FMGE Pharmacology Sample Paper – 3

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 pharmacologist compares the bioavailability of four drugs after oral administration. Drug W is given sublingually because its oral bioavailability is less than 2% despite complete GI absorption, due to an almost complete hepatic first-pass effect. Which of the following drugs has the HIGHEST hepatic extraction ratio and therefore undergoes the most extensive first-pass effect?

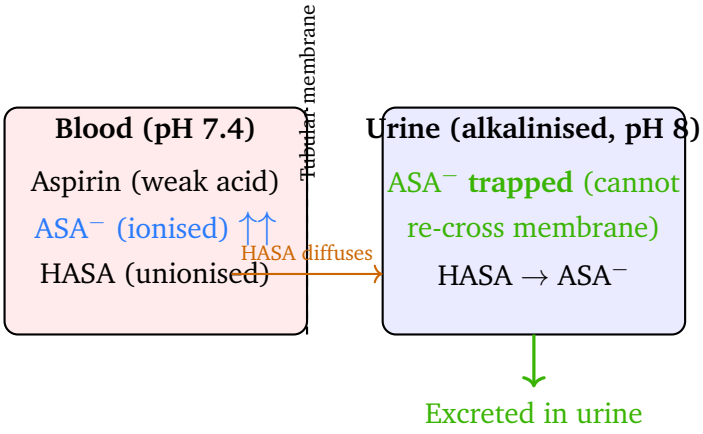
(A) Warfarin

(B) Diazepam

(C) Glyceryl trinitrate (GTN / nitroglycerin)

(D) Phenobarbitone

Q2. A 25-year-old medical student accidentally ingests a large dose of aspirin. On presentation, his blood pH is 7.38 and urine pH is 5.8. The treating physician orders intravenous sodium bicarbonate. The following diagram illustrates the principle of ion trapping:



To increase the urinary excretion of aspirin in this overdose, which of the following interventions is MOST appropriate?

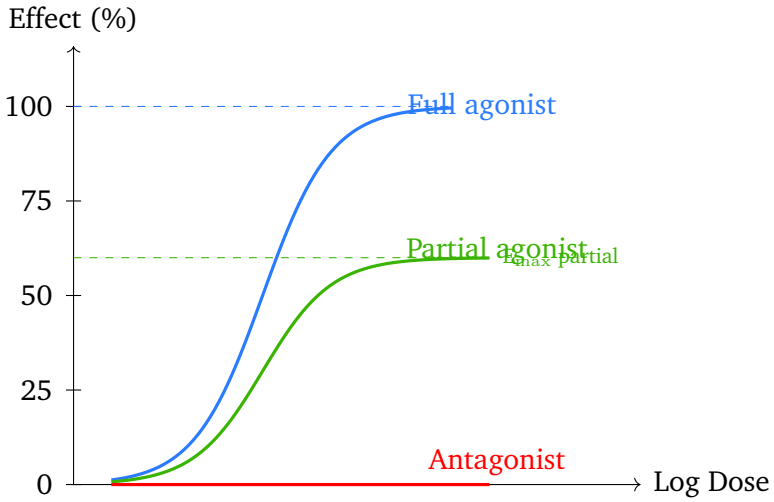
(A) Acidification of the urine with ammonium chloride

(B) Administration of activated charcoal to bind aspirin in the gut

(C) Forced diuresis with normal saline alone

(D) Alkalinisation of urine with sodium bicarbonate, increasing ionisation of aspirin (weak acid) in urine and promoting ion trapping

Q3. A pharmacologist studies three drugs at the same receptor. The following dose-response curves are obtained:



Based on the curves shown above, which statement BEST describes a partial agonist?

(A) It binds the receptor and produces a submaximal response (lower E_{max}) compared to a full agonist, even when all receptors are occupied

(B) It has no affinity for the receptor but reduces the effect of full agonists by allosteric mechanisms

(C) It produces the same maximal effect as a full agonist but requires a higher dose (rightward shift of EC_{50})

(D) It acts as a full agonist at high doses and antagonist at low doses

Q4. A 62-year-old man on warfarin therapy for atrial fibrillation is started on fluconazole for an oral candidiasis infection. Four days later, his INR has risen from 2.5 (therapeutic) to 6.8 (supratherapeutic), and he develops haematuria. Which of the following BEST explains this life-threatening drug interaction?

(A) Fluconazole displaces warfarin from plasma protein binding sites, increasing free warfarin concentration

(B) Fluconazole inhibits CYP2C9, the enzyme responsible for metabolising warfarin's S-enantiomer, thereby reducing warfarin clearance and increasing its plasma levels

(C) Fluconazole induces CYP3A4, increasing warfarin metabolism and paradoxically raising its levels

(D) Fluconazole increases gastrointestinal absorption of warfarin by reducing gut motility

Q5. A physiologist demonstrates the following experiment: A dog is given intravenous epinephrine (adrenaline), which causes a rise in blood pressure (BP). Phentolamine (a non-selective alpha blocker) is then administered, followed by a second dose of epinephrine. Surprisingly, the second dose of epinephrine now causes a FALL in blood pressure. What phenomenon is being demonstrated?

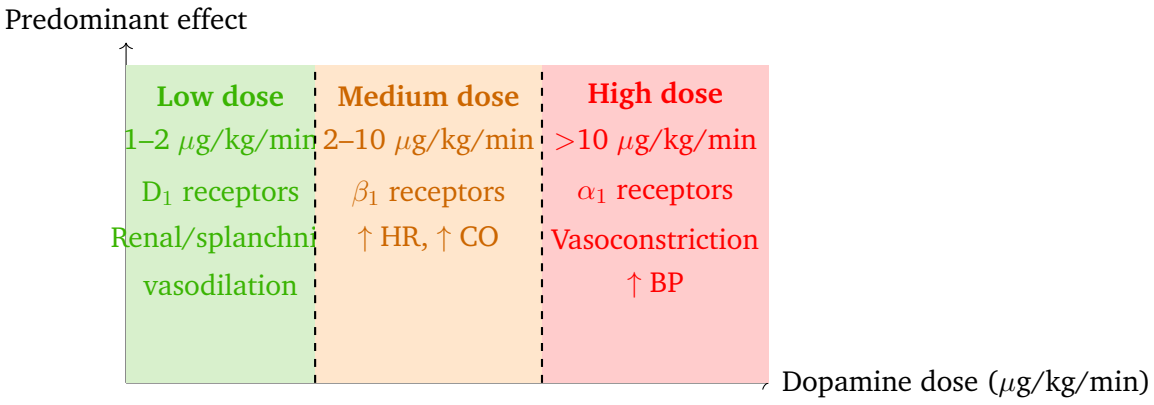
(A) Tachyphylaxis – epinephrine receptors are desensitised after the first dose

(B) Supersensitivity – phentolamine upregulates β-receptors causing an exaggerated response

(C) Dale's vasomotor reversal – after α-blockade, the vasodilatory β_2 effect of epinephrine is unmasked, causing BP to fall

(D) Phentolamine directly blocks β_1 receptors, preventing the pressor response

Q6. A 55-year-old patient is admitted to the ICU in cardiogenic shock. Intravenous dopamine is started and its dose is progressively increased. The following diagram shows the dose-dependent receptor profile of dopamine:



In a patient requiring a vasopressor for severe septic shock, the dopamine dose is escalated to 15 μg/kg/min. Which receptor effect predominantly mediates the haemodynamic response at this dose?

(A) D1 receptor stimulation causing renal vasodilation

(B) β_1 receptor stimulation causing increased myocardial contractility

(C) β_2 receptor stimulation causing peripheral vasodilation and reduced BP

(D) α_1 adrenergic stimulation causing vasoconstriction and increased blood pressure

Q7. A 58-year-old hypertensive patient on clonidine 0.2 mg twice daily abruptly stops his medication because he runs out of tablets during a holiday. Forty-eight hours later, he presents to the emergency department with

severe headache, BP 210/130 mmHg, sweating, and palpitations. Which of the following adverse effects of abrupt clonidine withdrawal BEST explains this clinical picture?

(A) Severe rebound hypertension with tachycardia due to a surge in sympathetic nervous system activity following withdrawal of central α_2 agonism

(B) Paradoxical bradycardia caused by vagal rebound after stopping the drug

(C) Acute pulmonary oedema from sudden loss of diuretic effect

(D) Hypokalaemia-induced cardiac arrhythmias after abrupt clonidine cessation

Q8. A 70-year-old man develops urinary retention 24 hours after an elective abdominal operation. Catheterisation reveals no mechanical obstruction. The urologist decides to use a direct-acting muscarinic agonist that is resistant to cholinesterase hydrolysis, primarily stimulates M3 receptors in the bladder detrusor muscle, and has no nicotinic effects. Which drug is most appropriate, and for which indication?

(A) Pilocarpine – for reducing intraocular pressure in glaucoma

(B) Bethanechol – for postoperative non-obstructive (neurogenic) urinary retention

(C) Carbachol – for increasing GI motility in paralytic ileus

(D) Methacholine – for bronchial provocation testing in suspected asthma

Q9. A 38-year-old farmer is brought unconscious to the emergency department with excessive salivation, lacrimation, urination, defaecation (SLUDGE), bronchospasm, bradycardia, and generalised muscle fasciculations after spraying pesticide. Organophosphate (OP) poisoning is suspected. Which of the following correctly describes the PRIORITY and sequence of treatment?

(A) Pralidoxime is given first to reactivate acetylcholinesterase, then atropine for muscarinic symptoms

(B) Diazepam alone is sufficient to control all features of OP poisoning

(C) High-dose atropine is given first (titrated to dry secretions and control bradycardia) followed by pralidoxime (within 24–48 hours before "aging" of the AChE-OP bond) to reactivate acetylcholinesterase

(D) Neostigmine is given to counteract nicotinic effects, and atropine for muscarinic effects

Q10. A 65-year-old patient with primary open-angle glaucoma has uncontrolled intraocular pressure (IOP) despite pilocarpine. Timolol 0.5% eye drops are added. The patient has well-controlled asthma. After two weeks, his asthma worsens with new-onset wheeze. Regarding timolol's mechanism of IOP reduction and its systemic risk, which of the following is CORRECT?

(A) Timolol increases aqueous humour outflow by relaxing the trabecular meshwork via β_1 blockade

(B) Timolol constricts the pupil (miosis), mechanically improving aqueous outflow

(C) Timolol inhibits carbonic anhydrase in the ciliary body, reducing aqueous humour formation

(D) Timolol reduces aqueous humour production by blocking β_2 receptors on the ciliary body epithelium; systemic absorption can cause bronchospasm in asthmatic patients

Q11. A 24-year-old man is brought to the emergency department unresponsive with pinpoint pupils, respiratory rate of 4/min, and a friend reports he injected heroin 30 minutes ago. Intravenous naloxone is administered and within 2 minutes the patient is alert and breathing normally. What is the mechanism by which naloxone reverses opioid-induced respiratory depression?

