FMGE Pharmacology Sample Paper – 1

Duration: 60 Minutes **Maximum Marks: 40**

Instructions

- This paper contains **40 Multiple Choice Questions** modelled on the **Pharmacology** section of FMGE.
- Each correct answer carries **+1 mark**. There is **no negative marking** – attempt all questions.
- Questions follow the clinically integrated pattern of the FMGE examination.
- Click a question number in the answer key to navigate to its solution.

FMGE Pharmacology – Q1 to Q40

Q1. A 45-year-old patient is prescribed an oral medication but achieves only 15% systemic bioavailability despite complete absorption from the gut. The drug is known to be extensively metabolised in the liver before reaching systemic circulation. Which of the following best explains this low bioavailability?

(A) Extensive first-pass hepatic metabolism reduces the fraction of absorbed drug reaching systemic circulation

(B) Rapid renal clearance eliminates the drug before it can achieve therapeutic concentrations

(C) High degree of plasma protein binding sequesters the drug and prevents distribution

(D) Very large volume of distribution causes the drug to be rapidly redistributed into peripheral tissues

Q2. A drug is administered intravenously as a 500 mg bolus dose. The initial plasma concentration (C_0) measured immediately after distribution

equilibrium is 0.5 mg/L. What does the very large apparent volume of distribution (Vd) calculated from this data indicate?

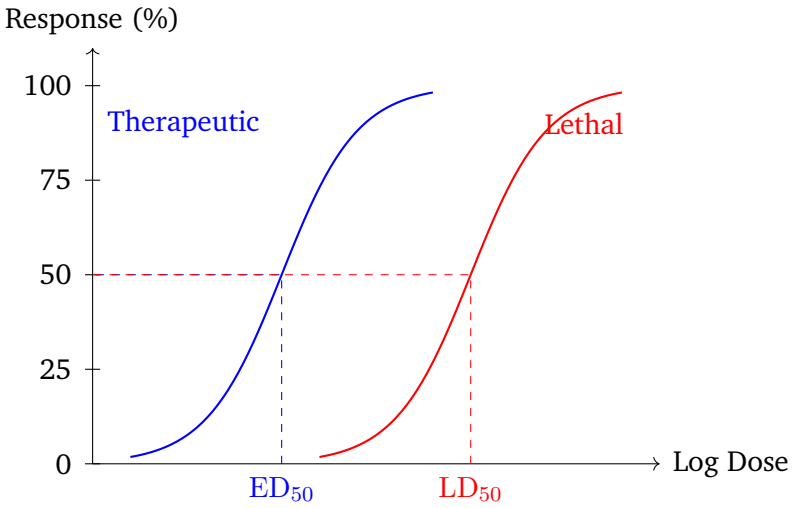
(A) The drug is extensively bound to plasma proteins and remains confined to the vascular compartment

(B) The drug is widely distributed into peripheral tissues and has low plasma concentrations relative to dose

(C) The drug undergoes rapid renal excretion leading to low plasma concentrations

(D) The drug has poor absorption resulting in low systemic availability

Q3. The following dose-response curves are obtained for a new analgesic drug in an animal study:



Based on the curves shown above, the therapeutic index of this drug is calculated as:

(A) ED_{50}/LD_{50}

(B) $LD_{50} \times ED_{50}$

(C) LD_{50}/ED_{50}

(D) LD_{99}/ED_{01}

Q4. A 28-year-old woman on oral contraceptive pills (OCPs) is started on rifampicin for pulmonary tuberculosis. She becomes pregnant three months

later. Which of the following statements about enzyme induction best explains this outcome?

(A) Enzyme induction decreases drug metabolism and raises plasma levels of co-administered drugs

(B) Enzyme induction occurs rapidly within hours of starting the inducing agent

(C) Enzyme induction reduces renal drug excretion, leading to drug accumulation

(D) Enzyme induction increases CYP450 enzyme activity, accelerating metabolism of co-administered drugs and reducing their plasma levels

Q5. A 62-year-old man is diagnosed with primary open-angle glaucoma. He is started on a miotic eye drop that acts as a direct muscarinic agonist and reduces intraocular pressure by increasing aqueous humour outflow through the trabecular meshwork via ciliary muscle contraction. Which drug is being described?

(A) Pilocarpine

(B) Timolol

(C) Latanoprost

(D) Acetazolamide

Q6. A 4-year-old child is brought to the emergency department with flushing, dry mouth, urinary retention, mydriasis, hyperthermia, and altered sensorium after accidentally ingesting tablets from the bedside table. The classic mnemonic for anticholinergic toxidrome applies. Which of the following is NOT a feature of atropine (anticholinergic) toxicity?

(A) Dry flushed skin and hyperthermia

(B) Diarrhoea

(C) Urinary retention and constipation

(D) Tachycardia and mydriasis

Q7. A 55-year-old hypertensive patient with a history of mild asthma is prescribed propranolol. Two days later, he presents with acute breathlessness and wheezing. Which of the following best explains this adverse effect of propranolol?

(A) Propranolol stimulates α_1 receptors in bronchial smooth muscle causing constriction

(B) Propranolol inhibits β_1 receptors in the myocardium causing reduced cardiac output and pulmonary oedema

(C) Propranolol blocks β_2 receptors in bronchial smooth muscle, removing the bronchodilatory tone and causing bronchoconstriction

(D) Propranolol releases histamine from mast cells triggering an allergic bronchoconstriction

Q8. A 68-year-old man with benign prostatic hyperplasia (BPH) and hypertension is started on prazosin. The next morning, he experiences severe dizziness and falls when getting up from bed. Which of the following correctly describes the mechanism underlying this adverse effect?

(A) Prazosin blocks β_1 receptors in the heart, causing excessive bradycardia and reduced cardiac output

(B) Prazosin stimulates central α_2 receptors, reducing sympathetic outflow and heart rate

(C) Prazosin inhibits angiotensin-converting enzyme, causing vasodilation and reflex tachycardia

(D) Prazosin blocks α_1 receptors in peripheral vasculature causing vasodilation; the first dose produces exaggerated postural hypotension

Q9. A 32-year-old woman presents with ptosis, diplopia, and fatigable proximal muscle weakness. She is diagnosed with myasthenia gravis. Neostigmine is started for symptomatic management. What is the mechanism of action of neostigmine?

(A) Reversible inhibition of acetylcholinesterase at the neuromuscular

junction, increasing the concentration and duration of action of acetylcholine

(B) Direct stimulation of nicotinic receptors at the neuromuscular junction, mimicking acetylcholine

(C) Irreversible inhibition of acetylcholinesterase leading to prolonged depolarization

(D) Release of acetylcholine from presynaptic terminals at the neuromuscular junction

Q10. A 40-year-old patient undergoing elective laparoscopic cholecystectomy receives succinylcholine for rapid sequence intubation. The anaesthetist notes initial muscle fasciculations before paralysis. Which of the following statements about succinylcholine is NOT correct?

(A) It causes initial muscle fasciculations due to depolarization of the motor end plate

(B) Its neuromuscular blockade is reliably reversed by neostigmine administration

(C) It is contraindicated in patients with extensive burns due to risk of life-threatening hyperkalaemia

(D) Prolonged exposure may lead to a Phase II (desensitization) block that resembles non-depolarizing blockade

Q11. A 58-year-old patient with advanced cancer is prescribed morphine for severe pain. During review, the medical team lists the expected pharmacological effects of morphine. Which of the following is NOT produced by morphine?

(A) Respiratory depression and reduced tidal volume

(B) Miosis (pupillary constriction) due to stimulation of the Edinger-Westphal nucleus

(C) Tachycardia and increased cardiac output

(D) Nausea, vomiting, and constipation due to action on gastrointestinal opioid receptors

Q12. A 35-year-old patient with generalised anxiety disorder is prescribed diazepam. The pharmacologist explains that benzodiazepines enhance GABA-A receptor-mediated inhibition. Which of the following correctly describes the molecular mechanism of benzodiazepines at GABA-A receptors?

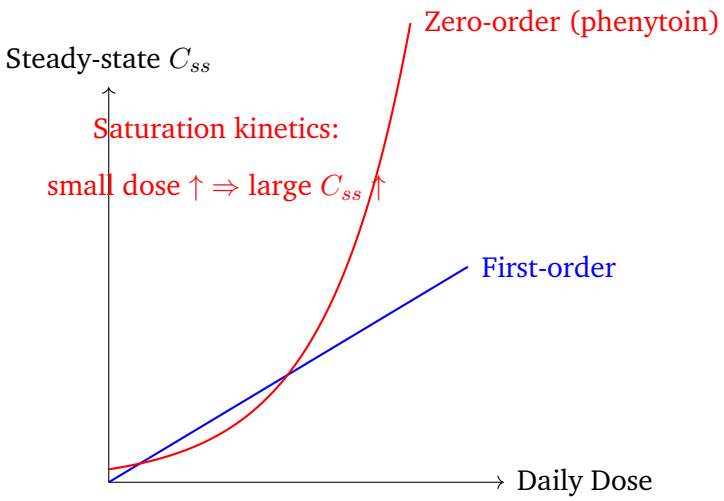
(A) They directly open Cl^- channels in the absence of GABA, producing inhibition

(B) They bind to the GABA recognition site and act as full agonists

(C) They prolong the duration of Cl^- channel opening per burst, similar to barbiturates

(D) They increase the frequency of Cl^- channel opening in the presence of GABA, without affecting duration

Q13. A 28-year-old epileptic patient on phenytoin 300 mg/day has a serum level of 12 μg/mL (therapeutic). The dose is increased by 50 mg/day, and two weeks later the serum level has risen disproportionately to 28 μg/mL (toxic). The following diagram illustrates the relationship between dose and steady-state plasma levels:



The best explanation for this disproportionate rise in phenytoin levels is:

(A) Phenytoin shows saturation (zero-order, Michaelis-Menten) kinetics at therapeutic doses; a small dose increase saturates hepatic enzymes, causing a disproportionate rise in plasma levels

(B) Phenytoin undergoes extensive first-pass metabolism; any dose increase proportionally reduces bioavailability

(C) Phenytoin has a very large volume of distribution; increased dose is sequestered in tissues

(D) Phenytoin competes with albumin binding sites; the dose increase displaces protein-bound drug, raising free levels

Q14. A 24-year-old patient with schizophrenia is started on chlorpromazine. After three weeks, he develops rigidity, bradykinesia, and a mask-like face. These extrapyramidal side effects are primarily caused by blockade of which receptor?

