FMGE Pharmacology Sample Paper – 2

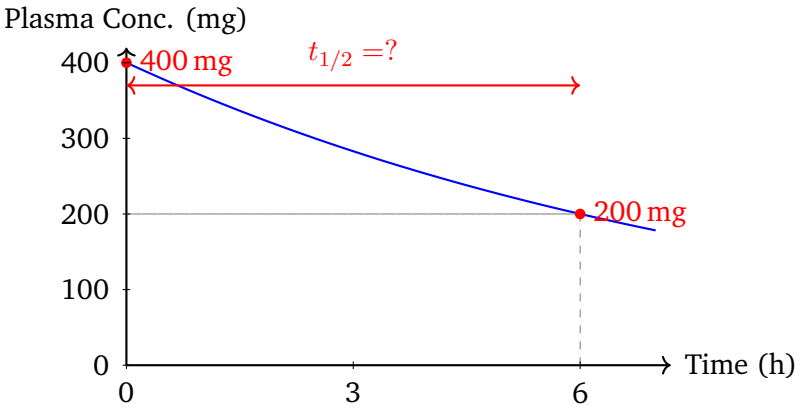
Duration: 60 Minutes **Maximum Marks: 40**

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 patient receives a 400 mg dose of a drug. The plasma concentration is 200 mg at 6 hours and 100 mg at 12 hours. The following graph represents the plasma drug concentration over time. What is the half-life ($t_{½}$) of this drug?



(A) 3 hours

(B) 6 hours

(C) 9 hours

(D) 12 hours

Q2. Zero-order kinetics means that a constant *amount* (not fraction) of drug is eliminated per unit time, regardless of plasma concentration. Which of the following drugs exhibits zero-order (saturation) kinetics even at **therapeutic doses**?

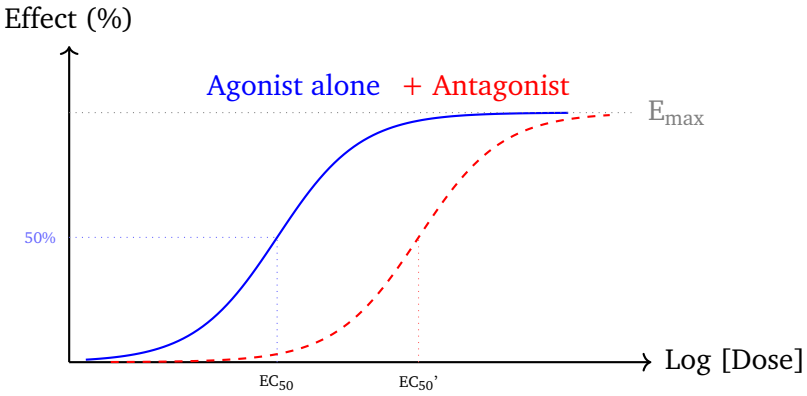
(A) Aspirin at analgesic doses

(B) Paracetamol at therapeutic doses

(C) Ethanol at any ingested dose

(D) Penicillin G at standard doses

Q3. The graph below shows two dose-response curves for an agonist alone and an agonist in the presence of a competitive antagonist. Which statement BEST describes the effect of a competitive antagonist on the agonist dose-response curve?



(A) E_{max} is decreased; EC_{50} is unchanged

(B) Both E_{max} and EC_{50} are decreased

(C) E_{max} is decreased; EC_{50} is increased

(D) E_{max} is unchanged; EC_{50} is increased (rightward shift)

Q4. A patient stabilised on warfarin therapy (99% protein-bound) is started on aspirin for a cardiovascular indication. Within days, unexpected bleeding occurs. What is the PRIMARY pharmacokinetic mechanism responsible?

(A) Displacement from plasma protein binding sites increases the free (unbound) drug concentration

(B) Aspirin induces hepatic CYP2C9, increasing warfarin metabolism

(C) Aspirin inhibits renal tubular secretion of warfarin

(D) Aspirin decreases gastric absorption of warfarin

Q5. Succinylcholine is a depolarising neuromuscular blocking agent (DNMB) that causes initial muscle fasciculations followed by flaccid paralysis. It is metabolised by plasma cholinesterase. Which of the following is a recognised CONTRAINDICATION to succinylcholine administration?

(A) Rapid sequence induction of anaesthesia

(B) Extensive burns or crush injuries (risk of severe hyperkalaemia)

(C) Intubation of a patient with a full stomach

(D) Neuromuscular monitoring during surgery

Q6. Methacholine is a selective muscarinic agonist (predominantly M2/M3) that is resistant to acetylcholinesterase. In clinical medicine, inhaled methacholine is used for which of the following diagnostic purposes?

(A) Treatment of open-angle glaucoma

(B) Reversal of non-depolarising neuromuscular block

(C) Bronchial provocation challenge test to diagnose airway hyperresponsiveness (asthma)

(D) Diagnosis of myasthenia gravis (Tensilon test)

Q7. A patient with hypertension and mild bronchial asthma requires a beta-blocker. Atenolol is preferred over propranolol in this clinical setting. Which property of atenolol accounts for its relative safety in asthmatic patients?

(A) Atenolol has intrinsic sympathomimetic activity (ISA)

(B) Atenolol blocks both α- and β-adrenergic receptors

(C) Atenolol undergoes extensive first-pass hepatic metabolism

(D) Cardioselective (β_1) blockade without significant β_2 receptor blockade

Q8. Amphetamine produces CNS stimulation, euphoria, anorexia, and tachycardia. It is classified as an indirect sympathomimetic agent. What is the PRIMARY mechanism of action of amphetamine?

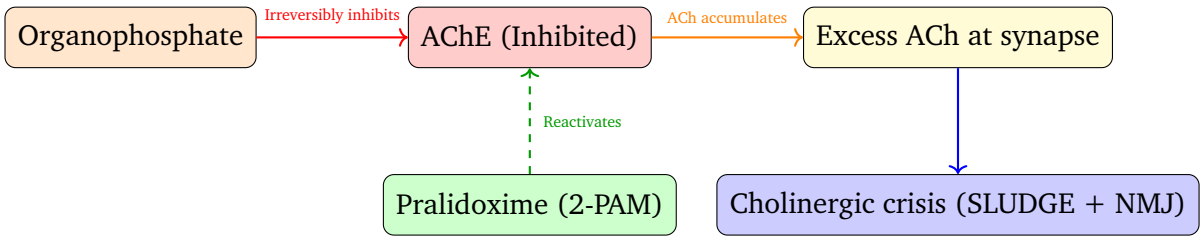
(A) Promotes release of norepinephrine and dopamine from presynaptic nerve terminals

(B) Directly activates postsynaptic α_1 and β_1 adrenergic receptors

(C) Inhibits monoamine oxidase (MAO), preventing NE degradation

(D) Blocks reuptake of norepinephrine via the NET transporter only

Q9. A farmer presents with profuse salivation, lacrimation, miosis, bradycardia, bronchospasm, and muscle fasciculations after spraying pesticides. The diagram below illustrates the mechanism of organophosphate (OPC) toxicity. Which drug specifically reactivates acetylcholinesterase (AChE) if given early?



(A) Atropine

(B) Pralidoxime (2-PAM)

(C) Physostigmine

(D) Pyridostigmine

Q10. Guanethidine is an adrenergic neuron-blocking agent used historically for severe hypertension. It produces sustained hypotension without reflex tachycardia. What is the mechanism of action of guanethidine?

(A) Blocks postsynaptic α_1 adrenergic receptors on vascular smooth muscle

(B) Inhibits synthesis of norepinephrine by blocking tyrosine hydroxylase

(C) It enters the adrenergic nerve terminal via uptake-1 and depletes norepinephrine from storage vesicles

(D) Stimulates presynaptic α_2 receptors to reduce NE release (central action)

Q11. A 58-year-old male presents to the emergency department with severe, colicky loin-to-groin pain and haematuria. Imaging confirms ureteric calculus. Which category of pain responds BEST to opioid analgesics?

(A) Superficial somatic pain (skin laceration)

(B) Neuropathic pain (diabetic peripheral neuropathy)

(C) Musculoskeletal pain (ankle sprain)

(D) Severe visceral pain (e.g., renal colic, myocardial infarction)

Q12. Both phenobarbitone and benzodiazepines act at the GABA-A receptor to enhance Cl^- influx, but they differ in their precise mechanism. Which statement about phenobarbitone is CORRECT?

