FMGE Biochemistry Sample Paper – 3

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 24-year-old woman in her first trimester is found to be taking high-dose vitamin A supplements (50,000 IU/day) for acne. She is counselled about embryonic risks. Isotretinoin (a synthetic retinoid) is absolutely contraindicated in pregnancy because excess retinoic acid is a potent teratogen. Which of the following defects is most characteristically associated with retinoic acid embryopathy?

(A) Cleft palate and conotruncal cardiac defects (e.g., transposition of great arteries)

(B) Neural tube defects (spina bifida, anencephaly)

(C) Limb reduction deformities (phocomelia)

(D) Neonatal hypocalcaemia and seizures

Q2. An enzyme has a K_m of 0.1 mM for its substrate, while a second enzyme catalysing the same reaction has a K_m of 5 mM. At a physiological substrate concentration of 0.5 mM, which statement best describes the clinical implication?

(A) Both enzymes are equally saturated at physiological substrate concentration

(B) The first enzyme (lower K_m) has higher affinity and operates near saturation; the second enzyme is far from saturation

(C) The second enzyme (higher K_m) has higher affinity for the substrate

(D) K_m has no relationship to enzyme affinity at physiological concentrations

Q3. A 6-day-old neonate presents with vomiting, lethargy, metabolic acidosis, and hyperammonemia. Urine organic acid analysis reveals elevated propionic acid and 3-hydroxypropionate. Plasma glycine is elevated. The deficient enzyme is biotin-dependent and normally carboxylates propionyl-CoA. Which enzyme is deficient?

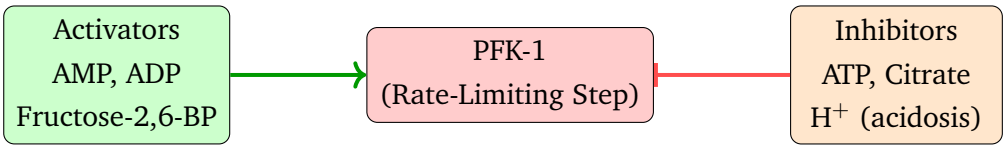
(A) Methylmalonyl-CoA mutase

(B) Propionyl-CoA carboxylase

(C) Pyruvate carboxylase

(D) Acetyl-CoA carboxylase

Q4. A biochemistry examination question depicts the regulation of phosphofructokinas 1 (PFK-1). The allosteric regulators shown below are tested. Which set of regulators correctly identifies the **activators** of PFK-1?



(A) AMP, ADP, and fructose-2,6-bisphosphate

(B) ATP, citrate, and H^+

(C) AMP and ATP equally activate PFK-1

(D) Glucagon activates PFK-1 directly

Q5. A patient with peripheral neuropathy, subacute combined degeneration of the spinal cord, and macrocytic anaemia has elevated urinary methyl-

malonic acid. Vitamin B12 is a required cofactor for which enzyme relevant to this elevated metabolite?

(A) Methionine synthase

(B) Thymidylate synthase

(C) Dihydrofolate reductase

(D) Methylmalonyl-CoA mutase

Q6. A 3-year-old child with a urea cycle disorder is started on sodium benzoate therapy. Sodium benzoate is used to treat hyperammonemia because it conjugates with an amino acid to form hippurate, which is excreted in the urine, thereby removing excess nitrogen. Which amino acid does sodium benzoate conjugate with?

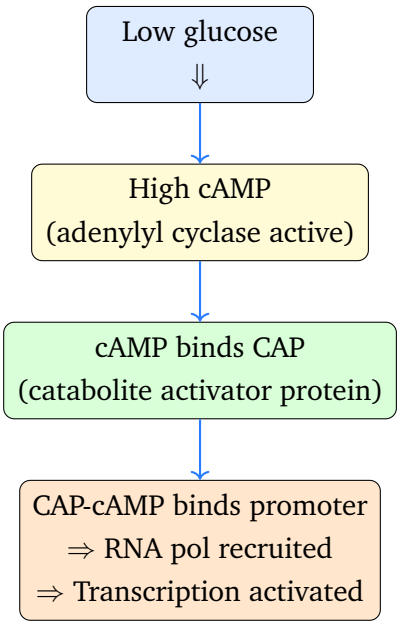
(A) Glutamine

(B) Glycine

(C) Alanine

(D) Aspartate

Q7. A molecular biology question describes the lac operon of *E. coli*. When lactose is absent and glucose is present, the lac operon is maximally repressed. When lactose is present and glucose is absent, the operon is maximally induced. Which mechanism best explains the **positive** control (activation) of the lac operon?



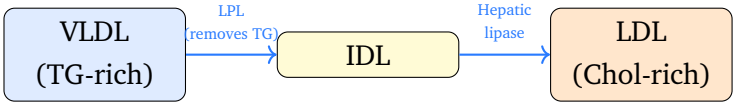
(A) Allolactose binds the CAP protein to allow RNA polymerase binding

(B) The lac repressor protein directly recruits RNA polymerase

(C) cAMP-CAP complex binds the promoter and enhances RNA polymerase binding (catabolite repression relief)

(D) High glucose increases cAMP and activates the operon

Q8. A 45-year-old man with hypertriglyceridaemia is found to have reduced lipoprotein lipase (LPL) activity. In the normal conversion of VLDL to LDL, LPL acts on VLDL in peripheral capillaries. Which sequence correctly describes VLDL catabolism?



(A) VLDL → HDL → LDL (HDL is the intermediate)

(B) VLDL → IDL → LDL (LPL removes TG; hepatic lipase acts on IDL)

(C) VLDL → LDL directly (no IDL intermediate)

(D) VLDL → chylomicron remnant → LDL

Q9. During prolonged starvation (3–4 weeks), the brain adapts to use an alternative fuel to spare muscle protein. Which statement correctly describes ketone body utilization by the brain in this context?

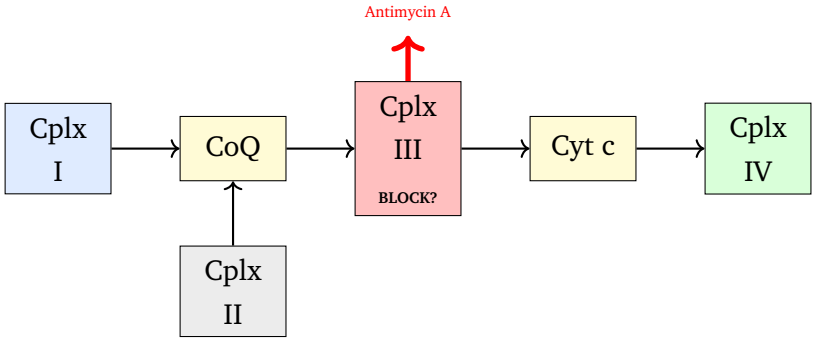
(A) The brain cannot use ketone bodies at any time; it is entirely glucose-dependent

(B) The brain adapts to use ketone bodies (acetoacetate and β-hydroxybutyrate) as its primary fuel, meeting 60–70% of energy needs

(C) The liver uses ketone bodies extensively during starvation

(D) Ketone body utilization by the brain requires insulin

Q10. A researcher adds antimycin A to an isolated mitochondrial preparation. Oxygen consumption falls dramatically and NADH accumulates. Antimycin A acts by blocking which component of the electron transport chain (ETC)?



(A) Complex I (NADH-ubiquinone oxidoreductase)

(B) Complex II (succinate dehydrogenase)

(C) Complex IV (cytochrome c oxidase)

(D) Complex III (cytochrome bc_1 complex)

Q11. A patient is transfused with blood stored for 4 weeks. Stored blood has depleted 2,3-bisphosphoglycerate (2,3-BPG). After transfusion, oxygen delivery to tissues is transiently impaired. Which condition causes a **left shift** of the oxygen-haemoglobin dissociation curve (increased O_2 affinity, impaired O_2 delivery)?

(A) Acidosis (pH 7.20)

(B) Fever (40°C)

(C) Increased 2,3-BPG (as in altitude acclimatisation)

(D) Decreased 2,3-BPG, alkalosis, or fetal haemoglobin (HbF)

Q12. A 55-year-old woman presents with fatigue, pallor, and a smooth, beefy-red tongue (glossitis). Her haemoglobin is 8.5 g/dL with an MCV of 110 fL (megaloblastic anaemia). Anti-intrinsic factor antibodies are detected. Gastric biopsy shows atrophic gastritis. This condition results from:

(A) Dietary iron deficiency

(B) Folate deficiency from malabsorption

(C) Autoimmune destruction of parietal cells $\rightarrow$ absent intrinsic factor $\rightarrow$ vitamin B12 malabsorption (pernicious anaemia)

(D) Haemolytic anaemia with compensatory reticulocytosis

Q13. During DNA replication, positive supercoiling accumulates ahead of the replication fork as the double helix is unwound. A specific topoisomerase relieves this tension by introducing transient double-strand breaks and is the target of fluoroquinolone antibiotics (e.g., ciprofloxacin). This enzyme is:

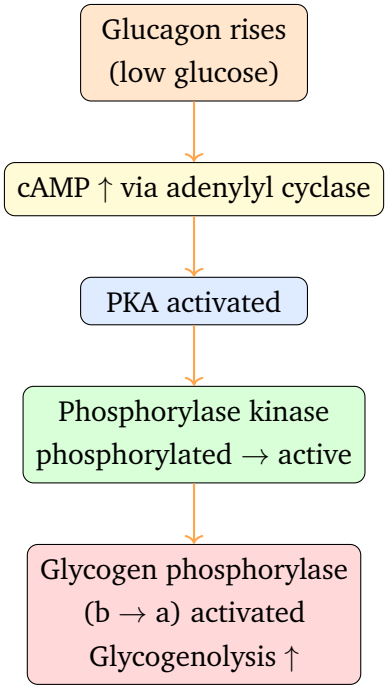
(A) Topoisomerase I (relaxes supercoils via single-strand nicks)

(B) Primase (synthesises RNA primers)

(C) Helicase (unwinds the double helix)

(D) DNA gyrase (topoisomerase II; introduces negative supercoils; target of fluoroquinolones)

Q14. A patient undergoes a 24-hour fast. As blood glucose falls, the glucagon-to-insulin ratio rises. Regarding hepatic glycogen metabolism during this fasting state, which sequence of events is correct?