(A) Muscarinic M1 receptors in the caudate nucleus

(B) D2 dopamine receptors in the nigrostriatal pathway

(C) Serotonin 5-HT2A receptors in the prefrontal cortex

(D) Histamine H1 receptors in the basal ganglia

Q15. A 70-year-old man with Parkinson's disease is prescribed levodopa-carbidopa combination. Prior to this, levodopa monotherapy caused severe nausea and postural hypotension at doses required for therapeutic effect. Why is carbidopa added to levodopa in this formulation?

(A) Carbidopa crosses the blood-brain barrier and inhibits central monoamine oxidase, preventing dopamine breakdown in the CNS

(B) Carbidopa acts as a dopamine agonist in the striatum, supplementing the effect of levodopa

(C) Carbidopa inhibits peripheral DOPA decarboxylase and does not cross the blood-brain barrier; this reduces peripheral conversion of levodopa to dopamine, decreasing side effects and increasing CNS delivery

(D) Carbidopa blocks the renal excretion of levodopa, prolonging its plasma half-life

Q16. During spinal anaesthesia with lignocaine, the anaesthetist explains that different nerve fibres are blocked in a predictable sequence depending on fibre size and myelination. Which nerve fibre type is blocked LAST (most resistant to local anaesthetic blockade)?

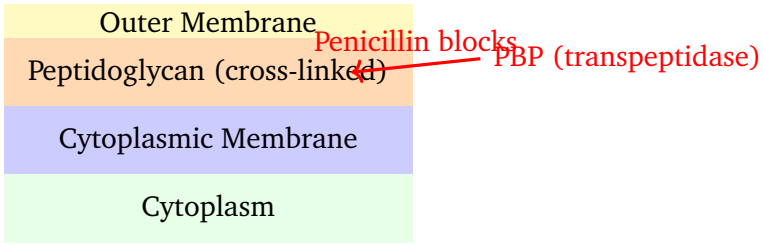
(A) C fibres (unmyelinated, pain and temperature)

(B) B fibres (preganglionic autonomic)

(C) A-delta fibres (myelinated, fast pain and temperature)

(D) A-alpha fibres (large myelinated motor fibres to skeletal muscle)

Q17. A 35-year-old patient with bacterial pneumonia is treated with benzylpenicillin. The diagram below illustrates the bacterial cell wall:



What is the primary mechanism of action of penicillin?

(A) Inhibition of transpeptidase (penicillin-binding proteins), preventing cross-linking of peptidoglycan strands in the bacterial cell wall

(B) Disruption of the cytoplasmic membrane, causing leakage of intracellular contents

(C) Inhibition of bacterial DNA gyrase, preventing DNA supercoiling required for replication

(D) Inhibition of the 30S ribosomal subunit, blocking protein synthesis

Q18. A patient with severe Gram-negative septicaemia is treated with gentamicin. The clinical pharmacist advises once-daily dosing to maximise efficacy and minimise toxicity. Which of the following statements about aminoglycosides is CORRECT?

(A) Aminoglycosides are bacteriostatic and their effect is time-dependent (efficacy depends on time above MIC)

(B) Aminoglycosides are concentration-dependent bactericidal agents; higher peak concentrations relative to MIC improve bacterial killing and justify once-daily dosing

(C) Aminoglycosides are well absorbed orally and can be used for systemic Gram-negative infections by the oral route

(D) Aminoglycosides primarily cause hepatotoxicity as their major dose-limiting adverse effect

Q19. A 7-year-old child with a Rickettsia infection is prescribed doxycycline for two weeks. The child's mother is concerned about long-term complications. What is the most significant complication of tetracycline use in children under 8 years of age?

(A) Nephrotoxicity due to accumulation of tetracycline in renal tubular cells

(B) Haemolytic anaemia due to oxidative stress on immature red blood cells

(C) Permanent discolouration and hypoplasia of developing teeth due to chelation of calcium in tooth enamel

(D) Hepatotoxicity due to fatty infiltration of the liver

Q20. A 30-year-old woman presents with dysuria, frequency, and pyuria. Urine culture grows *E. coli* sensitive to ciprofloxacin. She is prescribed a course of ciprofloxacin. What is the mechanism of action of ciprofloxacin?

(A) Inhibition of bacterial cell wall synthesis by blocking transpeptidase

(B) Inhibition of bacterial RNA polymerase, preventing mRNA synthesis

(C) Disruption of bacterial cell membrane integrity

(D) Inhibition of bacterial DNA gyrase (topoisomerase II) and topoisomerase IV, preventing DNA replication and repair

Q21. Metronidazole is being considered for several patients with different infections. For which of the following organisms is metronidazole NOT effective?

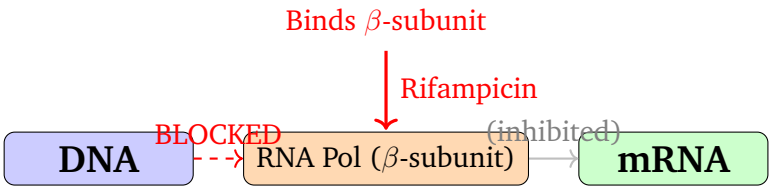
(A) Aerobic Gram-positive cocci (e.g., *Staphylococcus aureus*)

(B) *Trichomonas vaginalis*

(C) *Entamoeba histolytica*

(D) *Clostridium difficile* (pseudomembranous colitis)

Q22. A patient with sputum-positive pulmonary tuberculosis is started on rifampicin as part of RIPE therapy. The diagram below illustrates rifampicin's mechanism:



Which of the following correctly describes rifampicin's mechanism of action?

(A) It inhibits bacterial cell wall synthesis by blocking penicillin-binding proteins

(B) It inhibits bacterial DNA-dependent RNA polymerase by binding to the β-subunit, blocking mRNA synthesis

(C) It inhibits bacterial DNA gyrase, preventing DNA supercoiling

(D) It binds to the 50S ribosomal subunit, blocking peptide elongation

Q23. A 45-year-old HIV-positive patient with cryptococcal meningitis is treated with amphotericin B. After one week of therapy, his serum creatinine rises from 0.9 to 3.2 mg/dL. His physician explains that this is the most common dose-limiting toxicity of the drug. What is the mechanism of action of amphotericin B that explains its antifungal selectivity?

(A) It inhibits fungal DNA gyrase, which differs from the mammalian enzyme

(B) It blocks fungal cell wall synthesis by inhibiting β-glucan synthase

(C) It binds to ergosterol in the fungal cell membrane, forming pores that disrupt membrane integrity and cause leakage of cellular contents

(D) It inhibits fungal dihydropteroate synthase, blocking folate synthesis

Q24. A 22-year-old immunocompromised patient presents with herpes simplex encephalitis and is treated with intravenous acyclovir. The pharmacologist emphasises that acyclovir is selectively toxic to herpes-infected cells with minimal toxicity to normal host cells. What accounts for this selectivity?

(A) Acyclovir is actively transported into herpes-infected cells by a virus-encoded membrane transporter absent in normal cells

(B) Acyclovir selectively inhibits host cell RNA polymerase only in the presence of herpes virus

(C) Acyclovir irreversibly binds to herpes glycoproteins on the cell surface, preventing viral entry into uninfected cells

(D) Acyclovir is monophosphorylated to its active form exclusively by viral thymidine kinase (encoded by herpes virus) present only in infected cells, then further phosphorylated by host kinases to the active triphosphate that inhibits viral DNA polymerase

Q25. A traveller returning from a malaria-endemic region is diagnosed with *Plasmodium vivax* malaria and prescribed chloroquine. What is the primary mechanism by which chloroquine kills the malaria parasite?

(A) Prevention of heme polymerization (hemozoin formation) in the parasite's food vacuole, leading to accumulation of toxic free heme that kills the parasite

(B) Inhibition of dihydrofolate reductase in the parasite, blocking folate metabolism

(C) Disruption of the parasite's mitochondrial electron transport chain

(D) Alkylation of parasite DNA, preventing replication

Q26. Sulfamethoxazole is used in combination with trimethoprim for urinary tract infections. Sulfonamides are selectively toxic to bacteria but not

to mammalian cells. Which of the following best explains this selective toxicity?