(A) Phenobarbitone increases the *duration* of Cl^- channel opening (unlike benzodiazepines which increase *frequency*)

(B) Phenobarbitone increases the frequency of Cl^- channel opening

(C) Phenobarbitone directly opens the Cl^- channel independent of GABA

(D) Phenobarbitone blocks glycine receptors in addition to GABA-A receptors

Q13. Carbamazepine is a first-line antiepileptic used for partial seizures and trigeminal neuralgia. It acts via use-dependent sodium channel blockade. Which of the following is a recognised SERIOUS haematological adverse effect of carbamazepine?

(A) Thrombocytopenia only

(B) Aplastic anemia and agranulocytosis

(C) Megaloblastic anemia

(D) Haemolytic anemia in G6PD deficiency

Q14. A patient with bipolar affective disorder is commenced on lithium carbonate for mood stabilisation. Lithium has a narrow therapeutic index (therapeutic range 0.6–1.2 mEq/L). Which monitoring parameter is MOST essential to prevent toxicity?

(A) Serum potassium levels

(B) 24-hour urine creatinine clearance

(C) Regular serum lithium levels (every 3–6 months once stable)

(D) Electroencephalogram (EEG)

Q15. A 25-year-old woman is brought to the emergency department after ingesting a large quantity of amitriptyline (tricyclic antidepressant). She is unconscious, with a QRS width of 160 ms on ECG. What is the MOST COMMON cause of death in tricyclic antidepressant overdose?

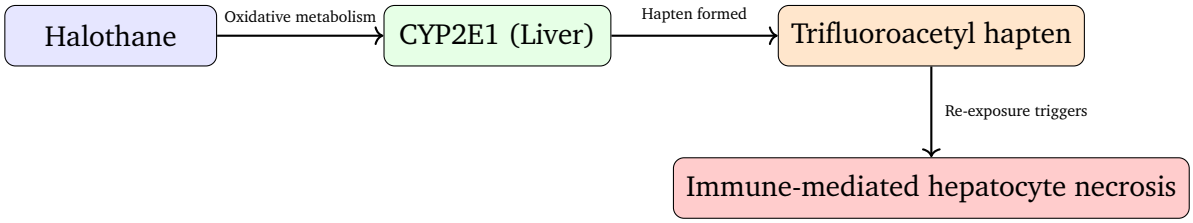
(A) Respiratory depression from muscarinic blockade

(B) Hyperthermia due to inhibition of sweating

(C) Hepatic necrosis from toxic metabolite accumulation

(D) Cardiac arrhythmias (due to Na^+ channel blockade causing QRS widening and ventricular tachycardia)

Q16. A 45-year-old patient undergoes a second surgery under halothane anaesthesia within three months of the first. Post-operatively she develops jaundice, fever, and markedly elevated liver enzymes. The following diagram illustrates halothane hepatic metabolism. What is the MOST SERIOUS complication of repeated halothane exposure?



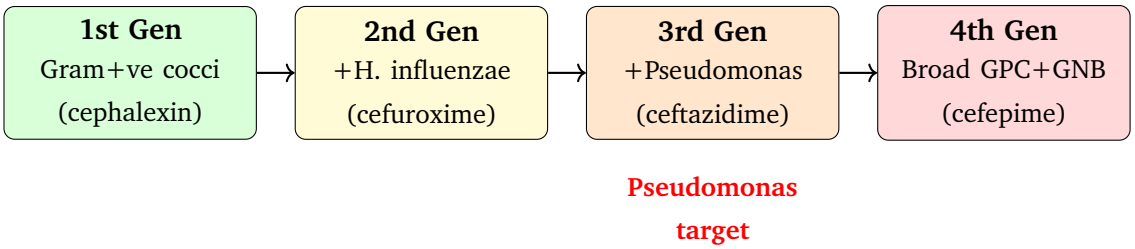
(A) Halothane hepatitis (immune-mediated fulminant hepatic necrosis on re-exposure)

(B) Malignant hyperthermia on first exposure

(C) Nephrotoxicity from fluoride ion release

(D) Cardiac sensitisation to epinephrine causing arrhythmia

Q17. The diagram below summarises the expanding antimicrobial spectrum across cephalosporin generations. Which cephalosporin has clinically significant activity against *Pseudomonas aeruginosa*?



(A) Cephalexin (1st generation)

(B) Ceftazidime (3rd generation)

(C) Cefuroxime (2nd generation)

(D) Cefazolin (1st generation)

Q18. A premature neonate treated with chloramphenicol develops abdominal distension, grey discolouration, vascular collapse, and death – the "grey baby syndrome." Chloramphenicol binds the 50S ribosomal subunit and inhibits peptidyl transferase. What is the mechanism of grey baby syndrome?

(A) Direct inhibition of mitochondrial ribosomes in neonatal cardiac myocytes

(B) Immune hypersensitivity reaction to chloramphenicol in neonates

(C) Immature glucuronosyltransferase in neonates cannot conjugate chloramphenicol, leading to toxic accumulation

(D) Chloramphenicol competes with bilirubin for albumin binding, causing kernicterus

Q19. Erythromycin is a macrolide antibiotic that binds the 23S rRNA of the 50S ribosomal subunit and inhibits translocation. Beyond its antibacterial action, erythromycin has an additional pharmacological property exploited clinically in gastroparesis. What is this property?

(A) Inhibition of CYP3A4, increasing levels of co-administered drugs

(B) H_2 receptor antagonism, reducing gastric acid secretion

(C) Leukotriene receptor antagonism with mild anti-inflammatory effect

(D) Prokinetic action via motilin receptor agonism – stimulates gastrointestinal motility

Q20. Amoxicillin-clavulanate (co-amoxiclav) is effective against organisms that would otherwise be resistant to amoxicillin alone. Clavulanate itself has minimal antibacterial activity. What is the mechanism of action of clavulanate?

(A) It irreversibly inhibits bacterial β-lactamase enzymes, protecting amoxicillin from degradation

(B) It competitively inhibits bacterial penicillin-binding proteins (PBPs)

(C) It enhances cellular uptake of amoxicillin through outer membrane porins

(D) It inhibits bacterial efflux pumps, preventing antibiotic expulsion

Q21. Clindamycin is frequently used for anaerobic infections above the diaphragm and skin/soft tissue infections. A patient treated with clindamycin for a dental abscess develops profuse, watery, bloody diarrhoea two weeks after completing the course. What is the MOST SERIOUS complication of clindamycin use?

(A) Nephrotoxicity and ototoxicity

(B) Pseudomembranous colitis (*Clostridioides difficile*-associated diarrhoea/colitis)

(C) Aplastic anemia (idiosyncratic bone marrow suppression)

(D) Steven-Johnson syndrome (severe cutaneous drug reaction)

Q22. Isoniazid (INH) is the cornerstone of anti-tuberculosis therapy. It inhibits InhA (enoyl-ACP reductase), blocking mycolic acid synthesis. A common dose-related adverse effect of INH is peripheral neuropathy, especially in malnourished patients and slow acetylators. Which vitamin should be co-administered with INH to prevent this adverse effect?

(A) Vitamin B12 (cyanocobalamin)

(B) Vitamin C (ascorbic acid)

(C) Pyridoxine (Vitamin B6)

(D) Thiamine (Vitamin B1)

Q23. Fluconazole is a triazole antifungal with excellent oral bioavailability and CSF penetration, used for Cryptococcal meningitis maintenance therapy. What is the primary mechanism of action of fluconazole?

(A) Binds ergosterol directly in the fungal cell membrane, forming pores

(B) Inhibits fungal β-1,3-glucan synthase, disrupting cell wall synthesis

(C) Inhibits fungal DNA topoisomerase II, causing DNA strand breaks

(D) Inhibits fungal lanosterol 14α-demethylase (CYP51), blocking ergosterol synthesis

Q24. Zidovudine (AZT) was the first antiretroviral drug approved for HIV infection. It belongs to the nucleoside reverse transcriptase inhibitor (NRTI) class. What is the mechanism by which zidovudine inhibits HIV replication?