(A) Glucagon → cAMP → PKA → phosphorylase kinase activated → glycogen phosphorylase activated → glycogenolysis; simultaneously gluconeogenesis (PEPCK) is induced

(B) Insulin activates glycogen phosphorylase directly during fasting

(C) Glucagon inhibits adenylyl cyclase to reduce glycogenolysis

(D) High glucagon activates glycogen synthase to store glucose

Q15. A 3-month-old infant presents with seizures, hypotonia, and a skin rash. Urine organic acid analysis shows elevated 3-methylcrotonylglycine, methylcitrate, and lactate. Serum biotinidase activity is undetectable. Biotin supplementation dramatically improves all symptoms. The diagnosis is:

(A) Holocarboxylase synthetase deficiency (neonatal form)

(B) Propionic acidemia due to propionyl-CoA carboxylase deficiency

(C) Biotinidase deficiency (late-onset multiple carboxylase deficiency)

(D) Biotin dietary deficiency from raw egg white consumption

Q16. A first-year medical student is studying glucose sensing by hepatic glucokinase (hexokinase IV) versus peripheral hexokinase (hexokinase I). Which statement correctly distinguishes glucokinase from hexokinase?

(A) Glucokinase has a low K_m ($\sim$0.1 mM) and is inhibited by glucose-6-phosphate

(B) Glucokinase has a high K_m ($\sim$10 mM), is not inhibited by glucose-6-phosphate, and shows sigmoidal (co-operative) kinetics – acting as a glucose sensor

(C) Both glucokinase and hexokinase have the same K_m and kinetics

(D) Hexokinase has a high K_m and is not inhibited by glucose-6-phosphate

Q17. A 40-year-old chronic alcohol user presents with elevated liver enzymes. His alcohol metabolism involves a microsomal ethanol oxidizing system (MEOS) that is induced by chronic alcohol. Which cytochrome P450 isoform mediates MEOS activity, and what is a key consequence of its induction?

(A) CYP3A4; reduced drug metabolism

(B) CYP1A2; increased tobacco carcinogen activation

(C) CYP2C9; impaired warfarin metabolism

(D) CYP2E1; increased ROS generation and hepatotoxicity; enhanced metabolism of other drugs/toxins

Q18. A premature neonate with respiratory distress syndrome (RDS) is also found to have haemolytic anaemia and is placed on vitamin E supplementation. Vitamin E (α-tocopherol) protects cell membranes from oxidative damage. Which mechanism best explains the antioxidant action of vitamin E?

(A) Vitamin E chelates iron ions, preventing Fenton reaction

(B) Vitamin E activates superoxide dismutase (SOD)

(C) Vitamin E donates electrons directly to molecular oxygen

(D) α-Tocopherol donates a hydrogen atom to lipid peroxide radicals, quenching the chain reaction; the resulting tocopheroxyl radical is recycled by vitamin C

Q19. A 30-year-old woman presents with fatigue, pallor, and a serum ferritin of 4 ng/mL (normal 20–200). Her serum iron is low and TIBC is elevated. Which statement about serum ferritin is correct?

(A) Serum ferritin is the best indicator of total body iron stores; low ferritin is diagnostic of iron deficiency; it is elevated in haemochromatosis and chronic disease (acute-phase reactant)

(B) Serum ferritin does not reflect body iron stores

(C) Serum ferritin is low in haemochromatosis

(D) Serum ferritin is not affected by inflammatory conditions

Q20. During prolonged exercise, skeletal muscle exports alanine to the liver. In the liver, alanine is transaminated to pyruvate, which enters gluconeogenesis to regenerate glucose sent back to muscle. This cycle is the glucose-alanine cycle. Which amino acid is the most important gluconeogenic amino acid released from muscle?

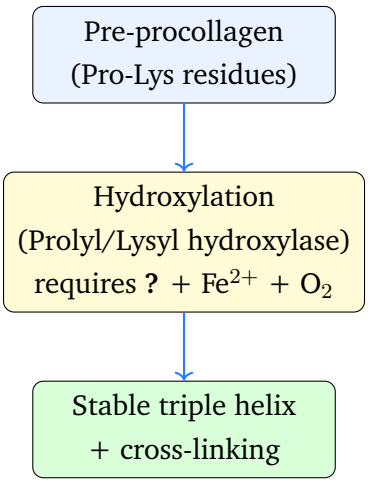
(A) Glutamine

(B) Leucine

(C) Aspartate

(D) Alanine

Q21. A 30-year-old man develops perifollicular haemorrhages, bleeding gums, and corkscrew hairs after months on a restricted diet. Wound healing is impaired. Collagen synthesis requires hydroxylation of proline and lysine residues in the endoplasmic reticulum. Which cofactor is required by prolyl hydroxylase and lysyl hydroxylase for collagen synthesis?



(A) Vitamin K (γ-carboxylase cofactor)

(B) Biotin (carboxylation reactions)

(C) Vitamin C (ascorbic acid) – maintains Fe^{2+} state for hydroxylase activity

(D) Vitamin B6 (pyridoxal phosphate)

Q22. IGF-1 (insulin-like growth factor 1) is produced by the liver in response to growth hormone (GH). Regarding the structure of IGF-1, which statement is correct?

(A) IGF-1 shares structural homology with proinsulin, containing A, B, C, and D domains; unlike insulin, the C-domain is NOT cleaved and remains in the mature molecule

(B) IGF-1 is structurally identical to insulin with a cleaved C-peptide

(C) IGF-1 is a steroid hormone synthesised in the adrenal cortex

(D) IGF-1 has no structural homology with insulin

Q23. A patient has been fasting for 5 weeks (experimental starvation study). Urinary nitrogen excretion, initially high, has now fallen significantly. Blood ketone levels are elevated at 6 mM. Which metabolic adaptation best explains the reduced urinary nitrogen loss after prolonged starvation?

(A) The brain switches entirely to glucose, sparing amino acids

(B) Liver gluconeogenesis from amino acids is maximally activated in prolonged starvation

(C) Brain adaptation to use ketone bodies as fuel (60–70% of energy needs) reduces the need to catabolise muscle protein for gluconeogenesis

(D) Muscle glycogen provides adequate glucose after 5 weeks of fasting

Q24. A patient with chronic kidney disease (CKD) has low serum calcium and elevated PTH. The active form of vitamin D (calcitriol) is deficient because the final hydroxylation step cannot occur. Which statement about calcitriol synthesis is correct?

(A) Calcitriol = 25-hydroxycholecalciferol; final hydroxylation occurs in the liver

(B) Calcitriol = 1,25-dihydroxycholecalciferol; synthesised entirely in the skin

(C) Calcitriol = 1,25-dihydroxycholecalciferol; 1α-hydroxylase in the kidney catalyses the final step; stimulated by PTH and low phosphate

(D) Calcitriol is the storage form of vitamin D; 25-OH-D_3 is the active form

Q25. A 50-year-old man with a history of MI is on low-dose aspirin (75 mg/day) for antiplatelet prophylaxis. Aspirin irreversibly inhibits cyclo-oxygenase (COX). Why is the antiplatelet effect of aspirin prolonged for 7–10 days (the platelet lifespan)?

(A) Platelets are anucleate and cannot synthesise new COX protein; therefore, aspirin's irreversible COX acetylation lasts for the platelet's entire lifespan

(B) Aspirin is slowly excreted, maintaining therapeutic blood levels for 7–10 days

(C) Platelets have a very slow turnover rate of 30 days

(D) Aspirin reversibly inhibits COX; the prolonged effect is due to active metabolites

Q26. S-adenosylmethionine (SAM) is the principal methyl donor in over 100 methylation reactions in the body. Which enzyme catalyses the formation of SAM from methionine and ATP?