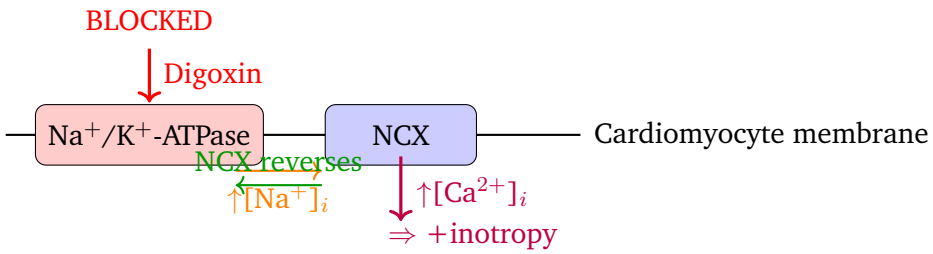
(A) Sulfonamides cannot penetrate mammalian cell membranes due to their large molecular size

(B) Bacteria must synthesise folate de novo from PABA and cannot utilise exogenous preformed folate; mammalian cells cannot synthesise folate and rely on dietary uptake, so they are unaffected by inhibition of folate synthesis

(C) Sulfonamides are inactivated by mammalian hepatic enzymes but remain active in bacterial cytoplasm

(D) Mammalian dihydropteroate synthase has a much higher affinity for sulfonamides than does the bacterial enzyme

Q27. A 72-year-old patient with chronic heart failure and atrial fibrillation is prescribed digoxin. The diagram below shows the mechanism of its positive inotropic effect:



What is the correct description of digoxin's mechanism of action?

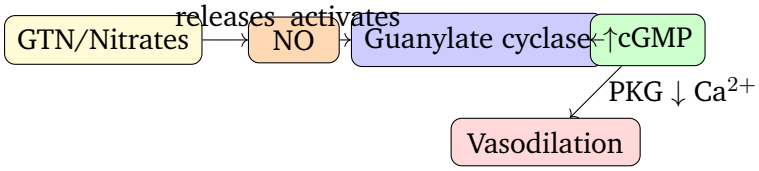
(A) Digoxin activates β_1 adrenergic receptors on cardiomyocytes, increasing intracellular cAMP and calcium

(B) Digoxin inhibits the Na^+/Ca^{2+} exchanger (NCX) directly, causing calcium accumulation

(C) Digoxin inhibits Na^+/K^+-ATPase, causing intracellular Na^+ accumulation; this reduces NCX activity (or reverses it), leading to increased intracellular Ca^{2+} and positive inotropy

(D) Digoxin opens L-type calcium channels directly, increasing calcium influx

Q28. A 60-year-old patient with stable angina uses sublingual glyceryl trinitrate (GTN) and gets relief within 2–3 minutes. The mechanism of nitrate action is shown below:



Regarding the haemodynamic effects of nitrates, which of the following is correct?

(A) Nitrates act primarily on arterioles, reducing systemic vascular resistance (afterload)

(B) Nitrates increase cardiac contractility by activating β_1 receptors

(C) Nitrates block L-type calcium channels in arterial smooth muscle

(D) Nitrates act primarily on venous capacitance vessels (venodilation), reducing venous return and preload, thereby decreasing cardiac work and myocardial oxygen demand

Q29. A 55-year-old woman with hypertension is started on hydrochlorothiazide. Routine blood tests after 6 weeks show elevated serum calcium (10.8 mg/dL). Which of the following metabolic effects is characteristically associated with thiazide diuretics and distinguishes them from loop diuretics?

(A) Hypercalcaemia due to enhanced calcium reabsorption in the distal convoluted tubule

(B) Hypocalcaemia due to increased urinary calcium excretion

(C) Hyperkalaemia due to impaired potassium excretion

(D) Hyperphosphataemia due to reduced renal phosphate excretion

Q30. A 58-year-old diabetic patient with hypertension and early diabetic nephropathy is prescribed ramipril. After 4 weeks, he develops a troublesome dry, persistent cough. Which of the following best explains this adverse effect of ACE inhibitors?

(A) ACE inhibitors block angiotensin II receptors in the bronchi, causing bronchoconstriction

(B) ACE inhibitors prevent the breakdown of bradykinin (which is normally degraded by ACE/kininase II); accumulated bradykinin stimulates sensory C-fibres in the airways, causing a dry cough

(C) ACE inhibitors increase prostaglandin synthesis in the lungs, irritating airway receptors

(D) ACE inhibitors reduce aldosterone, causing sodium and fluid retention in lung tissue

Q31. A 65-year-old patient with ischaemic heart disease is prescribed aspirin 100 mg daily for secondary prevention. At this low dose, what is the mechanism by which aspirin prevents platelet aggregation?

(A) Reversible inhibition of COX-2 in endothelial cells, reducing prostacyclin (PGI2) synthesis

(B) Competitive antagonism of ADP at the P2Y12 receptor on platelets

(C) Irreversible inhibition of COX-1 in platelets, preventing thromboxane A2 (TXA2) synthesis; since platelets lack nuclei, they cannot regenerate COX-1, resulting in prolonged antiplatelet effect

(D) Inhibition of thrombin by activating antithrombin III

Q32. A 52-year-old man with osteoarthritis and a history of peptic ulcer disease requires long-term NSAID therapy for joint pain management. He is at high risk of NSAID-induced GI complications. Which of the following is the most appropriate choice?

(A) Indomethacin – a potent non-selective NSAID with strong anti-inflammatory action

(B) Ibuprofen – widely available and well tolerated at low doses

(C) Naproxen – has a longer half-life allowing twice-daily dosing

(D) Celecoxib – a selective COX-2 inhibitor that spares COX-1-mediated gastric mucosal protection, significantly reducing the risk of peptic ulceration

Q33. A 28-year-old patient with severe bronchial asthma is treated with intravenous hydrocortisone. Corticosteroids provide broad anti-inflammatory action by reducing the synthesis of both prostaglandins and leukotrienes. What is the primary molecular mechanism underlying this effect?

(A) Induction of annexin-1 (lipocortin), which inhibits phospholipase A2, thereby reducing release of arachidonic acid and blocking both the COX and lipoxygenase pathways

(B) Direct inhibition of COX-1 and COX-2 enzymes, reducing prostaglandin synthesis

(C) Blockade of leukotriene receptors (CysLT1) on airway smooth muscle cells

(D) Inhibition of mast cell degranulation by stabilising the mast cell membrane

Q34. A 19-year-old type 1 diabetic patient presents in diabetic ketoacidosis (DKA) with blood glucose of 540 mg/dL, severe metabolic acidosis, and ketonuria. The treating physician decides to start an intravenous insulin infusion for acute management. Which insulin preparation is appropriate for intravenous administration in this setting?

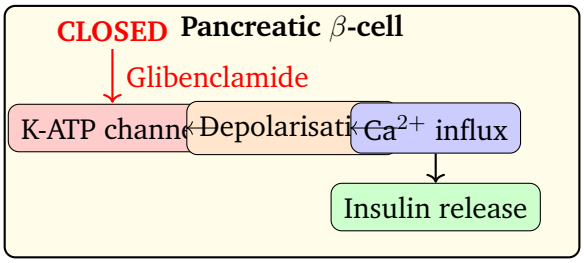
(A) Insulin glargine – long-acting, peakless insulin suitable for continuous infusion

(B) Regular (soluble) insulin – the only short-acting, clear insulin preparation suitable for intravenous infusion in acute settings such as DKA

(C) NPH insulin – intermediate-acting, can be given intravenously for faster onset

(D) Insulin lispro – rapid-acting insulin analogue used in insulin pumps

Q35. A 58-year-old patient with type 2 diabetes is prescribed glibenclamide. The drug causes an increase in insulin secretion from pancreatic β-cells. The following diagram illustrates the mechanism:



What is the mechanism of action of sulfonylureas such as glibenclamide?

(A) They activate PPAR-γ receptors in adipose tissue, increasing insulin sensitivity

(B) They inhibit hepatic gluconeogenesis by activating AMPK in hepatocytes

(C) They close ATP-sensitive K^+ channels in pancreatic β-cells, causing membrane depolarisation, Ca^{2+} influx, and subsequent insulin secretion

(D) They mimic GLP-1 by binding to GLP-1 receptors on β-cells, stimulating glucose-dependent insulin release

Q36. A 34-year-old woman with Graves' disease presents to the emergency department with hyperthermia (39.8°C), severe tachycardia, heart failure, and altered consciousness. She is diagnosed with thyroid storm. Among the antithyroid drugs, which is preferred in this acute situation, and why?

(A) Methimazole – because it acts more rapidly than PTU in blocking thyroid hormone synthesis

(B) Carbimazole – because it has fewer side effects than PTU and is preferred in all clinical settings

(C) Potassium iodide – because it immediately stops synthesis and release of thyroid hormones

(D) Propylthiouracil (PTU) – because in addition to blocking thyroid hormone synthesis, it also inhibits peripheral conversion of T4 to the more active T3 (by inhibiting type 1 deiodinase), rapidly lowering active hormone levels

Q37. A 45-year-old patient with erosive oesophagitis is prescribed omeprazole. The drug provides more effective and sustained acid suppression than H2-blockers. What is the mechanism of action of omeprazole?

(A) Irreversible inhibition of H^+/K^+-ATPase (the proton pump) on the luminal surface of gastric parietal cells, blocking the final common pathway of gastric acid secretion

(B) Competitive antagonism at histamine H2 receptors on parietal cells, reducing acid secretion

(C) Stimulation of prostaglandin synthesis in gastric mucosa, increasing mucus and bicarbonate secretion

(D) Neutralisation of gastric acid by acting as a weak base in the gastric lumen

Q38. A 19-year-old with acute severe asthma presents to the emergency room with breathlessness and wheeze. He is given nebulised salbutamol. What is the mechanism of action of salbutamol in relieving bronchoconstriction?

