Physiology

Sample Paper – 9

Questions:	25	**Duration:**	45 min
Total Marks:	100	**Marking:**	+4 / −1

Topics: Cardiovascular · Renal · Respiratory · Nervous · Biochemistry · Immune · Endocrine

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Quick Reference

Instructions

- This paper has **25 questions** carrying **100 marks**.
- Each correct answer: **+4 marks**. Each wrong answer: **−1 mark**. Unattempted: **0**.
- Suggested time: **45 minutes**. All questions are single-correct MCQs.
- Covers: Cardiovascular, Renal, Respiratory, Nervous systems, Biochemistry, Immunology, Endocrinology.
- Click a question number in the answer key to jump to its solution.

Q1. Plasma oncotic (colloid osmotic) pressure is primarily generated by proteins dissolved in the plasma. Which plasma protein is the **most important contributor** to this oncotic pressure, and what is its main physiological consequence?

(A) Fibrinogen — it forms a fibrin clot that seals blood vessel walls and prevents plasma leakage

(B) Globulins — they bind and transport hormones and generate ∼5 mmHg of oncotic pressure

(C) Albumin — the most abundant plasma protein (3.5–5 g/dL) — generates ∼25 mmHg of oncotic pressure, drawing water from the interstitium into capillaries; hypoalbuminaemia causes oedema

(D) Transferrin — it binds iron and maintains oncotic pressure by preventing iron-mediated fluid shifts

Q2. Blood viscosity is a key determinant of vascular resistance and cardiac workload. Which factor is the **primary determinant** of blood viscosity?

(A) Haematocrit (packed cell volume, the proportion of blood occupied by RBCs) — anaemia decreases viscosity, polycythaemia increases it

(B) Plasma fibrinogen concentration — elevated fibrinogen causes hyperviscosity syndrome

(C) Core body temperature — viscosity is fixed once temperature is set

(D) Serum albumin level — hypoalbuminaemia increases blood viscosity by reducing osmotic forces

Q3. Coronary blood flow supplying oxygen and nutrients to the myocardium is not uniform throughout the cardiac cycle. During which phase of the cardiac cycle does **most coronary artery filling** occur?

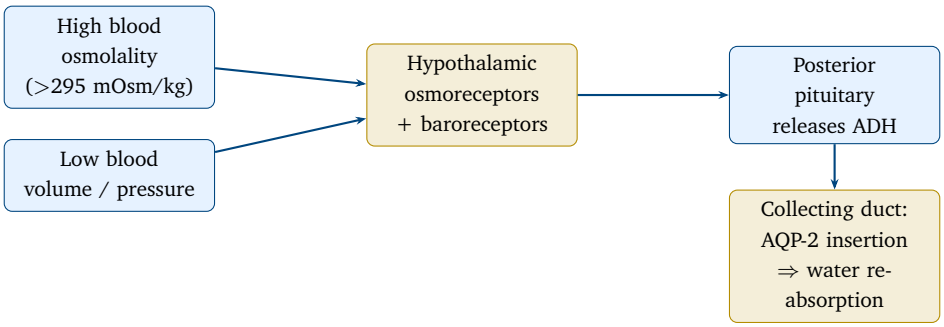
(A) Diastole — coronary perfusion occurs primarily during diastole when the myocardium relaxes and coronary vascular resistance drops; tachycardia shortens diastole and can reduce coronary perfusion

(B) Isovolumetric contraction — the brief phase before the aortic valve opens allows maximal coronary filling

(C) Systole — ventricular pressure peaks during systole, driving blood into the coronary ostia

(D) The late systolic ejection phase — maximal aortic pressure during rapid ejection perfuses the coronaries

Q4. Antidiuretic hormone (ADH, vasopressin) is a key regulator of water balance. The diagram below summarises the stimuli for ADH release and its renal action. Which statement **best describes** the mechanism of ADH release and its primary effect?



(A) ADH is released from the anterior pituitary when blood glucose rises; it acts on the proximal tubule to reabsorb sodium

(B) ADH is released from the posterior pituitary when blood osmolality rises (detected by hypothalamic osmoreceptors) OR when blood volume/pressure falls (detected by baroreceptors); it acts on V2 receptors in the collecting duct to insert aquaporin-2 (AQP2) water channels

(C) ADH is synthesised by the adrenal medulla and released during haemorrhage; it causes vasoconstriction only without affecting water reabsorption

(D) ADH is released from the anterior pituitary in response to hypokalaemia and acts on the distal tubule to increase potassium secretion

Q5. Ventilation is regulated by both central and peripheral chemoreceptors. What is the **primary stimulus** that activates the **peripheral chemoreceptors** (carotid and aortic bodies)?

(A) Decreased arterial P_{O_2} (hypoxaemia below ~60 mmHg) — peripheral chemoreceptors are uniquely sensitive to low P_{O_2}, unlike central chemoreceptors which respond primarily to CO_2/H^+

(B) Increased arterial P_{CO_2} above 40 mmHg — both central and peripheral chemoreceptors respond equally to hypercapnia

(C) Decreased blood pH below 7.30 — the peripheral chemoreceptors monitor pH only, not oxygen partial pressure

(D) Increased venous P_{CO_2} returning to the right heart — venous chemoreceptors signal the respiratory centre

Q6. Lysosomes are membrane-bound organelles found in virtually all eukaryotic cells. What is the **primary function** of lysosomes, and what is the clinical consequence of their dysfunction?