(A) Methionine synthase

(B) Cystathionine beta-synthase

(C) Homocysteine methyltransferase

(D) Methionine adenosyltransferase (MAT)

Q27. A cancer biologist notes that HeLa cells (immortal cell line) maintain telomere length despite repeated divisions, whereas normal human fibroblasts undergo progressive telomere shortening and eventually senesce (Hayflick limit). The enzyme responsible for telomere elongation in cancer and germ cells is:

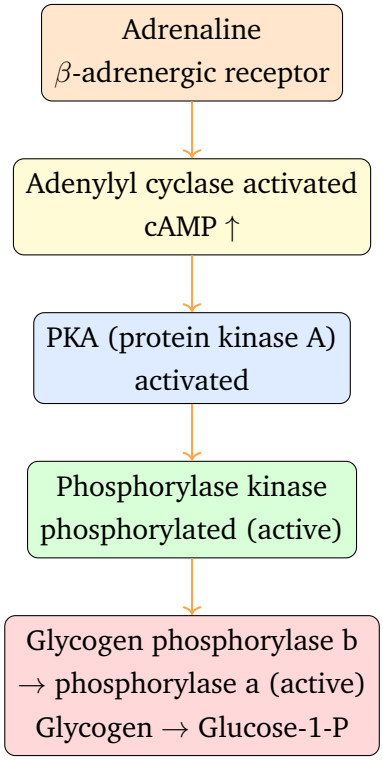
(A) DNA polymerase delta (synthesises lagging strand)

(B) Topoisomerase II (relieves supercoiling)

(C) Primase (synthesises RNA primers)

(D) Telomerase (a reverse transcriptase that uses its intrinsic RNA template to extend telomeric repeats)

Q28. An injection of adrenaline (epinephrine) rapidly mobilises glucose from liver glycogen. The signalling cascade activating glycogen phosphorylase involves multiple phosphorylation steps. Which sequence is correct?



(A) Adrenaline → cAMP → PKA → phosphorylase kinase (active) → glycogen phosphorylase b → a (active)

(B) Adrenaline → IP_3 → DAG → PKC → glycogen phosphorylase

(C) Glucagon → direct activation of glycogen phosphorylase (no second messenger)

(D) cAMP directly phosphorylates glycogen phosphorylase without PKA

Q29. A 2-day-old neonate has jaundice. Total bilirubin is 15 mg/dL with direct (conjugated) bilirubin of 0.5 mg/dL. The paediatrician explains that neonatal physiological jaundice results from immature hepatic conjugation. Which enzyme is responsible for conjugating bilirubin with glucuronic acid to form water-soluble direct bilirubin?

(A) Heme oxygenase (converts heme to biliverdin)

(B) Biliverdin reductase (converts biliverdin to bilirubin)

(C) Glutathione S-transferase (ligandin; binds bilirubin for transport)

(D) UDP-glucuronosyltransferase 1A1 (UGT1A1; conjugates bilirubin with glucuronic acid in the liver)

Q30. A 25-year-old man develops muscle cramps and dark (myoglobinuric) urine after moderate exercise. Serum CK is markedly elevated. A forearm ischaemic exercise test shows that venous lactate does NOT rise (normal: rises >3-fold). Ammonia rises normally. The diagnosis is:

(A) Pompe disease (GSD type II) – acid maltase deficiency

(B) Von Gierke disease (GSD type I) – glucose-6-phosphatase deficiency

(C) McArdle disease (GSD type V) – myophosphorylase deficiency; muscle cannot break down glycogen; no lactate rise with exercise

(D) Carnitine palmitoyltransferase I deficiency

Q31. Pre-mRNA processing in eukaryotes involves removal of introns by a large ribonucleoprotein complex. The spliceosome assembles at intron consensus sequences. Which snRNAs are components of the spliceosome, and what is the key intermediate formed during splicing?

(A) 16S and 23S rRNAs form the spliceosome; no intermediate is formed

(B) U1, U2, U4, U5, U6 snRNAs; lariat intermediate is formed by the branch-point adenosine attacking the 5' splice site (two transesterification reactions)

(C) The spliceosome uses only protein components; no RNA is involved

(D) mRNA splicing requires DNA template and reverse transcriptase

Q32. A patient with hypothyroidism undergoes radioiodine imaging. The synthesis of thyroid hormones T3 and T4 requires iodine. Which enzyme catalyses the organification (iodination) of tyrosine residues on thyroglobulin to form MIT and DIT?

(A) Thyroid peroxidase (TPO) – organifies iodide by coupling it to tyrosine residues; also catalyses coupling of MIT+DIT to form T3/T4; inhibited by propylthiouracil (PTU) and methimazole

(B) Thyroglobulin itself catalyses the iodination reaction

(C) Deiodinase performs iodination in the thyroid follicle

(D) Pendrin (iodide transporter) catalyses the oxidation of iodide

Q33. A 20-year-old is brought to the emergency department with a history of antifreeze ingestion. Urinalysis shows calcium oxalate crystals (envelope-shaped). Serum creatinine is rising rapidly. Which metabolic pathway explains the accumulation of oxalate in ethylene glycol poisoning?

(A) Ethylene glycol $\rightarrow$ glyoxylate $\rightarrow$ glycine (no oxalate formed)

(B) Ethylene glycol is directly excreted as oxalate without enzymatic conversion

(C) Ethylene glycol $\rightarrow$ glycolaldehyde $\rightarrow$ glycolate $\rightarrow$ glyoxylate $\rightarrow$ oxalate; oxalate combines with Ca^{2+} $\rightarrow$ calcium oxalate crystals in renal tubules, causing AKI

(D) Ethylene glycol competes with methanol for alcohol dehydrogenase, preventing oxalate formation

Q34. A student is asked to classify the branched-chain amino acids (BCAAs). Which of the following correctly identifies all three BCAAs and their metabolic properties?

(A) Leucine, phenylalanine, tryptophan – all ketogenic only

(B) Valine, alanine, leucine – all glucogenic

(C) Leucine, isoleucine, valine – all essential; catabolised primarily in muscle (not liver); isoleucine is both glucogenic and ketogenic

(D) Leucine, isoleucine, methionine – all catabolised in liver

Q35. A patient presents with easy bruising and a prolonged prothrombin time (PT/INR elevated), but a normal activated partial thromboplastin time (aPTT). This pattern points to extrinsic pathway deficiency. Which factor initiates the extrinsic pathway of coagulation?

(A) Factor XII (Hageman factor) – initiates the intrinsic pathway

(B) Factor VII binding to tissue factor (TF/Factor III); TF-VIIa complex activates Factor X; this is the extrinsic pathway; measured by PT/INR

(C) Factor VIII – intrinsic pathway; measured by aPTT

(D) Thrombin (Factor IIa) – final common pathway, not the initiating step

Q36. A patient on long-term warfarin therapy for atrial fibrillation requires dose adjustment after starting a new medication. Warfarin exerts its anticoagulant effect by inhibiting vitamin K recycling. Which enzyme does warfarin inhibit?

(A) γ-Glutamyl carboxylase (the enzyme that carboxylates clotting factors)

(B) Vitamin K epoxide reductase (VKOR) – warfarin blocks the regeneration of active (reduced) vitamin K from vitamin K epoxide, depleting active vitamin K

(C) Thrombin directly (warfarin is a direct thrombin inhibitor)

(D) Protein C activator (warfarin increases protein C first)

Q37. A pharmacology question describes the second messenger system activated by α_1-adrenergic, M_1-muscarinic, and H_1-histamine receptors. These receptors are coupled to which G-protein, and what are the downstream second messengers generated?

(A) Gs protein $\rightarrow$ adenylyl cyclase $\rightarrow$ cAMP $\rightarrow$ PKA

(B) Gi protein $\rightarrow$ inhibition of adenylyl cyclase $\rightarrow$ decreased cAMP

(C) Gq protein $\rightarrow$ PLC-β $\rightarrow$ PIP_2 cleaved into IP_3 (releases ER Ca^{2+}) + DAG (activates PKC)

(D) G12 protein $\rightarrow$ Rho-GTPase pathway

Q38. A newborn is diagnosed with atypical (malignant) PKU despite a normal phenylalanine hydroxylase (PAH) gene. Blood phenylalanine is elevated, but more critically, neurotransmitters (dopamine, serotonin, norepinephrine) are severely depleted despite dietary phenylalanine restriction. Which cofactor deficiency explains this presentation?

(A) Tetrahydrobiopterin (BH4) deficiency – BH4 is the cofactor for PAH, tyrosine hydroxylase, and tryptophan hydroxylase; BH4 deficiency

impairs both phenylalanine metabolism and catecholamine/serotonin synthesis

(B) Pyridoxal phosphate (B6) deficiency

(C) Thiamine pyrophosphate (TPP) deficiency

(D) Flavin adenine dinucleotide (FAD) deficiency

Q39. A patient with growth failure, hypogonadism, poor wound healing, and anosmia is found to have zinc deficiency. Zinc serves as a catalytic cofactor in multiple enzymes. Which of the following enzymes requires zinc as an essential cofactor at its active site?

(A) Carbonic anhydrase (Zn^{2+} as Lewis acid activates water for CO_2 hydration); also carboxypeptidase A, alcohol dehydrogenase, DNA polymerase

(B) Pyruvate carboxylase (requires Mn^{2+} and biotin)

(C) Glutathione peroxidase (requires selenium)

(D) Superoxide dismutase (Cu/Zn-SOD – actually requires Zn but the primary answer is carbonic anhydrase for the Lewis acid role)

Q40. A 12-year-old boy with haematuria is found to have sensorineural deafness and progressive renal insufficiency. Renal biopsy electron microscopy shows irregular thinning and splitting of the glomerular basement membrane (GBM). Genetics reveals a mutation in the gene encoding α5 chain of type IV collagen (X-linked form). Which type of collagen forms the meshwork of basement membranes and is defective in Alport syndrome?

