FMGE Biochemistry Sample Paper – 8

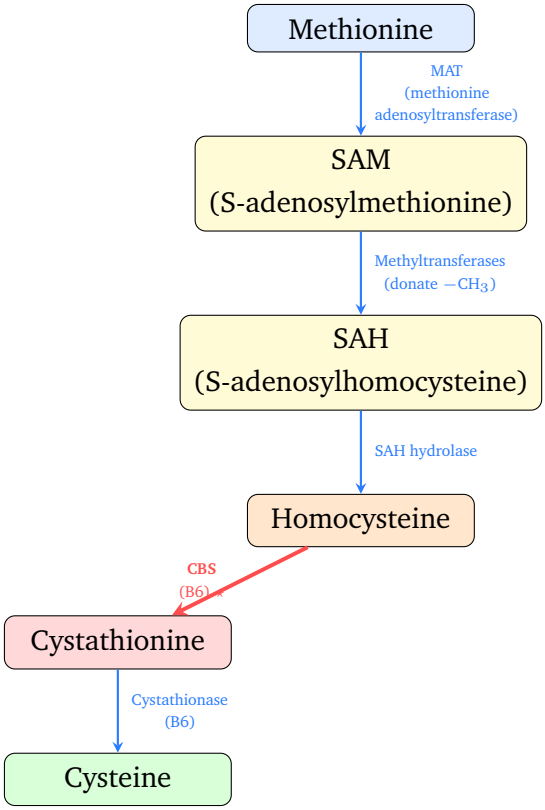
Duration: 60 Minutes **Maximum Marks: 40**

Instructions

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

FMGE Biochemistry – Q1 to Q40

Q1. A 35-year-old woman with recurrent deep vein thrombosis is found to have elevated plasma homocysteine. Genetic testing shows a mutation in cystathionine beta-synthase (CBS). Which of the following correctly describes the transsulfuration pathway shown below?



(A) Methionine donates methyl groups but not sulfur to cysteine

(B) The CBS enzyme uses pyridoxal phosphate (B6) as a cofactor to convert cystathionine to cysteine

(C) Methionine donates both methyl groups (via SAM) and sulfur (via homocysteine) to cysteine

(D) SAH is the primary methyl donor in one-carbon transfer reactions

Q2. In enzyme kinetics, the Michaelis-Menten equation describes a rectangular hyperbola when velocity is plotted against substrate concentration. A sigmoid (S-shaped) velocity curve, however, is produced by cooperative enzymes with a Hill coefficient (n) greater than 1. Which of the following enzymes would produce a **sigmoidal** substrate-saturation curve?

(A) Lactate dehydrogenase (LDH) acting on pyruvate

(B) Hexokinase acting on glucose in the liver

(C) Alkaline phosphatase in bone

(D) Phosphofructokinase-1 (PFK-1), an allosteric cooperative enzyme

Q3. A 6-year-old child presents with severe intellectual disability, behavioural disturbances (hyperactivity, aggression), and coarse facial features. Urine spot test shows elevated heparan sulfate. An enzyme assay reveals deficiency of heparan-N-sulfatase. Which mucopolysaccharidosis (MPS) does this child have?

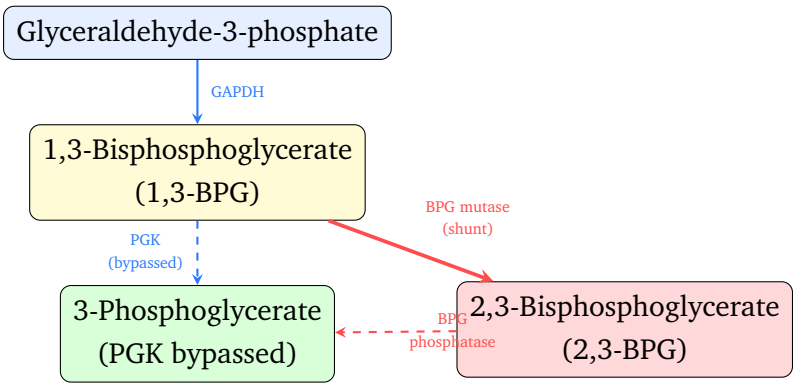
(A) MPS I (Hurler syndrome) – α-L-iduronidase deficiency

(B) MPS II (Hunter syndrome) – iduronate-2-sulfatase deficiency (X-linked)

(C) MPS VI (Maroteaux-Lamy syndrome) – N-acetylgalactosamine-4-sulfatase deficiency

(D) MPS III (Sanfilippo syndrome type A) – heparan-N-sulfatase deficiency

Q4. A 25-year-old woman living at high altitude has a lower than expected haemoglobin-oxygen saturation for her altitude. Her red blood cells show a markedly elevated level of 2,3-bisphosphoglycerate (2,3-BPG). Which of the following best describes the role of 2,3-BPG and the Rapoport-Luebering shunt shown below?



(A) 2,3-BPG binds oxyhaemoglobin (R-state) and increases O_2 affinity

(B) 2,3-BPG binds deoxyhaemoglobin (T-state) between the β-chains, stabilises it, and facilitates O_2 delivery to tissues

(C) The Rapoport-Luebering shunt generates extra ATP by bypassing phosphoglycerate kinase (PGK)

(D) 2,3-BPG binds the α-chains of haemoglobin and causes a left-shift in the O_2 dissociation curve

Q5. A 40-year-old volunteer on a research diet deficient in pantothenic acid develops dysaesthesia of the feet described as a "burning" sensation. Pantothenic acid (vitamin B5) is an essential component of which two key metabolic cofactors?

(A) NAD^+ and FAD

(B) Thiamine pyrophosphate (TPP) and pyridoxal phosphate (PLP)

(C) Tetrahydrofolate (THF) and biotin

(D) Coenzyme A (CoA) and acyl carrier protein (ACP)

Q6. A 3-year-old boy presents with spastic diplegia, progressive intellectual disability, and seizures. His serum ammonia is mildly elevated. Plasma amino acid analysis reveals markedly elevated **arginine**. Urine orotic acid is normal. The enzyme deficiency in this urea cycle disorder is:

(A) Ornithine transcarbamylase (OTC) – X-linked

(B) Argininosuccinate synthetase – citrullinaemia type I

(C) Arginase – hyperargininaemia

(D) Carbamoyl phosphate synthetase I (CPS-I)

Q7. During translation at the ribosome, peptide bond formation is catalysed by peptidyl transferase activity. In eukaryotes, this catalytic activity resides in the:

(A) 40S small ribosomal subunit (18S rRNA)

(B) eEF-2 elongation factor protein

(C) 28S rRNA of the 60S large ribosomal subunit (ribozyme activity)

(D) Peptidyl-tRNA at the P site

Q8. A 6-month-old infant presents to the emergency department in a comatose state after a 12-hour fast. Blood glucose is 1.8 mmol/L with paradoxically low or absent ketones (hypoketotic hypoglycaemia). Newborn screen shows elevated C8-acylcarnitine (octanoylcarnitine). Which metabolic disorder is most likely?

(A) MCADD (medium-chain acyl-CoA dehydrogenase deficiency)

(B) VLCADD (very-long-chain acyl-CoA dehydrogenase deficiency)

(C) Carnitine transporter deficiency

(D) Glycogen storage disease type I (Von Gierke disease)

Q9. In one complete turn of the tricarboxylic acid (TCA) cycle, which of the following correctly describes the **only substrate-level phosphorylation** step?

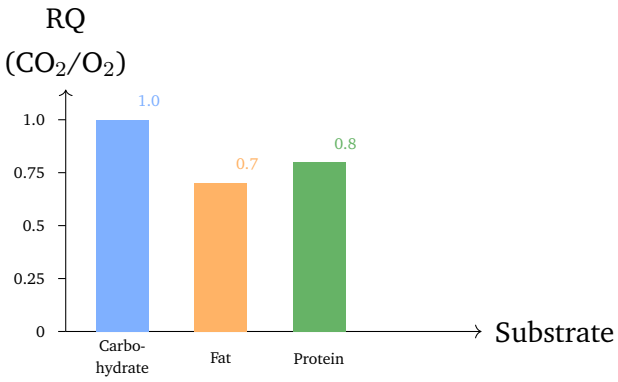
(A) Succinyl-CoA synthetase: succinyl-CoA + GDP + Pi $\rightarrow$ succinate + GTP + CoA

(B) Isocitrate dehydrogenase: isocitrate + NAD^+ $\rightarrow$ α-ketoglutarate + NADH + CO_2

(C) Malate dehydrogenase: malate + NAD^+ $\rightarrow$ oxaloacetate + NADH

(D) α-Ketoglutarate dehydrogenase: α-KG + NAD^+ + CoA $\rightarrow$ succinyl-CoA + NADH + CO_2

Q10. The respiratory quotient (RQ) is used in indirect calorimetry to determine fuel utilisation. In the bar chart shown below, which fuel substrate corresponds to an RQ of 1.0?



(A) Fat (RQ = 0.7)

(B) Protein (RQ $\approx$ 0.8)

(C) Carbohydrate (RQ = 1.0)

(D) Mixed diet (RQ = 0.85)

Q11. A 28-year-old man working in a chemical factory is rushed in after accidental inhalation of nitrite fumes. He is cyanosed despite normal pO_2. Co-oximetry shows 35% methaemoglobin. Which of the following is the correct treatment for symptomatic methaemoglobinaemia?

