FMGE Biochemistry Sample Paper – 9

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 malnourished woman with protein-energy malnutrition is found to have very low serum retinol despite adequate dietary vitamin A intake. She has no signs of liver disease. Further investigation reveals that retinol is not being transported from the liver to target tissues. Which of the following proteins is primarily responsible for transporting vitamin A (retinol) in the circulation?

(A) Retinol-binding protein (RBP)

(B) Albumin

(C) Transthyretin (TTR) alone

(D) Ceruloplasmin

Q2. An enzyme has optimal activity at pH 7.4 in the blood. The same enzyme, when exposed to pH 5.0, shows markedly reduced activity. Which of the following best explains why enzyme activity depends critically on pH?

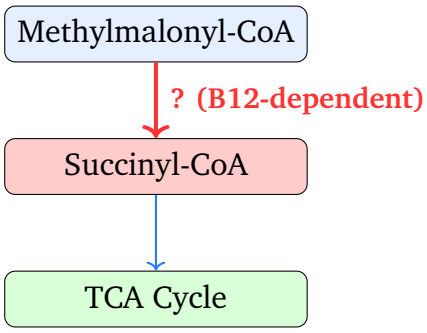
(A) Increased substrate concentration at acidic pH reduces V_{max}

(B) High pH denatures the enzyme by breaking peptide bonds

(C) Ionisation states of active-site residues (e.g., histidine, cysteine) are altered, disrupting catalysis and substrate binding

(D) Low pH increases the K_m by competitive inhibition

Q3. A 5-day-old neonate presents with metabolic acidosis, hyperammonaemia, hypoglycaemia, and lethargy. Urine organic acid analysis shows massively elevated methylmalonic acid. Blood cobalamin is normal but adenosylcobalamin is absent. The deficiency of which enzyme is responsible?



(A) Methylmalonyl-CoA mutase

(B) Propionyl-CoA carboxylase

(C) Methylmalonyl-CoA epimerase

(D) Succinyl-CoA synthetase

Q4. During the pay-off phase of glycolysis, 1,3-bisphosphoglycerate (1,3-BPG) is converted to 3-phosphoglycerate with the concomitant generation of ATP. This is the first substrate-level phosphorylation step in glycolysis. Which enzyme catalyses this reaction?

(A) Phosphoglycerate kinase (PGK)

(B) Phosphoglycerate mutase

(C) Enolase

(D) Pyruvate kinase

Q5. A physician is comparing the two dietary forms of vitamin D available for supplementation of patients with osteoporosis. Vitamin D2 (ergocalciferol) is derived from plant ergosterol by UV irradiation, while vitamin

D3 (cholecalciferol) is synthesised in human skin. Which of the following statements about the two forms is correct?

(A) D2 is more efficacious than D3 in raising serum 25-hydroxyvitamin D levels

(B) D3 is slightly more efficacious than D2 at raising serum 25-OH-D; both are hydroxylated by the same hepatic and renal enzymes

(C) D2 is synthesised from 7-dehydrocholesterol in skin on UV exposure

(D) D3 is derived from ergosterol in plants and fungi

Q6. A 40-year-old man with viral hepatitis has markedly elevated serum ALT. The reaction catalysed by alanine aminotransferase (ALT) is:

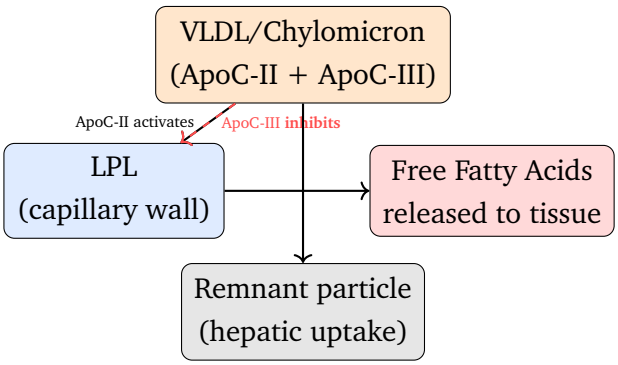
(A) Alanine + oxaloacetate $\rightleftharpoons$ pyruvate + aspartate

(B) Alanine + α-ketoglutarate $\rightleftharpoons$ pyruvate + glutamate

(C) Alanine + succinyl-CoA $\rightleftharpoons$ pyruvate + succinate

(D) Alanine + $NAD^+ \rightleftharpoons$ pyruvate + NADH + NH_3

Q7. A patient with hypertriglyceridaemia is found to have elevated circulating VLDL despite normal lipoprotein lipase (LPL) activity. A genetic study reveals loss-of-function mutation in LPL activator ApoC-II and overexpression of ApoC-III. Which of the following correctly describes ApoC-III's role in triglyceride metabolism?



(A) ApoC-III inhibits LPL activity and reduces hepatic remnant uptake, raising circulating triglycerides

(B) ApoC-III activates LPL, increasing triglyceride clearance

(C) ApoC-III is the structural protein of VLDL that binds LDL receptors

(D) ApoC-III transfers cholesterol ester to HDL via CETP

Q8. Linoleic acid (LA) and α-linolenic acid (ALA) are classified as essential fatty acids. Which of the following correctly identifies the structural features that make them essential in the human diet?

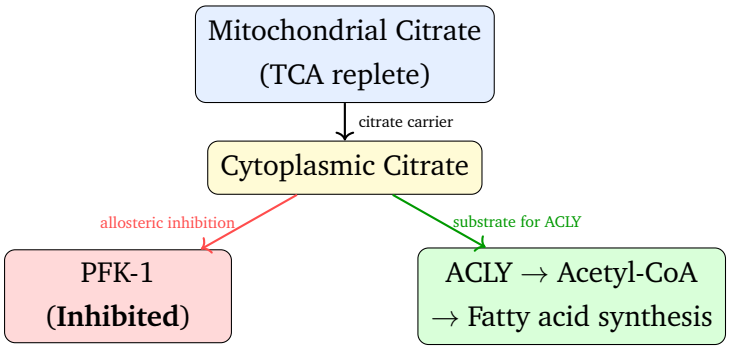
(A) LA is 20:4 Δ5,8,11,14 (n-6); ALA is 20:5 Δ5,8,11,14,17 (n-3)

(B) LA is 18:1 Δ9 (n-9); ALA is 18:2 Δ9,12 (n-6)

(C) Both have saturated backbones, but contain unusual methyl branches at the ω-end

(D) LA is 18:2 Δ9,12 (n-6); ALA is 18:3 Δ9,12,15 (n-3); humans lack Δ12 and Δ15 desaturases

Q9. After a high-carbohydrate meal, citrate accumulates in the mitochondria and is exported to the cytoplasm. In the cytoplasm, citrate performs two key roles. Which of the following correctly describes both roles of cytoplasmic citrate?



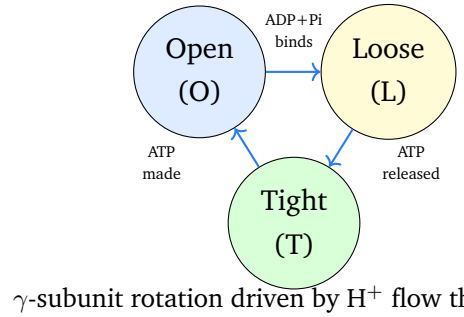
(A) Citrate inhibits pyruvate kinase and activates HMG-CoA synthase

(B) Citrate allosterically inhibits PFK-1 (signalling glycolysis is not needed) and provides acetyl-CoA for fatty acid synthesis via ATP-citrate lyase (ACLY)

(C) Citrate activates phosphofructokinase-2 and inhibits acetyl-CoA carboxylase

(D) Citrate activates glycogen synthase and inhibits glucose-6-phosphatase

Q10. Complex V (F_0F_1 ATP synthase) uses the proton gradient across the inner mitochondrial membrane to synthesise ATP. Which of the following correctly describes the binding-change mechanism of ATP synthase?



γ-subunit rotation driven by H^+ flow through F_0

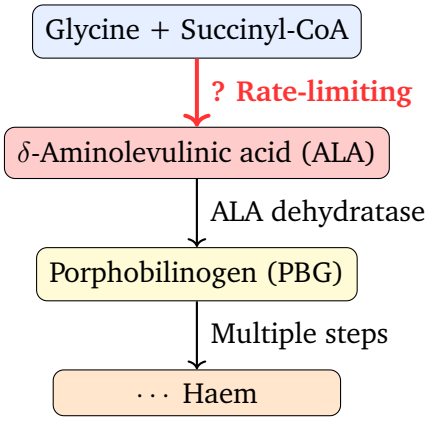
(A) Proton flow through the α-subunit of F_1 directly phosphorylates ADP

(B) Rotation of the F_0 ε-subunit alone generates a direct chemical bond between phosphate and ADP

(C) Proton flow through the F_0 c-ring drives rotation of the γ-subunit, inducing sequential conformational changes (O→L→T→O) in the three β-subunits of F_1 to synthesise ATP

(D) The β-subunits each synthesise ATP simultaneously when the proton gradient exceeds a threshold

Q11. A 28-year-old woman develops acute abdominal pain, neuropsychiatric symptoms, and port-wine coloured urine after starting oral contraceptive pills. Urine porphobilinogen (PBG) is markedly elevated. The first and rate-limiting step of haem biosynthesis, which is derepressed in acute porphyrias by drugs that induce CYP450, is catalysed by which enzyme?