(A) Type I collagen (fibrillar; tendons, bone, skin)

(B) Type IV collagen (non-fibrillar network; forms the meshwork of all basement membranes – GBM, lens capsule, alveolar BM; α3–α5 chain mutations cause Alport syndrome)

(C) Type II collagen (fibrillar; articular cartilage)

(D) Type III collagen (reticular fibres; liver, spleen, lymph nodes)

Detailed Solutions

Q1.

Solution

Concept – Vitamin A teratogenicity (Retinoic acid embryopathy): Excess retinoic acid during organogenesis (especially weeks 2–8) disrupts homeobox gene expression in neural crest cells, causing **conotruncal cardiac defects** (transposition of great arteries, VSD, truncus arteriosus), cleft palate, microtia (ear anomalies), and CNS malformations. Isotretinoin (13-cis-retinoic acid), used for severe acne, is a Category X teratogen. Neural tube defects are classically caused by **folate** deficiency, not vitamin A excess. Phocomelia is associated with thalidomide.

Distractors: (B) Neural tube defects $\rightarrow$ folate deficiency. (C) Phocomelia $\rightarrow$ thalidomide. (D) Hypocalcaemia $\rightarrow$ vitamin D deficiency or DiGeorge syndrome.

Final Answer: Cleft palate and conotruncal cardiac defects (retinoic acid embryopathy). $\Rightarrow \boxed{A}$

Answer: (A) Go Back to Q1

Q2.

Solution

Concept – K_m and enzyme affinity: K_m is inversely related to affinity: **lower K_m = higher affinity**. At a physiological substrate concentration of 0.5 mM, Enzyme 1 (K_m = 0.1 mM) is operating near saturation ($[S]$ is 5$\times$ its K_m), while Enzyme 2 (K_m = 5 mM) is far from saturation ($[S]$ is only 1/10 of its K_m). This concept explains why glucokinase (high K_m) acts as a glucose sensor, while hexokinase (low K_m) is always near saturation. Clinically, enzymes with low K_m are efficient at normal substrate levels; those with high K_m only activate when substrate is abundant.

Final Answer: Lower K_m = higher affinity; first enzyme operates near saturation. $\Rightarrow \boxed{B}$

Answer: (B) Go Back to Q2

Q3.

Solution

Concept – Propionic Acidemia (Propionyl-CoA Carboxylase Deficiency): **Propionyl-CoA carboxylase** (biotin-dependent) converts propionyl-CoA to

methylmalonyl-CoA in the catabolism of odd-chain fatty acids and branched-chain amino acids (isoleucine, valine, methionine, threonine). Deficiency leads to propionic acid accumulation, secondary hyperammonemia (propionic acid inhibits urea cycle enzymes), ketoacidosis, and hyperglycinaemia. Methylmalonyl-CoA mutase (B12-dependent) is the next step; its deficiency causes methylmalonic acidemia (MMA). Biotin supplementation helps only if biotinidase or holocarboxylase synthetase is deficient.

Distractors: (A) Methylmalonyl-CoA mutase deficiency $\rightarrow$ MMA, not propionic acidemia. (C) Pyruvate carboxylase $\rightarrow$ lactic acidosis and hypoglycaemia. (D) Acetyl-CoA carboxylase $\rightarrow$ fatty acid synthesis regulation.

Final Answer: Propionyl-CoA carboxylase deficiency. $\Rightarrow \boxed{B}$

Answer: (B) Go Back to Q3

Q4.

Solution

Concept – PFK-1 allosteric regulation: PFK-1 is the rate-limiting, committed step of glycolysis. **Activators:** AMP, ADP (signal low energy), and fructose-2,6-bisphosphate (signal fed state; made by PFK-2 stimulated by insulin). **Inhibitors:** ATP (signal high energy), citrate (signals TCA cycle saturation), and H^+ (acidosis – prevents worsening lactic acidosis). Glucagon does not directly activate PFK-1; instead, glucagon activates PFK-2 kinase/phosphatase to lower F-2,6-BP, thereby inhibiting PFK-1.

Distractors: (B) These are inhibitors. (C) ATP inhibits PFK-1. (D) Glucagon inhibits PFK-1 indirectly by reducing F-2,6-BP.

Final Answer: AMP, ADP, and fructose-2,6-bisphosphate are PFK-1 activators. $\Rightarrow \boxed{A}$

Answer: (A) Go Back to Q4

Q5.

Solution

Concept – Vitamin B12 as cofactor for methylmalonyl-CoA mutase: Vitamin B12 (cobalamin) serves as a cofactor for two enzymes: (i) **Methionine synthase** (5-methylTHF + homocysteine $\rightarrow$ methionine + THF) and (ii) **Methylmalonyl-CoA mutase** (methylmalonyl-CoA $\rightarrow$ succinyl-CoA), which is required for catabolism of odd-chain fatty acids, valine, isoleucine, methionine, and threonine. B12 deficiency causes elevated **methylmalonic acid** (MMA) in urine

– a diagnostic marker distinguishing B12 deficiency from folate deficiency (folate deficiency raises homocysteine but NOT MMA).

Distractors: (A) Methionine synthase deficiency raises homocysteine, not MMA. (B) Thymidylate synthase uses 5,10-methylene-THF. (C) DHFR uses folate, not B12.

Final Answer: Methylmalonyl-CoA mutase (vitamin B12-dependent). $\Rightarrow \boxed{D}$

Answer: (D) Go Back to Q5

Q6.

Solution

Concept – Hyperammonemia treatment with sodium benzoate: In urea cycle disorders, excess ammonia accumulates. **Sodium benzoate** conjugates with **glycine** to form hippurate (benzoylglycine), which is excreted in urine – effectively removing one nitrogen atom per molecule. **Sodium phenylbutyrate** is converted to phenylacetate, which conjugates with **glutamine** (two nitrogen atoms) to form phenylacetylglutamine – more efficient nitrogen scavenging. Both are used clinically to bypass the deficient urea cycle step. The mnemonic: Benzoate $\rightarrow$ **B**enzoate + **G**lycine = Hippurate (**B–G**).

Distractors: (A) Glutamine is conjugated by phenylacetate (from phenylbutyrate), not benzoate. (C) Alanine is not a substrate for benzoate conjugation. (D) Aspartate donates nitrogen directly in the urea cycle.

Final Answer: Glycine (sodium benzoate $\rightarrow$ hippurate). $\Rightarrow \boxed{B}$

Answer: (B) Go Back to Q6

Q7.

Solution

Concept – Lac operon: positive control (catabolite repression): The lac operon is under *dual control*: (i) Negative control by the lac repressor (inhibited by allolactose, a lactose metabolite). (ii) **Positive control** by the cAMP-CAP (catabolite activator protein) complex. When glucose is low, adenylyl cyclase activity rises, increasing intracellular **cAMP**. cAMP binds **CAP (CRP)**, and the cAMP-CAP complex binds upstream of the lac promoter, facilitating RNA polymerase binding and dramatically increasing transcription. This is "catabolite repression" – when glucose is present, cAMP is low and CAP cannot activate the operon.

Distractors: (A) Allolactose binds the repressor (negative control), not CAP. (B) The repressor blocks RNA pol; it does not recruit it. (D) High glucose *decreases*

cAMP and *reduces* lac operon activity.

Final Answer: cAMP-CAP complex activates the lac operon when glucose is absent. $\Rightarrow \boxed{C}$

Answer: (C) Go Back to Q7

Q8.

Solution

Concept – VLDL-to-LDL conversion: VLDL (very low-density lipoprotein) is secreted by the liver, rich in triglycerides (TG) and containing ApoB-100, ApoE, and ApoCII. In peripheral capillaries, **lipoprotein lipase (LPL)** (activated by ApoCII) hydrolyses TG, converting VLDL $\rightarrow$ **IDL** (intermediate-density lipoprotein). Hepatic lipase then removes remaining TG from IDL $\rightarrow$ **LDL** (low-density lipoprotein), which is predominantly cholesterol-rich and carries ApoB-100. LDL is cleared from circulation by LDL receptors on hepatocytes. In LPL deficiency, VLDL and chylomicrons accumulate (hypertriglyceridaemia).

Distractors: (A) HDL is not an intermediate in VLDL catabolism. (C) IDL is an obligate intermediate. (D) Chylomicrons are intestinal lipoproteins, not derived from VLDL.

Final Answer: VLDL $\rightarrow$ IDL (by LPL) $\rightarrow$ LDL (by hepatic lipase). $\Rightarrow \boxed{B}$

Answer: (B) Go Back to Q8

Q9.

Solution

Concept – Ketone body utilisation by the brain in starvation: The brain normally depends on glucose. After glycogen depletion (24–48 h), gluconeogenesis provides glucose, but this requires amino acid catabolism. After 3–4 weeks of starvation, elevated blood ketones (acetoacetate and β-hydroxybutyrate) are taken up by the brain and converted to acetyl-CoA via succinyl-CoA transferase (thiophorase). **The brain derives 60–70% of its energy from ketone bodies**, dramatically reducing the demand for glucose and thereby sparing muscle protein from gluconeogenesis. The **liver itself cannot use ketone bodies** (it lacks succinyl-CoA transferase).

Distractors: (A) False – the brain adapts to use ketones in starvation. (C) The liver produces ketones but cannot use them. (D) Ketone utilisation by brain does not require insulin.

Final Answer: Brain uses ketone bodies as primary fuel (60–70% energy) in pro-

longed starvation. $\Rightarrow \boxed{B}$

Answer: (B) Go Back to Q9

Q10.