(A) Hydroxyurea to reduce Hb polymerisation

(B) Supplemental oxygen alone is sufficient

(C) Deferoxamine (iron chelation therapy)

(D) Methylene blue (requires NADPH from G6PD) to reduce Fe^{3+} back to Fe^{2+}

Q12. Activation of α_1-adrenergic receptors on hepatocytes leads to a rise in intracellular calcium via the phosphoinositide signalling pathway. The enzyme that cleaves PIP_2 (phosphatidylinositol-4,5-bisphosphate) to generate IP_3 and DAG is:

(A) Phospholipase A_2 (PLA_2) – releases arachidonic acid

(B) Phospholipase D (PLD) – generates phosphatidic acid

(C) Phospholipase C-β (PLC-β), activated by G_q protein

(D) Adenylyl cyclase – generates cAMP from ATP

Q13. A patient with sickle cell disease has a point mutation in codon 6 of the β-globin gene (GAG $\rightarrow$ GTG), substituting valine for glutamic acid. This type of mutation that changes the identity of the encoded amino acid is called:

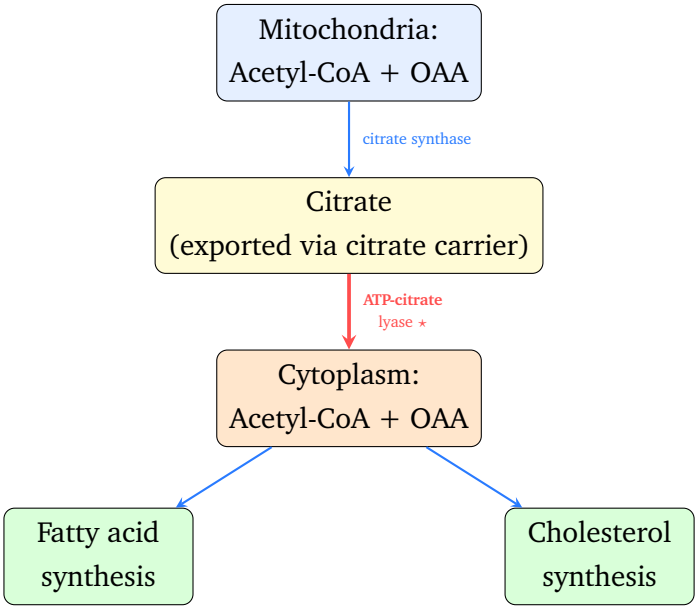
(A) Silent (synonymous) mutation – same amino acid retained

(B) Nonsense mutation – premature stop codon introduced

(C) Frameshift mutation – reading frame altered by insertion/deletion

(D) Missense mutation – different amino acid substituted

Q14. In the well-fed (postprandial) state, the liver exports citrate to the cytoplasm for fatty acid and cholesterol synthesis. Which enzyme converts cytoplasmic citrate back to acetyl-CoA and oxaloacetate, providing the substrate for lipogenesis?



(A) ATP-citrate lyase (ACL)

(B) Citrate synthase

(C) Aconitase

(D) Isocitrate dehydrogenase

Q15. A 2-year-old child presents with progressive loss of walking ability, spastic paraparesis, and peripheral neuropathy. MRI shows diffuse white matter changes (demyelination). Urine shows metachromatic granules (sulphatides). Nerve biopsy confirms demyelination. Enzyme assay shows deficiency of arylsulphatase A. The diagnosis is:

(A) Krabbe disease – galactocerebrosidase deficiency

(B) Metachromatic leukodystrophy (MLD) – arylsulphatase A deficiency

(C) Adrenoleukodystrophy (ALD) – ABCD1 transporter mutation (X-linked)

(D) Fabry disease – α-galactosidase A deficiency

Q16. A patient with severe hypertriglyceridaemia (type I hyperlipoproteinaemia) is found to have a mutation rendering apolipoprotein C-II non-functional. The basis for the marked elevation in chylomicrons is:

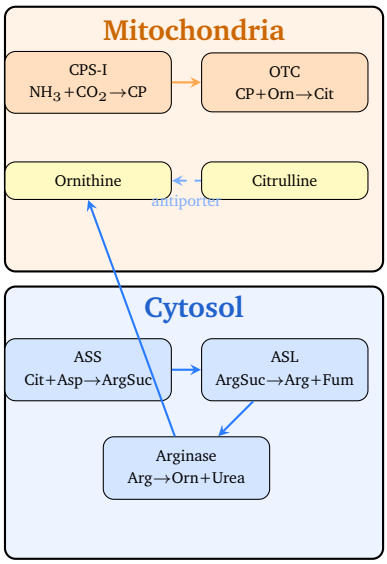
(A) ApoC-II is the obligatory activator of lipoprotein lipase (LPL), so its absence prevents chylomicron TG hydrolysis

(B) ApoC-II inhibits lipoprotein lipase; its loss causes overactivation and excess TG clearance

(C) ApoC-II is required for VLDL assembly in the liver

(D) ApoC-II mediates chylomicron remnant uptake by the liver LRP1 receptor

Q17. A neonate with hyperammonaemia is found to have citrullinaemia and elevated urinary orotic acid. The deficient enzyme is ornithine transcarbamylase (OTC). Regarding the compartmentalisation of the urea cycle shown below, which statement is correct?



(A) Arginase and OTC both function in the mitochondrial matrix

(B) CPS-I and OTC are mitochondrial; argininosuccinate synthetase (ASS), argininosuccinate lyase (ASL), and arginase are cytosolic

(C) All five urea cycle enzymes function exclusively in the cytosol

(D) Citrulline is synthesised in the cytosol and transported into the mitochondria

Q18. Cortisol exerts its anti-inflammatory and metabolic effects through a specific receptor. Unlike surface receptors for peptide hormones, the glucocorticoid receptor (GR) acts through which mechanism?

(A) Cortisol binds a G-protein-coupled receptor, generating cAMP via adenylyl cyclase

(B) Cortisol binds a tyrosine kinase receptor on the cell surface, activating the MAPK pathway

(C) Cortisol binds a ligand-gated ion channel, causing rapid membrane depolarisation

(D) Cortisol diffuses into the cell, binds cytoplasmic GR, dissociates from Hsp90, translocates to nucleus, and binds glucocorticoid response elements (GREs) to regulate transcription

Q19. During DNA replication, the leading strand is synthesised continuously while the lagging strand is synthesised in Okazaki fragments. The sliding clamp that encircles the DNA duplex and tethers DNA polymerase δ to the template, dramatically increasing processivity, is:

(A) RPA (replication protein A) – single-strand binding protein

(B) PCNA (proliferating cell nuclear antigen) – trimeric sliding clamp loaded by RFC

(C) RFC (replication factor C) – the clamp loader ATPase

(D) Topoisomerase I – relieves torsional stress ahead of the replication fork

Q20. A student studying amino acid metabolism notes that non-essential amino acids can be synthesised from common metabolic intermediates via transamination. The amino acid alanine is synthesised from which keto acid by the action of alanine aminotransferase (ALT/GPT)?

(A) Pyruvate (accepts amino group from glutamate $\rightarrow$ alanine + α-ketoglutarate)

(B) Oxaloacetate (accepts amino group $\rightarrow$ aspartate)

(C) α-Ketoglutarate (accepts amino group $\rightarrow$ glutamate via GDH)

(D) Succinyl-CoA (accepts amino group $\rightarrow$ δ-aminolaevulinic acid)

Q21. A dietitian advises patients with iron deficiency anaemia to consume vitamin C-rich foods along with their iron supplements. The biochemical basis for this recommendation is:

(A) Ascorbic acid reduces dietary non-haem iron from Fe^{3+} (ferric, poorly absorbed) to Fe^{2+} (ferrous, transported by DMT1) in the intestinal lumen, enhancing absorption

(B) Vitamin C increases haem oxygenase activity, releasing more iron from haem

(C) Ascorbic acid binds transferrin and increases its iron-loading capacity

(D) Vitamin C inhibits hepcidin secretion from the liver, reducing iron sequestration

Q22. A 6-month-old infant of Ashkenazi Jewish descent presents with progressive neurodegeneration, exaggerated startle response, and a cherry-red spot on fundoscopy. Hexosaminidase A enzyme assay shows marked deficiency. Which glycolipid accumulates in the lysosomes of neurons in this condition?

(A) Glucocerebroside (glucosylceramide) – in Gaucher disease

(B) Sphingomyelin – in Niemann-Pick disease type A

(C) Galactocerebrosidase – in Krabbe disease

(D) GM2 ganglioside – in Tay-Sachs disease

Q23. Proline is unique among the 20 standard amino acids because of its cyclic structure, in which the nitrogen is part of a five-membered pyrrolidine ring. What is the major structural consequence of proline residues in a polypeptide chain?

(A) Proline is an α-helix breaker that introduces a rigid kink in the peptide backbone due to restricted ϕ angle; it is abundant in collagen

(B) Proline forms disulfide bridges that stabilise the tertiary structure of proteins

(C) Proline is positively charged at physiological pH and promotes electrostatic interactions

(D) Proline is the only amino acid with a free α-amino group that reacts with 2,4-dinitrophenyl chloride

Q24. A pharmacology student is asked to distinguish between nucleosides and nucleotides. Which of the following correctly defines a nucleotide?

(A) A nucleotide consists of a nitrogenous base + a pentose sugar + one or more phosphate groups

(B) A nucleotide consists of only a nitrogenous base + a pentose sugar (no phosphate)

(C) A nucleotide consists of a purine base only + a deoxyribose sugar

(D) A nucleotide is any molecule that contains adenine linked to a ribose sugar

Q25. A 3-year-old child is brought to a metabolic clinic after autopsy of an older sibling revealed a lysosomal storage disease. The parents are counselled that lysosomal storage diseases share which common pathophysiological feature?

(A) They are all caused by defective mitochondrial membrane transport proteins

(B) All are caused by deficiency of lysosomal hydrolases (optimal pH 4.5-5.0), causing intralysosomal substrate accumulation and progressive organ dysfunction

(C) They are all X-linked recessive disorders exclusively affecting males

(D) They all present in the neonatal period with acute metabolic crisis and hyperammonaemia

Q26. A 45-year-old man with recurrent venous thromboembolism has a fasting plasma homocysteine of 28 μmol/L (normal $<$15). His B12 and folate are normal. He is a heavy smoker with hypertension. Elevated homocysteine is an independent risk factor for cardiovascular disease through which mechanism?