(A) Competitive antagonism at μ-opioid receptors in the brainstem respiratory centres, rapidly displacing opioids and restoring respiratory drive

(B) Stimulation of central sympathetic pathways to increase respiratory rate through adrenergic mechanisms

(C) Inhibition of opioid absorption from the bloodstream by acting as a chelating agent

(D) Activation of κ-opioid receptors, which exert an antagonistic effect on μ-opioid receptor signalling

Q12. A 40-year-old woman is brought to the emergency department after ingesting a large quantity of diazepam. She is deeply sedated with GCS 8. Flumazenil is administered intravenously and she regains consciousness. Thirty minutes later, she becomes drowsy and unresponsive again. Which of the following BEST explains this clinical deterioration?

(A) Flumazenil causes paradoxical stimulation of GABA-A receptors in some patients, causing delayed sedation

(B) Flumazenil has a shorter half-life (approximately 1 hour) than most benzodiazepines; as flumazenil is eliminated, the residual diazepam re-occupies GABA-A receptors causing resedation

(C) Diazepam induces its own metabolism, causing a rebound increase in its plasma levels after flumazenil wears off

(D) Flumazenil causes hepatic enzyme induction, accelerating the production of active diazepam metabolites

Q13. A 28-year-old woman with juvenile myoclonic epilepsy is on sodium valproate monotherapy and wishes to become pregnant. Her neurologist counsels her about teratogenicity. Sodium valproate is the antiepileptic drug MOST associated with which of the following major congenital malformations?

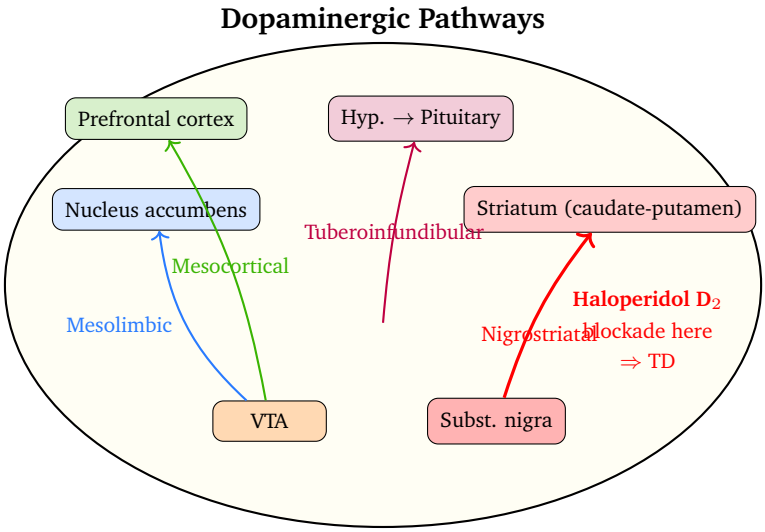
(A) Cleft palate and digital hypoplasia (foetal hydantoin syndrome)

(B) Choanal atresia and aplasia cutis congenita

(C) Neural tube defects (particularly spina bifida) due to interference with folate metabolism and other developmental pathways

(D) Cardiac septal defects and intrauterine growth restriction

Q14. A 45-year-old patient with chronic schizophrenia has been on haloperidol for 8 years. He now presents with involuntary repetitive lip-smacking, tongue protrusion, and choreiform movements of his limbs. He has been compliant with medication. The following diagram shows the major dopaminergic pathways in the brain:



This movement disorder (tardive dyskinesia) results from long-term D2 blockade in which dopaminergic pathway?

(A) Mesolimbic pathway (VTA → nucleus accumbens) – responsible for antipsychotic efficacy

(B) Mesocortical pathway (VTA → prefrontal cortex) – responsible for cognitive side effects

(C) Tuberoinfundibular pathway (hypothalamus → pituitary) – responsible for hyperprolactinaemia

(D) Nigrostriatal pathway (substantia nigra → striatum) – D2 receptor upregulation with chronic blockade leads to hypersensitivity and tardive dyskinesia

Q15. A psychiatrist is choosing between different SSRIs for a patient with major depressive disorder who has previously struggled with compliance and medication adherence. The psychiatrist mentions that one SSRI is much less likely to cause discontinuation (withdrawal) syndrome even if doses are missed, due to its unique pharmacokinetic profile. Which SSRI and which pharmacokinetic property are being described?

(A) Fluoxetine – its very long half-life (2–4 days) plus its active metabolite norfluoxetine (half-life 4–16 days) means plasma levels decline slowly, preventing withdrawal syndrome

(B) Paroxetine – its potent CYP2D6 inhibition reduces its own metabolism, maintaining stable levels

(C) Sertraline – its once-weekly extended-release formulation provides sustained plasma levels

(D) Escitalopram – its high selectivity for SERT means receptor occupancy is maintained even after a missed dose

Q16. A 12-year-old child with severe refractory asthma needs emergency surgery for an acute appendicitis. The anaesthetist wants an induction agent that will not worsen bronchospasm and may actually improve airway patency. Ketamine is selected. Which of the following BEST describes why ketamine is preferred in this patient and its mechanism of action?

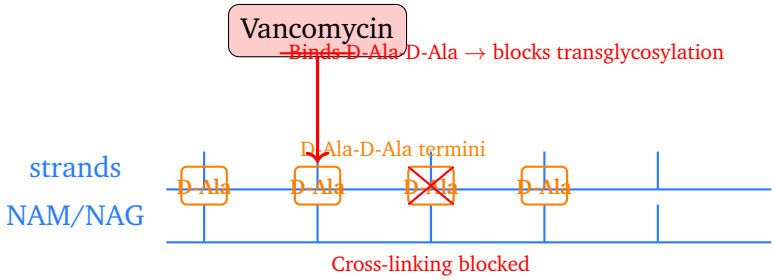
(A) Ketamine is preferred because it potentiates GABA-A receptors, producing deep sedation without affecting airway tone

(B) Ketamine is the preferred induction agent in asthmatic patients because it acts as an NMDA receptor antagonist that produces dissociative anaesthesia, and its sympathomimetic action releases catecholamines causing bronchodilation

(C) Ketamine is preferred because it inhibits muscarinic receptors in the bronchi, preventing bronchoconstriction during intubation

(D) Ketamine is preferred because it directly opens bronchial β_2 receptors, bypassing the need for catecholamines

Q17. A 55-year-old hospitalised patient with MRSA bacteraemia is started on vancomycin. Vancomycin has a completely different mechanism of action from β-lactam antibiotics, which explains why MRSA (with altered PBPs) remains susceptible. The following diagram illustrates vancomycin's mechanism:



What is the mechanism of action of vancomycin?

(A) Binding to penicillin-binding proteins (PBPs) to inhibit transpeptidation, similar to β-lactam antibiotics

(B) Inhibition of bacterial RNA polymerase, preventing transcription of genes encoding cell wall enzymes

(C) Binding to the D-Ala-D-Ala terminus of peptidoglycan precursors, physically blocking both transglycosylation and transpeptidation, preventing cell wall synthesis

(D) Disruption of the outer membrane of Gram-negative bacteria, causing leakage of intracellular contents

Q18. A patient with vancomycin-resistant Enterococcus faecium (VRE) bacteraemia is started on linezolid. The microbiologist explains that linezolid has a unique mechanism unlike all other available antibiotics, which is why there is no cross-resistance with other agents targeting the 50S subunit (e.g., erythromycin, chloramphenicol). What is linezolid's mechanism of action?

(A) Binding to the 30S ribosomal subunit, blocking aminoacyl-tRNA attachment to the A site

(B) Binding to the 50S ribosomal subunit at the same site as chloramphenicol, inhibiting peptidyl transferase activity

(C) Inhibition of bacterial DNA gyrase, preventing DNA replication

(D) Binding to 23S rRNA of the 50S subunit, preventing formation of the 70S initiation complex and blocking translation at the initiation stage – a unique mechanism with no cross-resistance

Q19. A 35-year-old patient is diagnosed with community-acquired pneumonia (CAP) caused by Mycoplasma pneumoniae. Azithromycin is prescribed as a 3-day course (500 mg daily). The patient is sceptical that a 3-day course can treat a 10-day illness. What pharmacokinetic property of azithromycin makes short-course therapy effective?

(A) Azithromycin has an exceptionally long tissue half-life (approximately 68 hours), with very high tissue concentrations maintained for 5–7 days after the last dose, allowing a 3-day course to achieve effective treatment duration

(B) Azithromycin is bactericidal at tissue concentrations, killing bacteria faster than bacteriostatic alternatives

(C) Azithromycin has potent CYP3A4 inhibition, which prolongs its own half-life by inhibiting hepatic metabolism

(D) Azithromycin is concentrated selectively in macrophages and phagocytes, which actively deliver it to infection sites within the first 24 hours

Q20. A patient with complicated intra-abdominal sepsis is prescribed imipenem-cilastatin. A medical student asks why cilastatin is always combined with imipenem, as cilastatin has no antibacterial activity of its own. What is the rationale for combining cilastatin with imipenem?

(A) Cilastatin enhances the penetration of imipenem across the bacterial outer membrane of Gram-negative organisms

(B) Cilastatin inhibits renal dihydropeptidase-I (DHP-I), the enzyme that inactivates imipenem in the renal tubule, thereby increasing urinary imipenem concentrations and reducing nephrotoxic metabolite accumulation

(C) Cilastatin is a β-lactamase inhibitor that protects imipenem from bacterial resistance enzymes

(D) Cilastatin prolongs the plasma half-life of imipenem by competing for renal tubular secretion

Q21. A 32-year-old woman presents with a recurrent lower urinary tract infection (UTI). Urine culture grows a Gram-negative organism. The physician prescribes nitrofurantoin. Nitrofurantoin is effective for uncomplicated lower UTI caused by most urinary pathogens. Which of the following organisms is NOT susceptible to nitrofurantoin?

(A) Escherichia coli (the most common cause of UTI)

(B) Staphylococcus saprophyticus

(C) Pseudomonas aeruginosa (intrinsically resistant; nitrofurantoin is also ineffective against Proteus and Serratia)

(D) Enterococcus faecalis

Q22. A 42-year-old patient is started on first-line anti-tuberculosis therapy (isoniazid, rifampicin, pyrazinamide, and ethambutol). After 6 weeks, he complains that he cannot distinguish between red and green colours on his computer screen. He is referred urgently to an ophthalmologist. This specific adverse effect is characteristically associated with which drug in his regimen?