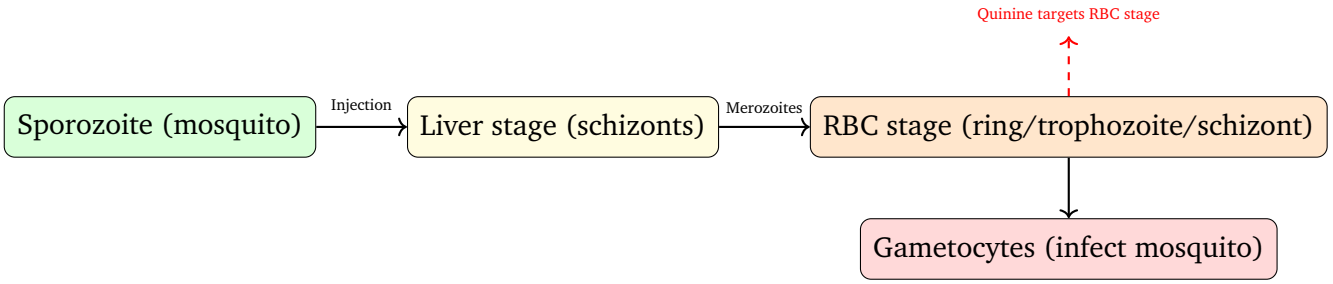
(A) It is incorporated into viral DNA by reverse transcriptase and terminates further chain elongation (lacks 3'-OH group)

(B) It competitively blocks the active site of HIV protease, preventing polyprotein cleavage

(C) It inhibits HIV integrase, preventing integration of viral DNA into the host genome

(D) It binds the CD4 receptor on T-lymphocytes, blocking viral entry

Q25. Quinine is used for severe falciparum malaria when artemisinin-based therapy is unavailable. The diagram below shows the simplified malaria life cycle and the stage targeted by blood schizontocides like quinine. Which adverse effect is CHARACTERISTICALLY associated with quinine?



(A) Blackwater fever in all patients

(B) Cinchonism (tinnitus, headache, nausea, vertigo)

(C) Haemolytic anemia in patients with normal G6PD

(D) Peripheral neuropathy with long-term use

Q26. Mebendazole and albendazole are benzimidazole anthelmintics used for intestinal nematode infections (roundworm, hookworm, pinworm) and tissue parasites (echinococcosis with albendazole). What is the mechanism of action of these drugs?

(A) They open chloride channels in nematode nerve/muscle, causing hyperpolarisation and paralysis

(B) They inhibit cholinesterase in helminths, leading to spastic paralysis

(C) Inhibition of microtubule polymerisation in helminths by binding β-tubulin, impairing glucose uptake

(D) They irreversibly activate glutamate-gated Cl^- channels in helminths (ivermectin mechanism)

Q27. Lidocaine is a Class Ib antiarrhythmic agent with use-dependent sodium channel blockade. Unlike Class Ia drugs, it shortens the action potential duration and refractory period. Which is the PRIMARY indication for intravenous lidocaine?

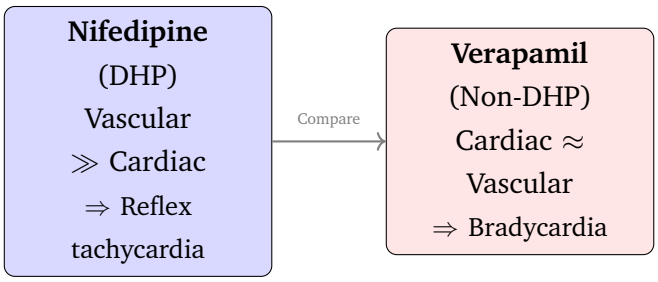
(A) Supraventricular tachycardia (SVT) refractory to adenosine

(B) Atrial fibrillation with rapid ventricular rate

(C) Complete heart block requiring rate support

(D) Ventricular tachyarrhythmias, especially post-myocardial infarction

Q28. A hypertensive patient on nifedipine (dihydropyridine CCB) complains of palpitations. Nifedipine acts predominantly on vascular smooth muscle L-type calcium channels. Verapamil acts on both vascular and cardiac calcium channels. The diagram compares their selectivity. Which side effect is MORE PRONOUNCED with nifedipine compared to verapamil?



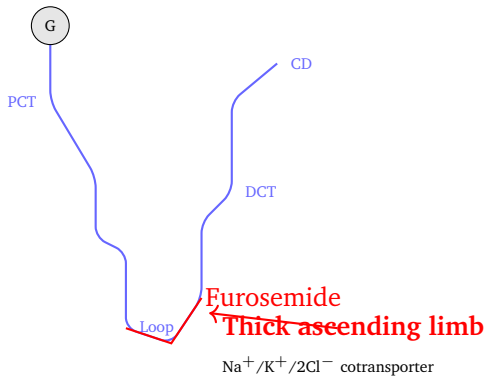
(A) Reflex tachycardia (due to selective vascular smooth muscle relaxation without direct cardiac effects)

(B) Bradycardia and AV block

(C) Constipation (smooth muscle relaxation in GI tract)

(D) Hyperkalaemia due to aldosterone suppression

Q29. Furosemide is the most potent diuretic in clinical use. The nephron diagram below shows the site of furosemide action. Which metabolic effect of furosemide is the OPPOSITE of that produced by thiazide diuretics?



(A) Hypokalaemia (both furosemide and thiazides cause this)

(B) Hypocalcaemia (furosemide causes Ca^{2+} wasting; thiazides cause Ca^{2+} retention)

(C) Hyperuricaemia (both furosemide and thiazides cause this)

(D) Hyponatraemia (both furosemide and thiazides cause this)

Q30. Statins (e.g., atorvastatin, simvastatin, rosuvastatin) are the most widely prescribed lipid-lowering agents. They reduce LDL-cholesterol by 30–60%. What is the PRIMARY mechanism of cholesterol reduction by statins?

(A) Inhibition of cholesterol absorption from the intestine (ezetimibe mechanism)

(B) Activation of lipoprotein lipase, enhancing triglyceride clearance

(C) Competitive inhibition of HMG-CoA reductase, the rate-limiting enzyme of cholesterol biosynthesis

(D) Sequestration of bile acids in the intestinal lumen (bile acid sequestrant mechanism)

Q31. A 22-year-old student presents 36 hours after ingesting 20 g of paracetamol (acetaminophen). He has right upper quadrant pain and markedly elevated liver enzymes (ALT 4800 U/L). Which toxic metabolite is responsible for paracetamol hepatotoxicity?

(A) Glucuronide conjugate of paracetamol

(B) Paracetamol sulfate ester

(C) Acetyl-CoA (formed during normal hepatic metabolism)

(D) NAPQI (N-acetyl-p-benzoquinone imine) formed by CYP2E1/CYP3A4

Q32. A premature neonate at 28 weeks gestation has a haemodynamically significant patent ductus arteriosus (PDA). Prostaglandins (PGE1, PGE2) maintain ductal patency. Which drug, based on its mechanism of COX inhibition, is used for pharmacological closure of PDA?

(A) Indomethacin (pharmacological closure of PDA in premature neonates)

(B) Celecoxib (selective COX-2 inhibitor)

(C) Naproxen (long half-life NSAID)

(D) Paracetamol (weak COX inhibitor)

Q33. Methotrexate (MTX) is a disease-modifying antirheumatic drug (DMARD) used in rheumatoid arthritis (RA) at low doses. It requires supplementation with folic acid to reduce adverse effects. What is the mechanism of action of methotrexate in RA?

(A) Inhibition of interleukin-6 (IL-6) signalling via JAK-STAT pathway

(B) Inhibition of dihydrofolate reductase (DHFR), reducing available folate for DNA synthesis in rapidly dividing immune cells

(C) Direct inhibition of TNF-α by forming a stable complex with the cytokine

(D) Depletion of B-lymphocytes via complement-mediated cytotoxicity

Q34. A physician needs to prescribe a corticosteroid with high glucocorticoid potency but virtually no sodium-retaining (mineralocorticoid) activity for a patient with cerebral oedema. Which statement about dexamethasone is CORRECT?