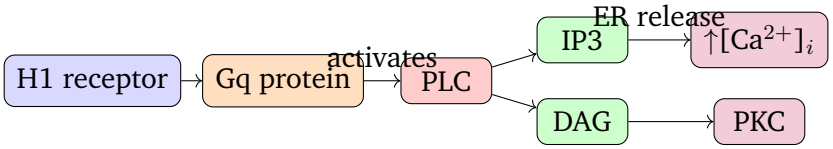
(A) Salbutamol antagonises muscarinic M3 receptors in airway smooth muscle, reducing parasympathetically mediated bronchoconstriction

(B) Salbutamol selectively stimulates β_2-adrenergic receptors in bronchial smooth muscle, activating adenylyl cyclase, increasing intracellular cAMP, activating PKA, and causing smooth muscle relaxation and bronchodilation

(C) Salbutamol inhibits phosphodiesterase, preventing cAMP breakdown and maintaining bronchodilation

(D) Salbutamol blocks leukotriene CysLT1 receptors, reducing leukotriene-mediated bronchoconstriction

Q39. A patient is given diphenhydramine (a first-generation H1 antihistamine) for an acute allergic reaction. Understanding the H1 receptor signal transduction pathway is important for rationalising drug design. The following diagram shows the H1 receptor pathway:



Which of the following correctly describes the signal transduction pathway activated by histamine at H1 receptors?

(A) H1 receptors are coupled to Gs protein, activating adenylyl cyclase and increasing intracellular cAMP

(B) H1 receptors are coupled to Gi protein, inhibiting adenylyl cyclase and decreasing intracellular cAMP

(C) H1 receptors are coupled to Gq protein, activating phospholipase C, generating IP3 and DAG, and increasing intracellular Ca^{2+}

(D) H1 receptors are ligand-gated ion channels that directly allow Ca^{2+} influx upon histamine binding

Q40. A 65-year-old patient with deep vein thrombosis is started on unfractionated heparin (UFH) infusion. The nurse asks which laboratory test should be used to monitor the adequacy and safety of heparin therapy. The correct answer is:

(A) Prothrombin time (PT/INR) – monitors the extrinsic and common coagulation pathways

(B) Platelet count – the most important monitoring parameter for heparin therapy

(C) Bleeding time – measures platelet plug formation and primary haemostasis

(D) Activated partial thromboplastin time (APTT) – monitors the intrinsic and common coagulation pathways; heparin (via antithrombin III) prolongs APTT, which is used to titrate the dose to 1.5–2.5 times the control value

Detailed Solutions

Q1.

Solution

Concept – First-pass effect and oral bioavailability: After oral administration, a drug is absorbed from the GI tract and passes through the portal circulation to the liver before reaching systemic circulation. Drugs that are extensively metabolised by the liver (high hepatic extraction ratio) undergo significant first-pass metabolism, leaving only a small fraction to reach the systemic circulation. This dramatically reduces oral bioavailability (e.g., morphine ∼25%, lignocaine ∼3%, propranolol ∼26%). First-pass metabolism does not apply to intravenous or sublingual routes because the drug bypasses the liver initially. Options (B), (C), and (D) describe other pharmacokinetic parameters that do not explain low bioavailability due to pre-systemic elimination.

Final Answer: Extensive first-pass hepatic metabolism reduces oral bioavailability $\Rightarrow \boxed{A}$

Answer: (A) Go Back to Q1

Q2.

Solution

Concept – Volume of distribution (Vd): Vd is a theoretical volume calculated as Vd = Dose/C_0. In this question: Vd = 500 mg ÷ 0.5 mg/L = 1000 L – far exceeding total body water (∼42 L). A very large Vd indicates the drug is widely distributed into peripheral tissues (e.g., fat, muscle) and has relatively low plasma concentrations. It does NOT mean the drug is confined to plasma (that would be a small Vd ≈ 3–5 L, seen with highly protein-bound drugs like warfarin staying in vascular space at lower concentrations). Drugs with large Vd include chloroquine (∼200–800 L/kg), amiodarone, and digoxin. Options (A), (C), and (D) incorrectly interpret a large Vd.

Final Answer: Large Vd indicates wide distribution into peripheral tissues $\Rightarrow \boxed{B}$

Answer: (B) Go Back to Q2

Q3.

Solution

Concept – Therapeutic Index: The therapeutic index (TI) is the ratio of the dose that produces toxicity (LD50) to the dose that produces the desired therapeutic

effect (ED50): TI = LD50/ED50. A higher TI indicates a safer drug (wider margin between effective and lethal doses). Drugs with narrow TI (e.g., digoxin, warfarin, lithium, phenytoin) require careful monitoring. From the dose-response curves shown: the blue curve (therapeutic) has its ED50 at a lower dose, and the red curve (lethal) has its LD50 at a higher dose. Option (A) inverts the ratio (would give a value less than 1 for a safe drug). Option (B) is a product, not a ratio. Option (D) is the more conservative "certain safety factor" (LD1/ED99 or LD5/ED95), not the standard TI.

Final Answer: Therapeutic index = LD_{50} / ED_{50} $\Rightarrow \boxed{C}$

Answer: (C) Go Back to Q3

Q4.

Solution

Concept – Enzyme induction by rifampicin: Rifampicin is one of the most potent inducers of hepatic CYP450 enzymes (especially CYP3A4, CYP2C9, and CYP2C19). Enzyme induction increases the synthesis and activity of these enzymes, accelerating the metabolism of co-administered drugs and reducing their plasma concentrations. OCPs (ethinyl oestradiol and progestins) are metabolised by CYP3A4; rifampicin-induced induction reduces their plasma levels below the contraceptive threshold, leading to contraceptive failure and unintended pregnancy. Enzyme induction takes days to weeks to develop and reverses slowly after the inducer is stopped. Option (A) is incorrect – induction increases metabolism and reduces levels, not the reverse. Option (B) is incorrect – induction is gradual. Option (C) is incorrect – induction affects hepatic, not renal, mechanisms.

Final Answer: Rifampicin induces CYP450 enzymes, accelerating OCP metabolism and reducing its efficacy $\Rightarrow \boxed{D}$

Answer: (D) Go Back to Q4

Q5.

Solution

Concept – Pilocarpine in open-angle glaucoma: Pilocarpine is a direct-acting muscarinic (M3) agonist used topically in open-angle glaucoma. It contracts the ciliary muscle, which pulls on the scleral spur and opens the trabecular meshwork, facilitating aqueous humour outflow and reducing intraocular pressure. It also contracts the sphincter pupillae causing miosis. Timolol (B) is a β-blocker that reduces aqueous production. Latanoprost (C) is a prostaglandin analogue that increases uveoscleral outflow. Acetazolamide (D) is a carbonic anhydrase in-

hibitor that reduces aqueous production. Among these, only pilocarpine is a direct muscarinic agonist that increases outflow via ciliary muscle contraction.

Final Answer: Pilocarpine is the direct muscarinic agonist used in open-angle glaucoma $\Rightarrow \boxed{A}$

Answer: (A) Go Back to Q5

Q6.

Solution

Concept – Atropine (anticholinergic) toxicity: The classic features of anticholinergic toxidrome are remembered by the mnemonic: "Dry as a bone" (anhidrosis, dry mouth), "Blind as a bat" (cycloplegia, mydriasis), "Red as a beet" (flushed skin due to cutaneous vasodilation), "Hot as a hare" (hyperthermia due to anhidrosis), "Mad as a hatter" (confusion, delirium, hallucinations), and "Full as a flask" (urinary retention). Additionally, atropine causes tachycardia (by blocking M2 receptors in the SA node) and constipation (reduced GI motility). **Diarrhoea is NOT a feature** – atropine reduces GI secretions and motility, causing constipation, not diarrhoea. Options (A), (C), and (D) are all genuine features of atropine toxicity.

Final Answer: Diarrhoea is NOT a feature of atropine toxicity (it causes constipation) $\Rightarrow \boxed{B}$

Answer: (B) Go Back to Q6

Q7.

Solution

Concept – Propranolol and bronchospasm: Propranolol is a non-selective β-adrenergic blocker, antagonising both β_1 (cardiac) and β_2 (bronchial, vascular) receptors. In the lungs, sympathetic tone through β_2 receptors maintains bronchodilation. Blockade of β_2 receptors by propranolol removes this dilatory tone, allowing unopposed parasympathetic bronchoconstriction. This is particularly dangerous in patients with asthma or COPD. Selective β_1-blockers (e.g., atenolol, metoprolol) are preferred in such patients when a beta-blocker is necessary. Option (A) is incorrect – propranolol does not stimulate α_1 receptors. Option (B) describes reduced cardiac output, not the primary cause of wheeze. Option (D) is not a pharmacological mechanism of propranolol.

Final Answer: Non-selective β_2 blockade by propranolol removes bronchodilatory tone, causing bronchoconstriction $\Rightarrow \boxed{C}$

Answer: (C) Go Back to Q7

Q8.

Solution

Concept – Prazosin and first-dose orthostatic hypotension: Prazosin is a selective α_1-adrenergic receptor antagonist used in BPH (relaxes internal urethral sphincter and prostatic smooth muscle) and hypertension. α_1 receptors in peripheral arterioles and venules maintain vascular tone; blockade leads to vasodilation and reduced peripheral resistance. With the first dose, the compensatory baroreceptor reflex (which would normally increase heart rate) is blunted because prazosin also blocks the α_1-mediated vasoconstriction that generates the signal. This results in exaggerated postural (orthostatic) hypotension, which can cause dizziness and syncope, particularly on rising from bed. Management: start with a low dose at bedtime. Options (A), (B), and (C) describe mechanisms of other drug classes.

Final Answer: Prazosin blocks α_1 receptors, causing first-dose orthostatic hypotension $\Rightarrow \boxed{D}$

Answer: (D) Go Back to Q8

Q9.