(A) Isoniazid – peripheral neuropathy due to pyridoxine depletion

(B) Rifampicin – optic nerve toxicity due to hepatic enzyme induction

(C) Pyrazinamide – hyperuricaemia causing crystal deposition in the optic nerve

(D) Ethambutol – retrobulbar optic neuritis causing colour vision deficiency (red-green colour blindness) and visual field defects; baseline and regular visual acuity testing is mandatory

Q23. A 28-year-old man presents with a pruritic, scaly, circular rash on his trunk and tinea unguium (onychomycosis). The dermatologist prescribes oral griseofulvin. A medical student asks about griseofulvin's spectrum of activity. For which of the following infections would griseofulvin be INEFFECTIVE?

(A) Oropharyngeal candidiasis caused by Candida albicans (griseofulvin has no activity against Candida, Aspergillus, or other non-dermatophyte

fungi)

(B) Tinea corporis caused by Trichophyton rubrum

(C) Tinea capitis caused by Microsporum canis

(D) Tinea pedis caused by Epidermophyton floccosum

Q24. During an influenza outbreak, a 45-year-old immunocompromised patient presents within 36 hours of symptom onset with fever, myalgia, and severe respiratory symptoms. Rapid antigen testing confirms influenza A. Oseltamivir is prescribed. What is the mechanism of action of oseltamivir?

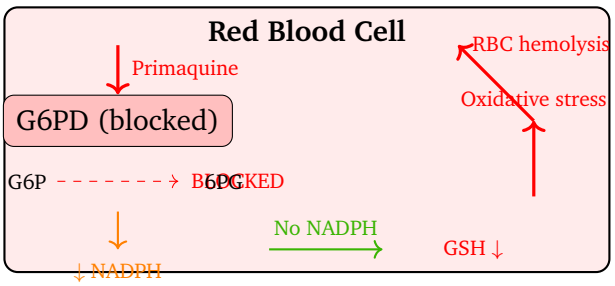
(A) Oseltamivir blocks the M2 ion channel of influenza A, preventing viral uncoating and release of viral RNA

(B) Oseltamivir inhibits influenza neuraminidase, preventing cleavage of sialic acid residues from host cell surface glycoproteins, thereby trapping new viral particles at the infected cell surface and blocking spread to neighbouring cells

(C) Oseltamivir inhibits influenza RNA-dependent RNA polymerase (RdRp), blocking viral replication

(D) Oseltamivir stimulates interferon production, enhancing the innate immune response against influenza

Q25. A 22-year-old man from a G6PD-deficient population is diagnosed with Plasmodium vivax malaria. After chloroquine treatment for the blood-stage infection, the physician wishes to add primaquine to achieve radical cure (eradicate hepatic hypnozoites). The following diagram illustrates the biochemical basis of the risk:



Which patient CANNOT safely receive primaquine for radical cure?

(A) A patient with sickle cell trait (HbAS), who has partial protection against malaria

(B) A patient with thalassaemia minor, who has mild microcytic anaemia at baseline

(C) A patient with G6PD deficiency, who is at high risk of severe intravascular haemolytic anaemia when exposed to primaquine

(D) A patient with iron-deficiency anaemia, who has a reduced haemoglobin level

Q26. A 30-year-old man from Bihar, India presents with prolonged fever for 3 months, massive splenomegaly, weight loss, and anaemia. Bone marrow biopsy reveals Leishmania donovani amastigotes. Which of the following is the FIRST-LINE treatment for this condition (visceral leishmaniasis / kala-azar) in most endemic regions?

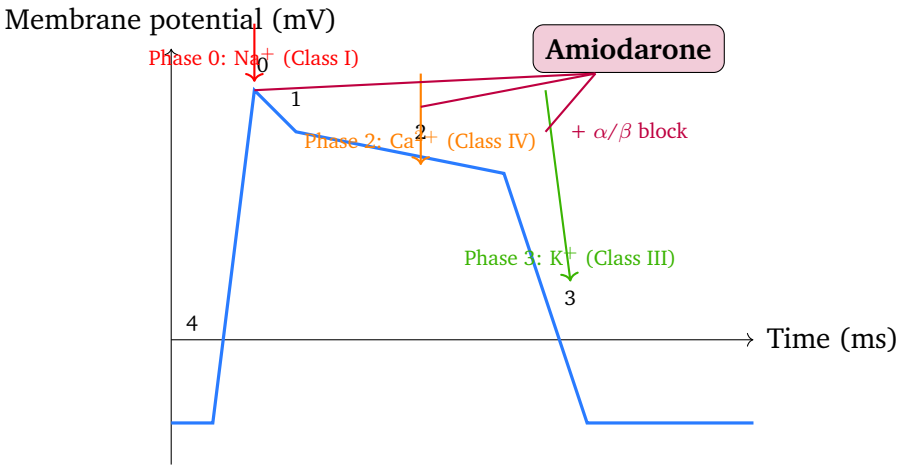
(A) Miltefosine – oral agent used when antimonials fail

(B) Paromomycin – aminoglycoside used as adjunctive therapy

(C) Amphotericin B liposomal – reserved for antimonial-resistant cases

(D) Sodium stibogluconate (pentavalent antimony compound) – first-line therapy for visceral leishmaniasis in most endemic regions, inhibiting leishmanial ATP synthesis

Q27. A 68-year-old patient presents with recurrent life-threatening ventricular tachycardia (VT). After failure of other antiarrhythmics, amiodarone is considered. The following diagram shows the cardiac action potential with the ion channels affected by amiodarone:



Which of the following BEST describes the mechanism and pharmacological profile of amiodarone?

(A) Amiodarone has effects on Na^+, Ca^{2+}, and K^+ channels, and additionally blocks α and β-adrenergic receptors, making it a broad-spectrum antiarrhythmic (Vaughan-Williams Classes I, II, III, and IV properties)

(B) Amiodarone acts exclusively on K^+ channels (Class III), prolonging the action potential duration and effective refractory period

(C) Amiodarone is a selective β_1 blocker (Class II) with additional weak Na^+ channel blocking properties

(D) Amiodarone selectively blocks L-type Ca^{2+} channels (Class IV), similar to verapamil, slowing AV nodal conduction

Q28. A 58-year-old patient with stable chronic systolic heart failure (EF 30%) on ACE inhibitor and furosemide is reviewed in the cardiology clinic. His cardiologist decides to add a β-blocker, despite traditional teaching that β-blockers are "contraindicated" in heart failure. Which β-blocker is specifically APPROVED for reducing mortality in stable chronic heart failure, and why are β-blockers beneficial in this setting?

(A) Atenolol – reduces heart rate and prevents tachycardia-induced cardiomyopathy

(B) Bisoprolol (β_1-selective) – approved for stable chronic HF; reduces mortality by attenuating chronic sympathetic overdrive and revers-

ing adverse cardiac remodelling (reduces myocyte apoptosis, fibrosis, and receptor downregulation)

(C) Propranolol – the original β-blocker used for HF due to its non-selective action on both β_1 and β_2 receptors

(D) Sotalol – approved for chronic HF because its Class III antiarrhythmic action prevents sudden cardiac death

Q29. A 65-year-old patient with chronic heart failure is already on enalapril (ACE inhibitor) and furosemide. His cardiologist adds spironolactone (based on the RALES trial mortality benefit). Two weeks later, routine electrolytes show: K^+ = 6.4 mEq/L, Na^+ = 138 mEq/L, creatinine = 1.8 mg/dL. What is the MOST SERIOUS concern with spironolactone in this clinical context?

(A) Hyponatraemia – spironolactone promotes excessive sodium excretion

(B) Hypocalcaemia – spironolactone blocks calcium reabsorption in the distal tubule

(C) Hyperkalaemia – spironolactone blocks aldosterone-mediated potassium excretion in the collecting duct; risk is amplified by concurrent ACE inhibitor use and renal impairment

(D) Metabolic alkalosis – spironolactone causes excessive bicarbonate retention

Q30. A 52-year-old diabetic patient with hypertension and CKD was switched from ramipril (ACE inhibitor) to losartan (an ARB – angiotensin receptor blocker) because of an intolerable dry cough. After 3 months on losartan, the cough has completely resolved. Which of the following BEST explains why ARBs do NOT cause the dry cough associated with ACE inhibitors?

(A) ARBs also inhibit ACE but to a lesser extent, causing less bradykinin accumulation

(B) ARBs block both AT1 and AT2 receptors, preventing any angiotensin II-mediated airway irritation

(C) ARBs stimulate bronchial prostaglandin synthesis, which counteracts the cough reflex

(D) ARBs block the AT1 receptor directly but do not inhibit the ACE enzyme; therefore, bradykinin (which is normally degraded by ACE) is not accumulated, and cough does not occur

Q31. A 55-year-old man presents with a sudden onset of exquisitely painful, swollen, hot, and red left first metatarsophalangeal joint – classic podagra. Serum uric acid is 10.2 mg/dL. He is given colchicine for the acute attack. What is the mechanism by which colchicine provides relief in acute gout?

(A) Inhibition of microtubule polymerisation by binding to tubulin, thereby preventing neutrophil migration into the affected joint and blocking release of inflammatory mediators

(B) Inhibition of xanthine oxidase, reducing uric acid synthesis and lowering serum urate levels acutely

(C) Competitive antagonism at urate transporters (URAT1) in the renal proximal tubule, promoting urate excretion

(D) Inhibition of prostaglandin synthesis via COX-1 and COX-2 blockade, reducing pain and swelling

Q32. A 48-year-old patient with gout and rheumatoid arthritis is started on allopurinol for hyperuricaemia. He is also on azathioprine for his rheumatoid arthritis. Two weeks later, he develops severe pancytopenia. Which drug interaction BEST explains this life-threatening complication?

(A) Allopurinol inhibits CYP3A4, increasing plasma levels of azathioprine's parent compound

(B) Allopurinol inhibits xanthine oxidase (XO), the enzyme that normally inactivates the active metabolite of azathioprine (6-mercaptopurine);

this leads to massive accumulation of 6-MP causing bone marrow suppression

(C) Allopurinol displaces azathioprine from plasma protein binding, dramatically increasing free azathioprine concentration

(D) Allopurinol competes with azathioprine for renal tubular secretion, reducing azathioprine elimination and causing toxicity

Q33. A 60-year-old man with osteoarthritis and a history of GI bleeding is prescribed celecoxib (selective COX-2 inhibitor) instead of a non-selective NSAID. While celecoxib reduces GI complications, his cardiologist warns him about a specific cardiovascular risk. What is the mechanism of the increased cardiovascular thrombotic risk associated with selective COX-2 inhibitors?