(A) Dexamethasone has the highest mineralocorticoid activity among all glucocorticoids

(B) Dexamethasone and hydrocortisone have equivalent mineralocorticoid activity

(C) Dexamethasone has virtually no mineralocorticoid activity (high glucocorticoid potency with minimal Na^+/water retention)

(D) Dexamethasone is preferred in Addison's disease because of its high mineralocorticoid effect

Q35. Metformin is the first-line oral antidiabetic drug for type 2 diabetes mellitus. Unlike sulfonylureas, it does NOT cause hypoglycaemia (eugly-

caemic agent). What is the PRIMARY mechanism of antidiabetic action of metformin?

(A) Stimulation of pancreatic β-cell insulin secretion via K_{ATP} channel closure

(B) Inhibition of intestinal α-glucosidase, delaying carbohydrate absorption

(C) Activation of PPAR-γ receptors in adipose tissue, improving insulin sensitivity

(D) Activation of AMPK leading to inhibition of hepatic gluconeogenesis and improved peripheral insulin sensitivity

Q36. A 24-year-old woman requests combined oral contraceptive pill (OCP) counselling. The pill contains both oestrogen and progestogen. What is the PRIMARY mechanism of contraceptive action of combined OCPs?

(A) Suppression of the mid-cycle LH surge, thereby preventing ovulation

(B) Direct cytotoxic effect on the fertilised ovum in the fallopian tube

(C) Inhibition of sperm motility within the seminal vesicles

(D) Thickening of the endometrium, preventing implantation only

Q37. H_2-receptor antagonists competitively block histamine H_2 receptors on gastric parietal cells, reducing acid secretion. A patient on warfarin, theophylline, and phenytoin is commenced on an H_2 blocker for peptic ulcer disease. His INR rises dangerously. Which H_2 blocker is a potent CYP450 inhibitor, causing significant drug interactions?

(A) Famotidine

(B) Cimetidine (inhibits CYP450, raising levels of warfarin, theophylline, and phenytoin)

(C) Ranitidine

(D) Nizatidine

Q38. Theophylline is a methylxanthine bronchodilator with a narrow therapeutic index. It requires plasma level monitoring (10–20 mcg/mL therapeutic range). Toxic effects include nausea, vomiting, tachycardia, and seizures at high plasma levels. What is the mechanism of bronchodilation produced by theophylline?

(A) Direct activation of β_2-adrenergic receptors in bronchial smooth muscle

(B) Blockade of muscarinic (M_3) receptors in bronchial smooth muscle

(C) Inhibition of phosphodiesterase (PDE), increasing intracellular cAMP in bronchial smooth muscle

(D) Blockade of leukotriene D_4 (LTD_4) receptors on bronchial smooth muscle

Q39. Ondansetron is the standard antiemetic for chemotherapy-induced nausea and vomiting (CINV) and post-operative nausea. Unlike metoclopramide, ondansetron does NOT cause extrapyramidal adverse effects. Which receptor does ondansetron antagonise?

(A) Dopamine D_2 receptor in the chemoreceptor trigger zone (CTZ)

(B) Histamine H_1 receptor in the vestibular nucleus

(C) Muscarinic M_1 receptor in the vomiting centre

(D) 5-Hydroxytryptamine type 3 (5-HT_3) receptor in the GI tract and CTZ

Q40. A 55-year-old male presents with an acute STEMI within 2 hours of symptom onset. The treating physician considers thrombolytic therapy with streptokinase. Streptokinase is antigenic and cannot be re-used within 12 months. What is the mechanism of action of fibrinolytics such as streptokinase?

(A) Conversion of plasminogen to plasmin, which then degrades fibrin clots

(B) Direct inhibition of thrombin (factor IIa) independent of antithrombin

(C) Inhibition of vitamin K epoxide reductase, reducing clotting factor synthesis

(D) Irreversible inhibition of platelet COX-1, preventing thromboxane A_2 formation

Detailed Solutions

Q1.

Solution

Concept – Plasma Half-Life ($t_{½}$): The half-life is the time required for the plasma drug concentration to fall by 50%. Here, the concentration halves from 200 mg (at 6 h) to 100 mg (at 12 h) – an interval of 6 hours. Alternatively, from the initial 400 mg to 200 mg also takes 6 hours. The formula is $t_{1/2} = 0.693/k_e$, but direct inspection of the data confirms the answer.

Key points: (1) For drugs following first-order kinetics, $t_{½}$ is constant regardless of initial concentration. (2) $t_{½}$ determines dosing interval and time to steady state (~5 half-lives).

Final Answer: The plasma concentration halves every 6 hours $\Rightarrow \boxed{B}$

Answer: (B) Go Back to Q1

Q2.

Solution

Concept – Zero-Order Kinetics: In zero-order kinetics, the rate of elimination is constant (independent of concentration) because the metabolic pathway is **saturated at all plasma levels**. Ethanol (alcohol dehydrogenase system saturates at very low blood alcohol concentrations) and aspirin in **overdose** show zero-order kinetics. Of the options, **ethanol** uniquely shows zero-order kinetics even at social/therapeutic doses.

Contrast with first-order: Most drugs follow first-order kinetics (constant % eliminated per unit time). Phenytoin also shows zero-order kinetics at therapeutic doses (capacity-limited; Michaelis-Menten kinetics).

Final Answer: Ethanol shows zero-order kinetics at all ingested doses $\Rightarrow \boxed{C}$

Answer: (C) Go Back to Q2

Q3.

Solution

Concept – Competitive Antagonism: A competitive (surmountable) antagonist binds reversibly to the same receptor as the agonist. Increasing agonist concentration can overcome the blockade. The dose-response curve shifts **to the right** (EC_{50} increases) but the maximum effect (E_{max}) remains **unchanged**.

Contrast with non-competitive antagonism: A non-competitive antagonist re-

duces E_{max} (irreversible or allosteric binding; the curve is depressed, not just shifted).

Mnemonic: "Competitive = Curve shifts Right with Same ceiling" (CRSS).

Final Answer: E_{max} is unchanged; EC_{50} is increased (rightward shift) $\Rightarrow \boxed{D}$

Answer: (D) Go Back to Q3

Q4.

Solution

Concept – Plasma Protein Binding Displacement: Warfarin is 99% protein-bound (to albumin). Only the free (unbound) fraction is pharmacologically active. When aspirin displaces warfarin from binding sites, the free warfarin concentration rises acutely, augmenting anticoagulant effect and increasing bleeding risk. This is a classic drug interaction exam point.

Note: Aspirin also has its own antiplatelet effect (irreversible COX-1 inhibition), further compounding bleeding risk.

Final Answer: Displacement from plasma protein binding sites increases free warfarin concentration $\Rightarrow \boxed{A}$

Answer: (A) Go Back to Q4

Q5.

Solution

Concept – Succinylcholine and Hyperkalaemia: Succinylcholine (suxamethonium) is a depolarising NMB. It activates ACh receptors, causing sustained depolarisation and initial muscle fasciculations. In patients with **extensive burns, crush injuries, prolonged immobility, upper/lower motor neuron lesions**, there is upregulation of extrajunctional ACh receptors across the entire muscle membrane. Succinylcholine activates all these receptors simultaneously, releasing large amounts of K^+ into the circulation, potentially causing **fatal cardiac arrest from hyperkalaemia**.

Safe uses of succinylcholine: Rapid sequence induction (RSI), anticipated difficult airway, full stomach.

Final Answer: Extensive burns or crush injuries (hyperkalaemia risk) $\Rightarrow \boxed{B}$

Answer: (B) Go Back to Q5

Q6.

Solution

Concept – Methacholine Challenge Test: Methacholine is a synthetic, selective muscarinic agonist (M2/M3) resistant to AChE hydrolysis. Inhaled methacholine causes bronchoconstriction. In **normal individuals**, a high concentration is required to produce a 20% fall in FEV_1 ($PC_{20} > 16\,mg/mL$). In **asthmatics** with airway hyperresponsiveness, bronchoconstriction occurs at much lower concentrations ($PC_{20} < 4\,mg/mL$). This is the **bronchial provocation challenge test** used to diagnose asthma when spirometry is normal at rest.

Final Answer: Bronchial provocation challenge test to diagnose airway hyperresponsiveness (asthma) $\Rightarrow \boxed{C}$

Answer: (C) Go Back to Q6

Q7.