Solution

Concept – Neostigmine in myasthenia gravis: Myasthenia gravis is an autoimmune disease with antibodies against nicotinic acetylcholine receptors (nAChR) at the neuromuscular junction (NMJ), reducing the number of functional receptors. Neostigmine is a reversible anticholinesterase (quaternary ammonium compound) that inhibits acetylcholinesterase at the NMJ. This prevents the enzymatic breakdown of ACh, increasing its concentration and duration of action in the synaptic cleft. More ACh is available to compete with the antibodies for the remaining receptors, improving neuromuscular transmission. Unlike organophosphates, neostigmine's binding to AChE is reversible. Option (B) is incorrect – neostigmine acts indirectly (not a direct agonist). Option (C) is incorrect – irreversible inhibition describes organophosphates. Option (D) describes aminopyridines, not neostigmine.

Final Answer: Neostigmine reversibly inhibits acetylcholinesterase, increasing ACh at the NMJ $\Rightarrow \boxed{A}$

Answer: (A) Go Back to Q9

Q10.

Solution

Concept – Succinylcholine: depolarizing neuromuscular blocker: Succinylcholine is the only depolarizing NMJ blocker in clinical use. It mimics ACh at nicotinic receptors, causing persistent depolarization of the end plate. Initial fasciculations result from this depolarization. Because the block is due to persistent depolarization (Phase I block), anticholinesterases like neostigmine do NOT reverse the block – they increase ACh, which would worsen the depolarizing block. **Neostigmine reverses non-depolarizing blockers (e.g., rocuronium, vecuronium), NOT succinylcholine.** With prolonged or repeated exposure, a Phase II (desensitization) block may develop, which resembles non-depolarizing block. Succinylcholine is contraindicated in burns, crush injury, and denervation due to upregulation of extrajunctional nAChRs, causing massive K^+ release and life-threatening hyperkalaemia.

Final Answer: Succinylcholine blockade is NOT reversed by neostigmine (it is a depolarizing blocker) $\Rightarrow \boxed{B}$

Answer: (B) Go Back to Q10

Q11.

Solution

Concept – Morphine effects: Morphine acts on μ, κ, and δ opioid receptors throughout the CNS and periphery. Established effects include: respiratory depression (reduced tidal volume and respiratory rate – the main cause of death in opioid overdose), miosis (pupillary constriction due to stimulation of the Edinger-Westphal nucleus – a parasympathetic nucleus), nausea/vomiting (stimulation of the chemoreceptor trigger zone), constipation (reduced GI motility), euphoria, sedation, cough suppression, biliary spasm, and urinary retention. Morphine causes **bradycardia** (vagally mediated and direct cardiac effects), **not tachycardia**. Tachycardia is not a recognised pharmacological effect of morphine; at therapeutic doses, heart rate is typically mildly reduced or unchanged. This makes option (C) the incorrect statement.

Final Answer: Tachycardia is NOT produced by morphine (it causes bradycardia) $\Rightarrow \boxed{C}$

Answer: (C) Go Back to Q11

Q12.

Solution

Concept – Benzodiazepine mechanism at GABA-A receptors: GABA-A receptors are pentameric ligand-gated Cl^- ion channels. GABA binding opens these channels, allowing Cl^- influx and hyperpolarization. Benzodiazepines bind at an allosteric site (between α and γ subunits), distinct from the GABA binding site (β subunit). They act as positive allosteric modulators: **in the presence of GABA, benzodiazepines increase the frequency of Cl^- channel opening** (but do not affect the duration of each opening or the conductance). Barbiturates, in contrast, increase the **duration** of Cl^- channel opening. Key distinction: Benzodiazepines require GABA to be present (they are modulators, not direct activators), which is why they have a ceiling effect and are relatively safer in overdose than barbiturates.

Final Answer: Benzodiazepines increase the frequency of Cl^- channel opening in the presence of GABA $\Rightarrow \boxed{D}$

Answer: (D) Go Back to Q12

Q13.

Solution

Concept – Phenytoin zero-order (saturation) kinetics: Most drugs follow first-order kinetics where a constant fraction is eliminated per unit time, giving linear proportionality between dose and steady-state plasma levels. Phenytoin is unique in following Michaelis-Menten (saturation/zero-order) kinetics at therapeutic doses. The hepatic enzymes responsible for phenytoin metabolism (CYP2C9, CYP2C19) become saturated at plasma concentrations within the therapeutic range. Once saturated, a constant amount (not fraction) is metabolised per unit time. Therefore, even a small increase in dose causes a disproportionately large increase in plasma concentration (as illustrated by the exponential curve in the diagram). This narrow therapeutic window and saturable kinetics make phenytoin difficult to manage – small dose adjustments can cause dramatic swings in plasma levels, leading to toxicity (nystagmus, ataxia, confusion).

Final Answer: Phenytoin shows saturation (zero-order) kinetics; small dose increase saturates enzymes causing disproportionate rise in levels $\Rightarrow \boxed{A}$

Answer: (A) Go Back to Q13

Q14.

Solution

Concept – Chlorpromazine and D2 receptor blockade: Chlorpromazine is a phenothiazine typical (first-generation) antipsychotic. Its antipsychotic effect is primarily due to D2 dopamine receptor blockade in the mesolimbic pathway. D2 blockade in other dopaminergic pathways causes adverse effects: (1) **Nigrostriatal pathway**: D2 blockade causes Parkinsonism (drug-induced extrapyramidal symptoms – rigidity, bradykinesia, mask-like face, as seen in this patient) and tardive dyskinesia with long-term use. (2) **Tuberoinfundibular pathway**: D2 blockade raises prolactin levels (hyperprolactinaemia – amenorrhoea, galactorrhoea). (3) **Mesocortical pathway**: D2 blockade may worsen negative symptoms. Chlorpromazine also blocks muscarinic, histaminergic, and α_1 receptors, contributing to its diverse side-effect profile, but D2 is the primary receptor for both efficacy and EPS.

Final Answer: Extrapyramidal side effects are caused by D2 dopamine receptor blockade in the nigrostriatal pathway $\Rightarrow \boxed{B}$

Answer: (B) Go Back to Q14

Q15.

Solution

Concept – Role of carbidopa in levodopa-carbidopa combination: Levodopa is the amino acid precursor of dopamine and crosses the blood-brain barrier (BBB) via large neutral amino acid transporters; dopamine itself cannot cross the BBB. When levodopa is given alone, ∼95–99% is converted to dopamine in the periphery by DOPA decarboxylase (aromatic amino acid decarboxylase) in gut, liver, kidney, and blood vessel walls. This peripheral dopamine causes severe nausea, vomiting, hypotension, and cardiac arrhythmias, while only ∼1% of the dose reaches the brain. Carbidopa is a DOPA decarboxylase inhibitor that does **not cross the BBB**. By blocking peripheral conversion of levodopa to dopamine, carbidopa: (1) reduces peripheral side effects dramatically, and (2) allows more levodopa to reach the brain, increasing the effective CNS dose 4–5 fold. Carbidopa has no anti-Parkinsonian activity of its own.

Final Answer: Carbidopa inhibits peripheral DOPA decarboxylase (without crossing BBB), reducing side effects and increasing CNS levodopa delivery $\Rightarrow \boxed{C}$

Answer: (C) Go Back to Q15

Q16.

Solution

Concept – Order of nerve fibre blockade by local anaesthetics: Local anaesthetics block voltage-gated Na^+ channels in nerve fibres. The sequence of blockade depends on fibre diameter (smaller fibres are blocked first) and myelination (myelinated fibres with nodes of Ranvier may be blocked at lower concentrations). The sequence from first blocked to last blocked is: **B fibres** (preganglionic autonomic, small myelinated) $\rightarrow$ **C fibres** (unmyelinated, pain/temperature) $\rightarrow$ **A-delta fibres** (small myelinated, fast pain/temperature) $\rightarrow$ **A-beta fibres** (touch/pressure) $\rightarrow$ **A-alpha fibres** (large myelinated, motor to skeletal muscle). In clinical spinal/epidural anaesthesia, autonomic block occurs first (vasodilation, hypotension), followed by sensory loss (pain, temperature, touch), and motor block last. Large myelinated A-alpha motor fibres are the most resistant because their large diameter requires more Na^+ channel blockade.

Final Answer: A-alpha (large myelinated motor) fibres are blocked LAST by local anaesthetics $\Rightarrow \boxed{D}$

Answer: (D) Go Back to Q16

Q17.

Solution

Concept – Penicillin mechanism (PBP/transpeptidase inhibition): Beta-lactam antibiotics (penicillins, cephalosporins, carbapenems) exert their bactericidal effect by inhibiting penicillin-binding proteins (PBPs), which are transpeptidase enzymes responsible for the final cross-linking (transpeptidation) of peptidoglycan strands in the bacterial cell wall. Inhibiting transpeptidase prevents cross-linking, leaving the peptidoglycan layer weakened and unable to withstand osmotic pressure. Autolysins then degrade the defective wall, causing cell lysis. As illustrated in the diagram, PBP (transpeptidase) is located in the peptidoglycan layer adjacent to the cytoplasmic membrane. Beta-lactams are selective for bacteria because mammalian cells lack cell walls and PBPs. Option (B) describes polymyxins. Option (C) describes fluoroquinolones. Option (D) describes aminoglycosides.

Final Answer: Penicillin inhibits transpeptidase (PBP), preventing peptidoglycan cross-linking $\Rightarrow \boxed{A}$

Answer: (A) Go Back to Q17

Q18.