(A) COX-2 inhibitors increase thromboxane A2 (TXA2) synthesis in platelets, directly promoting platelet aggregation

(B) COX-2 inhibitors block renal prostaglandin synthesis, causing sodium retention and hypertension that indirectly increases MI risk

(C) Selective COX-2 inhibition reduces prostacyclin (PGI2) production in vascular endothelium without affecting platelet TXA2 (which depends on COX-1), shifting the balance toward thrombosis and vasoconstriction

(D) COX-2 inhibitors directly activate coagulation Factor X, accelerating thrombin generation

Q34. A 32-year-old woman with Graves' disease in thyroid storm is admitted to the ICU with heart rate of 148 bpm, temperature 40.2°C, and thyroid hormone levels: T4 = 22 μg/dL, T3 = 540 ng/dL. In addition to β-blockers, iodine solution, and steroids, an antithyroid drug is urgently required. Which statement BEST explains why propylthiouracil (PTU) is preferred over methimazole in thyroid storm?

(A) PTU has a longer half-life than methimazole, reducing the risk of missed doses in the ICU

(B) PTU has superior anti-inflammatory properties that directly suppress thyroid storm cytokine release

(C) PTU causes fewer hepatotoxicity side effects than methimazole, making it safer in acutely ill patients

(D) PTU not only inhibits thyroid peroxidase (blocking new thyroid hormone synthesis) but also inhibits type 1 deiodinase in peripheral tissues, blocking the conversion of T4 to the more potent T3, thereby rapidly reducing active hormone levels

Q35. A 70-year-old woman with type 2 diabetes is newly started on glipizide (a second-generation sulfonylurea). Her daughter calls 3 days later because the patient is sweaty, trembling, and confused after skipping breakfast. Which of the following precautions is MOST IMPORTANT when initiating a patient on a sulfonylurea such as glipizide?

(A) Monitor blood glucose closely for hypoglycaemia, especially if meals are skipped, as sulfonylureas stimulate insulin secretion independently of blood glucose levels

(B) Monitor renal function monthly, as glipizide is primarily excreted unchanged by the kidneys

(C) Advise the patient to avoid all carbohydrates while on glipizide to prevent postprandial hyperglycaemia

(D) Monitor liver enzymes weekly, as glipizide causes hepatocellular damage within the first month of therapy

Q36. A 26-year-old woman has regular 28-day menstrual cycles. On day 21 (mid-luteal phase), her progesterone level is 18 ng/mL, confirming ovulation. The corpus luteum is the primary source of progesterone during this phase. What is the KEY physiological role of progesterone during the luteal phase of the menstrual cycle?

(A) To stimulate the LH surge from the anterior pituitary, triggering ovulation

(B) Maintenance of the secretory (post-ovulatory) endometrium, converting it to a "decidua-like" state suitable for implantation of a fertilised ovum, and suppression of further LH secretion to prevent luteolysis

(C) To stimulate endometrial proliferation (thickening) in preparation for the follicular phase

(D) To promote FSH release, stimulating growth of the next cohort of ovarian follicles

Q37. A 55-year-old woman with diabetic gastroparesis experiences nausea, vomiting, and early satiety. Her gastroenterologist prescribes metoclopramide. After two doses, she develops involuntary muscle spasms of her neck (torticollis) and an upward deviation of her eyes (oculogyric crisis). Which combination of receptor activities explains BOTH the therapeutic benefit AND the adverse effect in this case?

(A) α_1 receptor blockade (antiemetic) and muscarinic agonism (prokinetic)

(B) 5-HT3 receptor antagonism (antiemetic) and D2 agonism (prokinetic)

(C) D2 receptor antagonism in the chemoreceptor trigger zone (antiemetic) combined with 5-HT4 receptor agonism in the myenteric plexus (prokinetic); D2 blockade in the nigrostriatal pathway causes acute dystonic reactions

(D) H1 receptor antagonism (antiemetic) and ACh receptor agonism (prokinetic)

Q38. A 10-year-old child with allergic asthma and exercise-induced bronchospasm is reviewed by the paediatrician. The mother asks about sodium cromoglycate (cromolyn sodium), which she has read about online. She wants to know if she can give it during an acute asthma attack to relieve symptoms. Which of the following statements about sodium cromoglycate is CORRECT?

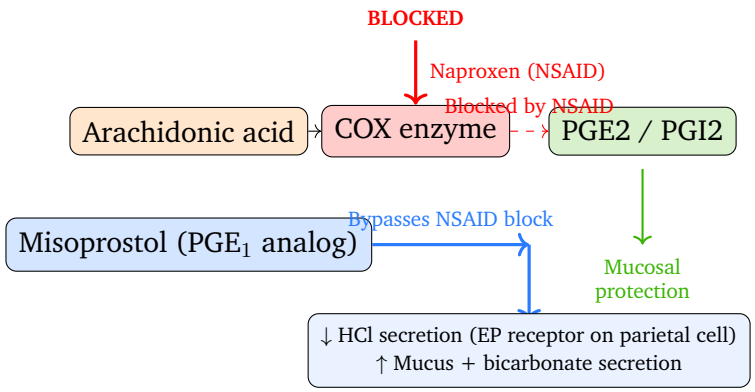
(A) Sodium cromoglycate is a potent bronchodilator that acts faster than salbutamol during acute attacks

(B) Sodium cromoglycate blocks H1 receptors, reducing histamine-mediated bronchoconstriction in acute attacks

(C) Sodium cromoglycate inhibits leukotriene synthesis and can be used to abort acute attacks as well as for prophylaxis

(D) Sodium cromoglycate stabilises mast cells (prevents calcium-dependent degranulation) and is used ONLY for prophylaxis – it has NO bronchodilator action and cannot relieve an acute asthma attack

Q39. A 55-year-old man who requires long-term naproxen therapy for ankylosing spondylitis has a history of peptic ulcer disease. His gastroenterologist co-prescribes misoprostol for gastroprotection. The following diagram illustrates the mechanism:



What is the PRIMARY mechanism by which misoprostol protects the gastric mucosa in a patient taking NSAIDs?

(A) Stimulation of EP (prostaglandin E) receptors on gastric parietal cells to reduce HCl secretion, and on mucous cells to increase mucus and bicarbonate secretion – replacing the cytoprotective prostaglandins suppressed by NSAID-mediated COX inhibition

(B) Irreversible inhibition of the H^+/K^+-ATPase (proton pump) on parietal cells, blocking acid secretion completely

(C) Competitive antagonism at histamine H2 receptors, reducing cAMP-mediated acid secretion

(D) Neutralisation of existing gastric acid by acting as a mucosal buffer

Q40. A 68-year-old obese woman (weight 118 kg) with renal impairment is admitted with a deep vein thrombosis. The haematologist prescribes enoxaparin (a low molecular weight heparin, LMWH). The nurse asks which laboratory test should be used to monitor LMWH therapy when monitoring is required (e.g., in renal impairment, pregnancy, or extreme body weight). Which is the CORRECT test?

(A) Prothrombin time (PT/INR) – used for monitoring warfarin therapy via the extrinsic pathway

(B) Anti-Xa activity assay – the appropriate test for monitoring LMWH when required, since LMWH does not reliably prolong the APTT due to its predominant anti-Xa (vs. anti-IIa) activity

(C) Activated partial thromboplastin time (APTT) – the standard test for unfractionated heparin, which is also used for LMWH

(D) Thrombin time (TT) – measures fibrinogen conversion to fibrin and is the standard LMWH monitor

Detailed Solutions

Q1.

Solution

Topic: Hepatic Extraction Ratio and First-Pass Effect

Answer: (C)

Glyceryl trinitrate (GTN / nitroglycerin) has a hepatic extraction ratio approaching 1.0 (nearly 100%), meaning almost all of an oral dose is metabolised during the first pass through the liver. This results in oral bioavailability of less than 2%, making oral administration impractical.

High extraction ratio drugs (first-pass effect is extensive):

- GTN / nitroglycerin (sublingual) – extraction ratio ≈ 0.98
- Morphine, propranolol, lignocaine (IV or sublingual/transdermal bypasses first-pass)
- Labetalol, verapamil, nifedipine

Low extraction ratio drugs (sensitive to protein binding changes, NOT first-pass):

- Warfarin, phenytoin, diazepam, phenobarbitone
- Their elimination rate is determined by the free (unbound) fraction and intrinsic clearance

Clinical relevance: GTN must be given sublingually, transdermally, or IV to bypass hepatic first-pass. Option A (warfarin) and B (diazepam) are low-extraction drugs. Option D (phenobarbitone) has moderate first-pass but is given orally. GTN has the *highest* extraction ratio of the options listed.

Go Back to Q1

Q2.

Solution

Topic: pH-Dependent Urinary Excretion – Ion Trapping

Answer: (D)

Aspirin (acetylsalicylic acid) is a weak acid (pKa ≈ 3.5). In the urine, the ionisation depends on urinary pH:

Henderson-Hasselbalch principle:

- Acidic urine (pH 5.8): aspirin is mostly in the *un-ionised* (lipid-soluble) form $\rightarrow$ reabsorbed across tubular membranes $\rightarrow$ poor excretion
- Alkaline urine (pH 8, after $NaHCO_3$): aspirin is mostly *ionised* (ASA^-) $\rightarrow$ **cannot cross** back across tubular membranes $\rightarrow$ ion trapping $\rightarrow$ excreted in urine

Key rule: Alkalinise urine to enhance excretion of *weak acids* (aspirin, phenobarbitone); acidify urine to enhance excretion of *weak bases* (amphetamine, quinine).

Options analysis:

- A – Wrong: acidification *reduces* aspirin excretion (more un-ionised form reabsorbed)
- B – Wrong: activated charcoal only works if given within 1–2 hours of ingestion (pre-absorption)
- C – Wrong: saline alone without alkalinisation does not promote ion trapping
- **D – CORRECT**: sodium bicarbonate alkalinises urine, ionising aspirin and trapping it for excretion

Go Back to Q2

Q3.

Solution

Topic: Partial Agonist – Definition and Dose-Response Characteristics

Answer: (A)

A **partial agonist** has:

- **Affinity**: binds the receptor (like a full agonist)
- **Intrinsic activity (efficacy)**: $0 < \alpha < 1$ – produces a submaximal response (lower E_{max}) even when all receptors are occupied
- It cannot produce the same maximal effect as a full agonist regardless of dose

Clinical examples of partial agonists:

- **Buprenorphine** – partial μ-opioid agonist (used in opioid dependence and pain)

- **Pindolol** – partial β-agonist (intrinsic sympathomimetic activity, ISA)
- **Buspirone** – partial 5-HT1A agonist (anxiolytic)

Partial agonist in the presence of a full agonist: acts as a *competitive antagonist* (blocks receptor but produces less effect), which is the principle behind buprenorphine's use in opioid overdose.

Options analysis:

- **A – CORRECT**: lower E_{max} even at maximal receptor occupancy
- B – Wrong: this describes an allosteric modulator or non-competitive antagonist
- C – Wrong: this describes a competitive antagonist (same E_{max}, higher EC_{50})
- D – Wrong: partial agonists do not switch between agonist and antagonist modes by dose

Go Back to Q3

Q4.

