MASTERING BIOCHEMISTRY

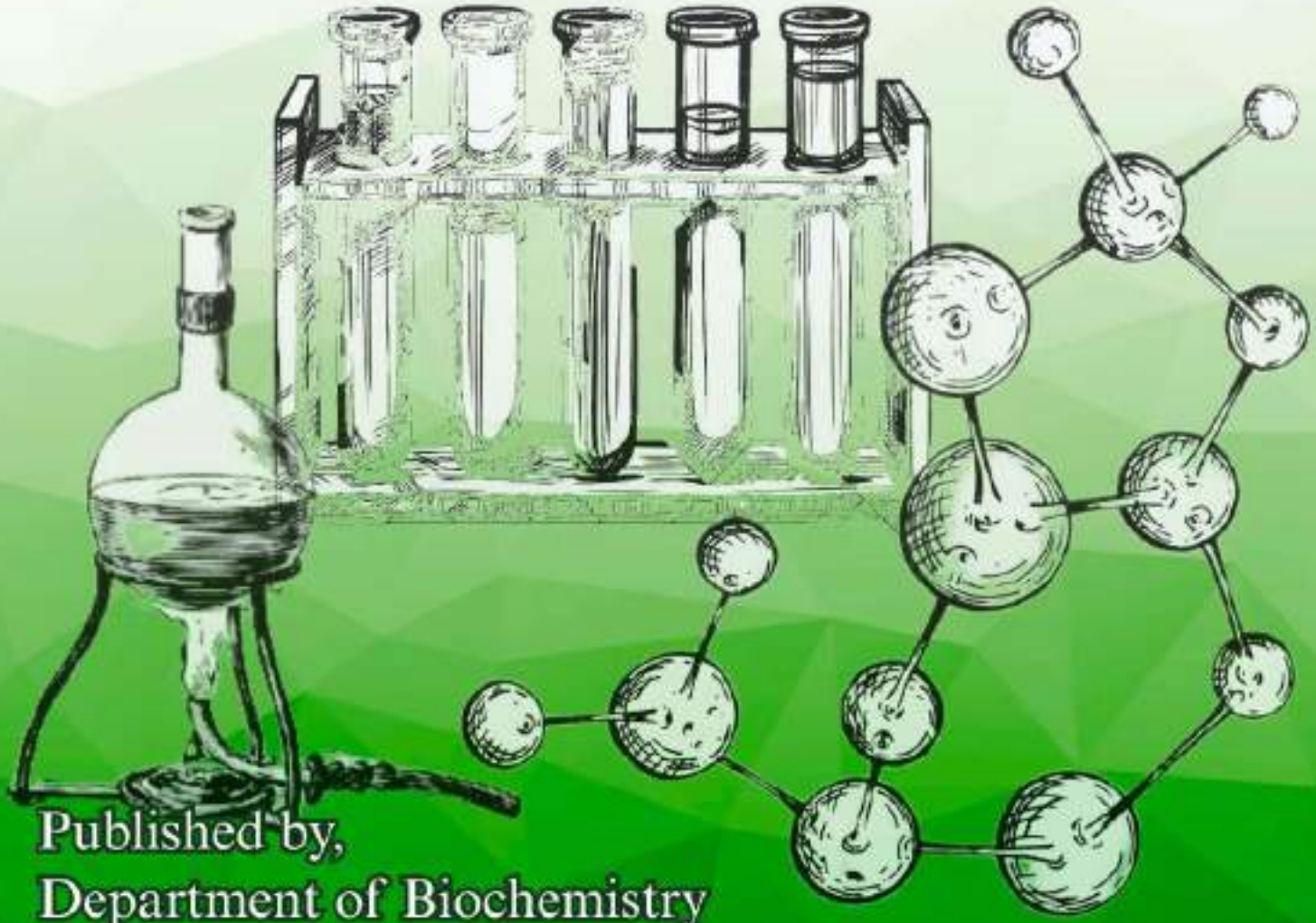
A Comprehensive Guide to MCQs, Essays, and OSPEs

Part II

Uva Wellassa University

Semester 2

- **Metabolism 1**
- **Metabolism 2**
- **Metabolism 3**
- **Inborn Errors of Metabolism**



Published by,
Department of Biochemistry
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Authored by:

Department of Biochemistry

Faculty of Medicine

Uva Wellassa University of Sri Lanka

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A Comprehensive Guide to
MCQs, Essays & OSPEs
Part II

Semester 2

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Message from the Vice Chancellor

Dear students,

It is with immense pleasure that I offer my warm congratulations and genuine appreciation to the Faculty of Medicine, Uva Wellassa University of Sri Lanka, including Senior Professor Muditha Vidanapathirana, Dean of the Faculty of Medicine, for this outstanding initiative in publishing "Mastering Biochemistry – Part II: A Comprehensive Guide to MCQs, Essays & OSPEs" successfully.

This book stands as an invaluable resource, providing substantial benefits not only for MBBS undergraduates of Uva Wellassa University of Sri Lanka, but also for medical students nationwide overall.

I encourage you to fully utilize the excellent resources created by the Faculty of Medicine to strengthen your academic journey. Resources like this guide can make your studies more focused, efficient, and truly rewarding overall experience.

Wishing you all the very best in your academic and professional endeavours.

Senior Professor Kolitha B. Wijesekara
B.Sc. (Hon.) (Peradeniya), M.Phil. (Peradeniya),
Dr. Sc. Agr. (Gottingen, Germany), M.Biol.
Vice Chancellor
Uva Wellassa University of Sri Lanka



Message from the Head of the Department

Dear Students,

As the Head of the Department of Biochemistry, it is both an honour and a privilege to be part of the team behind the publication of "Mastering Biochemistry: A Comprehensive Guide to MCQs, Essays, and OSPEs." This publication has been meticulously designed to align with the Biochemistry curriculum for Year 1, Semester 1, as offered by the Department of Biochemistry, Faculty of Medicine, Uva Wellassa University of Sri Lanka.

As aspiring medical professionals dedicated to excellence, this guide aims to support your academic journey by serving as a resource to prepare effectively for your examinations. It provides detailed insights into the components of MCQs, essays, and OSPEs, helping you navigate these formats with confidence. Furthermore, the publication is structured to assist in testing your comprehension and reinforcing the knowledge acquired through the curriculum.

I extend my heartfelt gratitude to Snr. Prof. Muditha Vidanapathirana, Founder Dean of the Faculty of Medicine, Uva Wellassa University, for conceptualizing this initiative and offering steadfast guidance throughout its development. My sincere appreciation also goes to all contributors who played a role in creating this valuable resource.

I hope this publication serves as a reliable guide and inspires you to excel in your academic endeavours.

Warm regards

Dr. Gayathri Rathnayake,
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BIOCHEMISTRY PRACTICE MCQs (T/F & SBA)

- **Metabolism 1**
- **Metabolism 2**
- **Metabolism 3**
- **Inborn errors of Metabolism**

(Q1) T/F regarding RBC glycolysis?

(A) Anaerobic glycolysis occurs when O_2 is deficient in RBC.
(B) Citrate allosterically enhances glycolytic activity.
(C) Defective glycolysis results in haemolysis.
(D) Reactions after the rate controlling reaction, do not consume energy.
(E) Synthesis of 2,3-bisphosphoglycerate lowers ATP yield.

(Q2) T/F regarding increases hepatic glycolysis?

(A) Decrease AMP.
(B) Decrease cAMP.
(C) Increase ATP.
(D) Increase fructose 2-6 bisphosphate.
(E) Increase in citrate.

(Q3) T/F regarding hepatic glycolysis?

(A) 2-3 BPG is a by-product.
(B) AMP is an allosteric activator.
(C) Enhanced in glucose 6 phosphatase deficiency.
(D) Increased rate in well fed state.
(E) Rate limiting step is regulated by hormone regulation.

(Q4) T/F regarding genetic code?

(A) 3rd position of the codon is subject to wobbling.
(B) AUG codes for methionine.
(C) Cellular and mitochondrial genetic codons are identical.
(D) Removal of a codon from DNA causes shifting of reading frame.
(E) There are 3 nonsense codes.

(Q5) T/F regarding the functions of nucleotide derivatives?

(A) Acyl carriers.
(B) Energy intermediates.
(C) Enzyme co-factors.
(D) Reducing equivalents.
(E) Secondary messengers.

(Q6) T/F regarding important factors for maintaining the double helix form in DNA?

(A) Base pair stacking.
(B) H bonding.
(C) Interchain cross-links.
(D) Phosphodiester bonds.
(E) Presence of histones.

(Q7) T/F regarding transamination?

(A) Aminotransferase is induced by glucocorticoids.
(B) Contribute to maintain blood glucose levels during fasting.
(C) Is essential for synthesis of non-essential amino acids.
(D) Pyridoxal phosphate act as a co-enzyme.
(E) This is the initiation of majority of amino acid regeneration.

(Q8) T/F regarding Ketone bodies?

(A) They are synthesized in liver.
(B) They are utilized by RBC for energy.
(C) Disturb bicarbonate buffer system in blood.
(D) Normally absent in blood.
(E) Synthesis depends on NADH: NAD^+ ratio.

(Q9) T/F regarding beta oxidation of fatty acids?

(A) Carnitine transports long chain fatty acids into mitochondria.
(B) It is induced by high insulin/glucagon ratio.
(C) It provides substrate to GNG.
(D) Malonyl CoA inhibits CAT-1.
(E) Takes place in mitochondria.

(Q10) T/F regarding the amino acids formed by free ammonia assimilation?

(A) Alanine
(B) Arginine
(C) Glutamate
(D) Glutamine
(E) Glycine

(Q11) T/F regarding metabolism of amino acids?

(A) Alanine is synthesized from an intermediate of TCA cycle.
(B) Arginine gives rise to Nitric Oxide.
(C) Glutamate is a substrate for ketone body synthesis.
(D) Impaired metabolism of Tyrosine gives rise to albinism.
(E) Serine provides carbon skeleton for synthesis of cysteine.

(Q12) T/F regarding conversions which are associated with the synthesis of glucose from alanine in the liver?

(A) Fructose 1,6 bisphosphate to Fructose 6 phosphate.
(B) Lactate to pyruvate.
(C) Oxaloacetate to phosphoenolpyruvate.
(D) Pyruvate to Acetyl CoA.
(E) Pyruvate to OAA.

(Q13) A 2-year-old boy presented with severe fasting hypoglycaemia. What is the deficient enzyme?

(A) Alanine aminotransferase
(B) Glucose 6-phosphatase
(C) Glycogen synthase
(D) Phosphoenolpyruvate carboxykinase
(E) Phosphofructokinase 1

(Q14) T/F regarding pentose phosphate pathway (PPP)?

(A) Glucose 6 phosphatase is the key regulatory enzyme.
(B) Individuals with deficiency of the main enzyme of PPP are susceptible for haemolysis.
(C) It is the alternative pathway for glucose oxidation.
(D) PPP is highly active in lactating mammary glands.
(E) Supplies NADH for FA synthesis.

(Q15) Which of the following is/are seen in LDL but not in chylomicron?

(A) Apolipoprotein B100
(B) Apolipoprotein A
(C) Cholesterols
(D) Cholesteryl esters
(E) Triglycerides

(Q16) Which of the following is/are required for the synthesis of urea?

(A) Ammonium ions
(B) Aspartic acid
(C) ATP
(D) Carbon dioxide
(E) Uric acid

(Q17) T/F regarding bile acids?

(A) Synthesized by polyunsaturated fatty acids.
(B) Conserved in body via extra hepatic circulation.
(C) Are important in protein digestion.
(D) Facilitate cholesterol absorption.
(E) Form by the activity of 1-alfa hydroxylase.

(Q18) T/F regarding the combination of antibiotic and its function?

(A) Chloramphenicol – inhibits peptide transferase.
(B) Erythromycin – inhibits ribosome translocation.
(C) Rifampicin – inhibits RNA synthesis.
(D) Streptomycin – inhibits initiation of translation.
(E) Tetracycline – inhibits the progression of translation.

(Q19) Which of the following is/are correctly matched with the elevated bilirubin level in blood?

(A) Cholestasis – Unconjugated Bilirubin
(B) Gilbert syndrome - Conjugated Bilirubin
(C) Malaria – unconjugated bilirubin
(D) Neonatal jaundice - Conjugated Bilirubin
(E) Viral hepatitis – both conjugated and unconjugated bilirubin

(Q20) T/F regarding eicosanoids?

(A) Aspirin inhibits lipoxygenase enzyme.
(B) Corticosteroids inhibit cyclooxygenase enzyme.
(C) Lipoxins are synthesized in immune cells.
(D) Omega 3 fatty acids promote production of series 3 eicosanoids.
(E) Thromboxane is produced by vascular wall endothelium.

(Q21) T/F regarding eicosanoids?

(A) Arachidonic acid is a precursor of group 2 eicosanoids.
(B) Prostacyclin is produced by platelets.
(C) Thromboxane and prostacyclin act as antagonists.
(D) Thromboxane is a vasoconstrictor.
(E) Thromboxane is synthesized by lipo-oxygenase.

(Q22) T/F regarding antioxidants?

(A) Alfa tocopherol
(B) Ascorbic acid
(C) Folate
(D) Oxidized glutathione
(E) Superoxide dismutase

(Q23) T/F regarding the steps included in in-vitro of human insulin production?

(A) Expression vector ligation.
(B) PCR amplification.
(C) Protein purification.
(D) Restriction digestion.
(E) Reverse transcription.

(Q24) T/F regarding obstructive jaundice?

(A) GGT activity increased in serum.
(B) Increase alkaline phosphatase activity in serum.
(C) Increase conjugated bilirubin in serum.
(D) Presence of bilirubin in urine.
(E) UCB increased in serum.

(Q25) Which of the following is/are involved in the progression of the cell cycle?

(A) Cyclin-dependent protein kinase (CDK)
(B) p21
(C) p53
(D) Protein Ku
(E) Retinoblastoma (Rb)

(Q26) T/F regarding the process of recombinant DNA technology?

(A) Genomic DNA can be used as a template to express mammalian genes on E. coli.
(B) Polymerase chain reaction (PCR) can be used for the introduction of restriction sites to the gene.
(C) Recombinant DNA introduced to E. coli through the cell membrane.
(D) Regulated gene expression in E. coli increases protein.
(E) Vector plasmids include multiple cloning sites to integrate foreign DNA.

(Q27) T/F regarding the enzymes that increase the hepatic cholesterol level?

(A) 7-α-hydroxylase
(B) Acetyl-CoA: Acyl transferase (ACAT)
(C) Cholesterol ester hydrolase
(D) Cholesterol ester transfer protein (CETP)
(E) HMG-CoA reductase

(Q28) T/F regarding inherited diseases associated with tyrosine metabolism?

(A) Albinism
(B) Alkaptonuria
(C) Homocystinuria
(D) Maple syrup disease
(E) Phenylketonuria

(Q29) What are the post-translational modifications that take place when procollagen converts into mature collagen?

(A) Amino-terminal and carboxy-terminal pro peptides are cleaved.
(B) Formation of cross-links between hydroxylysine and lysine.
(C) Glycosylation of hydroxyproline residues.
(D) N-terminal leading sequence is cleaved.
(E) Tropocollagen is arranged in a staggered manner.

(Q30) Which of the following is/are atherogenic risk of an individual can be assessed by?

(A) Atherogenic index of plasma
(B) Highly sensitive C-reactive protein
(C) Lipoprotein bound phospholipase A2 (Lp-A2)
(D) Ratio between LDL cholesterol and HDL cholesterol (LDL-C/HDL-C)
(E) Ratio between total cholesterol and HDL cholesterol (Total C/HDL-C)

(Q31) A man got pain and swelling in his right knee following a fall recently. What enzyme is inhibited in the prescription for the pain and swelling?

(A) Cyclooxygenase 1
(B) Cyclooxygenase 2
(C) Lipoxygenase
(D) Phospholipase A2
(E) Phospholipase A

BIOCHEMISTRY PRACTICE MCQ (T/F & SBA) ANSWERS

(Q1) T/F regarding RBC glycolysis?

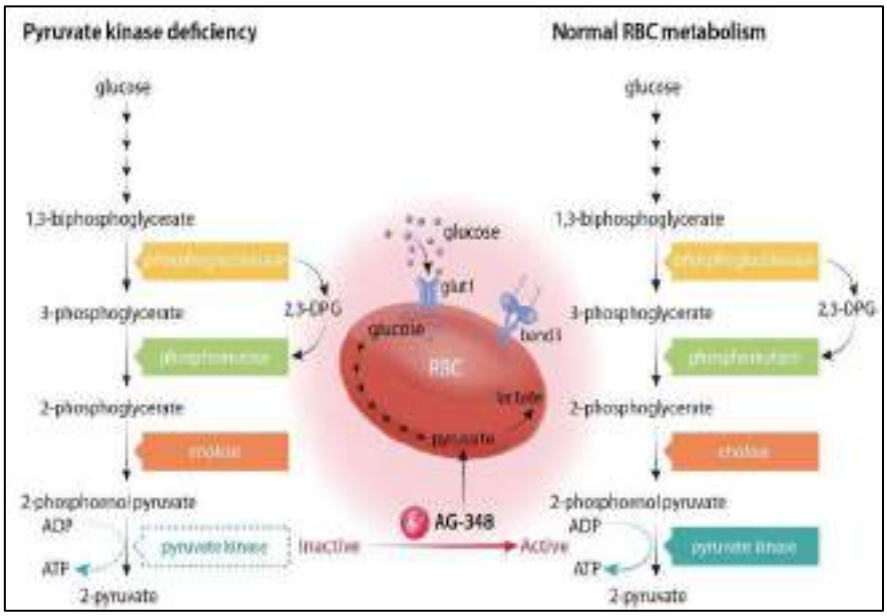

Figure 3-RBC Glycolysis

https://haematologica.org/article/view/10127

(A) Anaerobic glycolysis occurs when oxygen is deficient in RBC – True, because RBCs lack mitochondria and therefore always generate ATP anaerobically.
(B) Citrate allosterically enhances glycolytic activity – False, citrate actually inhibits phosphofructokinase-1 (PFK-1) and slows glycolysis.
(C) Defective glycolysis results in haemolysis – True, since ATP is essential to maintain membrane ion pumps in RBCs, and deficiency of glycolytic enzymes (e.g. pyruvate kinase deficiency) leads to haemolysis.
(D) Reactions after the rate-controlling reaction do not consume energy – True, after PFK-1 the pathway mainly generates ATP rather than consuming it.
(E) Synthesis of 2,3-bisphosphoglycerate lowers ATP yield – True, because diversion through the 2,3-BPG shunt bypasses an ATP-producing step.

(Q2) T/F regarding increases hepatic glycolysis?

(A) Decrease AMP – False, low AMP inhibits glycolysis whereas high AMP stimulates PFK-1.
(B) Decrease cAMP – True, low cAMP reduces PKA activity, dephosphorylates PFK-2 and increases F2,6BP, which activates glycolysis.
(C) Increase ATP – False, high ATP is inhibitory to PFK-1.
(D) Increase fructose 2,6 bisphosphate – True, F2,6BP is the most potent activator of hepatic PFK-1.
(E) Increase in citrate – False, citrate inhibits PFK-1 and slows glycolysis.

(Q3) T/F regarding hepatic glycolysis?

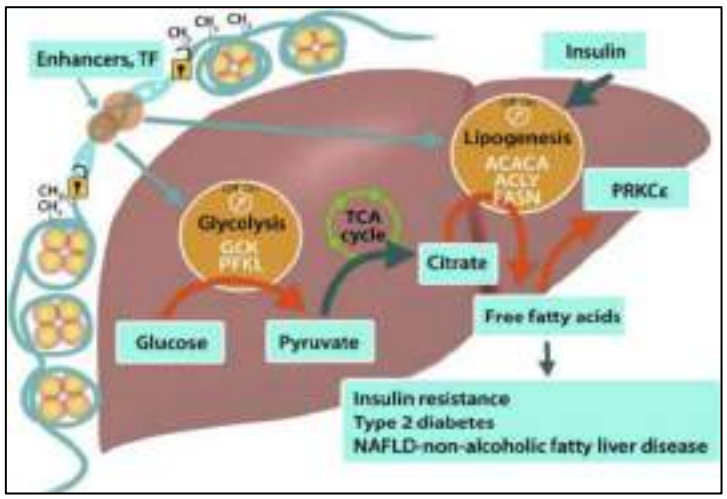

Figure 2- Hepatic glycolysis

https://www.researchgate.net/figure/Increased-hepatic-glycolysis-and-de-novo-lipogenesis-is-associated-with-DNA_fig4_291013840

(A) 2-3 BPG is a by-product – False, it is formed mainly in RBCs not in the liver.
(B) AMP is an allosteric activator – True, it stimulates PFK-1 activity in the liver.
(C) Enhanced in glucose 6-phosphatase deficiency – True, because glucose can't be released and is shunted into glycolysis.
(D) Increased rate in well-fed state – True, high insulin/low glucagon promotes glycolysis.
(E) Rate limiting step is regulated by hormone regulation – True, PFK-1 is indirectly controlled by hormones via F2,6BP.

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(Q4) T/F regarding genetic code,

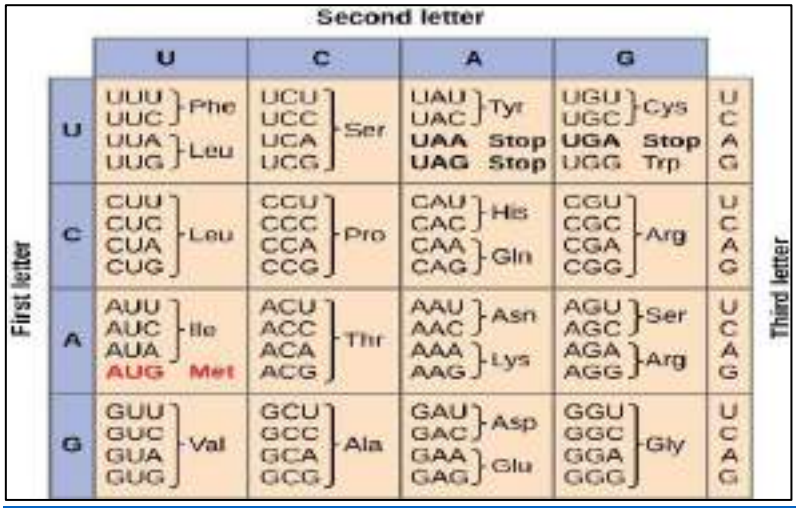


Figure 3- Genetic codes

https://vivaopen.oercommons.org/courseware/lesson/504/overview

(A) Third position of the codon is subject to wobbling – True, the wobble hypothesis allows degeneracy at the third base.
(B) AUG codes for methionine – True, it is the start codon for protein synthesis in eukaryotes.
(C) Cellular and mitochondrial genetic codons are identical – False, mitochondria have some differences in codon usage.
(D) Removal of a codon from DNA causes shifting of the reading frame – False, deletion of an entire codon (three bases) removes one amino acid but does not shift the frame; only non-triplet additions or deletions cause frameshifts.
(E) There are three nonsense codes – True, UAA, UAG and UGA terminate translation.

(Q5) T/F regarding the functions of nucleotide derivatives?

(A) Acyl carriers – True, for example coenzyme A carries acyl groups.
(B) Energy intermediates – True, ATP, GTP and related nucleotides store and transfer energy.
(C) Enzyme co-factors – True, many cofactors such as NAD^+, FAD and CoA contain nucleotide structures.
(D) Reducing equivalents – True, NADH and NADPH act as reducing equivalents.
(E) Secondary messengers – True, cAMP and cGMP act as second messengers in cell signalling.

(Q6) T/F regarding important factors for maintaining the double helix form in DNA?

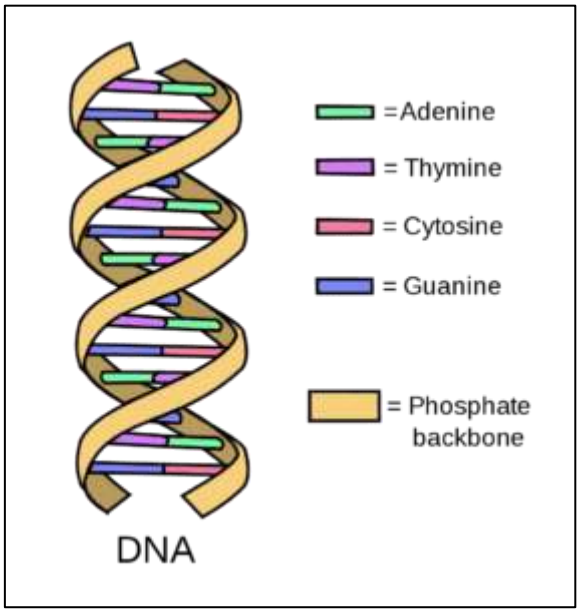


Figure 4-DNA double helix

https://www.ashg.org/discover-genetics/building-blocks/

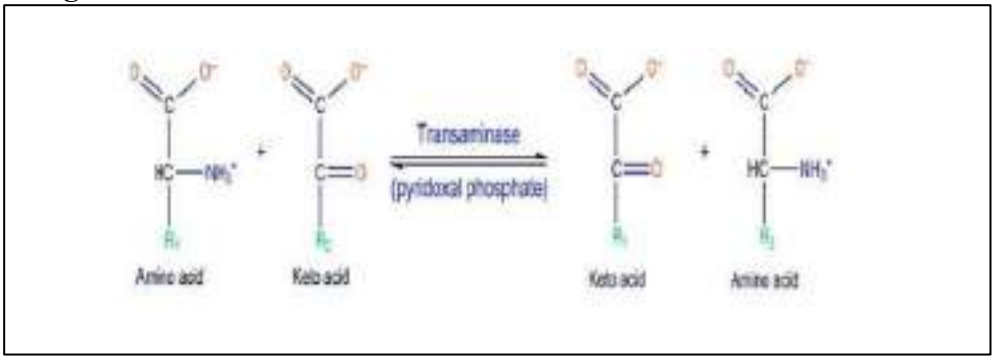
(A) Base pair stacking – **True**, hydrophobic interactions between stacked bases stabilize the DNA helix.
(B) Hydrogen bonding – **True**, complementary base pairing via H-bonds holds the two strands together.

(C) Interchain cross-links – **False**, normally no covalent crosslinks between strands occur in native DNA (crosslinks can occur after damage or drugs but not physiologically).

(D) Phosphodiester bonds – **True**, these covalent bonds form the sugar–phosphate backbone of each strand, essential for helical integrity.

(E) Presence of histones – **False**, histones help package DNA into chromatin but are not responsible for the helix itself; double helix exists even without histones.

(Q7) T/F regarding transamination?



https://www.pharmaguideline.com/2022/01/transamination-deamination-and-decarboxylation.html

(A) Aminotransferase is induced by glucocorticoids – **True**, glucocorticoids increase aminotransferase activity to mobilize amino acids.

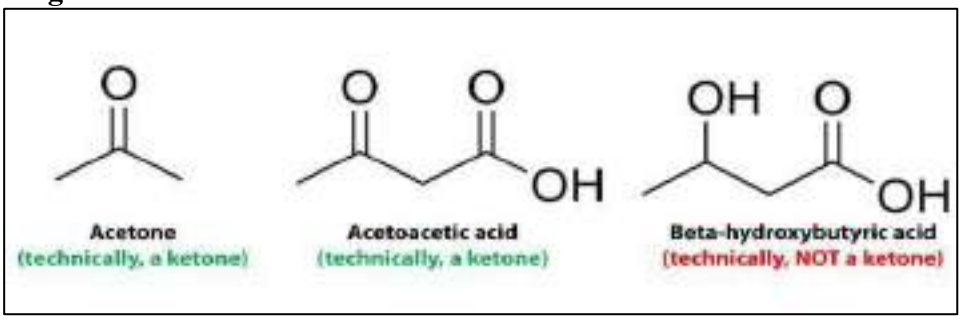
(B) Contribute to maintain blood glucose levels during fasting – **True**, transamination supplies amino groups and carbon skeletons for gluconeogenesis (glucose–alanine cycle).

(C) Is essential for synthesis of non-essential amino acids – **True**, transamination provides amino groups for synthesizing nonessential amino acids.

(D) Pyridoxal phosphate acts as a co-enzyme – **True**, PLP (vitamin B6 derivative) is the coenzyme for all aminotransferases.

(E) This is the initiation of majority of amino acid regeneration – **True**, transamination is the first step in catabolism and also in generating new amino acids.

(Q8) T/F regarding Ketone bodies?



http://peterattiamd.com/ketosis-advantaged-or-misunderstood-state-part-i/

(A) Are synthesized in liver – **True**, liver mitochondria form acetoacetate and β-hydroxybutyrate during fasting.

(B) Are utilized by RBC for energy – **False**, RBCs have no mitochondria and therefore cannot utilize ketone bodies.

(C) Disturb bicarbonate buffer system in blood – **True**, excess ketone bodies cause metabolic acidosis by buffering bicarbonate.
(D) Normally absent in blood – **True**, in healthy fed individual ketone bodies are present only in trace amounts.
(E) Synthesis depends on NADH: NAD^+ ratio – **True**, the ratio determines conversion of acetoacetate to β-hydroxybutyrate.

(Q9) T/F regarding beta oxidation of fatty acids?

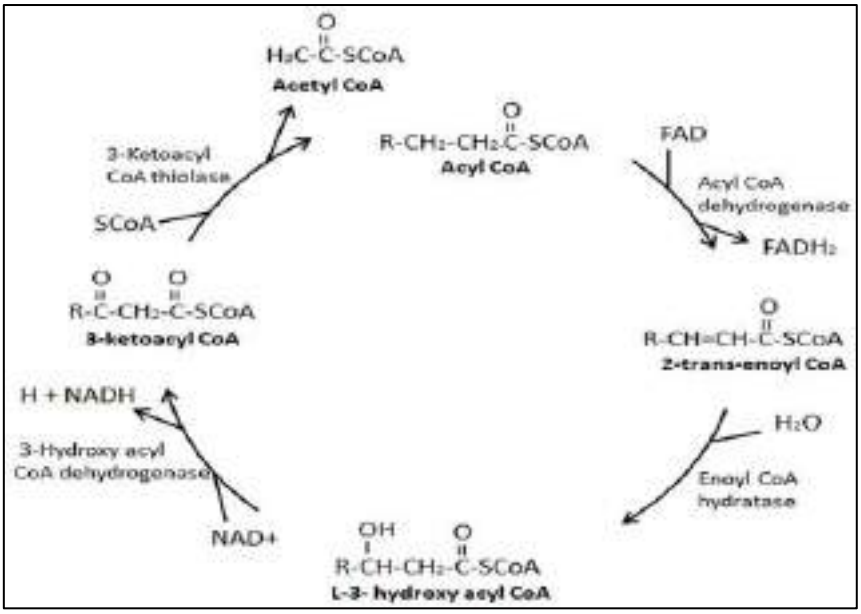


Figure 5-Beta oxidation of fatty acids

https://www.aocs.org/resource/fatty-acid-beta-oxidation/

(A) Carnitine transports long chain fatty acids into mitochondria – **True**, the carnitine shuttle moves long-chain fatty acyl-CoA into the mitochondrial matrix.
(B) It is induced by high insulin/glucagon ratio – **False**, high insulin inhibits lipolysis and β-oxidation; low insulin/high glucagon Favors β-oxidation.
(C) It provides substrate to gluconeogenesis – **True**, β-oxidation supplies ATP and also generates acetyl-CoA and NADH, and the glycerol backbone from TAG provides substrate for gluconeogenesis (though acetyl-CoA itself cannot become glucose, its energy drives gluconeogenesis).
(D) Malonyl CoA inhibits CAT-1 – **True**, malonyl-CoA (from fatty acid synthesis) inhibits carnitine acyltransferase-1 to prevent simultaneous oxidation and synthesis.
(E) Takes place in mitochondria – **True**, β-oxidation occurs in the mitochondrial matrix (very-long-chain fatty acids initially in peroxisomes).

(Q10) T/F regarding the amino acids formed by free ammonia assimilation?

(A) Alanine – **False**, alanine is formed from pyruvate mainly by transamination, not directly by free ammonia.
(B) Arginine – **False**, arginine is formed via the urea cycle and not directly by free ammonia assimilation.
(C) Glutamate – **True**, formed by glutamate dehydrogenase combining α-ketoglutarate with free ammonia.
(D) Glutamine – **True**, formed by glutamine synthetase adding another ammonia to glutamate.
(E) Glycine – **False**, formed from serine (or other sources) by transamination or hydroxy methyltransferase reactions, not by direct ammonia assimilation.

(Q11) T/F regarding metabolism of amino acids?

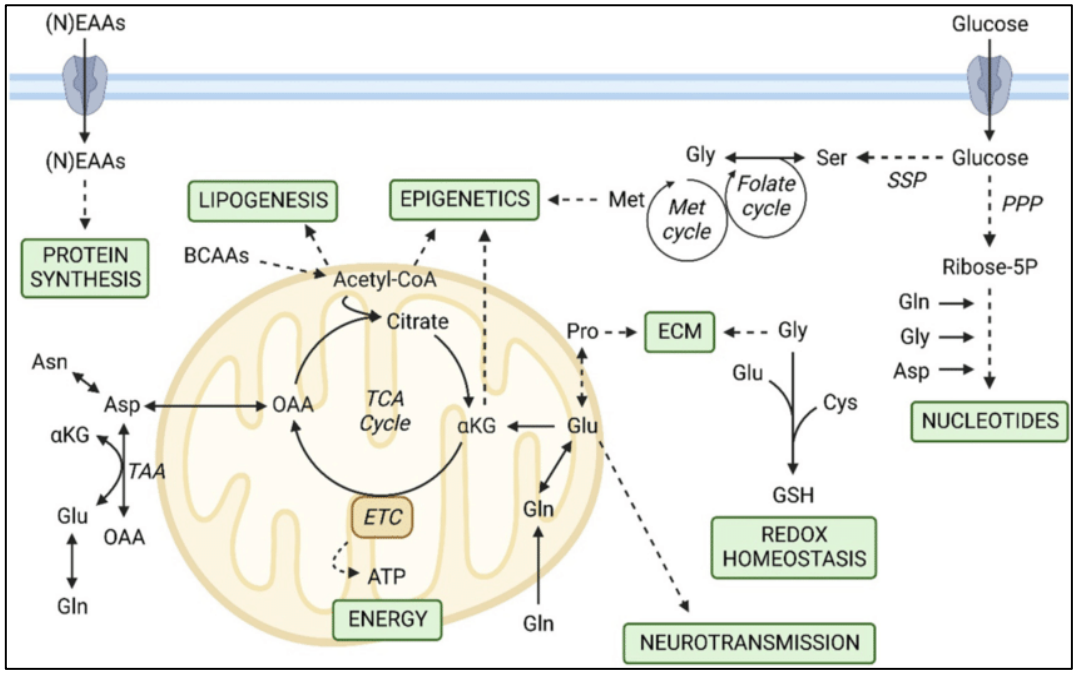


Figure 6- Amino acid metabolism

https://www.researchgate.net/figure/General-overview-of-amino-acids-metabolism-Scheme-showing-the-main-amino-acid-fueled-and_fig1_363389394

(A) Alanine is synthesized from an intermediate of TCA cycle: **False**. Alanine is typically synthesized from pyruvate via transamination, and pyruvate is an *entry point* into the TCA cycle, not an *intermediate* of the cycle itself. The direct intermediate is pyruvate.
(B) Arginine gives rise to Nitric Oxide: **True**. The enzyme nitric oxide synthase converts L-arginine to L-citrulline and nitric oxide (NO).
(C) Glutamate is a substrate for ketone body synthesis: **False**. Glutamate is a glucogenic amino acid, meaning it can be converted into glucose, not ketone bodies.

(D) Impaired metabolism of Tyrosine gives rise to albinism: **True**. Albinism results from defects in tyrosine metabolism, specifically affecting the production of melanin.

(E) Serine provides carbon skeleton for synthesis of cysteine: **True**. Serine provides the carbon backbone for cysteine synthesis, with the sulphur coming from methionine.

(Q12) T/F regarding conversions are associated with the synthesis of glucose from alanine in the liver?

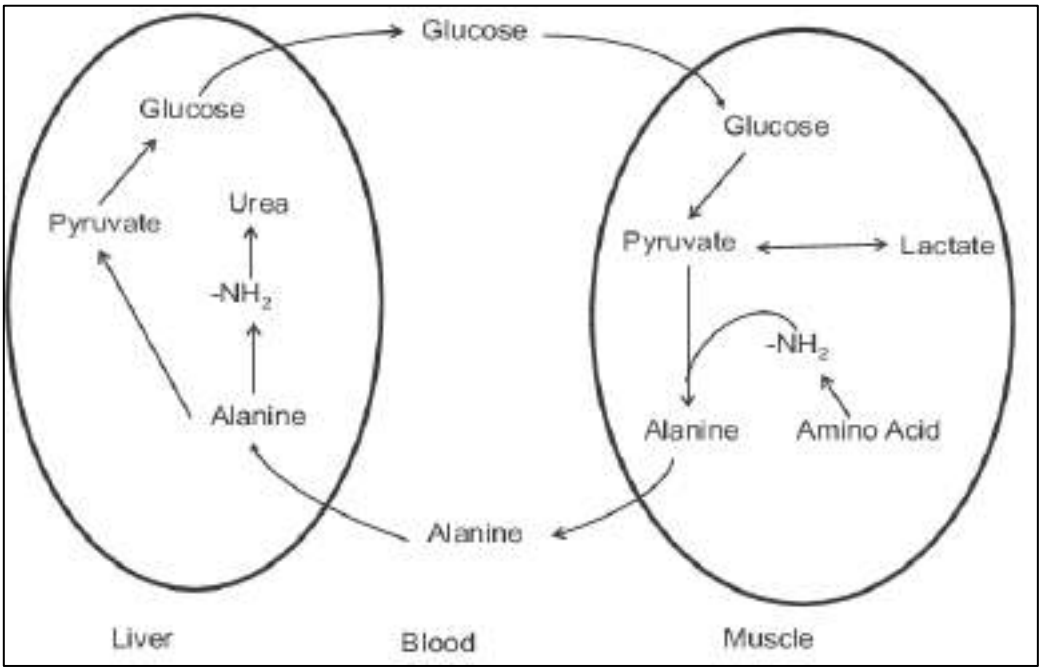


Figure 7-Glucose alanine cycle

https://www.researchgate.net/figure/The-glucose-alanine-cycle-Alanine-is-synthesized-in-muscle-by-transamination-of_fig1_255968302

(A) Fructose 1,6 bisphosphate to Fructose 6 phosphate: **True**. This dephosphorylation step is performed by fructose-1,6-bisphosphatase in gluconeogenesis.

(B) Lactate to pyruvate: **False**. Alanine is transaminase to pyruvate directly. Lactate dehydrogenase converts lactate to pyruvate.

(C) Oxaloacetate to phosphoenolpyruvate: **True**. This is a key regulatory step in gluconeogenesis catalysed by phosphoenolpyruvate carboxykinase (PEPCK).

(D) Pyruvate to Acetyl CoA: **False**. The conversion of pyruvate to Acetyl CoA is an irreversible step that leads to energy production via the TCA cycle or ketogenesis, not gluconeogenesis.

(E) Pyruvate to OAA: **True**. Pyruvate is converted to oxaloacetate (OAA) by pyruvate carboxylase in the liver mitochondria, the first step in gluconeogenesis from pyruvate.

(Q13) A 2-year-old boy presented with severe fasting hypoglycaemia. What is the deficient enzyme?

(A) Alanine aminotransferase: **False.** ALT is involved in amino acid metabolism and the alanine–glucose cycle. Its deficiency does not produce severe fasting hypoglycaemia.

(B) Glucose-6-phosphatase: **True.** Deficiency causes Von Gierke disease (Type I glycogen storage disease). It prevents the final step of gluconeogenesis and glycogenolysis, leading to severe fasting hypoglycaemia.

(C) Glycogen synthase: **False.** Deficiency impairs glycogen formation but does not cause severe fasting hypoglycaemia; patients rely on gluconeogenesis.

(D) Phosphoenolpyruvate carboxykinase: **False.** PEPCK deficiency impairs gluconeogenesis, but it typically causes less severe hypoglycaemia compared to a block at glucose-6-phosphatase.

(E) Phosphofructokinase-1: **False.** PFK-1 deficiency affects glycolysis, not fasting glucose maintenance, and does not produce severe fasting hypoglycaemia.

(Q14) T/F regarding pentose phosphate pathway (PPP)?