Solution

Concept – Aminoglycoside pharmacodynamics: Aminoglycosides (gentamicin, amikacin, tobramycin) are bactericidal antibiotics with **concentration-dependent killing**. Their bacterial killing depends on the peak concentration relative to the minimum inhibitory concentration (Cmax:MIC ratio). A higher peak concentration leads to more complete bacterial killing. This property justifies once-daily dosing (rather than divided doses), which achieves a higher peak concentration without increasing total daily dose or toxicity. An additional benefit is the post-antibiotic effect (PAE) – continued bacterial suppression even after drug concentrations fall below MIC. Once-daily dosing also reduces the risk of nephrotoxicity (trough-related toxicity) and ototoxicity. Option (A) is wrong – they are bactericidal, not bacteriostatic. Option (C) is wrong – aminoglycosides are poorly absorbed orally (polar compounds). Option (D) is wrong – the dose-limiting toxicity is nephrotoxicity and ototoxicity, not hepatotoxicity.

Final Answer: Aminoglycosides are concentration-dependent bactericidal agents, justifying once-daily dosing $\Rightarrow \boxed{B}$

Answer: (B) Go Back to Q18

Q19.

Solution

Concept – Tetracycline toxicity in children: Tetracyclines chelate divalent cations (Ca^{2+}, Mg^{2+}, Fe^{2+}) due to their polyketide structure. When given to children under 8 years or during pregnancy (after 4 months gestation), tetracyclines bind calcium in developing dental enamel and bone. In developing teeth, this causes **permanent yellow-brown discolouration and enamel hypoplasia**. Once formed, this staining cannot be reversed – hence the contraindication. Tetracyclines are also contraindicated in pregnancy (cross placenta, affect fetal teeth and bones) and should be avoided with milk, antacids, and iron supplements (chelation reduces absorption). Outdated tetracyclines cause Fanconi syndrome (proximal tubular dysfunction). Doxycycline is the preferred tetracycline for use in children $\geq$8 years for specific indications (e.g., rickettsiosis) when benefits outweigh risks.

Final Answer: Permanent teeth discolouration and enamel hypoplasia due to calcium chelation in developing teeth $\Rightarrow \boxed{C}$

Answer: (C) Go Back to Q19

Q20.

Solution

Concept – Fluoroquinolone mechanism (DNA gyrase/topoisomerase II inhibition): Fluoroquinolones (ciprofloxacin, levofloxacin, moxifloxacin) are broad-spectrum bactericidal antibiotics targeting two bacterial type II topoisomerases: **DNA gyrase (topoisomerase II)** – the primary target in Gram-negative organisms (inhibits DNA supercoiling required for replication), and **topoisomerase IV** – the primary target in Gram-positive organisms (inhibits decatenation of daughter chromosomes). Inhibition leads to double-strand DNA breaks and bacterial death. Human topoisomerase II has much lower affinity for fluoroquinolones, accounting for selective toxicity. Fluoroquinolones are absorbed well orally, concentrate in urine making them useful for UTIs, and have good tissue penetration. They should not be used in children and pregnant women (damage to developing cartilage in animal studies). Option (A) describes beta-lactams. Option (B) describes rifampicin. Option (C) describes polymyxins.

Final Answer: Ciprofloxacin inhibits bacterial DNA gyrase (topoisomerase II) and topoisomerase IV $\Rightarrow \boxed{D}$

Answer: (D) Go Back to Q20

Q21.

Solution

Concept – Metronidazole spectrum of activity: Metronidazole is a nitroimidazole that is selectively active against **strictly anaerobic organisms and certain protozoa**. The mechanism involves reduction of its nitro group by anaerobic electron transport systems (absent in aerobes) to form cytotoxic nitro radical anions that damage DNA. Therefore, aerobic organisms that lack this anaerobic reduction step are **not susceptible**. Metronidazole is effective against: (1) Anaerobic bacteria: *Bacteroides fragilis*, *Clostridium difficile*, *Fusobacterium*; (2) Protozoa: *Entamoeba histolytica*, *Giardia lamblia*, *Trichomonas vaginalis*. It is the drug of choice for pseudomembranous colitis (C. difficile), amoebiasis (intestinal and hepatic), Trichomonas vaginitis, and bacterial vaginosis (anaerobes). Aerobic Gram-positive cocci (e.g., *S. aureus*, *Streptococcus*) are obligate aerobes and are NOT susceptible. A notable side effect is disulfiram-like reaction with alcohol.

Final Answer: Aerobic Gram-positive cocci are NOT susceptible to metronidazole $\Rightarrow \boxed{A}$

Answer: (A) Go Back to Q21

Q22.

Solution

Concept – Rifampicin mechanism (RNA polymerase inhibition): Rifampicin belongs to the rifamycin class. It binds to the **β-subunit of bacterial DNA-dependent RNA polymerase** at the RNA polymerase-DNA-RNA complex. This binding **blocks the initiation step** of mRNA transcription – it sterically prevents extension of short RNA chains (fewer than 2–3 nucleotides). Importantly, it does not affect already elongating RNA chains. The bacterial RNA polymerase has $\sim$100,000-fold higher affinity for rifampicin than the mammalian RNA polymerase, providing selective toxicity. Rifampicin is bactericidal and turns body fluids (urine, sweat, tears, saliva) orange-red. It is a potent inducer of CYP450 enzymes. Resistance develops rapidly (single-step mutation in rpoB gene encoding the β-subunit) – hence it is always used in combination. As shown in the diagram, rifampicin blocks the flow of genetic information from DNA to mRNA.

Final Answer: Rifampicin inhibits bacterial DNA-dependent RNA polymerase by binding the β-subunit, blocking mRNA synthesis $\Rightarrow \boxed{B}$

Answer: (B) Go Back to Q22

Q23.

Solution

Concept – Amphotericin B: ergosterol binding and nephrotoxicity: Amphotericin B is a polyene macrolide antifungal that selectively binds to **ergosterol** in the fungal cell membrane. Ergosterol is the primary sterol in fungal membranes (analogous to cholesterol in mammalian membranes). Binding of amphotericin B to ergosterol creates transmembrane pores (channels), causing leakage of K^+, Mg^{2+}, and other cellular contents, leading to fungal cell death. While mammalian cell membranes contain cholesterol (not ergosterol), amphotericin B has some affinity for cholesterol, which accounts for its significant toxicity – particularly **nephrotoxicity** (renal tubular damage, reduced GFR, hypokalaemia, hypomagnesaemia) and infusion-related reactions (fever, rigors). Liposomal amphotericin B reduces nephrotoxicity. Option (B) describes echinocandins (caspofungin). Options (A) and (D) describe fluoroquinolones and sulfonamides respectively.

Final Answer: Amphotericin B binds ergosterol in fungal cell membrane, forming pores that disrupt membrane integrity $\Rightarrow \boxed{C}$

Answer: (C) Go Back to Q23

Q24.

Solution

Concept – Acyclovir selectivity via viral thymidine kinase: Acyclovir (aciclovir) is a guanosine analogue prodrug. Its selectivity for herpes-infected cells is achieved through a two-stage activation process: **Step 1:** Acyclovir enters all cells, but is monophosphorylated to acyclovir monophosphate **exclusively by viral thymidine kinase (TK)** encoded by herpes simplex virus (HSV). Uninfected cells have human TK, which has negligible affinity for acyclovir. **Step 2:** Host cell kinases then convert acyclovir monophosphate to the active triphosphate form. Acyclovir triphosphate: (1) Competitively inhibits viral DNA polymerase (1000× greater affinity than host polymerase), and (2) Acts as a chain terminator when incorporated into viral DNA (lacking the 3'-OH group needed for further extension). The high selectivity for infected cells and the chain terminator mechanism mean that acyclovir has very low toxicity to normal host cells.

Final Answer: Acyclovir is activated exclusively by viral thymidine kinase in herpes-infected cells, providing selectivity $\Rightarrow \boxed{D}$

Answer: (D) Go Back to Q24

Q25.

Solution

Concept – Chloroquine: prevention of heme polymerization: *Plasmodium* parasites digest haemoglobin within their food vacuole (a specialised lysosomal compartment) for amino acids. During digestion, free heme (ferriprotoporphyrin IX, or FP) is released. Free heme is toxic to the parasite. Normally, the parasite polymerises free heme into an insoluble, non-toxic crystalline form called **hemozoin** (malaria pigment). Chloroquine is a weak base that accumulates in the acidic food vacuole (ion trapping), where it **prevents heme polymerization (hemozoin formation)**. Accumulated free heme is toxic to the parasite's membranes, leading to its death. Chloroquine resistance in *P. falciparum* results from mutations in the PfCRT (chloroquine resistance transporter) gene, which pumps chloroquine out of the food vacuole. Chloroquine is effective against the blood stages (erythrocytic) of *P. vivax*, *P. ovale*, *P. malariae*, and sensitive *P. falciparum*.

Final Answer: Chloroquine prevents heme polymerization (hemozoin formation), causing toxic heme accumulation in the parasite $\Rightarrow \boxed{A}$

Answer: (A) Go Back to Q25

Q26.

Solution

Concept – Sulfonamide selective toxicity: Sulfonamides are structural analogues of para-aminobenzoic acid (PABA). They competitively inhibit **dihydropteroate synthase (DHPS)**, an enzyme required for bacterial folate synthesis. The key to selectivity: **bacteria must synthesise folate de novo** from PABA, pteridine, and glutamate – they cannot transport preformed folate from the environment. **Mammalian cells cannot synthesise folate** and must obtain it from dietary sources via specific folate transporters. Since mammalian cells never use DHPS and don't synthesise folate, sulfonamides have no effect on them. This is a classic example of selective toxicity exploiting a metabolic difference between pathogen and host. Trimethoprim acts synergistically by blocking the next step (dihydrofolate reductase – DHFR), achieving sequential blockade of folate synthesis. Option (A) is incorrect – size is not the reason. Option (C) is incorrect – sulfonamides are active in mammalian systems if DHPS were present. Option (D) is incorrect – mammalian DHPS has lower affinity for sulfonamides.