Solution

Topic: CYP450 Inhibition – Fluconazole and Warfarin Interaction

Answer: (B)

Warfarin's anticoagulant effect depends primarily on the **S-enantiomer**, which is metabolised by **CYP2C9**. Fluconazole is a potent **CYP2C9 inhibitor** (and also inhibits CYP3A4 and CYP2C19).

Mechanism of interaction:

- Fluconazole inhibits CYP2C9 $\rightarrow$ reduced metabolism of S-warfarin $\rightarrow$ plasma S-warfarin concentrations rise $\rightarrow$ excessive anticoagulation $\rightarrow$ INR elevation and bleeding risk
- This is one of the most clinically significant and dangerous drug interactions in clinical practice

Management: Reduce warfarin dose by 25–50% when adding azole antifungals; monitor INR closely within 3–5 days.

Other important CYP2C9 substrates: phenytoin, glipizide, losartan, NSAIDs (ibuprofen).

Options analysis:

- A – Wrong: protein displacement is a transient, usually minor interaction mechanism
- **B – CORRECT**: CYP2C9 inhibition reduces S-warfarin metabolism
- C – Wrong: fluconazole inhibits CYP3A4 (not induces); and CYP3A4 metabolises R-warfarin less relevantly
- D – Wrong: fluconazole does not affect GI warfarin absorption

Go Back to Q4

Q5.

Solution

Topic: Dale's Vasomotor Reversal – Epinephrine after Alpha-Blockade

Answer: (C)

Normal epinephrine response: At pharmacological doses, epinephrine stimulates *both* α_1 (vasoconstriction) and β_2 (vasodilation) receptors. The α_1 effect dominates in most vascular beds $\rightarrow$ net hypertension.

After phentolamine (α-blockade):

- α_1-mediated vasoconstriction is blocked
- β_2-mediated vasodilation is **unmasked**
- Second dose of epinephrine now causes **net hypotension**
- This reversal of the pressor response is called **Dale's vasomotor reversal**

Clinical importance: Explains why pure α-blockers should be used to treat hypertensive crises caused by epinephrine-secreting tumours (phaeochromocytoma) – never a β-blocker alone (would worsen hypertension by removing β_2 vasodilation and leaving α_1 unopposed).

Go Back to Q5

Q6.

Solution

Topic: Dopamine – Dose-Dependent Receptor Profile

Answer: (D)

Dopamine exhibits a unique dose-dependent receptor selectivity:

- **Low dose (1–2 μg/kg/min)**: D1 receptors $\rightarrow$ renal and splanchnic vasodilation ("renal-dose dopamine" – not proven to be nephroprotective in clinical trials)
- **Medium dose (2–10 μg/kg/min)**: β_1 receptors $\rightarrow$ increased heart rate (chronotropy) and cardiac output (inotropy)
- **High dose (>10 μg/kg/min)**: α_1 adrenergic receptors $\rightarrow$ peripheral vasoconstriction $\rightarrow$ increased SVR and blood pressure (vasopressor effect)

At 15 μg/kg/min (high dose), the α_1 adrenergic effect predominates, making dopamine a vasopressor. At this dose, its haemodynamic profile resembles norepinephrine rather than a cardiac stimulant.

Go Back to Q6

Q7.

Solution

Topic: Clonidine – Rebound Hypertension on Abrupt Withdrawal

Answer: (A)

Clonidine's mechanism: Central α_2 agonist (acts on presynaptic α_2 receptors in the brainstem, particularly the locus coeruleus and nucleus tractus solitarius) $\rightarrow$ reduces sympathetic outflow $\rightarrow$ lowers BP and HR.

Abrupt withdrawal syndrome:

- Sudden loss of central sympatholytic effect $\rightarrow$ **rebound surge in sympathetic nervous system activity**
- Symptoms: severe hypertension (may exceed pre-treatment levels), tachycardia, sweating, anxiety, headache
- Onset: 18–36 hours after last dose
- More severe than withdrawal of other antihypertensives

Management of clonidine withdrawal: Restart clonidine OR convert to another antihypertensive (e.g., labetolol, nitroprusside for hypertensive emergency).

Prevention: Never stop clonidine abruptly; taper over 1–2 weeks.

Go Back to Q7

Q8.

Solution

Topic: Bethanechol – Direct Muscarinic Agonist for Neurogenic Bladder

Answer: (B)

Bethanechol is a direct-acting muscarinic (cholinergic) agonist with the following key properties:

- **Predominantly M3 selective**: stimulates detrusor muscle of the urinary bladder and GI smooth muscle
- **Resistant to cholinesterase**: not hydrolysed by acetylcholinesterase or plasma cholinesterase → longer duration of action than ACh
- **No nicotinic activity**: no effects at the neuromuscular junction (unlike carbachol)
- **Primary indication**: postoperative non-obstructive urinary retention (neurogenic bladder) – stimulates detrusor contraction to initiate voiding

Contraindication: Do NOT use if there is mechanical obstruction (outlet obstruction, prostatic hypertrophy causing urinary obstruction) – increased bladder pressure with blocked outflow risks perforation or severe pain.

Go Back to Q8

Q9.

Solution

Topic: Organophosphate Poisoning – Treatment Priorities

Answer: (C)

Organophosphates irreversibly inhibit acetylcholinesterase → acetylcholine accumulates at all cholinergic synapses, producing the SLUDGE syndrome (muscarinic) plus nicotinic effects (fasciculations, paralysis).

Treatment sequence:

(a) **Atropine FIRST (and in high doses)**: competitive antagonist at muscarinic receptors. Titrate to endpoint of dry secretions and acceptable heart rate. May require 10–100 mg in severe poisoning. Does NOT affect nicotinic (NMJ) effects.

(b) **Pralidoxime (2-PAM) SECOND**: an oxime that reactivates (regenerates) the phosphorylated acetylcholinesterase if given *before "aging"* of the enzyme-

OP bond (typically within 24–48 hours, depending on the specific OP compound). Reverses both muscarinic and nicotinic toxicity.

(c) **Diazepam**: for seizure management.

Key concept – "aging": After a variable time, the OP-AChE bond undergoes a conformational change ("aging") that makes it permanently irreversible – pralidoxime is ineffective after aging occurs.

Go Back to Q9

Q10.

Solution

Topic: Timolol Eye Drops – Mechanism in Glaucoma and Systemic Risk

Answer: (D)

Timolol mechanism in glaucoma:

- Non-selective β-blocker (blocks β_1 and β_2 receptors)
- Reduces aqueous humour **production** by blocking β_2 receptors on the **ciliary body epithelium** (not outflow)
- Mechanism: β_2 blockade in ciliary epithelium $\rightarrow$ reduced cAMP $\rightarrow$ reduced active secretion of aqueous humour
- Net result: lowers intraocular pressure (IOP)

Systemic absorption risk:

- Timolol eye drops are absorbed through the nasolacrimal duct $\rightarrow$ systemic circulation
- In asthmatic patients: β_2 blockade in bronchi $\rightarrow$ bronchoconstriction (potentially life-threatening)
- **Contraindicated in asthma and COPD**

Options analysis:

- A – Wrong: timolol reduces aqueous production (not outflow); it targets ciliary epithelium β_2, not β_1
- B – Wrong: miosis (pupil constriction) and increased trabecular outflow is the mechanism of pilocarpine/miotics

- C – Wrong: carbonic anhydrase inhibition is the mechanism of acetazolamide/dorzolamide
- **D – CORRECT**: β_2 blockade in ciliary body reduces production; systemic absorption risks bronchospasm

Go Back to Q10

Q11.

Solution

Topic: Naloxone – Competitive Opioid Antagonist at μ-Receptors

Answer: (A)

Naloxone is a pure, competitive opioid receptor antagonist with affinity for all three opioid receptor subtypes ($\mu > \kappa = \delta$), but its primary clinical effect is through μ-opioid receptor blockade.

Mechanism of reversal of opioid toxicity:

- Rapidly displaces opioids from μ-opioid receptors in the brainstem respiratory centres (pre-Botzinger complex)
- Restores respiratory drive within 2 minutes when given IV
- Also reverses other μ-opioid effects: sedation, miosis, constipation

Important pharmacokinetic limitation:

- Half-life of naloxone: **30–90 minutes** (much shorter than most opioids)
- Risk of **re-narcotisation** (relapse into coma/respiratory depression) as naloxone wears off before the opioid does
- Management: repeat IV boluses or continuous infusion; monitor for at least 4–6 hours

Precipitates withdrawal: In opioid-dependent patients, naloxone causes acute withdrawal syndrome.

Go Back to Q11

Q12.

Solution

Topic: Flumazenil – Short Half-Life Causing Resedation

Answer: (B)

Flumazenil is a competitive BZD antagonist at the GABA-A receptor BZD binding site (does not directly affect chloride channel opening; blocks access of BZDs to their site).

Pharmacokinetic mismatch:

- Flumazenil half-life: ≈**60 minutes**
- Diazepam half-life: **24–72 hours** (plus active metabolite desmethyldiazepam: 36–200 hours)
- After flumazenil is eliminated, diazepam (still at high concentration) reoccupies GABA-A receptor BZD sites → **resedation**

Clinical management: Repeat flumazenil doses or infusion; monitor in ICU for resedation.

Additional risk: In BZD-dependent patients, flumazenil precipitates acute BZD withdrawal syndrome, including *seizures* – a potentially life-threatening complication.

Flumazenil does NOT reverse: Alcohol sedation, barbiturate sedation, GHB/opioid sedation (different receptors).

Go Back to Q12

Q13.

Solution

Topic: Valproate Teratogenicity – Neural Tube Defects

Answer: (C)

Valproate (sodium valproate) is the **most teratogenic** of all antiepileptic drugs used in clinical practice.

Major teratogenic risk:

- **Neural tube defects** (NTDs), particularly **spina bifida** – risk 1–2% vs 0.05% in the general population (20–40 times higher)
- NTDs occur at neural tube closure (days 18–28 post-conception – often before pregnancy is recognised)

- Mechanism: interferes with folate metabolism and inhibits histone deacetylase (epigenetic changes)

Additional risks of valproate in pregnancy:

- Cognitive impairment / autism spectrum disorder in the offspring
- Foetal valproate syndrome: cleft palate, limb defects, facial dysmorphism

Other antiepileptic teratogenic profiles:

- **Phenytoin**: foetal hydantoin syndrome (cleft palate, digital hypoplasia, facial anomalies)
- **Methimazole (NOT antiepileptic)**: choanal atresia, aplasia cutis
- **Carbamazepine**: spina bifida (lower risk than valproate)

Go Back to Q13

Q14.

Solution

Topic: Tardive Dyskinesia – Nigrostriatal Pathway D2 Upregulation

Answer: (D)

Tardive dyskinesia (TD) is a delayed, potentially irreversible movement disorder caused by long-term (months to years) use of dopamine D2 receptor antagonists (typical antipsychotics, metoclopramide).