(A) ALA dehydratase (porphobilinogen synthase)

(B) Uroporphyrinogen decarboxylase

(C) Ferrochelatase

(D) ALA synthase (ALAS)

Q12. A 45-year-old man of Northern European ancestry presents with fatigue, bronze skin discolouration, hepatomegaly, and impotence. Serum ferritin is 1800 ng/mL and transferrin saturation is 88%. Liver biopsy shows periportal iron deposition. Genetic testing reveals homozygous C282Y mutation in HFE gene. Which of the following laboratory findings is most characteristic of hereditary haemochromatosis?

(A) Transferrin saturation $>$50% (often $>$70–80%) with elevated serum ferritin

(B) Low serum ferritin with normal transferrin saturation

(C) Elevated TIBC with low transferrin saturation

(D) Normal transferrin saturation with elevated serum iron

Q13. A molecular biology laboratory is studying the regulation of TNF-α mRNA stability. They find that the mRNA has a very short half-life and is rapidly degraded after inflammatory stimuli resolve. Which RNA structural element, located in the 3′-UTR of cytokine and proto-oncogene mRNAs, promotes rapid mRNA decay by binding destabilising proteins that accelerate deadenylation?

(A) Internal ribosome entry site (IRES)

(B) Iron-response element (IRE) stem-loop

(C) AU-rich elements (AREs; AUUUA pentamers and UUAUUUAUU nonamers)

(D) Kozak sequence

Q14. A medical student is studying the regulation of blood glucose between meals. She notes that liver glycogen is the primary source of blood glucose, but muscle glycogen cannot directly release glucose into the blood.

The enzyme responsible for this difference, which is present in liver and kidney but absent in skeletal muscle, is:

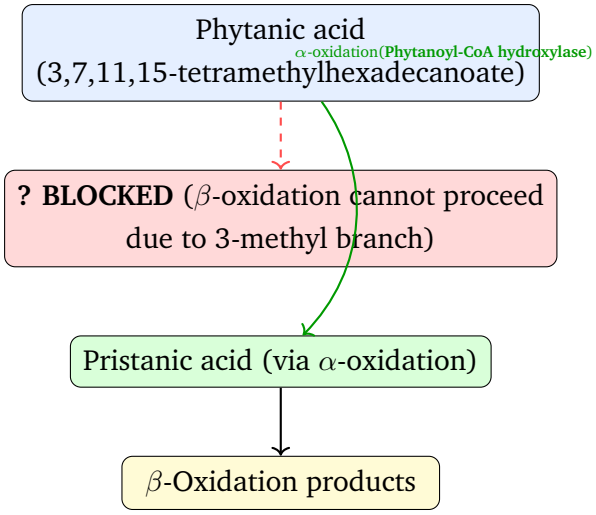
(A) Glycogen phosphorylase

(B) Glucose-6-phosphatase

(C) Glucokinase

(D) Glycogen synthase

Q15. A 20-year-old man presents with retinitis pigmentosa, polyneuropathy, cerebellar ataxia, and sensorineural deafness. His diet includes large amounts of dairy products and ruminant meat (rich in chlorophyll). Plasma phytanic acid is markedly elevated. The enzyme deficient in this peroxisomal disorder is:



(A) Very-long-chain acyl-CoA dehydrogenase (VLCAD)

(B) α-Methylacyl-CoA racemase (AMACR)

(C) Phytanoyl-CoA hydroxylase (α-phytanoyl-CoA dioxygenase)

(D) Pristanoyl-CoA oxidase

Q16. A researcher studying occupational toxins finds that the insecticide rotenone (used in organic farming and as a fish poison) causes selective degeneration of dopaminergic neurons in the substantia nigra, mimicking Parkinson's disease. Which complex of the mitochondrial electron transport chain is inhibited by rotenone?

(A) Complex II (succinate-CoQ reductase)

(B) Complex III (cytochrome bc_1 complex)

(C) Complex I (NADH-ubiquinone oxidoreductase)

(D) Complex IV (cytochrome c oxidase)

Q17. A newborn is identified on expanded newborn screening (MS/MS) by an elevated C4 acylcarnitine (butyrylcarnitine) peak. The infant has variable clinical findings including hypotonia and developmental delay. Urine organic acids show elevated ethylmalonic acid. The enzyme deficient in this condition catalyses the first step of β-oxidation of short-chain fatty acids. It is:

(A) Medium-chain acyl-CoA dehydrogenase (MCAD)

(B) Long-chain acyl-CoA dehydrogenase (LCAD)

(C) Glutaryl-CoA dehydrogenase

(D) Short-chain acyl-CoA dehydrogenase (SCAD)

Q18. A type 1 diabetic is brought to the emergency department with hypoglycaemia. To assess whether the hypoglycaemia is due to exogenous insulin injection (factitious hypoglycaemia) or endogenous hyperinsulinism (e.g., insulinoma), which laboratory test is most useful?

(A) Serum proinsulin only

(B) Fasting serum insulin level alone

(C) Serum C-peptide level

(D) Urinary ketones

Q19. In recombinant DNA technology, a gene of interest is cloned into a bacterial plasmid vector. Plasmids are useful as cloning vectors because of which fundamental property?

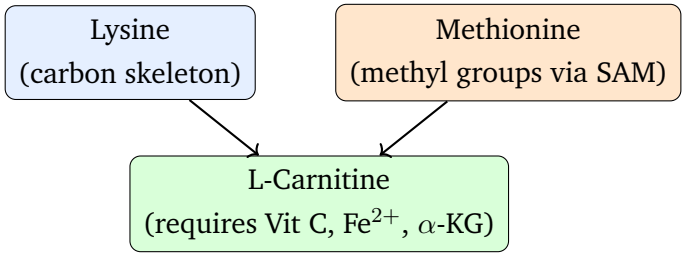
(A) Plasmids are linear DNA molecules that integrate into the bacterial chromosome

(B) Plasmids are circular extrachromosomal DNA with their own origin of replication, enabling autonomous replication in host cells

(C) Plasmids lack antibiotic resistance genes, making selection easier

(D) Plasmids require viral coat proteins to replicate inside bacteria

Q20. A premature infant in the ICU is found to have carnitine deficiency. Carnitine is essential for transport of long-chain fatty acids into mitochondria. The two amino acid precursors from which L-carnitine is biosynthesised are:



(A) Tryptophan and serine

(B) Lysine and methionine

(C) Tyrosine and leucine

(D) Arginine and glycine

Q21. A 12-year-old boy from a rural area presents with a photosensitive, pellagra-like rash on sun-exposed areas, cerebellar ataxia, and psychiatric disturbances. Urine amino acid analysis shows excess neutral aminoaciduria (including tryptophan). His symptoms improve with oral nicotinamide supplementation. Which transport defect explains this presentation?

(A) Defective cystine transporter (SLC3A1) in renal tubules

(B) Defective dibasic amino acid transporter causing elevated urine ornithine

(C) Defective SLC6A19 (B^0AT1) neutral amino acid transporter causing intestinal and renal tryptophan malabsorption (Hartnup disease)

(D) Defective PEPT1 dipeptide transporter in jejunum

Q22. A biochemistry student is calculating ATP yields. $FADH_2$ generated in the TCA cycle (e.g., by succinate dehydrogenase) donates electrons to ubiquinone (CoQ), bypassing Complex I. Using modern P/O ratios, what is the ATP yield per molecule of $FADH_2$ oxidised?