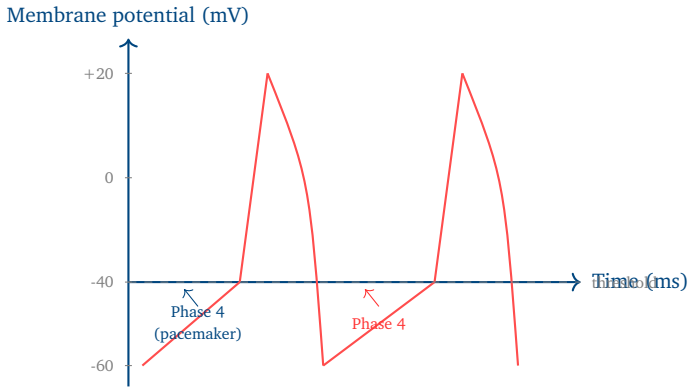
(A) Intracellular digestion — lysosomes contain acid hydrolases (pH ∼5) that break down worn-out organelles (autophagy), engulfed bacteria (phagocytosis), and macromolecules; lysosomal storage diseases (e.g., Gaucher's disease) result from enzyme deficiencies

(B) ATP synthesis — lysosomes generate ATP by oxidative phosphorylation within their acidic interior using proton gradients

(C) Protein synthesis — lysosomes bear ribosomes on their outer surface and synthesise lysosomal hydrolases directly at the organelle

(D) Lipid synthesis and packaging — lysosomes synthesise phospholipids and export them as VLDL for systemic distribution

Q7. The SA node generates spontaneous action potentials that pace the heart without external stimulation. The diagram below shows the pacemaker (Phase 4) depolarisation of an SA node cell. Which statement **correctly explains** the ionic basis of this automaticity?



(A) A rapid influx of Cl^- through leak channels during Phase 4 depolarises the SA node membrane toward threshold, triggering the action potential upstroke via fast Na^+ channels

(B) Phase 4 depolarisation is driven by an outward K^+ current (I_K) that progressively hyperpolarises the cell until a rebound depolarisation occurs through voltage-gated Na^+ channels

(C) The L-type Ca^{2+} channel alone is responsible for Phase 4 spontaneous depolarisation; the funny current (I_f) has no role in normal pacemaker activity

(D) A slow spontaneous depolarisation during diastole (Phase 4) driven by the 'funny current' I_f (HCN channels allowing Na^+/K^+ influx), $I_{Ca\text{-}T}$, and decreasing I_K — this pacemaker potential automatically brings the membrane to threshold and fires each heartbeat without external stimulation

Q8. The blood-brain barrier (BBB) is a selective barrier that tightly regulates passage of substances between the systemic circulation and the central nervous system. Which structural feature is **primarily responsible** for forming the BBB?

(A) Fenestrated capillary endothelium with large pores (>100 nm) — these fenestrae allow rapid passive filtration of nutrients into the brain
(B) Thick myelin sheaths surrounding brain capillaries — myelin prevents ion and water movement into the brain parenchyma
(C) Astrocyte cell bodies completely encasing capillaries — astrocyte soma directly block all transport between blood and neurones
(D) Tight junctions (zonulae occludentes) between adjacent brain capillary endothelial cells — these, together with pericytes and astrocyte end-feet, restrict paracellular passage of most hydrophilic molecules, ions, and pathogens; lipid-soluble molecules (O_2, CO_2, ethanol, many drugs) cross freely

Q9. The renin-angiotensin-aldosterone system (RAAS) is a critical hormonal cascade controlling blood pressure and fluid balance. What is the **first enzymatic step** in the RAAS cascade initiated by renin?

(A) Renin (an aspartyl protease from juxtaglomerular cells of the kidney) cleaves angiotensinogen (a liver glycoprotein) to form angiotensin I (10-amino-acid peptide), which is then converted to the vasoactive angiotensin II by ACE
(B) Renin directly converts angiotensin I to angiotensin II by removing two amino acids from the C-terminus in the pulmonary circulation
(C) Renin cleaves bradykinin to form angiotensin II, bypassing angiotensinogen and ACE entirely
(D) Renin is secreted by the adrenal cortex and acts on the liver to stimulate aldosterone release directly without forming angiotensin

Q10. Obstructive sleep apnoea (OSA) is a common sleep-related breathing disorder. Which statement **best describes** the pathophysiological mechanism of OSA?

(A) OSA is caused by failure of the respiratory centre in the medulla to send signals to the diaphragm during sleep, resulting in central apnoea without airway obstruction
(B) OSA results from bronchospasm of the lower airways during REM sleep, causing reduced airflow despite a patent upper airway
(C) OSA is primarily due to excessive mucus production narrowing the trachea and mainstem bronchi during supine sleep
(D) Repetitive collapse of the upper airway (pharyngeal walls) during sleep due to relaxation of pharyngeal dilator muscles, causing apnoeic episodes, oxygen desaturation, arousals, and daytime sleepiness; risk factors: obesity, retrognathia, large tonsils

Q11. Upper motor neurons that initiate voluntary movement originate from the primary motor cortex. Where is the **primary motor cortex** located?

(A) The postcentral gyrus of the parietal lobe — this strip processes somatosensory information and generates motor commands for fine movements
(B) The superior temporal gyrus of the temporal lobe — this region integrates auditory input and coordinates motor speech responses
(C) The precentral gyrus of the frontal lobe — the 'motor strip' — contains the primary motor cortex, where upper motor neurons (pyramidal cells of Betz) originate the corticospinal tract; the body is somatotopically mapped (homunculus)
(D) The cingulate gyrus of the limbic lobe — this region coordinates emotional motor responses via projections to the spinal cord

Q12. Pain perception begins with the activation of specialised sensory receptors called nociceptors. Which structure **serves as a nociceptor**?

(A) Meissner's corpuscles — encapsulated mechanoreceptors in the dermal papillae that detect light touch and respond to tissue-damaging stimuli
(B) Pacinian corpuscles — lamellated pressure receptors that detect vibration and are activated by high-intensity mechanical forces only
(C) Ruffini endings — slowly-adapting mechanoreceptors in the dermis that respond to skin stretch and sustained pressure but not to chemical pain signals
(D) Free nerve endings (bare unmyelinated or lightly myelinated axon terminals in skin, muscles, viscera) — they detect thermal, mechanical, and chemical stimuli that signal tissue damage; activated by bradykinin, prostaglandins, H^+, capsaicin, and ATP

Q13. Efficient gas exchange between the maternal and fetal circulations is essential for fetal oxygenation. Where does maternal-fetal gas exchange take place, and what structural feature of fetal haemoglobin facilitates oxygen transfer?