Solution

Concept – Cardioselective β-Blockers: Atenolol is a β_1-selective (cardioselective) blocker. At standard therapeutic doses it predominantly blocks cardiac β_1 receptors with minimal effect on β_2 receptors in the bronchi. Propranolol is **nonselective** (β_1 and β_2); blocking β_2 in asthmatic airways can precipitate severe bronchospasm.

Important caveat: Cardioselectivity is **relative, not absolute** – at high doses, atenolol also blocks β_2 receptors. It should be used with caution (not freely) in asthmatics.

Other cardioselective β-blockers: Metoprolol, bisoprolol, nebivolol.

Final Answer: Cardioselective β_1 blockade without significant β_2 receptor blockade $\Rightarrow \boxed{D}$

Answer: (D) Go Back to Q7

Q8.

Solution

Concept – Indirect Sympathomimetics (Amphetamine): Amphetamine does NOT directly activate adrenergic receptors. It is an indirect sympathomimetic: it enters the presynaptic nerve terminal via the norepinephrine/dopamine transporter (NET/DAT) and causes **carrier-mediated release** of norepinephrine and dopamine from storage vesicles into the synapse (reverse transport). It also inhibits reuptake (but the primary mechanism is release).

Effects: CNS stimulation (dopamine release in mesolimbic/mesocortical pathways), peripheral sympathomimetic effects (tachycardia, hypertension, vasoconstriction), anorexia (hypothalamic effect).

Final Answer: Promotes release of norepinephrine and dopamine from presynaptic nerve terminals $\Rightarrow \boxed{A}$

Answer: (A) Go Back to Q8

Q9.

Solution

Concept – Organophosphate Poisoning Treatment: Organophosphates (OPs) irreversibly phosphorylate the serine residue at the active site of AChE. This prevents ACh hydrolysis, causing cholinergic crisis (SLUDGE + nicotinic features: fasciculations, paralysis).

Treatment:

- **Atropine:** Blocks muscarinic effects (SLUDGE, bronchospasm, secretions) – given in large doses until secretions dry.
- **Pralidoxime (2-PAM):** Oxime that cleaves the phosphate-ester bond between OP and AChE, **reactivating AChE** – must be given **early** (before "ageing" – permanent irreversible binding occurs within hours to days depending on OP).
- Benzodiazepines for seizures.

Final Answer: Pralidoxime (2-PAM) reactivates AChE by cleaving the phosphoryl-enzyme bond $\Rightarrow \boxed{B}$

Answer: (B) Go Back to Q9

Q10.

Solution

Concept – Guanethidine (Adrenergic Neuron Blocker): Guanethidine is a highly polar drug that enters the adrenergic nerve terminal via the **norepinephrine uptake-1 transporter** (NET). Once inside, it:

(a) Replaces NE in storage vesicles, gradually depleting the NE pool.

(b) Blocks the release of NE in response to sympathetic nerve stimulation.

This results in sustained hypotension without compensatory tachycardia (because

sympathetic reflexes are also blocked). Tricyclic antidepressants block uptake-1, preventing guanethidine entry and abolishing its effect.

Final Answer: Enters adrenergic nerve terminal via uptake-1 and depletes NE from storage vesicles $\Rightarrow \boxed{C}$

Answer: (C) Go Back to Q10

Q11.

Solution

Concept – Opioid Analgesics and Pain Types: Opioids (morphine, fentanyl, pethidine) activate μ-opioid receptors in the spinal cord (substantia gelatinosa), supraspinal centres (PAG), and peripheral tissues. They are most effective for **severe visceral pain** (renal colic, biliary colic, MI, cancer pain, post-operative pain). Visceral pain has a high density of opioid receptors in afferent pathways.

Pain type response to opioids:

- Visceral pain: **excellent** response
- Somatic deep pain (bone, muscle): good response
- Neuropathic pain: **poor** response (better with TCAs, gabapentin)
- Superficial somatic pain: NSAIDs often sufficient

Final Answer: Severe visceral pain (e.g., renal colic, myocardial infarction) $\Rightarrow \boxed{D}$

Answer: (D) Go Back to Q11

Q12.

Solution

Concept – Barbiturates vs Benzodiazepines at GABA-A: Both drug classes potentiate GABA-A receptor-mediated Cl^- influx (hyperpolarisation), but at distinct binding sites and by different mechanisms:

Drug class	GABA-A effect	At high dose
Benzodiazepines	↑ **frequency** of Cl^- channel opening	Need GABA present
Barbiturates	↑ **duration** of Cl^- channel opening	Open channel directly

Barbiturates also directly open Cl^- channels at high doses (explaining their lower safety margin compared to benzodiazepines).

Mnemonic: "**B**arBiturates – **D**uration; **B**enzodiazepines – **F**requency" (BDF, BFF).

Final Answer: Phenobarbitone increases the *duration* of Cl^- channel opening $\Rightarrow$ $\boxed{A}$

Answer: (A) Go Back to Q12

Q13.

Solution

Concept – Carbamazepine Adverse Effects: Carbamazepine (CBZ) is a first-line AED for partial (focal) seizures and trigeminal neuralgia. It acts via use-dependent blockade of voltage-gated Na^+ channels. Important adverse effects:

- **Haematological (serious):** Aplastic anemia (rare, idiosyncratic) and agranulocytosis – require periodic blood count monitoring.
- **Dermatological:** Stevens-Johnson syndrome (SJS)/toxic epidermal necrolysis (TEN), especially in HLA-B*1502 carriers (South-East Asian populations).
- **Electrolyte:** Hyponatraemia (SIADH – CBZ stimulates ADH release).
- **Teratogenicity:** Neural tube defects (spina bifida) – use folic acid supplementation.
- **Enzyme inducer:** Induces CYP3A4, CYP2C9 – reduces efficacy of OCP, warfarin, other AEDs.

Final Answer: Aplastic anemia and agranulocytosis $\Rightarrow$ $\boxed{B}$

Answer: (B) Go Back to Q13

Q14.

Solution

Concept – Lithium Monitoring: Lithium has a very narrow therapeutic index (therapeutic range: 0.6–1.2 mEq/L; toxic above 1.5 mEq/L). It is not metabolised; excreted entirely by the kidney. Serum lithium levels must be monitored regularly (every 3–6 months when stable, more frequently when initiating or adjusting dose, or when clinical status changes).

Lithium toxicity signs: Fine tremor $\rightarrow$ coarse tremor $\rightarrow$ ataxia $\rightarrow$ confusion $\rightarrow$ seizures $\rightarrow$ coma. Toxicity precipitated by: dehydration, NSAIDs (reduce renal Li excretion), thiazides, ACE inhibitors.

Other monitoring: Thyroid function (hypothyroidism), renal function (nephro-

genic DI).

Final Answer: Regular serum lithium levels (narrow therapeutic index) $\Rightarrow \boxed{C}$

Answer: (C) Go Back to Q14

Q15.

Solution

Concept – TCA Overdose and Cardiac Toxicity: Tricyclic antidepressants (e.g., amitriptyline, imipramine) have multiple actions in overdose:

- **Fast Na^+ channel blockade** (membrane stabilising): Slows depolarisation $\rightarrow$ QRS widening $\rightarrow$ ventricular tachycardia/fibrillation. This is the **most common cause of death** in TCA overdose.
- Anticholinergic effects: Tachycardia, urinary retention, hyperthermia.
- α_1 blockade: Hypotension.
- α_1 CNS: Sedation, coma.

ECG hallmark: Prolonged QRS $>$ 100 ms predicts seizures; $>$ 160 ms predicts ventricular arrhythmias. **Treatment:** IV sodium bicarbonate (alkalinises blood, narrows QRS by reducing Na^+ channel blockade).

Final Answer: Cardiac arrhythmias (Na^+ channel blockade $\rightarrow$ QRS widening $\rightarrow$ ventricular tachycardia) $\Rightarrow \boxed{D}$

Answer: (D) Go Back to Q15

Q16.