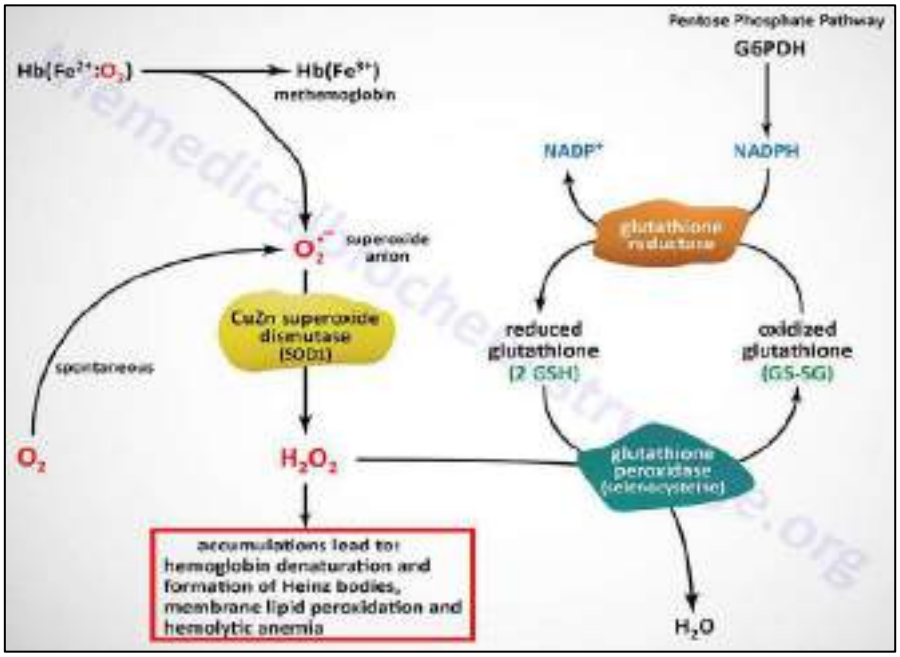


Figure 8-Pentose phosphate pathway

https://themedicalbiochemistrypage.org/pentose-phosphate-pathway/

(A) Glucose 6 phosphatase is the key regulatory enzyme: **False**. Glucose-6-phosphate dehydrogenase (G6PD) is the key regulatory enzyme of the PPP.

(B) Individuals with deficiency of the main enzyme of PPP are susceptible for haemolysis: **True**. G6PD deficiency leads to insufficient production of NADPH to protect red blood cells from oxidative stress, resulting in haemolytic anaemia when exposed to certain triggers.

(C) It is the alternative pathway for glucose oxidation: **True**. The PPP provides an alternative route for glucose 6-phosphate metabolism, running parallel to glycolysis.

(D) PPP is highly active in lactating mammary glands: **True**. The PPP provides the necessary NADPH for fatty acid synthesis, a key process in milk production in mammary glands.

(E) Supplies NADH for FA synthesis: **False**. The PPP primarily supplies **NADPH**, not NADH, for reductive biosynthesis reactions like fatty acid synthesis.

(Q15) What can be seen in LDL but not in chylomicron?

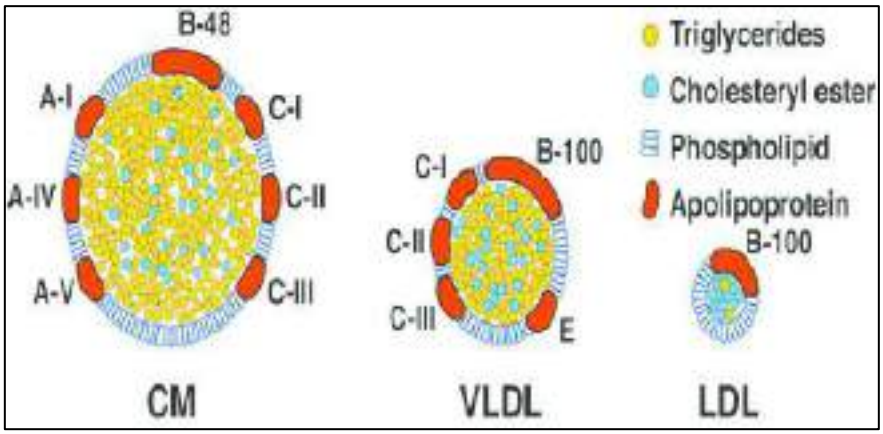


Figure 10- Lipoproteins

https://www.researchgate.net/figure/Apolipoproteins-present-in-chylomicrons-CM-very-low-density-lipoproteins-VLDL-and_fig3_335601355

(A) Apolipoprotein B100**: True.** LDL contains ApoB-100 as its structural apoprotein. Chylomicrons instead contain ApoB-48, not ApoB-100.

(B) Apolipoprotein A**: False.** ApoA is found in HDL and also present in chylomicrons, not specific to LDL.

(C) Cholesterols: **False.** Both LDL and chylomicrons contain cholesterol; LDL is richer, but it is not unique to LDL.

(D) Cholesteryl esters: **False.** Both lipoproteins contain cholesteryl esters, though LDL carries them in higher proportion.

(E) Triglycerides: **False.** Chylomicrons are highly enriched in triglycerides. LDL carries far fewer, but they are not absent from chylomicrons.

(Q16) Which of the following are required for the synthesis of urea?

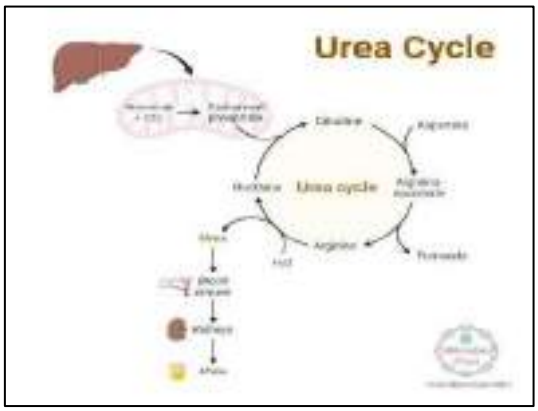


Figure 11- Urea cycle

https://microbenotes.com/urea-cycle-enzymes-and-steps/

(A) Ammonium ions: **True**. Ammonia is combined with bicarbonate in the first step of the urea cycle to form carbamoyl phosphate.
(B) Aspartic acid: **True**. Aspartate provides the second nitrogen atom for urea synthesis through condensation with citrulline to form argininosuccinate.
(C) ATP: **True**. ATP is required for several steps in the urea cycle, including the synthesis of carbamoyl phosphate (2 ATP) and the synthesis of argininosuccinate (1 ATP equivalent).
(D) Carbon dioxide: **True**. Bicarbonate (derived from CO2) provides the carbon atom for urea synthesis.
(E) Uric acid: **False**. Uric acid is a product of purine metabolism and is not involved in the synthesis of urea.

(Q17) T/F regarding bile acids?

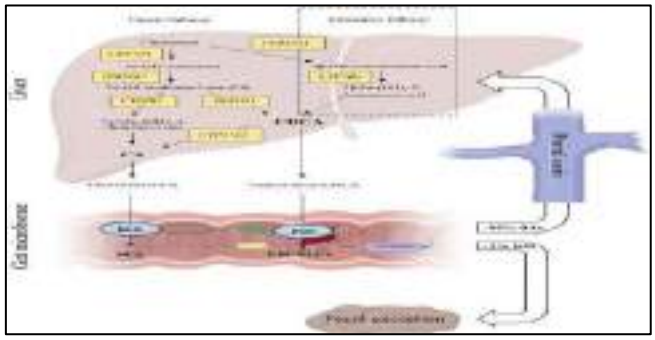


Figure 12- Bile acid synthesis

https://www.researchgate.net/figure/The-principal-bile-acid-synthesis-pathways-in-humans-Hepatocytes-are-the-primary-site-of_fig1_344862524

(A) Synthesized by polyunsaturated fatty acids: **False**. Bile acids are synthesized from cholesterol in the liver.
(B) Conserved in body via extra hepatic circulation: **False**. They are conserved through the enterohepatic circulation, involving the intestine and liver.
(C) Are important in protein digestion: **False**. Bile acids are important for the digestion and absorption of fats (lipids), not proteins.
(D) Facilitate cholesterol absorption: **True**. Bile acids form mixed micelles that facilitate the absorption of dietary fats and cholesterol in the small intestine.
(E) Form by the activity of 1-alfa hydroxylase: **False**. Cholesterol 7-alpha-hydroxylase is the key regulatory enzyme in bile acid synthesis, not 1-alpha.

(Q18) T/F combination of antibiotic and its function?

(A) Chloramphenicol – inhibits peptide transferase: **True**. Chloramphenicol binds to the 50S ribosomal subunit and inhibits the peptidyl transferase step of translation.
(B) Erythromycin – inhibits ribosome translocation: **True**. Erythromycin (a macrolide) binds to the 50S subunit and inhibits the translocation of the ribosome along the mRNA.
(C) Rifampicin – inhibits RNA synthesis: **True**. Rifampicin inhibits bacterial DNA-dependent RNA polymerase, thereby blocking RNA synthesis.
(D) Streptomycin – inhibits initiation of translation: **True**. Streptomycin (an aminoglycoside) binds to the 30S ribosomal subunit and prevents the formation of the initiation complex.
(E) Tetracycline – inhibits the progression of translation: **False**. Tetracycline inhibits the binding of aminoacyl-tRNA to the A site of the ribosome, thus preventing elongation/progression of translation.

(Q19) Which of the following is/are correctly matched with the elevated bilirubin level in blood?

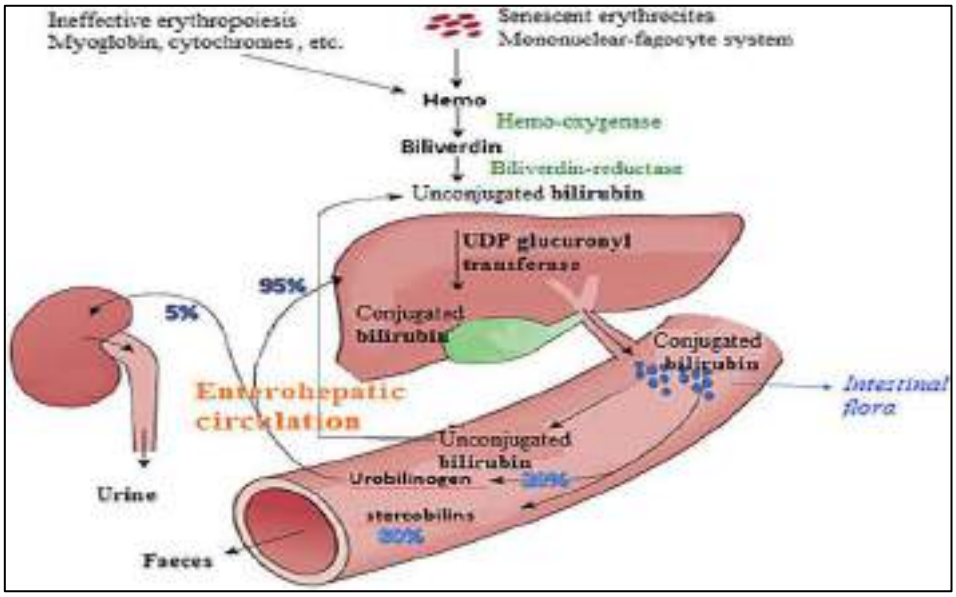


Figure 12-bilirubin metabolism

https://www.researchgate.net/figure/Bilirubin-metabolism-and-recirculation_fig3_353125938

(A) Cholestasis – Unconjugated Bilirubin: **False**. Cholestasis is bile flow obstruction, leading to an increase in **conjugated** bilirubin in the blood.

(B) Gilbert syndrome - Conjugated Bilirubin: **False**. Gilbert's syndrome is a deficiency in the conjugation enzyme (UGT1A1), leading to an increase in **unconjugated** bilirubin.

(C) Malaria – unconjugated bilirubin: **True**. Malaria causes haemolytic anaemia (destruction of red blood cells), resulting in an overproduction of unconjugated bilirubin that the liver cannot process fast enough.

(D) Neonatal jaundice - Conjugated Bilirubin: **False**. Physiologic neonatal jaundice is due to the immature liver's reduced ability to conjugate bilirubin, causing elevated **unconjugated** bilirubin.

(E) Viral hepatitis – both conjugated and unconjugated bilirubin: **True**. Viral hepatitis damages liver cells, affecting both the uptake/conjugation and excretion of bilirubin, leading to elevation in both forms.

(Q20) T/F regarding eicosanoids?

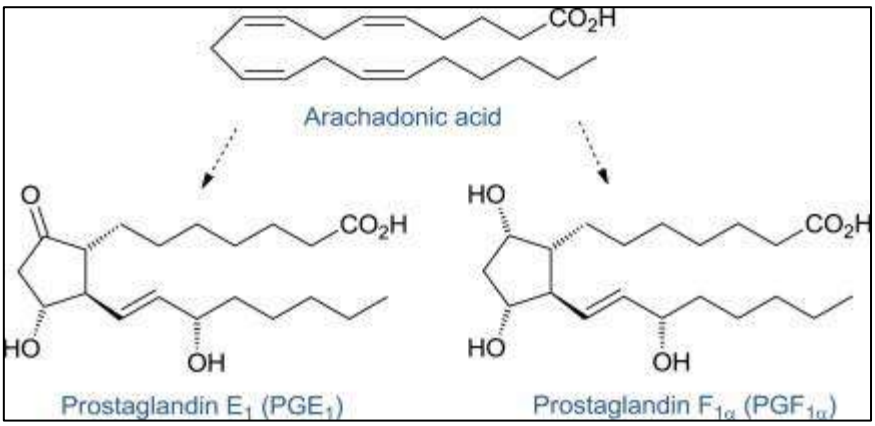


Figure 13-Eicosanoids

https://www.sciencedirect.com/topics/chemistry/eicosanoid

(A) Aspirin inhibits lipoxygenase enzyme: **False**. Aspirin inhibits the cyclooxygenase (COX-1 and COX-2) enzymes, not lipoxygenase (LOX).

(B) Corticosteroids inhibit cyclooxygenase enzyme: **False**. Corticosteroids inhibit phospholipase A2, thereby preventing the release of arachidonic acid, the precursor to both cyclooxygenase and lipoxygenase pathways.

(C) Lipoxins are synthesized in immune cells: **True**. Lipoxins are anti-inflammatory eicosanoids synthesized by the interaction of different immune cells (e.g., neutrophils and macrophages).

(D) Omega 3 fatty acids promote production of series 3 eicosanoids: **True**. Omega-3 fatty acids (like EPA) are precursors for series 3 prostaglandins and thromboxane, which are generally less inflammatory than series 2.

(E) Thromboxane is produced by vascular wall endothelium: **False**. Thromboxane A2 is primarily produced by platelets, while prostacyclin is produced by the vascular endothelium.

(Q21) T/F regarding eicosanoids?

(A) Arachidonic acid is a precursor of group 2 eicosanoids: **True**. Arachidonic acid (an omega-6 fatty acid) is the precursor for the 2-series prostaglandins, thromboxane, and 4-series leukotrienes.

(B) Prostacyclin is produced by platelets: **False**. Prostacyclin is produced by vascular endothelial cells, while thromboxane is produced by platelets.

(C) Thromboxane and prostacyclin act as antagonists: **True**. Thromboxane A2 promotes platelet aggregation and vasoconstriction, while prostacyclin (PGI2) inhibits platelet aggregation and is a vasodilator, making them functional antagonists.

(D) Thromboxane is a vasoconstrictor: **True**. Thromboxane A2 causes constriction of blood vessels.

(E) Thromboxane is synthesized by lipo-oxygenase: **False**. Thromboxane is synthesized by the cyclooxygenase (COX) pathway in platelets.

(Q22) T/F regarding antioxidants?

(A) Alfa tocopherol: **True**. Alpha-tocopherol is a form of Vitamin E, a major lipid-soluble antioxidant.

(B) Ascorbic acid: **True**. Ascorbic acid (Vitamin C) is a water-soluble antioxidant.

(C) Folate: **False**. Folate (Vitamin B9) is involved in DNA synthesis and methylation, not primarily as an antioxidant.

(D) Oxidized glutathione: **False**. Reduced glutathione is the active antioxidant form; oxidized glutathione (GSSG) needs to be recycled back to the reduced state (GSH).

(E) Superoxide dismutase: **True**. Superoxide dismutase (SOD) is an enzyme that catalyses the dismutation of the superoxide radical into oxygen and hydrogen peroxide, acting as a crucial enzymatic antioxidant defence.

(Q23) Which of the following is/are steps included in in-vitro of human insulin production?

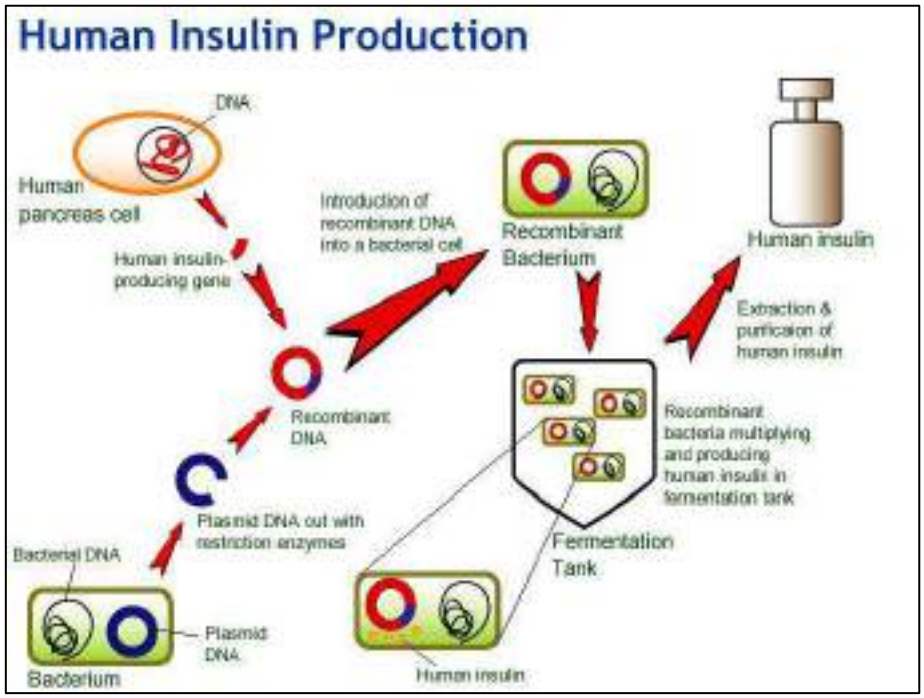


Figure 14- Human insulin production

https://www.eduhk.hk/biotech/eng/classrm/class_health5.html

(A) Expression vector ligation: **True**. The gene for insulin must be ligated into an expression vector.

(B) PCR amplification: **True**. PCR can be used to amplify the insulin gene insert from cDNA before ligation.

(C) Protein purification: **True**. The expressed insulin protein must be purified from the host organism culture.

(D) Restriction digestion: **True**. Restriction enzymes are used to cut both the vector and the insulin gene insert to allow ligation.

(E) Reverse transcription: **True**. Since insulin is a protein and the final gene used often doesn't contain introns, a cDNA copy is made from mRNA using reverse transcriptase.

(Q24) T/F regarding obstructive jaundice?

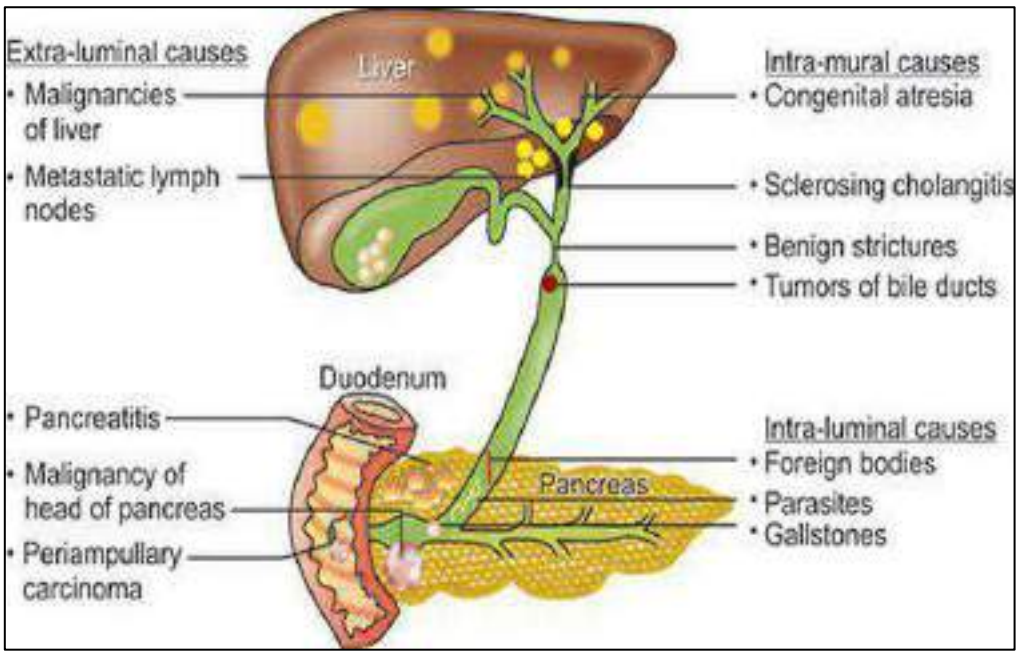


Figure 15- Obstructive jaundice

https://medizzy.com/feed/34109815

(A) GGT activity increased in serum: **True**. Gamma-glutamyl transferase (GGT) is typically elevated in cholestatic and obstructive liver diseases.

(B) Increase alkaline phosphatase activity in serum: **True**. Alkaline phosphatase (ALP) activity increases significantly in obstructive jaundice because of increased synthesis and release from the bile duct cells.

(C) Increase conjugated bilirubin in serum: **True**. Obstruction prevents the excretion of conjugated bilirubin into the bile/intestine, causing it to accumulate in the bloodstream.

(D) Presence of bilirubin in urine: **True**. Conjugated (water-soluble) bilirubin can be filtered by the kidneys and appears in the urine (dark urine), which does not happen with unconjugated bilirubin.

(E) UCB increased in serum: **False**. Unconjugated bilirubin (UCB) levels typically remain normal or near normal in pure obstructive jaundice; the increase is in the conjugated form.

(Q25) Which of the following is/are involved in the progression of the cell cycle?

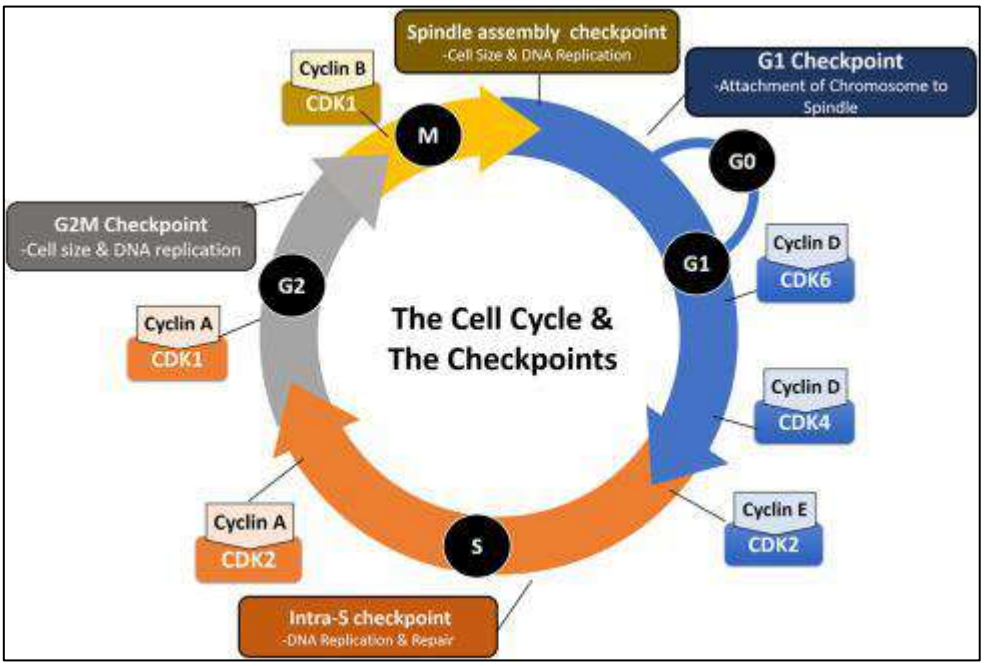


Figure 16- Cell cycle progression

https://www.sciencedirect.com/topics/immunology-and-microbiology/cell-cycle-progression

(A) Cyclin-dependent protein kinase (CDK): **True**. CDKs, in association with cyclins, are central regulators that drive the cell cycle forward.

(B) p21: **False**. p21 is a CDK inhibitor that halts the cell cycle progression, typically in response to DNA damage.

(C) p53: **False**. p53 is a tumour suppressor protein that **halts** the cell cycle (or induces apoptosis) in response to DNA damage or stress; it does not promote progression.

(D) Protein Ku: **False**. Protein Ku is involved in DNA repair (specifically non-homologous end joining), not directly in the overall progression of the cell cycle stages.

(E) Retinoblastoma (Rb**)**: **False**. Rb protein acts as a brake on the cell cycle in its active (hypo phosphorylated) state. When inactivated by phosphorylation by cyclin/CDK complexes, it *allows* progression into S phase, but it is fundamentally a regulator that *inhibits* progression until a signal is received.

(Q26) T/F regarding the process of recombinant DNA technology?

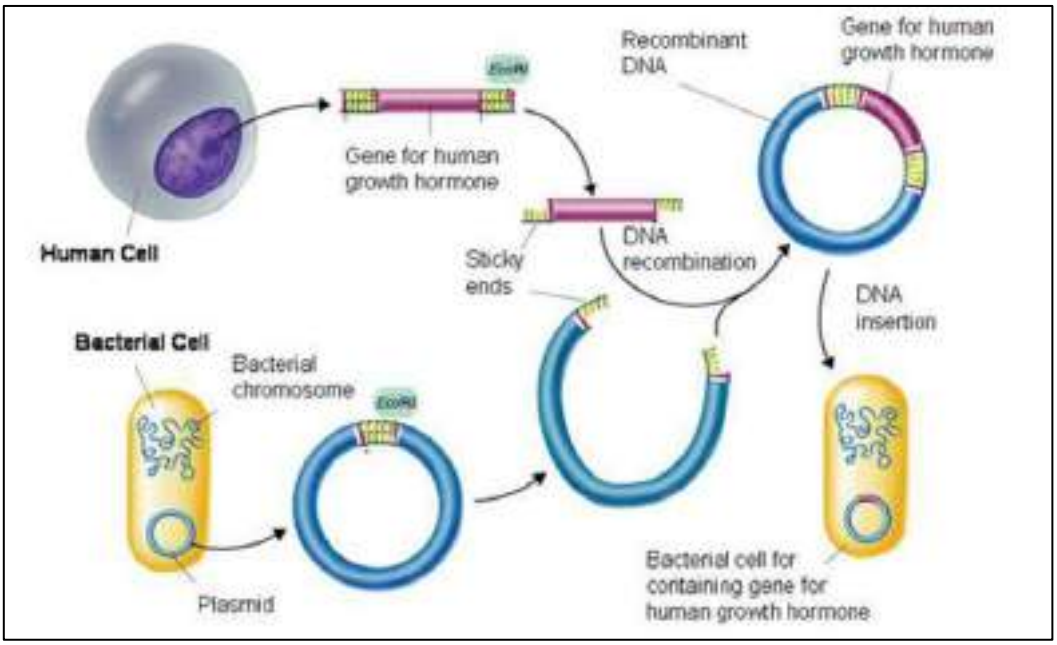


Figure 17-Recombinant DNA Technology

https://microbenotes.com/recombinant-dna-technology-steps-applications-and-limitations/

(A) Genomic DNA can be used as a template to express mammalian genes on E. coli: **False**. Genomic DNA from mammals contains introns, which *E. coli* cannot splice out. cDNA must be used for expression in bacteria.

(B) Polymerase chain reaction (PCR) can be used for the introduction of restriction sites to the gene: **True**. Primers used in PCR can be engineered to include specific restriction sites at their ends, allowing the amplified gene product to be easily cloned.

(C) Recombinant DNA introduced to E. coli through the cell membrane: **True**. Transformation involves making the cell membrane permeable, either chemically (calcium chloride) or by electroporation, allowing the DNA to pass through.

(D) Regulated gene expression in E. coli increases protein: **True**. Regulated expression allows the bacteria to grow to high density before the foreign protein is produced, maximizing yield and minimizing toxic effects during growth.

(E) Vector plasmids include multiple cloning sites to integrate foreign DNA: **True**. Multiple cloning sites (MCS) contain several different restriction enzyme recognition sequences clustered together, providing flexibility for inserting foreign DNA.

(Q27) Which of the following is/are enzymes that increase the hepatic cholesterol level?

(A) 7-α-hydroxylase: **False**. This enzyme is the rate-limiting step in bile acid synthesis, which *removes* cholesterol from the liver.

(B) Acetyl-CoA: Acyl transferase (ACAT): **True**. ACAT converts free cholesterol into cholesteryl esters for storage within the liver (and other cells), increasing the amount of stored cholesterol.

(C) Cholesterol ester hydrolase: **False**. This enzyme breaks down cholesteryl esters back into free cholesterol, making it available for processes like bile acid synthesis or secretion, not increasing total stored levels.

(D) Cholesterol ester transfer protein (CETP): **False**. CETP is involved in transferring cholesterol esters between lipoproteins in the plasma, not primarily increasing hepatic levels directly in this context.

(E) HMG-CoA reductase: **True**. HMG-CoA reductase is the rate-limiting enzyme in cholesterol biosynthesis. Inhibiting it with statins *lowers* cholesterol levels, so its activity *increases* hepatic cholesterol levels.

(Q28) Which of the following is/are inherited diseases are associated with tyrosine metabolism?

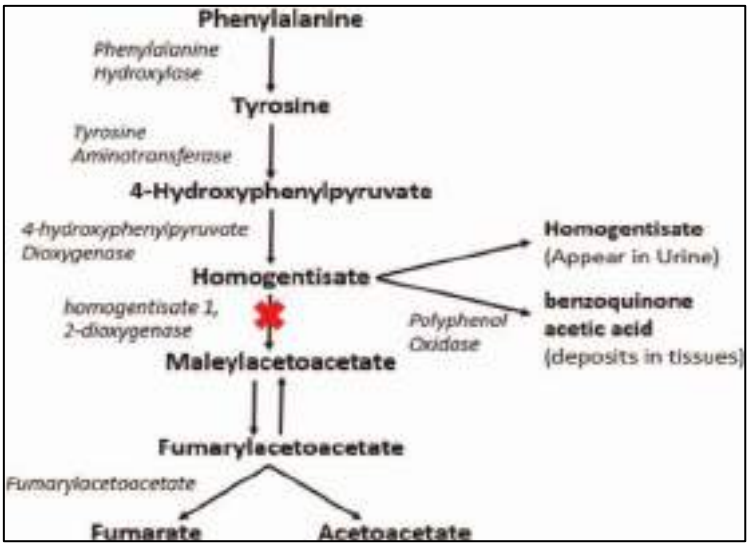


Figure 18-Tyrosine metabolism

https://www.researchgate.net/figure/The-metabolic-pathway-of-tyrosine-metabolism-showing-block-in-the-pathway-at-the-level_fig1_357297916

(A) Albinism: **True**. Albinism results from defects in the pathway of melanin synthesis, which starts from tyrosine.

(B) Alkaptonuria: **True**. Alkaptonuria is an IEM caused by a deficiency in homogentisate 1,2-dioxygenase, an enzyme in the breakdown pathway of tyrosine.

(C) Homocystinuria: **False**. Homocystinuria is associated with methionine metabolism.

(D) Maple syrup disease: **False**. Maple syrup urine disease involves the metabolism of branched-chain amino acids (leucine, isoleucine, valine).

(E) Phenylketonuria: **False**. Phenylketonuria (PKU) involves the metabolism of phenylalanine, the precursor to tyrosine.

(Q29) What are the post-translational modifications that take place when procollagen converts into mature collagen?

(A) Amino-terminal and carboxy-terminal pro peptides are cleaved: **True**. Specific peptidases cleave these extension peptides to form tropocollagen, which can then assemble into mature collagen fibrils extracellularly.

(B) Formation of cross-links between hydroxylysine and lysine: **True**. Covalent cross-links (involving deamination by lysyl oxidase) between lysine and hydroxylysine residues stabilize the collagen fibrils into mature Fibers.

(C) Glycosylation of hydroxyproline residues: **False**. Hydroxylysine residues are glycosylated, not hydroxyproline.

(D) N-terminal leading sequence is cleaved: **False**. The signal peptide is cleaved during translation into the ER; the pro peptides at the N and C terminals are cleaved *after* secretion.

(E) Tropocollagen is arranged in a staggered manner: **False**. This describes the self-assembly and structure of mature collagen fibrils, not a chemical post-translational modification step.

(Q30) Which of the following is/are atherogenic risk of an individual can be assessed by?

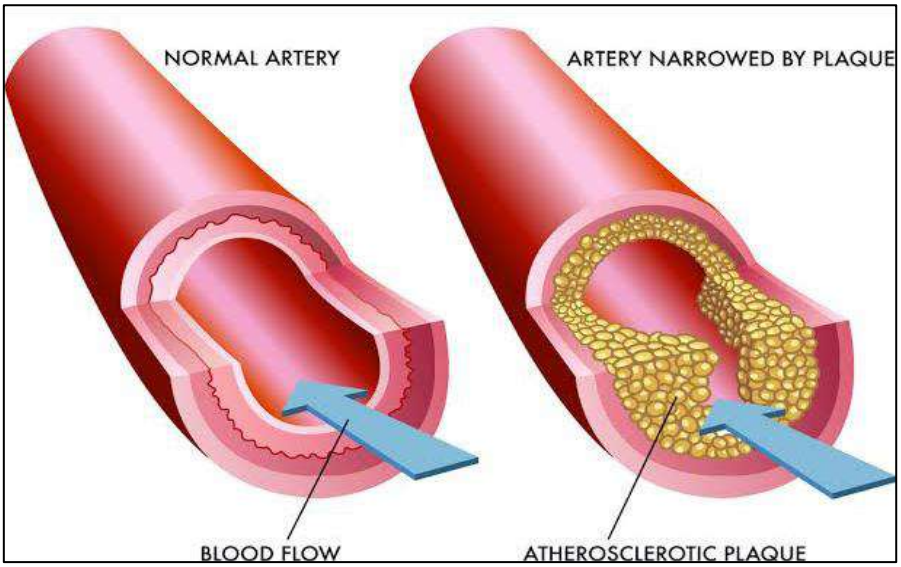


Figure18-Atherosclerosis

https://simshospitals.com/atherosclerosis/

(A) Atherogenic index of plasma: **True**. The Atherogenic Index of Plasma (AIP) is calculated as log (TG/HDL-C) and is a strong predictor of cardiovascular risk.

(B) Highly sensitive C-reactive protein: **True**. Hs-CRP is a biomarker for systemic inflammation, which is strongly associated with the development and progression of atherosclerosis.

(C) Lipoprotein bound phospholipase A2 (Lp-A2): **True**. Lp-PLA2 is a vascular inflammatory enzyme strongly associated with increased risk for heart attack and stroke.

(D) Ratio between LDL cholesterol and HDL cholesterol (LDL-C/HDL-C): **True**. This ratio is a good indicator of cholesterol balance and cardiovascular risk.

(E) Ratio between total cholesterol and HDL cholesterol (Total C/HDL-C): **True**. This is a widely used and effective measure for assessing overall atherogenic risk.

(Q31) A man got pain and swelling in his right knee following a fall recently. What enzyme is inhibited in the prescription for the pain and swelling?

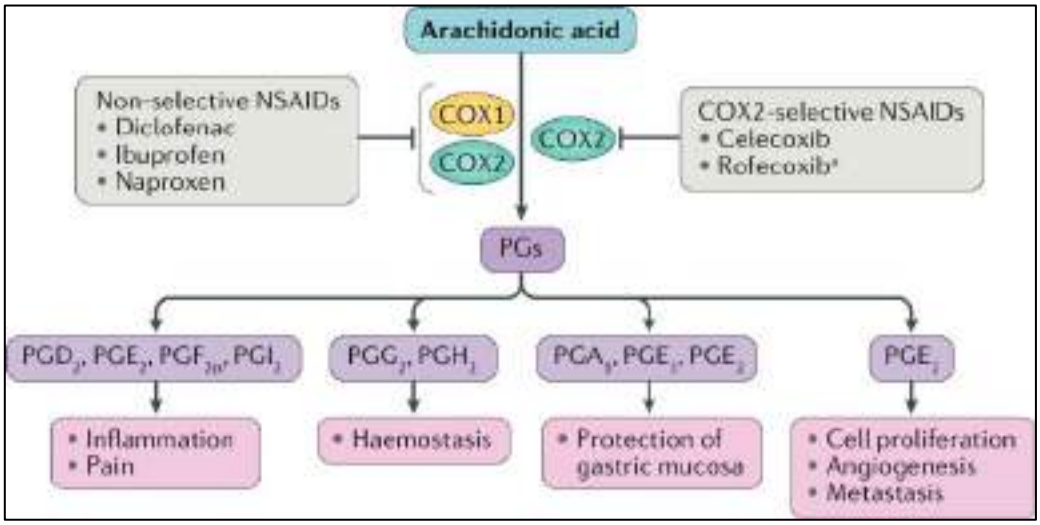


Figure 19-NSAID

https://www.nature.com/articles/s41569-020-0366-z

(A) Cyclooxygenase-1: **False.** COX-1 is constitutive and involved in gastric protection and platelet function. It is not the primary target when treating inflammation from injury.

(B) Cyclooxygenase-2: **True.** COX-2 is induced during inflammation and produces prostaglandins responsible for pain and swelling. NSAIDs used for post-injury inflammation primarily inhibit COX-2 to reduce these symptoms.

(C) Lipoxygenase: **False.** This enzyme forms leukotrienes in the inflammatory pathway, but NSAIDs do not inhibit lipoxygenase.

(D) Phospholipase A2**: False.** PLA_2 releases arachidonic acid from membrane phospholipids. It is inhibited by corticosteroids, not NSAIDs.

(E) Phospholipase A**: False.** NSAIDs do not act on this enzyme; it is not the main source of arachidonic acid in acute inflammation management.

COURSE 1- METABOLISM 1

TUTORIALS & ANSWERS

TUTORIAL 01

Carbohydrate Metabolism

(1) Explain in detail all the steps involved in the preparatory and payoff phases of carbohydrate metabolism?

(2) What are the key factors that regulate the activity of the enzyme PFK-1 in carbohydrate metabolism? Explain how each factor affects its function.

(3) Name the enzyme complex involved in the conversion of pyruvate to acetyl-CoA. List the enzymes and coenzymes required for this intermediate reaction and explain the role of each.

(4) Calculate the total ATP yield from one molecule of glucose during glycolysis and the intermediate step. Mention the specific steps where ATP is produced or consumed.

(5) Explain the role of B vitamins in the intermediate reaction that converts pyruvate to acetyl-CoA?

TUTORIAL 01

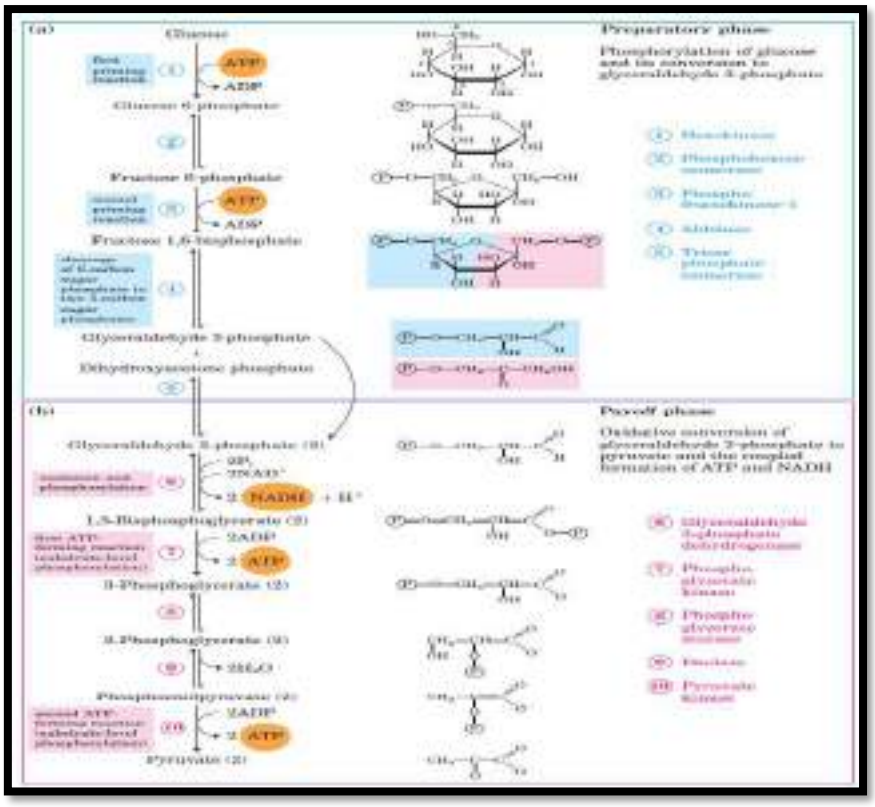
Carbohydrate Metabolism-Answers

(1) Explain in detail all the steps involved in the preparatory and payoff phases of carbohydrate metabolism?