(A) The umbilical vein — oxygen diffuses directly from maternal blood in the umbilical vein lumen into fetal red cells circulating in the adjacent umbilical artery by counter-current exchange
(B) The placenta (specifically the syncytiotrophoblast layer of chorionic villi) — O_2 and CO_2 exchange by simple diffusion; fetal haemoglobin (HbF) has higher O_2 affinity than adult HbA (shifted left dissociation curve), favouring O_2 transfer from mother to fetus
(C) The amniotic fluid — dissolved oxygen in amniotic fluid diffuses across the fetal skin in the second trimester before keratinisation is complete
(D) The chorion laeve (smooth chorion) — thin smooth chorion membranes lack vasculature but allow direct diffusion of gases driven by osmotic gradients

Q14. The human body employs several buffer systems to resist changes in blood pH. Which is the **most physiologically important** extracellular buffer system and why?

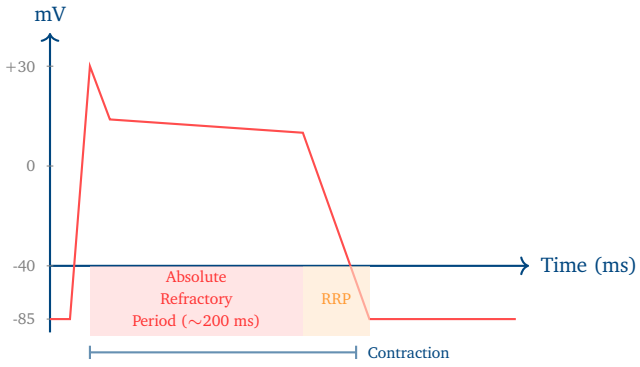
(A) The phosphate buffer system ($H_2PO_4^-/HPO_4^{2-}$) — it is the dominant plasma buffer because phosphate is present in high concentrations in the blood and reacts instantly with both acids and bases

(B) The protein buffer system (haemoglobin and plasma proteins) — haemoglobin is the single most important buffer because it is present at high concentration and reacts directly with H^+ without requiring respiratory or renal adjustment

(C) The bicarbonate-carbonic acid buffer system ($HCO_3^-/H_2CO_3 \rightleftharpoons CO_2 + H_2O$) — it is the most physiologically important buffer because its components are regulated by the lungs (CO_2/ventilation) and kidneys (HCO_3^- reabsorption/excretion), allowing rapid and precise pH control

(D) The ammonia buffer system (NH_3/NH_4^+) — it is the primary plasma buffer because ammonia is continuously generated by hepatic deamination of amino acids and rapidly neutralises acids in the blood

Q15. Cardiac muscle has a uniquely prolonged refractory period compared with skeletal muscle. The diagram below shows a ventricular action potential alongside the refractory period. Why is the **absolute refractory period** of cardiac muscle physiologically important?



(A) The absolute refractory period limits the maximum heart rate to 40 bpm by forcing a mandatory pause of 1500 ms between action potentials, which is set by the slow inactivation of L-type Ca^{2+} channels

(B) The absolute refractory period allows the heart to maintain a fixed stroke volume regardless of preload, because Na^+ channels cannot reopen until the ventricle has ejected all its blood

(C) Calcium released during the plateau phase binds troponin and simultaneously inactivates all ion channels, making the absolute refractory period a passive consequence of Ca^{2+} buffering

(D) The absolute refractory period of cardiac muscle (~200–250 ms, nearly as long as contraction itself) makes cardiac tetany impossible — the heart cannot be re-excited until it has fully relaxed, ensuring diastolic filling occurs with every beat

Q16. Laplace's law relates wall tension to pressure, radius, and wall thickness in hollow organs. How does Laplace's law explain the **increased oxygen demand** seen in dilated cardiomyopathy?

(A) Laplace's law predicts that wall tension decreases when the ventricular radius increases; dilated hearts therefore require less energy per beat, but the increased heart rate raises total oxygen consumption

(B) Laplace's law shows that increasing wall thickness (hypertrophy) in a dilated ventricle raises tension exponentially, independent of radius; this is why hypertrophied hearts consume more oxygen than dilated hearts

(C) According to Laplace's law (wall tension $T = P \times r/2h$), ventricular wall tension is proportional to the product of pressure and radius — this means a dilated ventricle (increased radius) must generate greater wall tension to produce the same pressure, increasing myocardial oxygen demand and explaining why dilated cardiomyopathy causes heart failure

(D) Laplace's law applies only to spherical thin-walled structures (like alveoli); the thick-walled ventricle does not obey this relationship, so dilation increases oxygen demand purely through neuro-hormonal activation

Q17. The oxygen-haemoglobin dissociation curve characterises how haemoglobin binds and releases oxygen. What is the **P50** of haemoglobin under normal physiological conditions, and what factors shift it to the right?

(A) Approximately 10–15 mmHg — haemoglobin is nearly fully saturated at these low oxygen tensions and the P50 is unaffected by changes in pH or temperature

(B) Approximately 26–27 mmHg — the partial pressure of O_2 at which haemoglobin is exactly 50% saturated under standard conditions (pH 7.4, 37°C, normal PCO_2); the P50 rises (rightward shift) with increased temperature, CO_2, 2,3-DPG, or acidosis, promoting O_2 unloading

(C) Approximately 40–45 mmHg — this corresponds to venous P_{O_2} and at this tension haemoglobin is 50% saturated only in severe anaemia

(D) Approximately 100 mmHg — this equals alveolar P_{O_2} and defines 50% saturation under hyperoxic conditions

Q18. Phenylketonuria (PKU) is a common inborn error of amino acid metabolism that causes intellectual disability if untreated. Which enzyme is deficient in classical PKU?