(A) Homocysteine activates the complement pathway, causing haemolysis

(B) Homocysteine is directly converted to fibrin and promotes clot formation without thrombin

(C) Homocysteine causes endothelial damage, promotes LDL oxidation, and has prothrombotic effects

(D) Homocysteine competes with arginine for nitric oxide synthase, abolishing vasodilation

Q27. A molecular biology laboratory uses Western blotting to confirm the presence of a specific protein in patient serum samples. Regarding the Western blot technique, which of the following is correct?

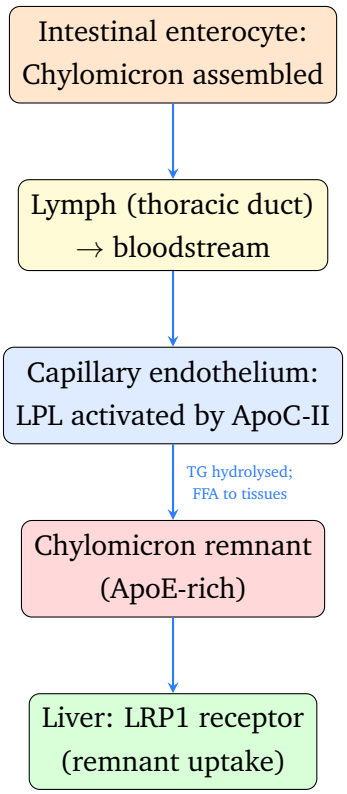
(A) Southern blot detects proteins; Western blot detects DNA sequences

(B) Western blot uses agarose gel for protein separation by charge under native conditions

(C) In Western blot, proteins are separated by SDS-PAGE (size), transferred to a membrane, and detected with specific antibodies (e.g., ECL chemiluminescence)

(D) Northern blot uses antibodies to detect specific mRNA species after gel electrophoresis

Q28. Chylomicrons are assembled in intestinal enterocytes after a fatty meal. Regarding their metabolism in the bloodstream, which of the following is correct?



(A) Chylomicrons enter the portal bloodstream directly, bypassing the lymphatic system

(B) ApoB-48 on chylomicrons activates lipoprotein lipase (LPL) at the capillary endothelium

(C) Chylomicron remnants are taken up by the spleen via the ApoC-II receptor

(D) Chylomicrons are assembled in the intestine, travel via lymph, and their triglycerides are hydrolysed by LPL (activated by ApoC-II); remnants are taken up by liver LRP1 receptor via ApoE

Q29. The protein C anticoagulant system provides a natural brake on coagulation. Regarding protein C and its cofactor protein S, which of the following is correct?

(A) Protein C is a vitamin K-independent serine protease activated by antithrombin III

(B) Protein C activates factors V and VIII to amplify clot formation (procoagulant)

(C) Activated protein C (APC), with protein S as cofactor, proteolytically inactivates factors Va and VIIIa; Factor V Leiden (Arg506Gln) is resistant to APC cleavage, causing thrombophilia

(D) Protein S is activated by thrombomodulin on the endothelial surface

Q30. Succinate dehydrogenase (Complex II) of the mitochondrial electron transport chain is the only complex that does NOT pump protons across the inner mitochondrial membrane. This is because:

(A) Complex II receives electrons from NADH, which carries insufficient energy for proton pumping

(B) Complex II is located in the outer mitochondrial membrane, outside the proton gradient

(C) Complex II uses a different electron acceptor (cytochrome c instead of ubiquinone) that bypasses proton pumping

(D) Complex II passes electrons from $FADH_2$ directly to ubiquinone (CoQ) without the conformational changes required for proton translocation; hence $FADH_2$ yields fewer ATP (1.5) than NADH (2.5)

Q31. When a glucose solution is allowed to stand in water, it undergoes mutarotation to reach an equilibrium mixture of α- and β-anomers. In the equilibrium mixture of D-glucose in aqueous solution, which anomer predominates and why?

(A) α-D-glucose predominates because its axial C1-OH forms more hydrogen bonds with water

(B) β-D-glucose predominates (approx. 64%) because the equatorial C1-OH at C1 is sterically less hindered and more stable

(C) The two anomers are present in exactly equal proportions (50:50) at equilibrium

(D) Open-chain (aldehyde) form predominates (>90%) in aqueous solution

Q32. Bile salts play a critical role in the digestion and absorption of dietary lipids in the small intestine. Which of the following best describes how bile salts facilitate fat absorption?

(A) Bile salts are lipases that directly hydrolyse dietary triglycerides in the intestinal lumen

(B) Bile salts form mixed micelles (with phospholipids and cholesterol) that solubilise the products of fat digestion (2-monoacylglycerol, fatty acids) and present them to enterocytes for absorption

(C) Bile salts are re-synthesised de novo in the intestinal lumen from dietary cholesterol

(D) Bile salts bind to the fat-soluble vitamins A, D, E, K and prevent their absorption

Q33. A newborn screening programme detects elevated phenylalanine in a male infant. Further testing shows elevated biopterin with a normal phenylalanine hydroxylase (PAH) gene. Urine neurotransmitter metabolites are markedly reduced (low HVA and 5-HIAA). The deficient enzyme, which regenerates BH4 from the quinonoid dihydrobiopterin (qBH2) product of PAH, is:

(A) Dihydropteridine reductase (DHPR) – regenerates BH4 from qBH2 using NADH; deficiency impairs both PAH and aromatic amino acid hydroxylases (TH, TPH) causing low dopamine and serotonin

(B) GTP cyclohydrolase I – first enzyme of BH4 biosynthesis de novo

(C) Sepiapterin reductase – reduces sepiapterin to BH4 in the salvage pathway

(D) Phenylalanine hydroxylase (PAH) – hydroxylates Phe to Tyr

Q34. Thyroid hormone bioactivity: T4 (thyroxine) is the major secretory product of the thyroid gland but has relatively low receptor affinity. The active hormone at the nuclear receptor level is T3 (triiodothyronine). Regarding the relationship between T4 and T3, which is correct?

(A) T4 is a prohormone; peripheral conversion by deiodinases (D1 in liver/kidney, D2 in brain/pituitary) produces T3 (3-5$\times$ more potent); D3 produces inactive reverse T3 (rT3)

(B) T3 is synthesised directly by the thyroid gland and is the sole circulating thyroid hormone

(C) rT3 (reverse T3) is the most biologically active thyroid hormone at the nuclear receptor

(D) T4 and T3 have identical receptor affinities but T4 has a shorter half-life

Q35. In the acute phase response triggered by infection or tissue injury, the liver reprioritises its protein synthesis. Which of the following plasma proteins is a **negative acute phase reactant** that **decreases** during the acute phase response?

(A) C-reactive protein (CRP) – a positive acute phase protein that rises $>$1000-fold

(B) Albumin – a negative acute phase protein whose synthesis is down-regulated (IL-1, IL-6, TNF-α mediated)

(C) Fibrinogen – a positive acute phase protein; elevated ESR reflects hyperfibrinogenaemia

(D) Serum amyloid A (SAA) – a positive acute phase protein; precursor of AA amyloid

Q36. Alpha-linolenic acid (ALA, 18:3 ω-3) is an essential fatty acid obtained from plant sources (flaxseed, chia). Its conversion to the long-chain ω-3 fatty acids EPA and DHA in the human body occurs by which process?

(A) ALA is directly activated to EPA by thiokinase without any elongation or desaturation

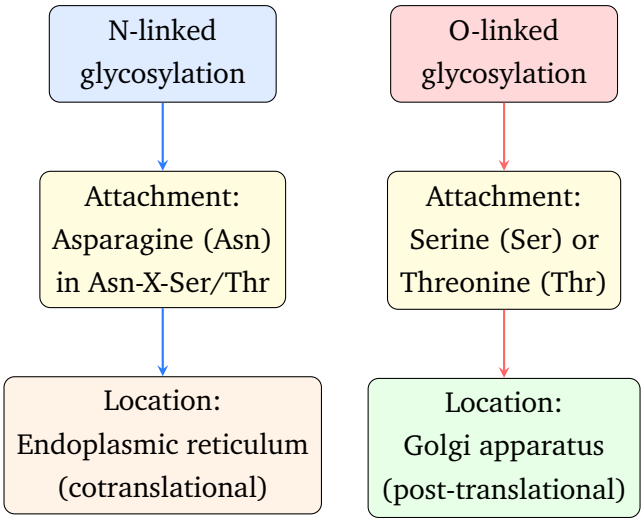
(B) ALA undergoes β-oxidation to release two-carbon units that are re-assembled into EPA by fatty acid synthase

(C) ALA undergoes sequential elongation (by elongases) and desaturation (by Δ5- and Δ6-desaturases, with Δ6-desaturase as the rate-

limiting step) to form EPA (20:5ω-3) and DHA (22:6ω-3); conversion is inefficient ($<$10%) in humans

(D) EPA and DHA cannot be synthesised from ALA; they must all come directly from the diet

Q37. Glycoproteins are proteins with covalently attached oligosaccharide chains. Regarding N-linked glycosylation versus O-linked glycosylation, which statement is correct?



(A) N-linked glycosylation occurs on serine residues in the Golgi apparatus; O-linked occurs on asparagine in the ER

(B) Both N-linked and O-linked glycosylation occur exclusively in the endoplasmic reticulum

(C) N-linked glycosylation occurs on asparagine (in Asn-X-Ser/Thr sequon) in the ER; O-linked glycosylation occurs on serine or threonine, predominantly in the Golgi

(D) N-linked glycosylation is initiated by transfer of GlcNAc from UDP-GlcNAc directly to the polypeptide in the cytoplasm

Q38. In the liver, primary bile acids (cholic acid and chenodeoxycholic acid) undergo conjugation before secretion into bile. This conjugation improves their properties as detergents. Which of the following correctly describes bile acid conjugation?