Solution

Concept – Antimycin A blocks Complex III (cytochrome bc_1 complex): Antimycin A is a classic ETC inhibitor that blocks the **Qi site of Complex III** (cytochrome bc_1), preventing electron transfer from cytochrome b to cytochrome c_1. Consequently, electrons cannot flow from CoQ to cytochrome c; NADH (and $FADH_2$) accumulate; O_2 consumption ceases. Other ETC inhibitors: rotenone/amytal block **Complex I**; malonate blocks **Complex II**; cyanide, CO, azide block **Complex IV**. ATP synthase is blocked by oligomycin.

Distractors: (A) Complex I is blocked by rotenone. (B) Complex II is blocked by malonate. (C) Complex IV is blocked by cyanide/CO.

Final Answer: Antimycin A inhibits Complex III (cytochrome bc_1 complex). $\Rightarrow \boxed{D}$

Answer: (D) Go Back to Q10

Q11.

Solution

Concept – Left shift of O_2-Hb dissociation curve (increased O_2 affinity): A left shift means haemoglobin **binds O_2 more tightly** and releases it less readily to tissues ($\downarrow P_{50}$). Causes include: **decreased 2,3-BPG** (stored blood), **alkalosis** (reversed Bohr effect), **decreased CO_2**, **decreased temperature (hypothermia)**, and **fetal haemoglobin (HbF)** (has γ-chains that bind 2,3-BPG less avidly, so HbF has higher O_2 affinity to extract O_2 from maternal blood). A right shift (Bohr effect) indicates decreased affinity and enhanced O_2 delivery.

Distractors: (A) Acidosis $\rightarrow$ right shift (Bohr effect). (B) Fever $\rightarrow$ right shift. (C) Increased 2,3-BPG $\rightarrow$ right shift.

Final Answer: Decreased 2,3-BPG, alkalosis, or HbF cause a left shift. $\Rightarrow \boxed{D}$

Answer: (D) Go Back to Q11

Q12.

Solution

Concept – Pernicious anaemia: Pernicious anaemia is an autoimmune disease in which **autoantibodies against parietal cells** (anti-H/K-ATPase) and/or **anti-intrinsic factor (IF) antibodies** destroy gastric parietal cells and/or neutralise IF. Without IF, vitamin B12 cannot be absorbed in the terminal ileum (the specific site for IF-B12 complex absorption). The result is vitamin B12 deficiency leading to megaloblastic anaemia, glossitis (Hunter's glossitis – smooth, beefy-red tongue), and subacute combined degeneration of the spinal cord. The Schilling test differentiates pernicious anaemia from other causes of B12 malabsorption.

Distractors: (A) Iron deficiency causes microcytic, hypochromic anaemia. (B) Folate deficiency does not cause neurological features; anti-IF antibodies are not present. (D) Haemolytic anaemia has reticulocytosis and normal/elevated B12.

Final Answer: Pernicious anaemia – autoimmune destruction of parietal cells, absent IF, B12 malabsorption. $\Rightarrow \boxed{C}$

Answer: (C) Go Back to Q12

Q13.

Solution

Concept – DNA Gyrase (Topoisomerase II) and fluoroquinolones: As the replication fork advances, the two strands are unwound by helicase, creating **positive supercoils** ahead. **DNA gyrase** (bacterial topoisomerase II) relieves this tension by introducing transient **double-strand breaks**, passing the DNA through, and religating – introducing negative supercoils. This is the target of **fluoroquinolone antibiotics** (ciprofloxacin, levofloxacin), which stabilise the gyrase-DNA cleavage complex, preventing religation and causing bacterial death. Eukaryotic topoisomerase II is the target of anticancer drugs (etoposide, doxorubicin).

Distractors: (A) Topoisomerase I cuts only one strand (no ATP required); not the fluoroquinolone target. (B) Primase makes RNA primers. (C) Helicase unwinds but does not relieve supercoiling.

Final Answer: DNA gyrase (topoisomerase II) – target of fluoroquinolones. $\Rightarrow \boxed{D}$

Answer: (D) Go Back to Q13

Q14.

Solution

Concept – Glucagon/insulin ratio in fasting and glycogenolysis: During fasting, the rising glucagon-to-insulin ratio activates: (i) **Glycogenolysis** via the cAMP-PKA cascade (glucagon → cAMP → PKA → phosphorylase kinase → glycogen phosphorylase b → a, active); simultaneously PKA **inhibits glycogen synthase**. (ii) **Gluconeogenesis** via induction of PEPCK (phosphoenolpyruvate carboxykinase). Glucagon also suppresses glycolysis (by reducing F-2,6-BP, inhibiting PFK-1) and activates fatty acid oxidation and ketogenesis.

Distractors: (B) Insulin activates glycogen synthase; glucagon has the opposite effect. (C) Glucagon activates, not inhibits, adenylyl cyclase. (D) Glucagon inhibits glycogen synthase (phosphorylation inactivates it).

Final Answer: Glucagon → cAMP → PKA → glycogenolysis + gluconeogenesis. ⇒ $\boxed{A}$

Answer: (A) Go Back to Q14

Q15.

Solution

Concept – Multiple Carboxylase Deficiency (Biotinidase deficiency): Biotinidase recycles biotin from biocytin (biotin-lysine) produced during protein turnover. Deficiency causes progressive biotin depletion, impairing all four biotin-dependent carboxylases: pyruvate carboxylase, propionyl-CoA carboxylase, 3-methylcrotonyl-CoA carboxylase, and acetyl-CoA carboxylase. Clinical features: seizures, hypotonia, skin rash (alopecia, dermatitis), and optic atrophy. Elevated urine organic acids (3-methylcrotonylglycine, methylcitrate, lactate). Dramatic response to pharmacological biotin doses. Newborn screening includes biotinidase assay in most countries. **Holocarboxylase synthetase deficiency** is the neonatal (early-onset) form, also biotin-responsive.

Distractors: (A) Holocarboxylase synthetase deficiency presents in the neonatal period (earlier onset). (B) Propionic acidemia lacks the skin/neurological features of biotinidase deficiency. (D) Raw egg white biotin deficiency is very rare and lacks biotinidase assay findings.

Final Answer: Biotinidase deficiency (late-onset multiple carboxylase deficiency). ⇒ $\boxed{C}$

Answer: (C) Go Back to Q15

Q16.

Solution

Concept – Glucokinase vs. Hexokinase (glucose sensing): Glucokinase (hexokinase IV) in liver and pancreatic β-cells: high K_m ($\sim$10 mM, above fasting blood glucose of $\sim$5 mM), **not inhibited by glucose-6-phosphate (G-6-P)**, shows sigmoidal (cooperative) kinetics (Hill coefficient $\approx$1.7). This makes glucokinase a **glucose sensor** – only active when blood glucose is high (postprandial). **Hexokinase (I-III)** in peripheral tissues: low K_m ($\sim$0.1 mM), **inhibited by G-6-P** (product inhibition), hyperbolic kinetics – always near saturation, provides constitutive glucose phosphorylation.

Distractors: (A) This describes hexokinase, not glucokinase. (C) They are different in K_m, product inhibition, and kinetics. (D) Hexokinase has a low K_m (opposite of what is stated) and IS inhibited by G-6-P.

Final Answer: Glucokinase has high K_m, not inhibited by G-6-P, sigmoidal kinetics – acts as a glucose sensor. $\Rightarrow \boxed{B}$

Answer: (B) Go Back to Q16

Q17.

Solution

Concept – Microsomal Ethanol Oxidizing System (MEOS) and CYP2E1: The MEOS uses **CYP2E1** (cytochrome P450 2E1) in the smooth endoplasmic reticulum (SER) to oxidise ethanol: **Ethanol + NADPH + O_2 $\rightarrow$ Acetaldehyde + $NADP^+$ + H_2O**. Chronic alcohol use **induces CYP2E1**, contributing to: (i) **increased ROS production** (superoxide, hydroxyl radicals) causing lipid peroxidation and hepatocyte damage; (ii) **metabolic tolerance** (faster ethanol clearance); (iii) enhanced metabolism and bioactivation of hepatotoxins (e.g., acetaminophen toxicity at lower doses in alcoholics). CYP2E1 induction also explains why alcoholics are at greater risk for drug-induced hepatotoxicity.

Distractors: (A) CYP3A4 metabolises most drugs but is not the primary MEOS enzyme. (B) CYP1A2 metabolises caffeine and activates carcinogens in tobacco but not ethanol primarily. (C) CYP2C9 metabolises warfarin, NSAIDs.

Final Answer: CYP2E1; induction increases ROS and hepatotoxicity. $\Rightarrow \boxed{D}$

Answer: (D) Go Back to Q17

Q18.

Solution

Concept – Vitamin E (α-tocopherol) antioxidant mechanism: Vitamin E is a **lipid-soluble** antioxidant located in cell membranes. It donates a **hydrogen atom ($H^{\bullet}$)** to lipid peroxyl radicals ($LOO^{\bullet}$), quenching the lipid peroxidation chain reaction and protecting polyunsaturated fatty acids (PUFAs) in membrane phospholipids. The resulting **tocopheroxyl radical** is relatively stable and is regenerated back to active tocopherol by **vitamin C (ascorbate)** at the membrane-aqueous interface. This vitamin E–vitamin C recycling is an important synergistic antioxidant system. Vitamin E deficiency causes haemolytic anaemia (in premature neonates) and neurological deficits (spinocerebellar ataxia).