(A) Tyrosinase — the enzyme that converts tyrosine to DOPA and ultimately to melanin; its deficiency causes phenylalanine accumulation and simultaneous albinism
(B) Homogentisate oxidase — the enzyme in the tyrosine degradation pathway; its deficiency causes alkaptonuria, not phenylketonuria
(C) Phenylalanine hydroxylase deficiency — this autosomal recessive enzyme normally converts phenylalanine to tyrosine; deficiency causes accumulation of phenylalanine and neurotoxic metabolites, resulting in intellectual disability, seizures, and fair skin/hair if untreated; managed with phenylalanine-restricted diet
(D) Branched-chain alpha-keto acid dehydrogenase — the enzyme whose deficiency causes maple syrup urine disease; it is sometimes confused with PKU because both present with amino acid accumulation

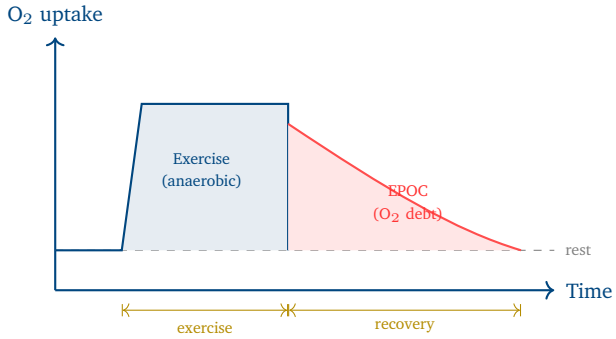
Q19. Insulin is essential for glucose uptake into muscle and adipose tissue. By what mechanism does insulin facilitate **glucose entry** into these insulin-responsive cells?

(A) Facilitated diffusion via GLUT4 transporter — insulin causes GLUT4 vesicles to translocate from intracellular stores to the plasma membrane, increasing glucose uptake without requiring ATP; the movement is down the concentration gradient (no active transport)
(B) Active transport via a Na^+/glucose co-transporter (SGLT) — insulin increases SGLT expression on muscle cell membranes, allowing glucose uptake against its concentration gradient using the Na^+ gradient
(C) Simple diffusion through lipid bilayer — insulin increases membrane fluidity, allowing glucose to dissolve in and diffuse across the phospholipid bilayer in proportion to its concentration gradient
(D) Endocytosis — insulin binds its receptor, triggering a clathrin-coated vesicle that engulfs extracellular glucose and deposits it directly into the cytoplasm

Q20. Eosinophils are granulocytes with a distinctive bilobed nucleus and large cytoplasmic granules. In which clinical conditions are eosinophils **most characteristically elevated**?

(A) Bacterial sepsis and acute viral infections — eosinophilia is a sensitive marker of systemic infection and rises in proportion to bacterial load
(B) Allergic/atopic conditions (asthma, hay fever, urticaria) and parasitic infections (especially tissue-invasive helminths) — eosinophils release major basic protein, eosinophil peroxidase, and cationic protein to kill parasites and modulate allergic inflammation
(C) Autoimmune haemolytic anaemia and SLE — eosinophilia is the hallmark of type II hypersensitivity reactions involving complement-mediated cell lysis
(D) Myocardial infarction and stroke — eosinophil degranulation contributes to reperfusion injury and eosinophilia peaks 24–48 hours after myocardial necrosis

Q21. After intense anaerobic exercise, oxygen consumption remains elevated above resting levels for a period — a phenomenon called excess post-exercise oxygen consumption (EPOC), or 'oxygen debt'. The diagram below illustrates the oxygen uptake curve during and after exercise. Which statement **best explains** the physiological basis of EPOC?



(A) EPOC occurs solely because elevated body temperature after exercise increases the basal metabolic rate; once the body cools to 37°C, oxygen consumption returns to rest immediately

(B) EPOC is caused by continued lactic acid production during recovery — the muscles continue anaerobic glycolysis for up to 2 hours after exercise ceases, requiring sustained oxygen delivery to drive this process

(C) Replenishment of ATP and creatine phosphate stores, oxidative conversion of accumulated lactate back to pyruvate/glucose (Cori cycle), restoration of myoglobin and haemoglobin O_2, and elevated body temperature/metabolism all contribute to EPOC

(D) EPOC is entirely accounted for by increased cardiac output during recovery; the heart's elevated work consumes extra oxygen while peripheral tissues are already at rest

Q22. Cells continuously move ions, nutrients, and waste products across their membranes. What is the **fundamental difference** between active transport and passive transport?

(A) Active transport moves substances against their electrochemical gradient and requires energy (ATP or ion gradients), whereas passive transport (diffusion, facilitated diffusion, osmosis) moves substances down their gradient without energy expenditure

(B) Active transport uses protein carriers while passive transport occurs only through lipid bilayer dissolution; no ion channels are involved in either form of passive transport

(C) Active transport is restricted to the apical membrane of epithelial cells, whereas passive transport occurs only at the basolateral membrane, giving directional (vectorial) transport

(D) Active transport requires a voltage difference across the membrane, while passive transport is driven solely by concentration differences; both can move solutes in either direction depending on conditions

Q23. Thyroid hormones (T_3 and T_4) regulate the metabolic rate of virtually all body cells. Which set of features is **characteristic of hypothyroidism**?

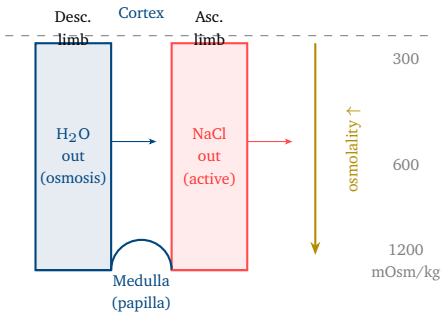
(A) Increased basal metabolic rate, weight loss, tachycardia, heat intolerance, diarrhoea, fine tremor, and exophthalmos — the constellation of hyperthyroidism (thyrotoxicosis)

(B) Increased sweating, warm moist skin, anxiety, proximal muscle weakness, and suppressed TSH — these are signs of excess thyroid hormone activity

(C) Elevated calcium, polyuria, nephrolithiasis, bone pain, and constipation — the clinical features of primary hyperparathyroidism, not thyroid disease

(D) Decreased basal metabolic rate (BMR), weight gain, bradycardia, cold intolerance, constipation, dry skin, fatigue, elevated TSH (primary hypothyroidism) — the opposite of hyperthyroidism; myxoedema is severe hypothyroidism with non-pitting oedema

Q24. The kidney generates a hyperosmotic medullary interstitium essential for producing concentrated urine. The diagram below shows the loop of Henle and the medullary osmotic gradient. Which statement **best describes** the countercurrent multiplier mechanism?