- Glycolysis converts one glucose molecule (6 carbons) into two molecules of pyruvate (3 carbons each).
- The process yields energy in the form of ATP and NADH.
- It consists of 10 enzyme-catalysed reactions divided into two phases,

  ➢ The Preparatory Phase

  ➢ The Payoff Phase

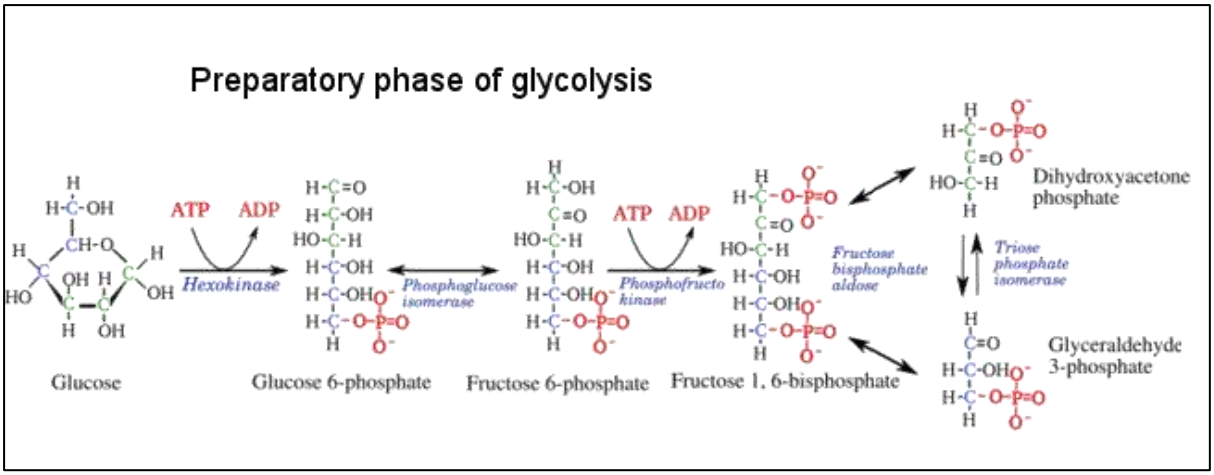


levelbiology.co.uk/notes/glycolysis-steps

Preparatory Phase/ Energy Investment Phase

- In this phase, glucose is primed for breakdown, consuming two ATP molecules
- It includes the following steps,

1. Phosphorylation of Glucose (6C)
2. Isomerization of Glucose-6-Phosphate (6C)
3. Phosphorylation of Fructose-6-Phosphate (6C)
4. . Cleavage of Fructose-1,6-Bisphosphate (6C)
5. Interconversion of Glyceraldehyde-3-Phosphate (3C) and Dihydroxyacetone Phosphate (3C)



https://reachingfordreams.com/bioscience/cellular-energy/cellular-respiration/10-steps-of-glycolysis-reactions-in-cytoplasm

Payoff Phase/ Energy Harvest Phase

• This phase generates energy, producing ATP and NADH.
• It includes the following steps,

6. Oxidation of Glyceraldehyde-3-Phosphate
7. Production of ATP
8. Isomerization of 3-Phosphoglycerate
9. Formation of Phosphoenolpyruvate (PEP)
10. Final ATP Production and Pyruvate Formation

(2) What are the key factors that regulate the activity of the enzyme PFK-1 in carbohydrate metabolism? Explain how each factor affects its function.

Regulation of Phosphofructokinase-1 (PFK-1)

➢ Allosteric Regulation: PFK-1 is the most important control site in glycolysis and is allosterically regulated by several molecules.

- Inhibition: High levels of ATP, citrate, and phosphoenolpyruvate reducing glycolytic flux when energy levels are high.
- Activation: AMP reverses the inhibitory effect of ATP, increasing energy (ATP) levels are low Energy Charge.
- As the cellular ATP/AMP ratio falls, glycolysis is stimulated.
- PFK-1 has two binding sites for ATP, one as a substrate and the other for inhibitory action.
- When AMP is present, it counteracts the inhibitory effect of ATP, thus increasing PFK-1 activity and promoting glycolysis under low energy conditions.

- Fructose 2,6-bisphosphate (F-2,6-BP): This is the most potent activator of PFK-1. It increases the enzyme's affinity for fructose 6-phosphate and reduces ATP's inhibitory effect.
- pH: Low pH (acidic conditions) inhibits PFK-1, especially in anaerobic conditions where lactic acid accumulates. This protects the muscle from damage due to excessive acidity.

(3) Name the enzyme complex involved in the conversion of pyruvate to acetyl-CoA. List the enzymes and coenzymes required for this intermediate reaction and explain the role of each.

Intermediate Reaction - Pyruvate to Acetyl CoA

- The conversion of Pyruvate to Acetyl of CoA is catalysed by the Pyruvate Dehydrogenase Complex (PDC).
- The Pyruvate Dehydrogenase Complex (PDC) is a large multi-enzyme complex made up of three enzymes,

1. Pyruvate Dehydrogenase (E1) – Catalyses the decarboxylation of pyruvate
2. Dihydrolipoyl Transacetylase (E2) – Transfers the acetyl group to CoA
3. Dihydrolipoyl Dehydrogenase (E3) – Regenerates the oxidized form of lipoamide and transfers electrons to NAD+ to form NADH

Five co-enzymes are required for this conversion

1. Thiamine Pyrophosphate (TPP) – A cofactor for Pyruvate Dehydrogenase (E1)
2. Lipoamide – Covalently attached to Dihydrolipoyl Transacetylase (E2), serves as a carrier for acyl groups
3. Coenzyme A (CoA) – Accepts the acetyl group to form acetyl CoA
4. FAD – Electron carrier in Dihydrolipoyl Dehydrogenase (E3)
5. NAD+ – Electron acceptor, reduced to NADH

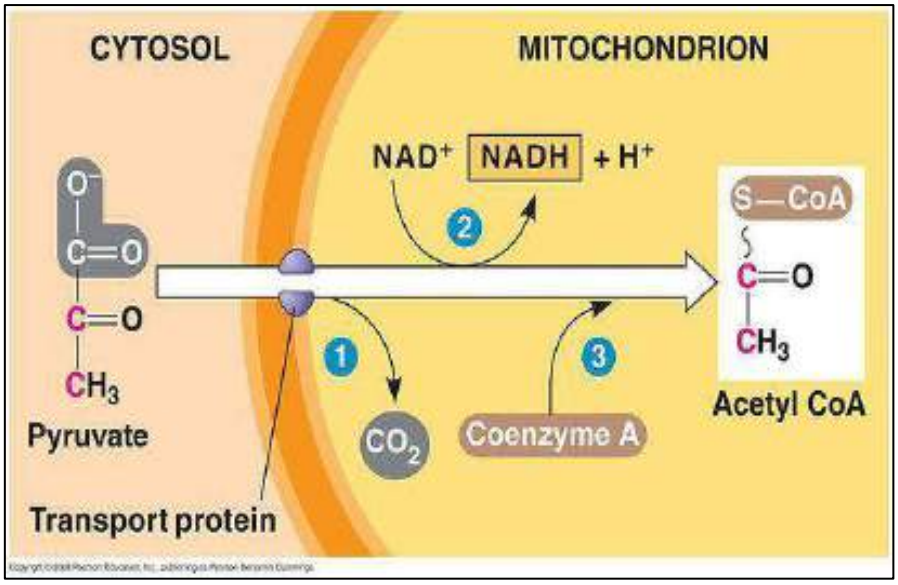


Figure 20- Intermediate Reaction - Pyruvate to Acetyl CoA

https://bio.libretexts.org/Bookshelves/Introductory_and_General_Biology/Map%3A_Raven_Biology_12th_Edition/07%3A_How_Cells_Harvest_Energy/7.03%3A_The_Oxidation_of_Pyruvate_Produces_Acetyl-CoA

(4) Calculate the total ATP yield from one molecule of glucose during glycolysis and the intermediate step. Mention the specific steps where ATP is produced or consumed.

ATP production during the Glycolysis

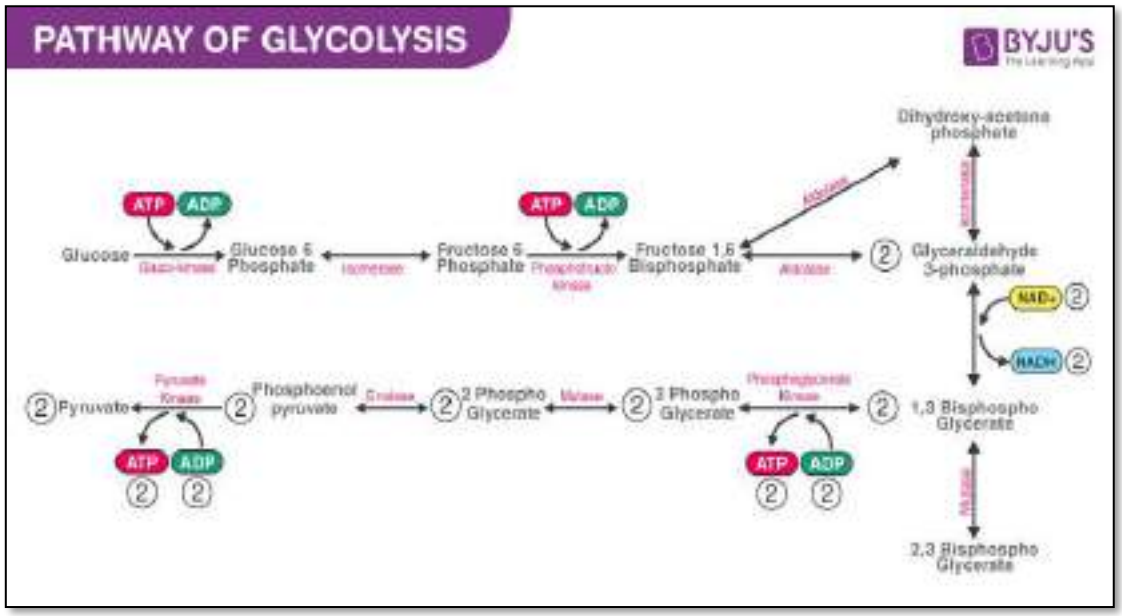


Figure 21- Pathway of Glycolysis

https://byjus.com/biology/glycolysis/

ATP Consumption from Glycolysis (Preparatory Phase)

- Glucose → Glucose-6-Phosphate = -1 ATP (Hexokinase) Phosphofructokinase-1)
- Fructose-6-Phosphate → Fructose-1,6-Bisphosphate = -1 ATP (Phosphofructokinase-1)
- Total ATP used in the investment phase = -2 ATP

ATP Produced from Glycolysis (payoff phase)

- NADH produced during glycolysis (Oxidative phosphorylation) = 2 NADH x 3 ATP = 6 ATP (Glyceraldehyde-3-phosphate dehydrogenase)
- Direct ATP (Substrate-level phosphorylation) = 4 ATP
- 1,3-BPG to 3-phosphoglycerate = 2 ATP (Phosphoglycerate kinase) ➢ PEP to pyruvate = 2 ATP (pyruvate kinase)
- Total ATP produced from Glycolysis = 10 ATP Net ATP Produced during the Glycolysis = 8 ATP

Intermediate step

ATP Produced from the Intermediate Step,

- NADH produced during the conversion of pyruvate to acetyl CoA (Oxidative phosphorylation) = 2 NADH x 3ATP = 6ATP (Pyruvate Dehydrogenase Complex)
- Total ATP from the Intermediate Step= 6 ATP
- Total ATP Yield from Glycolysis and the Intermediate Step: 8 ATP (from glycolysis) + 6 ATP (from the intermediate step) = 14 ATP

(5) Explain the role of B vitamins in the intermediate reaction that converts pyruvate to acetyl-CoA?

1. **Thiamine (Vitamin B1) – Thiamine Pyrophosphate (TPP)**

- In the first step, Pyruvate is decarboxylated (carbon is removed in the form of CO_2).
- This reaction is catalysed by pyruvate dehydrogenase, and the coenzyme involved is Thiamine Pyrophosphate (TPP) enzyme, derived from Vitamin B1 (Thiamine).

2. **Pantothenic Acid (Vitamin B5) – Coenzyme A (CoA)**

- After decarboxylation, the remaining two-carbon fragment (an acetyl group) is transferred to Coenzyme A (CoA), derived from pantothenic acid.
- CoA has a thiol group (-SH) that forms a thioester bond with the acetyl group, which is a high-energy bond, making acetyl-CoA highly reactive.

3. **Niacin (Vitamin B3) – Nicotinamide Adenine Dinucleotide (NAD^+)**

- The reduction of NAD^+ to NADH occurs in the oxidation step, where the two-carbon fragment is oxidized by the enzyme dihydrolipoyl dehydrogenase in the pyruvate dehydrogenase complex.
- NAD^+ accepts electrons and hydrogen to form NADH, which is derived from Niacin (Vitamin B3).

Tutorial 2

Carbohydrate Metabolism: Pentose Phosphate Pathway

Introduction

The Pentose Phosphate Pathway (PPP), also known as the hexose monophosphate (HMP) shunt, is an alternative pathway for glucose metabolism that operates in the cytoplasm. Unlike glycolysis, it does not directly produce ATP. Instead, its main roles are to generate NADPH for reductive biosynthesis and antioxidant defence, and to produce ribose-5-phosphate for nucleotide synthesis. The pathway has two distinct phases, oxidative (irreversible) and non-oxidative (reversible), which are interconnected with glycolysis and other metabolic routes.

Short Answer Questions

(1) Define the Pentose Phosphate Pathway?
(2) Name the two phases of the Pentose Phosphate Pathway and state one main function of each?
(3) List the major products of the oxidative phase of the PPP?
(4) Give two key benefits of the Pentose Phosphate Pathway in human cells?
(5) Explain briefly how the non-oxidative phase links the PPP to glycolysis?

Tutorial 2

Carbohydrate Metabolism: Pentose Phosphate Pathway- Answers.

(1) Define the Pentose Phosphate Pathway Pentose Phosphate Pathway (PPP)?

• The name emphasizes the production of pentose sugars and the involvement of phosphate biochemical reactions of this pathway.

- In the Oxidative phase Pentose in the sugar with phosphate group is synthesized (Ribose-5 phosphate).
- In all the reaction pathways, the Phosphate group involved in the intermediates throughout the pathway (Eg- Glucose-6 phosphate, Ribose-5-phosphate).

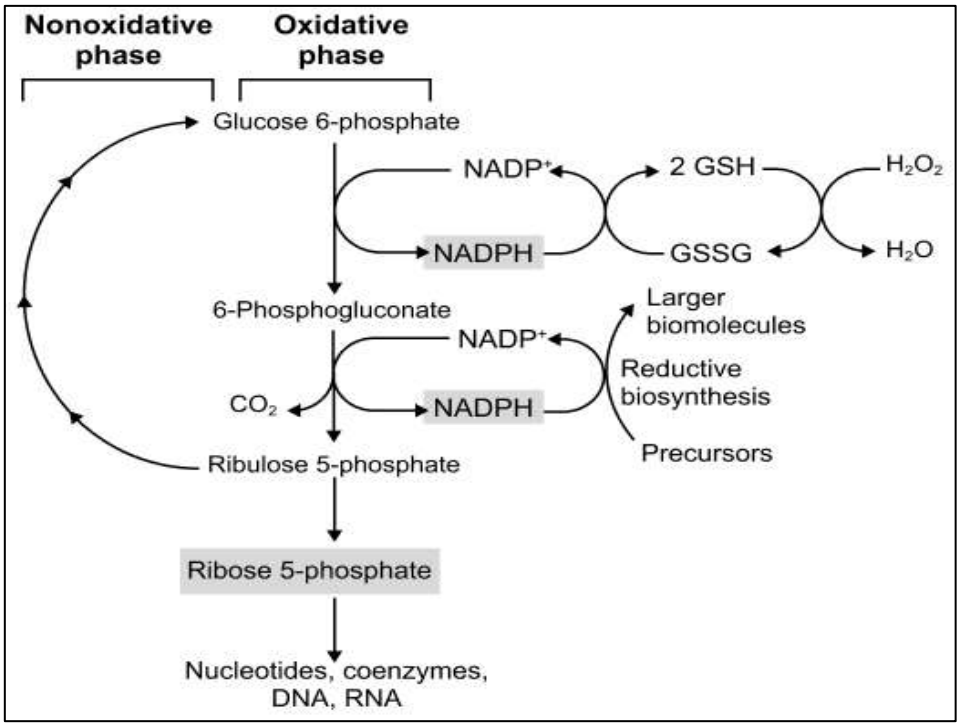
• The Pentose Phosphate Pathway occurs in the cytosol and is more complex than glycolysis.

• The process does not produce or consumption of ATP.

• It takes place with two distinct phases,

1. Anoxidative phase
2. Non-oxidative phase

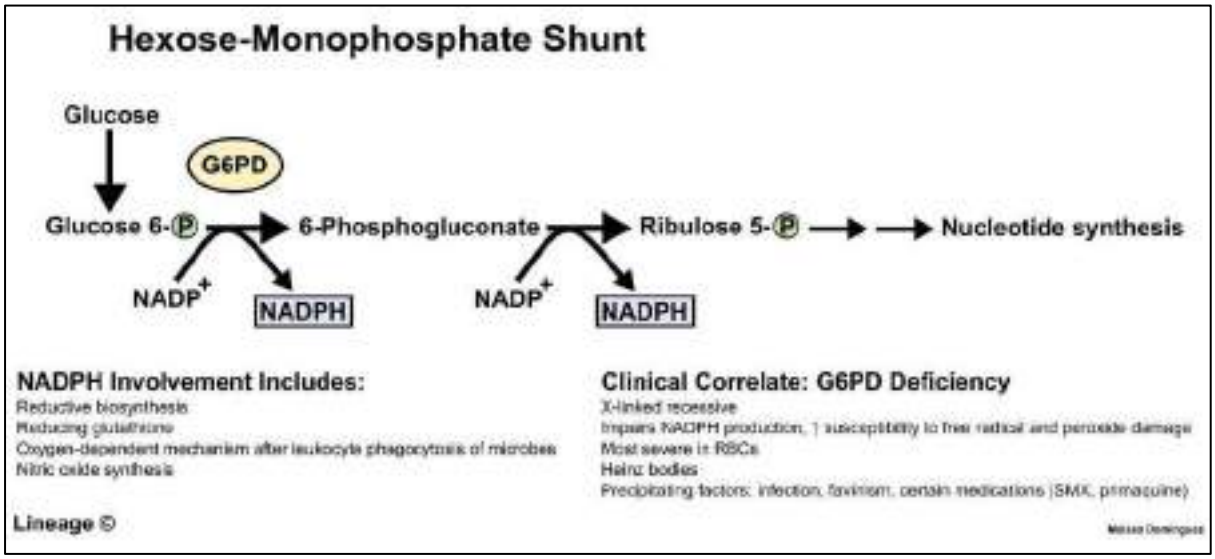
- Unlike glycolysis, the oxidation in PPP is achieved through dehydrogenation using $NADP^+$ instead of NAD^+.
- The pathway's primary functions are to produce NADPH antioxidant defence and to generate for biosynthetic processes and ribose-5-phosphate, a precursor for nucleotide synthesis.



https://www.khanacademy.org/test-prep/mcat/biological-sciences-practice/x04f6bc56:mcat-bio-biochem-foundation-1-passages/e/glucose-6-phosphate-dehydrogenase-and-the-most-important-function-of-the-pentose-phosphate-pathway

Hexose Monophosphate (HMP) shunt

• Pathway starts with Glucose-6-Phosphate (Hexose sugar with single Phosphate group) but this shunt (Changes the way) from the main glycolysis pathway to an alternative pathway to produce NADPH and ribose-5-phosphate.



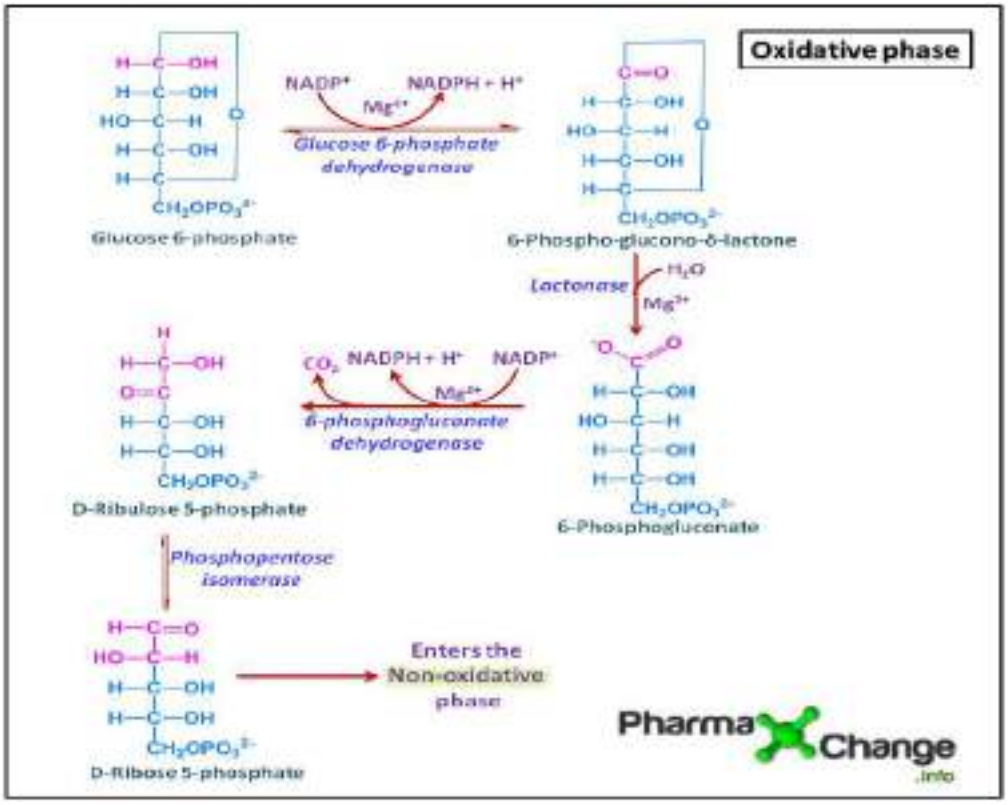
https://usmlestrike.com/topic/hmp-shunt/

(2) Name the two phases of the Pentose Phosphate Pathway and state one main function of each?

The pathway operates in two steps,

1. Oxidative phase (Irreversible)

- One molecule of and one 5 glucose-6-phosphate undergoes oxidation, producing one molecule of CO_2-carbon sugar (ribulose-5-phosphate) and the production of NADPH from $NADP^+$.



https://sciencevivid.com/hexose-monophosphate-pathway-hmp/#google_vignett

2. Non-oxidative phase (Reversible)

- The nonoxidative phase interconverts C3, C4, C5, C6 and C7 monosaccharides to other Carbon number sugars.
- Three 5-carbon sugars are rearranged to regenerate two phosphate and one molecule of glyceraldehyde-3-phosphate molecules of fructose-6.
- This phase allows the interconversion of sugar phosphates, linking the PPP with glycolysis.
- When demand for ribose is higher G3P and F6P help synthesis (Nucleic acids) than NADPH; of ribose 5 P without oxidative steps.

(3) What are the major products of the oxidative phase of the Pentose Phosphate Pathway?

From 1 molecule of Glucose -6- Phosphate

- 2 NADPH
- Ribulose -5- Phosphate
- Co2

(4) State two key benefits of the Pentose Phosphate Pathway in human cells?

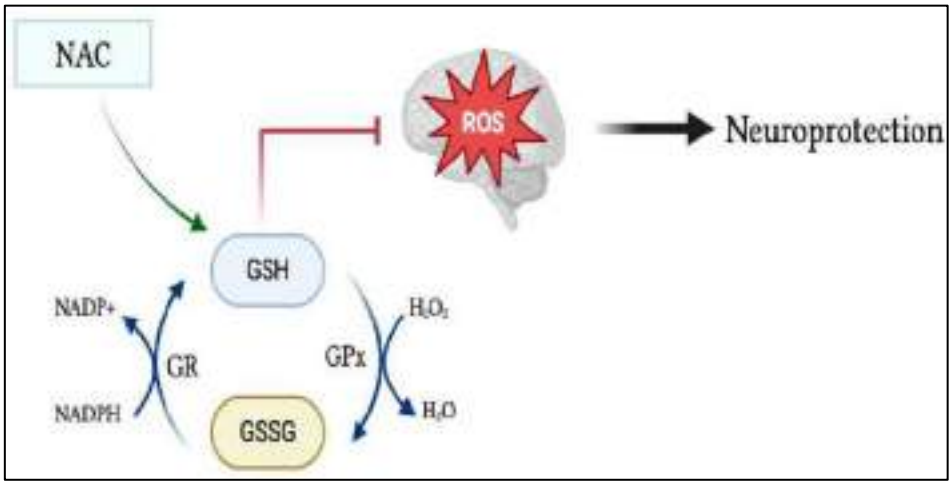
1. Major products of PPP are NADPH and Ribose -5-phosphate have several benefits to the human body

a. NADPH acts as a reducing agent

- Synthesis of Fatty acids
- Synthesis of Cholesterol
- Synthesis of Neurotransmitters

- Maintenance of the antioxidant system (Regeneration of reduced glutathione (GSH NADPH is essential for regenerating reduced glutathione (GSH), which neutralizes reactive oxygen species (ROS) and protects cells from oxidative damage.
- Involved in detoxification process - NADPH supports the activity of cytochrome P450.
- enzymes, which are involved in drug metabolism and detoxification.

Antioxidant system of NADPH



https://www.mdpi.com/2039-7283/13/4/70

Antioxidant system of NADPH

ROS and Oxidative Stress

- ROS are byproducts of metabolism that can cause oxidative damage to proteins, lipids, and DNA if uncontrolled.
- Glutathione's Role,
- Glutathione (GSH), a tripeptide, neutralizes ROS by donating electrons, converting itself into its oxidized form, glutathione disulfide (GSSG).

GSH Regeneration

- The enzyme glutathione reductase converts GSSG back to its active form, GSH, to maintain antioxidant defence.

Role of NADPH

- NADPH provides the reducing power needed for glutathione reductase to regenerate GSH from GSSG.

NADPH Production

- NADPH is primarily produced via the pentose phosphate pathway (PPP), ensuring a steady supply of antioxidant functions.

b. Ribose -5-phosphate will lead to the production of the compounds

Ribose-5-phosphate is a key building block for nucleotides, which are essential for the synthesis of Nucleotides such as,

- DNA
- RNA
- ATP
- NADH
- FADH
- Coenzyme A

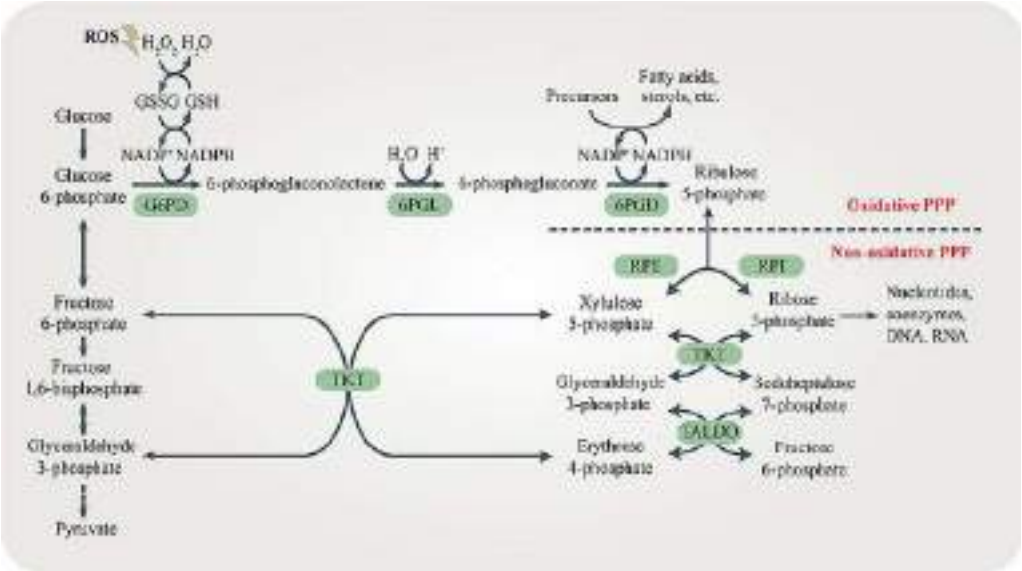
Ribose-5-phosphate is involved in the biosynthesis of histidine, an essential amino acid,

Pentose sugar from

2. Provide the mechanical pathway to break the diet.
3. Act as a pathway to interconvert 3 Carbon, 4 Carbon, 5 Carbon, 6 Carbon and 7 Carbon sugar molecules.

(5) Explain briefly how the non-oxidative phase links the PPP to glycolysis.

Ribose-5-phosphate and xylulose-5-phosphate are converted into fructose-6-phosphate and glyceraldehyde-3-phosphate, intermediates that can directly enter glycolysis.



https://www.frontiersin.org/journals/endocrinology/articles/10.3389/fendo.2020.00365/full

Tutorial 3

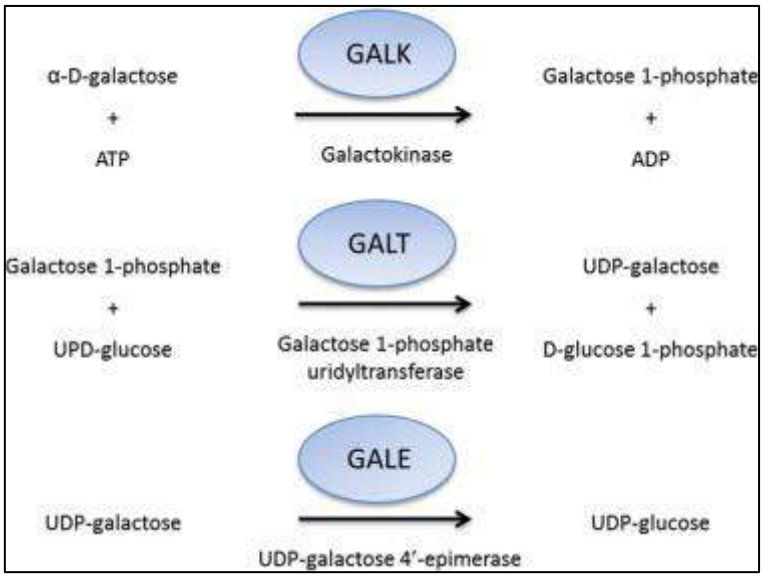
Disorders of Carbohydrate Metabolism

1. Explain the Leloir Pathway, including the enzymes involved and the four key steps.
2. Outline the biochemical basis of Galactosemia.
3. Explain the metabolic process of fructose in liver cells and other tissues.
4. What are the metabolic disorders of fructose metabolism, and how do Essential Fructosuria and Hereditary Fructose Intolerance (HFI) differ in their clinical presentation and biochemical consequences?
5. Explain how deficiency of glucose-6-phosphatase causes fasting hypoglycaemia.

Tutorial 3

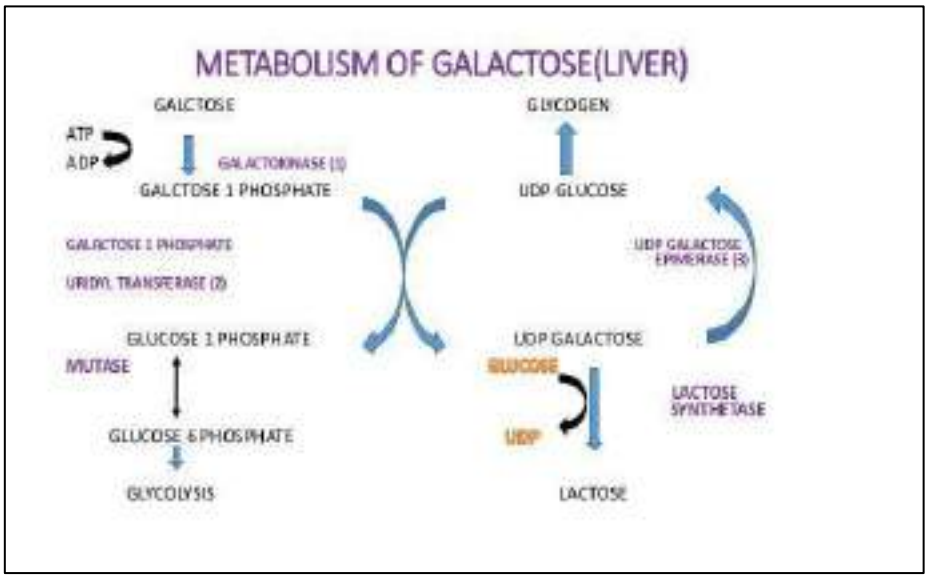
Disorders of Carbohydrate Metabolism -Answers

(1) Explain the Leloir Pathway, including the enzymes involved and the four key steps. Key steps in Leloir Pathway (Galactose Metabolic pathway).



https://www.sciencedirect.com/topics/agricultural-and-biological-sciences/leloir-pathway

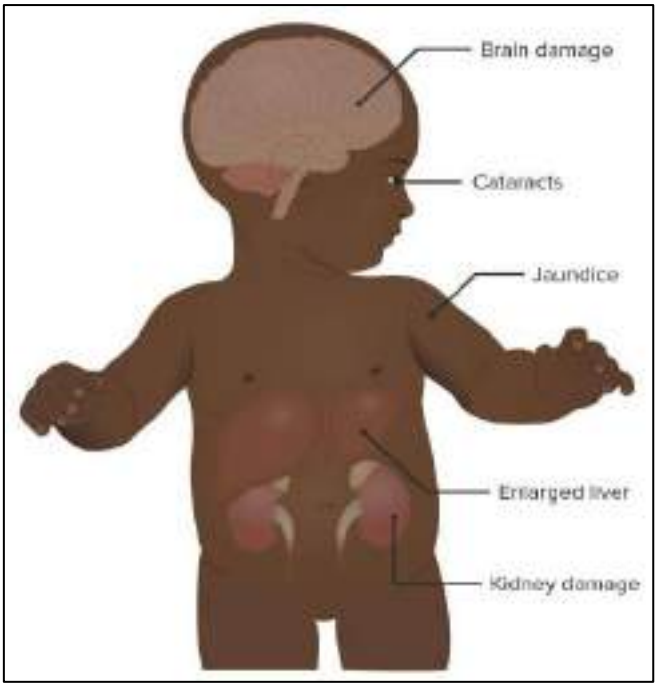
1. Conversion of Galactose to Galactose-1-Phosphate - Galactokinase
2. Conversion of Galactose-1-Phosphate to UDP-Galactose - Galactose-1-Phosphate Uridylyl transferase (GLAT)
3. Conversion of UDP-Galactose to UDP-Glucose - UDP-Galactose – 4- Epimerase
4. Conversion of Glucose-1-Phosphate to Glucose -6- Phosphate (For Glycolysis) - Phosphoglucomutase



https://microbenotes.com/galactose-metabolism/

Outline the biochemical basis of Galactosemia?

- Classic galactosemia is a metabolic disorder characterized by a deficiency galactose-1-phosphate uridylyl transferase (GALT).
- This condition leads to the incomplete metabolism of galactose.
- This condition is inherited in an autosomal recessive manner of the enzyme.
- The deficiency of GALT leads to the accumulation of galactose-1-phosphate and galactitol in various tissues, including the nerves, lens of the eye, liver, and kidneys.
- This accumulation disrupts normal cellular function and metabolism.
- Individuals with classic galactosemia may experience,
  - Cataracts- Due to galactitol accumulation in the lens of the eye
  - Intellectual disability- Resulting from neurological damage
  - Liver damage-From the toxic effects of galactose and its metabolites
  - Galactosemia- High levels of galactose in the blood
  - Galactosuria- Presence of galactose in the urine
  - Vomiting and diarrhoea- Often occurring in newborns after lactose-containing feeds
  - Jaundice- Due to liver dysfunction
- If left untreated, classic galactosemia can lead to persistent developmental delays, progressive liver damage, and ocular complications.



https://www.lecturio.com/concepts/galactosemia/

(2) Explain the metabolic process of fructose in liver cells and other tissues.

- Fructose undergoes different metabolic processes in liver cells and other tissues such as muscle and adipose tissue.

Fructose Metabolism in the Liver (Fructose 1-Phosphate Pathway)

- Step 1: Phosphorylation of Fructose Enzyme: Fructokinase Fructose is phosphorylated to fructose 1-phosphate using ATP.
- Step 2: Cleavage of Fructose 1-Phosphate Enzyme: Aldolase B (Fructose 1-Phosphate Aldolase) Fructose 1-phosphate is cleaved into two 3-carbon molecules (glyceraldehyde and dihydroxyacetone phosphate (DHAP)).
- Step 3: Glyceraldehyde Phosphorylation Enzyme: Triose Kinase Glyceraldehyde is phosphorylated to glyceraldehyde 3-phosphate using ATP, which, along with DHAP, enters the glycolysis pathway.

Fructose Metabolism in Muscle and Adipose Tissue (Fructose 6-Phosphate Pathway)

- Phosphorylation of Fructose Enzyme: Hexokinase In these tissues, fructose is phosphorylated directly to fructose 6-phosphate, which then enters the glycolysis pathway.

(3) What are the metabolic disorders of fructose metabolism, and how do Essential Fructosuria and Hereditary Fructose Intolerance (HFI) differ in their clinical presentation and biochemical consequences?

- Fructose metabolism disorders are caused by enzyme deficiencies that affect normal metabolic pathways.
- The two primary disorders are Essential Fructosuria and Hereditary Fructose Intolerance (HFI).

1. Essential Fructosuria

• Cause due to the deficiency of the enzyme fructokinase.
• It is an autosomal recessive inheritance.

•Biochemical Consequences

- Fructose cannot be phosphorylated, so it is excreted in the urine.
- No accumulation of toxic intermediates, making the condition benign.

•Clinical Features

- No serious symptoms.
- Fructose is excreted in urine, leading to fructosuria.

2. Hereditary Fructose Intolerance (HFI)

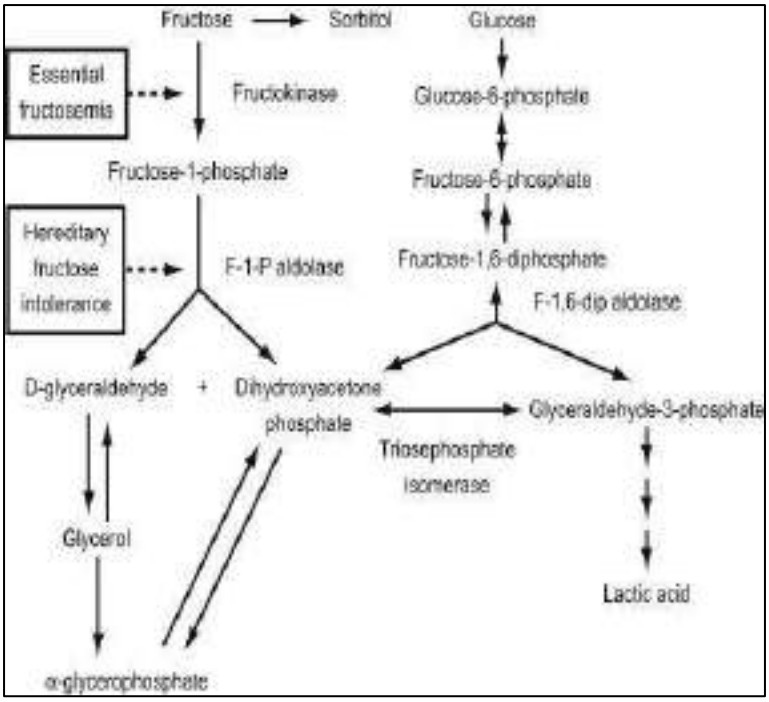
• Cause due to the deficiency of the enzyme Aldolase B.
• It is an autosomal recessive inheritance with a prevalence of 1:20,000.

Biochemical Consequences

- Fructose 1-phosphate accumulates inside cells.
- This leads to ATP depletion and increased degradation of AMP, causing hyperuricemia (high uric acid levels).
- The lack of ATP impairs gluconeogenesis and protein synthesis, leading to hypoglycaemia.
- Decreased inorganic phosphate in the liver affects hepatic glycogenolysis.

Clinical Features

- Symptoms appear after weaning, when babies are introduced to sucrose/ fructose-containing foods.
- Symptoms include severe hypoglycaemia, vomiting, jaundice, failure to thrive, and hyperuricemia.
- If untreated, HFI can cause liver damage, kidney dysfunction, and other systemic issues.



https://www.sciencedirect.com/topics/biochemistry-genetics-and-molecular-biology/fructose-1-phosphate

(6) Explain how deficiency of glucose-6-phosphatase causes fasting hypoglycaemia.