(A) Primary bile acids are conjugated with cholesterol to form bile salts in the mitochondria

(B) Primary bile acids are conjugated in hepatocytes with glycine or taurine, lowering their pKa so they remain ionised at intestinal pH, improving micelle formation and preventing passive reabsorption in the small intestine

(C) Conjugation of bile acids is performed by gut bacteria to convert primary into secondary bile acids

(D) Bile acid conjugation increases their pKa, making them uncharged and more lipid-soluble for passive absorption

Q39. A 55-year-old patient is given diisopropylfluorophosphate (DFP), an organophosphate compound, as part of a research study. DFP covalently phosphorylates the active-site serine of acetylcholinesterase. This illustrates which type of enzyme inhibition?

(A) Competitive inhibition – can be overcome by adding excess acetylcholine

(B) Uncompetitive inhibition – binds only the enzyme-substrate complex

(C) Non-competitive inhibition – binds allosteric site, unchanged K_m

(D) Irreversible (suicide) inhibition – covalent modification of active site; activity not restored by substrate addition or dialysis

Q40. Calcitriol (1,25-dihydroxyvitamin D_3), the active form of vitamin D, exerts its effects by binding to the vitamin D receptor (VDR). Regarding the mechanism of VDR action, which of the following is correct?

(A) VDR is a G-protein-coupled receptor (GPCR) that activates adenylyl cyclase upon calcitriol binding

(B) Calcitriol binds the nuclear receptor VDR; VDR-RXR heterodimer binds vitamin D response elements (VDREs) in gene promoters, upregulating calbindin (intestinal Ca^{2+} absorption), TRPV6, and RANKL (bone remodelling)

(C) VDR functions as a tyrosine kinase receptor on the plasma membrane, phosphorylating intracellular targets upon calcitriol binding

(D) VDR is located exclusively in kidney cells and only regulates calcium reabsorption in the distal tubule

Detailed Solutions

Q1.

Solution

Concept – Methionine transsulfuration pathway: Methionine serves as the universal methyl donor (via SAM – S-adenosylmethionine) and also donates its sulfur atom to cysteine via the transsulfuration pathway. The pathway: Methionine $\rightarrow$ SAM (by MAT) $\rightarrow$ SAH after methyl donation $\rightarrow$ Homocysteine (by SAH hydrolase) $\rightarrow$ Cystathionine (by CBS, requires vitamin B6/PLP) $\rightarrow$ Cysteine + homoserine (by cystathionase, also B6-dependent). Thus methionine is the source of both the methyl groups (via SAM) AND the sulfur (via homocysteine) that ends up in cysteine.

Distractors: (A) is wrong – methionine donates sulfur as well as methyl groups. (B) is wrong – CBS converts homocysteine to cystathionine (not cystathionine to cysteine; that is cystathionase). (D) is wrong – SAH is not a methyl donor; SAM is the methyl donor; SAH is the product after methyl transfer and it inhibits methyltransferases.

Final Answer: Methionine donates both methyl groups (via SAM) and sulfur (via homocysteine) to cysteine. $\Rightarrow \boxed{C}$

Answer: (C) Go Back to Q1

Q2.

Solution

Concept – Sigmoidal kinetics and cooperativity: Standard Michaelis-Menten enzymes (with a single active site, no cooperativity) display a hyperbolic v vs $[S]$ curve. A sigmoidal curve indicates cooperative binding – each substrate molecule bound increases the affinity of the remaining sites (positive cooperativity). This is characterised by a Hill coefficient $n > 1$. **PFK-1** is an allosteric, cooperative enzyme that shows sigmoidal kinetics with respect to its substrate fructose-6-phosphate; it also responds cooperatively to its allosteric activators (AMP, ADP, F-2,6-BP) and inhibitors (ATP, citrate).

Distractors: (A) LDH, (B) hexokinase, and (C) alkaline phosphatase are all single-site Michaelis-Menten enzymes displaying hyperbolic kinetics.

Final Answer: PFK-1 (allosteric cooperative enzyme, sigmoidal kinetics). $\Rightarrow \boxed{D}$

Answer: (D) Go Back to Q2

Q3.

Solution

Concept – Sanfilippo syndrome (MPS III): Sanfilippo syndrome is characterised by accumulation of **heparan sulfate** due to deficiency of one of four enzymes involved in its degradation. Type A (heparan-N-sulfatase), type B (α-N-acetylglucosaminidase), type C (acetyl-CoA:α-glucosaminide acetyltransferase), type D (N-acetylglucosamine-6-sulfatase). Clinically, MPS III presents with **severe intellectual disability and behavioural disturbances** (hyperactivity, aggression, sleep disturbances) but relatively mild somatic features – distinguishing it from MPS I (Hurler) and MPS II (Hunter) which have severe somatic and skeletal involvement.

Distractors: (A) MPS I (Hurler) – α-L-iduronidase deficiency, dermatan + heparan sulfate, gargoylism. (B) MPS II (Hunter) – iduronate-2-sulfatase, X-linked, dermatan + heparan sulfate. (C) MPS VI (Maroteaux-Lamy) – dermatan sulfate, N-acetylgalactosamine-4-sulfatase.

Final Answer: MPS III (Sanfilippo syndrome type A) – heparan-N-sulfatase deficiency. $\Rightarrow \boxed{D}$

Answer: (D) Go Back to Q3

Q4.

Solution

Concept – 2,3-BPG and Rapoport-Luebering shunt: 2,3-Bisphosphoglycerate (2,3-BPG) is unique to red blood cells. It is synthesised from 1,3-BPG by bisphosphoglycerate mutase (Rapoport-Luebering shunt), bypassing the phosphoglycerate kinase (PGK) step – **losing** one ATP per shunt activation. 2,3-BPG binds to the central cavity of **deoxyhaemoglobin** (T-state) between the β-chains through electrostatic interactions. This stabilises the T-state, lowers O_2 affinity, and **right-shifts** the O_2-dissociation curve, facilitating O_2 delivery to tissues. Increased at high altitude, in anaemia, and in chronic hypoxia.

Distractors: (A) Wrong – 2,3-BPG binds deoxy-Hb (T-state), not oxy-Hb. (C) Wrong – the shunt *bypasses* PGK and therefore sacrifices, not gains, ATP. (D) Wrong – 2,3-BPG binds β-chains (not α-chains) and causes a right-shift.

Final Answer: 2,3-BPG binds deoxyhaemoglobin (T-state) between β-chains, stabilises it, and facilitates O_2 delivery. $\Rightarrow \boxed{B}$

Answer: (B) Go Back to Q4

Q5.

Solution

Concept – Pantothenic acid (Vitamin B5) and its metabolic roles: Pantothenic acid (B5) is an essential constituent of **Coenzyme A (CoA)** and **acyl carrier protein (ACP)** – the two critical cofactors for fatty acid oxidation (β-oxidation uses CoA), fatty acid synthesis (ACP in FAS complex), and the TCA cycle (succinyl-CoA, acetyl-CoA). Deficiency causes "burning feet syndrome" (dysaesthesia of the lower extremities). True isolated B5 deficiency is extremely rare because it is widely distributed in foods.

Distractors: (A) NAD^+ and FAD are from niacin (B3) and riboflavin (B2) respectively. (B) TPP comes from thiamine (B1); PLP from pyridoxine (B6). (C) THF is derived from folate (B9); biotin is a separate vitamin.

Final Answer: Coenzyme A (CoA) and acyl carrier protein (ACP). $\Rightarrow \boxed{D}$

Answer: (D) Go Back to Q5

Q6.

Solution

Concept – Arginase deficiency (Hyperargininaemia): Arginase catalyses the final step of the urea cycle (arginine $\rightarrow$ ornithine + urea). Deficiency leads to **accumulation of arginine** and its derivatives (agmatine, guanidino compounds). Unlike other urea cycle defects, hyperammonaemia is typically mild because some urea is still synthesised via alternative routes. The clinical picture is distinctive: **progressive spastic diplegia, intellectual disability, seizures, and growth retardation** – resembling cerebral palsy. Urine orotic acid may be normal or mildly elevated. Treatment: low-protein diet with reduced arginine.

Distractors: (A) OTC deficiency causes hyperammonaemia + elevated urine orotic acid; it is X-linked. (B) ASS deficiency (citrullinaemia type I) causes elevated citrulline. (D) CPS-I deficiency presents with severe neonatal hyperammonaemia and LOW orotic acid.

Final Answer: Arginase deficiency (hyperargininaemia). $\Rightarrow \boxed{C}$

Answer: (C) Go Back to Q6

Q7.

Solution

Concept – Peptidyl transferase is a ribozyme: Peptide bond formation is catalysed by the peptidyl transferase centre of the large ribosomal subunit. Crucially,

the catalytic activity is intrinsic to the **rRNA** of the large subunit – it is a **ribozyme**. In eukaryotes, the large subunit is **60S** and contains **28S rRNA** (equivalent of prokaryotic 23S rRNA) that harbours the peptidyl transferase activity. This means rRNA, not ribosomal protein, is the enzyme. This discovery was fundamental in establishing RNA as a catalytic molecule.

Distractors: (A) The 40S small subunit (18S rRNA) is responsible for decoding (mRNA binding, anticodon recognition), not peptidyl transfer. (B) eEF-2 mediates translocation, not peptide bond formation. (D) The peptidyl-tRNA at the P site is the substrate, not the catalyst.

Final Answer: 28S rRNA of the 60S large ribosomal subunit (ribozyme activity). $\Rightarrow \boxed{C}$

Answer: (C) Go Back to Q7

Q8.

Solution

Concept – MCADD (Medium-Chain Acyl-CoA Dehydrogenase Deficiency): MCADD is the **most common fatty acid oxidation disorder** (incidence 1:10,000-15,000). Medium-chain fatty acids (C6-C12) cannot be oxidised. During fasting, when glucose stores are depleted, the inability to oxidise fatty acids leads to: (i) **hypoglycaemia** (no gluconeogenic substrates from β-oxidation) AND (ii) **paradoxically low ketones** (hypoketosis – because medium-chain fats are not oxidised to acetyl-CoA for ketogenesis). Diagnosis: elevated **C8-acylcarnitine (octanoylcarnitine)** on tandem mass spectrometry newborn screen. Sudden infant death is a well-recognised presentation.