Pathophysiology:

- Chronic D2 receptor blockade in the **nigrostriatal pathway** $\rightarrow$ D2 receptor upregulation (increased density and sensitivity) – as a compensatory response
- This hypersensitivity manifests as involuntary movements: choreiform movements, lip-smacking, tongue protrusion, grimacing, athetosis
- More common with: long duration of treatment, older age, higher doses, prior EPS, female sex

Dopaminergic pathway – adverse effect profile:

- **Mesolimbic** (VTA $\rightarrow$ nucleus accumbens): D2 blockade = antipsychotic efficacy

- **Mesocortical** (VTA → PFC): D2 blockade = cognitive blunting, negative symptom worsening
- **Nigrostriatal** (SN → striatum): D2 blockade → acute EPS (dystonia, parkinsonism, akathisia); **chronic** → **TD**
- **Tuberoinfundibular** (hypothalamus → pituitary): D2 blockade → hyperprolactinaemia (galactorrhoea, amenorrhoea, gynaecomastia)

Management of TD: Reduce/withdraw offending drug; switch to atypical antipsychotic (clozapine, quetiapine – lower EPS risk); valbenazine or deutetrabenazine (VMAT2 inhibitors – approved for TD).

Go Back to Q14

Q15.

Solution

Topic: Fluoxetine – Long Half-Life and Minimal Discontinuation Syndrome

Answer: (A)

Fluoxetine's unique pharmacokinetic advantage:

- Fluoxetine half-life: **1–4 days** (plasma)
- Active metabolite **norfluoxetine** half-life: **4–16 days**
- Combined effective half-life: the plasma level declines very slowly after stopping
- This slow, self-tapering decline prevents the withdrawal (discontinuation) syndrome

SSRI discontinuation syndrome ("FINISH" mnemonic): Flu-like symptoms, Insomnia, Nausea, Imbalance, Sensory disturbances ("electric shocks"), Hyperarousal – occurs within 2–4 days of stopping shorter half-life SSRIs.

Comparison of SSRI half-lives:

- **Fluoxetine**: longest (> 4 days) → almost no discontinuation syndrome
- **Paroxetine**: shortest (≈ 21 hours) → most severe discontinuation syndrome
- Sertraline, citalopram, escitalopram: intermediate

Note: Paroxetine (option B) causes its OWN severe discontinuation syndrome due to SHORT half-life – the opposite of what option B claims.

Go Back to Q15

Q16.

Solution

Topic: Ketamine – NMDA Antagonist, Preferred in Asthmatic Patients

Answer: (B)

Ketamine is unique among induction agents:

- **Mechanism**: Non-competitive antagonist at **NMDA (glutamate) receptors** in the CNS
- Produces **dissociative anaesthesia**: eyes open, patient appears awake but is unaware and analgesic; associated with amnesia

Unique cardiovascular and respiratory profile:

- **Sympathomimetic**: stimulates release of catecholamines $\rightarrow$ increases BP, HR, and cardiac output (unlike most other induction agents which cause hypotension)
- **Bronchodilator**: due to catecholamine release (β_2 stimulation of bronchial smooth muscle) $\rightarrow$ **preferred induction agent in asthmatic patients**
- Maintains pharyngeal/laryngeal reflexes better than other agents

Adverse effects:

- **Emergence phenomena**: vivid hallucinations, dysphoria, "bad trips" during recovery – prevented by premedication with BZDs (diazepam or midazolam)
- Increased secretions (give atropine premedication)
- Raises ICP and IOP (avoid in head injury, penetrating eye injury)

Go Back to Q16

Q17.

Solution

Topic: Vancomycin – D-Ala-D-Ala Binding Mechanism

Answer: (C)

Vancomycin is a glycopeptide antibiotic with a completely different mechanism from β-lactam antibiotics:

- Binds non-covalently to the **D-Ala-D-Ala** terminus of the peptidoglycan pen-

tapeptide precursor (NAM-NAG-L-Ala-D-iGlu-L-Lys-D-Ala-**D-Ala**)

- This physical binding sterically prevents **transglycosylation** (linking of NAM-NAG units) and **transpeptidation** (cross-linking of peptide side chains)
- Net result: cell wall synthesis is blocked → osmotic lysis

Why MRSA is susceptible:

- MRSA is resistant to β-lactams due to *altered PBP2a* (mecA gene)
- Vancomycin does not interact with PBPs – it acts upstream (at the D-Ala-D-Ala terminus), bypassing this resistance mechanism

Vancomycin resistance (VRE – vancomycin-resistant Enterococcus):

- VanA gene cluster: replaces D-Ala-D-Ala with **D-Ala-D-Lactate** (or D-Ala-D-Serine)
- Vancomycin cannot bind D-Ala-D-Lac effectively → resistance

Adverse effects: Red-man syndrome (non-immune histamine release if infused rapidly – slow infusion over 1–2 hours), nephrotoxicity, ototoxicity.

Go Back to Q17

Q18.

Solution

Topic: Linezolid – Prevents 70S Initiation Complex by Binding 23S rRNA

Answer: (D)

Linezolid (oxazolidinone) has a unique mechanism unlike all other antibacterials:

- Binds to the **23S ribosomal RNA** of the **50S subunit**
- Prevents formation of the **70S initiation complex** (prevents the 30S-fMet-tRNA-mRNA complex from joining the 50S subunit)
- Blocks protein synthesis at the **initiation stage** – a unique mechanism
- No cross-resistance with other 50S inhibitors (erythromycin, chloramphenicol, clindamycin – which all bind at different 50S sites and act after initiation complex formation)

Spectrum: Gram-positive organisms including MRSA, VRE, drug-resistant Mycobacterium tuberculosis, Listeria.

Adverse effects:

- **Reversible myelosuppression**: thrombocytopenia, anaemia (monitor CBC weekly)
- **Serotonin syndrome**: linezolid has weak MAO-inhibitory activity – avoid SSRIs, SNRIs, pethidine, tramadol
- **Optic and peripheral neuropathy**: with prolonged use ($>$ 28 days)
- **Lactic acidosis**: rare, due to mitochondrial protein synthesis inhibition

Go Back to Q18

Q19.

Solution

Topic: Azithromycin – Long Tissue Half-Life Enabling Short Course

Answer: (A)

Azithromycin's distinctive pharmacokinetics:

- Plasma half-life: $\approx$**68 hours** (exceptional among macrolides; erythromycin $\approx$ 1.5 hours)
- Very high tissue-to-plasma concentration ratio ($>$ 50:1 in some tissues)
- Tissue levels remain above MIC for susceptible organisms for **5–7 days** after the last dose
- A 3-day (or even 1-day) course achieves effective tissue drug exposure equivalent to 7–10 days with older antibiotics

Mechanism: Macrolide – binds to the 23S rRNA of the 50S ribosomal subunit, inhibiting translocation (peptide chain elongation).

Spectrum and uses:

- Atypical pneumonia (Mycoplasma, Chlamydophila, Legionella)
- Chlamydia trachomatis STI (single 1g dose)
- Community-acquired pneumonia (CAP)

Fewer drug interactions: Unlike erythromycin (strong CYP3A4 inhibitor), azithromycin is a weak CYP3A4 inhibitor – fewer interactions.

Go Back to Q19

Q20.

Solution

Topic: Imipenem-Cilastatin – Cilastatin Inhibits Renal DHP-I

Answer: (B)

Imipenem is a carbapenem – the broadest-spectrum β-lactam, active against Gram-positive cocci, Gram-negative bacilli (including Pseudomonas), and anaerobes.

Why cilastatin is necessary:

- Imipenem is inactivated in the renal tubule by the enzyme **dihydropeptidase-I (DHP-I)**
- DHP-I hydrolyses the β-lactam ring of imipenem $\rightarrow$ generates nephrotoxic metabolites AND reduces urinary drug concentration
- **Cilastatin inhibits renal DHP-I**, protecting imipenem from tubular inactivation
- Result: higher urinary imipenem concentrations (important for urinary tract infections), reduced nephrotoxic metabolite accumulation

Note on other carbapenems:

- **Meropenem, ertapenem, doripenem**: stable to DHP-I, do NOT require a DHP-I inhibitor
- Only imipenem requires cilastatin

Cilastatin is NOT a β-lactamase inhibitor: It does not protect imipenem from bacterial β-lactamases (imipenem is stable to most β-lactamases, but not metallo-β-lactamases).

Go Back to Q20

Q21.

Solution

Topic: Nitrofurantoin – Intrinsic Resistance of Pseudomonas and Proteus

Answer: (C)

Nitrofurantoin: urinary antiseptic active within the urinary tract due to high concentration in urine.

Mechanism: Reduced to reactive intermediates by bacterial nitrofuran reductase → damages bacterial DNA, ribosomes, and metabolic enzymes.

Spectrum (susceptible organisms in UTI):

- *Escherichia coli* (most common UTI pathogen – highly susceptible)
- *Staphylococcus saprophyticus*
- *Enterococcus faecalis*
- *Klebsiella* (variable susceptibility)

Intrinsically resistant organisms (NOT susceptible):

- ***Pseudomonas aeruginosa*** – lacks the nitrofuran reductase; intrinsically resistant
- ***Proteus* spp.** – urine alkalinised by urease activity reduces nitrofurantoin activity; also intrinsic resistance
- *Serratia, Morganella*

Adverse effects: Pulmonary toxicity (acute pneumonitis or chronic pulmonary fibrosis), peripheral neuropathy (especially in renal impairment where drug accumulates), GI upset, haemolysis in G6PD deficiency.

Go Back to Q21

Q22.

Solution

Topic: Ethambutol – Optic Neuritis and Colour Vision Defects

Answer: (D)

Ethambutol is a first-line anti-tuberculosis drug with a unique mechanism and specific toxicity:

Mechanism of action:

- Inhibits **arabinosyl transferase** (encoded by the embB gene)
- Prevents synthesis of **arabinogalactan**, a key component of the mycobacterial cell wall
- Active only against mycobacteria (not other bacteria)

The ONE major adverse effect – optic neuritis:

- **Retrobulbar optic neuritis**: dose- and duration-dependent
- Presents as: **red-green colour blindness** (earliest sign), decreased visual acuity, central scotoma
- Visual field defects: central or peripheral
- Usually reversible if drug is stopped early; may be permanent with prolonged exposure
- **Mandatory monitoring**: baseline visual acuity and colour vision testing; repeat monthly (Ishihara charts for colour, Snellen chart for acuity)

Prevention: Avoid in children $<$ 5 years old (cannot reliably report visual changes); reduce dose in renal impairment (ethambutol is renally excreted).

Go Back to Q22

Q23.

Solution

Topic: Griseofulvin – Active Only Against Dermatophytes, NOT Candida

Answer: (A)

Griseofulvin: antifungal for dermatophytosis only.