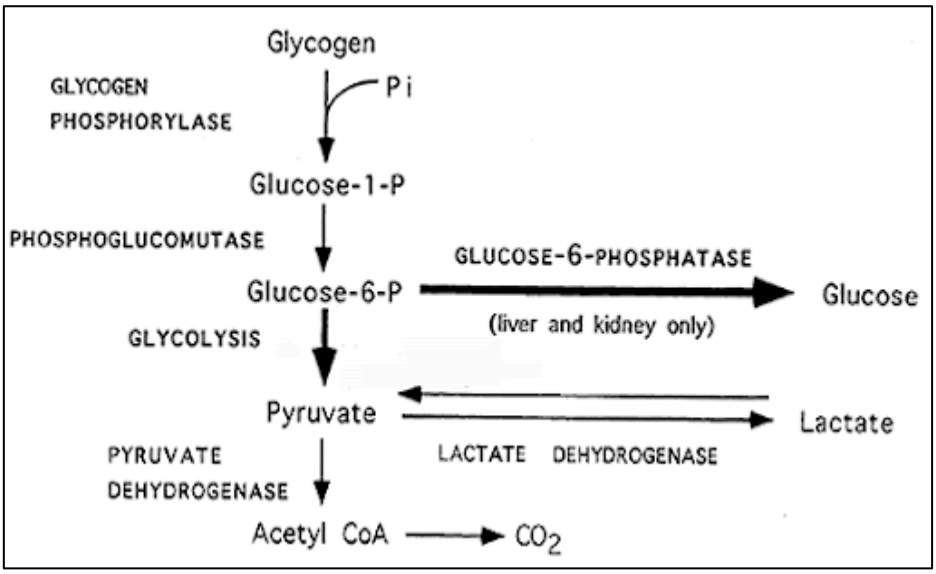
- In muscle cells, glucose-6-phosphate directly enters glycolysis for energy production.
- In the liver, glucose-6-phosphate can be further converted to free glucose by glucose-6-phosphatase and released into the bloodstream to regulate blood glucose level.
- Glycolysis- In muscle and other tissues, G6P enters glycolysis to produce energy (ATP) for cellular activities.
- In the liver, G6P can be converted to free glucose by glucose-6-phosphatase and released into the bloodstream to maintain blood glucose levels.
- Pentose Phosphate Pathway- G6P can enter the pentose phosphate pathway to produce NADPH and ribose-5 phosphate.

Glucose-6-phosphatase (enzyme of liver, kidney) converts,

glucose-6-phosphate → free glucose

In its absence (Von Gierke's disease):

- Glycogen breakdown and gluconeogenesis both produce G6P, but cannot release free glucose → trapped in cells.
- Results in severe fasting hypoglycaemia.
- Excess G6P shunted to glycolysis → ↑ lactate (lactic acidosis) & uric acid (hyperuricemia).



http://chemistry.gravitywaves.com/CHE452/04_Glycogen.htm

SGDs & ANSWERS

SGD 01

Carbohydrate Metabolism

(1) Explain the process of carbohydrate digestion and absorption in the human body, highlighting the specific bonds digested and the enzymes involved.
(2) What is Metabolism, and Differentiate Catabolism and Anabolism with Examples?
(3) Explain the process of glycolysis in detail, highlighting the key steps, intermediates, and enzymes involved. Additionally, differentiate between the preparatory phase and the payoff phase of glycolysis, outlining the role and significance of each.
(4) Name four kinase enzymes involved in glycolysis and classify them based on the reversibility of their reactions.
(5) How does phosphofructokinase-1 (PFK-1) regulate the rate of glycolysis, and what are the key factors influencing its activity?
(6) Describe the intermediate reaction that converts pyruvate into acetyl CoA. Name the enzyme complex involved and list the enzymes and co-enzymes required for this conversion.

SGD 01

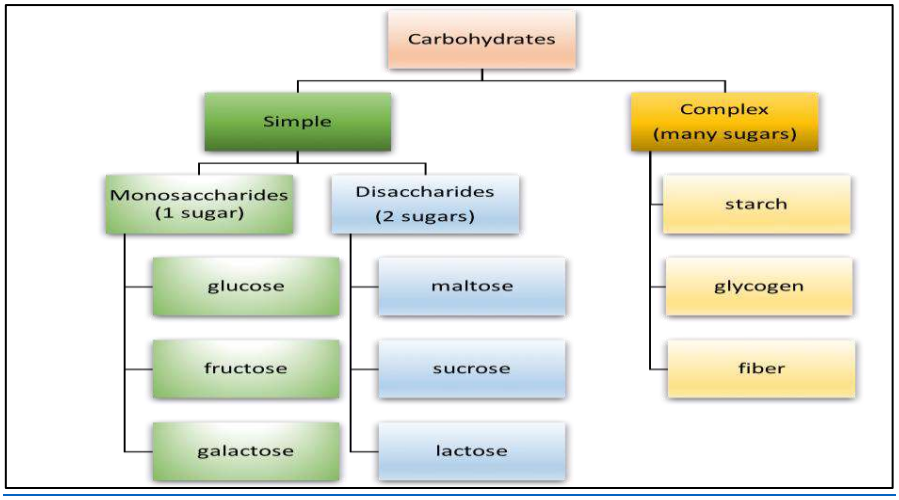
Carbohydrate Metabolism-Answers

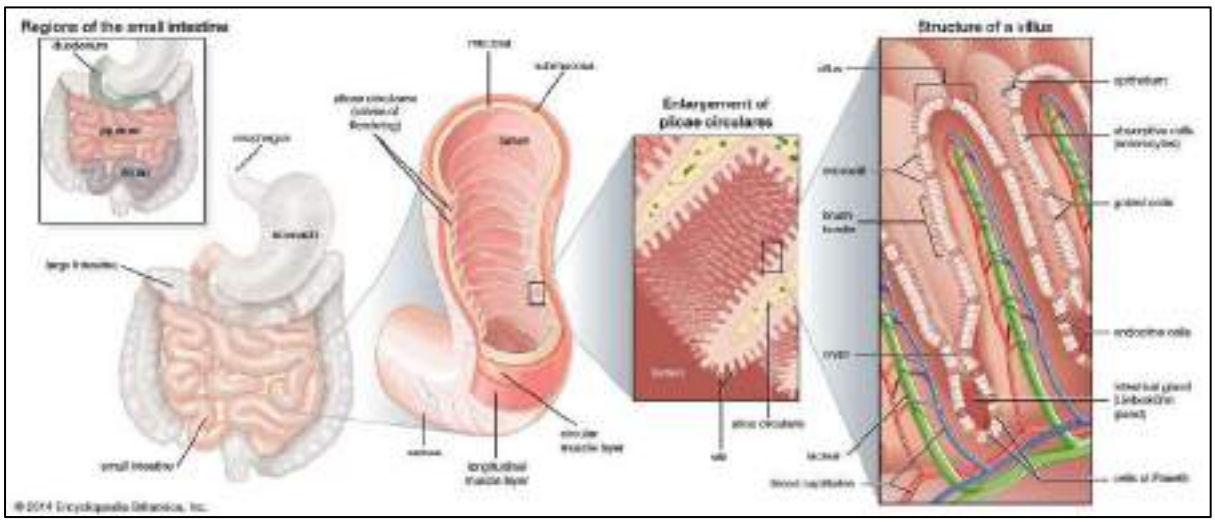
(1) Explain the process of carbohydrate digestion and absorption in the human body, highlighting the specific bonds digested and the enzymes involved.

Carbohydrate Digestion and Absorption

➢ Intestine Can Only Transport Monosaccharides

- The intestinal cells (enterocytes) are specialized to absorb only monosaccharides such as glucose, fructose, and galactose.
- Larger carbohydrates like disaccharides and polysaccharides must be broken down.





https://www.britannica.com/science/duodenum

Two Phases of Carbohydrate Digestion

1. **Luminal Digestion**
   - Enzymes involved are Salivary amylase (in the mouth) and Pancreatic amylase (in the small intestine).
   - Complex carbohydrates (starch and glycogen) are broken down into disaccharides (maltose, sucrose, lactose) and oligosaccharides tract.
2. **Brush-Border Digestion**
   - within the lumen of the digestive Membrane-bound hydrolases on the microvilli of enterocytes sucrase, lactase).
   - Disaccharides (e.g., maltase, and oligosaccharides are further broken down into monosaccharides at the brush-border of the enterocytes, allowing them to be absorbed into the bloodstream.

Luminal Digestion

➢**Salivary α-amylase (mouth)**

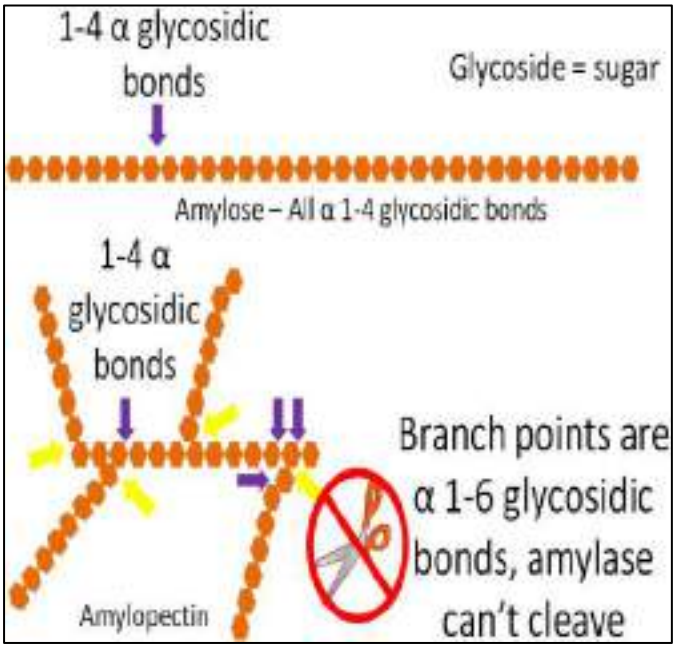
- Digestion starts in the mouth with smaller polysaccharides.
- It functions best at a pH of 7 salivary α-amylase, which breaks down starch.
- However, salivary amylase is inactivated when it reaches the acidic environment of the stomach.

➢**Pancreatic α-amylase (small intestine)**

- This enzyme acts primarily in the duodenum.
- Sodium bicarbonate ($NaHCO_3$) is secreted into the duodenum by the pancreas a key role in neutralizing the acidic chyme.
- Pancreatic amylase cleaves α-1,4 bonds in starch, but cannot break α-1,6 bonds (branch points) or terminal α-1,4 bonds.

➢**The breakdown products include**

- Maltose (a disaccharide of glucose).
- Maltotriose (a trimer of glucose).
- α-limit dextrins (branched chains of glucose derived from amylopectin).
- Oligomers containing 2-9 glucose units.
- Disaccharides remain undigested by amylase.



https://courses.lumenlearning.com/suny-nutrition/chapter/3-42-carbohydrate-digestion-in-the-small-intestine/

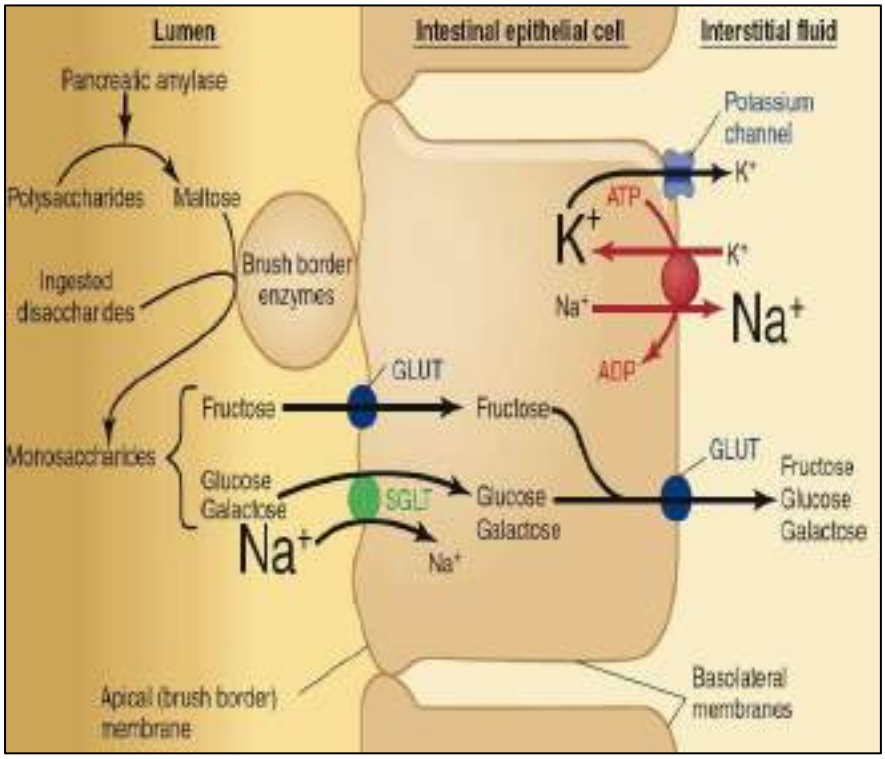
Brush-Border Digestion

➢**Membrane-bound hydrolases**

- Digestion is completed by enzymes present on the brush border of the small intestine's epithelial cells (enterocytes).
- Substrates acted upon include,
- Maltose, Sucrose and lactose
- Linear glucose oligomers,
- α-limit dextrins (branched oligosaccharides from amylopectin).

➢Key enzymes involved in the brush border

- Glucoamylase: Breaks down glucose oligomers into glucose (Cleaves α-1,4 bonds).
- Isomaltase: Cleaves α-limit dextrins, releasing glucose (Cleves both α-1,4 and α-1,6 bonds).
- Maltase: Breaks Maltose to Glucose (Cleaves α-1,4 glycosidic bonds).
- Sucrase: Splits Sucrose into glucose and fructose (Cleaves the α-1, β-2 glycosidic bond).
- Lactase: Breaks down Lactose into glucose and galactose (Cleves β-1,4 glycosidic bonds.



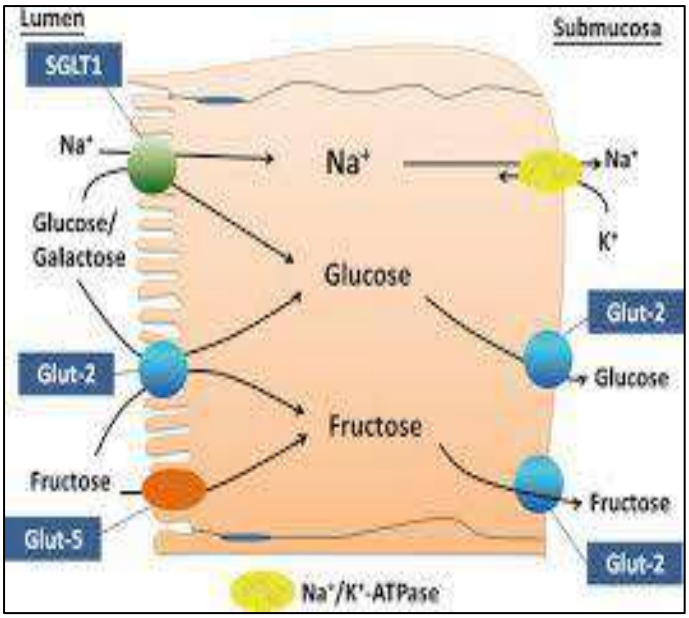
https://biosiva.50webs.org/digestion.html

Absorption

➢ Only monosaccharides (glucose, galactose, fructose) are absorbable.

➢ Absorption primarily occurs in the duodenum Transport Mechanisms and jejunum.

- SGLT-1 (Sodium-Dependent Glucose Transporter 1)
- Actively transports glucose and galactose into enterocytes.
- Uses secondary active transport coupled with sodium ions.
- GLUT-5
- Facilitates passive transport of fructose
- GLUT-2 into enterocytes
- Facilitates the efflux of these mono-saccharides bloodstream from the enterocytes into the allowing them to enter the hepatic portal vein and reach the liver.



https://link.springer.com/chapter/10.1007/978-94-017-8771-0_6

Indigestible Carbohydrates Cellulose

- Composed of glucose units linked by β-1,4 glycosidic bonds.
- Human enzymes cannot break these bonds.
- Acts as dietary Fiber, aiding digestion Enzyme deficiency.
- A genetic deficiency in Iso-maltase.
- Deficiency of Sucrase leads to starch malabsorption results in an intolerance of ingested sucrose.
- Low Lactase activity causes lactose intolerance.

(2) What is Metabolism, and Differentiate Catabolism and Anabolism with Examples Metabolism?

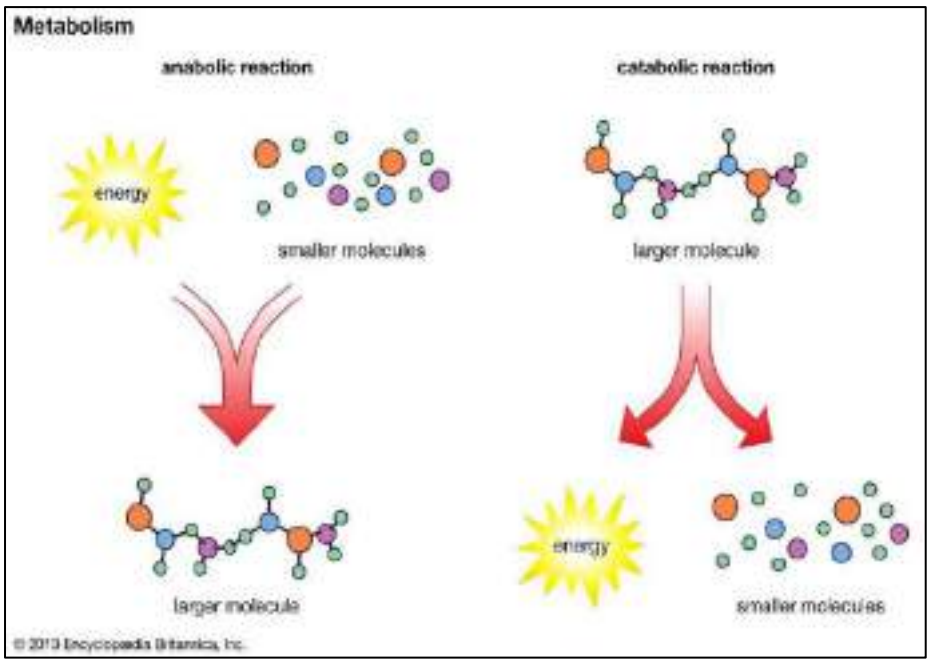
- Metabolism refers to the entire set of chemical reactions that occur in a living cell to enable growth, division, maintenance, and survival.
- These processes ensure that the cell obtains energy, synthesizes necessary molecules, and breaks down substances as needed.
- Metabolism consists of two broad categories,

- Catabolism – The breakdown of complex molecules and simpler compounds.
- Anabolism – The synthesis of complex molecules to produce energy from simpler ones, requiring energy.

Key Differences Between Catabolism and Anabolism

Feature	**Catabolism**	**Anabolism**
Definition	Breakdown of complex molecules into simpler ones	Synthesis of complex molecules from simpler ones
Energy	**Releases energy** (exergonic)	**Requires energy** (endergonic)
Purpose	Provides ATP and building blocks	Builds macromolecules and tissues
Examples	Glycolysis, β-oxidation, protein degradation	Protein synthesis, glycogenesis, fatty acid synthesis
Coenzymes	Uses **NAD^+** (oxidizing agent)	Uses **NADPH** (reducing agent)
Location	Often in **mitochondria**	Often in **cytosol**
Effect on Molecules	Produces CO_2, H_2O, ATP	Produces macromolecules (proteins, lipids, glycogen)
Overall Goal	Energy generation	Growth, repair, storage

Examples of Catabolic and Anabolic Processes Catabolism



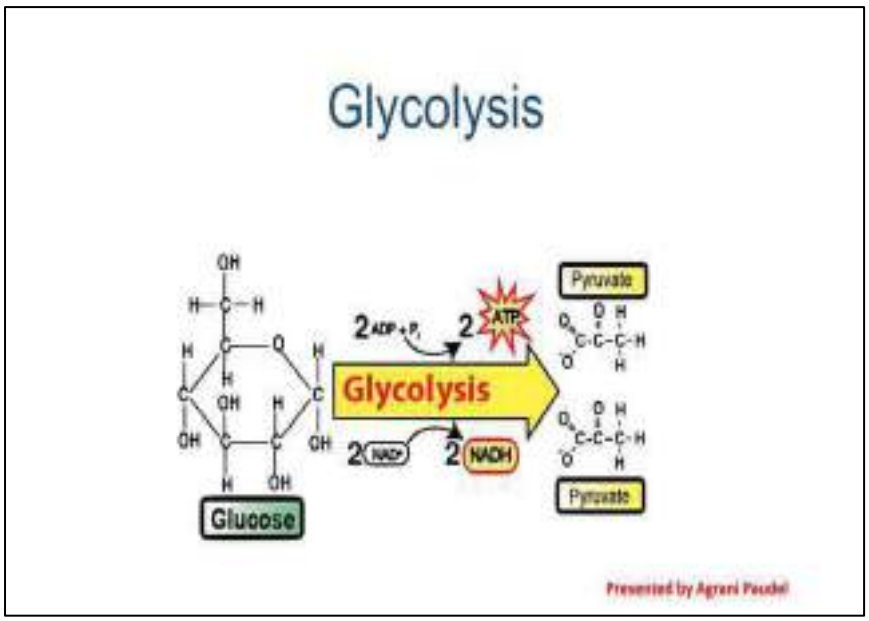
https://www.britannica.com/science/catabolism

- Glycogen is broken down into glucose for energy in muscles.
- Triglycerides are converted into fatty acids and glycerol in adipose tissue.
- Proteins are degraded into amino acids for various functions, including energy generation Anabolism.
- Glucose is stored as glycogen.
- Fatty acids and glycerol in the liver and muscles for later energy use are synthesized into triglycerides.
- Amino acids are built into proteins for long-term energy storage for cell structure, enzyme function, and repair.

(3) Explain the process of glycolysis in detail, highlighting the key steps, intermediates, and enzymes involved. Additionally, differentiate between the preparatory phase and the payoff phase of glycolysis, outlining the role and significance of each.

Glycolysis

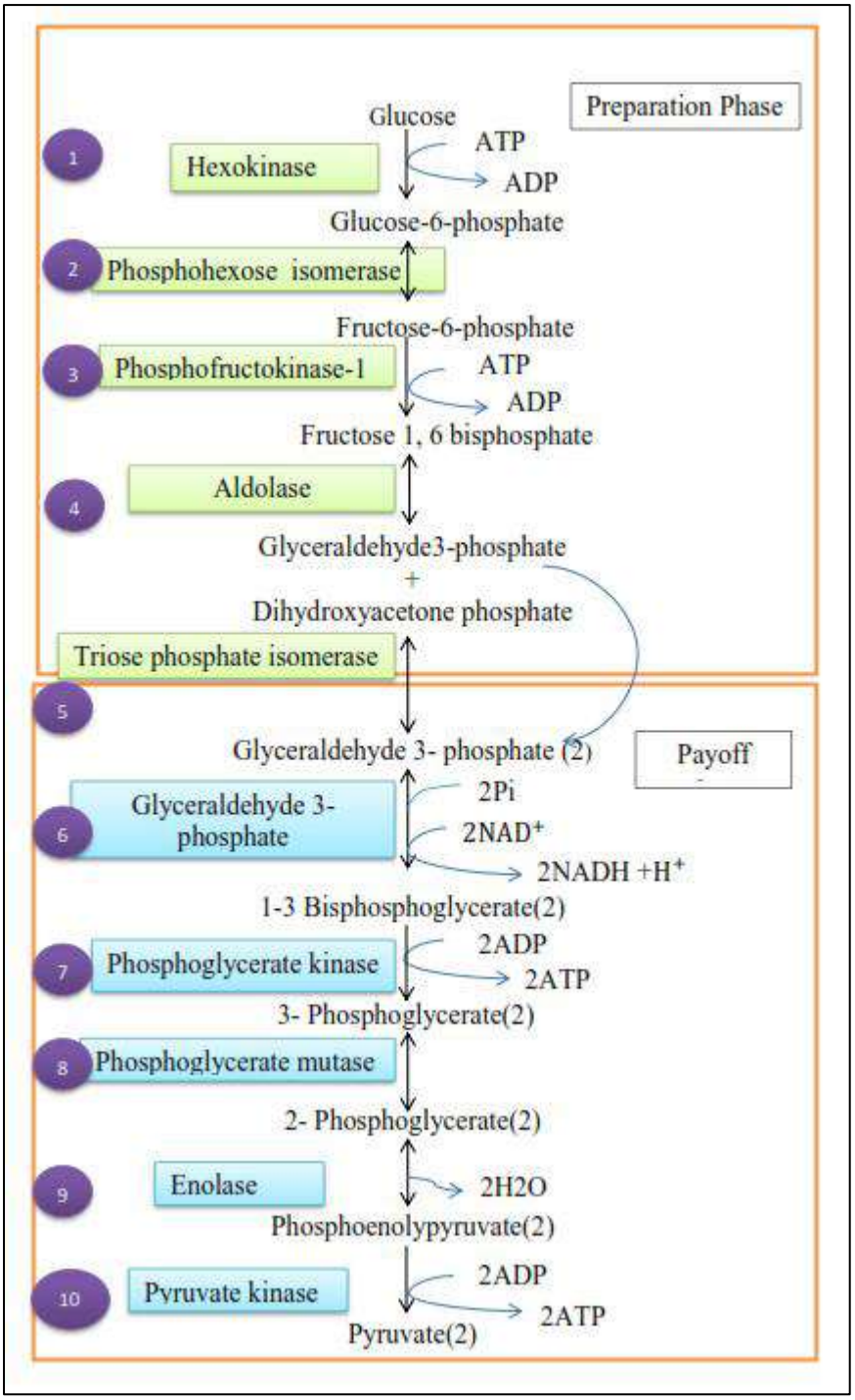
- Glycolysis is a fundamental metabolic pathway that breaks down glucose into energy.
- The term "glycolysis" comes from the Greek words glycos (sugar) and lysis (dissolution), indicating the breakdown of sugar.
- This pathway occurs in the cytoplasm aerobic and anaerobic organisms of all cells and is essential for both aerobic and anaerobic organisms.



https://www.slideshare.net/slideshow/glycolysis-246693977/246693977

- Glycolysis converts one glucose molecule (6 carbons) into two molecules of pyruvate carbons each).

- The process yields energy in the form of ATP (3 and NADH).
- It consists of 10 enzyme-catalysed reactions divided into two phases,
    - ➢ The Preparatory Phase
    - ➢ The Payoff Phase



https://www.simplynotes.in/e-notes/bio-technology/biochemistry/glycolysis/

Preparatory Phase/ Energy Investment Phase

- In this phase, glucose is primed for breakdown, consuming two ATP molecules
- It includes the following steps,

1. Phosphorylation of Glucose (6C).

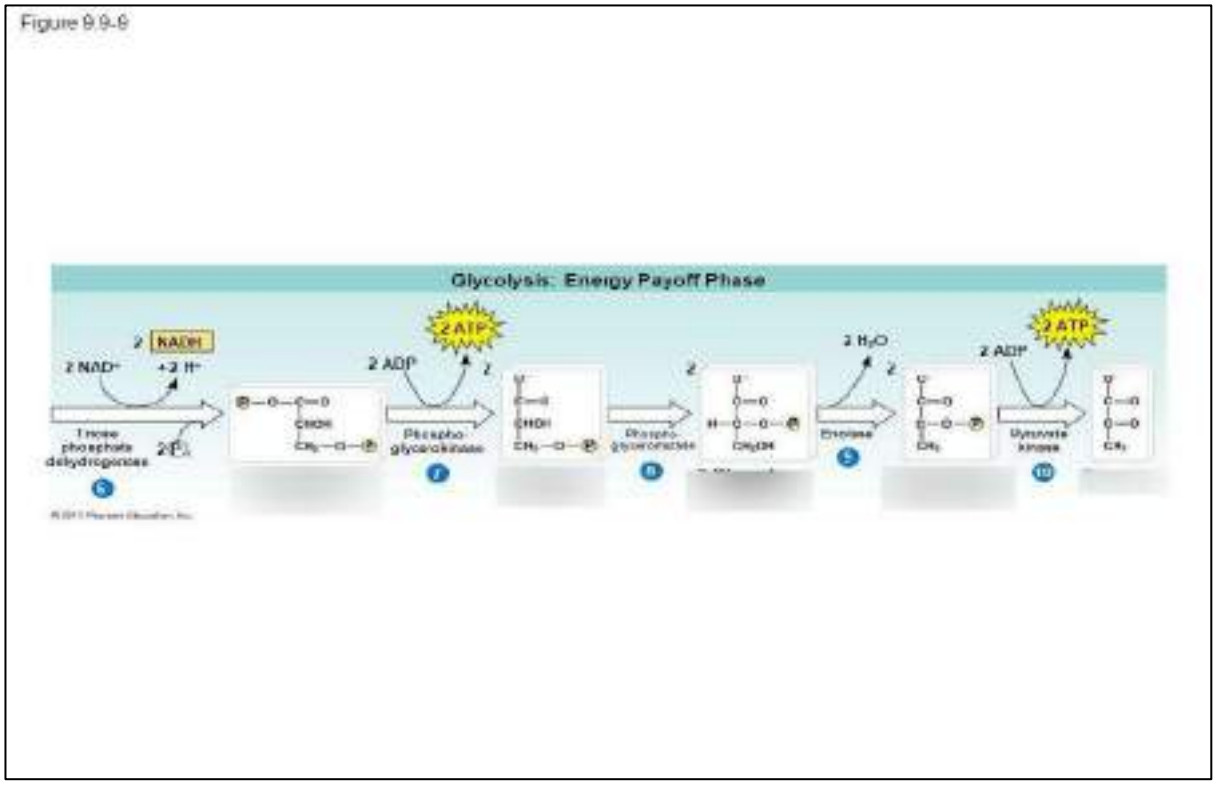
2. Isomerization of Glucose-6-Phosphate (6C).
3. Phosphorylation of Fructose-6-Phosphate (6C).
4. Cleavage of Fructose-1,6-Bisphosphate (6C).
5. Interconversion of Glyceraldehyde-3-Phosphate (3C) and Dihydroxyacetone Phosphate (3C).

Payoff Phase/ Energy Harvest Phase

- This phase generates energy, producing ATP and NADH.
- It includes the following steps,

6. Oxidation of Glyceraldehyde-3-Phosphate.
7. Production of ATP.
8. Isomerization of 3-Phosphoglycerate.
9. Formation of Phosphoenolpyruvate (PEP).
10. Final ATP Production and Pyruvate Formation.

Payoff Phase



https://quizlet.com/337148180/glycolysis-energy-payoff-phase-diagram/

1. **Phosphorylation of Glucose**
   - The enzyme hexokinase catalyses the phosphorylation of glucose glucose-6-phosphate (G6P) using one ATP molecule.
   - This step is irreversible and marks the beginning of glycolysis.
2. **Isomerization of Glucose-6-Phosphate**

- Glucose-6-phosphate is converted to phosphoglucose fructose-6-phosphate (F6P) by isomerase through an aldose-ketose isomerization.
- Aldo to Keto isomerization.
- This is a reversible step,

3. Phosphorylation of Fructose-6-Phosphate

- Phosphofructokinase-1 (PFK-1), a key regulatory enzyme, catalyses the conversion offructose-6-phosphate to using another ATP molecule.
- This irreversible fructose-1,6-bisphosphate (F1,6BP) step is also the rate-limiting step of glycolysis.

4. Cleavage of Fructose-1,6-Bisphosphate

- Aldolase splits fructose-1,6-bisphosphate into two 3-carbon molecules glyceraldehyde-3-phosphate (G3P) and dihydroxyacetone phosphate (DHAP).
- This is a reversible step.

5. Interconversion of Glyceraldehyde-3-Phosphate and Dihydroxyacetone Phosphate

- The enzyme triosephosphate isomerase converts DHAP into G3P, ensuring that two G3P molecules proceed to the next phase of glycolysis.
- Keto-aldo isomerization.
- This is a reversible step.

6. Oxidation of Glyceraldehyde-3-Phosphate

- Glyceraldehyde-3-phosphate dehydrogenase catalyses the oxidation of G3P to 1,3-bisphosphoglycerate (1,3-BPG), producing NADH from NAD^+.
- First production of high-energy intermediates.
- This is a reversible step.

7. Production of ATP

- Phosphoglycerate kinase forming ATP and transfers a phosphate group from 3-phosphoglycerate.
- This is the first substrate-level phosphorylation of glycolysis 1,3-BPG to ADP,
- This is a reversible step.

8. Isomerization of 3-Phosphoglycerate

- Phosphoglycerate mutase converts 3-phosphoglycerate.
- Phosphate is shifted from the OH on C3.
- This is a reversible step to the OH on C2 2-phosphoglycerate.

9. Formation of Phosphoenolpyruvate (PEP)

- Enolase catalyses the dehydration of phosphoenolpyruvate 2-phosphoglycerate to form (PEP), a high-energy intermediate.
- Involves the dehydration.
- This is a reversible step.

10. Final ATP Production and Pyruvate Formation

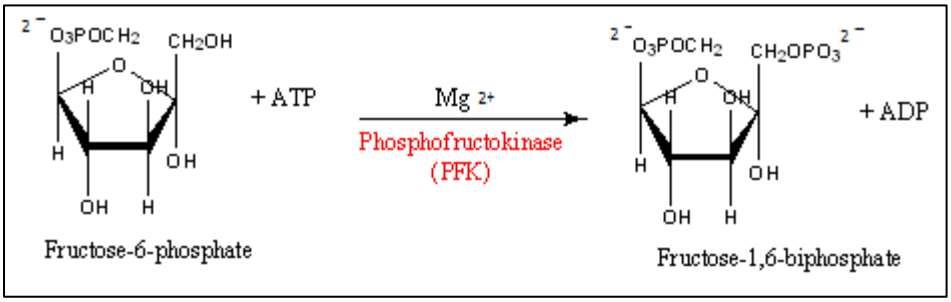
- In the last step, pyruvate kinase from PEP catalyses the transfer of a phosphate group to ADP, forming ATP and pyruvate.
- This is another substrate-level phosphorylation.
- This step is irreversible.

(4) Name four kinase enzymes involved in glycolysis and classify them based on the reversibility of their reactions.

Kinase Enzymes in Glycolysis

- **Hexokinase** - Catalyses the phosphorylation of glucose to glucose-6 phosphate (irreversible).
- **Phosphofructokinase-1 (PFK-1)** - Phosphorylates fructose-6-phosphate to fructose-1,6-bisphosphate (irreversible).
- **Phosphoglycerate kinase** - Converts 1,3-bisphosphoglycerate to 3-phosphoglycerate(reversible).
- **Pyruvate kinase** - Converts phosphoenolpyruvate to pyruvate (irreversible).

(5) How does phosphofructokinase-1 (PFK-1) regulate the rate of glycolysis, and what are the key factors influencing its activity?



https://collab.its.virginia.edu

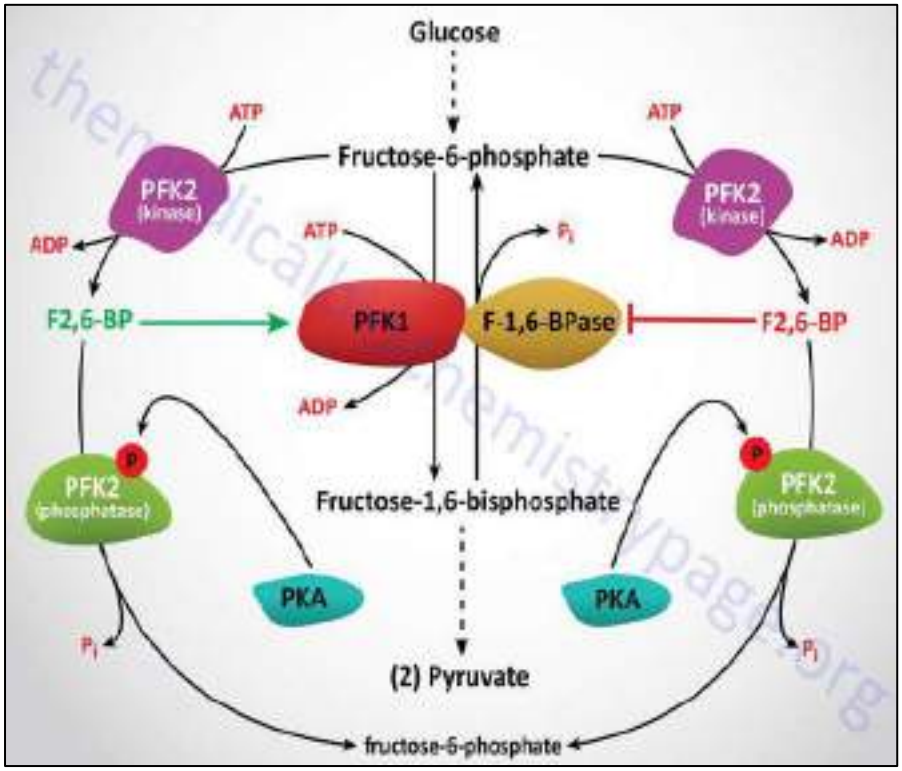
Regulation of Phosphofructokinase-1 (PFK-1)

- Allosteric Regulation: PFK-1 is the most important control site in glycolysis and is allosterically regulated by several molecules.
- Inhibition: High levels of ATP, citrate, and phosphoenolpyruvate reducing glycolytic flux when energy levels are high.
- Activation: AMP reverses the inhibitory effect of ATP, increasing energy (ATP) levels are low.
- Fructose (PEP) inhibit PFK-1, PFK-1 activity when 2,6-bisphosphate (F-2,6-BP): This is the most potent activator of PFK-1. It increases the enzyme's affinity for fructose-6-phosphate and reduces ATP's inhibitory effect.
- pH: Low pH (acidic conditions) inhibits PFK-1, especially in anaerobic conditions where lactic acid accumulates. This protects the muscle from damage due to excessive acidity.

Energy Charge

- As the cellular ATP/AMP ratio falls, glycolysis is stimulated.

- PFK-1 has two binding sites for ATP, one as a substrate and the other for inhibitory action.
- When AMP is present, it counteracts the inhibitory effect of ATP, thus increasing PFK-1 activity and promoting glycolysis under low energy conditions.



https://themedicalbiochemistrypage.org/glycolysis-and-the-regulation-of-blood-glucose/

Activator Effect on PFK-1

- Insulin -Activates Increases glycolysis by promoting the activity of PFK-2, which increases F-2,6-BP levels.
- PFK-2 - Activates Produces F-2,6-BP from fructose-6-phosphate, enhancing PFK-1 activity.
- Fructose-2,6-Bisphosphate (F-2,6-BP) - Activates Allosteric activator: Increases affinity of PFK-1 for fructose-6-phosphate and diminishes ATP inhibition.
- AMP - Activates Signals low energy; reverses ATP's inhibitory effect, promoting glycolysis.

ADP – Activates Indicates low energy levels, stimulating PFK-1 to increase glycolytic flux.

Inhibitor Effect on PFK-1

- Glucagon- Inhibits Decreases F-2,6-BP synthesis via activation of Fructose Bisphosphatase-2 (FBPase-2), reducing PFK-1 activity.
- Fructose Bisphosphatase-2 (FBPase-2) - Inhibits Breaks down F-2,6-BP, leading to reduced PFK-1 activity.

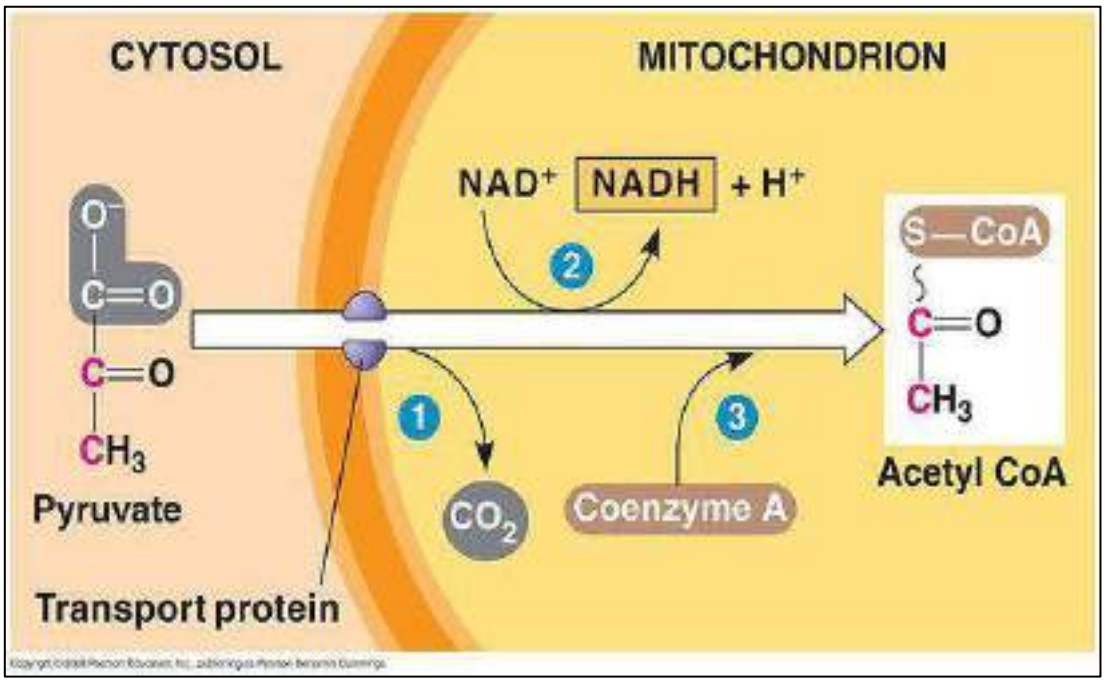
- ATP – Inhibits Signals high energy levels and reduces the rate of glycolysis by inhibiting PFK-1 allosterically.
- Acidic pH (low pH)- Inhibits Prevents excessive acid accumulation by inhibiting PFK 1, especially during anaerobic respiration.
- Citrate- Inhibits Signals abundant energy from the citric acid cycle, reducing PFK-1 activity.
- Phosphoenolpyruvate (PEP)- Inhibits Product of glycolysis, feeds back to inhibit PFK-1.