(A) 1.5 ATP

(B) 2.5 ATP

(C) 2.0 ATP

(D) 3.0 ATP

Q23. A 50-year-old man with type 2 diabetes undergoes a glucose clamp study. His pancreatic β-cells release insulin proportionally to rising blood glucose even at high glucose concentrations (14–20 mM), unlike other tissues that respond maximally at lower concentrations. This is because the glucose-sensing enzyme in β-cells has a high K_m and is not inhibited by its product, glucose-6-phosphate. This enzyme is:

(A) Glucokinase (hexokinase IV)

(B) Hexokinase I

(C) Phosphoglucose isomerase

(D) Glucose-6-phosphatase

Q24. A patient is started on low-dose aspirin for secondary prevention of myocardial infarction. Aspirin irreversibly inhibits COX-1 in platelets, reducing the synthesis of a potent platelet aggregator and vasoconstrictor derived from arachidonic acid. This prostaglandin-like mediator with a very short half-life (approximately 30 seconds) is:

(A) Prostacyclin (PGI_2)

(B) Leukotriene B_4 (LTB_4)

(C) Prostaglandin E_2 (PGE_2)

(D) Thromboxane A_2 (TXA_2)

Q25. In multiple sclerosis (MS) research, a protein is being investigated as a target of autoimmune demyelination. This protein is the major structural protein of compact myelin in the central nervous system, is highly positively charged (rich in lysine and arginine), and interacts with the cytoplasmic faces of the myelin lipid bilayer. Antibodies to this protein are used in experimental autoimmune encephalomyelitis (EAE) models. This protein is:

(A) Myelin basic protein (MBP)

(B) Myelin-associated glycoprotein (MAG)

(C) Proteolipid protein (PLP)

(D) Myelin oligodendrocyte glycoprotein (MOG)

Q26. Phytanic acid accumulates in Refsum disease because it cannot undergo β-oxidation directly. The specific structural feature of phytanic acid that prevents direct β-oxidation, and the oxidation pathway that must first be used, are:

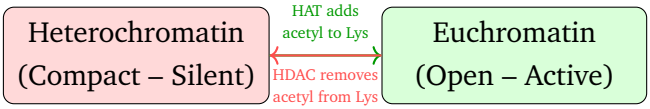
(A) Phytanic acid is a very-long-chain fatty acid (>22 carbons) and requires peroxisomal β-oxidation before mitochondrial β-oxidation

(B) Phytanic acid is polyunsaturated and requires an isomerase before β-oxidation

(C) Phytanic acid contains an odd-carbon chain and produces propionyl-CoA requiring B12-dependent mutase

(D) Phytanic acid has a methyl group at the β-carbon (C-3) that blocks β-oxidation; it first undergoes α-oxidation (removing C-1 as CO_2) to produce pristanic acid, which can then undergo β-oxidation

Q27. A haematologist is studying lymphoma cells and finds that treatment with an HDAC inhibitor (vorinostat) reactivates silenced tumour-suppressor genes. Which of the following best describes the mechanism by which histone acetylation leads to gene activation?



(A) Acetylation adds a negative charge to lysine, increasing histone binding to negatively charged DNA

(B) Acetylation methylates cytosine residues in DNA, silencing gene expression

(C) Acetylation of the ε-amino group of histone lysines neutralises the positive charge, loosening histone-DNA interactions and making chromatin accessible to transcription factors

(D) Acetylation cross-links histone tails to the major groove of DNA, stabilising the nucleosome

Q28. A student calculates the number of protons pumped per NADH oxidised through the full mitochondrial electron transport chain (Complexes I, III, and IV). Considering the established stoichiometry for each complex, what is the total number of protons translocated per NADH oxidised?

(A) 6 H^+ per NADH

(B) 8 H^+ per NADH

(C) 12 H^+ per NADH

(D) 10 H^+ per NADH (4 by Complex I + 4 by Complex III + 2 by Complex IV)

Q29. A patient with classical PKU is placed on a strict phenylalanine-restricted diet. The dietitian notes that even on this diet, tyrosine must be supplemented. This is because tyrosine, which is normally synthesised from phenylalanine by phenylalanine hydroxylase (PAH), becomes essential in PKU. In what other clinical condition does tyrosine become conditionally essential?

(A) When PAH enzyme is deficient or when dietary phenylalanine is severely restricted; also in premature infants with immature PAH

(B) When dietary protein intake exceeds 2 g/kg/day

(C) In renal failure due to impaired amino acid reabsorption

(D) In vitamin C deficiency because ascorbate is required for tyrosine synthesis

Q30. A 25-year-old medical student of West African descent is told he is a carrier of sickle cell trait (HbAS). His physician explains that he has relative protection against a life-threatening infection. Against which pathogen does sickle cell heterozygosity confer partial protection, explaining the high prevalence of HbS in certain geographic regions?

(A) *Mycobacterium tuberculosis*

(B) *Plasmodium falciparum* (malaria)

(C) *Leishmania donovani*

(D) *Trypanosoma brucei*

Q31. A newly synthesised protein destined for secretion is found to be translated on ribosomes bound to the rough endoplasmic reticulum. The co-translational targeting of this protein to the ER membrane is initiated by which structural feature at the N-terminus of the nascent polypeptide?

(A) A C-terminal KDEL retention sequence

(B) A mannose-6-phosphate (M6P) tag added in the Golgi

(C) An N-terminal hydrophobic signal peptide recognised by the signal recognition particle (SRP)

(D) A GPI anchor addition in the ER lumen

Q32. A researcher studying adipokines finds that a patient with morbid obesity has very low circulating levels of an adipose-tissue-derived hormone that normally activates AMPK, increases fatty acid oxidation, and improves insulin sensitivity. Serum levels of this adipokine are inversely proportional to body fat mass. This adipokine is:

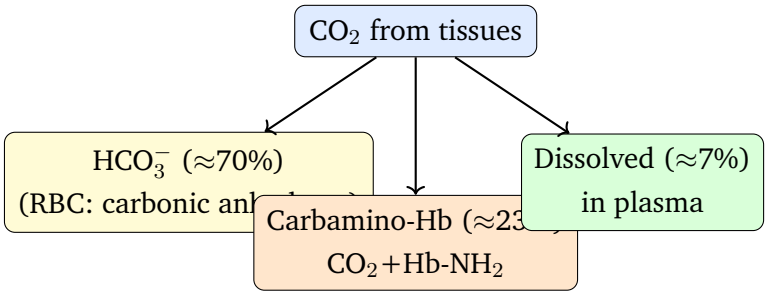
(A) Leptin

(B) Adiponectin

(C) Resistin

(D) TNF-α

Q33. A medical student studying respiratory physiology reviews CO_2 transport in blood. Approximately 70% is carried as bicarbonate (HCO_3^-), 23% as carbamino-haemoglobin, and 7% dissolved in plasma. Which of the following statements about CO_2 transport is correct?



(A) CO_2 combines with albumin to form carbamino complexes in plasma (primary transport form)

(B) The majority of CO_2 is transported dissolved as CO_2 gas in plasma

(C) Haemoglobin binds CO_2 at its iron-containing haem groups

(D) The largest fraction of CO_2 is transported as HCO_3^- formed in RBCs by carbonic anhydrase; the H^+ generated is buffered by haemoglobin (Haldane effect)

Q34. In a clinical laboratory, enzyme activity is reported in International Units (IU or U). A biochemist asks a junior colleague the standard definition of one International Unit of enzyme activity. The correct answer is:

(A) The amount of enzyme that converts 1 micromole (μmol) of substrate per minute under specified conditions (temperature, pH, substrate concentration)

(B) The amount of enzyme that produces 1 mole of product per second (this is the SI unit, katal)

(C) The amount of enzyme that raises absorbance at 340 nm by 1 unit per minute

(D) The amount of enzyme present in 1 mL of serum

Q35. A 4-day-old neonate presents with non-ketotic hypoglycaemia, elevated plasma dicarboxylic acids, and metabolic acidosis. Plasma 3-hydroxy-3-methylglutaric acid is markedly elevated. The parents are found to be

consanguineous. The deficient mitochondrial enzyme in this condition, which is distinct from the cytoplasmic enzyme targeted by statins, is:

(A) HMG-CoA reductase (mitochondrial isoform)

(B) HMG-CoA synthase

(C) β-Ketothiolase (mitochondrial acetoacetyl-CoA thiolase)

(D) HMG-CoA lyase

Q36. A physician treating a patient with pyruvate dehydrogenase complex (PDC) deficiency considers using dichloroacetate (DCA) therapy. DCA acts by inhibiting pyruvate dehydrogenase kinase (PDK). In the normal regulation of PDC, PDK phosphorylates and inactivates the E1 subunit. Which signals activate PDK, leading to PDC inactivation?

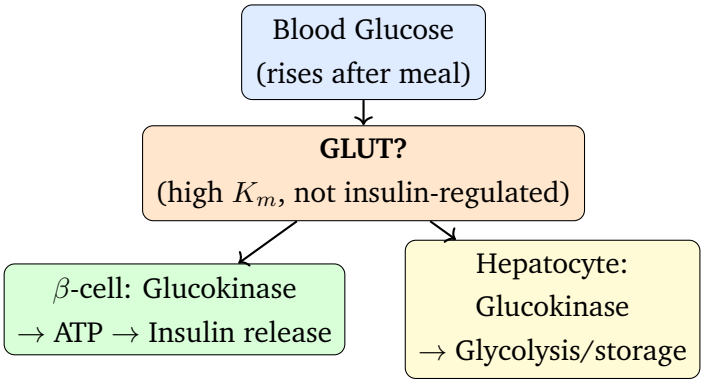
(A) Low NADH/NAD^+ ratio, low acetyl-CoA/CoA ratio, low ATP

(B) High AMP, high pyruvate, low NADH

(C) Low acetyl-CoA, high CoA, elevated pyruvate

(D) High NADH/NAD^+ ratio, high acetyl-CoA/CoA ratio, high ATP (signals of mitochondrial energy sufficiency)

Q37. A biochemist studying glucose transporters notes that pancreatic β-cells and hepatocytes express a glucose transporter that is not saturated at normal fasting blood glucose levels (5 mM) because its K_m for glucose is very high (15–20 mM). This transporter is not regulated by insulin and functions as a glucose sensor. It is:



(A) GLUT4 (insulin-regulated, found in muscle and adipose)

(B) GLUT2 (high K_m glucose sensor in liver and pancreatic β-cells)

(C) GLUT1 (ubiquitous, low K_m, constitutively active)

(D) GLUT3 (brain, very high affinity for glucose)

Q38. A patient with familial defective ApoB-100 (FDB) has elevated LDL-cholesterol because LDL particles are not efficiently cleared from circulation. The full-length ApoB-100 is the sole apolipoprotein on LDL, IDL, and VLDL, and is essential for LDL receptor binding. Which specific mutation in ApoB-100 causes familial defective ApoB-100 (FDB)?