Solution

Concept – Halothane Hepatotoxicity: Halothane is metabolised oxidatively (primarily by CYP2E1) to a trifluoroacetyl (TFA) chloride hapten. This hapten covalently binds to hepatic proteins, creating **neo-antigens** that trigger a T-cell-mediated immune response on re-exposure. This causes **massive centrilobular hepatic necrosis** (fulminant halothane hepatitis) – mortality 50–75%.

Risk factors: Female sex, obesity, middle age, multiple exposures, short interval between exposures.

Other halothane adverse effects (also tested):

- Malignant hyperthermia trigger (ryanodine receptor mutation – treat with dantrolene)

- Myocardial sensitisation to catecholamines (arrhythmias if adrenaline used)
- Minor hepatotoxicity (transaminase rise) in ~20% on first exposure (not immune-mediated)

Final Answer: Halothane hepatitis (immune-mediated fulminant hepatic necrosis on re-exposure) $\Rightarrow \boxed{A}$

Answer: (A) Go Back to Q16

Q17.

Solution

Concept – Cephalosporin Generations and Spectrum:

Generation	Key organisms	Examples
1st	Gram+ve cocci (MSSA, Strep)	Cephalexin, cefazolin
2nd	+H. influenzae, Moraxella	Cefuroxime, cefaclor
3rd	+GNB, *Pseudomonas* (ceftazidime)	Ceftriaxone, **ceftazidime**
4th	Broad GPC+GNB+*Pseudomonas*	Cefepime

Among 3rd-generation cephalosporins, **ceftazidime** and cefoperazone have anti-pseudomonal activity; ceftriaxone does NOT. Cefepime (4th generation) also covers Pseudomonas.

Clinical pearl: *Pseudomonas aeruginosa* infections (ICU pneumonia, burns, CF lung disease) require anti-pseudomonal coverage.

Final Answer: Ceftazidime (3rd generation) is active against *Pseudomonas aeruginosa* $\Rightarrow \boxed{B}$

Answer: (B) Go Back to Q17

Q18.

Solution

Concept – Grey Baby Syndrome: Chloramphenicol is normally inactivated in the liver by **UDP-glucuronosyltransferase (UGT)** to an inactive glucuronide conjugate that is renally excreted. Neonates (especially premature) have immature UGT activity. Consequently, chloramphenicol accumulates to toxic concentrations, causing:

- Abdominal distension, vomiting, refusal to feed
- Grey skin colour (due to circulatory collapse, tissue hypoperfusion)

- Hypothermia, flaccidity, cardiovascular collapse
- Death within 2–3 days if untreated

Grey baby syndrome = neonatal immature glucuronidation → chloramphenicol accumulation → toxicity.

Note: Chloramphenicol also causes aplastic anemia (idiosyncratic, not dose-related – check FBC regularly).

Final Answer: Immature glucuronosyltransferase in neonates cannot conjugate chloramphenicol, leading to toxic accumulation $\Rightarrow \boxed{C}$

Answer: (C) Go Back to Q18

Q19.

Solution

Concept – Erythromycin as Prokinetic: Erythromycin (at subantimicrobial doses) acts as an agonist at **motilin receptors** in the GI tract. Motilin is a peptide hormone that initiates migrating motor complexes (MMC – the "housekeeper" contractions of the GI tract). Erythromycin mimics motilin:

- Accelerates gastric emptying
- Used in **gastroparesis** (diabetic gastroparesis, post-vagotomy)
- Also used to clear blood from the stomach before emergency endoscopy

Note on CYP3A4: Erythromycin also inhibits CYP3A4 (important drug interaction – raises levels of warfarin, theophylline, digoxin, statins), but this is a pharmacokinetic interaction, not an "additional pharmacological property."

Final Answer: Prokinetic action via motilin receptor agonism – stimulates GI motility $\Rightarrow \boxed{D}$

Answer: (D) Go Back to Q19

Q20.

Solution

Concept – β-Lactamase Inhibitors: Clavulanate (clavulanic acid) is a **"suicide substrate" or irreversible inhibitor** of bacterial β-lactamase enzymes. It binds to the active site of β-lactamase, forms a stable acyl-enzyme complex, and is irreversibly inactivated along with the enzyme ("mechanism-based" irreversible inhi-

bition). This protects co-administered amoxicillin from enzymatic hydrolysis.

Other β-lactamase inhibitors: Sulbactam (ampicillin-sulbactam), tazobactam (piperacillin-tazobactam).

Clinical application: Amoxicillin-clavulanate covers β-lactamase-producing organisms: MSSA, Haemophilus, Moraxella, E. coli, Klebsiella, anaerobes.

Final Answer: Clavulanate irreversibly inhibits bacterial β-lactamase, protecting amoxicillin from degradation $\Rightarrow \boxed{A}$

Answer: (A) Go Back to Q20

Q21.

Solution

Concept – Clindamycin and *C. difficile*: Clindamycin binds the 50S ribosomal subunit (peptidyl transferase centre) and inhibits translocation, like erythromycin. It is highly effective against anaerobes above the diaphragm and Gram-positive cocci. However, it disrupts normal colonic flora, allowing overgrowth of *Clostridioides difficile* (spore-forming, toxin-producing anaerobe).

***C. difficile* colitis:**

- Toxin A (enterotoxin): watery diarrhoea, mucosal oedema.
- Toxin B (cytotoxin): mucosal necrosis, pseudomembrane formation.
- Treatment: Stop clindamycin; oral metronidazole or vancomycin; fidaxomicin for recurrence.

Other high-risk antibiotics for *C. diff*: Ampicillin/amoxicillin, fluoroquinolones, 3rd-gen cephalosporins.

Final Answer: Pseudomembranous colitis (*C. difficile*-associated diarrhoea/colitis) $\Rightarrow \boxed{B}$

Answer: (B) Go Back to Q21

Q22.

Solution

Concept – INH Peripheral Neuropathy and Pyridoxine: Isoniazid competes with **pyridoxal phosphate (active form of Vitamin B6)** for the enzyme pyridoxal phosphokinase, and also combines with pyridoxine to form an inactive hydrazone, causing functional B6 deficiency. This leads to peripheral neuropathy (sensorimo-

tor, dose-related, more common in:

- Slow acetylators (higher INH plasma levels)
- Malnourished patients, alcoholics, diabetics, HIV-positive patients
- Pregnant women

Prevention and treatment: **Pyridoxine (Vitamin B6) 10–50 mg/day** co-administered with INH.

Other INH side effects: Hepatotoxicity (monitor LFTs), lupus-like syndrome, enzyme inhibitor (raises phenytoin/carbamazepine levels in slow acetylators).

Final Answer: Pyridoxine (Vitamin B6) should be co-administered with INH $\Rightarrow$ $\boxed{C}$

Answer: (C) Go Back to Q22

Q23.

Solution

Concept – Triazole Antifungals (Fluconazole) Mechanism: Fluconazole inhibits the fungal cytochrome P450 enzyme **lanosterol 14α-demethylase (CYP51)**, which converts lanosterol to ergosterol. Ergosterol is an essential component of the fungal cell membrane (analogous to cholesterol in human cells). Ergosterol depletion:

- Increases cell membrane permeability
- Impairs function of membrane-bound enzymes
- Results in fungistatic (not fungicidal) effect

Clinical uses: Candidiasis (oral, vaginal, oesophageal, invasive), Cryptococcal meningitis (maintenance), dermatophytosis.

Drug interaction: Fluconazole inhibits CYP2C9 $\rightarrow$ raises warfarin levels (INR monitoring required).

Final Answer: Inhibition of fungal lanosterol 14α-demethylase (CYP51) blocking ergosterol synthesis $\Rightarrow$ $\boxed{D}$

Answer: (D) Go Back to Q23

Q24.

Solution

Concept – NRTI Mechanism (Zidovudine): NRTIs are prodrugs that are phosphorylated intracellularly to their active triphosphate form. Zidovudine triphosphate (AZTMP):

(a) Is incorporated into the growing viral DNA chain by HIV reverse transcriptase (competing with natural dTTP substrate).

(b) Acts as a **chain terminator**: it lacks a 3'-hydroxyl (-OH) group, so no further nucleotide can be added (no phosphodiester bond formation).

This selectively inhibits HIV replication (human DNA polymerases have much lower affinity for AZTMP).

Side effects of zidovudine: Bone marrow suppression (anemia, neutropenia), myopathy (mitochondrial toxicity), lactic acidosis (class effect of NRTIs).

