume and chloride depletion can maintain the alkalosis by increasing renal bicarbonate reabsorption and limiting bicarbonate secretion.

218. D. Cerebral perfusion pressure is commonly approximated as MAP minus ICP, assuming venous pressure is not higher than ICP. As ICP rises at a given MAP, the pressure gradient driving cerebral blood flow falls. Severe elevation can therefore threaten cerebral perfusion even when systemic blood pressure appears adequate.

219. D. Lysyl oxidase is a copper-dependent extracellular enzyme that helps cross-link collagen and elastin. Impaired cross-linking weakens connective tissue. Hydroxylation of proline and lysine occurs intracellularly and depends on vitamin C, iron, oxygen, and other cofactors.

220. B. Human placental lactogen has growth hormone-like metabolic effects that increase maternal lipolysis and insulin resistance, making more glucose available for placental transfer to the fetus. Other placental and maternal hormones also contribute. Excessive insulin resistance can contribute to gestational diabetes in susceptible patients.

221. A. Low effective arterial volume lowers renal perfusion and often distal NaCl delivery. The macula densa signals for increased renin and altered arteriolar tone, while renal sympathetic beta-1 stimulation also promotes renin release. These mechanisms activate the renin-angiotensin-aldosterone system to conserve sodium and support pressure.

222. E. The vagus is central to the cephalic phase of gastric secretion and contributes to gastric accommodation and motility. Hormonal and enteric mechanisms can still support digestion after vagotomy, so intestinal absorption and endocrine responses are not simply abolished. The main loss is neural anticipatory stimulation.

223. A. Cardiac beta-1 receptors are Gs coupled and increase cAMP. In pacemaker cells this enhances funny current and calcium currents, steepening phase 4 and shortening the time to threshold. Parasympathetic M2 signaling has the opposite effect.

224. A. Sensitized mast cells bear allergen-specific IgE on high-affinity Fc epsilon receptors. Re-exposure cross-links receptor-bound IgE and triggers rapid degranulation with histamine release, followed by lipid mediators and cytokines. This is the classic immediate mechanism of type I hypersensitivity.

225. B. Evaporation depends on a vapor-pressure gradient between water at the skin surface and the surrounding air. High humidity reduces that gradient, so sweating becomes less effective even if sweat production remains high. This can sharply reduce the body's capacity to dissipate metabolic heat.

226. C. Methemoglobin contains ferric iron, which cannot bind oxygen effectively. In addition, oxidation increases oxygen affinity at remaining ferrous sites, reducing unloading. Tissue hypoxia can therefore occur even when arterial PO2 is preserved.

227. C. ABO incompatibility can trigger rapid antibody binding to donor erythrocyte antigens and complement-mediated intravascular hemolysis. This is a type II antibody-mediated cytotoxic hypersensitivity reaction. Erythrocytes do not express the MHC pattern needed for the NK-cell mechanism described.

228. E. Angiotensin II directly stimulates proximal sodium reabsorption, including sodium-hydrogen exchange, and also promotes aldosterone secretion and vasoconstriction. Efferent arteriolar constriction can raise filtration fraction, increasing peritubular oncotic pressure and further favoring proximal reabsorption. These combined effects conserve sodium and water.

229. E. Pure water crosses cell membranes freely and distributes throughout total body water. Because intracellular fluid is the largest compartment, most of the added water ultimately resides inside cells, while a smaller fraction remains extracellular. Plasma receives only a portion of the extracellular share.

230. D. Serum sickness is a type III hypersensitivity reaction caused by deposition of soluble immune complexes. Complement activation and recruited inflammatory cells then damage tissues, often producing fever, rash, arthralgia, and renal findings. The mechanism differs from immediate IgE-mediated allergy and fixed-cell type II reactions.

231. A. Gastric distention and meal-related hormonal and neural signals can increase colonic motility through the gastrocolic reflex. This helps explain the urge to defecate after meals in some people. The migrating motor complex is primarily an interdigestive small-intestinal pattern rather than the fed colonic response.

232. E. Progesterone increases ventilatory drive in pregnancy, lowering PaCO2. The kidneys compensate by excreting bicarbonate, so maternal pH is only mildly alkalemic despite chronic hypocapnia. The lower maternal PaCO2 also facilitates fetal-to-maternal carbon dioxide transfer.