Distractors: (A) Iron chelation is performed by deferoxamine, not vitamin E. (B) SOD activity is independent of vitamin E. (C) Vitamin E does not donate electrons to O_2 directly.

Final Answer: α-Tocopherol donates $H^{\bullet}$ to lipid peroxyl radicals; recycled by vitamin C. $\Rightarrow \boxed{D}$

Answer: (D) Go Back to Q18

Q19.

Solution

Concept – Serum ferritin as a marker of iron stores: Serum ferritin is the best single laboratory test for assessing total body iron stores. Ferritin is an intracellular iron storage protein; small amounts leak into the serum, reflecting total body iron. **Low ferritin** ($<$12 ng/mL) is pathognomonic of **iron deficiency** – the most specific test (TIBC is elevated, serum iron is low). **Elevated ferritin** is seen in haemochromatosis, ferritin is also an **acute-phase reactant** (elevated in infection, inflammation, malignancy, liver disease), which can mask coexisting iron deficiency. In chronic disease anaemia, ferritin is normal or elevated despite reduced iron availability.

Distractors: (B) Ferritin is the best indirect measure of body iron stores. (C) Ferritin is elevated (not low) in haemochromatosis. (D) Ferritin IS an acute-phase reactant and rises with inflammation.

Final Answer: Serum ferritin reflects total body iron stores; low $\Rightarrow$ iron deficiency; elevated in haemochromatosis and inflammation. $\Rightarrow \boxed{A}$

Answer: (A) Go Back to Q19

Q20.

Solution

Concept – Alanine as the primary gluconeogenic amino acid from muscle: During fasting and exercise, muscle catabolises BCAAs (leucine, isoleucine, valine) and transaminating the amino group to α-ketoglutarate $\rightarrow$ glutamate, then to pyruvate $\rightarrow$ **alanine** (via alanine aminotransferase, ALT). Alanine is released into the bloodstream and taken up by the liver, where ALT regenerates pyruvate (and glutamate), and pyruvate enters gluconeogenesis. This is the **glucose-alanine cycle**. Alanine is quantitatively the most important gluconeogenic amino acid from muscle. Glutamine is the major gluconeogenic amino acid released by gut and kidney.

Distractors: (A) Glutamine is important for gut/kidney but not the primary muscle-derived gluconeogenic amino acid. (B) Leucine is purely ketogenic – it cannot be used for gluconeogenesis. (C) Aspartate is a gluconeogenic AA but not the major one from muscle.

Final Answer: Alanine – glucose-alanine cycle. $\Rightarrow \boxed{D}$

Answer: (D) Go Back to Q20

Q21.

Solution

Concept – Vitamin C and collagen hydroxylation: Collagen synthesis requires hydroxylation of **proline** (to hydroxyproline) and **lysine** (to hydroxylysine) residues in the endoplasmic reticulum, catalysed by **prolyl hydroxylase** and **lysyl hydroxylase**. Both require: **ascorbic acid (Vitamin C)**, Fe^{2+}, O_2, and α-ketoglutarate. Vitamin C keeps iron in the reduced Fe^{2+} form essential for enzyme activity. Without hydroxylation, the collagen triple helix is thermally unstable at body temperature and cannot be properly cross-linked. This causes **scurvy**: perifollicular haemorrhages, bleeding gums, impaired wound healing.

Distractors: (A) Vitamin K is required for γ-carboxylation of clotting factors, not collagen. (B) Biotin is for carboxylation reactions. (D) Vitamin B6 is for transamination and cross-link formation but not for the hydroxylation step.

Final Answer: Vitamin C (ascorbic acid) is the cofactor for prolyl and lysyl hydroxylases. $\Rightarrow \boxed{C}$

Answer: (C) Go Back to Q21

Q22.

Solution

Concept – IGF-1 structure (proinsulin homology): IGF-1 (somatomedin C) shares 50% structural homology with **proinsulin**. Like proinsulin, IGF-1 has **A and B domains** (similar to insulin's A and B chains) connected by a **C-domain**. However, unlike insulin processing, the C-domain of IGF-1 is **NOT cleaved** – it remains in the mature circulating molecule. IGF-1 also has an additional **D-domain** at the C-terminus. IGF-1 is synthesised primarily by the liver in response to GH and mediates most of GH's anabolic effects (somatic growth). It acts via tyrosine kinase receptors (IGF-1R) with strong sequence homology to the insulin receptor.

Distractors: (B) In insulin biosynthesis the C-peptide IS cleaved from proinsulin; IGF-1 retains its C-domain. (C) IGF-1 is a peptide hormone (not steroid), produced by liver. (D) IGF-1 has significant structural homology with proinsulin.

Final Answer: IGF-1 shares proinsulin homology; A, B, C, D domains; C-domain not cleaved. $\Rightarrow \boxed{A}$

Answer: (A) Go Back to Q22

Q23.

Solution

Concept – Brain adaptation to ketone bodies in prolonged starvation: After glycogen stores are depleted ($\sim$24 h), gluconeogenesis from amino acids becomes essential, leading to negative nitrogen balance. However, after **3–4 weeks**, the brain adapts to use **ketone bodies (β-hydroxybutyrate and acetoacetate)** for 60–70% of its energy needs. This dramatically **reduces the demand for gluconeogenesis from amino acids**, thereby **reducing muscle protein catabolism and urinary nitrogen excretion**. The remaining glucose is provided from glycerol (from lipolysis) and the small amount of gluconeogenesis still required. This adaptation is the key survival mechanism that allows humans to survive weeks to months of starvation.

Distractors: (A) The brain does NOT remain entirely glucose-dependent in prolonged starvation – it adapts to ketones. (B) Gluconeogenesis from amino acids is *reduced* in prolonged starvation (not maximally activated). (D) Muscle glycogen cannot provide glucose to other tissues (lacks glucose-6-phosphatase); it is depleted within hours of exercise.

Final Answer: Brain ketone body adaptation reduces proteolysis and urinary nitrogen. $\Rightarrow \boxed{C}$

Answer: (C) Go Back to Q23

Q24.

Solution

Concept – Active form of vitamin D (Calcitriol): Vitamin D_3 (cholecalciferol) from skin/diet $\rightarrow$ **25-hydroxylation in liver** (by CYP2R1/CYP27A1) $\rightarrow$ 25-OH-D_3 (calcidiol; major circulating form, measured clinically) $\rightarrow$ **1α-hydroxylation in kidney** (by CYP27B1, 1α-hydroxylase) $\rightarrow$ **1,25-(OH)$_2$-D$_3$ (calcitriol; the active form)**. Renal 1α-hydroxylase is **stimulated** by PTH, low calcium, and low phosphate; **inhibited** by FGF-23 (phosphatonin) and calcitriol itself. In CKD, renal 1α-hydroxylase activity is lost $\rightarrow$ calcitriol deficiency $\rightarrow$ secondary hyperparathyroidism, renal osteodystrophy.

Distractors: (A) 25-OH-D_3 is the storage/circulating form, not the active form. (B) Both skin AND liver AND kidney are required; calcitriol is not synthesised entirely in skin. (D) 25-OH-D_3 is the storage form; calcitriol is the active form (not vice versa).

Final Answer: Calcitriol = 1,25-$(OH)_2$-D_3; 1α-hydroxylation in kidney is the final step. $\Rightarrow \boxed{C}$

Answer: (C) Go Back to Q24

Q25.

Solution

Concept – Aspirin: irreversible COX inhibition in platelets: Aspirin **irreversibly acetylates** a serine residue (Ser-530 of COX-1, Ser-516 of COX-2) in the active channel of cyclooxygenase, blocking prostaglandin and thromboxane A_2 (TXA_2) synthesis. Platelets are **anucleate** (no nucleus, no ribosomes) and **cannot synthesise new COX protein**. Therefore, the inhibition lasts for the platelet's entire lifespan of **7–10 days**. Nucleated cells (endothelial cells, which produce prostacyclin PGI_2) can regenerate COX, so the antiplatelet effect is relatively selective. This is the basis of low-dose aspirin for antiplatelet prophylaxis.

Distractors: (B) Aspirin is rapidly absorbed and hydrolysed; its plasma half-life is short ($\sim$15–20 min); prolonged effect is due to irreversible COX inhibition in platelets, not persistent drug levels. (C) Platelet lifespan is 7–10 days, not 30 days. (D) Aspirin is an irreversible inhibitor.

Final Answer: Platelets are anucleate; cannot regenerate COX; aspirin's effect lasts platelet lifespan. $\Rightarrow \boxed{A}$

Answer: (A) Go Back to Q25

Q26.

Solution

Concept – SAM formation by Methionine Adenosyltransferase (MAT): Methionine adenosyltransferase (MAT) catalyses the transfer of the adenosyl group from ATP to methionine to form **S-adenosylmethionine (SAM)** – the principal biological methyl donor (active methionine). SAM donates its methyl group in over 100 reactions (methylation of DNA, RNA, histones, neurotransmitters, phospholipids, creatine synthesis). The product **S-adenosylhomocysteine (SAH)** is a potent product inhibitor of all methyltransferases; it is hydrolysed to homocysteine + adenosine. MAT is highly expressed in the liver; liver disease impairs SAM synthesis, affecting transmethylation reactions.