Final Answer: Incorporated into viral DNA by RT; terminates chain elongation (lacks 3'-OH) $\Rightarrow \boxed{A}$

Answer: (A) Go Back to Q24

Q25.

Solution

Concept – Quinine Adverse Effects: Quinine is an alkaloid derived from cinchona bark. It acts as a blood schizontocide (kills RBC stage of *Plasmodium falciparum* by inhibiting haemozoin formation). Its adverse effects include:

- **Cinchonism (characteristic):** Tinnitus, headache, nausea, vertigo, blurred vision, hearing loss. Dose-related, at therapeutic levels.
- Hypoglycaemia (stimulates pancreatic insulin release – especially during IV infusion).
- Blackwater fever: haemoglobinuria due to intravascular haemolysis – occurs in G6PD-deficient patients, but also rarely in non-G6PD patients with repeated quinine exposure.
- Cinchona alkaloid hypersensitivity (thrombocytopenia, urticaria).
- QTc prolongation (IV quinine $\rightarrow$ ventricular arrhythmia).

Final Answer: Cinchonism (tinnitus, headache, nausea, vertigo) is the characteristic quinine adverse effect $\Rightarrow \boxed{B}$

Answer: (B) Go Back to Q25

Q26.

Solution

Concept – Benzimidazole Anthelmintics: Mebendazole and albendazole bind selectively to β-**tubulin** in helminths (much higher affinity than mammalian β-tubulin). This:

- Inhibits microtubule polymerisation $\rightarrow$ disrupts cytoskeletal integrity.
- Impairs glucose uptake (helminth-specific energy metabolism).
- Inhibits secretory granule transport and egg hatching.

Result: the worm is slowly killed (not acutely paralysed – unlike pyrantel pamoate or ivermectin).

Albendazole vs mebendazole: Albendazole is better absorbed (with fatty meal) and used for tissue parasites (cysticercosis, echinococcosis, toxocariasis). Mebendazole is poorly absorbed and best for intestinal helminths.

Final Answer: Inhibition of microtubule polymerisation by binding β-tubulin in helminths $\Rightarrow \boxed{C}$

Answer: (C) Go Back to Q26

Q27.

Solution

Concept – Lidocaine (Class Ib Antiarrhythmic): Lidocaine blocks voltage-gated fast Na^+ channels in a use-dependent manner (preferentially blocks channels in the open/inactivated state – more effective at rapid heart rates). In ischaemic myocardium (post-MI), depolarised tissues are disproportionately blocked.

Class Ib features: Shortens action potential duration (APD) and effective refractory period (ERP) – opposite to Class Ia. Does NOT prolong QT interval.

Indications for IV lidocaine:

- **Ventricular tachycardia (VT)** – especially post-MI
- Ventricular fibrillation (VF) after defibrillation
- Digitalis-induced ventricular arrhythmias

Note: Lidocaine is ineffective for supraventricular arrhythmias (SVT, AF, AFL).

Final Answer: Ventricular tachyarrhythmias, especially post-myocardial infarction $\Rightarrow \boxed{D}$

Answer: (D) Go Back to Q27

Q28.

Solution

Concept – Dihydropyridine vs Non-DHP Calcium Channel Blockers: L-type Ca^{2+} channels are present in both vascular smooth muscle and cardiac muscle. The two subclasses differ in selectivity:

Property	Nifedipine (DHP)	Verapamil (Non-DHP)
Vascular selectivity	High	Moderate
Cardiac depression	Minimal	Significant
Heart rate	↑ (reflex tachycardia)	↓ (bradycardia)
AV conduction	Unaffected	Prolonged

Nifedipine causes profound peripheral vasodilation → baroreceptor-mediated reflex sympathetic activation → **reflex tachycardia**. This is undesirable in angina (increases cardiac oxygen demand). Long-acting amlodipine has a slower onset and less reflex tachycardia.

Final Answer: Reflex tachycardia (due to selective vascular smooth muscle relaxation) $\Rightarrow \boxed{A}$

Answer: (A) Go Back to Q28

Q29.

Solution

Concept – Loop Diuretics vs Thiazides and Calcium: Furosemide inhibits the $Na^+/K^+/2Cl^-$ (NKCC2) cotransporter in the **thick ascending limb of the loop of Henle**. This abolishes the lumen-positive electrical potential that normally drives Ca^{2+} (and Mg^{2+}) reabsorption paracellularly. Result: **urinary Ca^{2+} wasting** → **hypocalcaemia**.

Thiazides act on the NCC cotransporter in the **distal convoluted tubule** and paradoxically **increase** Ca^{2+} reabsorption (by stimulating Na^+/Ca^{2+} exchange in DCT) → **hypercalcaemia**.

Clinical applications of this difference:

- Furosemide: hypercalcaemia emergency ("flush" Ca^{2+} out)

- Thiazides: hypercalciuria/calcium oxalate stones (retain Ca^{2+}, reduce urinary calcium)

Final Answer: Hypocalcaemia (furosemide wastes Ca^{2+}; thiazides retain Ca^{2+}) $\Rightarrow$ $\boxed{B}$

Answer: (B) Go Back to Q29

Q30.

Solution

Concept – Statin Mechanism: Statins are structural analogues of HMG-CoA (hydroxymethylglutaryl-CoA). They **competitively inhibit HMG-CoA reductase**, the enzyme that converts HMG-CoA to mevalonate – the **rate-limiting step** in hepatic cholesterol biosynthesis. Consequences:

(a) $\downarrow$ intracellular cholesterol $\rightarrow$ upregulation of **LDL receptors** on hepatocytes $\rightarrow \uparrow$ clearance of circulating LDL.

(b) $\downarrow$ VLDL production (modest triglyceride lowering).

(c) $\uparrow$ HDL (modest).

Adverse effects: Myopathy (myalgia $\rightarrow$ CK elevation $\rightarrow$ rhabdomyolysis – especially with CYP3A4 inhibitors like erythromycin, azole antifungals); hepatotoxicity (monitor LFTs); teratogenicity (Category X).

Final Answer: Competitive inhibition of HMG-CoA reductase, the rate-limiting enzyme of cholesterol biosynthesis $\Rightarrow$ $\boxed{C}$

Answer: (C) Go Back to Q30

Q31.

Solution

Concept – Paracetamol Hepatotoxicity and NAPQI:

- **Normal therapeutic doses:** 90% paracetamol is conjugated to glucuronide or sulfate conjugates (non-toxic) and excreted. A small fraction ($\sim$5%) is oxidised by CYP2E1 and CYP3A4 to **NAPQI** (N-acetyl-p-benzoquinone imine), which is rapidly detoxified by **glutathione** (GSH).
- **Overdose:** Glucuronide and sulfate pathways saturate. Increased NAPQI production overwhelms GSH stores. Free NAPQI covalently binds hepatic macromolecules $\rightarrow$ **centrilobular (zone 3) hepatic necrosis**.

Treatment: N-acetylcysteine (NAC) replenishes glutathione stores – most effective within 8–10 hours, still beneficial up to 24 h. Use Rumack-Matthew nomogram (paracetamol level vs time since ingestion) to determine NAC need.

Final Answer: NAPQI (N-acetyl-p-benzoquinone imine) is the toxic metabolite responsible for paracetamol hepatotoxicity $\Rightarrow \boxed{D}$

Answer: (D) Go Back to Q31

Q32.

Solution

Concept – PDA Closure with Indomethacin: The ductus arteriosus is kept patent in the foetus by **prostaglandin E_2 (PGE_2)** and prostacyclin (PGI_2). After birth, PGE_2 levels fall and the duct closes. In premature neonates, elevated PGE_2 keeps the duct open.

Indomethacin (a potent, non-selective COX-1/COX-2 inhibitor) inhibits PGE_2 synthesis, promoting ductal constriction and closure. This avoids the need for surgical ligation.

Contraindications to indomethacin for PDA: Renal failure, IVH (intraventricular haemorrhage), necrotising enterocolitis, thrombocytopenia (platelet count $<$ 60,000).

Alternative: Ibuprofen (also used for PDA closure). Oral paracetamol has also been used (weak COX inhibitor, different mechanism).