233. D. Rectal distention triggers the rectoanal inhibitory reflex, causing relaxation of the internal anal sphincter, which is smooth muscle. The external anal sphincter is skeletal muscle under voluntary pudendal control and can be contracted to defer defecation. Coordinated pelvic parasympathetic and enteric activity supports defecation.

234. B. Infants have high metabolic and cerebral glucose requirements relative to body size, while their absolute energy reserves are limited. They can perform glycogenolysis and gluconeogenesis, but prolonged fasting can exhaust available substrate more quickly than in adults. This combination increases susceptibility to hypoglycemia.

235. B. The Ferguson reflex is a classic positive-feedback loop: cervical stretch promotes oxytocin release, which increases uterine contractions and produces more stretch. Local prostaglandins and changing myometrial responsiveness also contribute to labor. Positive feedback continues until delivery removes the stimulus.

236. E. Dopamine from the hypothalamus tonically inhibits prolactin secretion through D2 receptors on anterior pituitary lactotrophs. Suckling reduces this inhibitory input, allowing prolactin to rise and support milk synthesis. Oxytocin is released separately to mediate milk ejection.

237. D. The tuberculin reaction is a delayed type IV hypersensitivity response. Antigen-specific T cells release cytokines that recruit and activate macrophages, producing induration over 24 to 72 hours. Immediate mast-cell degranulation would occur much earlier and is not the basis of this test.

238. A. The AV node depends heavily on calcium currents for conduction. Vagal M2 activation reduces cAMP and calcium current and increases potassium conductance, slowing conduction and increasing AV nodal refractoriness. This effect underlies the PR-interval prolongation seen with increased vagal tone.

239. E. Growth hormone stimulates production of IGF-1, especially in the liver and also locally in tissues. IGF-1 mediates many effects on bone and soft-tissue growth and provides negative feedback on the growth hormone axis. Growth hormone also has direct metabolic actions, including lipolysis and reduced insulin sensitivity.

240. A. Isotonic saline adds sodium and water to the extracellular compartment without creating a major transcellular osmotic gradient. It therefore expands plasma and interstitial volumes while intracellular volume changes little. The infused fluid does not stay exclusively in plasma because capillary exchange distributes it through the extracellular space.

241. D. Neutrophils are key rapid effector cells for phagocytosis and killing of extracellular bacteria and fungi in acute inflammation. Severe neutropenia therefore greatly increases infection risk. Adaptive antibody production, MHC I presentation, and platelet aggregation are mediated by other cells and proteins.

242. B. Carbon dioxide readily crosses the blood-brain barrier and generates hydrogen ions in brain extracellular fluid, producing potent cerebral vasodilation. Hypercapnia therefore increases cerebral blood flow and can raise intracranial blood volume. Hypocapnia has the opposite vasoconstrictor effect.

243. B. Hypocapnia raises brain extracellular pH and causes cerebral vasoconstriction, reducing cerebral blood flow. This effect is why short-term hyperventilation can transiently lower intracranial pressure in selected emergencies. Excessive or prolonged hypocapnia can also reduce cerebral oxygen delivery.

244. C. Acute hypotonic hyponatremia lowers extracellular effective osmolality, so water enters cells and can cause brain swelling. Over time, brain cells adapt by losing osmolytes, which reduces swelling but creates vulnerability to overly rapid correction. The key initial mechanism is transcellular water movement.

245. C. Benzodiazepines are positive allosteric modulators of GABA-A receptors and increase the frequency of chloride-channel opening in the presence of GABA. The result is enhanced inhibitory signaling. Barbiturates classically increase channel-opening duration, whereas GABA-B receptors are metabotropic rather than ligand-gated chloride channels.

246. A. Mu-opioid receptors are Gi/o coupled. Activation decreases adenylyl cyclase activity, promotes potassium efflux postsynaptically, and reduces calcium-dependent transmitter release presynaptically. These actions hyperpolarize neurons and suppress nociceptive signaling.

247. A. When renal perfusion falls but tubular function is preserved, sympathetic, renin-angiotensin, and other signals increase sodium and water reabsorption. Urinary sodium and fractional excretion of sodium are therefore often low. Intrinsic tubular injury can blunt this conservation response.