Distractors: (B) VLCADD shows elevated C14:1 acylcarnitine. (C) Primary carnitine deficiency shows low total carnitine with low acylcarnitine. (D) Von Gierke disease presents with hypoglycaemia but elevated, not low, lactate, and without elevated acylcarnitines.

Final Answer: MCADD (medium-chain acyl-CoA dehydrogenase deficiency). $\Rightarrow \boxed{A}$

Answer: (A) Go Back to Q8

Q9.

Solution

Concept – Substrate-level phosphorylation in the TCA cycle: The TCA cycle produces energy carriers (3 NADH, 1 $FADH_2$, 1 GTP) per turn. The **only substrate-**

level phosphorylation step is catalysed by **succinyl-CoA synthetase** (also called succinate thiokinase): succinyl-CoA + GDP (or ADP) + Pi $\rightarrow$ succinate + GTP (or ATP) + CoA-SH. This reaction couples the energy of the thioester bond in succinyl-CoA directly to nucleoside diphosphate phosphorylation without the involvement of the ETC or ATP synthase. The three dehydrogenase steps (isocitrate DH, α-KG DH, malate DH) produce NADH and succinate DH produces $FADH_2$ – all fed into the ETC (oxidative phosphorylation).

Distractors: (B), (C), and (D) are all oxidative reactions producing NADH or $FADH_2$; they are NOT substrate-level phosphorylation steps.

Final Answer: Succinyl-CoA synthetase – the only substrate-level phosphorylation in the TCA cycle. $\Rightarrow \boxed{A}$

Answer: (A) Go Back to Q9

Q10.

Solution

Concept – Respiratory Quotient (RQ) and fuel utilisation: RQ = VCO_2/VO_2 (volume CO_2 produced / volume O_2 consumed). For glucose ($C_6H_{12}O_6 + 6O_2 \rightarrow 6CO_2 + 6H_2O$): RQ = 6/6 = **1.0**. For fat (palmitic acid, $C_{16}H_{32}O_2 + 23O_2 \rightarrow 16CO_2 + 16H_2O$): RQ = 16/23 = **0.7**. For protein: RQ $\approx$ **0.8** (estimated). Mixed diet RQ $\approx$ 0.85. RQ $>$ 1.0 indicates active lipogenesis from carbohydrate (excess CHO converted to fat, producing more CO_2 than O_2 consumed). Used in ICU nutrition assessment and indirect calorimetry.

Distractors: (A) Fat has RQ = 0.7. (B) Protein has RQ $\approx$ 0.8. (D) Mixed diet RQ is 0.85, not 1.0.

Final Answer: Carbohydrate (RQ = 1.0). $\Rightarrow \boxed{C}$

Answer: (C) Go Back to Q10

Q11.

Solution

Concept – Methaemoglobinaemia treatment: In methaemoglobinaemia, haem iron is oxidised from Fe^{2+} (ferrous) $\rightarrow$ Fe^{3+} (ferric), which cannot bind O_2. Causes: nitrites (amyl/sodium nitrite, well-water), dapsone, benzocaine, aniline dyes. The normal pathway of MetHb reduction uses NADH-cytochrome b5 reductase (cytochrome b5 reductase). Treatment: **methylene blue** – it is reduced to leucomethylene blue by NADPH (provided by G6PD in the HMP shunt), and leucomethylene blue then reduces Fe^{3+} back to Fe^{2+}. If G6PD-deficient, methylene

blue is ineffective and ascorbic acid may be used as an alternative.

Distractors: (A) Hydroxyurea is used in sickle cell disease. (B) Supplemental O_2 alone is insufficient for significant MetHb. (C) Deferoxamine chelates iron in haemochromatosis, not MetHb.

Final Answer: Methylene blue (requires NADPH from G6PD). $\Rightarrow \boxed{D}$

Answer: (D) Go Back to Q11

Q12.

Solution

Concept – Phospholipase C-β and the phosphoinositide signalling pathway: Receptors coupled to Gq protein (e.g., α_1-adrenergic, M1/M3-muscarinic, angiotensin II AT1, H1-histamine) activate **phospholipase C-β (PLC-β)**, which cleaves **PIP2** (phosphatidylinositol-4,5-bisphosphate) into two second messengers: (i) **IP3** (inositol-1,4,5-trisphosphate) – diffuses to ER and triggers Ca^{2+} release; (ii) **DAG** (diacylglycerol) – remains in the membrane and activates protein kinase C (PKC). This dual second messenger system mediates smooth muscle contraction, glandular secretion, and glycogenolysis.

Distractors: (A) PLA_2 releases arachidonic acid from membrane phospholipids; not the primary pathway here. (B) PLD generates phosphatidic acid (PA); not involved in α_1 signalling. (D) Adenylyl cyclase generates cAMP via G_s (β-adrenergic), not Gq/α_1.

Final Answer: Phospholipase C-β (PLC-β), activated by Gq protein. $\Rightarrow \boxed{C}$

Answer: (C) Go Back to Q12

Q13.

Solution

Concept – Types of gene mutations: A **missense mutation** changes a single nucleotide such that the codon now encodes a different amino acid. In sickle cell disease, GAG (glutamic acid, codon 6) $\rightarrow$ GTG (valine): the protein sequence is altered, changing the properties of haemoglobin and causing sickling under deoxygenation. A silent (synonymous) mutation changes a codon but the same amino acid is encoded (wobble position). A nonsense mutation creates a premature stop codon. A frameshift arises from insertions/deletions not in multiples of three, altering all downstream codons.

Distractors: (A) Silent mutation: same amino acid retained. (B) Nonsense: stop codon. (C) Frameshift: insertion/deletion. The key here is that the valine substi-

tution for glutamate is the classic example of a **missense** mutation.

Final Answer: Missense mutation – different amino acid substituted. $\Rightarrow \boxed{D}$

Answer: (D) Go Back to Q13

Q14.

Solution

Concept – ATP-citrate lyase and cytoplasmic lipogenesis: In the well-fed state, excess mitochondrial acetyl-CoA combines with oxaloacetate (via citrate synthase) to form citrate. Citrate is exported from the mitochondria to the cytoplasm via the tricarboxylate transport system (citrate carrier). In the cytoplasm, **ATP-citrate lyase (ACL)** cleaves citrate back into acetyl-CoA + OAA, using ATP and CoA. Cytoplasmic acetyl-CoA is the substrate for (i) fatty acid synthesis (via ACC $\rightarrow$ malonyl-CoA $\rightarrow$ FAS) and (ii) cholesterol synthesis (via HMG-CoA synthase $\rightarrow$ HMG-CoA $\rightarrow$ mevalonate).

Distractors: (B) Citrate synthase is the TCA enzyme that makes citrate from acetyl-CoA + OAA. (C) Aconitase converts citrate to isocitrate. (D) Isocitrate dehydrogenase decarboxylates isocitrate to α-ketoglutarate.

Final Answer: ATP-citrate lyase (ACL). $\Rightarrow \boxed{A}$

Answer: (A) Go Back to Q14

Q15.

Solution

Concept – Metachromatic Leukodystrophy (MLD): MLD is caused by deficiency of **arylsulphatase A (cerebroside sulphatase)**, which normally degrades **sulphatide** (3-sulphogalactocerebrosidase) in myelin sheaths. Sulphatide accumulation causes progressive demyelination in the CNS and PNS. The term "metachromatic" refers to the granules in urine sediment and nerve biopsy that stain red-brown (rather than blue) with cresyl violet dye (metachromasia). Late-infantile form (most common): onset 1-2 years, motor regression, then intellectual decline. Allogeneic HSCT can halt progression in pre-symptomatic patients.

Distractors: (A) Krabbe: galactocerebrosidase deficiency, globoid cells. (C) ALD: ABCD1 mutation, very-long-chain fatty acid accumulation, X-linked. (D) Fabry: α-galactosidase A, globotriaosylceramide accumulation, X-linked, renal/cardiac/skin features.

Final Answer: Metachromatic leukodystrophy (MLD) – arylsulphatase A deficiency. $\Rightarrow \boxed{B}$

Answer: (B) Go Back to Q15

Q16.

Solution

Concept – ApoC-II as obligatory LPL activator: Lipoprotein lipase (LPL), located on the luminal surface of capillary endothelium in adipose, muscle, and heart, hydrolyses triglycerides from chylomicrons and VLDL into free fatty acids (taken up by tissues) and glycerol. **ApoC-II** is the obligatory activator of LPL – without it, LPL is essentially inactive. Familial ApoC-II deficiency presents identically to LPL deficiency: severe hyperchylomicronaemia (type I), massive hypertriglyceridaemia, eruptive xanthomas, pancreatitis. Note: ApoC-III *inhibits* LPL; ApoA-V activates LPL.

Distractors: (B) Wrong – ApoC-II activates (not inhibits) LPL. (C) Wrong – ApoC-II is on chylomicrons/VLDL, not involved in VLDL assembly. (D) ApoE (not ApoC-II) is the ligand for LRP1 (chylomicron remnant receptor) on liver.

Final Answer: ApoC-II is the obligatory activator of LPL. $\Rightarrow \boxed{A}$

Answer: (A) Go Back to Q16

Q17.

Solution

Concept – Urea cycle compartmentalisation: The urea cycle spans two compartments. **Mitochondria:** (1) CPS-I (carbamoyl phosphate synthetase I) synthesises carbamoyl phosphate from NH_3 + CO_2 + 2ATP; (2) OTC (ornithine transcarbamylase) condenses carbamoyl phosphate + ornithine $\rightarrow$ citrulline. Citrulline is then exported to the cytosol. **Cytosol:** (3) ASS (argininosuccinate synthetase) links citrulline + aspartate $\rightarrow$ argininosuccinate; (4) ASL (argininosuccinate lyase) cleaves argininosuccinate $\rightarrow$ arginine + fumarate; (5) Arginase cleaves arginine $\rightarrow$ ornithine + urea. Ornithine is returned to the mitochondria.