(A) Deletion of the first 48 amino acids of ApoB (truncation causing ApoB-48 phenotype)

(B) Loss-of-function mutation in the LDLR gene (this causes FH, not FDB)

(C) Gain-of-function mutation in PCSK9 causing increased LDLR degradation

(D) Arg3500Gln (R3500Q) missense mutation that reduces ApoB-100 binding to LDL receptor

Q39. A premature neonate at 30 weeks gestation develops haemolytic anaemia on day 10 of life. The mother's vitamin intake during pregnancy was not monitored. Laboratory investigations reveal haemolysis with elevated plasma malondialdehyde (lipid peroxidation marker). Peripheral smear shows eccentrocytes. This form of haemolytic anaemia in premature infants is caused by deficiency of which fat-soluble vitamin?

(A) Vitamin A

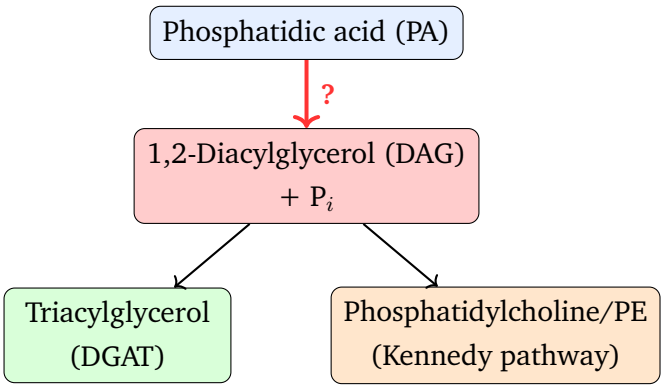
(B) Vitamin E (α-tocopherol)

(C) Vitamin D

(D) Vitamin K

Q40. In the synthesis of triacylglycerols (TG) in liver cells, phosphatidic acid (PA) is a key intermediate. PA must be dephosphorylated to 1,2-diacylglycerol

(DAG) before TG or phospholipid synthesis can proceed. The enzyme that catalyses this dephosphorylation is:



(A) Diacylglycerol acyltransferase (DGAT)

(B) Phospholipase D (PLD)

(C) Phosphatidate phosphatase (lipin-1)

(D) Lysophosphatidic acid acyltransferase (LPAAT)

Detailed Solutions

Q1.

Solution

Concept – Retinol-binding protein (RBP): Vitamin A (retinol) is transported in the bloodstream bound to **retinol-binding protein (RBP)**, which is synthesised in the liver. RBP circulates as a complex with **transthyretin (TTR)**, which prevents renal filtration of the small RBP molecule. In protein-energy malnutrition, RBP synthesis is impaired despite adequate liver retinol stores – this causes functional vitamin A deficiency even without dietary insufficiency. RBP4, an adipokine isoform, is linked to insulin resistance.

Distractors: Albumin binds fatty acids, bilirubin, and drugs but not retinol specifically. TTR alone does not bind retinol; it binds RBP. Ceruloplasmin transports copper, not retinol.

Final Answer: Retinol-binding protein (RBP). $\Rightarrow \boxed{A}$

Answer: (A) Go Back to Q1

Q2.

Solution

Concept – pH and enzyme activity: Each enzyme has an optimal pH at which its active-site residues are in the correct ionisation states for substrate binding and catalysis. Histidine (pKa ≈6), cysteine, lysine, and glutamate are common active-site residues. Deviation from optimal pH **alters ionisation** of these residues (protonation or deprotonation), disrupting their ability to act as acid-base catalysts or to interact with substrate – reducing V_{max} and/or K_m. Extreme pH causes irreversible denaturation (breaking non-covalent interactions, not peptide bonds).

Distractors: Substrate concentration does not change with pH. Peptide bonds are hydrolysed only by extreme acid/base or proteases, not physiological pH ranges. pH changes enzyme activity, not K_m via competitive inhibition.

Final Answer: Ionisation of active-site residues is altered. $\Rightarrow \boxed{C}$

Answer: (C) Go Back to Q2

Q3.

Solution

Concept – Methylmalonyl-CoA mutase deficiency: Methylmalonyl-CoA mutase is a vitamin B12 (adenosylcobalamin)-dependent enzyme that converts

methylmalonyl-CoA → succinyl-CoA. Deficiency results in accumulation of methylmalonic acid (methylmalonic acidaemia/aciduria). Two forms: mut^0 (no residual enzyme – adenosylcobalamin unresponsive) and mut^- (responsive). Neonatal presentation: metabolic acidosis, hyperammonaemia, hypoglycaemia, and neurological deterioration. Treatment: protein restriction, vitamin B12 supplementation (in responsive forms), carnitine.

Distractors: Propionyl-CoA carboxylase (biotin-dependent) converts propionyl-CoA to methylmalonyl-CoA – a preceding step. Methylmalonyl-CoA epimerase converts D-methylmalonyl-CoA to L-form. Succinyl-CoA synthetase is a TCA enzyme downstream.

Final Answer: Methylmalonyl-CoA mutase. $\Rightarrow \boxed{A}$

Answer: (A) Go Back to Q3

Q4.

Solution

Concept – Phosphoglycerate kinase (PGK) – first ATP-generating step of glycolysis: Phosphoglycerate kinase (PGK) catalyses the transfer of the high-energy phosphate from the C-1 acyl-phosphate of 1,3-BPG to ADP, generating ATP and 3-phosphoglycerate. This is the **first substrate-level phosphorylation** in glycolysis. The reaction requires Mg^{2+}. PGK1 deficiency (X-linked) causes haemolytic anaemia, myopathy, and neurological dysfunction. Note: substrate-level phosphorylation means the phosphate comes directly from the substrate molecule.

Distractors: Phosphoglycerate mutase converts 3-PG to 2-PG (no ATP). Enolase converts 2-PG to PEP (no ATP). Pyruvate kinase generates the second ATP in the pay-off phase (PEP → pyruvate).

Final Answer: Phosphoglycerate kinase (PGK). $\Rightarrow \boxed{A}$

Answer: (A) Go Back to Q4

Q5.

Solution

Concept – Vitamin D2 vs D3: Vitamin D3 (cholecalciferol) is synthesised in human skin from 7-dehydrocholesterol upon UV-B irradiation (previtamin D3 → D3 by thermal isomerisation). **Vitamin D2 (ergocalciferol)** is derived from plant sterol ergosterol by UV irradiation. Both are hydroxylated by CYP27A1/CYP2R1 in liver (to 25-OH-D) and CYP27B1 in kidney (to 1,25-OH_2-D, calcitriol – the active form). D3 is slightly more efficacious at raising serum 25-OH-D levels due to

higher affinity for vitamin D-binding protein (VDBP), giving it a longer half-life.

Distractors: D2 is less, not more, efficacious. D3 comes from 7-dehydrocholesterol in skin, not ergosterol. D2 (not D3) is derived from ergosterol in plants.

Final Answer: D3 is slightly more efficacious; both share the same hepatic and renal hydroxylation enzymes. $\Rightarrow \boxed{B}$

Answer: (B) Go Back to Q5

Q6.

Solution

Concept – ALT (Alanine aminotransferase) reaction: ALT catalyses the reversible transamination: **alanine + α-ketoglutarate $\rightleftharpoons$ pyruvate + glutamate**. The cofactor is pyridoxal phosphate (PLP, vitamin B6). ALT is found predominantly in the liver cytosol, making it the most liver-specific aminotransferase. ALT is significantly elevated in viral hepatitis, where ALT>AST. In alcoholic liver disease, AST>ALT (ratio >2:1) because alcohol specifically damages mitochondria (raising mitochondrial AST).

Distractors: Aspartate aminotransferase (AST) uses aspartate + α-ketoglutarate $\rightleftharpoons$ oxaloacetate + glutamate. ALT does not interact with succinyl-CoA or NAD^+ directly.

Final Answer: Alanine + α-ketoglutarate $\rightleftharpoons$ pyruvate + glutamate. $\Rightarrow \boxed{B}$

Answer: (B) Go Back to Q6

Q7.