248. D. Increasing hemoglobin can improve arterial oxygen content, but higher hematocrit also increases blood viscosity. At sufficiently high levels, the rise in vascular resistance and impaired microvascular flow can offset some benefit in oxygen delivery and increase thrombotic risk.

249. C. Case-control studies are efficient for rare outcomes because investigators deliberately sample cases rather than waiting for uncommon events to develop in a large cohort. They estimate odds ratios and are particularly useful when the disease has a long latency.

250. D. The posterior hypothalamus is important for heat conservation and production, including sympathetic vasoconstriction and shivering-related responses. The anterior hypothalamus is more closely associated with heat dissipation through sweating and vasodilation. Damage to posterior pathways therefore compromises cold defense.

251. C. IGF-1 is a key mediator of growth hormone effects on linear growth and tissue proliferation. When IGF-1 production or action is severely impaired, growth failure can occur despite normal or elevated growth hormone. Low IGF-1 also reduces negative feedback, often allowing growth hormone concentrations to rise.

252. E. Helminths are often too large to be phagocytosed. Eosinophils can bind antibody-coated parasites and release cytotoxic granule proteins, including major basic protein, onto their surfaces. IL-5 supports eosinophil growth and activation rather than being simply eliminated by them.

253. A. Increasing extracellular potassium reduces the concentration gradient for potassium efflux and makes EK less negative. Because resting ventricular membrane voltage is strongly influenced by potassium conductance, the resting potential depolarizes. With substantial hyperkalemia, sodium-channel inactivation can slow conduction and produce dangerous arrhythmias.

254. A. Arrector pili are smooth muscles under sympathetic adrenergic control. Contraction produces piloerection, which has limited thermoregulatory value in humans but is part of the cold-defense response. Somatic motor neurons innervate skeletal muscle, not these dermal smooth muscles.

255. C. Cold activates hypothalamic and sympathetic heat-conservation responses. Vasoconstriction reduces skin perfusion and conductive and convective heat loss, while shivering and nonshivering thermogenesis increase heat production.

256. B. Bone adapts to mechanical loading through mechanosensitive signaling involving osteocytes and remodeling units. Prolonged unloading favors bone loss, with resorption exceeding formation. This contributes to osteoporosis during immobilization or microgravity.

257. D. Normal bowel relaxation depends on inhibitory enteric motor neurons using transmitters such as nitric oxide. When enteric ganglia are absent, the affected segment cannot relax appropriately and remains functionally obstructed, while proximal bowel can dilate. The problem is neural coordination rather than absence of smooth-muscle contractile machinery.

258. C. Hypocalcemia tends to prolong ventricular repolarization and the QT interval, whereas hypercalcemia tends to shorten it. Ventricular phase 0 is primarily mediated by fast sodium channels, so low extracellular calcium does not simply eliminate the QRS complex. Calcium remains crucial for the plateau and excitation-contraction coupling.

259. D. Systemic stress activates catecholamines, cortisol, glucagon, and inflammatory mediators. These favor mobilization of glucose, amino acids, and fatty acids and can produce a catabolic state, particularly when illness is prolonged.

260. A. Growth hormone secretion is stimulated by GHRH and ghrelin and inhibited by somatostatin. Secretion is pulsatile and influenced by sleep, exercise, nutrition, and IGF-1 feedback. Dopamine is better known for tonic inhibition of prolactin.

261. A. Natural killer cells integrate activating and inhibitory signals; recognition of self MHC class I provides an important inhibitory signal. Some infected or transformed cells downregulate MHC I, reducing inhibition and permitting NK-mediated cytotoxicity. NK cells do not use clonally rearranged antigen receptors like T and B lymphocytes.

262. D. Transparent communication distinguishes established facts from probabilities and unknowns. Explaining how uncertainty will be addressed supports trust and informed decision-making without false reassurance or unwarranted certainty.

263. B. High distal NaCl delivery signals that upstream filtration or flow may be excessive. Macula densa-derived mediators promote afferent constriction and suppress renin, decreasing glomerular pressure and single-nephron GFR. Low NaCl delivery produces the opposite tendency.

264. D. The kidney can markedly reduce urinary potassium excretion during depletion. Principal-cell secretion falls, and H/K-ATPase in alpha-intercalated cells can contribute to potassium reabsorption. Aldosterone and distal sodium delivery strongly modulate potassium secretion, but low potassium itself promotes conservation.