Distractors: (A) Arginase is cytosolic. (C) CPS-I and OTC are mitochondrial. (D) Citrulline is made IN the mitochondria and exported to the cytosol.

Final Answer: CPS-I and OTC are mitochondrial; ASS, ASL, and arginase are cytosolic. $\Rightarrow \boxed{B}$

Answer: (B) Go Back to Q17

Q18.

Solution

Concept – Glucocorticoid receptor (GR) – nuclear receptor superfamily: Cortisol (and other glucocorticoids) is a lipophilic steroid that diffuses freely across the plasma membrane. In the cytoplasm it binds the **glucocorticoid receptor (GR)**, which is maintained in an inactive state by the chaperone **Hsp90**. Cortisol binding dissociates Hsp90, allowing GR homodimerisation and **nuclear translocation**. The GR dimer binds **glucocorticoid response elements (GREs)** in gene promoters to either activate (metabolic enzymes, anti-inflammatory molecules) or repress (inflammatory cytokines, CRH, ACTH) gene transcription. This is the genomic (slow) mechanism; non-genomic (rapid) effects also exist.

Distractors: (A) GPCR/cAMP mechanism is used by glucagon, adrenaline (β), PTH. (B) Tyrosine kinase receptor is used by insulin, growth hormone, IGF-1. (C) Ligand-gated ion channels are used by fast neurotransmitters (GABA, acetylcholine nicotinic, glutamate).

Final Answer: Cortisol diffuses into cell, binds cytoplasmic GR, dissociates from Hsp90, translocates to nucleus, binds GREs. $\Rightarrow \boxed{D}$

Answer: (D) Go Back to Q18

Q19.

Solution

Concept – PCNA (Proliferating Cell Nuclear Antigen) – the eukaryotic sliding clamp: PCNA is a **homotrimeric ring** that encircles double-stranded DNA. It is loaded onto DNA at the primer-template junction by **RFC (replication factor C)**, which is the clamp loader (ATPase). Once loaded, PCNA tethers **DNA polymerase** δ (lagging strand synthesis) and **DNA polymerase** ε (leading strand) to the template, dramatically increasing processivity (the enzyme can synthesise thousands of bases without dissociating). PCNA is also a key scaffold in DNA repair (NER, MMR, BER) and cell cycle regulation (p21 binds PCNA to inhibit CDK activity).

Distractors: (A) RPA (replication protein A) is the eukaryotic SSB that stabilises ssDNA. (C) RFC is the clamp loader, not the clamp itself. (D) Topoisomerase I relieves torsional strain but is not the sliding clamp.

Final Answer: PCNA (proliferating cell nuclear antigen) – trimeric sliding clamp loaded by RFC. $\Rightarrow \boxed{B}$

Answer: (B) Go Back to Q19

Q20.

Solution

Concept – Transamination and non-essential amino acid synthesis: Transamination reactions are catalysed by aminotransferases (also called transaminases) and require pyridoxal phosphate (PLP/B6) as cofactor. The general reaction: amino acid + α-keto acid $\leftrightarrow$ new α-keto acid + new amino acid. **Alanine aminotransferase (ALT/GPT):** glutamate + **pyruvate** $\leftrightarrow$ **alanine** + α-ketoglutarate. This reaction is central to the glucose-alanine cycle (Cahill cycle): muscles export amino groups as alanine to the liver, where ALT regenerates pyruvate for gluconeogenesis. Oxaloacetate $\rightarrow$ aspartate (via AST/GOT). α-Ketoglutarate $\rightarrow$ glutamate (reductive amination by GDH, not transamination).

Distractors: (B) Oxaloacetate + glutamate $\rightarrow$ aspartate (catalysed by AST). (C) α-Ketoglutarate $\rightarrow$ glutamate via GDH (not ALT). (D) Succinyl-CoA is a TCA cycle intermediate used in porphyrin synthesis, not direct transamination to an amino acid.

Final Answer: Pyruvate (accepts amino group from glutamate $\rightarrow$ alanine + α-ketoglutarate). $\Rightarrow \boxed{A}$

Answer: (A) Go Back to Q20

Q21.

Solution

Concept – Vitamin C and non-haem iron absorption: Dietary iron exists as haem iron (from meat, highly bioavailable $\sim$25%) and non-haem iron (from plants, bioavailability 1-10%). Non-haem iron must be in the **ferrous (Fe^{2+}) form** to be transported across the enterocyte brush border by **DMT1 (divalent metal transporter 1)**. Dietary non-haem iron is predominantly in the **ferric (Fe^{3+})** form. **Ascorbic acid (vitamin C)** in the intestinal lumen **reduces Fe^{3+} $\rightarrow$ Fe^{2+}** AND chelates iron to keep it soluble at the alkaline intestinal pH, markedly enhancing absorption. This is why orange juice with iron supplements significantly improves absorption.

Distractors: (B) Haem oxygenase acts on haem (intracellular), not dietary non-haem iron. (C) Transferrin is a plasma transport protein; it does not interact with ascorbic acid at the intestinal level. (D) Hepcidin regulation by vitamin C has some evidence but is not the primary established mechanism.

Final Answer: Ascorbic acid reduces dietary non-haem iron from Fe^{3+} to Fe^{2+}, absorbed by DMT1. $\Rightarrow \boxed{A}$

Answer: (A) Go Back to Q21

Q22.

Solution

Concept – Tay-Sachs disease and GM2 ganglioside accumulation: Tay-Sachs disease is an autosomal recessive lysosomal storage disorder caused by deficiency of **hexosaminidase A** (α-subunit, HexA). HexA normally degrades **GM2 ganglioside** in neurons. Without HexA, GM2 accumulates within lysosomes of neurons, causing progressive neurodegeneration. Gangliosides are complex glycosphingolipids containing ceramide, oligosaccharides, and one or more sialic acid (NANA) residues. They are particularly abundant in the grey matter of the brain. The cherry-red spot on fundoscopy reflects normal foveal colour against a whitish ganglioside-engorged macula.

Distractors: (A) Glucocerebroside accumulates in Gaucher disease (glucocerebrosidase deficiency). (B) Sphingomyelin accumulates in Niemann-Pick disease A/B (sphingomyelinase deficiency). (C) Galactocerebrosidase is an enzyme (galactocerebrosidase deficiency causes Krabbe disease); galactocerebroside/psychosine accumulates.

Final Answer: GM2 ganglioside accumulates in Tay-Sachs disease. $\Rightarrow \boxed{D}$

Answer: (D) Go Back to Q22

Q23.

Solution

Concept – Proline as an imino acid and helix breaker: Proline is the only amino acid in which the side chain is cyclically bonded to the backbone nitrogen, forming a **pyrrolidine ring**. This: (i) makes the nitrogen a secondary amine (imino acid) with no N-H bond to donate hydrogen bonds; (ii) severely restricts the ϕ dihedral angle of the backbone; (iii) introduces a rigid **kink** in the peptide chain. Therefore proline **disrupts α-helices** (cannot fit into the regular hydrogen-bonding pattern). In collagen, proline is abundant (Gly-X-Y repeat; X is often Pro, Y often 4-hydroxyproline) and contributes to the rigid, kinked structure of each α-chain that forms the triple helix.

Distractors: (B) Disulfide bridges are formed by cysteine. (C) Positively charged amino acids at pH 7 are lysine, arginine, histidine – not proline (it is uncharged). (D) All amino acids react with DNP-Cl via their α-amino group; proline does so but is not the "only" such amino acid.

Final Answer: Proline is an α-helix breaker, introduces rigid kink; abundant in collagen. $\Rightarrow \boxed{A}$

Answer: (A) Go Back to Q23

Q24.

Solution

Concept – Nucleoside vs nucleotide: A **nucleoside** = nitrogenous base (purine or pyrimidine) + pentose sugar (ribose or deoxyribose), linked by an N-glycosidic bond. A **nucleotide** = nucleoside + **one or more phosphate groups** (monophosphate NMP, diphosphate NDP, or triphosphate NTP) esterified at the 5'-OH of the sugar. Examples: adenosine (nucleoside) vs AMP/ADP/ATP (nucleotides); deoxyguanosine (nucleoside) vs dGMP/dGDP/dGTP (nucleotides). Nucleotides serve as: energy currency (ATP), signalling molecules (cAMP, cGMP), enzyme cofactors (NAD^+, FAD, CoA), and building blocks for DNA and RNA.

Distractors: (B) Describes a nucleoside, not a nucleotide. (C) Limits to purine + deoxyribose only; nucleotides include pyrimidine bases and ribose as well. (D) Too narrow (only adenine-ribose).

Final Answer: Nucleotide = nitrogenous base + pentose sugar + one or more phosphate groups. $\Rightarrow \boxed{A}$

Answer: (A) Go Back to Q24

Q25.

Solution

Concept – Common feature of lysosomal storage diseases: All lysosomal storage diseases share the **same fundamental mechanism**: deficiency of a **lysosomal hydrolase** (acid hydrolase, optimal activity at pH 4.5-5.0 within lysosomes) causes the enzyme's specific substrate to accumulate within lysosomes. The engorged lysosomes progressively disrupt cell function, especially in cells with high turnover of complex macromolecules (neurons, macrophages). Most are autosomal recessive (exception: Fabry, Hunter – X-linked). Diagnosis via enzyme assay in leucocytes/fibroblasts, or urine metabolite analysis. Some (Gaucher, Fabry, Pompe) are amenable to enzyme replacement therapy (ERT).

Distractors: (A) Mitochondrial membrane transport defects are the basis of disorders like carnitine deficiency, not LSDs. (C) Only Fabry and Hunter are X-linked; most LSDs are autosomal recessive. (D) Neonatal hyperammonaemia is characteristic of urea cycle defects, not LSDs.

Final Answer: All LSDs result from lysosomal hydrolase deficiency causing intralysosomal substrate accumulation. $\Rightarrow \boxed{B}$

Answer: (B) Go Back to Q25

Q26.