(6) Describe the intermediate reaction that converts pyruvate into acetyl CoA. Name the enzyme complex involved and list the enzymes and co-enzymes required for this conversion.

Intermediate Reaction - Pyruvate to Acetyl CoA

- This reaction is an essential link between Glycolysis and the Citric Acid Cycle (TCA cycle) because acetyl CoA, the product of this reaction, enters the TCA cycle for further oxidation and energy production.
- This reaction involves the oxidative decarboxylation of pyruvate, resulting in the removal of one carbon atom in the form of CO2, and the production NADH and acetyl CoA.
- This reaction is irreversible and crucial for tissues for aerobic metabolism.
- The conversion of Pyruvate to Acetyl of CoA is catalysed by the Pyruvate Dehydrogenase Complex (PDC).

Pyruvate + CoA + NAD+ → Acetyl CoA + CO2 + NADH Pyruvate to Acetyl CoA



https://www.nursinghero.com/study-guides/boundless-biology/oxidation-of-pyruvate-and-the-citric-acid-cycle

- The Pyruvate Dehydrogenase Complex (PDC) is a large multi-enzyme complex made up of three enzymes,

1. Pyruvate Dehydrogenase (E1) – Catalyses the decarboxylation of pyruvate
2. Dihydrolipoyl Transacetylase (E2) – Transfers the acetyl group to CoA
3. Dihydrolipoyl Dehydrogenase (E3) – Regenerates the oxidized form of lipoamide and transfers electrons to NAD+ to form NADH

- Five co-enzymes are required for this conversion.

4. Thiamine Pyrophosphate (TPP) – A cofactor for Pyruvate Dehydrogenase (E1)
5. Lipoamide – Covalently attached to Dihydrolipoyl Transacetylase (E2),
6. Coenzyme A (CoA) – Accepts the acetyl group to form acetyl CoA
7. FAD – Electron carrier in Dihydrolipoyl Dehydrogenase (E3)
8. NAD+ – Electron acceptor, reduced to NADH.

SGD 2

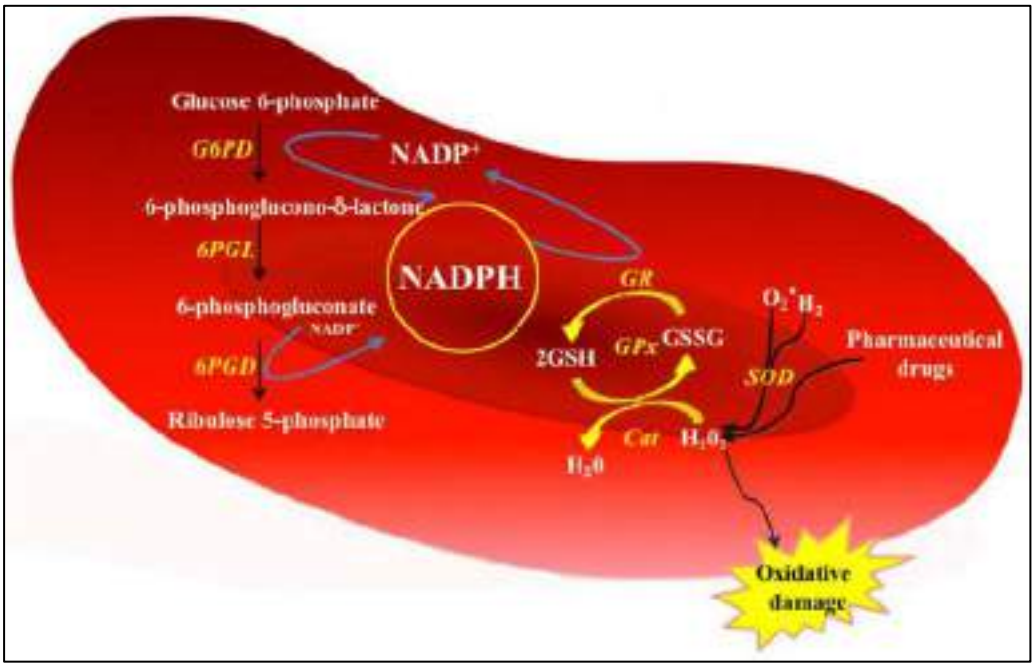
Disorders of Carbohydrate Metabolism

- Glucose -6-phosphate dehydrogenase (G6PD) deficiency is the most common enzyme defect in humans, inherited in an X-linked recessive manner.
- It is particularly important in malaria -endemic regions.
- Red blood cells (RBCs) depend on the pentose phosphate pathway to generate NADPH, which protects them against oxidative stress.
- In G6PD deficiency, exposure to oxidant drugs, infections, or fava beans can trigger acute haemolysis, leading to anaemia and jaundice.

(1) Explain the role of G6PD in the red cell metabolism.
(2) Why does haemolysis occur after oxidant drug exposure?
(3) Discuss the clinical features and diagnosis of G6PD deficiency.

Disorders of Carbohydrate Metabolism- Answers

(1) Explain the role of G6PD in the red cell metabolism.



https://www.researchgate.net/figure/Function-of-G6PD-enzyme-in-the-PPP-from-red-blood-cells-In-G6PD-normal-red-cells-the_fig3_311551182

- G6PD catalyses the first step in the pentose phosphate pathway (PPP).

- Generates NADPH, which is essential for keeping glutathione in reduced form (GSH).
- Reduced glutathione neutralizes reactive oxygen species (ROS), protecting haemoglobin
  and the RBC membrane.
- RBCs rely entirely on this pathway since they lack mitochondria → G6PD is crucial for their survival.

(2) Why does haemolysis occur after oxidant drug exposure?

- Oxidant drugs (e.g., primaquine, sulphonamides, nitrofurantoin) generate free radicals.
- In G6PD deficiency → insufficient NADPH → reduced glutathione is not regenerated.
- Haemoglobin gets oxidized → forms Heinz bodies.
- RBC membrane damage → extravascular and intravascular haemolysis → anaemia, jaundice, dark urine.

3. Discuss the clinical features and diagnosis of G6PD deficiency.

Clinical Features:

- Usually asymptomatic until exposed to oxidant stress (drugs, infections, fava beans).
- Acute haemolytic anaemia: pallor, jaundice, dark urine, fatigue.
- Neonatal jaundice in some cases.

Diagnosis:

- Peripheral smear → "bite cells", Heinz bodies (with supravital staining).
- Enzyme assay → low G6PD activity.
- Genetic testing (in some cases).

4. How can this condition be prevented/managed in endemic areas?

Prevention:

- Screening programs in malaria -endemic areas.
- Avoidance of known oxidant drugs/foods (e.g., fava beans, sulpha drugs,
- primaquine).

Management:

- Treat acute haemolysis with hydration, oxygen, blood transfusion if severe.
- Manage neonatal jaundice with phototherapy or exchange transfusion.
- Education of patients/families about triggers.

SGD 3

Diabetes Mellitus

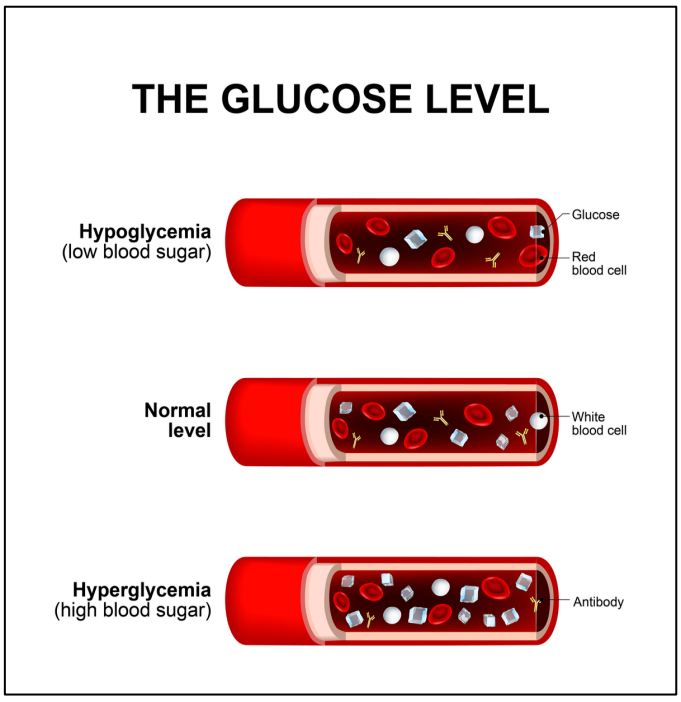
(1) What is meant by the term "Diabetes Mellitus"? Explain its definition and significance in clinical practice.
(2) Explain the aetiology of blood glucose regulation Discuss the key factors and mechanisms involved.
(3) What are the major causes of Type 1 Diabetes Mellitus? Discuss the underlying mechanisms contributing to its development.
(4) How does Type 2 Diabetes Mellitus differ from Type 1 Diabetes Mellitus? Highlight the key differences in aetiology, pathophysiology, and clinical features.
(5) What are the risk factors for Type 2 Diabetes Mellitus? Explain how these factors contribute to its development.
(6) What is gestational diabetes? Explain its definition, causes, and potential implications for both the mother and baby.
(7) How is diabetes diagnosed? Discuss the diagnostic criteria, tests, and their interpretation for different types of diabetes.
(8) What are the signs and symptoms of Diabetes Mellitus? Describe the common clinical manifestations associated with the condition.
(9) What are the major complications of Diabetes Mellitus?

SGD 03

Diabetes Mellitus -Answers

(1) What is meant by the term "Diabetes Mellitus"? Explain its definition and significance in clinical practice

- Diabetes Mellitus (DM) is a chronic metabolic disorder marked by persistently high blood glucose levels (hyperglycaemia).
- It occurs due to (inherited or acquired).
- A deficiency in insulin production.
- The ineffectiveness of the insulin produced by the pancreas.



https://www.drdogood.health/blogs/normal-blood-sugar-level-whats-healthy-when-to-worry

Significance in Clinical Practice

- DM is critical to manage due to its long -term impact on health.
- Uncontrolled DM can lead to severe complications, including,
- Cardiovascular diseases Increased risk of heart attack and stroke.
- Kidney failure: Progressive damage to the kidneys.
- Neuropathy Nerve damage causing pain or loss of sensation.
- Retinopathy Vision impairment or blindness.
- Increased susceptibility to infections Poor wound healing and immune response.

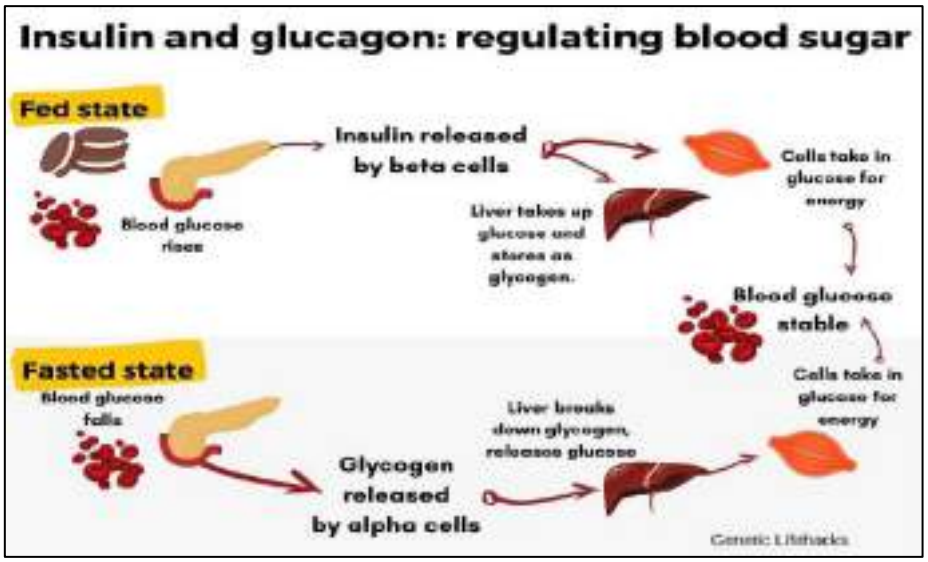
- Early diagnosis and effective management are essential to improve the quality of life and prevent.

complications

(2) Explain the aetiology of blood glucose regulation. Discuss the key factors and mechanisms involved.

Blood Glucose Regulation

Role of the Pancreas



https://www.geneticlifehacks.com/blood-glucose-levels-how-your-genes-impact-blood-sugar-regulation/

- The pancreas contains specialized endocrine cells in the islets of Langerhans, which regulate blood glucose levels.

Two main types of endocrine cells are,

1) Beta cells - produce insulin, a hormone that lowers blood glucose by facilitating glucose uptake into cells.
2) Alpha cells - Produce glucagon, a hormone that raises blood glucose by stimulating glucose release from the liver.

Dynamic Hormonal Balance

- Beta and alpha cells continuously adjust their hormone secretion levels based on glucose levels in the bloodstream.
- Insulin and glucagon work together to maintain blood glucose balance (homeostasis).

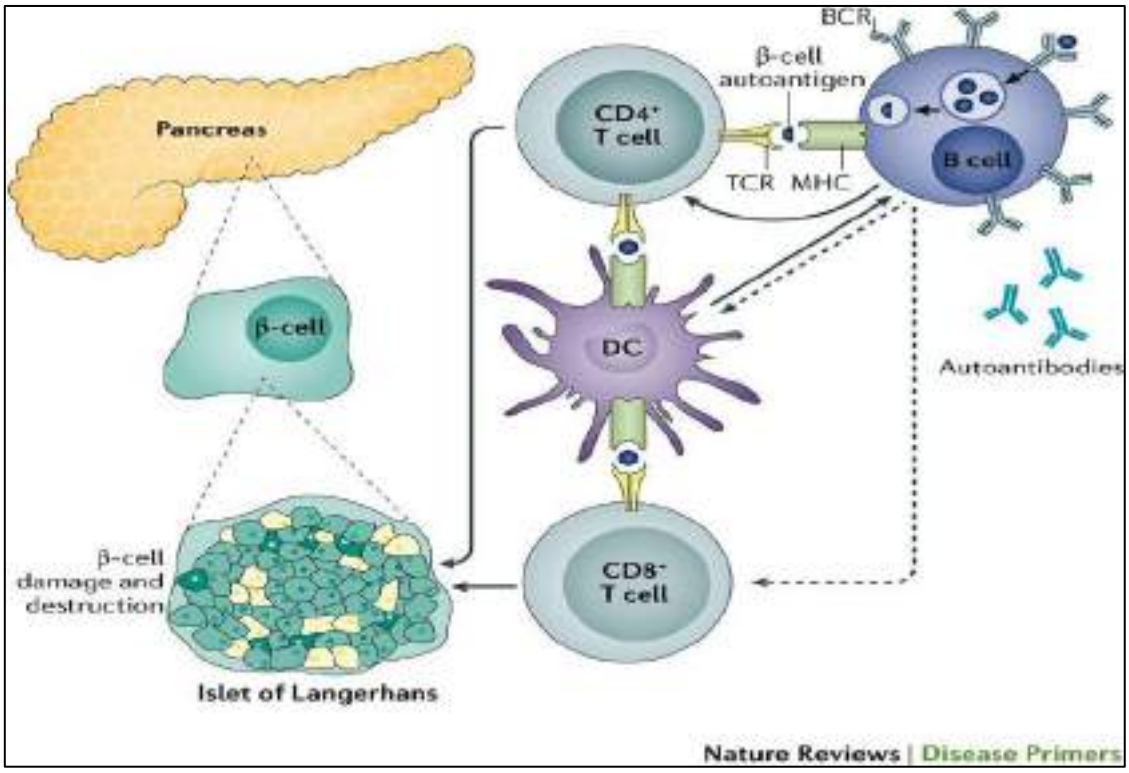
Imbalance in Diabetes Mellitus (DM)

DM occurs when there is

- Insulin deficiency - Insulin production by beta cells is reduced or absent.

- Impaired insulin action (insulin resistance) - Cells fail to respond properly to insulin.
- This disruption leads to hyperglycaemia, where blood glucose levels become excessively high.

3) What are the major causes of Type 1 Diabetes Mellitus? Discuss the underlying mechanisms contributing to its Development.



https://www.nature.com/articles/nrdp201716

- T1DM is also known as Insulin -Dependent Diabetes Mellitus.
- It results from the destruction of pancreatic beta cells, causing an absolute deficiency of insulin production.

Underlying Mechanisms

(1) Autoimmune Destruction

- The immune system attacks beta cells in the pancreas.
- This is the primary mechanism in most cases of T1D.

(2) Idiopathic Causes

- In some cases, the exact cause remains unknown.

Clinical Implications

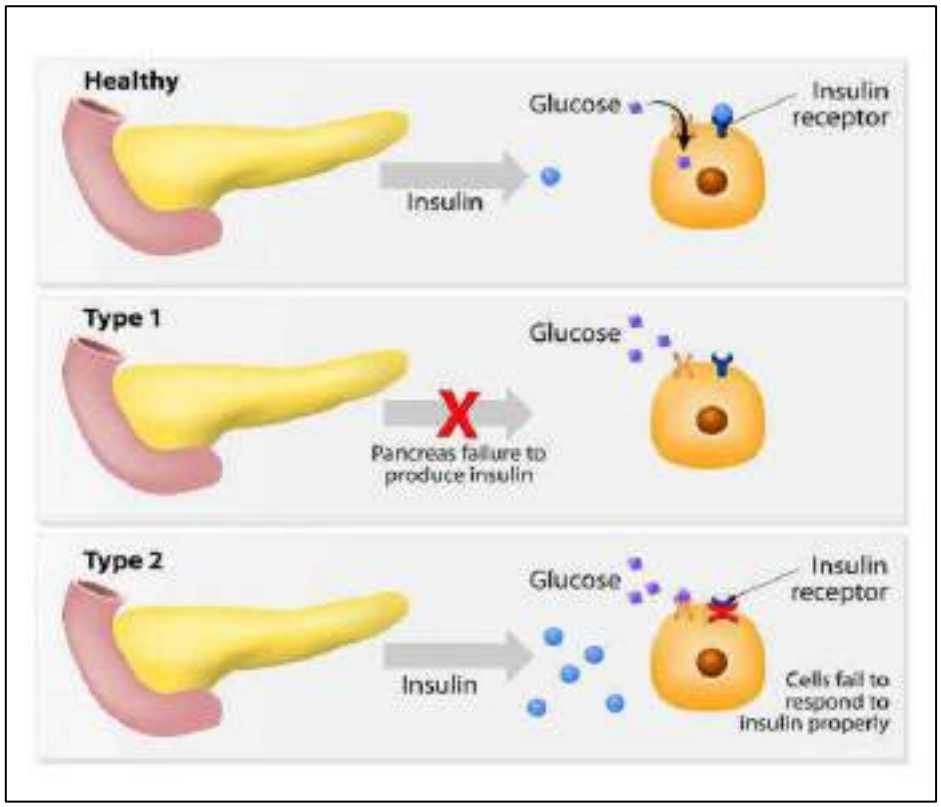
- Lifelong dependency on insulin therapy is required for glucose control.

Key Features of T1DM

- **Absolute Insulin Deficiency**
- Total loss or extremely low levels of insulin in circulation.

- **Prone to Ketosis**
- Lack of insulin leads to ketone body production and a risk of diabetic ketoacidosis.
- **Population Affected**
- Typically develops in children and adolescents but cases are increasing in adults under 40 years.
- T1DM accounts for approximately 10% of all diabetes cases.

(3) How does Type 2 Diabetes Mellitus differ from Type 1 Diabetes Mellitus? Highlight the key differences in aetiology, pathophysiology, and clinical features.



https://www.hsmc.ae/our-clinics/endocrinology/diabetes-mellitus/

Aetiology

Type 1 Diabetes Mellitus (T1DM)

- Autoimmune destruction of pancreatic beta cells.
- Results in an absolute insulin deficiency.
- Commonly develops in children or young adults.

Type 2 Diabetes Mellitus (T2DM)

- Caused by insulin resistance —cells fail to respond properly to insulin.
- Associated with lifestyle factors (e.g., obesity, physical inactivity) and aging.
- Has a stronger hereditary component than T1DM.

Pathophysiology

T1DM

- Complete or near -complete loss of insulin production.
- Prone to ketosis due to absence of insulin.

T2DM

- Insulin levels may be low, normal, or high, but insulin sensitivity is reduced.
- Imbalance between insulin levels and sensitivity leads to hyperglycaemia.

Clinical Features

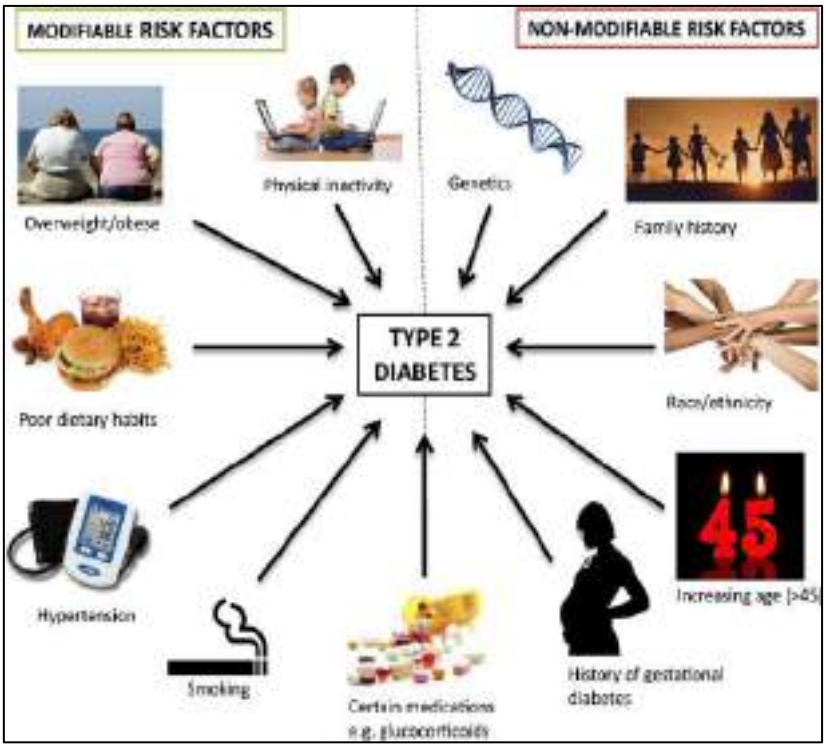
•T1DM

- Rapid onset of symptoms, including weight loss, polyuria, polydipsia, and fatigue.
- Requires lifelong insulin therapy.
- Accounts for approximately 10% of all diabetes cases.

•T2DM:

- Gradual onset, often asymptomatic in early stages.
- Over 90% of diabetes cases are T2DM.
- Often managed with lifestyle changes, oral medications, or insulin in advanced stages.

(3) What are the risk factors for Type 2 Diabetes Mellitus? Explain how these factors contribute to its development.



https://www.researchgate.net/figure/Modifiable-and-non-modifiable-risk-factors-of-Type-2-Diabetes-Mellitus_fig8_335684432

Modifiable Risk Factors

- Obesity - Strongly associated with insulin resistance and T2DM, especially in women.
- Physical inactivity - Lack of exercise exacerbates insulin resistance.
- Unhealthy eating habits - Diets high in sugar and unhealthy fats contribute to obesity and dyslipidaemia.
- High blood pressure and dyslipidaemia - Associated with metabolic syndrome and increased T2DM risk.
- Smoking - Both active and passive smoking increase the risk.
- Poor sleep quality/quantity - Disrupts glucose metabolism and increases T2DM risk.

Non -Modifiable Risk Factors

- Advanced age -Risk increases after age 45.
- Family history of diabetes - Strong hereditary component, particularly with first -degree relatives.
- Ethnicity - Some populations are more predisposed due to genetic variations in insulin sensitivity.

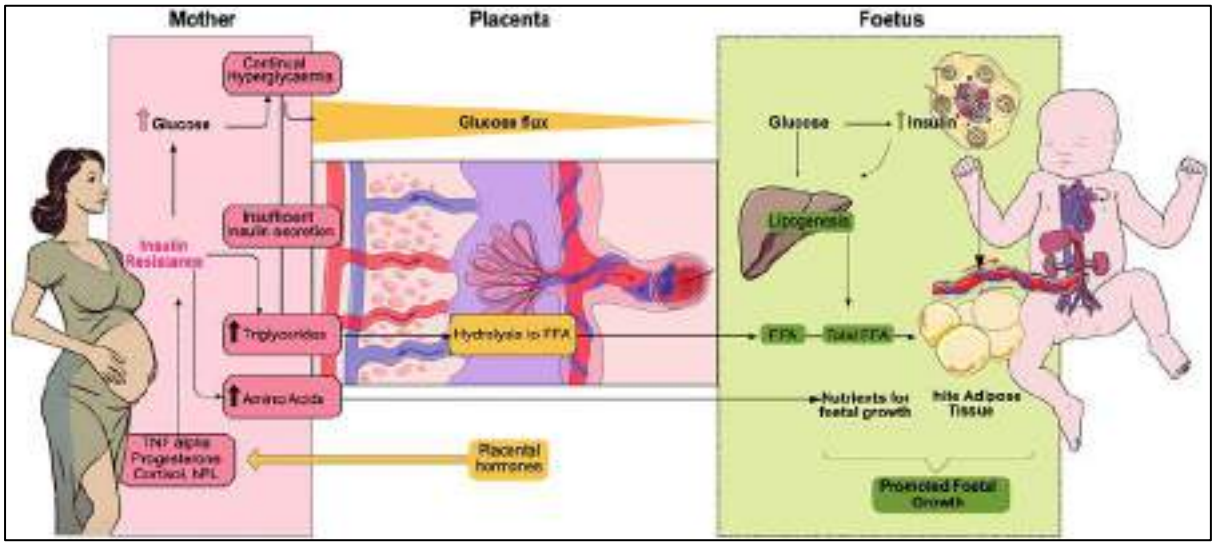
Additional Risk Factors

- Gestational diabetes history - Increases lifetime risk of T2DM.
- Socioeconomic status - Lower income and education levels contribute to higher prevalence through associated.
- lifestyle factors.

Mechanism of Risk Factors

- Obesity and inactivity lead to insulin resistance, causing glucose buildup in the blood.
- Genetics and age further exacerbate this functional imbalance between insulin levels and sensitivity.

(4) What is gestational diabetes? Explain its definition, causes, and potential implications for both the mother and baby.



https://open-research-europe.ec.europa.eu/articles/4-164

Gestational Diabetes

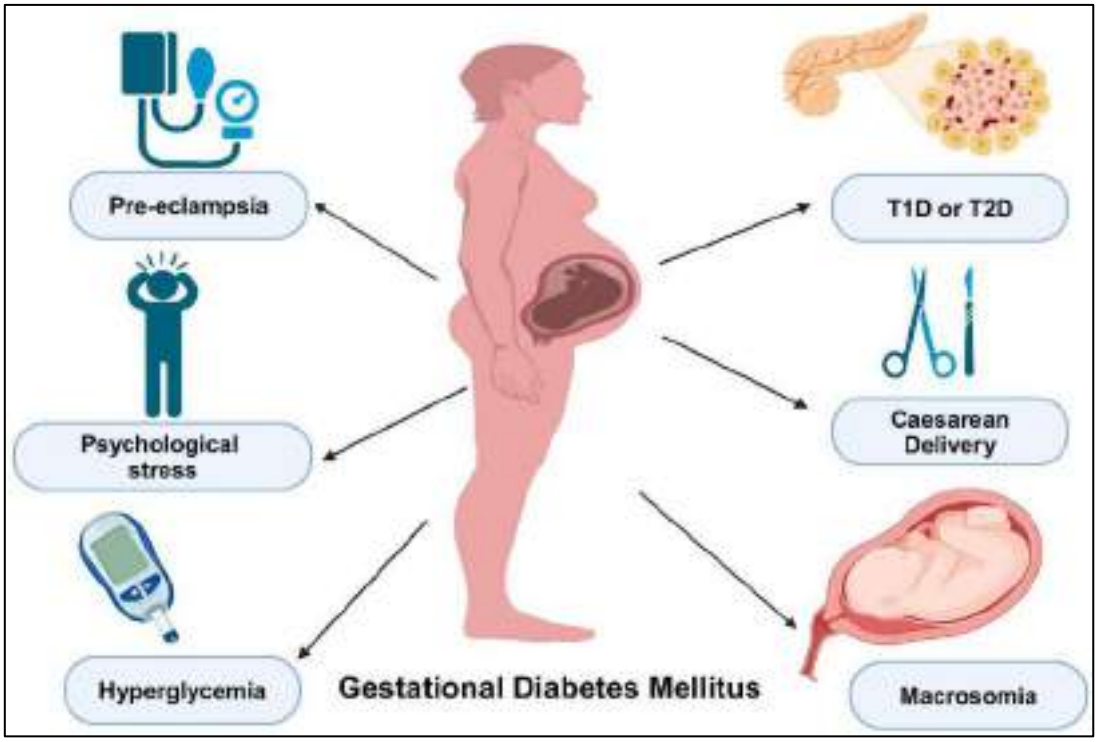
- A form of diabetes that develops during pregnancy due to elevated blood glucose levels.
- Typically appears between 24 and 28 weeks of pregnancy y and resolves after delivery.

Causes

- Hormones produced by the placenta (e.g., progesterone, cortisol, and human placental lactogen) interfere with insulin function, causing insulin resistance.
- Glucose builds up in the blood as a result.

Risk Factors

- Obesity or being overweight
- Family history of Type 2 Diabetes
- Advanced maternal age
- Polycystic ovary syndrome (PCOS)
- History of gestational diabetes or prediabetes
- Heart disease or high blood pressure



https://www.mdpi.com/1422-0067/26/5/2320

Implications for Mother

- Increased risk of preeclampsia (high blood pressure during pregnancy).
- Potential complications during labour, including a higher likelihood of Caesarean delivery.
- Higher risk of developing Type 2 Diabetes later in life.

Implications for the Baby

- Excessive birth weight (macrosomia), leading to delivery complications.

- Hypoglycaemia (low blood sugar) after birth.
- Respiratory problems and increased risk of premature birth.
- Higher likelihood of obesity and Type 2 Diabetes in later life.

Postpartum Considerations

- Blood glucose levels usually return to normal after delivery.
- Women should undergo a glucose test six weeks postpartum to rule out persistent type 2 Diabetes.

(5) How is diabetes diagnosed? Discuss the diagnostic criteria, tests, and their interpretation for different types of diabetes.



https://www.shutterstock.com/image-vector/diabetes-test-concept-mans-hand-glucometer-1174720045?dd_referrer=https%3A%2F%2Fwww.google.com%2F

Type 1 Diabetes Mellitus (T1DM)

- Diagnosis is based on elevated blood glucose levels and a characteristic clinical history.
- Diagnostic criteria include,
- Fasting glucose > 126 mg/dL
- Random glucose > 200 mg/dL
- HbA1c > 6.5%
- Testing for antibodies (e.g., GAD or insulin antibodies) may be used in some cases.

Type 2 Diabetes Mellitus (T2DM)

- Fasting glucose levels or HbA1c are used for diagnosis.
- Diagnostic criteria include,
- HbA1c ≥ 6.5%
- Fasting glucose ≥ 126 mg/dL
- 2-hour OGTT plasma glucose ≥ 200 mg/dL
- Prediabetes is diagnosed with,
- Fasting glucose 100 -125 mg/dL
- 2-hour post -OGTT glucose 140 -199 mg/dL

- Oral glucose tolerance test (OGTT) can be used for borderline cases.

Gestational Diabetes

- Screening is done between 24 -28 weeks of pregnancy.
- Initial test – 1 hour glucose challenge test (A non-fasting test where the pregnant woman drinks a glucose solution and then has her blood glucose measured 1 hour later).
- If glucose is > 140 mg/dL, a 3 -hour OGTT is performed.
- Diagnosis is confirmed if at least one value is abnormal during the 3 -hour test (The woman must be fasting for at least 8 hours before the test. After the fasting blood sample is taken, she
- drinks a glucose solution and has her blood glucose measured at 1, 2, and 3 hours after drinking the solution).
- 1-hour > 180 mg/dL
- 2-hour > 155 mg/dL
- 3-hour > 140 mg/dL

Screening Guidelines

- Adults aged 45+ or those aged 40 -70 with risk factors (overweight, family history, etc.) should be screened.

(6) What are the signs and symptoms of Diabetes Mellitus? Describe the common clinical manifestations associated with the condition.

Common Clinical Manifestations

- Polyuria (frequent urination) - Excessive glucose in the blood spills into the urine, leading to large volumes of urine production.
- Polydipsia (increased thirst) - Excessive urination causes dehydration, triggering increased thirst.
- Polyphagia (increased hunger) - Loss of calories in the urine leads to heightened hunger.
- Weight loss - Particularly in Type 1 diabetes, due to calorie loss in urine and fat breakdown.

Additional Symptoms

- Blurred vision
- Fatigue
- Nausea
- Drowsiness
- Decreased endurance during physical activity.

Specific Symptoms in Type 2 Diabetes

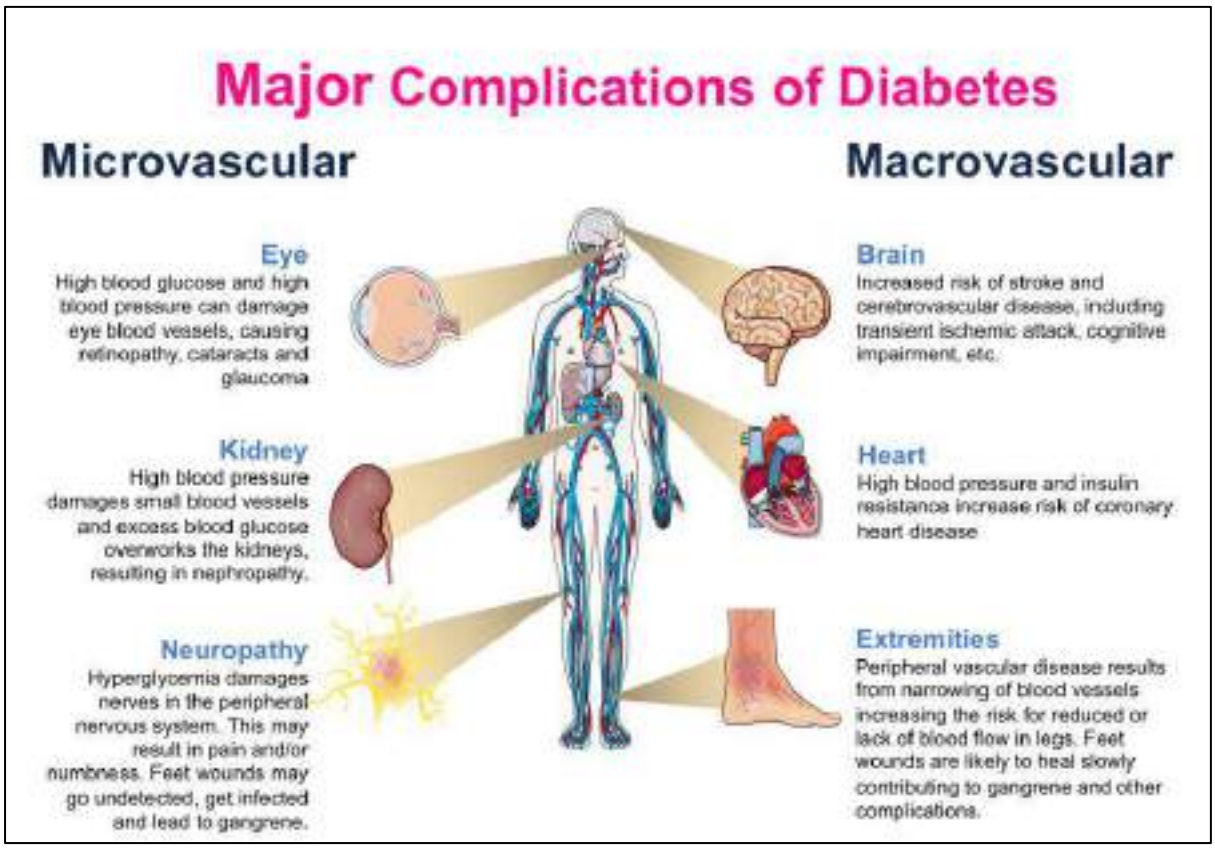
- Symptoms often develop gradually over time.
- Early symptoms may include mild polyuria and polydipsia.
- Advanced symptoms: Fatigue, blurred vision, dehydration, and mental confusion in severe cases.
- Rarely, hyperosmolar hyperglycaemic state (HHS).

- Extremely high glucose levels (>1,000 mg/dL), leading to dehydration, mental confusion, seizures, and drowsiness.

Specific Symptoms in Type 1 Diabetes

- Symptoms often appear suddenly on quick onset.
- May progress to diabetic ketoacidosis (DKA).
- Symptoms include nausea, vomiting, fatigue, abdominal pain (especially in children), fruity -smelling breath, and deep, rapid breathing (Kussmaul respirations).
- Can lead to coma or death without treatment.

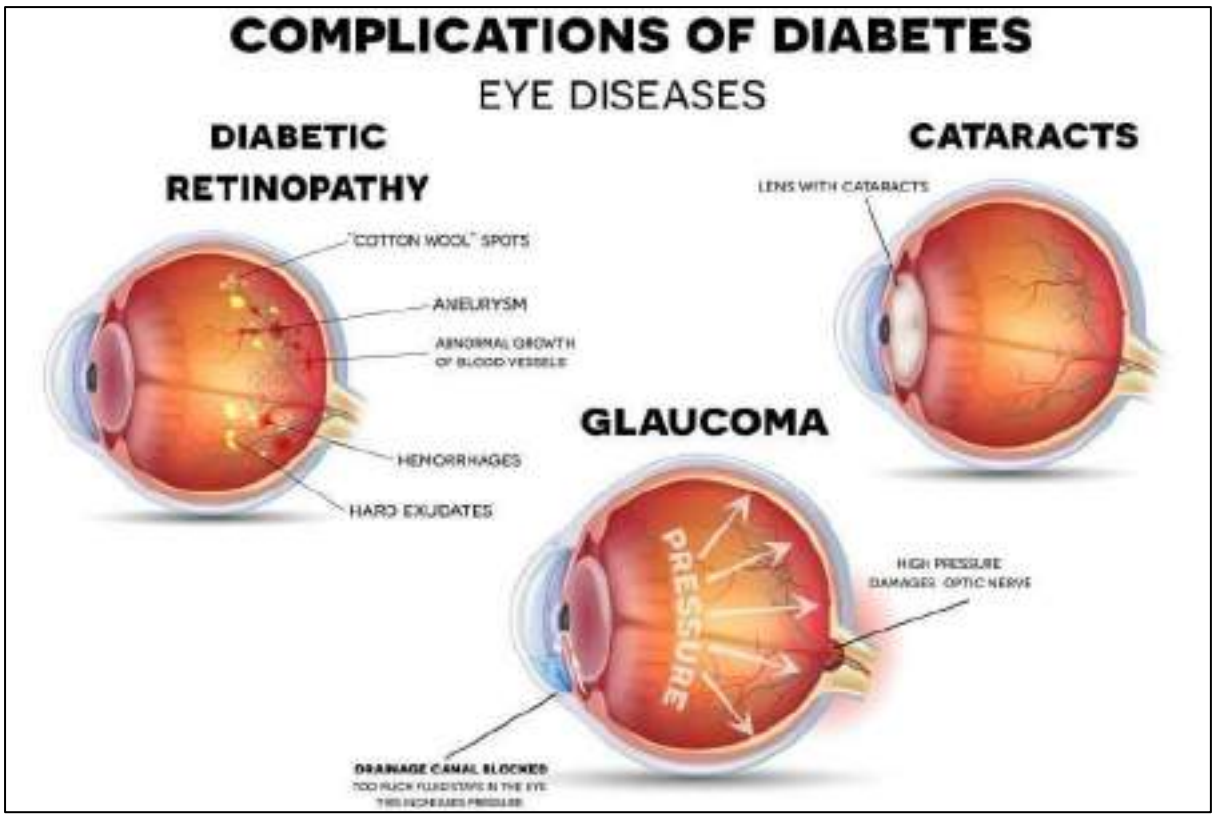
(7) What are the major complications of Diabetes Mellitus?



https://pdb101.rcsb.org/global-health/diabetes-mellitus/monitoring/complications

- Hyperglycaemia (very reactive with tissues)
- Protein glycosylation
- glucose + protein → glycosylated protein
- Glycosylation products can accumulate Leading to cellular dysfunction.
- Especially in tissues exposed to the blood (Blood vessels, kidneys, etc).
- Diabetes mellitus can cause serious complications, especially in organs affected by blood vessels and nerves.
- The major complications of diabetes include,

Eyes (Diabetic Retinopathy)

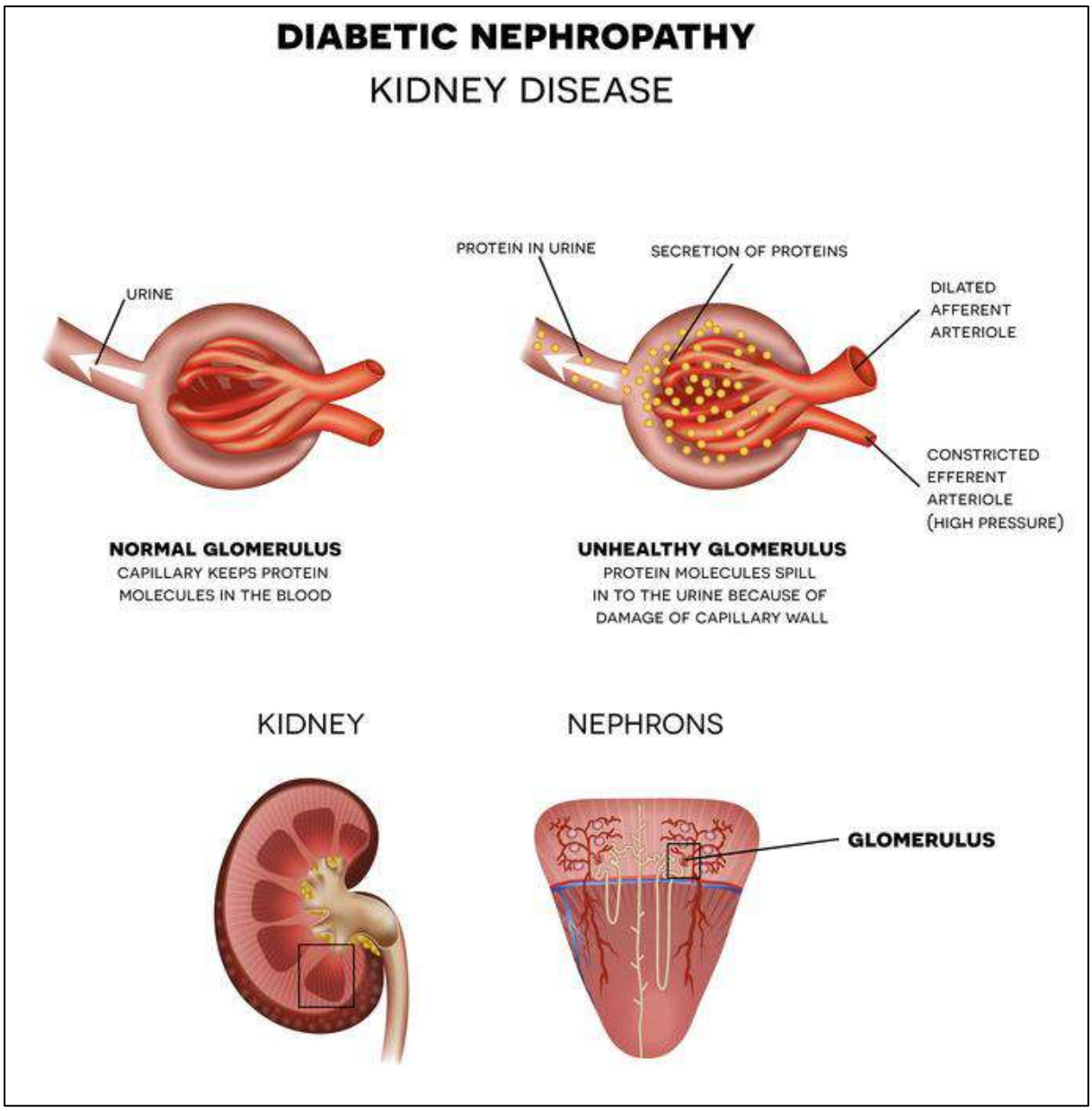


https://invisioncare.com/diabetic-eye-disease/

- Non proliferative Diabetic Retinopathy - In this early stage, small blood vessels in the retina leak fluid or blood, causing swelling that may impair vision.
- The damage may be minimal initially, but vision may gradually worsen as fluid leaks into the central retina (macula), causing blurred central vision or macular oedema.
- Proliferative Diabetic Retinopathy - This more severe stage involves the growth of abnormal blood vessels in the retina These vessels can bleed, causing vision loss or retinal detachment.
- The abnormal blood vessels can also lead to neovascular glaucoma where high eye pressure causes additional vision loss.
- Symptoms of Proliferative Diabetic Retinopathy - Blurred vision, floaters (black spots), flashing lights, or sudden vision loss.