265. C. Early strength gains from resistance training are strongly influenced by neural adaptations such as better recruitment, rate coding, and intermuscular coordination. Hypertrophy contributes increasingly over later weeks and months. Capillary and mitochondrial adaptations are more prominent in endurance training than as the primary driver of early maximal strength.

266. C. Higher capillary hydrostatic pressure favors filtration of fluid into the interstitium. The lymphatic system can increase removal of filtered fluid, but if filtration exceeds lymphatic capacity edema develops. Plasma oncotic pressure opposes filtration but does not automatically rise to cancel the hydrostatic change.

267. B. The suprachiasmatic nucleus of the hypothalamus is the principal circadian pacemaker and receives retinal input through the retinohypothalamic tract. It coordinates daily rhythms in sleep-wake behavior, hormone secretion, and other functions. The listed motor and sensory functions are mediated by different neural structures.

268. A. Capacity is decision-specific and generally concerns understanding, appreciation, reasoning, and communication of a choice. A patient may have a psychiatric or neurologic diagnosis and still retain capacity, and choosing differently from the clinician does not itself prove incapacity.

269. A. Advance directives preserve patient autonomy when capacity is lost. When a directive clearly applies, it should guide care. Surrogates help interpret and implement the patient's values rather than substitute their own preferences.

270. E. Tendons mechanically connect muscle to bone and transmit contractile force to the skeleton. A complete rupture can therefore produce major loss of functional torque even if the muscle fibers and motor nerve remain intact. Tendons also store and return elastic energy but do not generate action potentials or neurotransmitter.

271. A. Nephrogenic diabetes insipidus reflects renal resistance to vasopressin, so exogenous desmopressin produces little improvement in urine concentration. In central diabetes insipidus,

desmopressin can markedly increase urine osmolality. The distinction localizes the defect to hormone availability versus renal response.

272. D. The ventricular action-potential plateau reflects sustained inward L-type calcium current opposed by outward potassium current. The long plateau lengthens refractory time and couples electrical excitation to calcium-dependent contraction. Fast sodium channels are largely inactivated during this phase.

273. D. Broca aphasia is a nonfluent expressive aphasia caused by injury to dominant inferior frontal language networks. Comprehension is relatively preserved, although complex grammar may be difficult, and patients are often aware of the deficit. Fluent impaired-comprehension speech is more typical of Wernicke aphasia.

274. A. Wernicke aphasia produces fluent but often nonsensical speech with impaired comprehension and impaired repetition. Patients may be less aware of the deficit than those with Broca aphasia. Nonfluent effortful speech with relatively preserved comprehension points toward Broca-area dysfunction instead.

275. E. In SIADH, vasopressin remains inappropriately active despite low plasma osmolality. Collecting ducts reabsorb water, producing dilutional hyponatremia and concentrated urine relative to the hypo-osmolar plasma. Secondary natriuresis can limit volume expansion but water retention is the initiating abnormality.

276. D. Small amounts of plasma protein normally enter the interstitium and are returned to the blood through lymphatics. Obstruction impairs this return, allowing protein and fluid to accumulate. The higher interstitial protein concentration can further retain water and contribute to chronic tissue changes.

277. B. Myogenic autoregulation allows vascular smooth muscle to constrict when stretched by higher pressure and dilate when pressure falls. This adjusts resistance to stabilize flow over a range of perfusion pressures. Metabolic mechanisms also contribute in many tissues.

278. D. Structured bad-news communication emphasizes setting, patient perception and preferences, clear knowledge sharing, empathic response to emotion, and a plan. Information is best given in manageable pieces with opportunities for questions.

279. C. Protein retained in glomerular capillary plasma creates an oncotic force opposing filtration. Increasing plasma protein concentration therefore lowers net filtration pressure and tends to reduce GFR if hydrostatic pressures and filtration coefficient are unchanged. Bowman space normally contains little protein, so its oncotic pressure is low.

280. D. Right parietal association cortex contributes attention to both hemispaces, while the left hemisphere is more strongly biased toward the right. A right-sided lesion can therefore produce profound left hemispatial neglect because the intact left hemisphere does not fully compensate. Neglect is an attentional disorder, not simply a primary visual-field deficit.