(A) The loop of Henle functions as a countercurrent exchanger (like the vasa recta) in which osmolality is uniform throughout its length; the gradient is established by active urea secretion in the descending limb, not NaCl transport

(B) The countercurrent multiplier mechanism — the descending limb is permeable to water (osmotic water loss) but not NaCl; the ascending limb actively transports NaCl out (impermeable to water), building a hyperosmotic medullary interstitium ($\sim$1200 mOsm/kg at papilla) that drives water reabsorption from the collecting duct when ADH is present

(C) The ascending limb reabsorbs water and the descending limb secretes NaCl; together they dilute the medullary interstitium to create a hypo-osmotic environment that forces passive urea retention in the papilla

(D) Both limbs of the loop of Henle are equally permeable to water and NaCl; the medullary gradient is established solely by active H^+ secretion in the collecting duct under aldosterone control

Q25. Cyclic AMP (cAMP) is a ubiquitous second messenger that mediates the intracellular effects of many hormones and neurotransmitters. Which enzyme **synthesises cAMP**, and how is it activated?

(A) Phosphodiesterase (PDE) — this enzyme converts ATP to cAMP in response to G_s-coupled receptor activation; it is inhibited by caffeine and theophylline, which thereby raise intracellular cAMP levels

(B) Adenylyl cyclase (adenylate cyclase) — located on the inner plasma membrane, it catalyses conversion of ATP to cAMP when activated by G_s-coupled receptors (e.g., beta-adrenergic receptors, glucagon receptors, TSH receptor); cAMP then activates PKA to phosphorylate target proteins

(C) Guanylyl cyclase — this membrane-bound enzyme converts GTP to cGMP (not cAMP) in response to nitric oxide and atrial natriuretic peptide; cAMP is synthesised by a different enzyme

(D) Protein kinase A (PKA) — this enzyme both synthesises cAMP from ATP and propagates the second-messenger signal by auto-phosphorylation of its regulatory subunits

Answer Key — Physiology Sample Paper 9

1	C	2	A	3	A	4	B	5	A
6	A	7	D	8	D	9	A	10	D
11	C	12	D	13	B	14	C	15	D
16	C	17	B	18	C	19	A	20	B
21	C	22	A	23	D	24	B	25	B

Detailed Solutions

Solution

Q1. (C) Albumin generates ∼25 mmHg of oncotic pressure

Albumin (MW ≈ 67 kDa) constitutes ≈60% of total plasma protein (3.5–5 g/dL normal) and is responsible for ≈75% of plasma colloid osmotic (oncotic) pressure (≈25–28 mmHg total). This oncotic pressure opposes the hydrostatic pressure driving fluid out of capillaries, keeping fluid in the intravascular space (Starling forces). In *hypoalbuminaemia* (liver disease, malnutrition, nephrotic syndrome, protein-losing enteropathy), oncotic pressure falls and fluid accumulates in the interstitium, causing pitting oedema. Fibrinogen and globulins contribute minimally to oncotic pressure due to their large size and lower molar concentrations. Transferrin is present in trace amounts.

Solution

Q2. (A) Haematocrit is the primary determinant of blood viscosity

Blood viscosity (normal ≈ 3–4 mPa·s, about 3–4× water) is determined primarily by **haematocrit** (Hct, normal 40–54% men, 37–47% women). Each 10% rise in Hct roughly doubles viscosity. *Polycythaemia* (Hct >55%) dramatically increases viscosity, raising peripheral resistance and cardiac workload; risk of thrombosis. *Anaemia* decreases viscosity, reducing afterload — a compensatory benefit. Plasma proteins (especially fibrinogen) contribute secondarily. Temperature affects viscosity (blood is more viscous when cold) but is not the primary determinant under physiological conditions.

Solution

Q3. (A) Diastole — coronary perfusion occurs primarily during diastole

Unlike most organs perfused during systole, the **left coronary circulation** fills predominantly during **diastole**. During systole, myocardial contraction compresses intramyocardial vessels, especially in the subendocardium, impeding flow. When the myocardium relaxes in diastole, extravascular compression is relieved and coronary resistance drops, allowing perfusion. The right coronary artery has some systolic flow because right ventricular pressures are lower. Clinical implication: *tachycardia* shortens diastole disproportionately more than systole, reducing coronary filling time and oxygen supply — relevant in angina and critical in coronary artery disease.

Solution

Q4. (B) ADH released from posterior pituitary; acts via AQP-2

ADH (arginine vasopressin) is synthesised in the *hypothalamus* (supraoptic and paraventricular nuclei) and stored/released from the **posterior pituitary**. Two stimuli trigger release: (1) rising plasma osmolality (>285–295 mOsm/kg), detected by hypothalamic osmoreceptors; (2) falling blood volume (>10% loss) or pressure, detected by low-pressure (atrial) and arterial baroreceptors. ADH binds **V2 receptors** on collecting duct principal cells → cAMP → PKA → phosphorylation of **aquaporin-2 (AQP2)** vesicles → insertion into apical membrane → water reabsorption. Syndrome of inappropriate ADH secretion (SIADH) causes hyponatraemia; diabetes insipidus (central or nephrogenic) causes dilute polyuria.

Solution

Q5. (A) Decreased arterial P_{O_2} (hypoxaemia) — primary peripheral chemoreceptor stimulus

Peripheral chemoreceptors (carotid bodies at the carotid bifurcation; aortic bodies near the aortic arch) contain glomus (type I) cells that are exquisitely sensitive to *decreased arterial* P_{O_2}. They are significantly stimulated when P

Solution

Q6. (A) Intracellular digestion — lysosomes contain acid hydrolases

Lysosomes are membrane-bound organelles (0.1–1 μm) containing >60 hydrolytic enzymes (acid hydrolases) active at pH ≈4.5–5.0, maintained by V-type H^+-ATPases. Their functions: *autophagy* (digestion of damaged organelles, e.g., mitochondria via mitophagy), *heterophagy* (digestion of phagocytosed bacteria, e.g., in macrophages and neutrophils), and receptor-mediated endocytosis. When lysosomal enzyme genes are mutated, undegraded substrates accumulate, causing **lysosomal storage diseases**: Gaucher's (glucocerebrosidase), Tay-Sachs (hexosaminidase A), Pompe's (acid maltase/GAA). The lysosomal membrane protects the cytoplasm from these destructive enzymes.