Solution

Concept – ApoC-III inhibits LPL: ApoC-III is present on VLDL and chylomicrons and acts as an endogenous inhibitor of lipoprotein lipase (LPL). It competes with **ApoC-II** (the LPL activator) and also inhibits hepatic remnant uptake by blocking ApoE-receptor interactions. High ApoC-III levels $\rightarrow$ reduced TG clearance $\rightarrow$ hypertriglyceridaemia. Loss-of-function mutations in ApoC-III $\rightarrow$ very low TG and reduced cardiovascular disease risk. Volanesorsen (ApoC-III antisense oligonucleotide) is approved for familial chylomicronaemia syndrome.

Distractors: ApoC-II (not C-III) activates LPL. ApoC-III is not the structural protein of VLDL (that is ApoB-100). CETP mediates CE transfer between HDL and VLDL (not ApoC-III).

Final Answer: ApoC-III inhibits LPL and reduces hepatic remnant uptake, raising triglycerides. $\Rightarrow \boxed{A}$

Answer: (A) Go Back to Q7

Q8.

Solution

Concept – Essential fatty acid structure: Linoleic acid (LA): 18:2 Δ9,12 (n-6/omega-6 family). α**-Linolenic acid (ALA)**: 18:3 Δ9,12,15 (n-3/omega-3 family). Humans lack Δ12 and Δ15 desaturases and thus cannot introduce double bonds at the n-6 or n-3 positions – making LA and ALA **essential** (must be obtained from diet). LA is the precursor of arachidonic acid (20:4, n-6); ALA is the precursor of EPA and DHA (n-3, synthesised inefficiently). Sources: LA – sunflower/soybean oil; ALA – flaxseed, walnuts, chia.

Distractors: Option A describes arachidonic acid (LA metabolite) and EPA (ALA metabolite), not LA and ALA themselves. Option B describes oleic acid and LA (incorrect assignments). Option C is incorrect – EFAs are polyunsaturated, not saturated.

Final Answer: LA is 18:2 Δ9,12 (n-6); ALA is 18:3 Δ9,12,15 (n-3); humans lack Δ12 and Δ15 desaturases. $\Rightarrow \boxed{D}$

Answer: (D) Go Back to Q8

Q9.

Solution

Concept – Cytoplasmic citrate dual role: When the TCA cycle is replete, citrate exits the mitochondria via the citrate carrier (tricarboxylate transporter). In the cytoplasm: (1) **Allosteric inhibition of PFK-1** – citrate directly inhibits phosphofructokinase-1, signalling that energy status is high and glycolysis is not needed; (2) **Substrate for ATP-citrate lyase (ACLY)** – ACLY cleaves citrate into acetyl-CoA + oxaloacetate, providing the acetyl-CoA building block for de novo fatty acid synthesis. Cytoplasmic citrate also activates acetyl-CoA carboxylase (ACC), the first committed enzyme of fatty acid synthesis.

Distractors: Citrate does not inhibit pyruvate kinase (that is alanine and ATP). Citrate activates, not inhibits, ACC. Citrate has no direct effect on glycogen synthase or glucose-6-phosphatase.

Final Answer: Citrate inhibits PFK-1 and provides acetyl-CoA for fatty acid synthesis via ACLY. $\Rightarrow \boxed{B}$

Answer: (B) Go Back to Q9

Q10.

Solution

Concept – F_0F_1 ATP synthase binding-change mechanism: Protons flow through the **F_0 c-ring** (10 subunits in humans) driven by the electrochemical gradient. This drives rotation of the c-ring, which is coupled to the **γ-subunit** (central stalk) of F_1. The rotating γ-subunit sequentially induces conformational changes in the three β-subunits of F_1 (the catalytic sites): **Open (O)** – substrate release; **Loose (L)** – ADP + Pi bind; **Tight (T)** – spontaneous ATP synthesis. Approximately 3 H^+ per ATP (= 10 H^+ per turn / 3 β-sites). Boyer (Nobel 1997).

Distractors: The α-subunit is structural, not the proton channel. The ε-subunit assists coupling but does not directly phosphorylate ADP. All three β-subunits work sequentially, not simultaneously.

Final Answer: Proton flow through F_0 c-ring drives γ-subunit rotation $\rightarrow$ O$\rightarrow$L$\rightarrow$T$\rightarrow$O conformational changes in β-subunits. $\Rightarrow \boxed{C}$

Answer: (C) Go Back to Q10

Q11.

Solution

Concept – ALA synthase (ALAS) – rate-limiting step of haem biosynthesis: The first and rate-limiting step of haem biosynthesis is catalysed by **ALA synthase (ALAS)**: glycine + succinyl-CoA $\rightarrow$ δ-aminolevulinic acid (ALA) + CO_2. This reaction requires **pyridoxal phosphate (PLP, vitamin B6)** and occurs in the **mitochondrial matrix**. ALAS1 (hepatic) is regulated by haem feedback inhibition and induced by drugs that induce CYP450 (e.g., OCP, barbiturates, rifampicin) – explaining acute porphyria attacks. ALAS2 (erythroid) is regulated by iron (iron-response element).

Distractors: ALA dehydratase is the second step (two ALA $\rightarrow$ PBG). Uroporphyrinogen decarboxylase is deficient in porphyria cutanea tarda. Ferrochelatase inserts Fe^{2+} into protoporphyrin IX (last step – inhibited by lead).

Final Answer: ALA synthase (ALAS). $\Rightarrow \boxed{D}$

Answer: (D) Go Back to Q11

Q12.

Solution

Concept – Hereditary haemochromatosis (HFE gene, C282Y): In hereditary haemochromatosis, the HFE C282Y mutation prevents normal hepcidin regulation $\rightarrow$ hepcidin levels are inappropriately low $\rightarrow$ excess ferroportin activity $\rightarrow$ uncontrolled iron absorption from gut and release from macrophages. This leads to iron overload with: **transferrin saturation >50% (often 70–90%)** and markedly elevated serum ferritin. Clinical features: bronze diabetes, hepatic cirrhosis, cardiomyopathy, hypogonadism, arthropathy. Treatment: phlebotomy. Transferrin saturation is the most sensitive early screening test.

Distractors: Low ferritin with normal transferrin saturation suggests iron deficiency (opposite). Elevated TIBC with low saturation is also iron deficiency. Normal saturation with elevated serum iron does not match haemochromatosis.

Final Answer: Transferrin saturation >50%, elevated serum ferritin. $\Rightarrow \boxed{A}$

Answer: (A) Go Back to Q12

Q13.

Solution

Concept – AU-rich elements (AREs) in mRNA 3′-UTR: AU-rich elements (AREs) are RNA sequences containing AUUUA pentamers (and UUAUUUAUU nonamers) located in the 3′-UTR of short-lived mRNAs encoding cytokines (TNF-α, GM-CSF, IL-2), proto-oncogenes (c-fos, c-jun), and growth factors. ARE-binding proteins (ARE-BPs) promote rapid mRNA deadenylation, decapping, and degradation, enabling cells to rapidly shut off inflammatory responses. This is a critical post-transcriptional gene regulatory mechanism.

Distractors: IRES allows cap-independent translation initiation (found in viral/stress mRNAs). IRE stem-loops regulate iron metabolism (ferritin, TfR) by binding IRP proteins. The Kozak sequence is near the AUG start codon for ribosome recognition.

Final Answer: AU-rich elements (AREs). $\Rightarrow \boxed{C}$

Answer: (C) Go Back to Q13

Q14.

Solution

Concept – Glucose-6-phosphatase distribution: Glucose-6-phosphatase (an ER membrane enzyme) is present only in **liver, kidney cortex, and intestinal**

epithelium – tissues capable of releasing glucose into the blood. It is completely absent from skeletal muscle and brain. Therefore, muscle glycogen can only be used locally (for muscle energy), it cannot export glucose to maintain blood glucose. Liver glycogen is the primary buffer between meals; a 70 kg adult has ∼100 g liver glycogen providing ∼8–12 hours of fasting glucose.

Distractors: Glycogen phosphorylase is present in both liver and muscle (different isoforms). Glucokinase is in liver and β-cells. Glycogen synthase is ubiquitous.

Final Answer: Glucose-6-phosphatase. $\Rightarrow \boxed{B}$

Answer: (B) Go Back to Q14

Q15.

Solution

Concept – Refsum disease (α-phytanoyl-CoA hydroxylase deficiency): Refsum disease is an autosomal recessive peroxisomal disorder due to deficiency of **phytanoyl-CoA hydroxylase** (also called α-phytanoyl-CoA dioxygenase, encoded by PHYH gene). Phytanic acid (from phytol in chlorophyll, dairy, ruminant fat) accumulates because it has a methyl group at the β-carbon preventing β-oxidation – it requires α-oxidation first. Clinical tetrad: **retinitis pigmentosa, polyneuropathy, cerebellar ataxia, sensorineural deafness**; also ichthyosis. Treatment: restrict phytanic acid-containing foods (dairy, beef, mutton).

Distractors: VLCAD deficiency presents with hypoketotic hypoglycaemia, not Refsum syndrome. AMACR deficiency causes adult-onset sensorimotor neuropathy. Pristanoyl-CoA oxidase deficiency would block a later step.