Mechanism of action:

- Binds to **tubulin** (spindle microtubule proteins), inhibiting fungal mitosis
- Disrupts fungal cell division
- Deposits in **newly formed keratin-containing tissues** (skin, hair, nails) – the drug reaches infection sites via this keratin deposition

Spectrum (ONLY dermatophytes):

- *Trichophyton* spp. (tinea pedis, unguium, cruris, capitis, corporis)
- *Microsporum* spp. (tinea capitis in children)
- *Epidermophyton* spp. (tinea pedis, cruris)

NOT active against:

- ***Candida* spp.** – griseofulvin has NO activity against any Candida species

- *Aspergillus* spp.
- Any other yeasts or dimorphic fungi (Cryptococcus, Histoplasma)
- Systemic infections (griseofulvin is not used systemically for deep-seated mycoses)

Adverse effects: Hepatotoxicity, photosensitivity, drug interactions (enzyme inducer – reduces warfarin efficacy).

Go Back to Q23

Q24.

Solution

Topic: Oseltamivir – Neuraminidase Inhibitor, Prevents Viral Spread

Answer: (B)

Influenza virus replication:

- Influenza binds to sialic acid residues on host cell surface glycoproteins via **haemagglutinin (HA)**
- After replication, new viral particles bud from the infected cell surface
- **Neuraminidase (NA)** cleaves sialic acid residues $\rightarrow$ releases new virions from the cell surface $\rightarrow$ allows spread to neighbouring cells

Oseltamivir (Tamiflu) mechanism:

- Inhibits influenza A and B **neuraminidase**
- New viral particles remain attached to infected cell surface (sialic acid not cleaved) $\rightarrow$ cannot spread
- Reduces duration and severity of influenza by $\approx$ 1–2 days; most effective when started within 48 hours of symptom onset

Option A describes amantadine/rimantadine (M2 ion channel blockers – active only against influenza A, not B; now largely obsolete due to resistance). **Option C** describes baloxavir marboxil (cap-dependent endonuclease inhibitor, a newer agent). **Option D** is not a direct antiviral mechanism of oseltamivir.

Go Back to Q24

Q25.

Solution

Topic: Primaquine – Haemolysis in G6PD Deficiency

Answer: (C)

Primaquine is an 8-aminoquinoline active against:

- **Hepatic hypnozoites** of *P. vivax* and *P. ovale* (the only class of drugs to achieve radical cure)
- Gametocytes of *P. falciparum*

G6PD deficiency and haemolysis:

- G6PD (glucose-6-phosphate dehydrogenase) is the enzyme that catalyses the first step of the **pentose phosphate pathway**
- G6PD produces **NADPH** → regenerates **glutathione (GSH)** → protects RBCs from oxidative damage
- Primaquine is metabolised to reactive oxygen species that generate **oxidative stress** in RBCs
- In G6PD-deficient patients: cannot regenerate GSH → oxidised haemoglobin forms Heinz bodies → **intravascular haemolysis** → haemolytic anaemia, haemoglobinuria (dark urine)

Mandatory G6PD testing before prescribing primaquine (or dapsone, rasburicase, methylene blue, nalidixic acid, nitrofurantoin).

Alternative for G6PD-deficient patients: Weekly low-dose primaquine (0.75 mg/kg weekly for 8 weeks) is better tolerated; tafenoquine (requires single dose but same contraindication).

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Q26.

Solution

Topic: Visceral Leishmaniasis (Kala-Azar) – First-Line Treatment

Answer: (D)

Visceral leishmaniasis (kala-azar) is caused by *Leishmania donovani*, transmitted by the sandfly.

Treatment options:

- **Sodium stibogluconate (SSG)** / meglumine antimoniate: pentavalent antimony (Sb^V) compounds – historically the first-line treatment in most endemic regions (India, East Africa). Mechanism: converted to active trivalent antimony (Sb^{III}), which inhibits leishmanial enzymes involved in ATP synthesis and fatty acid oxidation.
- **Liposomal amphotericin B**: now the preferred treatment in India (where antimonial resistance is $>$ 60%), used in a short-course (1–5 days). Also first-line in Europe/USA.
- **Miltefosine**: oral first-line in India for antimonial-resistant VL. Teratogenic – contraindicated in pregnancy.
- **Paromomycin (aminoglycoside)**: parenteral, used in combination regimens.

In the context of "most endemic regions" where resistance to antimonials is not yet predominant (Africa, parts of Asia), **sodium stibogluconate** remains the first-line agent per this question's framing.

Go Back to Q26

Q27.

Solution

Topic: Amiodarone – Multi-Channel Antiarrhythmic (All 4 Vaughan-Williams Classes)

Answer: (A)

Amiodarone is the most complex and broad-spectrum antiarrhythmic drug:

Vaughan-Williams Class effects:

- **Class I (Na^+ channel block)**: Phase 0 slowing, reduces conduction velocity
- **Class II (β-blockade)**: Both α and β adrenergic receptor blockade – reduces heart rate
- **Class III (K^+ channel block)**: Prolongs Phase 3, extends action potential duration (APD) and effective refractory period (ERP) – the dominant antiarrhythmic mechanism
- **Class IV (Ca^{2+} channel block)**: Slows AV nodal conduction

Amiodarone's toxicity profile (long half-life 40–55 days means accumulation and prolonged toxicity):

- **Pulmonary**: interstitial pneumonitis/fibrosis (monitor with annual CXR and PFTs)
- **Thyroid**: both hypothyroidism (more common) and hyperthyroidism (amiodarone is 37% iodine by weight)
- **Corneal microdeposits**: almost universal ($>$ 90%), usually asymptomatic
- **Photosensitivity/blue-grey skin discolouration**
- **Hepatotoxicity**: transaminase elevation; rarely cirrhosis
- **Peripheral neuropathy**
- **Proarrhythmic**: can prolong QT and cause torsades de pointes (rare)

Go Back to Q27

Q28.

Solution

Topic: Beta-Blockers in Chronic Heart Failure – Bisoprolol Mortality Benefit

Answer: (B)

Paradox of β-blockers in heart failure:

- In **acute decompensated HF**: β-blockers are contraindicated (reduce inotropy and HR, worsening acute haemodynamics)
- In **stable chronic systolic HF**: three β-blockers are approved and reduce mortality (by 30–35%):
  - **Bisoprolol** (β_1-selective) – CIBIS-II trial
  - **Carvedilol** (non-selective β- + α_1-blocker) – COPERNICUS trial
  - **Metoprolol succinate** (extended-release β_1-selective) – MERIT-HF trial

Why β-blockers are beneficial in chronic HF:

- Attenuate **chronic sympathetic overdrive** (the maladaptive response in HF that accelerates cardiac damage)
- Reduce myocyte apoptosis and hypertrophy (**reverse cardiac remodelling**)
- Reduce β_1 receptor downregulation (restores receptor density)
- Reduce sudden cardiac death (ventricular arrhythmias)
- Long-term: improve EF and clinical symptoms

Atenolol (option A) is NOT approved for HF (lacks evidence); **propranolol** (option C) is not used for HF; **sotalol** (option D) is not indicated for HF.

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Q29.

Solution

Topic: Spironolactone – Hyperkalaemia as Most Serious Adverse Effect

Answer: (C)

Spironolactone is a competitive antagonist at the aldosterone (mineralocorticoid) receptor in the late distal tubule and collecting duct.

Mechanism:

- Blocks aldosterone $\rightarrow$ reduces expression of Na^+/K^+-ATPase and epithelial Na^+ channels (ENaC)
- Result: less Na^+ reabsorbed, less K^+ (and H^+) secreted $\rightarrow$ **potassium-sparing diuresis**
- Natriuresis reduces fluid overload; K^+ retention can cause hyperkalaemia

Risk of hyperkalaemia is amplified by:

- Concurrent ACE inhibitor/ARB (also reduces aldosterone-mediated K^+ excretion)
- Renal impairment (reduced K^+ excretion capacity)
- High K^+ diet or potassium supplements

In this question: $K^+ = 6.4$ mEq/L is dangerous (risk of fatal arrhythmias). The patient is also on enalapril.

Other spironolactone adverse effects:

- **Gynaecomastia/painful breast enlargement**: antiandrogen effect (binds androgen receptors)
- Menstrual irregularities in pre-menopausal women
- **Note**: Eplerenone (selective mineralocorticoid receptor antagonist) causes fewer hormonal side effects

Go Back to Q29

Q30.

Solution

Topic: ARBs vs ACE Inhibitors – No Bradykinin Accumulation, No Cough

Answer: (D)

ACE inhibitor (e.g., ramipril) mechanism and cough:

- ACE (= kininase II) normally metabolises bradykinin → inactive peptides
- ACE inhibition → **bradykinin accumulates** → stimulates sensory C-fibres (unmyelinated) in the airways via prostaglandin and substance P release → **dry cough** (non-productive, tickling)
- Cough incidence: 10–15% in European patients; 30–40% in Asian patients (higher sensitivity)

ARB (e.g., losartan) – why NO cough:

- ARBs block the **AT1 receptor** directly – they do NOT inhibit the ACE enzyme
- ACE enzyme remains functional → continues to degrade bradykinin normally
- **Bradykinin levels are not elevated** with ARBs → no airway sensory nerve stimulation → no cough

Additional note on losartan: It has a unique uricosuric effect (blocks URAT1 in renal proximal tubule, reducing uric acid reabsorption) – beneficial in hypertensive patients with gout.

Go Back to Q30

Q31.

Solution

Topic: Colchicine in Acute Gout – Microtubule Inhibition, Anti-Neutrophil

Answer: (A)

Colchicine mechanism:

- Binds to **tubulin dimers** and inhibits their polymerisation into microtubules
- **Prevents neutrophil migration** (chemotaxis) into the synovial joint – neutrophils require functional microtubules for locomotion
- Blocks neutrophil degranulation and release of inflammatory cytokines (IL-

1β, IL-6, TNF)

- Inhibits NLRP3 inflammasome activation (which produces IL-1β – the key driver of acute gout inflammation)

What colchicine does NOT do:

- Does NOT lower serum uric acid (not uricosuric, not xanthine oxidase inhibitor)
- Does NOT remove urate crystals from the joint
- Has no analgesic action on COX pathway

Main adverse effect: Severe GI toxicity (nausea, vomiting, cramping, profuse diarrhoea) – dose-limiting; stop the drug at first sign of GI symptoms. Long-term: myopathy, neuropathy.

Uses: Acute gout attack (most effective if given within first 12–24 hours), gout prophylaxis (low dose), familial Mediterranean fever (FMF), pericarditis.

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Q32.

Solution

Topic: Allopurinol – Drug Interaction with Azathioprine/6-Mercaptopurine

Answer: (B)

Allopurinol inhibits **xanthine oxidase (XO)**, the enzyme that converts hypoxanthine $\rightarrow$ xanthine $\rightarrow$ uric acid (the final steps in purine catabolism).