Solution

Q7. (D) Phase 4 pacemaker potential driven by I_f, $I_{Ca\text{-}T}$, and decreasing I_K

SA node cells lack a stable resting potential. During **Phase 4** (diastolic depolarisation), three ionic currents drive spontaneous depolarisation toward threshold (≈ -40 mV): (1) the **funny current I_f** — carried by HCN (hyperpolarisation-activated cyclic nucleotide-gated) channels opening at -60 to -70 mV, allowing mixed Na^+/K^+ inward current; (2) **$I_{Ca\text{-}T}$** — transient T-type Ca^{2+} current activated near threshold; (3) progressive decay of I_K (outward K^+ current). Once threshold is reached, **L-type Ca^{2+} channels** (not fast Na^+ channels as in ventricular muscle) drive the upstroke (Phase 0). Ivabradine selectively blocks I_f to slow heart rate — used in heart failure and stable angina.

Solution

Q8. (D) Tight junctions between brain capillary endothelial cells form the BBB

The **blood-brain barrier** is formed structurally by: (1) *Tight junctions* (claudin-5, occludin, ZO-1) between adjacent cerebral endothelial cells — these eliminate paracellular pathways, the major route of entry in systemic capillaries; (2) *Pericytes* ensheathing capillaries and regulating permeability; (3) *Astrocyte end-feet* covering ∼99% of capillary surface and inducing/maintaining barrier properties. Lipid-soluble substances (O_2, CO_2, ethanol, anaesthetic agents, many drugs) diffuse freely. Polar/large molecules (antibiotics, chemotherapy) have poor CNS penetration. Specific nutrients (glucose via GLUT1, amino acids) use dedicated transporters. The BBB is disrupted in meningitis, tumours, and stroke (vasogenic oedema).

Solution

Q9. (A) Renin cleaves angiotensinogen to angiotensin I

Renin is released from juxtaglomerular (JG) cells of the afferent arteriole in response to: (1) decreased renal perfusion pressure (baroreceptor mechanism); (2) decreased NaCl delivery to the macula densa; (3) sympathetic stimulation (β_1 receptors on JG cells). Renin is an **aspartyl protease** that cleaves the Leu–Val bond of *angiotensinogen* (a 452-amino-acid α_2-globulin synthesised in the liver) to release **angiotensin I** (10-amino-acid decapeptide). Angiotensin-converting enzyme (ACE), mainly in pulmonary endothelium, cleaves two C-terminal amino acids to yield **angiotensin II** (8-mer) — the potent vasoconstrictor and aldosterone secretagogue. ACE inhibitors block this step; ARBs block angiotensin II at its receptor.

Solution

Q10. (D) Repetitive pharyngeal collapse during sleep — the mechanism of OSA

In **obstructive sleep apnoea**, sleep-related muscle atonia reduces tone in pharyngeal dilator muscles (genioglossus, tensor palatini). The resulting upper airway instability causes repetitive collapse of the oropharynx, producing apnoeic episodes ($>$10 seconds cessation of airflow). Each episode causes: progressive O_2 desaturation (SpO_2 may fall below 80%), CO_2 accumulation, arousal from sleep (fragmented sleep architecture), and sympathetic surges. Chronic consequences: systemic hypertension, pulmonary hypertension, atrial fibrillation, daytime somnolence, cognitive impairment. Risk factors: obesity (fat deposition around pharynx), retrognathia, macroglossia, large tonsils, neck circumference $>$40 cm. Treatment: CPAP (gold standard), mandibular advancement, surgery.

Solution

Q11. (C) Precentral gyrus of the frontal lobe — primary motor cortex

The **primary motor cortex** (Brodmann area 4) lies in the *precentral gyrus*, anterior to the central sulcus. It contains the **giant pyramidal (Betz) cells** whose axons form the *corticospinal (pyramidal) tract*, descending through the internal capsule and pyramids to synapse on lower motor neurons in the spinal cord. The body is represented **somatotopically** (the motor homunculus): face/tongue/hand have disproportionately large representations (fine motor control); trunk and lower limb occupy the medial surface (supplied by anterior cerebral artery). Lesions cause contralateral spastic paralysis (upper motor neuron signs: spasticity, hyperreflexia, Babinski sign). The *postcentral gyrus* (parietal lobe) = primary somatosensory cortex.

Solution

Q12. (D) Free nerve endings — nociceptors detecting pain

Nociceptors are high-threshold sensory receptors that detect potentially harmful stimuli. They are morphologically **free nerve endings** — bare, unmyelinated (C-fibres, slow dull aching pain) or thinly myelinated (Aδ-fibres, sharp fast pain) terminals distributed throughout skin, muscles, joints, and viscera. They are activated by: (1) *thermal stimuli* ($>$43°C or $<$15°C via TRPV1/TRPM8 channels); (2) *mechanical stimuli* (high threshold, membrane deformation); (3) *chemical mediators* of tissue injury: bradykinin (most potent), prostaglandins (sensitise rather than directly activate, explaining analgesic effect of NSAIDs), H^+, K^+, ATP, histamine, substance P, capsaicin (via TRPV1). Meissner's and Pacinian corpuscles detect touch/vibration, not pain.

Solution

Q13. (B) Placenta (syncytiotrophoblast) — site of maternal-fetal gas exchange

The **placenta** is the functional organ of gas exchange, nutrition, and waste elimination for the fetus. In the chorionic villi, the **syncytiotrophoblast** (a continuous multinucleate layer) separates maternal blood (in intervillous spaces) from fetal capillary blood. O_2 and CO_2 cross by simple diffusion driven by partial pressure gradients. **HbF** ($\alpha_2\gamma_2$) has *higher O_2 affinity* than HbA ($\alpha_2\beta_2$) because γ-chains bind 2,3-DPG less avidly — the fetal curve is shifted *left*, enabling O_2 uptake at the lower P_{O_2} of the placenta. Additionally, the *double Bohr effect* enhances transfer: CO_2 from the fetus acidifies maternal blood (rightward shift, O_2 release) while fetal blood is alkalinised (leftward shift, O_2 binding).