Distractors: (A) Methionine synthase converts homocysteine $\rightarrow$ methionine (the preceding step to SAM formation). (B) CBS converts homocysteine $\rightarrow$ cystathionine (transsulfuration pathway). (C) Homocysteine methyltransferase is another name for methionine synthase.

Final Answer: Methionine adenosyltransferase (MAT) forms SAM. $\Rightarrow \boxed{D}$

Answer: (D) Go Back to Q26

Q27.

Solution

Concept – Telomerase: reverse transcriptase for telomere maintenance: Telomerase is a ribonucleoprotein enzyme with an intrinsic **RNA template** (TERC) that guides extension of the 3' end of chromosomes with TTAGGG repeats (telomeric sequences). It is a specialised **reverse transcriptase** (TERT subunit). Telomerase is active in **germ cells, stem cells, and most cancer cells** (allowing immortal replication). In most normal somatic cells, telomerase is absent or minimal, so telomeres shorten with each division, eventually causing cell senescence (Hayflick limit, $\sim$50 divisions). Telomere shortening is a tumour suppressor mechanism; cancer cells reactivate telomerase to bypass this limit.

Distractors: (A) DNA polymerase δ cannot replicate telomere ends (end-replication problem). (B) Topoisomerase II relieves supercoiling. (C) Primase makes short RNA primers for replication initiation.

Final Answer: Telomerase – reverse transcriptase using RNA template to extend telomeres. $\Rightarrow \boxed{D}$

Answer: (D) Go Back to Q27

Q28.

Solution

Concept – Glycogen phosphorylase activation cascade: Adrenaline (or glucagon) binds β-adrenergic receptors $\rightarrow$ Gs $\rightarrow$ adenylyl cyclase $\rightarrow$ **cAMP** $\uparrow \rightarrow$ **PKA** activated $\rightarrow$ PKA phosphorylates **phosphorylase kinase** (inactive $\rightarrow$ active) $\rightarrow$ active phosphorylase kinase phosphorylates **glycogen phosphorylase b** $\rightarrow$ **phosphorylase a** (active) $\rightarrow$ glycogen $\rightarrow$ glucose-1-phosphate. Simultaneously, PKA phosphorylates **glycogen synthase** (active $\rightarrow$ inactive), preventing simultaneous glycogen synthesis and breakdown. This cascade amplifies the hormonal signal $\sim 10^6$-fold.

Distractors: (B) IP_3/DAG/PKC is the Gq pathway (α_1-adrenergic); adrenaline acts via β-adrenergic/Gs/cAMP for glycogen mobilisation. (C) Glucagon does require a second messenger (cAMP). (D) PKA is the kinase that phosphorylates downstream targets; cAMP activates PKA, not phosphorylase directly.

Final Answer: Adrenaline $\rightarrow$ cAMP $\rightarrow$ PKA $\rightarrow$ phosphorylase kinase $\rightarrow$ glycogen phosphorylase b$\rightarrow$a. $\Rightarrow \boxed{A}$

Answer: (A) Go Back to Q28

Q29.

Solution

Concept – Bilirubin conjugation by UGT1A1: Unconjugated (indirect) bilirubin is water-insoluble and bound to albumin. In hepatocytes, it is conjugated with **glucuronic acid** by **UDP-glucuronosyltransferase 1A1 (UGT1A1)**, forming **direct (conjugated) bilirubin**, which is water-soluble and excreted in bile. **Neonatal physiological jaundice** occurs because UGT1A1 is functionally immature at birth (low expression). **Gilbert syndrome**: reduced UGT1A1 expression (mild unconjugated hyperbilirubinaemia, benign). **Crigler-Najjar syndrome** (types I and II): more severe UGT1A1 deficiency. Phenobarbitone induces UGT1A1 (used in Crigler-Najjar type II).

Distractors: (A) Heme oxygenase is in the spleen/macrophages – converts heme $\rightarrow$ biliverdin (green). (B) Biliverdin reductase converts biliverdin $\rightarrow$ unconjugated bilirubin (still indirect). (C) Glutathione S-transferase (ligandin) transports bilirubin to the SER but does not conjugate it.

Final Answer: UDP-glucuronosyltransferase 1A1 (UGT1A1) conjugates bilirubin. $\Rightarrow \boxed{D}$

Answer: (D) Go Back to Q29

Q30.

Solution

Concept – McArdle Disease (GSD Type V, Myophosphorylase Deficiency): **Myophosphorylase** (muscle-specific glycogen phosphorylase) is deficient in McArdle disease. Muscle cannot break down glycogen during exercise → **no lactate rise** on forearm ischaemic exercise test (lactate fails to rise because glycolysis from glycogen is blocked), while ammonia rises normally (purine nucleotide cycle intact). Features: exercise-induced **muscle cramps**, **myoglobinuria** (dark urine), **second wind phenomenon** (exercise tolerance improves after resting, when free fatty acids become available). CK is elevated at rest and dramatically after exercise. Treatment: avoid strenuous exercise; sucrose/glucose before exercise.

Distractors: (A) Pompe disease – acid maltase (alpha-glucosidase) deficiency; presents with cardiomegaly and hypotonia in infants. (B) Von Gierke – glucose-6-phosphatase deficiency; presents with fasting hypoglycaemia and hepatomegaly. (D) CPT-I deficiency causes hypoketotic hypoglycaemia and hepatomegaly, not exercise-induced myoglobinuria.

Final Answer: McArdle disease – myophosphorylase deficiency; no lactate rise with exercise. $\Rightarrow \boxed{C}$

Answer: (C) Go Back to Q30

Q31.

Solution

Concept – mRNA Splicing by the Spliceosome: Eukaryotic pre-mRNA contains exons and introns. Intron removal is catalysed by the **spliceosome**, a large ribonucleoprotein complex containing five **snRNAs: U1, U2, U4, U5, and U6** (as snRNPs – small nuclear ribonucleoproteins). Splicing proceeds by **two sequential transesterification reactions**: (i) The 2'-OH of the **branch point adenosine** (within the intron, ∼18–40 nt upstream of 3' splice site) attacks the 5' splice site → **lariat intermediate** (intron looped, still attached to exon 2). (ii) The free 3'-OH of exon 1 attacks the 3' splice site → exons joined; lariat intron released and degraded.

Distractors: (A) 16S/23S are ribosomal RNAs of bacteria; the spliceosome uses snRNAs, not rRNAs. (C) RNA components (snRNAs) are essential catalytic components of the spliceosome. (D) mRNA splicing is a co-transcriptional nuclear process, not reverse transcription.

Final Answer: U1/U2/U4/U5/U6 snRNAs; lariat intermediate formed by branch-point A attack. $\Rightarrow \boxed{B}$

Answer: (B) Go Back to Q31

Q32.

Solution

Concept – Thyroid peroxidase (TPO) and thyroid hormone synthesis: The biosynthesis of T3 and T4 involves: (i) Iodide uptake by the sodium-iodide symporter (NIS) at the basolateral membrane. (ii) **Organification**: **thyroid peroxidase (TPO)** oxidises iodide ($I^- \rightarrow I^0$) and iodates tyrosine residues on thyroglobulin $\rightarrow$ forming **MIT** (monoiodotyrosine) and **DIT** (diiodotyrosine). (iii) **Coupling**: TPO also couples MIT + DIT $\rightarrow$ T3 (triiodothyronine); DIT + DIT $\rightarrow$ T4 (thyroxine). **Propylthiouracil (PTU) and methimazole** inhibit TPO (and PTU also inhibits peripheral conversion of T4 $\rightarrow$ T3 by inhibiting deiodinase).

Distractors: (B) Thyroglobulin is the protein scaffold; it does not catalyse iodination itself. (C) Deiodinase removes iodine (for T4$\rightarrow$T3 conversion), not for organification. (D) Pendrin is the apical iodide transporter (iodide from cytoplasm to follicular lumen); it does not oxidise iodide.

Final Answer: Thyroid peroxidase (TPO) catalyses organification and coupling; inhibited by PTU and methimazole. $\Rightarrow \boxed{A}$

Answer: (A) Go Back to Q32

Q33.

Solution

Concept – Ethylene Glycol Poisoning and Oxalate Accumulation: Ethylene glycol (antifreeze) is metabolised by alcohol dehydrogenase (ADH): **Ethylene glycol** $\rightarrow$ **glycolaldehyde** $\rightarrow$ **glycolate** $\rightarrow$ **glyoxylate** $\rightarrow$ **oxalate**. Oxalate combines with calcium $\rightarrow$ **calcium oxalate monohydrate crystals** (envelope-shaped or dumbbell-shaped on urinalysis). Crystal deposition in renal tubules causes direct tubular toxicity and **acute kidney injury (AKI)**. Other features: high anion gap metabolic acidosis (glycolic and oxalic acids), early CNS depression (ethylene glycol itself), osmolar gap. Treatment: fomepizole (ADH inhibitor), ethanol, haemodialysis.

Distractors: (A) Glyoxylate IS converted to oxalate (not glycine primarily). (B) Ethylene glycol is not directly excreted; enzymatic conversion is required. (D) Ethanol competes with ethylene glycol for ADH (therapeutic use), but does not prevent oxalate formation when ethylene glycol is the substrate.

Final Answer: Ethylene glycol $\rightarrow$ glycolate $\rightarrow$ glyoxylate $\rightarrow$ oxalate $\rightarrow$ calcium oxalate crystals and AKI. $\Rightarrow \boxed{C}$

Answer: (C) Go Back to Q33

Q34.