Mechanism of the dangerous interaction:

- **Azathioprine** is a prodrug $\rightarrow$ converted in the body to **6-mercaptopurine (6-MP)** $\rightarrow$ 6-MP is normally inactivated by **xanthine oxidase** (and TPMT)
- Allopurinol **blocks XO** $\rightarrow$ 6-MP is NOT inactivated $\rightarrow$ accumulates to toxic levels
- Toxic 6-MP concentrations: severe **bone marrow suppression** (pancytopenia – thrombocytopenia, leucopenia, anaemia)

Clinical management: If allopurinol MUST be given with azathioprine/6-MP (e.g., in inflammatory bowel disease), reduce the azathioprine/6-MP dose by 75% and monitor CBC closely.

Alternative approach: Use febuxostat (non-purine XO inhibitor) instead of allopurinol – but febuxostat also inhibits XO and carries the same risk with 6-MP/azathioprine.

Go Back to Q32

Q33.

Solution

Topic: COX-2 Inhibitors – Increased Cardiovascular Thrombotic Risk

Answer: (C)

Vascular endothelium and platelet balance:

- **Platelets**: express COX-1 only → produce **thromboxane A2 (TXA2)** → promotes platelet aggregation and vasoconstriction
- **Vascular endothelium**: expresses **both COX-1 and COX-2** → produces **prostacyclin (PGI2)** → inhibits platelet aggregation and causes vasodilation

How selective COX-2 inhibitors shift this balance:

- Celecoxib blocks **vascular COX-2** → reduces PGI2 (prostacyclin) synthesis in endothelium
- Platelets still produce TXA2 via COX-1 (which celecoxib does not block)
- **TXA2 predominates → pro-thrombotic, pro-vasoconstrictive state → increased MI and stroke risk**

This mechanism led to the withdrawal of rofecoxib (Vioxx) from the market in 2004 (VIGOR trial demonstrated excess MI risk).

Options analysis:

- A – Wrong: COX-2 inhibitors do not increase platelet TXA2 (platelets express COX-1)
- B – Also a valid contributing mechanism (sodium retention) but NOT the main answer for cardiovascular thrombotic risk
- **C – CORRECT**: imbalance between reduced PGI2 and unchanged TXA2
- D – Wrong: COX-2 inhibitors are not coagulation factor activators

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Q34.

Solution

Topic: PTU in Thyroid Storm – Dual Mechanism (Synthesis + T4 to T3 Conversion Block)

Answer: (D)

Antithyroid drugs – comparison:

- **Both PTU and methimazole** (and carbimazole):
  - Inhibit **thyroid peroxidase (TPO)** → block iodination of tyrosine residues on thyroglobulin → reduce synthesis of T3 and T4
- **PTU additionally**:
  - Inhibits **type 1 iodothyronine deiodinase** in peripheral tissues (liver, kidney, thyroid)
  - This enzyme converts T4 (tetraiodothyronine, less active) → T3 (triiodothyronine, 3–5 times more potent and biologically active)
  - Blocking this conversion rapidly lowers the concentration of the most active thyroid hormone (T3) in tissues

Why this matters in thyroid storm:

- In thyroid storm, the immediate threat is excessive T3 activity
- Methimazole only blocks new synthesis – existing T4 continues converting to T3
- PTU blocks both synthesis AND conversion → more rapid reduction in T3 levels → preferred in thyroid storm

Caveat: PTU is also preferred in the **first trimester of pregnancy** (methimazole causes choanal atresia and aplasia cutis).

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Q35.

Solution

Topic: Glipizide (Sulfonylurea) – Hypoglycaemia if Meals Skipped

Answer: (A)

Sulfonylureas (glipizide, glibenclamide, glimepiride, gliclazide) stimulate insulin secretion by closing **ATP-sensitive K^+ channels (K-ATP)** in pancreatic β-cells:

- K-ATP channel closure $\rightarrow$ membrane depolarisation $\rightarrow$ voltage-gated Ca^{2+} channel opening $\rightarrow$ Ca^{2+} influx $\rightarrow$ insulin vesicle exocytosis
- This mechanism is **independent of blood glucose** – insulin is released even if blood glucose is low

Consequence: Hypoglycaemia is the major adverse effect, especially if a meal is skipped or delayed.

Important precautions:

- **Take 30 minutes before a meal** (for maximum effect at mealtime insulin release)
- Never skip meals
- **Glipizide is shorter-acting** than glibenclamide – safer in the elderly (glibenclamide's long-acting metabolites cause prolonged hypoglycaemia in elderly/renally impaired)
- Avoid in severe hepatic or renal impairment

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Q36.

Solution

Topic: Progesterone – Maintains Secretory Endometrium in Luteal Phase

Answer: (B)

Role of progesterone in the menstrual cycle:

Follicular phase (Days 1–14):

- Oestrogen dominates $\rightarrow$ endometrial proliferation (thickening)
- Rising oestrogen eventually triggers the **LH surge** at midcycle $\rightarrow$ ovulation

Luteal phase (Days 15–28) – after ovulation:

- Ruptured follicle $\rightarrow$ corpus luteum forms $\rightarrow$ produces **progesterone** (and some oestrogen)

- Progesterone converts proliferative endometrium into **secretory (decidua-like) endometrium**:
  - Increases glandular secretions (glycogen-rich) for nourishing a blastocyst
  - Reduces endometrial receptivity to further oestrogen stimulation
- Progesterone suppresses LH secretion (negative feedback) → prevents further ovulation
- If no implantation: corpus luteum degenerates → progesterone falls → endometrium sheds (menstruation)
- If implantation: hCG from trophoblast maintains corpus luteum → progesterone continues to maintain pregnancy

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Q37.

Solution

Topic: Metoclopramide – D2 Antagonism (Antiemetic) + 5-HT4 Agonism (Prokinetic)

Answer: (C)

Metoclopramide's dual pharmacology:

- **D2 receptor antagonism in the chemoreceptor trigger zone (CTZ/area postrema)** (outside blood-brain barrier):
  - Blocks D2 receptors → prevents dopamine-mediated nausea and vomiting → **antiemetic**
- **5-HT4 receptor agonism in the myenteric plexus of the gut**:
  - Increases acetylcholine release from myenteric neurons → increases GI smooth muscle contraction and coordination → **prokinetic effect** (faster gastric emptying, increased LES tone)

Adverse effects – D2 blockade in the nigrostriatal pathway:

- **Acute dystonia**: oculogyric crisis, torticollis, trismus (as in this question) – treat with IV procyclidine or diphenhydramine (anticholinergic)
- Akathisia (restlessness), parkinsonism with long-term use

- Tardive dyskinesia (with prolonged use)
- Hyperprolactinaemia (tuberoinfundibular pathway D2 blockade)

High-risk groups for acute dystonia: Young women and children.

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Q38.

Solution

Topic: Sodium Cromoglycate – Mast Cell Stabiliser, Only Prophylactic, No Bronchodilator Action

Answer: (D)

Sodium cromoglycate (cromolyn sodium) mechanism:

- Stabilises **mast cells** by blocking calcium-dependent chloride channels in the mast cell membrane
- Prevents **degranulation** of mast cells upon allergen exposure
- Reduces release of histamine, leukotrienes, prostaglandins, tryptase, and other inflammatory mediators

Critical clinical point:

- **PROPHYLACTIC ONLY**: must be taken before allergen exposure or exercise (e.g., 15–20 minutes before exercise for exercise-induced asthma)
- **Has NO bronchodilator action**: cannot relieve an acute asthma attack (does not relax bronchial smooth muscle)
- **Cannot be given during an acute attack**: it will have no effect on existing bronchoconstriction
- Very safe profile (virtually no systemic absorption – acts locally in the airway)

Uses:

- Prophylaxis of allergic asthma (especially children)
- Exercise-induced bronchospasm prophylaxis
- Allergic rhinitis (as nasal spray)
- Allergic conjunctivitis (as eye drops)

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Q39.

Solution

Topic: Misoprostol – PGE1 Analog, Reduces HCl and Increases Mucus/Bicarbonate

Answer: (A)

Misoprostol is a synthetic **prostaglandin E1 (PGE1) analog** that acts on **EP receptors** (specifically EP3 on parietal cells, EP4 on mucous cells).

Mechanism of gastroprotection:

- **EP3 receptors on gastric parietal cells**: Gi-coupled → reduces adenylyl cyclase → reduces cAMP → **reduces H^+/K^+-ATPase activity** → **decreases HCl secretion**
- **On mucous and epithelial cells**: **increases mucus and bicarbonate secretion** → strengthens the mucosal defence barrier
- **Bypasses the NSAID block**: NSAIDs inhibit COX, reducing endogenous PGE2/PGI2. Misoprostol directly activates EP receptors, replacing the lost prostaglandin cytoprotective function

Additional uses of misoprostol:

- **Medical abortion**: combined with mifepristone (RU-486) for termination of pregnancy
- **Cervical ripening/labour induction**: stimulates uterine smooth muscle (EP/FP receptors)
- **Postpartum haemorrhage**: uterotonic (WHO-approved)

Adverse effects: Diarrhoea and abdominal cramps (dose-dependent), uterine contractions (contraindicated in pregnancy when used for GI protection).

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Q40.

Solution

Topic: LMWH Monitoring – Anti-Xa Activity Assay (Not APTT)

Answer: (B)

Comparison of UFH vs LMWH:

- **Unfractionated heparin (UFH)**: inhibits both Factor Xa AND Factor IIa (thrombin) via antithrombin III enhancement, in equal proportions (anti-Xa:anti-IIa ratio = 1:1) $\rightarrow$ reliably prolongs **APTT** $\rightarrow$ monitored by APTT (therapeutic target: 1.5–2.5 $\times$ control)
- **Low molecular weight heparin (LMWH, e.g., enoxaparin, dalteparin)**:
  - Selectively inhibits **Factor Xa** $\gg$ Factor IIa (anti-Xa:anti-IIa ratio $\approx$ 4:1)
  - Does NOT significantly prolong APTT (APTT is insensitive to anti-Xa activity)
  - Predictable pharmacokinetics $\rightarrow$ weight-based dosing, **no routine monitoring** required in most patients

When LMWH monitoring IS required and the correct test:

- Renal impairment (LMWH accumulates – renally cleared)
- Extreme body weight (obese $>$ 100 kg or very underweight)
- Pregnancy (volume of distribution changes)
- Test: **Anti-Xa activity level** (target: 0.5–1.0 IU/mL for twice-daily dosing; 1.0–2.0 IU/mL for once-daily dosing)
- Timing: 4 hours after subcutaneous injection (peak levels)

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Answer Key – FMGE Pharmacology Sample Paper 3

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