Final Answer: Bacteria must synthesise folate de novo (no uptake of preformed folate); mammalian cells cannot synthesise folate and are unaffected $\Rightarrow \boxed{B}$

Answer: (B) Go Back to Q26

Q27.

Solution

Concept – Digoxin: Na^+/K^+-ATPase inhibition and positive inotropy: Digoxin inhibits the **Na^+/K^+-ATPase** (sodium pump) on the cardiomyocyte membrane. This pump normally maintains intracellular Na^+ at a low concentration by extruding 3 Na^+ for every 2 K^+ imported. Inhibition by digoxin leads to **intracellular Na^+ accumulation**. The Na^+/Ca^{2+} exchanger (NCX) normally uses the Na^+ gradient (high outside, low inside) to extrude 1 Ca^{2+} in exchange for 3 Na^+ entering. With increased intracellular Na^+, this gradient is reduced, so NCX operates less effectively (or may even reverse), resulting in **increased intracellular Ca^{2+}**. Elevated intracellular Ca^{2+} enhances excitation-contraction coupling in the heart, producing **positive inotropy**. As shown in the diagram, the sequence is: Digoxin $\rightarrow$ blocks Na^+/K^+-ATPase $\rightarrow \uparrow[Na^+]_i \rightarrow$ NCX reversal $\rightarrow \uparrow[Ca^{2+}]_i \rightarrow$ positive inotropy.

Final Answer: Digoxin inhibits Na^+/K^+-ATPase $\rightarrow \uparrow[Na^+]_i \rightarrow \uparrow[Ca^{2+}]_i \rightarrow$ positive inotropy $\Rightarrow \boxed{C}$

Answer: (C) Go Back to Q27

Q28.

Solution

Concept – Nitrates: preload reduction via venodilation: Organic nitrates (GTN, isosorbide dinitrate, isosorbide mononitrate) are converted to **nitric oxide (NO)** in vascular smooth muscle. NO activates soluble **guanylate cyclase**, increasing intracellular **cGMP**. cGMP activates protein kinase G (PKG), which phosphorylates myosin light chain kinase (MLCK) and reduces cytoplasmic Ca^{2+}, leading to vascular smooth muscle relaxation. At low therapeutic doses, nitrates preferentially dilate **venous capacitance vessels** (venodilation) more than arterioles. This reduces venous return to the heart, decreasing **preload** (end-diastolic volume and pressure). Reduced preload lowers myocardial wall tension (by Laplace's law) and decreases myocardial O_2 demand, relieving angina. At higher doses, arteriolar dilation also occurs (reducing afterload). As shown in the diagram: GTN $\rightarrow$ NO $\rightarrow$ guanylate cyclase $\rightarrow \uparrow$cGMP $\rightarrow$ vasodilation.

Final Answer: Nitrates act primarily via venodilation, reducing venous return and preload, decreasing myocardial O_2 demand $\Rightarrow \boxed{D}$

Answer: (D) Go Back to Q28

Q29.

Solution

Concept – Thiazide diuretics and hypercalcaemia: Thiazide diuretics (hydrochlorothiazide, chlorthalidone, indapamide) inhibit the **Na^+/Cl^- cotransporter (NCC)** in the distal convoluted tubule (DCT). This is the unique characteristic of thiazides: while they increase urinary Na^+, K^+, Mg^{2+}, and urate excretion, they paradoxically **reduce urinary calcium excretion** (i.e., increase Ca^{2+} reabsorption). Mechanism: Na^+ depletion activates Na^+/Ca^{2+} exchange in the DCT basolateral membrane, increasing Ca^{2+} reabsorption. This property makes thiazides useful in preventing nephrolithiasis (calcium oxalate stones) and in treating idiopathic hypercalciuria. **Loop diuretics** (frusemide) increase urinary Ca^{2+} excretion (used in hypercalcaemia). Other metabolic effects of thiazides: hypokalaemia, hyperuricaemia (gout), hyperglycaemia (impaired insulin secretion), and hyperlipidaemia. Hypercalcaemia is the hallmark metabolic effect that distinguishes thiazides from loop diuretics.

Final Answer: Hypercalcaemia (due to increased Ca^{2+} reabsorption in DCT) is the characteristic effect of thiazides $\Rightarrow \boxed{A}$

Answer: (A) Go Back to Q29

Q30.

Solution

Concept – ACE inhibitor dry cough due to bradykinin accumulation: ACE (angiotensin-converting enzyme, also called kininase II) has two main substrates: (1) It converts angiotensin I (inactive) to **angiotensin II** (vasoconstrictor, aldosterone-stimulating), and (2) It inactivates **bradykinin** (a potent vasodilator and bronchoconstrictor peptide). ACE inhibitors (ramipril, enalapril, lisinopril) block ACE, thereby: (1) Reducing angiotensin II formation (therapeutic benefit), and (2) Preventing bradykinin breakdown. Accumulated bradykinin stimulates B2 receptors on sensory C-fibres in the airways and lung, causing release of substance P and prostaglandins, which irritate airways and produce a **dry, tickling, persistent cough**. This occurs in $\sim$10–20% of patients (more common in women, Asians). ACE inhibitor-induced cough is a class effect – switching to an ARB (e.g., losartan), which does not affect bradykinin, resolves the cough.

Final Answer: Bradykinin accumulation (due to reduced ACE-mediated inactivation) stimulates airway C-fibres causing dry cough $\Rightarrow \boxed{B}$

Answer: (B) Go Back to Q30

Q31.

Solution

Concept – Aspirin antiplatelet effect via irreversible COX-1 inhibition: Aspirin (acetylsalicylic acid) irreversibly inhibits cyclooxygenase (COX) enzymes by covalent acetylation of a serine residue (Ser529 in COX-1, Ser516 in COX-2). At low doses ($\leq$325 mg/day), aspirin preferentially inhibits **COX-1 in platelets**. This prevents the synthesis of **thromboxane A2 (TXA2)**, a potent platelet aggregator and vasoconstrictor. Since platelets are anucleate cells, they **cannot regenerate COX-1**. Therefore, aspirin's antiplatelet effect lasts for the entire platelet lifespan ($\sim$7–10 days) – a single low dose permanently disables each platelet it contacts. This contrasts with endothelial cells, which can regenerate COX-2 and resume prostacyclin (PGI2) synthesis. The net effect is reduced platelet aggregation, explaining aspirin's use in ischaemic heart disease and stroke prevention. Option (A) is incorrect – PGI2 is anti-aggregatory and is reduced by high-dose aspirin. Option (B) describes clopidogrel. Option (D) describes heparin.

Final Answer: Aspirin irreversibly inhibits COX-1, preventing TXA2 synthesis in nucleate-free platelets permanently $\Rightarrow \boxed{C}$

Answer: (C) Go Back to Q31

Q32.

Solution

Concept – Selective COX-2 inhibitors in peptic ulcer history: NSAIDs inhibit cyclooxygenase enzymes. **COX-1** is constitutively expressed in gastric mucosa, platelets, and kidneys. In the stomach, COX-1-derived prostaglandins (PGE2, PGI2) stimulate mucus and bicarbonate secretion and increase mucosal blood flow – forming the "cytoprotective" gastric mucosal barrier. Non-selective NSAIDs (aspirin, ibuprofen, naproxen, indomethacin) inhibit both COX-1 and COX-2, disrupting this mucosal protection and causing peptic ulceration. **Celecoxib** is a selective COX-2 inhibitor. It provides anti-inflammatory and analgesic effects (COX-2-mediated) while **sparing COX-1 in the gastric mucosa**, thus causing significantly fewer GI ulcers. However, selective COX-2 inhibitors increase cardiovascular risk (prostacyclin from endothelial COX-2 is reduced, while platelet TXA2 via COX-1 is preserved). For a patient with peptic ulcer history needing NSAID, celecoxib is the most appropriate choice.

Final Answer: Celecoxib (selective COX-2 inhibitor) spares gastric COX-1 mucosal protection, safest in peptic ulcer history $\Rightarrow \boxed{D}$

Answer: (D) Go Back to Q32

Q33.

Solution

Concept – Corticosteroid anti-inflammatory mechanism via annexin-1 (lipocortin): Glucocorticoids (hydrocortisone, prednisolone, dexamethasone) exert their broad anti-inflammatory effects through nuclear steroid receptors. After entering cells, glucocorticoids bind cytoplasmic glucocorticoid receptors (GR), which then translocate to the nucleus and activate gene transcription. A key mechanism is the induction of **annexin-1 (lipocortin-1)**, a protein that **inhibits phospholipase A2 (PLA2)**. PLA2 catalyses the release of **arachidonic acid (AA)** from membrane phospholipids. AA is the common precursor for both: (1) Prostaglandins and thromboxanes (via COX pathway), and (2) Leukotrienes (via lipoxygenase/LOX pathway). By inhibiting PLA2, corticosteroids block **both pathways simultaneously** – reducing all eicosanoids (prostaglandins, thromboxanes, leukotrienes). This is why corticosteroids are more broadly anti-inflammatory than NSAIDs (which only block COX). Option (B) is incorrect – that is the mechanism of NSAIDs. Options (C) and (D) describe mechanisms of montelukast and sodium cromoglicate respectively.

Final Answer: Corticosteroids induce annexin-1 (lipocortin), inhibiting phospholipase A2 and blocking both COX and LOX pathways $\Rightarrow \boxed{A}$

Answer: (A) Go Back to Q33

Q34.