Final Answer: Phytanoyl-CoA hydroxylase. $\Rightarrow \boxed{C}$

Answer: (C) Go Back to Q15

Q16.

Solution

Concept – Rotenone inhibits Complex I: Rotenone is a plant-derived toxin (used as fish poison and insecticide) that **blocks electron transfer from the Fe-S clusters of Complex I to ubiquinone (CoQ)**. With Complex I inhibited, NADH cannot be oxidised → NADH accumulates → TCA cycle slows → ATP production falls. Dopaminergic neurons of the **substantia nigra** are particularly sensitive due to high energy demands and low antioxidant capacity → rotenone exposure in animals produces a model of Parkinson's disease. Fish suffocate at very low O_2 concentrations, explaining its use as a fish poison.

Distractors: Complex II is inhibited by malonate (competitive inhibitor of succinate dehydrogenase). Complex III is inhibited by antimycin A. Complex IV is inhibited by cyanide and CO.

Final Answer: Complex I (NADH-ubiquinone oxidoreductase). $\Rightarrow \boxed{C}$

Answer: (C) Go Back to Q16

Q17.

Solution

Concept – Short-chain acyl-CoA dehydrogenase deficiency (SCADD): SCAD catalyses the first step of β-oxidation of short-chain fatty acyl-CoAs (C4-C6, primarily butyryl-CoA). Deficiency leads to accumulation of **butyrylcarnitine (C4 acylcarnitine)** on MS/MS newborn screen and **ethylmalonic acid** in urine. Phenotype is highly variable: many affected individuals are asymptomatic. When symptomatic: hypotonia, developmental delay, seizures, and metabolic acidosis. The gene is ACADS. Unlike MCAD deficiency, SCADD rarely causes life-threatening hypoketotic hypoglycaemia.

Distractors: MCAD deficiency elevates C8 acylcarnitine (octanoylcarnitine). LCAD deficiency elevates C14 acylcarnitines. Glutaryl-CoA dehydrogenase deficiency (glutaric aciduria type 1) elevates glutarylcarnitine.

Final Answer: Short-chain acyl-CoA dehydrogenase (SCAD). $\Rightarrow \boxed{D}$

Answer: (D) Go Back to Q17

Q18.

Solution

Concept – C-peptide clinical significance: Proinsulin (86 aa) is cleaved in secretory granules by prohormone convertases PC1/3 and PC2 into **insulin** (51 aa, A+B chains) + **C-peptide** (31 aa, connecting peptide), released in equimolar amounts. **C-peptide** has a longer half-life (30–35 min vs 5 min for insulin) and is not present in exogenous insulin preparations. Therefore: exogenous insulin injection $\rightarrow$ **low C-peptide + high insulin**; insulinoma $\rightarrow$ **high C-peptide + high insulin**. Also used to distinguish type 1 DM (very low) from type 2 DM (normal/high).

Distractors: Proinsulin alone is not routinely used for this distinction. Fasting insulin alone cannot distinguish exogenous from endogenous. Urinary ketones assess metabolic state, not insulin source.

Final Answer: Serum C-peptide. $\Rightarrow \boxed{C}$

Answer: (C) Go Back to Q18

Q19.

Solution

Concept – Plasmid biology: Plasmids are autonomously replicating, circular (usually), extrachromosomal double-stranded DNA elements found in bacteria (and some eukaryotes). They carry their own **origin of replication (ori)** and are replicated by the host cell's replication machinery. Copy number varies: high-copy plasmids (20–50/cell), low-copy (5–10/cell), stringent (1–2/cell). Plasmids naturally carry antibiotic resistance genes, virulence factors, and metabolic genes. In molecular biology, they serve as cloning **vectors** (with selectable markers, multiple cloning sites, reporter genes).

Distractors: Plasmids are circular, not linear (most; some are linear). Most cloning vectors do carry antibiotic resistance for selection. Plasmids replicate using host machinery without viral coat proteins.

Final Answer: Circular extrachromosomal DNA with their own ori – autonomous replication. $\Rightarrow \boxed{B}$

Answer: (B) Go Back to Q19

Q20.

Solution

Concept – Carnitine biosynthesis precursors: L-carnitine is biosynthesised from two amino acids: **lysine** (provides the carbon skeleton – the ε-amino group of lysine is trimethylated using SAM) and **methionine** (provides three methyl groups via S-adenosylmethionine/SAM). The four-step pathway includes two hydroxylation reactions requiring: **vitamin C (ascorbate)**, Fe^{2+}, α-ketoglutarate, and O_2 (as cofactors for dioxygenases). Carnitine is synthesised in liver, brain, and kidney; skeletal muscle cannot synthesise it. Carnitine deficiency (primary or secondary) impairs long-chain fatty acid oxidation.

Distractors: Tryptophan is the precursor of niacin and serotonin. Tyrosine/leucine are not carnitine precursors. Arginine and glycine are precursors of creatine (not carnitine).

Final Answer: Lysine and methionine. $\Rightarrow \boxed{B}$

Answer: (B) Go Back to Q20

Q21.

Solution

Concept – Hartnup disease (SLC6A19 defect): Hartnup disease is caused by deficiency of **SLC6A19 (B^0AT1)**, the neutral amino acid transporter in intestinal and renal tubular epithelium. Impaired intestinal absorption of tryptophan reduces the tryptophan $\rightarrow$ NAD^+/niacin conversion pathway $\rightarrow$ functional niacin deficiency $\rightarrow$ **pellagra-like photosensitive rash, cerebellar ataxia, and psychiatric symptoms**. Neutral aminoaciduria is also present. Symptoms are episodic and triggered by fasting, sunlight, fever. Treated with **nicotinamide** supplementation (bypasses the tryptophan pathway).

Distractors: SLC3A1 defect causes cystinuria (kidney stones). Dibasic amino acid transporter defect causes lysinuric protein intolerance. PEPT1 dipeptides can partially compensate in Hartnup disease (explaining why symptoms are not always severe).

Final Answer: Defective SLC6A19 (B^0AT1) transporter – Hartnup disease. $\Rightarrow \boxed{C}$

Answer: (C) Go Back to Q21

Q22.

Solution

Concept – P/O ratio for $FADH_2$ (modern values): $FADH_2$ donates electrons directly to ubiquinone (CoQ) via Complex II (succinate dehydrogenase) or ETF-QO (in β-oxidation), **bypassing Complex I**. Since Complex I pumps 4 H^+ per 2 electrons, $FADH_2$ results in fewer protons pumped per electron pair – only Complexes III (4 H^+) and IV (2 H^+) contribute, totalling 6 H^+ vs 10 H^+ for NADH. With $\approx$4 H^+ per ATP (Complex V): $FADH_2$ yields $\approx$**1.5 ATP** (modern consensus: Nelson & Cox; Stryer). Older estimates: 2 ATP for $FADH_2$, 3 for NADH.

Distractors: 2.5 ATP is the P/O ratio for NADH (not $FADH_2$). 2.0 ATP is the older (classical) estimate for $FADH_2$, now revised downward. 3.0 ATP is the classical estimate for NADH.

Final Answer: 1.5 ATP per $FADH_2$. $\Rightarrow \boxed{A}$

Answer: (A) Go Back to Q22

Q23.

Solution

Concept – Glucokinase (hexokinase IV) as glucose sensor: Glucokinase has a high K_m for glucose ($\approx$10 mM), sigmoidal (cooperative) kinetics, is not inhibited

by its product glucose-6-phosphate (G-6-P), and is induced by insulin. Present in **hepatocytes** (regulates glycolysis and glycogen synthesis proportional to portal glucose) and **pancreatic β-cells** (glucose sensor – coupled with GLUT2 to trigger insulin release proportional to blood glucose). In fasting, glucokinase regulatory protein (GKRP) sequesters glucokinase in the nucleus, reducing its activity. In type 2 DM, glucokinase activity is reduced.

Distractors: Hexokinase I has a low K_m ($\approx$0.1 mM) and is product-inhibited by G-6-P (not a sensor). Phosphoglucose isomerase converts G-6-P to F-6-P (glycolytic, not sensor). Glucose-6-phosphatase releases free glucose (opposite function).

Final Answer: Glucokinase (hexokinase IV). $\Rightarrow \boxed{A}$

Answer: (A) Go Back to Q23

Q24.

Solution

Concept – Thromboxane A_2 (TXA_2): TXA_2 is synthesised from arachidonic acid by the sequential actions of **COX-1** and **thromboxane synthase** in platelets. TXA_2 is a potent **platelet aggregator and vasoconstrictor**. It has an extremely short half-life ($\approx$30 seconds), spontaneously hydrolysing to the inactive TXB_2. Aspirin **irreversibly acetylates** Ser^{530} of COX-1 in platelets (anucleate platelets cannot synthesise new COX-1), reducing TXA_2 production for the platelet's lifetime ($\approx$7–10 days). Endothelial PGI_2 (prostacyclin) opposes TXA_2 – endothelial cells can regenerate COX-1.