Solution

Q14. (C) Bicarbonate buffer system — most important physiological extracellular buffer

The **HCO_3^-/CO_2 buffer system** ($H^+ + HCO_3^- \rightleftharpoons H_2CO_3 \rightleftharpoons CO_2 + H_2O$, pKa = 6.1) is paradoxically the most important extracellular buffer despite its pKa being far from physiological pH (7.4). Its power lies in the regulatory integration: the *lungs* rapidly adjust P_{aCO_2} (minutes), and the *kidneys* adjust HCO_3^- (hours to days) — making both components of the buffer independently regulable (open system). By Henderson-Hasselbalch: $pH = 6.1 + \log([HCO_3^-]/[H_2CO_3]) = 6.1 + \log(24/1.2) = 7.4$. The phosphate and protein buffers are important intracellularly and in urine but have limited extracellular buffering capacity. Ammonia is a renal urinary buffer, not a plasma buffer.

Solution

Q15. (D) Absolute refractory period makes cardiac tetany impossible

Ventricular muscle has an **absolute refractory period (ARP)** of ≈200–250 ms, attributable to the prolonged **plateau (Phase 2)** of the cardiac action potential maintained by sustained L-type Ca^{2+} channel opening and balanced K^+ efflux. During the ARP, fast Na^+ channels remain inactivated (h-gates closed) and no new action potential can be triggered regardless of stimulus strength. Since the ARP extends through almost the entirety of mechanical systole (≈300 ms), the heart *cannot undergo tetanic contraction* — unlike skeletal muscle whose ARP is ∼1–2 ms (much shorter than twitch duration). This ensures complete relaxation and diastolic filling between every beat. The *relative refractory period* follows (partially recovered Na^+ channels), during which a suprathreshold stimulus can trigger an *extrasystole* (premature beat) followed by a compensatory pause.

Solution

Q16. (C) Laplace's law: dilated ventricle requires greater wall tension

Laplace's law for a thick-walled sphere: $T = \dfrac{P \times r}{2h}$, where T = wall tension, P = transmural pressure, r = inner radius, h = wall thickness. In a **dilated cardiomyopathy**: r increases (and h may decrease relative to r), so *wall tension rises* for any given pressure. Since myocardial oxygen consumption is proportional to tension development (Fenn effect/tension-time index), the dilated heart must expend more energy per unit pressure generated — a *vicious cycle*: dilation → increased wall stress → increased O_2 demand → ischaemia → further dilation. Laplace's law also explains why: (a) alveoli of different sizes would collapse (smaller alveoli, lower T; mitigated by surfactant); (b) aortic aneurysms expand progressively; (c) ventricular hypertrophy (increased h) partially normalises wall stress.

Solution

Q17. (B) P50 ≈ 26–27 mmHg under standard physiological conditions

The **P50** is the P_{O_2} at which haemoglobin is 50% saturated — a measure of O_2 affinity (lower P50 = higher affinity = leftward shift; higher P50 = lower affinity = rightward shift). Under standard conditions (pH 7.4, 37°C, P_{CO_2} 40 mmHg, normal 2,3-DPG), P50 ≈ **26–27 mmHg**. *Rightward shifts* (higher P50, lower affinity, facilitates O_2 *unloading* to tissues): increased temperature, CO_2, H^+ (Bohr effect), 2,3-DPG (binds β-chains, stabilises deoxy form), altitude (chronic, via increased 2,3-DPG). *Leftward shifts* (lower P50, higher affinity, facilitates O_2 *loading*): HbF, CO poisoning, methaemoglobinaemia, hypothermia, alkalosis, low 2,3-DPG.

Solution

Q18. (C) Phenylalanine hydroxylase deficiency causes PKU

Classical PKU (incidence $\approx$ 1:10 000–15 000, autosomal recessive, PAH gene on chromosome 12q) results from deficiency of **phenylalanine hydroxylase (PAH)**, which normally catalyses: phenylalanine + O_2 + tetrahydrobiopterin (BH4) $\rightarrow$ tyrosine + BH2 + H_2O. Accumulated phenylalanine is transaminated to **phenylpyruvate** (phenylketone, excreted in urine — Guthrie test/tandem MS at birth), phenyllactate, and phenylacetate (musty odour). Excess phenylalanine competitively inhibits transport of other large neutral amino acids across the BBB, impairing neurotransmitter synthesis $\rightarrow$ intellectual disability, seizures, microcephaly, fair hair/skin/eyes (tyrosine needed for melanin). Treatment: phenylalanine-restricted diet (phenylalanine is essential — must not eliminate entirely) $\pm$ BH4 (sapropterin) for responsive mutations.

Solution

Q19. (A) Facilitated diffusion via GLUT4 — insulin-stimulated glucose uptake

Glucose enters cells by **facilitated diffusion** (no ATP required, down concentration gradient) via GLUT (glucose transporter) family proteins. **GLUT4** is the insulin-sensitive transporter expressed in *skeletal muscle*, *cardiac muscle*, and *adipose tissue* — the major insulin-responsive tissues. In the basal (fasting) state, GLUT4-containing vesicles are sequestered intracellularly. Insulin binds its tyrosine kinase receptor $\rightarrow$ IRS-1 phosphorylation $\rightarrow$ PI3K $\rightarrow$ PIP3 $\rightarrow$ Akt/PKB $\rightarrow$ phosphorylation of AS160/TBC1D4 $\rightarrow$ GLUT4 vesicle translocation to and fusion with the plasma membrane $\rightarrow$ rapid glucose influx. This explains why insulin-resistant states (type 2 diabetes) impair glucose uptake despite elevated plasma glucose. GLUT1 (brain, RBCs) and GLUT2 (liver, pancreatic β-cells) are constitutively expressed; SGLT is used in the kidney/gut (active cotransport, not insulin-regulated).