Kidneys (Diabetic Nephropathy)

- Diabetes can lead to kidney damage, causing chronic kidney disease (CKD). Early signs are often detected through urine tests for protein.
- Treatment - Early intervention includes controlling blood sugar, blood pressure, and using medications like ACE inhibitors or ARBs to slow kidney damage.

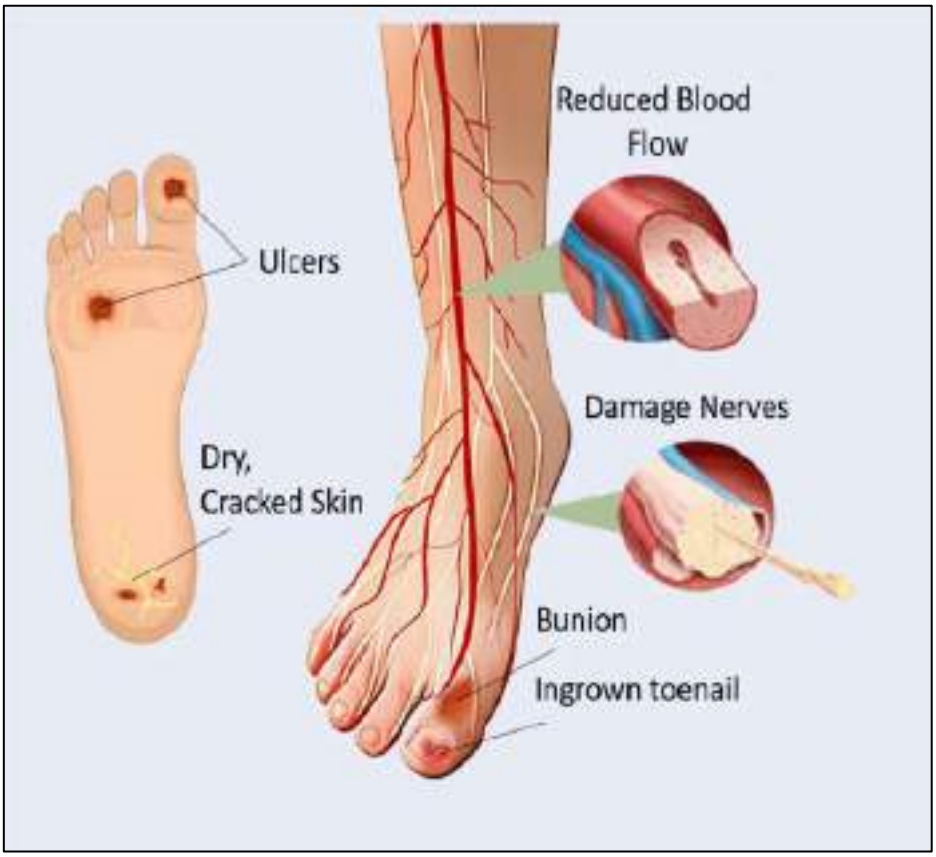


https://www.rsnhope.org/health-library/nephropathy-diabetes-kidney-disease/

Nerves (Diabetic Neuropathy)

- Diabetes can cause nerve damage, leading to diabetic neuropathy.
- This often affects the legs and feet, leading to symptoms like numbness, tingling, pain, or weakness.
- Due to impaired sensation, people with diabetic neuropathy may not feel injuries or infections, which can worsen over time.
- **Foot Complications**: Poor circulation and nerve damage make the feet more vulnerable to infections and ulcers, which may not heal properly and can result in gangrene, leading to amputation in severe cases.

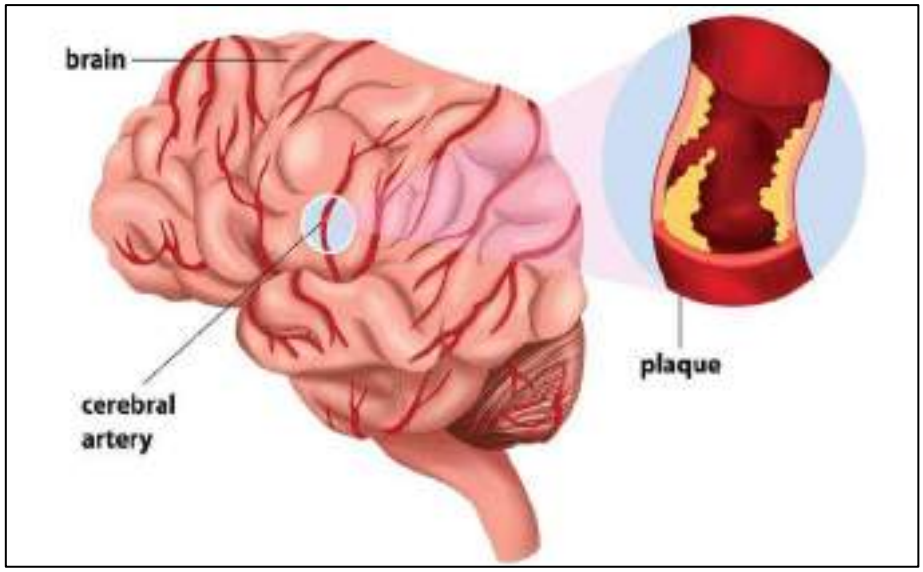
- hyperglycaemia promotes the formation of advanced glycation end-products (AGEs) which increase oxidative stress and inflammation, impairing vascular function.
- Chronic inflammation, oxidative stress, and lipid abnormalities lead to the formation of plaques in arteries.
- Insulin resistance leads to abnormal fat metabolism, causing high levels of triglycerides, LDL (more atherogenic), and low levels of HDL cholesterol These abnormalities exacerbate atherosclerosis.



https://www.researchgate.net/figure/Complications-in-a-diabetic-foot_fig2_361034769

Brain [Stroke/ cerebrovascular accident (CVA)]

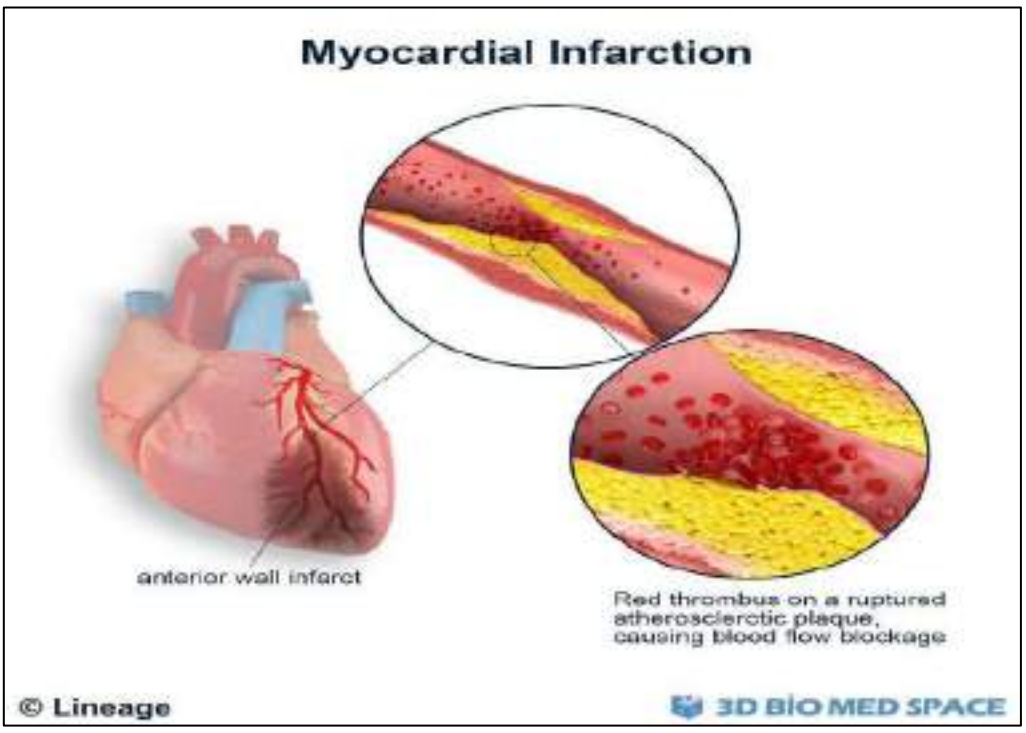
- Diabetes increases the risk of stroke due to its contribution to atherosclerosis (narrowing of blood vessels), which restricts blood flow to the brain.



https://sabclinic.com/cva-stroke/

Heart [Heart Attack / myocardial infarction (MI)]

- Diabetes accelerates the development of atherosclerosis, increasing the risk of heart attacks and heart failure due to the narrowing of blood vessels.



https://step2.medbullets.com/cardiovascular/120011/myocardial-infarction

Liver Problems

- Fatty Liver Disease (Steatosis Liver Disease) Diabetes is associated with abnormal fat buildup in the liver, which can progress to cirrhosis if not managed.

COURSE 2 - METABOLISM 02

TUTORIALS & ANSWERS

TUTORIAL 01

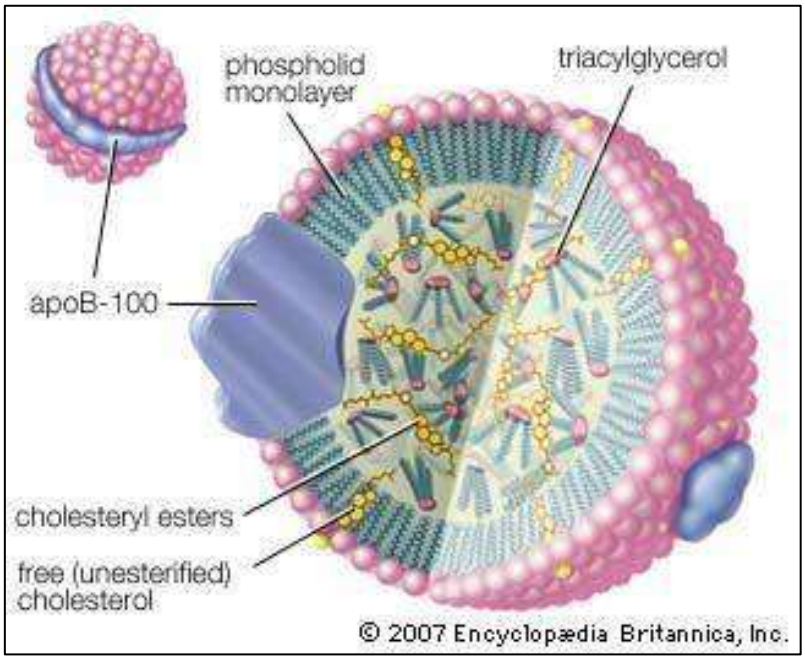
Lipid Metabolism

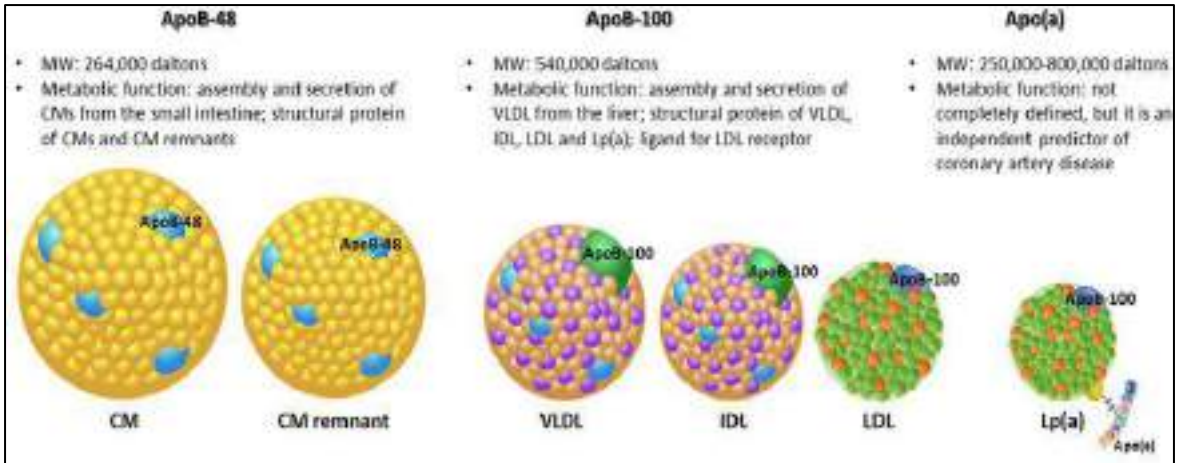
(1) Describe the structure and classification of lipoproteins. (30 Marks)
(2) Discuss the lipid and protein components that determine function of lipoproteins. (20Marks)
(3) Explain how lipoproteins facilitate the transport of lipids in the blood stream. (20 Marks)
(4) Discuss the role of apolipoproteins in lipoprotein function and receptor interaction. (30 Marks)

TUTORIAL 01

Lipid Metabolism-Answers

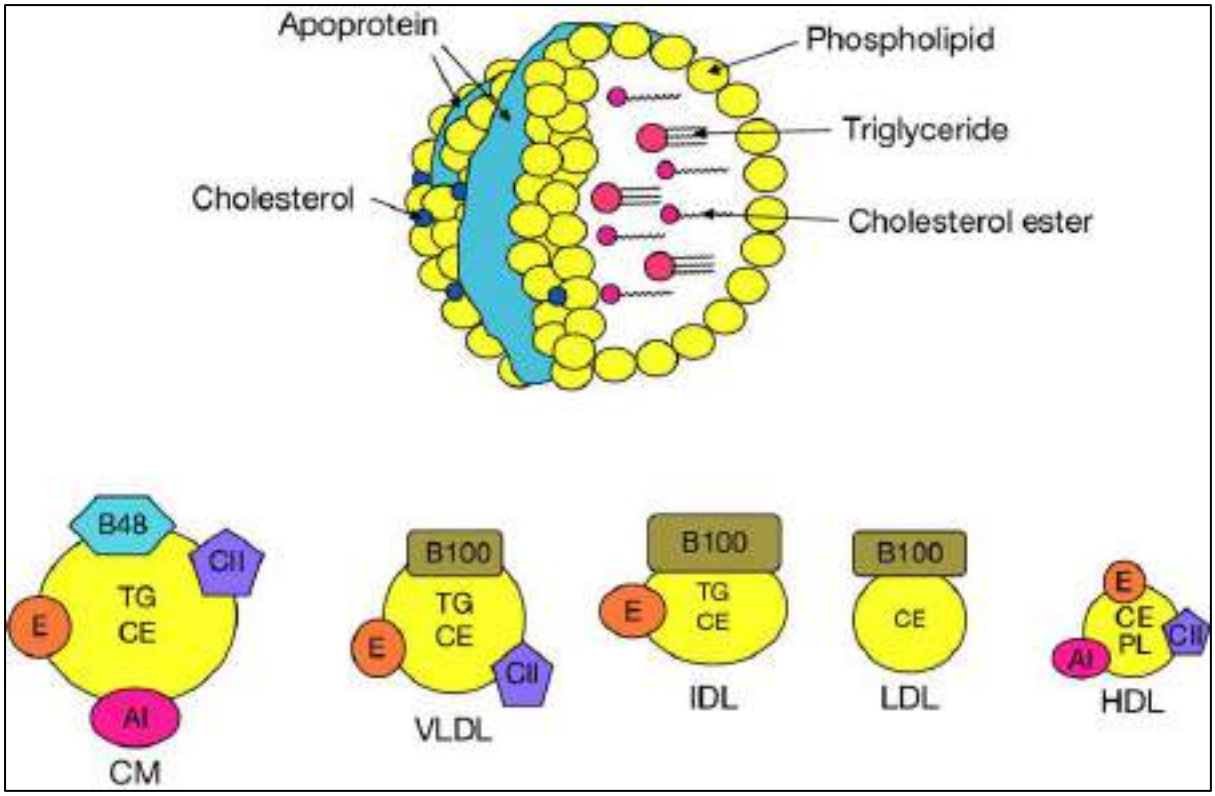
(1) Describe the structure and classification of lipoproteins. (30 Marks)





	CM	CM remnant	VLDL	IDL	LDL	Lp(a)
Source	Intestine	CM	liver (intestine)	VLDL	VLDL	liver
Density (g/dl)	<0.95	<1.006	0.95-1.006	1.006-1.019	1.019-1.063	1.05-1.12
Diameter (nm)	75-1200	45-150	30-80	25-35	18-25	about 25
Molecular weight (daltons)	400 x10^6	unknown	10-80 x10^6	5-10 x10^6	2.3 x10^6	about 4 x10^6
Structural components	99-98% total lipid and 1-2% total protein	94-92% total lipid and 6-8% total protein	93% total lipid and 7% total protein	85% total lipid and 15% total protein	80% total lipid and 20% total protein	80% total lipid and 20% total protein
Apolipoprotein composition	A-I, A-II, A-IV, B-48, C-I, C-II, C-III, E	B-48, E	B-100, C-I, C-II, C-III, E	B-100, C-I, C-II, C-III, E	B-100	B-100, Apo(a)

(2) Discuss the lipid and protein components that determine function of lipoproteins. (20Marks)



https://www.researchgate.net/figure/Lipoprotein-structures-Lipoproteins-contain-a-hydrophobic-core-of-TG-and-CE-and-an_fig5_271910276

1. Chylomicrons

- **Density:** Lowest (largest size).
- **Composition:** High triglyceride content (85-90%), low protein.
- **Function:** Transport dietary triglycerides and cholesterol from the intestines to peripheral tissues (e.g., muscle, adipose tissue) and the liver.
- **Source:** Produced in the intestines.
- **Clinical relevance:** Elevated chylomicrons may be seen in conditions like **hyperchylomicronaemia**.

2. Very Low-Density Lipoproteins (VLDL)

- **Density:** Low (second-largest size).
- **Composition:** High in triglycerides (55-65%), moderate protein and cholesterol.
- **Function:** Transport triglycerides synthesized by the liver to peripheral tissues.
- **Source:** Produced in the liver.
- **Clinical relevance:** Elevated VLDL is associated with **hypertriglyceridemia** and can lead to **atherosclerosis**.

3. Intermediate-Density Lipoproteins (IDL)

- **Density:** Intermediate between VLDL and LDL.

- **Composition:** Rich in cholesterol (30-40%) and intermediate protein content.
- **Function:** Transition from between VLDL and LDL as triglycerides are removed from VLDL.
- **Source:** Formed from VLDL in circulation.
- **Clinical relevance:** Elevated IDL can contribute to the development of atherosclerosis.

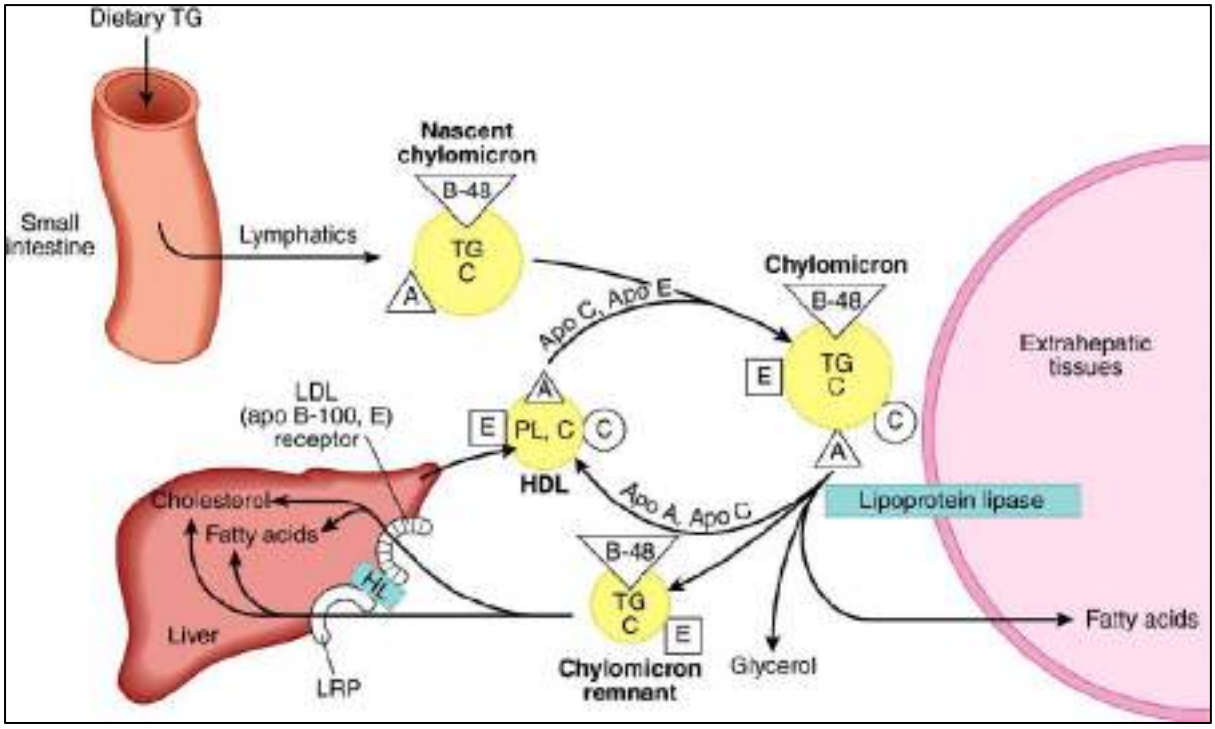
4. Low-Density Lipoproteins (LDL)

- **Density:** Higher (small size, denser).
- **Composition:** High cholesterol content (45-50%), low triglycerides.
- **Function:** Transport cholesterol from the liver to peripheral tissues.
- **Source:** Formed from IDL in circulation.
- **Clinical relevance:** Often referred to as "bad cholesterol"; high levels of LDL are strongly associated with **atherosclerosis** and **cardiovascular disease** (CVD).

5. High-Density Lipoproteins (HDL)

- **Density:** Highest (smallest size, most protein-rich).
- **Composition:** High protein content (40-50%), low cholesterol and triglycerides.
- **Function:** Reverse cholesterol transport – carries cholesterol from peripheral tissues back to the liver for excretion.
- **Source:** Produced in the liver and intestines.
- **Clinical relevance:** Referred to as "good cholesterol"; high levels of HDL are protective against **CVD**.

3. Explain how lipoproteins facilitate the transport of lipids in the blood stream. (20 Marks)



https://basicmedicalkey.com/lipid-transport-storage/

- **Lipid Packaging**: Lipoproteins package hydrophobic lipids like triglycerides and cholesterol within their core, surrounded by a hydrophilic shell of phospholipids, cholesterol, and apolipoproteins.
- **Transport in Blood**: The hydrophilic shell allows lipoproteins to move through the bloodstream while carrying hydrophobic lipids.
- **Lipid Delivery**: Lipoproteins transport lipids to tissues for energy production, storage, or structural use.
- **Reverse Transport**: HDL helps remove excess cholesterol from tissues, protecting against atherosclerosis by preventing cholesterol buildup in blood vessels.

4. Discuss the role of apolipoproteins in lipoprotein function and receptor interactions.

(30Marks)

1. Structural Role:

- **Stabilizing Lipoprotein Particles:**

Apolipoproteins are amphipathic, meaning they have both hydrophilic (water-attracting) and hydrophobic (water-repelling) regions. This structure allows them to maintain the integrity of lipoproteins by surrounding the hydrophobic core (containing triglycerides and cholesterol esters) with a hydrophilic outer shell (composed of apolipoproteins, phospholipids, and free cholesterol). This makes lipoproteins soluble in the aqueous environment of the bloodstream.

- **Key Example:** Apolipoprotein B-100 (ApoB-100) is the structural protein of **VLDL**, **IDL**, and **LDL**, and it helps maintain the particle's structure as it delivers lipids to tissues.

2. Enzyme Activation and Regulation:

Apolipoproteins act as activators or inhibitors of enzymes that are crucial in lipid metabolism.

- **Apo C-II:** Activates **lipoprotein lipase (LPL)**, an enzyme that hydrolyses triglycerides in chylomicrons and VLDL into free fatty acids, enabling their uptake by muscle and adipose tissues for energy or storage.
- **Apo A-I:** Activates **lecithin-cholesterol acyltransferase (LCAT)**, an enzyme that esterifies free cholesterol on the surface of high-density lipoproteins (HDL), aiding in cholesterol transport back to the liver (reverse cholesterol transport).
- **Apo C-III:** Inhibits lipoprotein lipase, regulating triglyceride breakdown and preventing excessive clearance of triglyceride-rich lipoproteins.

3. Receptor Interaction and Lipid Uptake:

Apolipoproteins serve as ligands for specific receptors on cell surfaces, facilitating the uptake and clearance of lipoproteins and their lipid cargo.

- **ApoB-100 and LDL Receptor Interaction:**
  LDL particles, which primarily carry cholesterol, are recognized and taken up by cells via the **LDL receptor (LDL-R)**. ApoB-100 acts as the ligand for LDL receptors, facilitating the internalization of LDL particles into cells, where the cholesterol is used for membrane synthesis, hormone production, or stored.
- **Apo E and Lipoprotein Clearance:**
  Apo E is a key apolipoprotein involved in the clearance of remnant lipoproteins (such as chylomicron remnants and IDL) from circulation. ApoE acts as a ligand for receptors such as the **LDL receptor** and **LDL receptor-related protein (LRP)**, allowing these remnants to be taken up by the liver for metabolism and excretion.
    - **Example:** In individuals with **ApoE deficiency or mutations** (as seen in conditions like **Type III hyperlipoproteinemia**), the clearance of remnants is impaired, leading to elevated blood lipid levels and an increased risk of atherosclerosis.

4. Reverse Cholesterol Transport:

One of the critical roles of apolipoproteins is in reverse cholesterol transport, which involves the removal of excess cholesterol from peripheral tissues and its transport back to the liver for excretion.

- **Apo A-I and HDL:**
  Apo A-I is the major apolipoprotein in HDL particles and plays a vital role in reverse cholesterol transport. It interacts with the **ABCA1 (ATP-binding cassette transporter A1)** on peripheral cells, promoting the efflux of cholesterol onto HDL. Apo A-I also activates LCAT, which converts free cholesterol into cholesteryl esters, making it easier to transport cholesterol back to the liver for clearance.
- **Importance in Atherosclerosis Prevention:**
  Apo A-I and HDL are often referred to as "good cholesterol" because they help remove excess cholesterol from tissues, especially arterial walls, reducing the risk of plaque formation and atherosclerosis.

5. Lipoprotein Recycling and Remodelling:

Apolipoproteins also play a role in the remodelling and recycling of lipoprotein particles:

- **Exchange of Apolipoproteins:**
  Apolipoproteins like **Apo C-II**, **Apo C-III**, and **Apo E** can be transferred between different lipoproteins (e.g., from HDL to VLDL and vice versa), allowing lipoproteins to adapt to changing metabolic needs and environmental conditions.
- **Remnant Clearance:**
  Chylomicrons and VLDL lose triglycerides through the action of lipoprotein lipase, transforming into smaller remnants that are cleared from circulation by liver receptors. **Apo E** plays a critical role in recognizing these remnants for clearance.

6. Clinical Relevance:

- **Apolipoprotein Deficiencies:**
  Genetic mutations or deficiencies in apolipoproteins can lead to dyslipidaemias, increasing the risk of cardiovascular disease. For example:
  - **ApoB-100 mutations** can impair LDL receptor binding, leading to familial hypercholesterolemia and premature atherosclerosis.
  - **Apo E mutations** can impair the clearance of remnants, causing Type III hyperlipoproteinemia.
- **Apo A-I Deficiency:**
  A deficiency in Apo A-I can reduce HDL levels, impair reverse cholesterol transport and increase the risk of atherosclerosis.

(Total: 100Marks)

SGDs & ANSWERS

SGD 01

Lipid Metabolism

(1)

(1.1.) List five (05) common classes of lipids. (10 Marks)

(1.2.) Briefly describe the process of processing of dietary lipids in the small intestine before the enzymatic digestion. (20 Marks)

(1.3.) List the enzymes involved in processing of dietary lipids in stomach, the gland which secrete that enzyme and the function. (30 Marks)

Enzyme	**Gland of origin**	**Location of digestion**	**Reaction**

(1.4.) Briefly describe the control of lipid digestion. (40 Marks)

(Total:100Marks)

(2)

(2.1.)

(2.1.1.) List three (03) primary products of lipid digestion in the jejunum. (06 Marks)

(2.1.2.) State the fate of primary products of lipid digestion in the enterocytes. (14Marks)

(2.2.) Briefly describe the role of the microsomal TAG transfer protein in chylomicron formation. (30 Marks)

(2.3.)

(2.3.1.) Briefly describe the process by which chylomicrons are released from enterocytes and transported through the lymphatic system. (20 Marks)

(2.3.2.) Explain the distinction between chyle and chyme. (20 Marks)

(2.4.) Briefly describe the pathway chylomicrons follow from the small intestine to the bloodstream. (10 Marks)

(Total:100Marks)

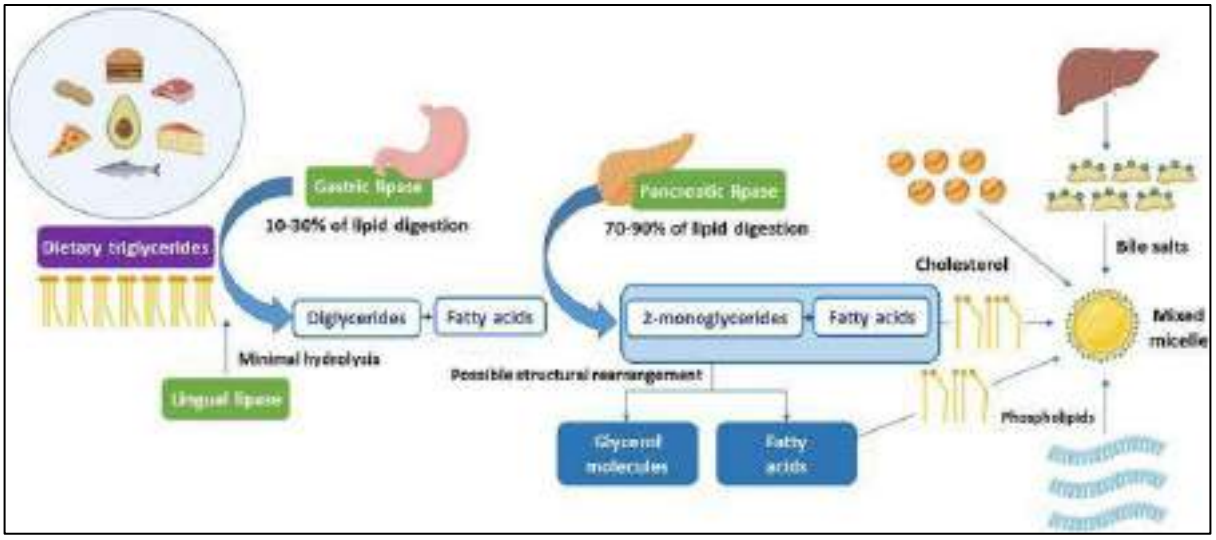
SGD 01

Lipid Metabolism- Answers

(1.1.) List five (05) common classes of lipids. (10 Marks)

Fatty acids
Triacylglycerol
Phospholipid
Steroid
Glycolipid

(1.2.) Briefly describe the process of processing of dietary lipids in the small intestine before the enzymatic digestion.



https://www.sciencedirect.com/science/article/pii/S0308814624038019

- Emulsification of dietary lipids Occurs in the duodenum.
- This process increases the surface area of the hydrophobic lipid droplets.
- Increase the effectiveness of digestive enzymes.

Two complementary mechanisms involved,

a. Use of the detergent properties of bile salts.
b. Mechanical mixing due to peristalsis.

(1.3.) List the enzymes involved in processing of dietary lipids in stomach, the gland which secrete that enzyme and the function. (30 Marks)

Enzyme	**Gland of origin**	**Location of digestion**	**Reaction**
Lipase (lingual lipase)	Glands at the back of the tongue	Stomach	TAG Molecules containing fatty acids of short or medium-chain length
Gastric lipase	Gastric mucosa	Stomach	TAG Molecules containing fatty acids of short or medium-chain length

Cholesteryl esterase	Pancreas	Small intestine	Cholesteryl ester → cholesterol
Lipases	Pancreas	Small intestine	Phosphatidylcholine (a phospholipid) → Glyceryl phosphorylcholine
Pancreatic lipases	Pancreas	Small intestine	Triacylglycerol → 2-monoacylglycerol

(1.4.) Briefly describe the control of lipid digestion. (40 Marks)

- Pancreatic secretion of the hydrolytic enzymes is hormonally controlled.
- Cholecystokinin (CCK) a small polypeptide hormone.
- Produced by lower duodenum and jejunum.
- In response to the presence of lipids and partially digested proteins entering these regions.
- Acts on the gallbladder,
    - Causing it to contract and release bile (mixture of bile salts, phospholipids and free cholesterol).
    - Act on exocrine cells of the pancreas causing them to release digestive enzymes.
    - Decreases gastric motility, resulting in a slower release of gastric contents into the small intestine.
- Secretin causes the pancreas and the liver to release a solution rich in bicarbonate that helps neutralize the pH of the intestinal contents.

(1.5.)

(1.5.1.) List three (03) primary products of lipid digestion in the jejunum.

(06 Marks)

Free fatty acids
Free cholesterol
2-monoacylglycerol

(1.5.2.) State the fate of primary products of lipid digestion in the enterocytes.

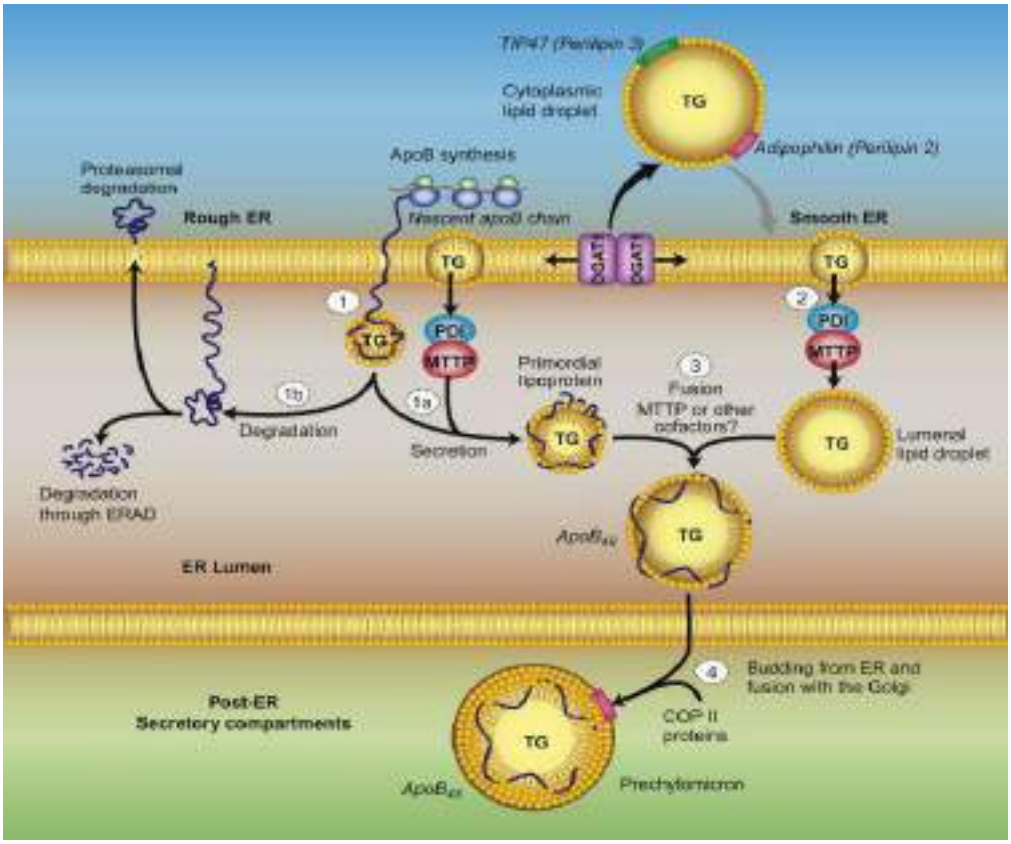
(14Marks)

- Migrate to the endoplasmic reticulum.
- Biosynthesis of complex lipids.
- Fatty acids conversion to activated form – fatty acyl-CoA synthetase (thiokinase).
- 2-monoacylglycerols → TAGs (TAG synthase).
- Cholesterol is esterified to fatty acids (acyl CoA:cholesterol acyltransferase).
- Lysophospholipids are reacylated to form phospholipids.

- Short and medium chain length fatty acids are not converted to their CoA derivatives, released in to the portal circulation.

(1.6.) Briefly describe the role of the microsomal TAG transfer protein in chylomicron formation.

(30 Marks)



https://www.sciencedirect.com/topics/nursing-and-health-professions/microsomal-triglyceride-transfer-protein

- Since resynthesized TAGs and cholesteryl esters are very hydrophobic, it is necessary to be packaged as particles of lipid droplets surrounded by a thin layer composed of phospholipids, unesterified cholesterol and apolipoprotein B-48.
- The microsomal triglyceride (TAG) transfer protein is essential for the assembly of triglyceride (TAG)-rich apolipoprotein B-containing lipoproteins in the endoplasmic reticulum (ER) of enterocytes.
- It facilitates the incorporation of TAG into apolipoprotein B, resulting in the formation of chylomicrons.
- Without this protein, chylomicron assembly is impaired, affecting fat absorption and transport.

(1.7.)

(1.7.1.) Briefly describe the process by which chylomicrons are released from enterocytes and transported through the lymphatic system.