Distractors: PGI_2 (prostacyclin) is the endothelial counter-regulatory eicosanoid (inhibits aggregation). LTB_4 is a leukotriene (not made by COX pathway) – chemotactic. PGE_2 is produced by COX but has complex effects and longer half-life.

Final Answer: Thromboxane A_2 (TXA_2). $\Rightarrow \boxed{D}$

Answer: (D) Go Back to Q24

Q25.

Solution

Concept – Myelin basic protein (MBP): **MBP** is a major structural protein of compact myelin in the CNS. It is highly **positively charged** (rich in lysine and arginine residues, with a pI $\approx$10.5) and interacts electrostatically with the **negatively charged phospholipid head groups** on the cytoplasmic faces of the myelin bilayer, gluing the two cytoplasmic faces together ("zippering" of compact myelin). MBP is the major antigen used to induce experimental autoimmune

encephalomyelitis (EAE), the animal model of MS. Anti-MBP antibodies are found in some MS patients.

Distractors: MAG is on the periaxonal membrane, involved in axon-myelin signalling. PLP (proteolipid protein) is the most abundant protein of CNS myelin but is hydrophobic and spans the membrane (different structure). MOG is an outer surface glycoprotein – target in NMOSD and some MS.

Final Answer: Myelin basic protein (MBP). $\Rightarrow \boxed{A}$

Answer: (A) Go Back to Q25

Q26.

Solution

Concept – Phytanic acid α-oxidation: Phytanic acid (3,7,11,15-tetramethylhexadecanoic acid) has a **methyl substituent at the β-carbon (C-3)**, which **blocks β-oxidation** (the β-carbon must be free for the β-oxidation sequence). Therefore, phytanic acid must first undergo **α-oxidation** in peroxisomes: phytanoyl-CoA is hydroxylated at the α-carbon (C-2) by phytanoyl-CoA hydroxylase, then the C-1 carbon is released as formyl-CoA/CO_2, generating **pristanic acid** (2,6,10,14-tetramethylpentadecanoic acid) – which now has the methyl branch at C-2, allowing normal β-oxidation to proceed.

Distractors: Phytanic acid is C16 (not very long chain >C22). It is fully saturated (no double bonds requiring isomerase). It is even-chain (no propionyl-CoA issue relevant here).

Final Answer: Methyl group at β-carbon blocks β-oxidation; α-oxidation first produces pristanic acid. $\Rightarrow \boxed{D}$

Answer: (D) Go Back to Q26

Q27.

Solution

Concept – Histone acetylation and chromatin: Histone acetyltransferases (HATs) transfer an acetyl group from acetyl-CoA to the ε-amino group ($-NH_3^+$) of specific lysine residues on histone tails. **Acetylation neutralises the positive charge** on lysine, reducing electrostatic attraction between positively charged histone tails and the negatively charged DNA backbone. This **loosens chromatin structure** $\rightarrow$ **euchromatin** $\rightarrow$ accessible to transcription factors and RNA polymerase $\rightarrow$ gene activation. **HDACs** remove acetyl groups, restoring positive charge $\rightarrow$ chromatin compaction $\rightarrow$ heterochromatin $\rightarrow$ gene silencing. HDAC inhibitors

(vorinostat, romidepsin) are used in T-cell lymphoma.

Distractors: Acetylation decreases (not increases) histone-DNA binding. DNA methylation (not histone acetylation) silences genes. Acetylation does not cross-link histones to DNA.

Final Answer: Acetylation neutralises lysine positive charge $\rightarrow$ loosened histone-DNA interaction $\rightarrow$ euchromatin. $\Rightarrow \boxed{C}$

Answer: (C) Go Back to Q27

Q28.

Solution

Concept – Proton pumping stoichiometry of ETC: Per NADH oxidised through the full ETC: **Complex I**: 4 H^+ pumped per $2e^-$; **Complex III**: 4 H^+ pumped per $2e^-$; **Complex IV**: 2 H^+ pumped per $2e^-$ (per $\frac{1}{2}$ O_2 reduced). Total = $4+4+2=$ **10 H^+** per NADH. For $FADH_2$ (bypasses Complex I): $4+2=6$ H^+. With $\approx$4 H^+ needed per ATP by Complex V: NADH $\rightarrow 10/4 \approx 2.5$ ATP; $FADH_2 \rightarrow 6/4 \approx 1.5$ ATP. These are the modern P/O ratios.

Distractors: 6 H^+ is the yield for $FADH_2$ only (not NADH). 8 H^+ is between the old and new estimates (not the accepted value). 12 H^+ is an overestimate.

Final Answer: 10 H^+ per NADH (4 + 4 + 2 from Complexes I, III, IV respectively). $\Rightarrow \boxed{D}$

Answer: (D) Go Back to Q28

Q29.

Solution

Concept – Tyrosine as conditionally essential amino acid: Tyrosine is normally a **non-essential** amino acid synthesised from phenylalanine by **phenylalanine hydroxylase (PAH)**. It becomes **conditionally essential** when: (1) **PAH is deficient** (as in phenylketonuria/PKU) – since phenylalanine cannot be converted to tyrosine; (2) **Dietary phenylalanine is severely restricted** (PKU management) – insufficient substrate for tyrosine synthesis; (3) In **premature infants** with immature PAH expression. Therefore tyrosine must be supplemented in PKU patients even while restricting phenylalanine.

Distractors: Protein intake amount does not affect PAH sufficiency. Renal failure primarily causes accumulation of non-essential amino acid metabolites, not tyrosine deficiency. Vitamin C is required for tyrosine degradation (fumarylacetoacetase pathway) but not for tyrosine synthesis from phenylalanine.

Final Answer: Tyrosine becomes essential when PAH is deficient (PKU) or phenylalanine is severely restricted; also in premature infants. $\Rightarrow \boxed{A}$

Answer: (A) Go Back to Q29

Q30.

Solution

Concept – Sickle cell heterozygote (HbAS) advantage against malaria: The high prevalence of the HbS allele in malaria-endemic regions of sub-Saharan Africa, the Mediterranean, Middle East, and India is explained by **heterozygote advantage**: individuals with HbAS (sickle cell trait) have relative protection against *Plasmodium falciparum* malaria. Proposed mechanisms include: (i) sickling of infected RBCs at low O_2 tension $\rightarrow$ phagocytosis by macrophages; (ii) reduced intraerythrocytic parasite growth; (iii) cross-reactive immune responses; (iv) impaired parasite cytoadherence. HbAS individuals rarely have clinical sickle cell disease but have $50 - -90\%$ protection against severe/cerebral malaria.

Distractors: Sickle cell trait does not protect against tuberculosis, leishmaniasis, or trypanosomiasis – these require different immune mechanisms.

Final Answer: *Plasmodium falciparum* (malaria). $\Rightarrow \boxed{B}$

Answer: (B) Go Back to Q30

Q31.

Solution

Concept – Signal peptide for ER targeting: Proteins destined for secretion, the plasma membrane, or lysosomes are synthesised with an **N-terminal signal peptide** (15–30 amino acids, with a hydrophobic core). As the signal peptide emerges from the ribosome, it is recognised by the **signal recognition particle (SRP)**, which pauses translation and docks the ribosome-mRNA-nascent chain complex to the **SRP receptor on the ER membrane**. Translocation into the ER lumen occurs cotranslationally through the Sec61 translocon. The signal peptide is then cleaved by **signal peptidase** in the ER lumen.

Distractors: KDEL is a C-terminal ER retention sequence (retrieves escaped ER-resident proteins from Golgi). M6P tag is added in the Golgi to target proteins to lysosomes. GPI anchors are added posttranslationally in the ER lumen to membrane-anchored proteins.

Final Answer: N-terminal hydrophobic signal peptide recognised by SRP. $\Rightarrow \boxed{C}$

Answer: (C) Go Back to Q31

Q32.

Solution

Concept – Adiponectin: Adiponectin is an adipokine secreted exclusively by adipocytes. It is **inversely proportional to body fat mass**: levels are **low in obesity and type 2 diabetes** and high with caloric restriction. Adiponectin activates **AMPK** in liver and muscle $\rightarrow$ increased fatty acid oxidation, decreased hepatic glucose production, and improved insulin sensitivity. It also has anti-inflammatory effects. Low adiponectin is an independent risk factor for metabolic syndrome, cardiovascular disease, and type 2 diabetes.

Distractors: Leptin is proportional to body fat (not inversely) and signals satiety to the hypothalamus. Resistin is pro-inflammatory and associated with insulin resistance (not anti-inflammatory). TNF-α is a pro-inflammatory cytokine produced by macrophages (elevated in obesity, not decreased).

Final Answer: Adiponectin. $\Rightarrow \boxed{B}$

Answer: (B) Go Back to Q32

Q33.