Solution

Q20. (B) Eosinophilia in allergic conditions and parasitic infections

Eosinophils (normal 1–4% of WBC, 100–400 cells/μL) are distinguished by large red-staining granules containing: *major basic protein* (MBP), *eosinophil cationic protein* (ECP), *eosinophil peroxidase* (EPO), and *eosinophil-derived neurotoxin*. These toxic granule contents kill parasites (especially helminth larvae too large to phagocytose) by membrane disruption. Eosinophilia ($>0.5\times10^9$/L) is classically caused by: (1) *Allergic/atopic disease* — IgE-mediated (asthma, allergic rhinitis, eczema, food allergy): eosinophils are recruited by IL-5, eotaxin; (2) *Parasitic infections* — tissue-invasive helminths (Ascaris, Toxocara, Strongyloides, Schistosoma, filaria); (3) Drug hypersensitivity; (4) Eosinophilic granulomatosis with polyangiitis (Churg-Strauss). Mnemonic: **NAACP** — Neoplasm, Addison's, Allergy, Collagen vascular disease, Parasites.

Solution

Q21. (C) EPOC: multiple physiological processes restore homeostasis after anaerobic exercise

Excess post-exercise oxygen consumption (EPOC), originally termed 'oxygen debt' (Hill, 1923), persists because several processes require oxygen after exercise ceases: (1) **Restoration of ATP and phosphocreatine stores** (≈50% of O_2 debt) — creatine kinase re-phosphorylates creatine using ATP from aerobic metabolism; (2) **Lactate clearance** — accumulated lactate is oxidised to pyruvate and CO_2 in the heart and slow-twitch fibres, or converted to glucose by the liver (Cori cycle); (3) **Restoration of O_2 stores** — myoglobin and haemoglobin replenishment; (4) **Elevated temperature** — higher BMR as long as core temperature is raised; (5) **Elevated circulating catecholamines** — adrenaline/noradrenaline continue to stimulate metabolism until cleared. EPOC magnitude correlates with exercise intensity and duration.

Solution

Q22. (A) Active vs passive transport: energy requirement and gradient direction

Passive transport (simple diffusion, facilitated diffusion via channels/carriers, osmosis) moves substances *down* their electrochemical gradient — no metabolic energy consumed; direction is thermodynamically spontaneous. **Active transport** moves substances *against* their gradient — requires energy input: *primary active transport* uses ATP directly (Na^+/K^+-ATPase, Ca^{2+}-ATPase, H^+/K^+-ATPase); *secondary active transport* harnesses ion gradients established by primary pumps (SGLT1/2, Na^+-amino acid co-transporters). Key examples: Na^+/K^+-ATPase maintains low intracellular Na^+ (active); GLUT4 moves glucose into muscle cells (passive, facilitated); Na^+/glucose SGLT moves glucose into gut/kidney epithelium (secondary active). Active transport can occur at apical or basolateral membranes; passive transport occurs wherever a gradient exists.

Solution

Q23. (D) Hypothyroidism: decreased BMR, weight gain, bradycardia, cold intolerance

Thyroid hormones (T_3 > T_4 in potency) act on nuclear receptors to increase expression of Na^+/K^+-ATPase and thermogenic proteins, raising BMR. In **primary hypothyroidism** (most commonly Hashimoto's thyroiditis in iodine-replete regions, or iodine deficiency globally): TSH rises (negative feedback loss), T_3/T_4 fall. Clinical features: *decreased BMR* (fatigue, weight gain despite poor appetite, cold intolerance), *cardiovascular* (bradycardia, diastolic hypertension, prolonged QT, pericardial effusion), *GI* (constipation, delayed relaxation of ankle reflexes), *skin* (dry, coarse hair, hair loss, non-pitting oedema/myxoedema), *neurological* (cognitive slowing, depression, carpal tunnel syndrome, cerebellar ataxia). Cretinism = congenital hypothyroidism causing irreversible intellectual disability if untreated. Treatment: levothyroxine (T_4).

Solution

Q24. (B) Countercurrent multiplier: descending (H_2O permeable) + ascending (NaCl active transport)

The **countercurrent multiplier** in the loop of Henle creates a corticomedullary osmotic gradient (≈300 mOsm/kg cortex → ∼1200 mOsm/kg papilla): (1) **Descending limb** (thin, H_2O permeable, impermeable to NaCl): tubular fluid equilibrates osmotically with the hypertonic medullary interstitium — water leaves by osmosis, concentrating the tubular fluid. (2) **Ascending limb** (thick, impermeable to water): **Na^+-K^+-$2Cl^-$ cotransporter (NKCC2)** actively reabsorbs NaCl without water, progressively diluting tubular fluid while hyperosmolarity is maintained in the interstitium. The descending limb flows counter-currently to the ascending limb — each pass 'multiplies' the small single-effect into a large gradient. The *vasa recta* (countercurrent exchanger) preserves the gradient by equilibrating slowly without washing it out. ADH then enables water reabsorption from the collecting duct into this hyperosmotic interstitium, producing concentrated urine. Loop diuretics (furosemide) block NKCC2, abolishing the gradient.

Solution

Q25. (B) Adenylyl cyclase synthesises cAMP from ATP

Adenylyl cyclase (also called adenylate cyclase) is a transmembrane enzyme with 12 transmembrane domains and a cytoplasmic catalytic domain. It catalyses: ATP $\xrightarrow{\text{adenylyl cyclase}}$ cAMP + PP_i. It is activated when **G**α_s (from G_s-coupled receptors) dissociates and binds the catalytic domain. Key G_s-coupled receptors: β_1/β_2-adrenergic, glucagon, TSH, PTH, ACTH, FSH, LH, D1/D5 dopamine, H2 histamine. cAMP activates **protein kinase A (PKA)**, which phosphorylates diverse targets (phosphorylase kinase, CREB, cardiac ion channels, etc.). cAMP is rapidly degraded by **phosphodiesterase (PDE)** to 5'-AMP — inhibited by caffeine, theophylline, sildenafil. G_i-coupled receptors (α_2, M2, D2, opioid) inhibit adenylyl cyclase. Guanylyl cyclase produces cGMP (not cAMP) in response to NO or ANP.