Solution

Concept – Homocysteine and cardiovascular risk: Elevated plasma homocysteine (>15 μmol/L = hyperhomocysteinaemia) is an independent risk factor for atherosclerosis and thromboembolism via multiple mechanisms: (i) **endothelial damage**: homocysteine is directly toxic to vascular endothelium (oxidative stress, impairs eNOS, reduces NO bioavailability); (ii) **prothrombotic effects**: activates platelets, increases tissue factor expression, inhibits thrombomodulin; (iii) **LDL oxidation**: promotes oxidative modification of LDL $\rightarrow$ foam cell formation. Causes of elevated Hcy: B12/B6/folate deficiency (most common), CBS deficiency, MTHFR C677T polymorphism, renal failure, hypothyroidism.

Distractors: (A) Homocysteine does not activate complement. (B) Fibrin is formed from fibrinogen by thrombin; Hcy does not directly polymerise. (D) Hcy does reduce eNOS activity but through oxidative stress mechanisms, not direct arginine competition.

Final Answer: Homocysteine causes endothelial damage, promotes LDL oxidation, and has prothrombotic effects. $\Rightarrow \boxed{C}$

Answer: (C) Go Back to Q26

Q27.

Solution

Concept – Western blot technique: The **Western blot** (immunoblot) is a technique to detect specific **proteins** in a sample. Steps: (1) proteins separated by **SDS-PAGE** (sodium dodecyl sulphate-polyacrylamide gel electrophoresis) by molecular weight; (2) transferred (blotted) from gel onto **nitrocellulose or PVDF membrane**; (3) membrane blocked to prevent non-specific binding; (4) incubated with **primary antibody** (specific to target protein), then **secondary antibody** (enzyme-conjugated); (5) detected by **ECL (enhanced chemiluminescence)** or colorimetric reaction. Clinical use: HIV confirmation (detects anti-gp120/gp41 antibodies in patient serum), Lyme disease confirmation, Creutzfeldt-Jakob disease (PrP^{Sc} detection).

Distractors: (A) Southern blot detects *DNA*; Northern blot detects *RNA*; Western blot detects proteins. (B) SDS-PAGE separates by size (under denaturing conditions), not by charge under native conditions. (D) Northern blot detects RNA using probes (not antibodies).

Final Answer: Western blot: SDS-PAGE $\rightarrow$ membrane transfer $\rightarrow$ antibody detection (ECL). $\Rightarrow \boxed{C}$

Answer: (C) Go Back to Q27

Q28.

Solution

Concept – Chylomicron metabolism: Chylomicrons are the largest lipoprotein particles. They are assembled in intestinal **enterocytes** (contain ApoB-48, ApoA-I/IV) after dietary fat absorption. They enter the lymphatic system via the lacteals and travel through the thoracic duct to the **bloodstream**. In the capillaries of adipose, muscle, and heart tissue, **lipoprotein lipase (LPL)** – activated by **ApoC-II** (acquired from HDL in blood) – hydrolyses triglycerides, releasing fatty acids for tissue uptake. The resulting **chylomicron remnants** (enriched in ApoE, cholesterol) are taken up by the **liver** via the **LRP1 receptor** (low-density lipoprotein receptor-related protein 1), which recognises ApoE.

Distractors: (A) Chylomicrons enter *lymph* (not portal blood); only short/medium-chain FAs enter portal blood directly. (B) ApoB-48 is structural; ApoC-II activates LPL. (C) ApoE is the liver ligand; LRP1 is the receptor; chylomicron remnants go to the liver, not spleen.

Final Answer: Chylomicrons travel via lymph; LPL (activated by ApoC-II) hydrolyses TG; remnants taken up by liver LRP1 via ApoE. $\Rightarrow \boxed{D}$

Answer: (D) Go Back to Q28

Q29.

Solution

Concept – Protein C anticoagulant system: Protein C is a **vitamin K-dependent serine protease** synthesised by the liver. It is activated by the **thrombomodulin-thrombin complex** on the endothelial surface (thrombin switches from procoagulant to anticoagulant role when bound to thrombomodulin). **Activated protein C (APC)**, with its cofactor **protein S** (also vitamin K-dependent), **proteolytically inactivates Factor Va and Factor VIIIa**, inhibiting the coagulation cascade. **Factor V Leiden** (Arg506Gln mutation) is resistant to APC cleavage, the most common inherited thrombophilia.

Distractors: (A) Antithrombin III (ATIII) is a different anticoagulant (serine protease inhibitor, serpine); it inactivates thrombin and Xa. (B) Protein C INACTIVATES Va and VIIIa (anticoagulant), not activates them. (D) Protein S is the cofactor; thrombomodulin-thrombin activates protein C (not protein S).

Final Answer: APC + protein S inactivates factors Va and VIIIa; Factor V Leiden

is APC-resistant, causing thrombophilia. $\Rightarrow \boxed{C}$

Answer: (C) Go Back to Q29

Q30.

Solution

Concept – Complex II does not pump protons: The mitochondrial ETC consists of four complexes. Complexes I, III, and IV pump protons across the inner mitochondrial membrane, generating the proton motive force that drives ATP synthase (Complex V). **Complex II (succinate dehydrogenase)** is different: it accepts electrons from **$FADH_2$** (not NADH) and passes them **directly to ubiquinone (CoQ)** without any proton translocation. The thermodynamic reason: $FADH_2$ carries electrons at a higher energy potential than the threshold needed for proton pumping through Complex I; instead, these electrons bypass Complex I entirely and enter at CoQ. Therefore, $FADH_2$ yields fewer ATP than NADH per molecule (1.5 vs 2.5 by modern P/O ratios).

Distractors: (A) Complex II receives electrons from $FADH_2$ (not NADH). (B) Complex II is embedded in the *inner* mitochondrial membrane. (C) Complex II transfers electrons to ubiquinone (CoQ), not directly to cytochrome c.

Final Answer: Complex II passes electrons from $FADH_2$ directly to CoQ without proton translocation; $FADH_2$ yields 1.5 ATP vs NADH 2.5 ATP. $\Rightarrow \boxed{D}$

Answer: (D) Go Back to Q30

Q31.

Solution

Concept – Anomers of D-glucose and mutarotation: In aqueous solution, open-chain D-glucose cyclises to form the pyranose ring through attack of C5-OH on the C1 aldehyde. This creates a new chiral centre at C1 (the anomeric carbon). In **α-D-glucose**, the C1-OH is **axial** (below the ring in Haworth representation). In **β-D-glucose**, the C1-OH is **equatorial** (above the ring). At equilibrium in water: approximately **36%** α and **64%** β. **β-D-glucose predominates** because the equatorial OH at C1 is sterically less strained. The interconversion ($\alpha \leftrightarrow$ open chain $\leftrightarrow \beta$) is called **mutarotation** and is catalysed by mutarotase (aldose 1-epimerase).

Distractors: (A) α-glucose is the minority anomer (36%). (C) The equilibrium is 64:36 (β:α), not 50:50. (D) The open-chain (aldehyde) form is present in $<$0.1% at equilibrium in aqueous solution.

Final Answer: β-D-glucose predominates ($\sim$64%) – equatorial C1-OH is sterically

more stable. $\Rightarrow \boxed{B}$

Answer: (B) Go Back to Q31

Q32.

Solution

Concept – Bile salt micelles and fat absorption: Bile salts are amphipathic molecules (hydrophilic ionic head + hydrophobic steroid ring) synthesised in the liver from cholesterol. They are secreted into bile and enter the duodenum. In the small intestinal lumen, pancreatic lipase hydrolyses dietary triglycerides into **2-monoacylglycerols (2-MAG) and free fatty acids (FFAs)**. Bile salts then form **mixed micelles** (together with phospholipids, cholesterol, 2-MAG, and FFAs) – spherical aggregates with hydrophilic exterior and hydrophobic core. These micelles **solubilise the fat-digestion products** and shuttle them to the brush border of enterocytes for passive absorption. Fat-soluble vitamins A, D, E, K are also absorbed via micelles.

Distractors: (A) Pancreatic lipase (not bile salts) hydrolyses triglycerides. (C) Bile acids are synthesised de novo from cholesterol in the *liver*, not in the intestinal lumen. (D) Bile salts facilitate fat-soluble vitamin absorption (not prevent it).

Final Answer: Bile salts form mixed micelles that solubilise fat-digestion products for absorption by enterocytes. $\Rightarrow \boxed{B}$

Answer: (B) Go Back to Q32

Q33.

Solution

Concept – Dihydropteridine reductase (DHPR) deficiency – variant PKU: Phenylalanine hydroxylase (PAH) requires the cofactor **BH4 (tetrahydrobiopterin)**. During the reaction, BH4 is oxidised to **qBH2 (quinonoid dihydrobiopterin)**. **DHPR (dihydropteridine reductase)** regenerates BH4 from qBH2 using NADH. Crucially, BH4 is also the cofactor for **tyrosine hydroxylase (TH)** and **tryptophan hydroxylase (TPH)**, which synthesise DOPA (precursor of dopamine/noradrenaline) and 5-hydroxytryptophan (precursor of serotonin) respectively. DHPR deficiency causes hyperphenylalaninaemia PLUS **severely reduced neurotransmitters** (dopamine, serotonin), leading to a more severe neurological outcome than classic PKU if treated only with a phenylalanine-restricted diet.

Distractors: (B) GTP cyclohydrolase I is the first enzyme in de novo BH4 syn-

thesis; its deficiency causes Dopa-responsive dystonia (Segawa syndrome). (C) Sepiapterin reductase is in the BH4 salvage pathway. (D) PAH is the enzyme whose gene is mutated in classic PKU (question specifies PAH gene is normal in this variant).

Final Answer: Dihydropteridine reductase (DHPR) – regenerates BH4; deficiency also impairs TH and TPH causing low dopamine and serotonin. $\Rightarrow \boxed{A}$

Answer: (A) Go Back to Q33

Q34.