(20 Marks)

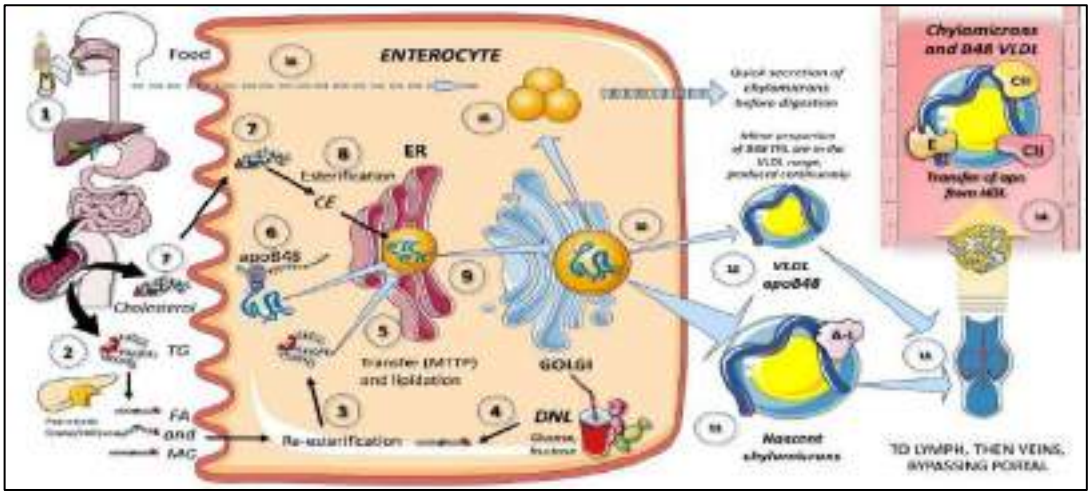
- After assembly in the ER, chylomicrons are released from enterocytes by exocytosis.
- These particles enter the lacteals, which are lymphatic vessels located in the villi of the small intestine.
- The presence of chylomicrons gives the lymph a milky appearance, known as chyle.
- The chylomicrons are then transported via the lymphatic system, following a path to the thoracic duct, which eventually empties into the bloodstream at the left subclavian vein.

(1.7.2.) Explain the distinction between chyle and chyme. (20 Marks)

- Chyle is a product of lipid absorption.
- Chyle is the milky fluid found in the lymphatic system, particularly after a lipid-rich meal, due to the presence of chylomicrons.

- Chyme is associated with the digestion of food.
- Chyme, on the other hand, refers to the semifluid mass of partially digested food that moves from the stomach to the duodenum during digestion.

(1.8.) Briefly describe the pathway chylomicrons follow from the small intestine to the bloodstream. (10 Marks)



https://www.frontiersin.org/journals/endocrinology/articles/10.3389/fendo.2023.1322869/full

Chylomicrons are absorbed into the lacteals from the small intestine's enterocytes. From the lacteals, they travel through the lymphatic vessels, which ultimately converge at the thoracic duct.

The thoracic duct then drains into the left subclavian vein, allowing the chylomicrons to enter the bloodstream, where they are distributed for fat metabolism and energy utilization.

COURSE 3- METABOLISM 3

TUTORIALS & ANSWERS

Tutorial 01

Protein Metabolism-1

(1)

(1.1.) List three (03) examples for non-essential amino acids. (03 Marks)

(1.2.) List three (03) examples for amphibolic intermediates of non-essential amino acids synthesis. (03 Marks)

(1.3.) Define dispensable and indispensable amino acids. (14 Marks)

(1.4.) Illustrate and explain the major metabolic pathways of amino acids. (30 Marks)

(Total: 50 Marks)

(2)

(2.1.) Define the term transamination. (05 Marks)

(2.2.) Illustrate a typical transamination reaction. (05 Marks)

(2.3.) List three (03) occasions where Amino Acid catabolism occurs. (15 Marks)

(2.4.) Explain the main two (02) steps of amino acid catabolism. (25 Marks)

(Total: 50 Marks)

(3)

(3.1.) List the major metabolic pathways that lead to the production of ammonia in the human body.

(10 Marks)

(3.2.) Explain how ammonia is transported from tissues to the liver for detoxification.

(10 Marks)

(3.3.) Describe the role of glutamine and alanine in the transport of ammonia in the blood.

(15 Marks)

(3.4.) Explain what are the potential consequences of elevated ammonia levels in the blood, and how does the body prevent ammonia toxicity? (15 Marks)

(Total: 50 Marks)

Tutorial 01

Protein Metabolism-1- Answers

(1)

(1.1.) List three (03) examples for non-essential amino acids. (03 Marks)

Glycine	Glutamic acid
Alanine	Glutamine
Proline	Tyrosine
Aspartic acid	Serine
Asparagine	Cysteine

(1.2.) List three (03) examples for amphibolic intermediates of non-essential amino acids synthesis. **(03 Marks)**

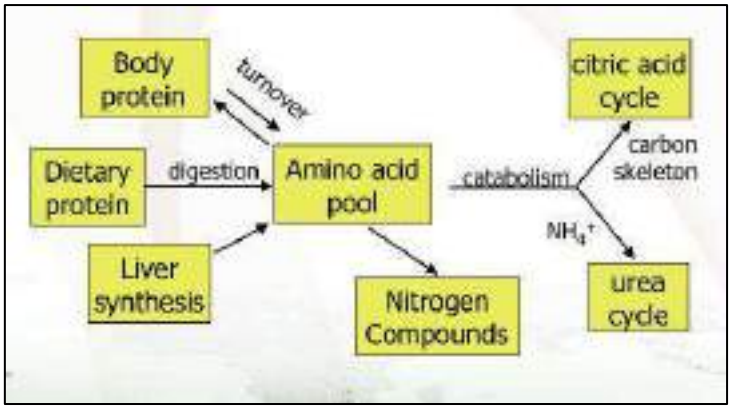
∝-KG/ OAA/ pyruvate

(1.3.) Define dispensable and indispensable amino acids. (14 Marks)

indispensable (essential) amino acids are those that must be obtained through the diet, while dispensable (non-essential) amino acids can be produced by the body itself.

(1.4.) Illustrate and explain the major metabolic pathways of amino acids.

(30 Marks)



The amino acid pool of the body is provided with amino acids by 03 majors sources,

a. Amino acids provided by the degradation of endogenous (body) proteins.
b. Amino acids derived from exogenous (dietary) protein.
c. Nonessential amino acids synthesized from simple intermediates of metabolism.

Conversely, the amino acid pool is depleted by three routes,

a. Synthesis of body protein.
b. Consumption of amino acids as precursors of essential nitrogen-containing small molecules.
c. Conversion of amino acids to glucose, glycogen, fatty acids and ketone bodies or oxidation to $CO_2 + H_2O$.

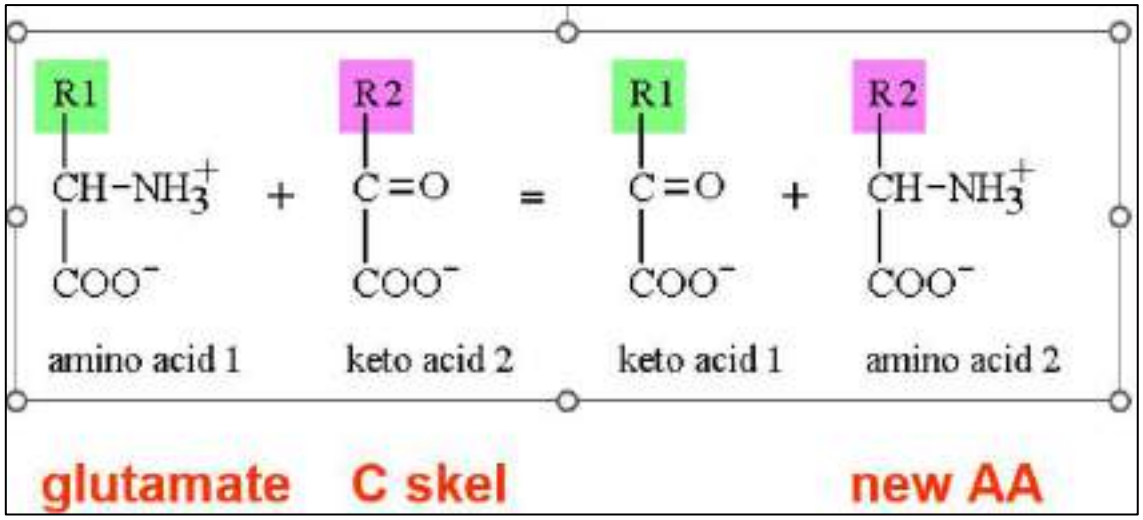
(2)

(2.1.) Define the term transamination. (05 Marks)

A reversible reaction in which NH_2 group of one amino acid is transferred to a keto acid giving rise to a new AA & a new keto acid.

(e.g.: keto acids - OAA, pyruvate, α-KG)

(2.2.) Illustrate a typical transamination reaction. (05 Marks)



(2.3.) List three (03) occasions where Amino Acid catabolism occurs. (15 Marks)

a. When surplus AA are ingested (high glutamate) (cannot be stored thus degraded) = 'E'.

b. Normal dynamic turnover of protein.

(continued degradation /synthesis)

c. When CHO are not being utilized/ (muscle protein degradation) (fasting /DM, AA as fuel).

(2.4.) Explain the main two (02) steps of amino acid catabolism. (25 Marks)

Amino acid catabolism involves 02 main steps,

- Removal of NH_2 from AA by,
  a. Transamination
  b. Oxidative deamination / other enzymes
- Conversion of C-skeleton to other products.

Removal of NH_2 by Transamination (reverse reaction in catabolism)

Eg

Asp + α-KG ↔ glutamate + OAA

(AST)

Ala + α-KG ↔ glutamate + pyruvate

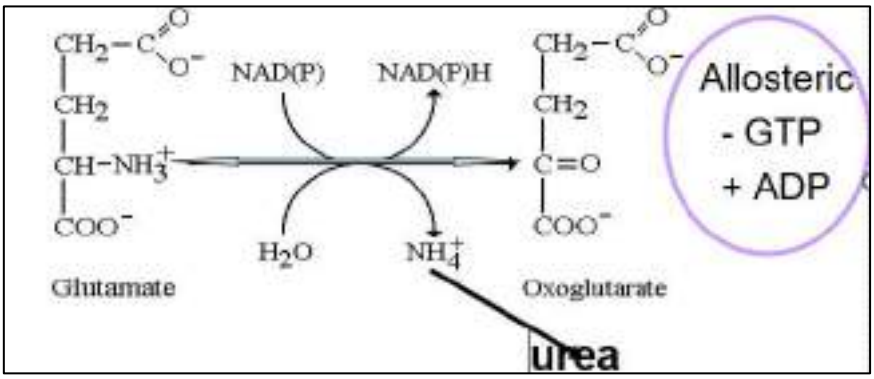
(ALT)

All amino acids including isoleucine/ leucine/ valine (branched chain amino acids).

Removal of NH_2 by Oxidative deamination/ other enzymes

Deamination of glutamate (oxidative deamination)

'N' of AA is removed as NH4+



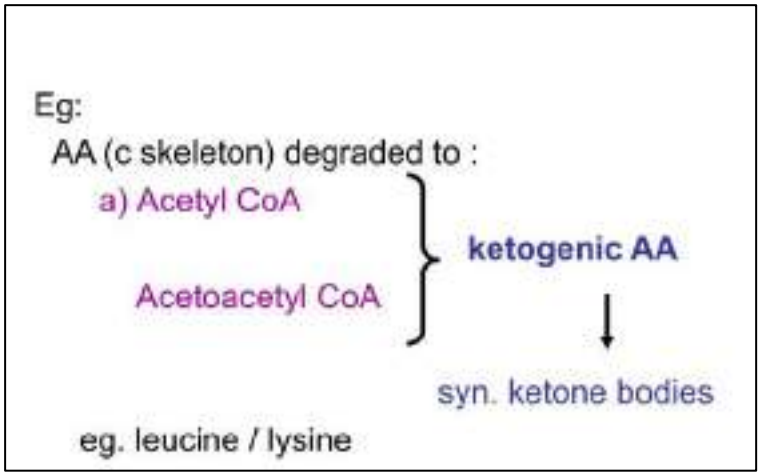
Deamination occurs in liver/ kidney.

This reaction is reversible.

Conversion of C. skeleton to other products

Conversion of resulting C. skeleton of AA to an intermediate capable of entering the TCA cycle & glycolytic pathway.

- 20 AA - funnelled into 7 molecules.
- Can be converted to glucose / oxidized in TCA cycle.
- Each AA has its own path way(s) to use up its C skeleton.



Metabolism of the common intermediates.

- Oxidation – all amino acids can be oxidized in TCA cycle with energy production.
- Fatty acid synthesis – some amino acids provide acetyl CoA (ketogenic amino acids).

- Gluconeogenesis – ketoacids derived from amino acids are used for synthesis of glucose (is important in starvation).

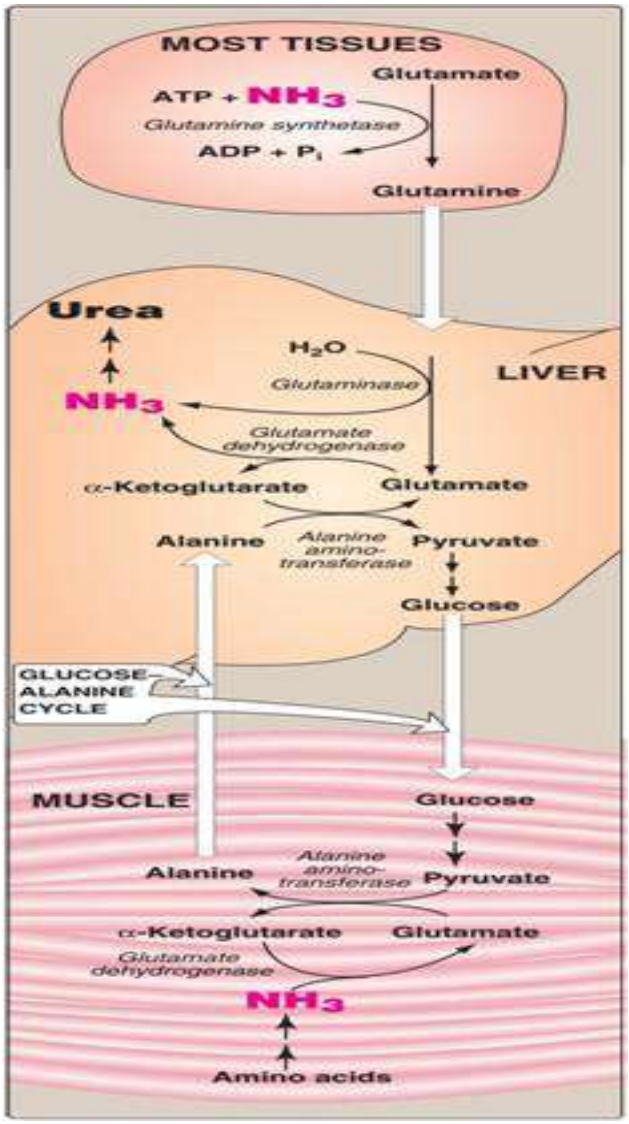
(3)

(3.1.) List the major metabolic pathways that lead to the production of ammonia in the human body? (10 Marks)

- Deamination of amino acids.
- Catabolism of purines and pyrimidines.
- Action of intestinal bacteria.
- Breakdown of glutamine.
- Transamination reactions

(3.2.) Explain how ammonia is transported from tissues to the liver for detoxification. (10 Marks)

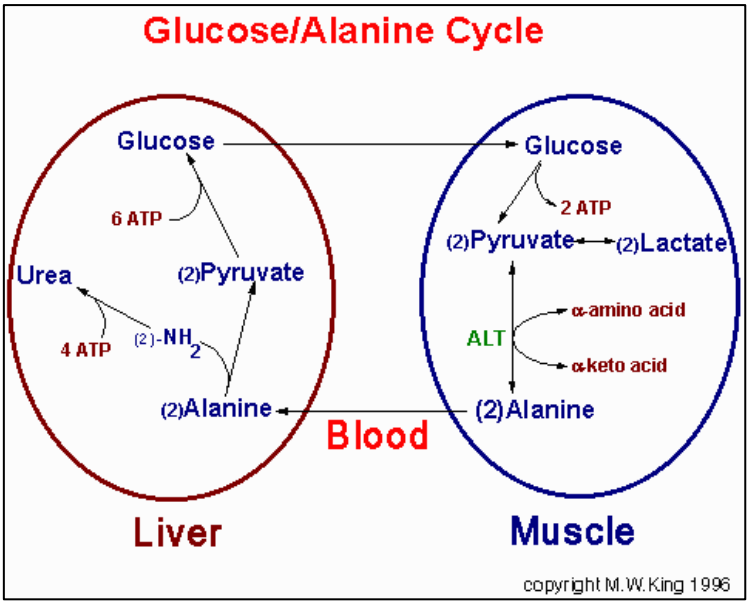
- Glutamine formation- In most tissues, ammonia combines with glutamate to form glutamine via the enzyme glutamine synthetase. Glutamine is a non-toxic carrier of ammonia that transports it through the bloodstream to the liver.
- Glucose-alanine cycle - In muscles, ammonia combines with pyruvate to form alanine, which is transported to the liver. In the liver, alanine undergoes deamination, releasing ammonia for detoxification.
- Direct transport - In the case of intestinal ammonia, it is transported directly via the portal vein to the liver for processing and detoxification.



(3.3.) Describe the role of glutamine and alanine in the transport of ammonia in the blood. (15 Marks)

- Glutamine
    - Glutamine serves as a safe carrier of ammonia.
    - It is synthesized from ammonia and glutamate in tissues such as the brain, muscles, and liver.
    - Glutamine can travel through the blood without raising ammonia toxicity and is later broken down in the liver or kidneys, releasing ammonia for urea production or excretion.
- Alanine
    - Alanine is primarily involved in transporting ammonia from muscles to the liver through the glucose-alanine cycle.

- In muscle tissue, pyruvate reacts with ammonia to form alanine, which is transported to the liver.
- There, alanine is converted back to pyruvate, releasing ammonia for detoxification via the urea cycle.



(3.4.) Explain what are the potential consequences of elevated ammonia levels in the blood, and how does the body prevent ammonia toxicity? (15 Marks)

- Consequences of elevated ammonia levels
  - High levels of ammonia in the blood, a condition known as hyper ammonia, can lead to serious health issues, including hepatic encephalopathy, characterized by confusion, tremors, and in severe cases, coma. Elevated ammonia disrupts neurotransmitter balance and brain function.
- Prevention of ammonia toxicity
  - Urea cycle: In the liver, ammonia is detoxified by converting it into urea via the urea cycle. Urea is then excreted by the kidneys.
  - Glutamine synthesis: Ammonia is detoxified by combining it with glutamate to form glutamine, which is non-toxic and safely transported to the liver or kidneys for further processing.
  - Efficient liver function: Proper liver function ensures that ammonia absorbed from the gut or released from tissues is quickly converted to urea, preventing accumulation in the bloodstream.

Tutorial 2

Protein Metabolism-2

(1)

(1.1.) List four (04) examples for glucogenic amino acids . (20 Marks)

(1.2.) List four (04) examples for glucogenic & ketogenic amino acids. (20 Marks)

(1.3.) List five (05) intermediates of TCA cycle where amino acids can be entered for the energy production of the body. (20 Marks)

(1.4.) Illustrate and describe the Glucose/ Alanine cycle. (40 Marks)

(Total: 100 Marks)

(2)

(2.1.) List two (02) biologically and physiologically important metabolites of amino acids and list three (03) functions each amino acid metabolite listed. (50 Marks)

Amino acid	**Metabolite**	**Function**
a. ……	……	i. …… ii. …… iii. ……
b. ……	……	i. …… ii. …… iii. ……

(2.2.) Briefly describe the steps of creatine production, storage, metabolism and excretion with the aid of an illustration. (50 Marks)

Tutorial 2

Protein Metabolism 2- Answers

(1)

(1.1.) List four (04) examples for glucogenic amino acids. (20 Marks)

Ala, ser, gly, cys, arg, his, pro, glu, gln, val, met, asp, asn

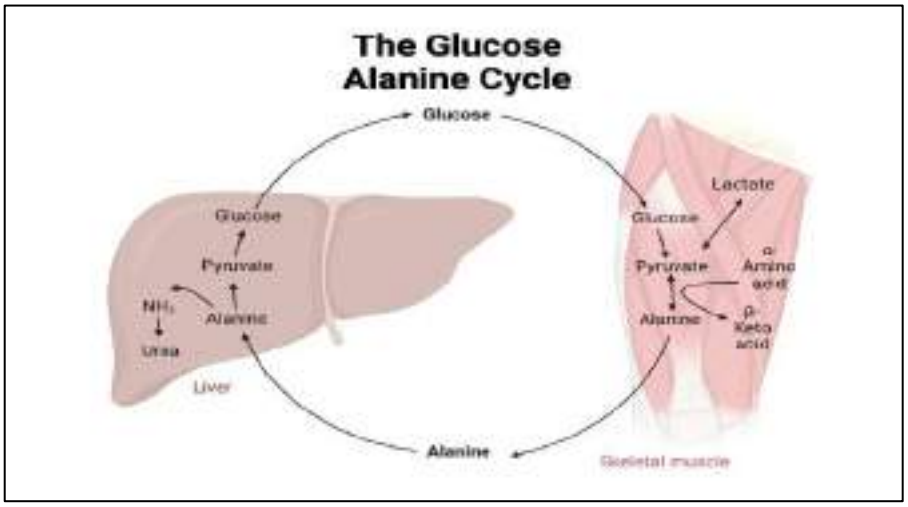
(1.2.) List four (04) examples for glucogenic & ketogenic amino acids. (20 Marks)

Phe, tyr, trp, ile, thr

(1.3.) List five (05) intermediates of TCA cycle where amino acids can be entered for the energy production of the body. (20 Marks)

Pyruvate
acetyl CoA
Acetoacetyl CoA
α-ketoglutarate
succinyl CoA
fumarate
oxaloacetate

(1.4.) Illustrate and describe the Glucose/ Alanine cycle.



https://www.biorender.com/template/glucose-alanine-cycle (40 Marks)

(10 Marks for the illustration)

Steps of the Glucose/Alanine Cycle

1. **<u>Amino Acid Catabolism in Muscle</u>**

- During prolonged exercise or fasting, proteins in muscle tissue are broken down into amino acids.
- These amino acids undergo **transamination** to form glutamate.

2. **Transamination to Form Alanine**
   - Glutamate transfers its amino group to **pyruvate**, a key glycolysis intermediate, forming **alanine** through the action of the enzyme **alanine aminotransferase** (ALT).
3. **Alanine Transport to Liver**
   - Alanine is then transported via the bloodstream from muscle to the liver.
4. **Alanine Conversion to Pyruvate in the Liver**
   - In the liver, **alanine aminotransferase** converts alanine back into pyruvate by transferring the amino group to α-ketoglutarate, forming glutamate and regenerating pyruvate.
5. **Glutamate's Role in Nitrogen Removal**
   - The glutamate formed in this reaction can release ammonia through **oxidative deamination**.
   - Ammonia is then converted into **urea** in the **urea cycle**, which is excreted by the kidneys.
6. **Gluconeogenesis in the Liver**
   - The pyruvate produced from alanine is used to synthesize **glucose** through the process of **gluconeogenesis**.
7. **Glucose Transport Back to Muscle**
   - The newly synthesized glucose is released into the bloodstream, where it is transported back to the muscle to be used as a fuel source, particularly during times of low glucose availability.

(Total: 100 Marks)

(2)

(2.1.) List two (02) biologically and physiologically important metabolites of amino acids and list three (03) functions each amino acid metabolite listed.

Amino acid (5*2)	Metabolite (5*2)	Function (5*6)
Histidine	Histamine	o Contracts smooth muscles including airways & GIT o Increases venular permeability o Induces nasal mucous production o Bronchodilation o Increases Vaso-permeability & dilation (blood pressure) o Stimulates gastric acid secretion
Dopamine	Tyrosine Phenylalanine	o Co-ordination & movement o Immunity o Wakefulness /attention
Nitric oxide	Arginine	o Dilates blood vessels o Reduces platelet stickiness

		○ Reduces monocyte stickiness (prevent formation of plaque). ○ Reduces multiplication of smooth muscle cells of the artery wall. ○ Reduces release of superoxide radicals. ○ Reduces oxidation of LDL cholesterol (major component of plaque).

SGDs & ANSWERS

SGD 01

Protein Metabolism

(1)

(1.1.)

(1.1.1.) State the significance of presence of α-amino group in amino acids. (10 Marks)

(1.1.2.) State the significance of the urea cycle. (10 Marks)

(1.2.) Illustrate the chemical reactions occur in urea cycle. (20 Marks)

(1.3.) Briefly describe the rate limiting step of the urea cycle. (20 Marks)

(1.4.) Briefly describe the regulation of the urea cycle. (30 Marks)

(Total: 100 Marks)

(2)

(2.1.)

(2.1.1.) Define hyperammonaemia. (10 Marks)

(2.1.2.) State why hyperammonaemia is considered as a medical emergency? (10 Marks)

(2.2.)

(2.2.1.) List the two (02) types of hyperammonaemia. (05 Marks)

(2.2.2.) List six (06) serum markers/ tests that can used to identify the common cause of acquired hyperammonaemia in adults. (15 marks)

(2.3.)

(2.3.1.) Give two (02) examples for aminotransferases. (10 Marks)

(2.3.2.) Briefly describe the diagnostic value of aminotransferases. (20 Marks)

(2.4.)

(2.4.1.) List four (04) methods of management of urea cycle disorders. (20 Marks)

(2.4.2.) Briefly explain the biochemical rationale for the methods listed in 2.4.1. (10 Marks)

(Total: 100 Marks)

SGD 01& 02

Protein Metabolism-Answers

(1)

(1.1.)

(1.1.1.) State the significance of presence of α-amino group in amino acids?

(10 Marks)

The presence of the α-amino group keeps amino acids safely locked away from oxidative breakdown.

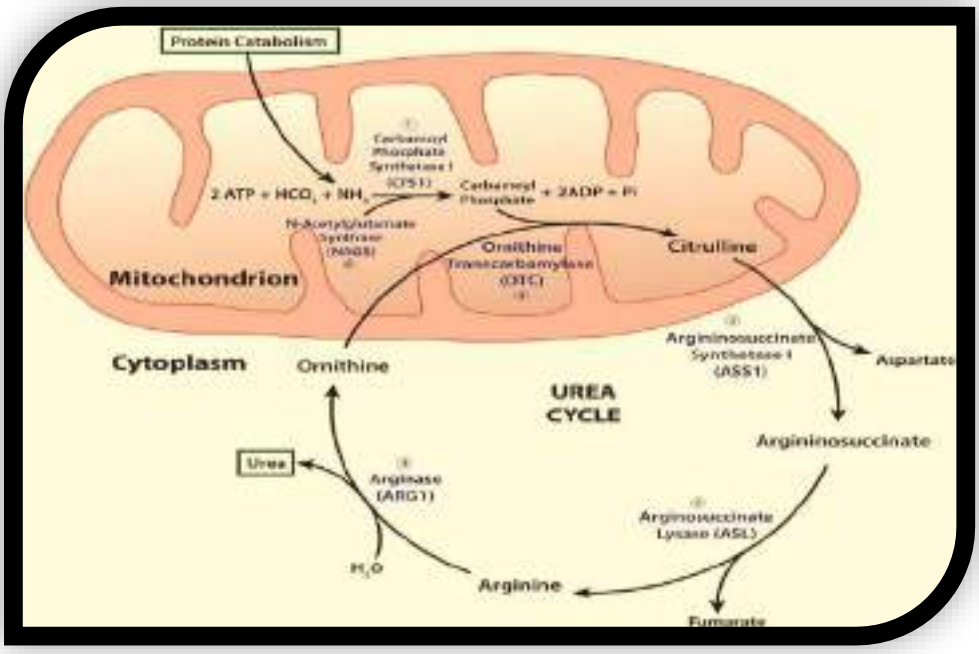
Removing the α-amino group is essential for producing energy from any amino acid and is an obligatory step in the catabolism of amino acids.

(1.1.2.) State the significance of the urea cycle (10 Marks)

it the main metabolic mechanism involved in the elimination of nitrogenous wastes generated by the breakdown of protein and other nitrogen-containing molecules.

(1.2.) Illustrate the chemical reactions occur in urea cycle.

(20 Marks)



(1.3.) Briefly describe the rate limiting step of the urea cycle. (20 Marks)

Carbamoyl Phosphate Synthesis

- Mitochondrial carbamoyl phosphate synthetase I (CPS I) catalyse the condensation of NH_4^+ ions with CO_2 (HCO_3^-) to generate carbamoyl phosphate.
- irreversible and rate-limiting, require 2 ATP.
- CPS I requires N-acetyl glutamate to function.

- Pyrimidine production: carbamoyl phosphate synthetase II (CPS-II), found in the cytosol accepts the amino group from glutamine BUT does not need N-acetyl glutamate to function.

(1.4.) Briefly describe the regulation of the urea cycle. (30 Marks)

- Urea cycle enzymes' activity is influenced by:
  - **Substrate concentrations: Glutamate**
  - **Allosteric activators:**
    - **N- acetyl glutamate** - activator of CPSI
    - **Arginine** – activator for synthesis of N-acetyl-glutamate by glutamate & acetyl Co A.

  - **Interactions with other metabolic processes:**
    - **CPSI** & **glutamate dehydrogenase** in mitochondria are needed for carbamoyl phosphate & NH_3 synthesis.
    - Other 4 enzymes are primarily regulated by the concentration of their respective substrates.

(Total: 100 Marks)

(2)

(2.1.)

(2.1.1.) Define hyperammonaemia. (10 Marks)

medical condition characterized by an abnormally high level of ammonia in the blood. Level of serum ammonia is normally low (5–35 μmol/L).

(2.1.2.) State why hyperammonaemia is considered as a medical emergency? (10Marks)

Ammonia has a direct neurotoxic effect on the CNS.

(2.2.)

(2.2.1.) List the two (02) types of hyperammonaemia. (05 Marks)

Acquired hyperammonaemia.
Congenital hyperammonaemia.

(2.2.2.) List six (06) serum markers/ tests that can used to identify the common cause of acquired hyperammonaemia in adults. (15 marks)

Liver disease is a common cause of acquired hyperammonaemia in adults.
Bilirubin.

ALT
AST
Alkaline phosphatase
Albumin
Total protein
Gamma glutamyl transferase
Lactate dehydrogenase
Ammonia
Prothrombin time

(2.3.)

(2.3.1.) Give two (02) examples for aminotransferases. (10 Marks)

Aspartate aminotransferase
Alanine aminotransferase

(2.3.2.) Briefly describe the diagnostic value of aminotransferases. (20 Marks)

Amino transferases are normally intracellular enzymes, with the low levels found in the plasma representing the release of cellular contents during normal cell turnover.

Elevated plasma levels of aminotransferases indicate damage to the cells rich in these enzymes.

- Hepatic diseases: Plasma AST and ALT are elevated in nearly all hepatic diseases but are particularly high in conditions that cause extensive cell necrosis. Viral hepatitis, toxic injury, and prolonged circulatory collapse.
- Non-hepatic diseases: aminotransferases may be elevated in non-hepatic diseases such as those that cause damage to cardiac or skeletal muscle. However, these disorders can usually be distinguished clinically from liver disease.

(2.4.)

(2.4.1.) List four (04) methods of management of urea cycle disorders. (20 Marks)

- Reversal of the catabolic state through caloric supplementation: dextrose and Interlipid.
- In extreme cases, hormonal suppression of protein catabolism (glucose and insulin drip).
- Ammonia scavengers (Sodium benzoate, phenylbutyrate).
- Remove protein from intake (PO (by mouth [per os] or TPN).

(2.4.2.) Briefly explain the biochemical rationale for the methods listed in 2.4.1.

(10 Marks)

- Reducing ammonia production.
- Enhancing ammonia removal from the bloodstream.

- Compensating for enzyme deficiencies to minimize toxic effect.
- Providing alternative ways to detoxify ammonia.

(Total:100Marks)

Recognize the metabolic changes in diseases and injuries and its clinical applications SGD_1

Question 01: Urine Collection Methods/Types of Urine Specimens

A 30-year-old female comes to the clinic complaining of painful urination and frequent urgency. The doctor suspects a urinary tract infection (UTI). A midstream urine sample is requested, but the patient is confused about how to collect it correctly.

(1) Explain the importance of using a midstream urine specimen for UTI diagnosis.
(2) What are the potential consequences of improper urine collection on diagnostic accuracy?
(3) Discuss the types of urine specimens used for specific clinical investigations.

Question 02: Physical and Chemical Analysis of Urine

A 60-year-old male with a history of hypertension and heart failure presents with swelling in the lower limbs. His urine is frothy, and he reports reduced urine output. A dipstick test reveals significant proteinuria but no glucose or ketones.

(1) Interpret the significance of frothy urine and proteinuria in this patient.
(2) Discuss the underlying mechanisms that cause proteinuria in conditions like heart failure and kidney disease.
(3) How would you differentiate between glomerular and tubular causes of proteinuria?

Question 03: Urine Sediment Analysis

A 25-year-old male presents with dark-coloured urine and lower back pain following a recent sore throat infection. Urinalysis reveals the presence of red blood cells and red cell casts in the urine sediment. He is diagnosed with post-streptococcal glomerulonephritis.

(1) Explain the significance of red blood cells and red cell casts in the urine sediment.
(2) Discuss other findings that might be observed in urine sediment analysis in cases of glomerulonephritis.
(3) How does urine sediment analysis help differentiate between glomerular and non-glomerular causes of haematuria?

Recognize the metabolic changes in diseases and injuries and its clinical applications SGD_1 Answers

Question 01: Urine Collection Methods/Types of Urine Specimens

A 30-year-old female comes to the clinic complaining of painful urination and frequent urgency. The doctor suspects a urinary tract infection (UTI). A midstream urine sample is requested, but the patient is confused about how to collect it correctly.

(1) Explain the importance of using a midstream urine specimen for UTI diagnosis.

- minimizes contamination from bacteria and cells that are naturally present in the lower part of the urethra and external genitalia.
    - reduce contamination.
    - improves diagnostic accuracy.
    - standardization for reliable results.

(2) What are the potential consequences of improper urine collection on diagnostic accuracy?

- False positive results.
- Misidentification of pathogens.
- Inaccurate antibiotic sensitivity testing.
- Increased healthcare cost and time.

(3) Discuss the types of urine specimens used for specific clinical investigations.

- **Midstream Urine Specimen**: Collected after discarding the first part of urine to minimize contamination. Used for **UTI diagnosis**, **urine culture**, and **microscopic analysis**.
- **First Morning Urine (FMU)**: Collected upon waking when urine is most concentrated. Ideal for **pregnancy tests**, **proteinuria**, **hormone measurements**, and **urine cytology**.
- **Random Urine Specimen**: Collected at any time of the day. Used for **routine urinalysis**, **urine dipstick tests**, and general screening for conditions like glucose or blood in the urine.
- **24-Hour Urine Specimen**: Collected over a 24-hour period for **quantitative analysis** of substances like **proteinuria**, **creatinine clearance**, and **electrolyte levels**.
- **Catheterized Urine Specimen**: Collected using a sterile catheter, particularly when a clean-catch is not possible. Used for **UTI diagnosis** and when contamination risk is high.

- **Suprapubic Aspiration Specimen**: Collected directly from the bladder using a needle, used when other collection methods are not feasible, often in **infants** or **UTI cases**.
- **First Void Urine (FVU)**: The first urine voided after waking, used for **urine cytology**, **bladder cancer screening**, and **STI testing**.
- **Timed Urine Specimen**: Collected at specific times or intervals, used for measuring **hormone levels**, **creatinine clearance**, or **metabolic excretion rates**.

Question 02: Physical and Chemical Analysis of Urine

A 60-year-old male with a history of hypertension and heart failure presents with swelling in the lower limbs. His urine is frothy, and he reports reduced urine output. A dipstick test reveals significant proteinuria but no glucose or ketones.

(1) Interpret the significance of frothy urine and proteinuria in this patient.

frothy urine along with **proteinuria** suggests a potential issue with kidney function, likely involving glomerular damage or nephrotic syndrome.

(2) Discuss the underlying mechanisms that cause proteinuria in conditions like heart failure and kidney disease.

In heart failure, proteinuria can arise from several mechanisms.

- **Increased Hydrostatic Pressure**: This can cause fluid to leak from the bloodstream into surrounding tissues (oedema) and into the renal interstitium. Increased pressure in the renal capillaries may enhance the filtration of proteins, leading to proteinuria.
- **Renal Hypoperfusion**: In heart failure, reduced cardiac output can lead to renal hypoperfusion (decreased blood flow to the kidneys). This triggers compensatory mechanisms, including activation of the renin-angiotensin-aldosterone system (RAAS). Increased angiotensin II levels lead to glomerular efferent arteriolar constriction, which may initially help maintain glomerular filtration rate (GFR), but chronic activation can lead to kidney damage and increased permeability of the glomerular filtration barrier, resulting in proteinuria.
- **Increased Glomerular Permeability**: Heart failure can result in glomerular structural changes, including mesangial expansion and podocyte dysfunction. This affects the integrity of the glomerular filtration barrier, allowing proteins (especially albumin) to pass into the urine.

(3) How would you differentiate between glomerular and tubular causes of proteinuria?

Glomerular Proteinuria

Glomerular proteinuria is caused by damage to the glomeruli, the filtering units of the kidneys, leading to increased permeability of the glomerular filtration barrier.

Typically involves larger proteins like albumin; can also include immunoglobulins.

Tubular Proteinuria

Tubular proteinuria results from dysfunction of the renal tubules, leading to an inability to reabsorb proteins that are normally filtered by the glomeruli.

Usually involves smaller proteins, such as low molecular weight proteins (e.g., beta-2-microglobulin, light chains), and may also include amino acids.

Question 03: Urine Sediment Analysis

A 25-year-old male presents with dark-coloured urine and lower back pain following a recent sore throat infection. Urinalysis reveals the presence of red blood cells and red cell casts in the urine sediment. He is diagnosed with post-streptococcal glomerulonephritis.

(1) Explain the significance of red blood cells and red cell casts in the urine sediment.



https://www.medical-labs.net/red-blood-cells-casts-in-renal-hematuria-408/

Red Blood Cells (RBCs)- Glomerular injury (e.g., glomerulonephritis, lupus nephritis, Goodpasture syndrome), Renal vascular injury (e.g., renal artery thrombosis, hypertension), Lower urinary tract injury (e.g., trauma, infection, stones) Red Blood Cell Casts - Pathognomonic for glomerular diseases, Acute glomerulonephritis (AGN), Indicative of renal parenchymal injury.

(2) Discuss other findings that might be observed in urine sediment analysis in cases of glomerulonephritis.

4. **Dysmorphic RBCs**: The high osmotic gradient and mechanical trauma as RBCs pass through the disrupted glomerular basement membrane and renal tubules cause them to become deformed and misshapen, often appearing as ring-shaped cells with blebs (acanthocytes).

5. **Proteinuria**: Increased protein in the urine is an almost universal finding in glomerulonephritis due to damage to the glomerular filtration barrier. The amount is typically mild to moderate (though can be in the nephrotic range in some cases).

6. **White Blood Cells (WBCs) and WBC Casts**: Polymorphonuclear leukocytes (a type of WBC) are often present in the urine of patients with acute

glomerulonephritis, especially during the early phase, reflecting the inflammatory process. White cell casts may also be present.

7. **Granular and Hyaline Casts**: Granular casts can be present, indicative of general kidney injury, along with hyaline casts, which form due to protein concentration.
8. **Urine Appearance**: The urine often appears dark, brown, or "cola-coloured" rather than bright red or pink due to the degradation of haemoglobin in the acidic environment of the tubules.

(4) How does urine sediment analysis help differentiate between glomerular and non-glomerular causes of haematuria?

Urine sediment analysis is a key tool in differentiating the source of bleeding:

- **RBC Morphology**:
  - **Glomerular haematuria** is characterized by **dysmorphic (deformed, fragmented) RBCs** due to passage through the damaged glomerulus and tubules.
  - **Non-glomerular haematuria** (e.g., from the bladder, ureters, or urethra due to infection, stones, or trauma) typically presents with **eumorphic (normal-shaped) RBCs**.
- **Presence of Casts**:
  - **Red cell casts are highly specific to glomerular disease**.
  - Casts are generally absent in non-glomerular causes of haematuria.
-
- **Urine Colour and Clots**:
  - **Glomerular bleeding** usually results in **brown or tea-coloured urine** and no blood clots.
  - **Non-glomerular bleeding** is often associated with **pink or bright red urine** and the potential for blood clots to be passed.
- **Proteinuria**:
  - Significant proteinuria (e.g., >300 mg/g creatinine) usually co-occurs with glomerular haematuria.
  - Proteinuria is typically minimal or absent in non-glomerular haematuria.
- **Clinical Presentation**:
  - **Glomerular haematuria** is often painless, as described in the case, and can be associated with oedema and hypertension.

Non-glomerular haematuria may be accompanied by pain (flank or abdominal), fever, or urinary tract symptoms like dysuria and frequency.

Bilirubin Metabolism
SGD

(1) Bilirubin Metabolism and Its Clinical Implications

(1.1.) Describe the process of bilirubin metabolism from its production to excretion.