Solution

Concept – Insulin preparations: only regular insulin for IV use: Different insulin preparations vary in onset, peak, and duration based on their formulation. **Regular insulin** (soluble, short-acting): clear solution, neutral pH – the **only insulin preparation that can be given intravenously**. This is essential in DKA and hyperosmolar hyperglycaemic state (HHS) where continuous IV insulin infusion is required for precise glucose control. **NPH insulin** (Neutral Protamine Hagedorn): cloudy suspension (protamine delays absorption), intermediate-acting – cannot be given IV. **Insulin glargine**: long-acting, clear, acidic pH (pH 4) – forms microprecipitates at neutral tissue pH providing peakless 24-hour release; acidic pH means it **cannot be mixed** with other insulins and should **never be given IV**. **Insulin lispro** (rapid-acting analogue): modified amino acid sequence (B28-B29 reversed), very rapid onset – used in pens and pumps, not for IV in DKA. Regular insulin is the safest and only validated option for IV infusion.

Final Answer: Regular (soluble) insulin is the only preparation suitable for intravenous infusion in DKA $\Rightarrow \boxed{B}$

Answer: (B) Go Back to Q34

Q35.

Solution

Concept – Sulfonylurea mechanism: K-ATP channel closure in β-cells: Pancreatic β-cells have **ATP-sensitive potassium channels (K-ATP channels)** on their surface. These channels maintain the resting membrane potential. When blood glucose rises: glucose $\rightarrow$ glycolysis $\rightarrow$ increased ATP $\rightarrow$ K-ATP channels close $\rightarrow$ membrane depolarises $\rightarrow$ voltage-gated L-type Ca^{2+} channels open $\rightarrow$ Ca^{2+} influx $\rightarrow$ insulin granule exocytosis. Sulfonylureas (glibenclamide, glipizide, gliclazide) bind to the **SUR1 subunit** of K-ATP channels and close them directly, **bypassing the glucose-sensing step**. This triggers the same cascade as high glucose, stimulating insulin release regardless of blood glucose levels. This explains why sulfonylureas can cause hypoglycaemia even in fasting states – a key safety concern compared to glucose-dependent secretagogues (e.g., GLP-1 agonists). As illustrated in the diagram, glibenclamide closes K-ATP channels $\rightarrow$ depolarisation $\rightarrow$ Ca^{2+} influx $\rightarrow$ insulin release.

Final Answer: Sulfonylureas close K-ATP channels in pancreatic β-cells, causing

depolarisation, Ca^{2+} influx, and insulin secretion $\Rightarrow \boxed{C}$

Answer: (C) Go Back to Q35

Q36.

Solution

Concept – PTU preferred in thyroid storm for peripheral T4→T3 inhibition: Both propylthiouracil (PTU) and methimazole/carbimazole inhibit the enzyme **thyroid peroxidase** (TPO), blocking the organification of iodide and synthesis of T3 and T4. However, PTU has an **additional mechanism**: it inhibits **type 1 deiodinase** (5'-deiodinase) in peripheral tissues (liver, kidney, pituitary), which catalyses the conversion of T4 (less active prohormone) to T3 (the more active form). In **thyroid storm**, extremely high levels of both T4 and T3 are present. Rapid reduction of T3 is critical. PTU's ability to block peripheral T4→T3 conversion provides a faster reduction in the concentration of the biologically active hormone. Methimazole does not have this additional action. Therefore, PTU is the antithyroid drug of choice in thyroid storm. Methimazole is preferred in non-urgent settings (once-daily dosing, lower risk of agranulocytosis and hepatotoxicity). In pregnancy, methimazole is avoided in the first trimester due to teratogenicity; PTU is used instead.

Final Answer: PTU is preferred in thyroid storm because it also inhibits peripheral T4→T3 conversion by inhibiting type 1 deiodinase $\Rightarrow \boxed{D}$

Answer: (D) Go Back to Q36

Q37.

Solution

Concept – Proton pump inhibitors: irreversible H^+/K^+-ATPase inhibition: Omeprazole is a **prodrug** (inactive at neutral pH). It is absorbed from the small intestine, reaches the systemic circulation, and is delivered to the **secretory canaliculi** of gastric parietal cells, where the highly acidic environment (pH $\leq$2) converts it to the active sulphenamide form. The active drug **covalently binds to cysteine residues** on the luminal surface of the **H^+/K^+-ATPase (proton pump)**, irreversibly inhibiting it. This pump is the final common pathway for acid secretion, regardless of whether stimulation comes from histamine, acetylcholine, or gastrin. Therefore, PPIs provide the most complete and sustained acid suppression. Acid secretion recovers only when new proton pump protein is synthesised ($\sim$18–24 hours). PPIs should be taken 30 minutes before meals (when proton pumps are actively secreting) for maximum efficacy. They are indicated in GORD,

peptic ulcer disease, Zollinger-Ellison syndrome, and H. pylori eradication regimens.

Final Answer: Omeprazole irreversibly inhibits H^+/K^+-ATPase (proton pump) on gastric parietal cells, blocking acid secretion $\Rightarrow \boxed{A}$

Answer: (A) Go Back to Q37

Q38.

Solution

Concept – Salbutamol: selective β_2-adrenergic receptor agonist: Salbutamol (albuterol) is a **short-acting, selective β_2-adrenergic receptor agonist (SABA)**. β_2 receptors in bronchial smooth muscle are coupled to Gs protein $\rightarrow$ adenylyl cyclase $\rightarrow \uparrow$cAMP $\rightarrow$ protein kinase A (PKA) activation $\rightarrow$ phosphorylation of myosin light chain kinase (MLCK, inactivating it) and reduced intracellular Ca^{2+} $\rightarrow$ smooth muscle relaxation $\rightarrow$ **bronchodilation**. Salbutamol also has additional effects: mast cell stabilisation (reducing mediator release), increased mucociliary clearance, and uterine relaxation (tocolysis in preterm labour). Side effects include tremor (skeletal muscle β_2 receptors), tachycardia (some β_1 cross-reactivity at high doses), and **hypokalaemia** (K^+ driven into cells via β_2-stimulated Na^+/K^+-ATPase). Option (A) describes ipratropium (anticholinergic). Option (C) describes theophylline/aminophylline (PDE inhibitor). Option (D) describes montelukast (leukotriene receptor antagonist).

Final Answer: Salbutamol selectively stimulates β_2-adrenergic receptors in bronchial smooth muscle, increasing cAMP and causing bronchodilation $\Rightarrow \boxed{B}$

Answer: (B) Go Back to Q38

Q39.

Solution

Concept – H1 receptor signal transduction (Gq/PLC pathway): Histamine H1 receptors are **G protein-coupled receptors (GPCRs)** coupled to the **Gq protein**. When histamine binds to H1 receptors, Gq activates **phospholipase C (PLC)**, which cleaves phosphatidylinositol-4,5-bisphosphate (PIP2) into two second messengers: (1) **Inositol-1,4,5-trisphosphate (IP3)** – releases Ca^{2+} from the endoplasmic reticulum, increasing intracellular Ca^{2+}, and (2) **Diacylglycerol (DAG)** – activates protein kinase C (PKC). The resulting increase in intracellular Ca^{2+} mediates many H1 effects: vascular smooth muscle contraction, increased vascular permeability, bronchoconstriction, and pruritus. First-generation H1 antihistamines (diphenhydramine, chlorpheniramine) block these receptors and cross the BBB

causing sedation. Second-generation antihistamines (loratadine, cetirizine) are non-sedating (poor CNS penetration). As shown in the diagram, the pathway: H1 $\rightarrow$ Gq $\rightarrow$ PLC $\rightarrow$ IP3 + DAG $\rightarrow \uparrow Ca^{2+}$ + PKC.

Final Answer: H1 receptors are coupled to Gq protein, activating PLC, generating IP3/DAG, and increasing intracellular $Ca^{2+} \Rightarrow \boxed{C}$

Answer: (C) Go Back to Q39

Q40.

Solution

Concept – Heparin monitoring by APTT: Unfractionated heparin (UFH) acts by binding **antithrombin III (ATIII)**, inducing a conformational change that dramatically accelerates ($\sim$1000-fold) ATIII's inhibition of thrombin (factor IIa), factor Xa, and to a lesser extent factors IXa, XIa, and XIIa. Since heparin primarily enhances inhibition of intrinsic pathway factors, it prolongs the **activated partial thromboplastin time (APTT)**, which measures the intrinsic and common coagulation pathways (factors XII, XI, IX, VIII, X, V, II, fibrinogen). APTT is used to monitor UFH therapy – the target is 1.5–2.5 times the control APTT (typically 60–100 seconds). **PT/INR** monitors the extrinsic pathway (factor VII) and is used for warfarin monitoring. Heparin-induced thrombocytopenia (HIT, type II) requires platelet count monitoring but APTT is the primary dosing guide. Heparin is reversed by **protamine sulphate** (1 mg neutralises 100 units heparin). Low molecular weight heparins (LMWH, e.g., enoxaparin) do not reliably prolong APTT; they are monitored by anti-Xa levels if needed.

Final Answer: APTT (activated partial thromboplastin time) is used to monitor unfractionated heparin therapy $\Rightarrow \boxed{D}$

Answer: (D) Go Back to Q40

Answer Key – FMGE Pharmacology Sample Paper 1

1	A	2	B	3	C	4	D	5	A
6	B	7	C	8	D	9	A	10	B
11	C	12	D	13	A	14	B	15	C
16	D	17	A	18	B	19	C	20	D
21	A	22	B	23	C	24	D	25	A
26	B	27	C	28	D	29	A	30	B
31	C	32	D	33	A	34	B	35	C
36	D	37	A	38	B	39	C	40	D