Solution

Concept – T4 as prohormone; T3 as active hormone: The thyroid gland secretes predominantly **T4** ($\sim$80%) and only 20% T3. T4 circulates bound to TBG (thyroxine-binding globulin), albumin, and transthyretin. In peripheral tissues, **deiodinases** convert T4 to T3 or rT3: **D1** (liver, kidney, thyroid): converts T4 $\rightarrow$ T3 (5'-deiodination, active) or T4 $\rightarrow$ rT3; **D2** (brain, pituitary, brown adipose tissue): converts T4 $\rightarrow$ T3 locally; **D3** (brain, placenta, liver): converts T4 $\rightarrow$ **rT3** (reverse T3, biologically inactive) and T3 $\rightarrow$ T2. T3 is **3-5$\times$ more potent** than T4 at the nuclear thyroid hormone receptor. In sick euthyroid syndrome: low T3, high rT3 (D3 preferentially active).

Distractors: (B) T3 is produced predominantly by peripheral conversion, not direct thyroid secretion. (C) rT3 is inactive. (D) T4 and T3 have very different receptor affinities; T4 half-life is longer (7 days vs 1 day for T3).

Final Answer: T4 is a prohormone; deiodinases produce active T3 or inactive rT3. $\Rightarrow \boxed{A}$

Answer: (A) Go Back to Q34

Q35.

Solution

Concept – Negative acute phase reactants: The acute phase response is triggered by pro-inflammatory cytokines (IL-1, IL-6, TNF-α) released during infection, trauma, or surgery. The liver redirects its synthetic capacity away from "housekeeping" proteins toward **positive acute phase proteins** (CRP, fibrinogen, SAA, haptoglobin, α_1-antitrypsin, ferritin, complement proteins). Simultaneously, synthesis of **negative acute phase proteins** decreases: **albumin**, transferrin, transthyretin (prealbumin), retinol-binding protein, and alpha-2-HS glycoprotein. Decreased albumin in acute illness leads to oedema and affects drug

binding. Decreased transthyretin/prealbumin is a sensitive marker of nutritional status and acute illness.

Distractors: (A) CRP is the quintessential positive APP (>1000-fold rise). (C) Fibrinogen is a positive APP (elevated ESR results from hyperfibrinogenaemia). (D) SAA (serum amyloid A) is a positive APP; chronic elevation leads to AA amyloidosis.

Final Answer: Albumin is a negative acute phase protein whose synthesis decreases during the acute phase response. $\Rightarrow \boxed{B}$

Answer: (B) Go Back to Q35

Q36.

Solution

Concept – ALA conversion to EPA and DHA (elongation and desaturation): ALA (18:3 ω-3) is an essential ω-3 fatty acid. Humans can convert ALA to longer-chain ω-3 fatty acids by alternating **desaturation** (by Δ6-desaturase = rate-limiting, Δ5-desaturase) and **elongation** (by elongases ELOVL2, ELOVL5) in the ER, plus one cycle of peroxisomal β-oxidation (for DHA). The pathway: ALA (18:3ω-3) $\xrightarrow{\Delta 6\text{-des}}$ 18:4ω-3 $\xrightarrow{\text{elong}}$ 20:4ω-3 $\xrightarrow{\Delta 5\text{-des}}$ **EPA** (20:5ω-3) $\xrightarrow{\text{elong}}$ 22:5ω-3 $\xrightarrow{\text{elong},\Delta 6\text{-des}}$ 24:5 $\xrightarrow{\text{perox}}$ **DHA** (22:6ω-3). This conversion is very inefficient (<10%) in humans; direct dietary EPA/DHA (oily fish) is more effective.

Distractors: (A) Thiokinase (acyl-CoA synthetase) only activates ALA; it does not elongate it. (B) β-Oxidation degrades fatty acids; fatty acid synthase makes saturated C16/C18 from scratch, not unsaturated long-chain. (D) While inefficient, some conversion does occur in humans.

Final Answer: ALA $\rightarrow$ EPA and DHA via elongation and desaturation (Δ6-desaturase rate-limiting); conversion <10%. $\Rightarrow \boxed{C}$

Answer: (C) Go Back to Q36

Q37.

Solution

Concept – N-linked vs O-linked glycosylation: N-linked glycosylation: Occurs *co-translationally* in the **endoplasmic reticulum**. A 14-sugar oligosaccharide ($Glc_3Man_9GlcNAc_2$) is transferred from dolichol-PP (a lipid carrier in the ER membrane) to the **asparagine** (Asn) residue in the consensus sequence **Asn-X-Ser/Thr** (where X is any amino acid except Pro). Subsequent trimming and processing occur in the ER and Golgi. **O-linked glycosylation:** Occurs post-translationally,

mainly in the **Golgi apparatus**. Sugars are added one at a time (no dolichol-PP intermediate) to the hydroxyl of **serine or threonine** residues. No strict consensus sequence. Mucins are heavily O-glycosylated (sialomucins). Cytoplasmic O-GlcNAc modification on Ser/Thr is distinct and occurs in the cytoplasm.

Distractors: (A) Reverses the location/residue assignments. (B) O-linked occurs in the Golgi, not the ER. (D) N-linked uses the dolichol-PP intermediate, not direct transfer from UDP-GlcNAc in the cytoplasm.

Final Answer: N-linked on Asn (Asn-X-Ser/Thr) in ER; O-linked on Ser/Thr predominantly in Golgi. $\Rightarrow \boxed{C}$

Answer: (C) Go Back to Q37

Q38.

Solution

Concept – Bile acid conjugation in the liver: Primary bile acids (cholic acid, chenodeoxycholic acid) synthesised from cholesterol in hepatocytes undergo conjugation with either **glycine** (to form glycocholic/glycochenodeoxycholic acid) or **taurine** (taurocholic/taurochenodeoxycholic acid). The conjugation reaction occurs via formation of an amide bond between the C24 carboxyl of the bile acid and the amino group of glycine or the sulphonate of taurine. Key consequences: (i) **lowers pKa** of the bile acid from $\sim$6 to $\sim$2 (glycine-conjugated) or 1 (taurine-conjugated); (ii) at intestinal pH 6-7, conjugated bile acids remain **ionised (charged)** and cannot be passively reabsorbed in the small intestine; (iii) they remain in the lumen to form micelles; (iv) they are actively reabsorbed in the terminal ileum (enterohepatic circulation). Bacteria in the colon deconjugate and convert them to secondary bile acids (deoxycholic, lithocholic).

Distractors: (A) Conjugation is with glycine or taurine (not cholesterol), and occurs in hepatocytes (not mitochondria). (C) Deconjugation by bacteria produces secondary bile acids; primary $\rightarrow$ secondary conversion is bacterial dehydroxylation. (D) Conjugation *lowers* (not increases) pKa, making bile salts more ionised at intestinal pH.

Final Answer: Primary bile acids conjugated with glycine or taurine in hepatocytes; lowered pKa keeps them ionised at intestinal pH, preventing passive absorption and improving micelle formation. $\Rightarrow \boxed{B}$

Answer: (B) Go Back to Q38

Q39.

Solution

Concept – Irreversible (covalent) enzyme inhibition: Irreversible inhibitors form covalent bonds with the enzyme, permanently modifying the active site. The enzyme activity is not restored by removing the inhibitor (dialysis), adding excess substrate, or any reversible means. New enzyme protein must be synthesised to restore activity. Examples: (i) **organophosphates** (DFP, sarin nerve agents, malathion insecticides) – covalently phosphorylate the active-site serine of acetylcholinesterase; (ii) **aspirin** – irreversibly acetylates the active-site serine of cyclooxygenase (COX-1 and COX-2); (iii) DFMO (difluoromethylornithine) – suicide inhibitor of ornithine decarboxylase. The clinical consequence of AChE inhibition: accumulation of acetylcholine $\rightarrow$ cholinergic crisis (SLUDGE: Salivation, Lacrimation, Urination, Defaecation, GI distress, Emesis + bradycardia, bronchospasm, miosis).

Distractors: (A) Competitive inhibition is reversible and overcome by excess substrate. (B) Uncompetitive inhibition binds enzyme-substrate complex (reversible). (C) Non-competitive inhibition binds allosteric site (reversible).

Final Answer: Irreversible (suicide) inhibition – covalent modification of active site; not reversed by substrate or dialysis. $\Rightarrow \boxed{D}$

Answer: (D) Go Back to Q39

Q40.

Solution

Concept – Vitamin D receptor (VDR) – nuclear receptor superfamily: The **vitamin D receptor (VDR)** belongs to the nuclear receptor superfamily (same family as steroid hormone receptors, thyroid hormone receptor, retinoic acid receptor). Calcitriol (1,25-dihydroxyvitamin D_3) is lipophilic and crosses the plasma membrane. It binds cytoplasmic/nuclear VDR $\rightarrow$ VDR heterodimerises with **RXR (retinoid X receptor)** $\rightarrow$ VDR:RXR dimer binds **VDREs (vitamin D response elements)** in gene promoters. Target genes include: **calbindin-D9k** (intestinal Ca^{2+} transport), **TRPV6** (apical Ca^{2+} channel in intestine), **RANKL** (bone remodelling), **CYP24A1** (25-OH-D catabolism, feedback). Non-genomic VDR actions also exist (rapid opening of Ca^{2+} channels).

Distractors: (A) GPCR-cAMP is the mechanism for PTH (which also regulates Ca^{2+}), not calcitriol. (C) Tyrosine kinase receptors are for peptide hormones (insulin, GH, EGF). (D) VDR is expressed ubiquitously (intestine, kidney, bone, immune cells, etc.), not exclusively in the kidney.

Final Answer: Calcitriol binds nuclear VDR; VDR-RXR heterodimer binds VDREs, upregulating calbindin, TRPV6, RANKL. $\Rightarrow \boxed{B}$

Answer: (B) Go Back to Q40

Answer Key – FMGE Biochemistry Sample Paper 8

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