Solution

Concept – Branched-Chain Amino Acids (BCAAs): The three **BCAAs are leucine, isoleucine, and valine** – all essential (cannot be synthesised by humans). They have a branched aliphatic side chain. Key features: (i) **Catabolised primarily in muscle** (not liver), because the initial transaminase (BCAA aminotransferase) is present in muscle, not liver. (ii) The second step (oxidative decarboxylation) is catalysed by **branched-chain α-keto acid dehydrogenase (BCKDH)**; deficiency causes MSUD. (iii) Metabolic fate: **Valine** – purely glucogenic; **Leucine** – purely ketogenic; **Isoleucine – both glucogenic and ketogenic** (the only BCAA with dual fate).

Distractors: (A) Phenylalanine and tryptophan are essential but not BCAAs by structural classification. (B) Alanine is not a BCAA; valine is glucogenic but leucine is not. (D) Methionine is not a BCAA; BCAAs are catabolised in muscle, not liver.

Final Answer: Leucine, isoleucine, valine; catabolised in muscle; isoleucine is glucogenic + ketogenic. $\Rightarrow \boxed{C}$

Answer: (C) Go Back to Q34

Q35.

Solution

Concept – Extrinsic pathway of coagulation (Factor VII + Tissue Factor): The **extrinsic pathway** is initiated when **Factor VII** binds **tissue factor (TF, Factor III)** exposed on subendothelial cells after vascular injury. The **TF-VIIa complex** activates **Factor X** (joining the common pathway) and also Factor IX. This pathway is measured by the **prothrombin time (PT/INR)**. The extrinsic pathway is physiologically the dominant initiating mechanism of haemostasis. Factor VII has the shortest half-life of all clotting factors ($\sim$4–6 h), so PT is the first test to become abnormal in warfarin therapy or liver disease.

Distractors: (A) Factor XII initiates the *intrinsic* (contact) pathway – measured by aPTT; Factor XII deficiency does not cause clinical bleeding. (C) Factor VIII is an intrinsic pathway cofactor; its deficiency causes haemophilia A (prolonged aPTT). (D) Thrombin (IIa) is the final common pathway product, not the initiating step.

Final Answer: Factor VII + Tissue Factor (TF) initiates the extrinsic pathway; measured by PT. $\Rightarrow \boxed{B}$

Answer: (B) Go Back to Q35

Q36.

Solution

Concept – Warfarin mechanism: inhibition of Vitamin K Epoxide Reductase (VKOR): Vitamin K is required for γ-carboxylation of clotting factors II, VII, IX, X, and anticoagulant proteins C and S. During this reaction, vitamin K (KH_2, reduced form) is oxidised to vitamin K epoxide (KO). **Vitamin K epoxide reductase (VKOR/VKORC1)** normally regenerates active KH_2 from KO. **Warfarin competitively inhibits VKOR**, depleting active vitamin K and impairing γ-carboxylation. The affected factors are not functional and cannot bind Ca^{2+}/phospholipid membranes. Warfarin resistance is caused by VKORC1 mutations; sensitivity is affected by CYP2C9 polymorphisms (metabolism) and VKORC1 haplotype.

Distractors: (A) γ-Glutamyl carboxylase uses vitamin K as cofactor; warfarin depletes the cofactor rather than inhibiting the enzyme directly. (C) Warfarin is an indirect anticoagulant; direct thrombin inhibitors include dabigatran and bivalirudin. (D) Warfarin actually reduces protein C levels (along with other vitamin K-dependent factors), causing a transient hypercoagulable state at initiation.

Final Answer: Warfarin inhibits Vitamin K Epoxide Reductase (VKOR), depleting active vitamin K. $\Rightarrow \boxed{B}$

Answer: (B) Go Back to Q36

Q37.

Solution

Concept – Gq/PLC-β/IP_3/DAG second messenger system: Receptors coupled to **Gq protein** activate **phospholipase C-β (PLC-β)**, which cleaves membrane **PIP_2** (phosphatidylinositol 4,5-bisphosphate) into two second messengers: (i) **IP_3** (inositol 1,4,5-trisphosphate) $\rightarrow$ binds IP_3R on endoplasmic reticulum $\rightarrow$ releases Ca^{2+} $\rightarrow$ activates calmodulin, protein kinases; (ii) **DAG** (diacylglycerol) $\rightarrow$ remains in membrane $\rightarrow$ activates **PKC**. Gq-coupled receptors: **α_1-adrenergic, M_1/M_3-muscarinic, H_1-histamine, vasopressin V_1, angiotensin AT_1, GnRH, TRH**.

Distractors: (A) Gs $\rightarrow$ cAMP $\rightarrow$ PKA: β-adrenergic, H_2, D_1, glucagon. (B) Gi $\rightarrow$ inhibits adenylyl cyclase: α_2-adrenergic, M_2, D_2, opioid. (D) G12 $\rightarrow$ Rho pathway: role in cell shape/migration.

Final Answer: Gq $\rightarrow$ PLC-β $\rightarrow$ IP_3 (Ca^{2+} release) + DAG (PKC activation). $\Rightarrow \boxed{C}$

Answer: (C) Go Back to Q37

Q38.

Solution

Concept – Tetrahydrobiopterin (BH4) deficiency: Atypical PKU: BH4 (tetrahydrobiopterin) is the essential cofactor for three aromatic amino acid hydroxylases: (i) **Phenylalanine hydroxylase** (Phe $\rightarrow$ Tyr), (ii) **Tyrosine hydroxylase** (Tyr $\rightarrow$ DOPA $\rightarrow$ dopamine/catecholamines), and (iii) **Tryptophan hydroxylase** (Trp $\rightarrow$ 5-hydroxytryptophan $\rightarrow$ serotonin). BH4 is also a cofactor for nitric oxide synthase. BH4 deficiency (from defects in GTP cyclohydrolase I, 6-pyruvoyltetrahydropterin synthase, or dihydrobiopterin reductase) causes **atypical PKU**: elevated phenylalanine + **severe neurological deterioration despite dietary restriction** because neurotransmitter synthesis is also impaired. Treatment requires BH4 supplementation + neurotransmitter precursors.

Distractors: (B) PLP (B6) is a cofactor for amino acid decarboxylases and transaminases, not hydroxylases. (C) TPP is for decarboxylation reactions (PDC, BCKDH). (D) FAD is for oxidative reactions; not the cofactor for aromatic hydroxylases.

Final Answer: BH4 deficiency impairs PAH + catecholamine/serotonin synthesis (atypical PKU). $\Rightarrow \boxed{A}$

Answer: (A) Go Back to Q38

Q39.

Solution

Concept – Zinc as enzyme cofactor: Zinc (Zn^{2+}) is the most abundant intracellular trace element after iron. It acts as a **Lewis acid** (electron pair acceptor) at enzyme active sites, activating water molecules for nucleophilic reactions. Key zinc-dependent enzymes: (i) **Carbonic anhydrase** (CA): $CO_2 + H_2O \rightleftharpoons HCO_3^- + H^+$; Zn^{2+} activates the water molecule. (ii) **Carboxypeptidase A** (digestion). (iii) **Alcohol dehydrogenase** (ethanol metabolism). (iv) **DNA polymerase and RNA polymerase** (Zn-finger domains). (v) **Superoxide dismutase** (Cu/Zn-SOD). Clinical features of zinc deficiency: growth retardation, hypogonadism, poor wound healing, **anosmia**, dysgeusia (loss of taste), dermatitis (acrodermatitis), immune deficiency.

Distractors: (B) Pyruvate carboxylase requires Mn^{2+} and biotin (not Zn). (C) Glutathione peroxidase requires **selenium** (as selenocysteine). (D) Cu/Zn-SOD does require zinc, but the Lewis acid catalytic role is most classically illustrated by carbonic anhydrase.

Final Answer: Zinc is the Lewis acid cofactor in carbonic anhydrase, carboxypep-

tidase, alcohol dehydrogenase, and DNA polymerase. $\Rightarrow \boxed{A}$

Answer: (A) Go Back to Q39

Q40.

Solution

Concept – Collagen Type IV and Alport Syndrome: Type IV collagen is a **non-fibrillar** collagen that forms a **sheet-like meshwork** (chicken-wire pattern) in all basement membranes, including the glomerular basement membrane (GBM), lens capsule, alveolar BM, and cochlear BM. It is composed of six α-chains ($\alpha 1$ through $\alpha 6$) in different combinations. **Alport syndrome** is caused by mutations in **COL4A3, COL4A4** (autosomal recessive/dominant) or **COL4A5** (X-linked; most common). Clinical features: **haematuria, progressive CKD, sensorineural hearing loss**, and anterior lenticonus. EM shows **irregular thinning, thickening, and splitting of the GBM** (basket-weave/lamellation pattern).

Distractors: (A) Type I collagen – fibrillar; major collagen of tendons, bone, skin, cornea, sclera; mutated in osteogenesis imperfecta. (C) Type II – fibrillar; articular cartilage, vitreous; mutated in chondrodysplasias. (D) Type III – reticular fibres; liver sinusoids, spleen, lymph nodes; low in Ehlers-Danlos type IV.

Final Answer: Type IV collagen – basement membrane meshwork; defective in Alport syndrome. $\Rightarrow \boxed{B}$

Answer: (B) Go Back to Q40

Answer Key – FMGE Biochemistry Sample Paper 3

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