Solution

Concept – CO_2 transport in blood: CO_2 is transported in three forms: (1) $\approx$**70% as bicarbonate (HCO_3^-)**: $CO_2 + H_2O \xrightarrow{\text{carbonic anhydrase in RBCs}} H_2CO_3 \rightarrow H^+ + HCO_3^-$; HCO_3^- exits RBC in exchange for Cl^- (chloride shift/Hamburger phenomenon); H^+ is buffered by deoxyHb; (2) $\approx$**23% as carbaminohaemoglobin**: CO_2 + Hb-$NH_2 \rightarrow$ Hb-$NHCOO^-$ (at terminal amino groups of globin, not haem iron); (3) $\approx$**7% dissolved** in plasma. The **Haldane effect**: deoxygenated Hb has higher affinity for CO_2 (both carbamino and H^+ buffering).

Distractors: CO_2 binds to haemoglobin's amino groups (not haem iron). CO_2 dissolved in plasma is only $\approx$7%, not the majority. CO_2 binds to Hb terminal amino groups (carbamino), not albumin primarily.

Final Answer: Largest fraction is HCO_3^- formed in RBCs by carbonic anhydrase; H^+ buffered by Hb (Haldane effect). $\Rightarrow \boxed{D}$

Answer: (D) Go Back to Q33

Q34.

Solution

Concept – International Unit (IU) of enzyme activity: One **International Unit (IU or U)** of enzyme activity is defined as the amount of enzyme that catalyses the conversion of **1 micromole (μmol) of substrate per minute** under specified standard conditions (defined temperature, pH, and substrate concentration). The **SI unit** is the **katal** (kat): 1 kat = 1 mole of substrate converted per second; 1 IU = 16.67 nanokatal (nkat). **Specific activity** = IU/mg protein (measure of enzyme purity). A pure enzyme has maximum specific activity.

Distractors: The katal (1 mole per second) is the SI unit, not the IU. Absorbance changes are used to measure activity spectrophotometrically but do not define the unit. IU does not refer to volume (mL).

Final Answer: Amount of enzyme converting 1 μmol of substrate per minute. $\Rightarrow$ $\boxed{A}$

Answer: (A) Go Back to Q34

Q35.

Solution

Concept – HMG-CoA lyase deficiency: HMG-CoA lyase is a **mitochondrial** enzyme that cleaves HMG-CoA $\rightarrow$ **acetoacetate** + acetyl-CoA – the **ketogenic step**. Deficiency results in impaired ketogenesis $\rightarrow$ **hypoketotic hypoglycaemia** despite fasting (no ketone bodies to spare glucose or feed brain). Clinical features: severe hypoglycaemia, metabolic acidosis, elevated 3-hydroxy-3-methylglutaric acid (the substrate of HMG-CoA lyase) and 3-methylglutaconic acid in urine. It must be distinguished from **HMG-CoA reductase** (cytoplasmic, cholesterol synthesis – target of statins, entirely different function) – a common exam trap.

Distractors: HMG-CoA reductase is cytoplasmic, not mitochondrial. HMG-CoA synthase deficiency (mitochondrial) also causes hypoketotic hypoglycaemia (but more benign). β-Ketothiolase deficiency (acetoacetyl-CoA thiolase) causes episodic ketoacidosis (different presentation).

Final Answer: HMG-CoA lyase. $\Rightarrow$ $\boxed{D}$

Answer: (D) Go Back to Q35

Q36.

Solution

Concept – PDK (pyruvate dehydrogenase kinase) regulation: Pyruvate dehydrogenase kinase (PDK) phosphorylates and **inactivates** the E1 (α) subunit of pyruvate dehydrogenase complex (PDC). PDK is **activated** (PDC is inactivated) when mitochondria signal energy sufficiency: **high NADH/NAD$^+$** (product of β-oxidation/TCA), **high acetyl-CoA/CoA** (signal of fatty acid oxidation), and **high ATP** (energy replete). PDK is **inhibited** by pyruvate, ADP, and NAD$^+$ – signalling need for more acetyl-CoA. **Dichloroacetate (DCA)** inhibits PDK $\rightarrow$ activates PDC $\rightarrow$ used in PDC deficiency and lactic acidosis treatment.

Distractors: Low NADH, low acetyl-CoA, and low ATP would activate PDC (not inhibit). High AMP and pyruvate inhibit PDK (they activate PDC, promoting more acetyl-CoA production). Low acetyl-CoA/high CoA ratio signals active β-oxidation proceeding – PDK would actually be activated in this context only with high NADH.

Final Answer: High NADH/NAD$^+$, high acetyl-CoA/CoA, high ATP (mitochondrial energy sufficiency). $\Rightarrow \boxed{D}$

Answer: (D) Go Back to Q36

Q37.

Solution

Concept – GLUT2 as glucose sensor: GLUT2 is a facilitative glucose transporter with a very high K_m for glucose (≈15–20 mM), meaning it is not saturated at normal fasting blood glucose (5 mM) and glucose uptake is proportional to blood glucose concentration. It is present in **hepatocytes, kidney tubules, small intestinal epithelium, and pancreatic β-cells**. It is **not regulated by insulin**. In β-cells, GLUT2 works together with glucokinase to act as a glucose sensor: rising postprandial glucose $\rightarrow$ proportional glucose entry $\rightarrow$ glucokinase generates G-6-P $\rightarrow$ glycolysis $\rightarrow$ ATP $\rightarrow$ K^{ATP} channel closes $\rightarrow$ depolarisation $\rightarrow$ Ca^{2+} influx $\rightarrow$ insulin exocytosis.

Distractors: GLUT4 is insulin-regulated and found in skeletal muscle and adipose (not liver/β-cells). GLUT1 is ubiquitous with low K_m (≈1 mM) – constitutively transports glucose at normal blood glucose. GLUT3 is in neurons (very high affinity, K_m ≈1.5 mM).

Final Answer: GLUT2. $\Rightarrow \boxed{B}$

Answer: (B) Go Back to Q37

Q38.

Solution

Concept – ApoB-100 and familial defective ApoB-100 (FDB): ApoB-100 (4536 amino acids, encoded by APOB gene) is the sole apolipoprotein on LDL, IDL, and VLDL. ApoB-100 contains the **LDL receptor-binding domain** centred around **Arg**^{3500} (residue 3500). The **Arg3500Gln (R3500Q)** missense mutation (≈1:600 in Europeans) reduces ApoB-100's affinity for the LDL receptor by ≈50%, impairing LDL clearance and causing **familial defective ApoB-100** – a hypercholesterolaemic phenotype similar to but less severe than familial hypercholesterolaemia (FH; LDLR mutation).

Distractors: ApoB-48 is the truncated form produced by RNA editing (intestine, chylomicrons). LDLR mutations cause FH, not FDB. PCSK9 gain-of-function causes hypercholesterolaemia by degrading LDLR (not a mutation in ApoB).

Final Answer: Arg3500Gln (R3500Q) missense mutation in ApoB-100. $\Rightarrow \boxed{D}$

Answer: (D) Go Back to Q38

Q39.

Solution

Concept – Vitamin E deficiency haemolytic anaemia in premature neonates: Vitamin E (α-tocopherol) is the major lipid-soluble antioxidant in cell membranes. Premature infants have: (i) very low vitamin E stores (placental transfer is limited, predominantly in the last trimester); (ii) high PUFA content in their RBC membranes (PUFA-rich formula diet). Without adequate vitamin E, RBC membranes undergo **lipid peroxidation** by free radicals $\rightarrow$ haemolytic anaemia, characterised by eccentrocytes and elevated malondialdehyde. This typically presents at 1–2 months of age in premature neonates fed low-vitamin-E formula. Genetic: abetalipoproteinaemia also causes severe vitamin E deficiency.

Distractors: Vitamin A deficiency causes night blindness and xerophthalmia, not haemolytic anaemia. Vitamin D deficiency causes rickets, not haemolysis. Vitamin K deficiency causes coagulopathy (bleeding), not haemolytic anaemia.

Final Answer: Vitamin E (α-tocopherol). $\Rightarrow \boxed{B}$

Answer: (B) Go Back to Q39

Q40.

Solution

Concept – Phosphatidate phosphatase (lipin-1): Phosphatidate phosphatase (PAP), encoded by LPIN1 (lipin-1), dephosphorylates **phosphatidic acid (PA)** to yield **1,2-diacylglycerol (DAG)** + inorganic phosphate. DAG is the branch-point intermediate for two major lipid synthesis pathways: (1) **Triacylglycerol (TG) synthesis**: DGAT (diacylglycerol acyltransferase) adds a third acyl chain; (2) **Phospholipid synthesis (Kennedy pathway)**: DAG + CDP-choline $\rightarrow$ phosphatidylcholine, or DAG + CDP-ethanolamine $\rightarrow$ PE. Lipin-1 mutations cause **lipodystrophy, acute pancreatitis, and exercise-induced rhabdomyolysis** in humans.

Distractors: DGAT adds the third fatty acid to DAG to form TG (a downstream step, not the PA dephosphorylation). PLD cleaves phospholipid head groups producing PA (reverse direction). LPAAT adds acyl groups to lysophosphatidic acid to produce PA (a preceding step).

Final Answer: Phosphatidate phosphatase (lipin-1). $\Rightarrow \boxed{C}$

Answer: (C) Go Back to Q40

Answer Key – FMGE Biochemistry Sample Paper 9

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