Final Answer: Indomethacin for pharmacological closure of patent ductus arteriosus in premature neonates $\Rightarrow \boxed{A}$

Answer: (A) Go Back to Q32

Q33.

Solution

Concept – Methotrexate Mechanism in RA: Methotrexate (MTX) is a folate analogue that competitively inhibits **dihydrofolate reductase (DHFR)**. This reduces the regeneration of tetrahydrofolate (THF), depleting the pool of folate coenzymes required for:

- Purine synthesis (de novo)
- Thymidylate synthesis (dTMP)
- Ultimately DNA and RNA synthesis

In RA (low-dose weekly MTX), the anti-inflammatory effect is partly through adenosine pathway (adenosine release suppresses inflammation) and partly through anti-proliferative effects on immune cells.

Monitoring: FBC (myelosuppression), LFTs (hepatotoxicity), chest X-ray/PFTs (pulmonary toxicity). Supplement with **folic acid** to reduce GI and haematological toxicity without compromising anti-inflammatory efficacy.

Final Answer: Inhibition of DHFR, reducing available folate for DNA synthesis in rapidly dividing immune cells $\Rightarrow \boxed{B}$

Answer: (B) Go Back to Q33

Q34.

Solution

Concept – Relative Potencies of Corticosteroids:

Drug	Glucocorticoid potency	Mineralocorticoid potency
Hydrocortisone	1 (reference)	1
Prednisolone	4	0.8
Methylprednisolone	5	0.5
Dexamethasone	**25–30**	$\approx$ **0 (negligible)**
Fludrocortisone	10	125 (pure mineralocorticoid use)

Dexamethasone is the **most potent glucocorticoid** (weight for weight) with virtually no mineralocorticoid activity – no Na^+/water retention or hypertension from mineralocorticoid effects. This makes it ideal for cerebral oedema, croup, antiemesis, and dexamethasone suppression testing.

Final Answer: Dexamethasone has virtually no mineralocorticoid activity (high glucocorticoid, minimal Na^+/water retention) $\Rightarrow \boxed{C}$

Answer: (C) Go Back to Q34

Q35.

Solution

Concept – Metformin Mechanism: Metformin's primary mechanism involves **activation of AMP-activated protein kinase (AMPK)** in hepatocytes. AMPK is a cellular energy sensor activated when AMP:ATP ratio rises (metformin inhibits mitochondrial Complex I, mildly reducing ATP production). Activated AMPK:

(a) **Inhibits hepatic gluconeogenesis** (primary mechanism – major glucose-lowering effect)

(b) Increases peripheral glucose uptake (skeletal muscle via GLUT4 upregulation)

(c) Reduces intestinal glucose absorption (minor)

Key features: Does NOT stimulate insulin secretion (no hypoglycaemia as monotherapy); may cause mild weight loss; reduces cardiovascular mortality (UKPDS). Contraindicated in eGFR < 30 mL/min (lactic acidosis risk from impaired lactate clearance).

Final Answer: Activation of AMPK leading to inhibition of hepatic gluconeogenesis $\Rightarrow \boxed{D}$

Answer: (D) Go Back to Q35

Q36.

Solution

Concept – Mechanism of Combined OCP: The combined OCP (oestrogen + progestogen) works by three mechanisms, in order of importance:

(a) **Inhibition of the LH surge** (primary): Oestrogen + progestogen suppress GnRH pulsatility and directly inhibit pituitary LH release $\rightarrow$ prevents ovulation. This is the most reliable mechanism.

(b) **Cervical mucus thickening** (progestogen): Thick, viscous mucus impedes sperm penetration.

(c) **Endometrial thinning** (progestogen): Atrophic endometrium less receptive to implantation.

Oestrogen also suppresses FSH $\rightarrow$ prevents follicular development and provides a stable hormonal environment to prevent breakthrough bleeding.

Final Answer: Suppression of the mid-cycle LH surge, thereby preventing ovulation $\Rightarrow \boxed{A}$

Answer: (A) Go Back to Q36

Q37.

Solution

Concept – H_2 Blocker Drug Interactions (Cimetidine): Cimetidine is unique among H_2 blockers in being a **potent inhibitor of multiple CYP450 enzymes** (CYP1A2, CYP2C9, CYP2D6, CYP3A4). This raises plasma levels of co-administered drugs metabolised by these enzymes:

- **Warfarin** (CYP2C9): ↑ INR, bleeding risk
- **Theophylline** (CYP1A2): ↑ toxicity (seizures, tachycardia)
- **Phenytoin** (CYP2C9): ↑ phenytoin toxicity (nystagmus, ataxia)
- Lidocaine, propranolol, metoprolol, diazepam

Ranitidine, famotidine, nizatidine do NOT significantly inhibit CYP450 – they are safer alternatives when polypharmacy is a concern.

Final Answer: Cimetidine inhibits CYP450, raising levels of warfarin, theophylline, and phenytoin $\Rightarrow \boxed{B}$

Answer: (B) Go Back to Q37

Q38.

Solution

Concept – Theophylline Mechanism of Bronchodilation: Theophylline is a non-selective **phosphodiesterase (PDE) inhibitor**. PDE normally degrades cyclic AMP (cAMP) and cyclic GMP (cGMP) to their inactive 5'-monophosphates. Inhibiting PDE:

- ↑ intracellular cAMP in bronchial smooth muscle → activates PKA → phosphorylates myosin light-chain kinase (MLCK) → smooth muscle relaxation → **bronchodilation**
- Also ↑ cAMP in mast cells → reduced mediator release (anti-inflammatory)

Additional mechanism: Adenosine receptor antagonism (adenosine causes bronchoconstriction) contributes to bronchodilatory effect; also stimulates the respiratory centre.

Drug interactions: Erythromycin, ciprofloxacin, cimetidine, allopurinol – all raise theophylline levels (narrow TI – toxicity risk).

Final Answer: Inhibition of phosphodiesterase, increasing intracellular cAMP in bronchial smooth muscle $\Rightarrow \boxed{C}$

Answer: (C) Go Back to Q38

Q39.

Solution

Concept – Ondansetron (5-HT$_3$ Antagonist): Serotonin (5-hydroxytryptamine, 5-HT) is released from enterochromaffin cells in the GI mucosa in response to chemotherapy cytotoxicity. It activates:

- **5-HT$_3$ receptors** on vagal afferents in the GI tract $\rightarrow$ afferent signals to the vomiting centre
- **5-HT$_3$ receptors** in the chemoreceptor trigger zone (CTZ) in the area postrema

Ondansetron selectively blocks 5-HT$_3$ receptors at both sites. It does not block dopamine receptors (unlike metoclopramide/prochlorperazine) – therefore **no extrapyramidal side effects** (no akathisia, tardive dyskinesia, dystonia).

Uses: Chemotherapy-induced nausea/vomiting (CINV), post-operative nausea/vomiting (PONV), radiation-induced emesis.

Final Answer: 5-Hydroxytryptamine type 3 (5-HT$_3$) receptor in the GI tract and CTZ $\Rightarrow \boxed{D}$

Answer: (D) Go Back to Q39

Q40.

Solution

Concept – Fibrinolytic (Thrombolytic) Drugs: Fibrinolytics restore coronary (or cerebral) artery patency by dissolving thrombi. The endogenous fibrinolytic system depends on **plasmin**, a serine protease that degrades fibrin.

Mechanism of streptokinase:

(a) Streptokinase forms a 1:1 stoichiometric complex with plasminogen (or plasmin).

(b) This complex has plasminogen activator activity.

(c) It **converts free plasminogen to plasmin** throughout the circulation (systemic fibrinolytic state).

(d) Plasmin then degrades fibrin, fibrinogen, and other clotting factors.

Comparison with tPA (alteplase): tPA is **fibrin-specific** (binds fibrin in the clot

before activating plasminogen) $\rightarrow$ less systemic fibrinolysis $\rightarrow$ safer. Streptokinase is non-specific (systemic activation).

Monitoring: Thrombin time (most sensitive), fibrinogen levels.

Final Answer: Conversion of plasminogen to plasmin, which then degrades fibrin clots $\Rightarrow \boxed{A}$

Answer: (A) Go Back to Q40

Answer Key – FMGE Pharmacology Sample Paper 2

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