(1.2.) Explain the differences between unconjugated and conjugated hyperbilirubinemia.

(2) Enzymatic and Genetic Disorders of Bilirubin Metabolism

(2.1.) Describe the role of the UGT1A1 enzyme in bilirubin metabolism.

(2.2.) Differentiate between Type I and Type II Crigler-Najjar syndrome in terms of severity and inheritance.

(2.3.) Explain the genetic mutation responsible for Gilbert's syndrome.

(3) A 23-year-old male presents to the clinic with yellowing of the skin and eyes (jaundice) that began two weeks ago. He reports fatigue, dark-coloured urine, and light-coloured stools. He has no history of alcohol use, and his family history is unremarkable. Blood tests reveal elevated total bilirubin (6 mg/dL), predominantly unconjugated bilirubin. His liver function tests show mildly elevated ALT and AST levels. No significant findings are observed in an ultrasound of the liver and biliary tract.

(1.1.) Explain the biochemical pathway of bilirubin metabolism and identify where in the pathway the problem might be occurring in this patient.

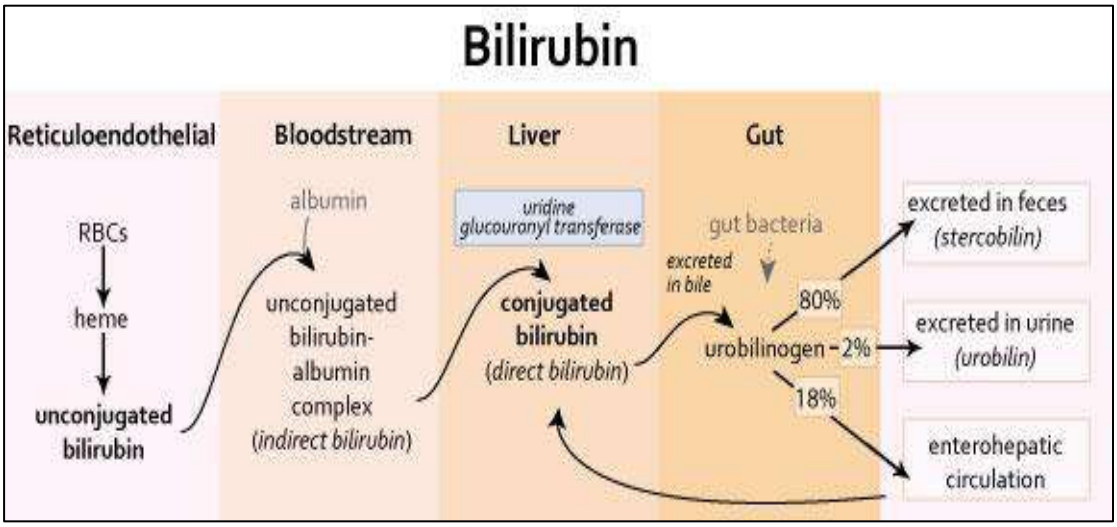
(1.2.) What are the possible causes of predominantly unconjugated hyperbilirubinemia in this patient?

(1.3.) Discuss the diagnostic approach and management options for this patient.

Bilirubin Metabolism -Answers
SGD

(1) Bilirubin Metabolism and Its Clinical Implications

(1.1.) Describe the process of bilirubin metabolism from its production to excretion.



(1.2.) Explain the differences between unconjugated and conjugated hyperbilirubinemia.

Feature	Unconjugated hyperbilirubinemia	Conjugated hyperbilirubinemia
Bilirubin type	Indirect	Direct
Water solubility	Lipid soluble	Water soluble
Primary causes	Haemolysis, hepatic uptake/ conjugation defect	Hepatocellular disease, biliary obstruction
Urine colour	Typically, normal	Dark (bilirubinuria)
Stool colour	Normal	Pale (in obstructive jaundice)
Complications	Kernicterus (in severe cases)	Pruritus*, jaundice, possible liver damage
Diagnosis and Lab Findings	• Elevated total bilirubin with a higher proportion of indirect bilirubin • liver function tests (e.g., ALT, AST) may be normal or mildly elevated if there is no underlying liver damage.	• Elevated direct bilirubin • typically, with abnormal liver function tests (ALT, AST, ALP). • Imaging (e.g., ultrasound or CT scan) may help identify obstructive causes.

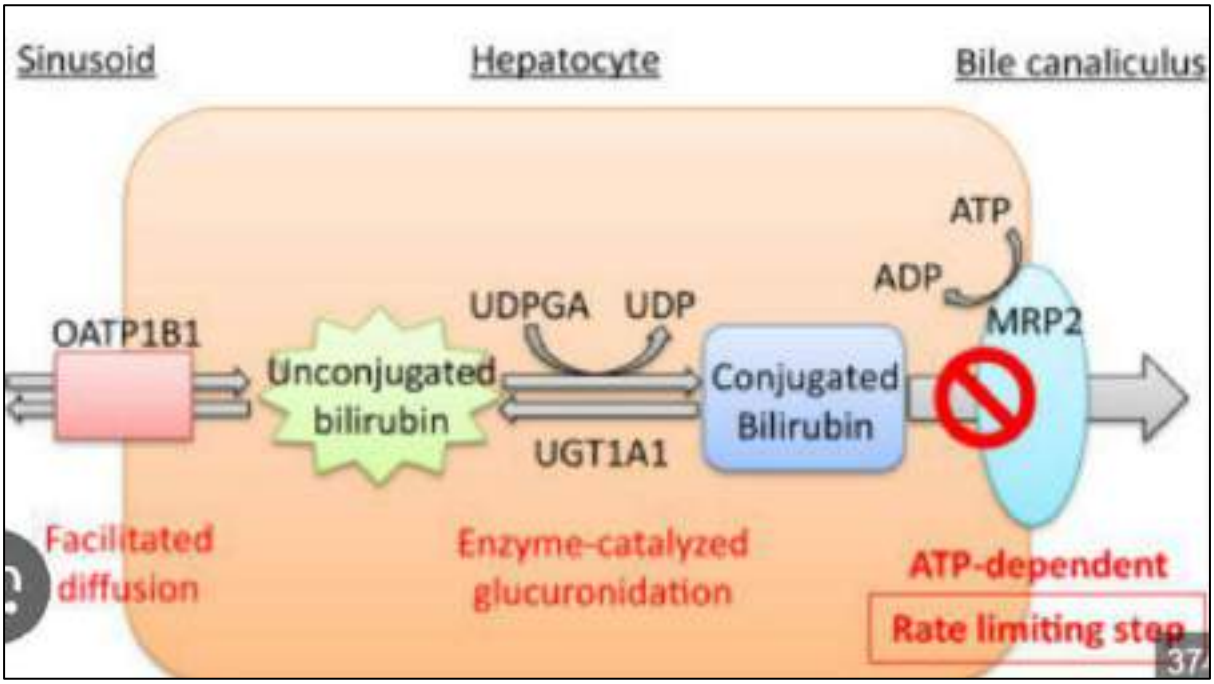
*Commonly known as itching, is an uncomfortable sensation on the skin that triggers the urge to scratch.

(2) Enzymatic and Genetic Disorders of Bilirubin Metabolism

(2.1.) Describe the role of the UGT1A1 enzyme in bilirubin metabolism.

UDP-glucuronosyltransferase 1A1

responsible for the conjugation of bilirubin.
process essential for transforming bilirubin from a lipid-soluble form to a water-soluble form.



(2.2.) Differentiate between Type I and Type II Crigler-Najjar syndrome in terms of severity and inheritance.

	Crigler-Najjar Syndrome Type I	Crigler-Najjar Syndrome Type II
Severity	• Type I is the more severe form. • complete or near-complete absence of UGT1A1 enzyme activity. • extremely high levels of unconjugated bilirubin, which can reach life-threatening levels.	• Type II is a milder form. • have some residual UGT1A1 enzyme activity. • partial bilirubin conjugation. • Although jaundice is still present, it is generally less severe and the risk of kernicterus is lower.
Inheritance	autosomal recessive inheritance	autosomal recessive

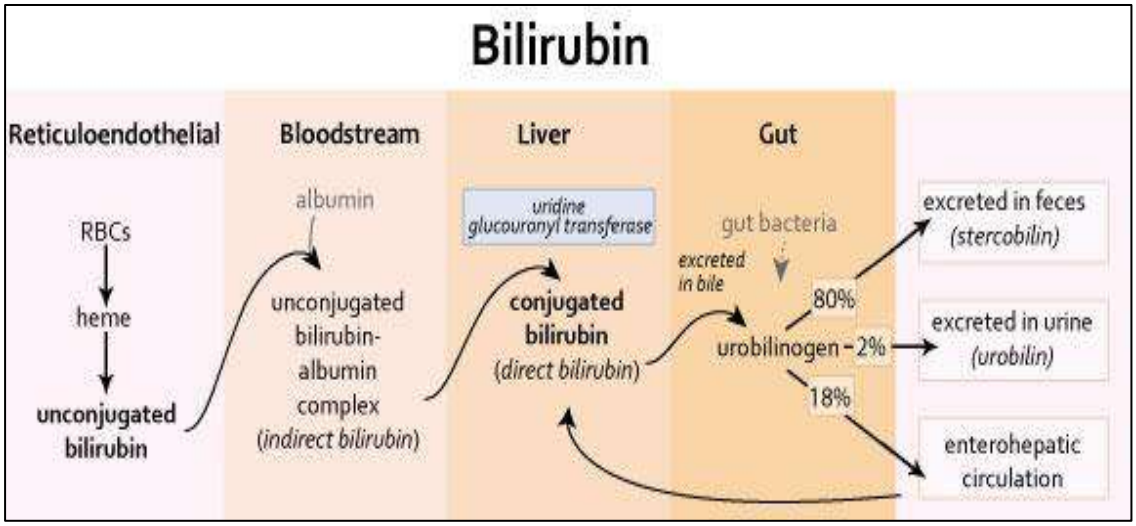
(2.3.) Explain the genetic mutation responsible for Gilbert's syndrome.
mild hereditary condition caused by a genetic mutation in the UGT1A1 gene
is inherited in an autosomal recessive pattern.

(3) A 23-year-old male presents to the clinic with yellowing of the skin and eyes (jaundice) that began two weeks ago. He reports fatigue but denies any history of alcohol use, and his family history is unremarkable. Blood tests reveal elevated total

bilirubin (6 mg/dL), predominantly unconjugated bilirubin. His liver function tests show mildly elevated ALT and AST levels. No significant findings are observed in an ultrasound of the liver and biliary tract.

(1.4.) Explain the biochemical pathway of bilirubin metabolism and identify where in the pathway the problem might be occurring in this patient.

- Jaundice
- Elevated total bilirubin, predominantly unconjugated bilirubin
- Mildly elevated ALT and AST
- No significant ultrasound or liver and biliary tract.



(1.5.) What are the possible causes of predominantly unconjugated hyperbilirubinemia in this patient?

Genetic Conditions Affecting Bilirubin Conjugation:

- **Gilbert's Syndrome**: A common benign condition characterized by mild UGT1A1 deficiency, leading to intermittent, mild hyperbilirubinemia, often triggered by stress, fasting, or illness.
- **Crigler-Najjar Syndrome (Type I or Type II)**: A rare condition with severe UGT1A1 deficiency (Type I) or partial deficiency (Type II), leading to high levels of unconjugated bilirubin.

Increased Haemolysis:

- Haemolytic anaemias (e.g., G6PD deficiency, hereditary spherocytosis) can lead to an increase in bilirubin production, overwhelming the liver's conjugation capacity and resulting in elevated unconjugated bilirubin.

Other Considerations:

- Although the patient's family history is unremarkable, the possibility of a mild or latent haemolytic disorder or an inherited bilirubin metabolism disorder should still be considered.

(1.6.) Discuss the diagnostic approach and management options for this patient.

Laboratory Tests:

- Complete Blood Count (CBC): To rule out haemolysis or anaemia.
- Reticulocyte Count and Peripheral Blood Smear: To check for signs of haemolysis.
- Haemolysis Markers: Lactate dehydrogenase (LDH), haptoglobin, and direct Coombs test if haemolysis is suspected.
- Genetic Testing for UGT1A1 Mutation: Testing for Gilbert's syndrome can confirm the diagnosis by identifying the common UGT1A1*28 variant in the promoter region.

Liver Function Tests:
Monitor ALT, AST, ALP, and GGT levels to assess for any progressive liver involvement or to rule out hepatocellular injury.

COURSE 4-INBORN ERRORS OF METABOLISM

TUTORIALS & SGDs WITH ANSWERS

SGD 1- Amino acid metabolism

(1)

(1.1.) Define the term “Inborn Errors of metabolism” and explain the occurrence, causes, and consequences of such errors.

(1.2.) List the main types of inborn errors of metabolism giving examples for each.

(1.3.) Explain the biochemical basis, clinical manifestations, diagnostic approach, and management strategies for phenylketonuria (PKU) as an inborn error of amino acid metabolism.

Tutorial 1- Amino acid metabolism

(1) Regarding the biochemical basis of Maple syrup urine disease?

(A) MSUD is caused by a deficiency in the branched-chain alpha-keto acid dehydrogenase complex (BCKDC).

(B) The accumulation of branched-chain amino acids (leucine, isoleucine, and valine) and their corresponding keto acids is characteristic of MSUD.

(C) MSUD is an autosomal dominant disorder.

(D) BCKDC deficiency affects the metabolism of aromatic amino acids.

(E) Mutations in genes encoding the E1, E2, or E3 components of BCKDC can lead to MSUD.

(2) Regarding clinical manifestations of Maple syrup urine disease?

(A) A hallmark feature of MSUD is a sweet or "maple syrup" Odor in the urine.

(B) Infants with MSUD may present with lethargy, feeding difficulties, and vomiting within the first week of life.

(C) Untreated MSUD does not result in any neurological complications.

(D) Hypotonia or hypertonia may be observed in infants with MSUD.

(E) Hypoglycaemia is the primary biochemical abnormality in MSUD.

(3) Regarding diagnostic approach of Maple syrup urine disease?

(A) Plasma amino acid analysis reveals elevated levels of leucine, isoleucine, and valine in MSUD.

(B) Tandem mass spectrometry is not useful for newborn screening of MSUD.

(C) Elevated levels of all amino acids are a diagnostic hallmark of MSUD.

(D) Detection of branched-chain keto acids in the urine is diagnostic for MSUD.

(E) Genetic testing can confirm the specific mutations causing MSUD.

(4) Regarding Management Strategies Maple syrup urine disease?

(A) The mainstay of MSUD management is a lifelong protein-free diet.

(B) Dietary restriction of branched-chain amino acids is essential for managing MSUD.
(C) Thiamine supplementation may benefit patients with thiamine-responsive MSUD.
(D) Liver transplantation can provide a definitive cure for MSUD.
(E) Regular plasma amino acid monitoring is unnecessary once dietary management is established.

(5) Regarding Prognosis and Outcomes of Maple syrup urine disease?
(A) Early diagnosis and treatment of MSUD can prevent severe neurological damage.
(B) Even with treatment, patients with MSUD are at risk of metabolic crises during illness or stress.
(C) Most untreated patients with MSUD have a normal lifespan.
(D) Intellectual disability is a potential complication of poorly managed MSUD.
(E) Patients with MSUD are never able to consume protein-containing foods.

(6) Regarding biochemical basis and types of albinism?
(A) Albinism is caused by a deficiency in the production or distribution of melanin.
(B) Oculocutaneous albinism affects only the eyes.
(C) Tyrosinase-negative albinism results from mutations in the tyrosinase enzyme, essential for melanin synthesis.
(D) Albinism is always inherited in an autosomal recessive pattern.
(E) Affected individuals with albinism may have normal melanin levels but defective melanosome distribution.

(7) Regarding Clinical Manifestations and Diagnosis of Albinism?
(A) Photophobia and nystagmus are common ophthalmologic features of albinism.
(B) Individuals with albinism have an increased risk of skin cancer due to decreased melanin protection.
(C) Genetic testing is not useful in diagnosing albinism.
(D) Albinism always results in completely white skin and hair.
(E) Vision problems in albinism are due to abnormal retinal development and misrouting of optic nerves.

(8) Regarding the Biochemical Basis Homocystinuria?
(A) Homocystinuria is caused by a defect in the metabolism of methionine and homocysteine.
(B) The most common form of homocystinuria is due to a deficiency of cystathionine beta-synthase (CBS).
(C) Vitamin B12 and folate deficiencies are unrelated to homocystinuria.
(D) Elevated levels of homocysteine are toxic to the vascular endothelium.
(E) Homocystinuria does not involve the transsulfuration or remethylation pathways of methionine metabolism.

(9) Regarding Clinical Manifestations and Diagnosis of Homocystinuria?

(A) Homocystinuria often presents with ectopia lentis (lens dislocation).
(B) Intellectual disability is a common feature of untreated homocystinuria.
(C) Homocystinuria does not increase the risk of thromboembolic events.
(D) Plasma amino acid analysis shows elevated levels of methionine and homocysteine in homocystinuria.
(E) The diagnosis of homocystinuria can be confirmed by measuring CBS enzyme activity.

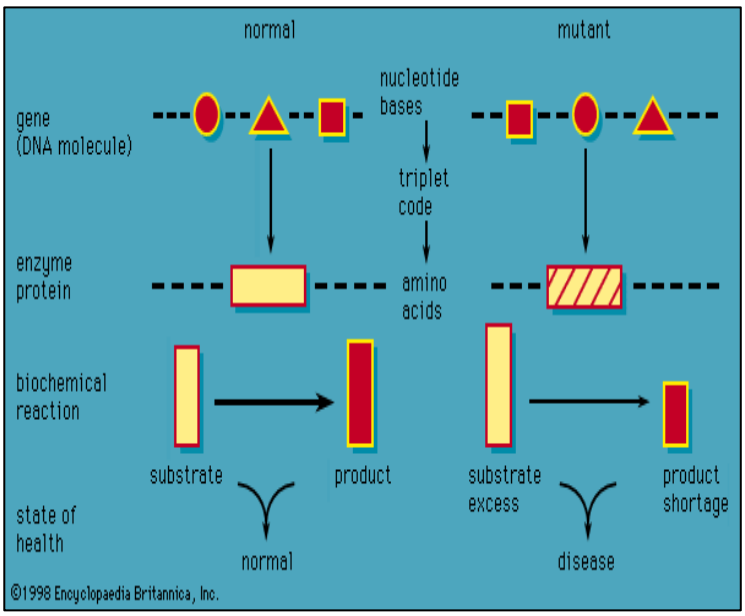
(10) Regarding Management and Prognosis of Homocystinuria?

(A) Dietary restriction of methionine is part of the management of homocystinuria.
(B) Supplementation with pyridoxine (vitamin B6) is beneficial in pyridoxine-responsive homocystinuria.
(C) Untreated homocystinuria typically has no long-term complications.
(D) Regular monitoring of plasma homocysteine levels is crucial in managing homocystinuria.
(E) Homocystinuria is fully cured with dietary and vitamin interventions.

Inborn errors of metabolism
Tutorials and SGDs

SGD 1- Amino acid metabolism -Answers

(1) Define the term "Inborn Errors of metabolism" and explain the occurrence, causes and consequences of such errors.



https://www.britannica.com/science/inborn-error-of-metabolism

• Inborn errors of metabolism are commonly caused by mutant genes that generally result in abnormal proteins, most often enzymes.

• The inherited defects may be expressed as a total loss of enzyme activity or, more frequently, as a partial deficiency in catalytic activity.

• Without treatment, the inherited defects of amino acid metabolism almost invariably result in mental retardation or other developmental abnormalities as a consequence of harmful accumulation of metabolites.

• Although more than 50 of these disorders have been described, many are rare, occurring in less than 1 per 250,000 in most populations.

• Collectively, however, they constitute a very significant portion of paediatric genetic diseases.

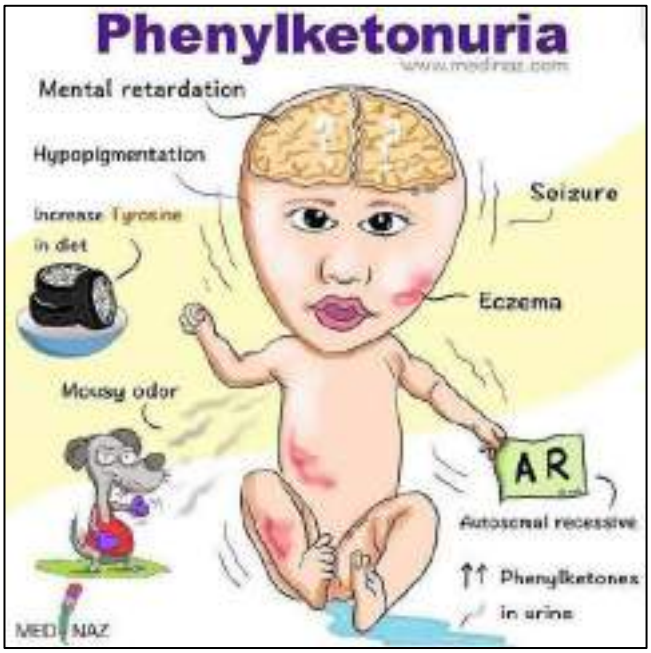
(2) List the main types of inborn errors of metabolism giving examples for each

The main types of inborn errors of metabolism include:

- **Disorders of Carbohydrate Metabolism:** These disorders affect the breakdown and use of sugars and glycogen.
    - **Examples:** Galactosemia, Glycogen Storage Diseases (GSD, e.g., Pompe disease, Von Gierke's disease), and Fructose Intolerance.
- **Disorders of Amino Acid Metabolism (Aminoacidopathies):** These conditions involve problems in metabolizing certain amino acids, leading to the accumulation of waste products that can damage the nervous system.
    - **Examples:** Phenylketonuria (PKU), Maple Syrup Urine Disease (MSUD), and Tyrosinemia.
- **Urea Cycle Disorders (UCDs):** Defects in this cycle prevent the body from properly converting ammonia (a byproduct of protein metabolism) into urea for excretion, resulting in high levels of ammonia (hyperammonaemia) in the blood.
    - **Examples:** Ornithine transcarbamylase (OTC) deficiency and Citrullinemia.
- **Organic Acidemias (Organic Acidurias):** These are a group of disorders where the body cannot break down certain amino acids, fats, or carbohydrates, leading to the accumulation of organic acids in the blood and urine, which can cause severe metabolic acidosis.
    - **Examples:** Propionic acidaemia, Methylmalonic acidaemia, and Isovaleric acidaemia.
- **Fatty Acid Oxidation (FAO) Disorders:** The body has difficulty breaking down fats into energy, especially during periods of fasting or illness, often leading to a lack of ketones and low blood sugar (hypoketotic hypoglycaemia).
    - **Examples:** Medium-chain acyl-CoA dehydrogenase (MCAD) deficiency and long-chain 3-hydroxyacyl-CoA dehydrogenase (LCHAD) deficiency.
- **Lysosomal Storage Disorders (LSDs):** These conditions involve the accumulation of complex molecules within the lysosomes of cells due to enzyme deficiencies, causing progressive organ dysfunction.
    - **Examples:** Gaucher disease, Tay-Sachs disease, and Niemann-Pick disease.

- **Peroxisomal Disorders:** These are caused by defects in peroxisomal enzymes or the formation of peroxisomes themselves, leading to a variety of symptoms often affecting multiple organ systems.
    - **Examples:** Zellweger syndrome.
- **Mitochondrial Disorders:** These disorders affect the mitochondria, the cell's primary energy producers, leading to insufficient energy production and a wide range of systemic symptoms.
    - **Examples:** Mitochondrial encephalomyopathy, lactic acidosis, and stroke-like episodes (MELAS) syndrome.

(3) Explain the biochemical basis, clinical manifestations, diagnostic approach, and management strategies for phenylketonuria (PKU) as an inborn error of amino acid metabolism.



https://medizzy.com/feed/35561885

Introduction

Phenylketonuria (PKU) is one of the most common inborn errors of amino acid metabolism. It is an autosomal recessive disorder caused by mutations in the gene encoding phenylalanine hydroxylase (PAH), which is responsible for converting phenylalanine to tyrosine. This results in elevated levels of phenylalanine in the blood and its toxic metabolites in tissues, leading to a spectrum of clinical manifestations.

Biochemical Basis:

1. Normal Pathway:
    - Phenylalanine is an essential amino acid obtained from dietary protein.

- Phenylalanine hydroxylase catalyses the hydroxylation of phenylalanine to tyrosine in the liver, with tetrahydrobiopterin (BH4) as a cofactor.

2. Pathophysiology in PKU:
   - A deficiency of phenylalanine hydroxylase or its cofactor BH4 leads to the accumulation of phenylalanine.
   - Excess phenylalanine undergoes alternative metabolic pathways, producing phenylpyruvate, phenyl lactate, and phenylacetate, which are neurotoxic.

Clinical Manifestations,

1. Neurological Symptoms:
   - Intellectual disability (if untreated)
   - Seizures
   - Microcephaly
   - Developmental delay
2. Behavioural and Psychological Issues:
   - Hyperactivity
   - Anxiety
   - Social difficulties
3. Physical Symptoms:
   - Hypopigmentation of skin, hair, and eyes due to reduced melanin synthesis (tyrosine is a precursor of melanin).
   - Musty or mousy body odour due to phenylacetate excretion.

Diagnostic Approach

1) Newborn Screening:

a) Blood phenylalanine levels are measured using tandem mass spectrometry.

b) Diagnosis is confirmed by genetic testing or enzyme activity assays.

2) Differential Diagnosis:

a) Conditions like BH4 deficiency should be excluded by specific tests.

Management Strategies

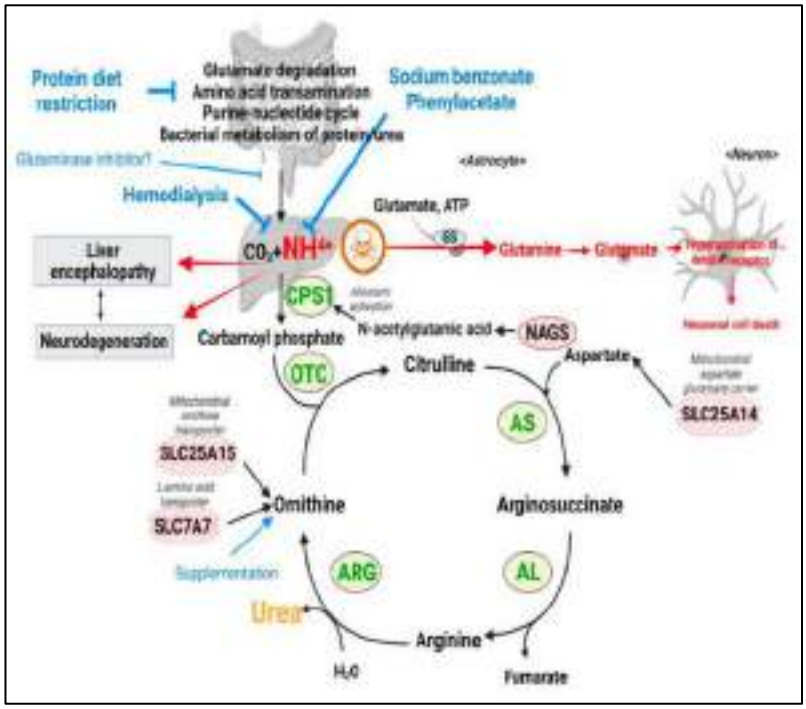
1. Dietary Management:
   - A low-phenylalanine diet is the cornerstone of treatment, initiated early to prevent neurotoxicity.
   - Specialized medical formulas are used to provide adequate protein without excess phenylalanine.
2. Pharmacological Treatment:
   - Sapropterin dihydrochloride (synthetic BH4) may be effective in some cases.
   - Pegvaliase, an enzyme substitution therapy, is available for severe cases.
3. Monitoring:
   - Regular blood phenylalanine level monitoring to ensure optimal control.

- Lifelong adherence to treatment is recommended, as relaxation in dietary restrictions may result in cognitive or psychological impairments.

4. Supportive Care:
   - Genetic counselling for families.
   - Psychological and developmental support for affected individuals.

• Outline the metabolic pathways and explain the errors associated with:

- Amino acid metabolism



https://www.mdpi.com/2218-1989/12/6/527

Tutorial 1- Amino acid metabolism -Answers

(1) Regarding the biochemical basis of Maple syrup urine disease?



https://www.emaze.com/@aqllrirq/Maple-Syrup-Urine-Disease

(A) MSUD is caused by a deficiency in the branched-chain alpha-keto acid dehydrogenase complex (BCKDC). (True)

(B) The accumulation of branched-chain amino acids (leucine, isoleucine, and valine) and their corresponding keto acids is characteristic of MSUD. (True)
(C) MSUD is an autosomal dominant disorder. (False)
(D) BCKDC deficiency affects the metabolism of aromatic amino acids. (False)
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(2) Regarding clinical manifestations of Maple syrup urine disease?

(A) A hallmark feature of MSUD is a sweet or "maple syrup" odour in the urine. (True)
(B) Infants with MSUD may present with lethargy, feeding difficulties, and vomiting within the first week of life. (True)
(C) Untreated MSUD does not result in any neurological complications. (False)
(D) Hypotonia or hypertonia may be observed in infants with MSUD. (True)
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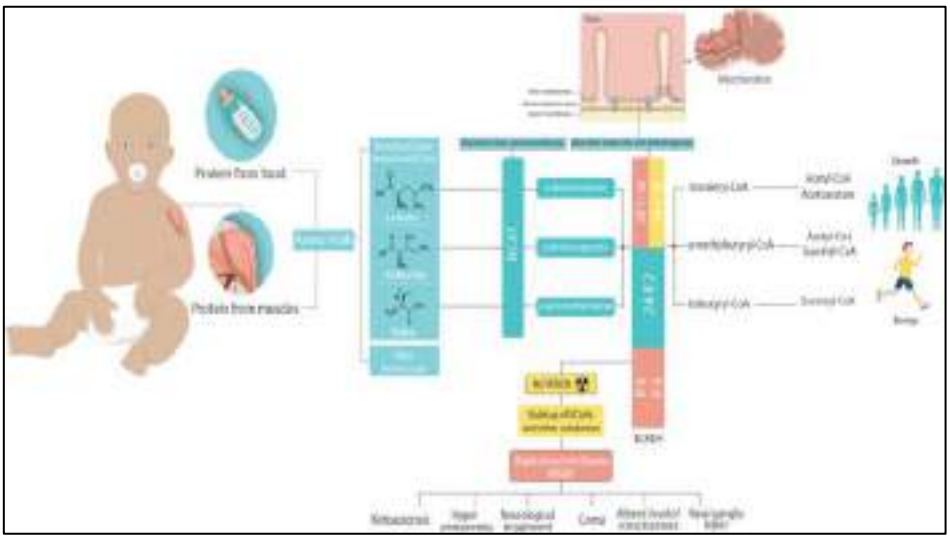

https://www.researchgate.net/figure/Schematic-representation-of-the-pathology-of-maple-syrup-urine-disease-depicting-the_fig6_333301297

(3) Regarding diagnostic approach of Maple syrup urine disease?

(A) Plasma amino acid analysis reveals elevated levels of leucine, isoleucine, and valine in MSUD. (True)
(B) Tandem mass spectrometry is not useful for newborn screening of MSUD. (False)
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(D) Detection of branched-chain keto acids in the urine is diagnostic for MSUD. (True)
(E) Genetic testing can confirm the specific mutations causing MSUD. (True)

(4) Regarding Management Strategies Maple syrup urine disease?

(A) The mainstay of MSUD management is a lifelong protein-free diet. (False)

(B) Dietary restriction of branched-chain amino acids is essential for managing MSUD. (True)
(C) Thiamine supplementation may benefit patients with thiamine-responsive MSUD. (True)
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(A) Early diagnosis and treatment of MSUD can prevent severe neurological damage. (True)
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(E) Patients with MSUD are never able to consume protein-containing foods. (False)

(6) Regarding biochemical basis and types of albinism?



https://www.azolifesciences.com/article/Genetics-of-Albinism.aspx

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(E) Affected individuals with albinism may have normal melanin levels but defective melanosome distribution. (True)

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(B) Individuals with albinism have an increased risk of skin cancer due to decreased melanin protection. (True)
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(8) Regarding the Biochemical Basis Homocystinuria?



https://disorders.eyes.arizona.edu/disorders/homocystinuria-beta-synthase-deficiency

(A) Homocystinuria is caused by a defect in the metabolism of methionine and homocysteine. (True)
(B) The most common form of homocystinuria is due to a deficiency of cystathionine beta-synthase (CBS). (True)
(C) Vitamin B12 and folate deficiencies are unrelated to homocystinuria. (False)
(D) Elevated levels of homocysteine are toxic to the vascular endothelium. (True)
(E) Homocystinuria does not involve the transsulfuration or remethylation pathways of methionine metabolism. (False)

(9) Regarding Clinical Manifestations and Diagnosis of Homocystinuria?

(A) Homocystinuria often presents with ectopia lentis (lens dislocation). (True)
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(10) Regarding Management and Prognosis of Homocystinuria?

(A) Dietary restriction of methionine is part of the management of homocystinuria. (True)
(B) Supplementation with pyridoxine (vitamin B6) is beneficial in pyridoxine-responsive homocystinuria. (True)

(C) Untreated homocystinuria typically has no long-term complications. (False)
(D) Regular monitoring of plasma homocysteine levels is crucial in managing homocystinuria. (True)
(E) Homocystinuria is fully cured with dietary and vitamin interventions. (False)

SGD 02: Carbohydrate metabolism, Lipid metabolism, Lysosome metabolism, Porphyrin metabolism, Mineral metabolism, Purine metabolism

Please answer the following MCQs (True/ False type) giving reasons for False answers.

(Q1) Regarding Inborn Errors of Carbohydrate Metabolism?

a) Glycogen storage diseases are caused by enzymatic defects in glycogen metabolism.
b) Von Gierke disease is due to a deficiency of glucose-6-phosphate dehydrogenase.
c) Galactosemia results from a deficiency of galactose-1-phosphate uridyltransferase.
d) Hereditary fructose intolerance is caused by aldolase B deficiency.
e) McArdle disease involves defective muscle glycogen phosphorylase.

(Q2) Regarding Inborn Errors of Carbohydrate Metabolism?

a) Glucose-6-phosphate dehydrogenase deficiency leads to haemolytic anaemia.
b) Fructosuria is caused by a deficiency of fructokinase.
c) Classical galactosemia causes cataracts in newborns.
d) Pompe disease is due to lysosomal acid maltase deficiency.
e) Glycogen storage diseases are all X-linked disorders.

(Q3) Regarding Inborn Errors of Lipid Metabolism?

a) Medium-chain acyl-CoA dehydrogenase deficiency (MCAD) impairs fatty acid oxidation.
b) MCAD deficiency presents with hypoketotic hypoglycaemia.
c) Carnitine deficiency results in impaired transport of long-chain fatty acids into mitochondria.
d) Refsum disease is caused by a defect in branched-chain fatty acid oxidation.
e) Gaucher disease is an inborn error of lipid metabolism.

(Q4) Regarding Inborn Errors of Lipid Metabolism?

a) Niemann-Pick disease involves sphingomyelin accumulation.
b) Zellweger syndrome is caused by peroxisomal defects.
c) Fabry disease is inherited in an X-linked recessive manner.
d) Tay-Sachs disease results from a deficiency of hexosaminidase A.
e) Adrenoleukodystrophy involves the accumulation of very-long-chain fatty acids.

(Q5) Regarding Inborn Errors of Lysosome Metabolism?

a) Lysosomal storage diseases result in the accumulation of undegraded macromolecules.
b) Gaucher disease is caused by a deficiency of beta-glucocerebrosidase.
c) Fabry disease involves the accumulation of ceramide trihexoside.
d) Hurler syndrome is caused by a deficiency of alpha-iduronidase.
e) Niemann-Pick disease is caused by a defect in mitochondrial function.

(Q6) Regarding Inborn Errors of Lysosome Metabolism?

a) Mucopolysaccharidoses involve defective degradation of glycosaminoglycans.
b) Krabbe disease results from the accumulation of galactosylceramide.
c) I-cell disease involves defective trafficking of lysosomal enzymes.
d) Pompe disease is a glycogen storage disease with lysosomal involvement.
e) Lysosomal storage diseases are inherited in an autosomal dominant manner.

(Q7) Regarding Inborn Errors of Porphyrin Metabolism?

a) Porphyria's are inherited disorders of heme biosynthesis.
b) Acute intermittent porphyria results from a deficiency of porphobilinogen deaminase.
c) Heme biosynthesis occurs entirely in the cytoplasm.
d) Porphyria cutanea tarda is the most common porphyria.
e) Ferrochelatase deficiency results in erythropoietic protoporphyria.

(Q8) Regarding Inborn Errors of Porphyrin Metabolism?

a) Lead poisoning inhibits delta-aminolevulinic acid synthase.
b) Congenital erythropoietic porphyria is caused by a deficiency of uroporphyrinogen III synthase.
c) Acute intermittent porphyria is associated with neurovisceral symptoms.
d) Heme oxygenase is involved in the breakdown of heme.
e) All porphyria's present with photosensitivity.

(Q9) Regarding Inborn Errors of Mineral Metabolism?

a) Wilson's disease is caused by a defect in copper transport.
b) Menkes disease is caused by defective copper absorption.
c) Hemochromatosis leads to excessive iron absorption.
d) Hypoparathyroidism results in hypercalcemia.
e) Vitamin D-resistant rickets is caused by a defect in renal phosphate reabsorption.

(Q10) Regarding Inborn Errors of Mineral Metabolism?

a) Calcitriol promotes calcium absorption in the gut.
b) PTH increases serum calcium and decreases serum phosphate.
c) Hypophosphatasia is due to a deficiency of alkaline phosphatase.
d) Excess zinc interferes with copper absorption.
e) Magnesium deficiency does not affect PTH secretion.

(Q11) Regarding Errors of Purine Metabolism?

a) Lesch-Nyhan syndrome is caused by hypo-xanthine-guanine phosphoribosyl transferase (HGPRT) deficiency.
b) Adenosine deaminase deficiency leads to severe combined immunodeficiency (SCID).
c) Xanthine oxidase deficiency results in decreased uric acid production.
d) Gout is caused by the accumulation of inosine.
e) Allopurinol inhibits xanthine oxidase.

(Q12) Regarding Errors of Purine Metabolism?

a) PRPP synthetase is overactive in gout.
b) Purine nucleoside phosphorylase deficiency results in T-cell immunodeficiency.
c) Hypoxanthine is converted to IMP by HGPRT.
d) Salvage of purines prevents their excessive degradation to uric acid.
e) Gout is associated with calcium pyrophosphate crystal deposition.

(Q13) Regarding Inborn Errors of metabolism?

a) Glycogen storage diseases are inherited in an autosomal dominant manner.
b) Medium-chain acyl-CoA dehydrogenase deficiency causes fasting hypoglycaemia.
c) Niemann-Pick disease involves the accumulation of sphingomyelin.
d) Acute intermittent porphyria is caused by a defect in delta-aminolaevulinic acid synthase.
e) Wilson's disease causes copper accumulation in the liver.

(Q14) Regarding Inborn Errors of metabolism?

a) Hurler syndrome involves a defect in mucopolysaccharide degradation.
b) G6PD deficiency leads to haemolytic anaemia under oxidative stress.
c) Hyperuricemia is a hallmark of Lesch-Nyhan syndrome.
d) Pompe disease involves lysosomal acid maltase deficiency.
e) Hypocalcaemia is common in hyperparathyroidism.

(Q15) Regarding Inborn Errors of metabolism?

a) MCAD deficiency is a defect in mitochondrial fatty acid oxidation.
b) Gaucher disease involves the accumulation of glucocerebrosides.
c) Xanthine oxidase deficiency causes xanthinuria.
d) Acute intermittent porphyria presents with photosensitivity.
e) Galactosemia is due to a deficiency of galactose kinase.

SGD 02: 1.Carbohydrate metabolism, Lipid metabolism, Lysosome metabolism, Porphyrin metabolism, Mineral metabolism, Purine Metabolism-Answers

(1) Regarding Inborn Errors of Carbohydrate Metabolism?

(A) Glycogen storage diseases are caused by enzymatic defects in glycogen metabolism. (True)

(B) Von Gierke disease is due to a deficiency of glucose-6-phosphate dehydrogenase. (False)

(C) Galactosemia results from a deficiency of galactose-1-phosphate uridyltransferase. (True)

(D) Hereditary fructose intolerance is caused by aldolase B deficiency. (True)

(E) McArdle disease involves defective muscle glycogen phosphorylase. (True)

(2) Regarding Inborn Errors of Carbohydrate Metabolism?

(A) Glucose-6-phosphate dehydrogenase deficiency leads to haemolytic anaemia. (True)

(B) Fructosuria is caused by a deficiency of fructokinase. (True)

(C) Classical galactosemia causes cataracts in newborns. (True)

(D) Pompe disease is due to lysosomal acid maltase deficiency. (True)

(E) Glycogen storage diseases are all X-linked disorders. (False)

(3) Regarding Inborn Errors of Lipid Metabolism?

(A) Medium-chain acyl-CoA dehydrogenase deficiency (MCAD) impairs fatty acid oxidation. (True)

(B) MCAD deficiency presents with hypoketotic hypoglycaemia. (True)

(C) Carnitine deficiency results in impaired transport of long-chain fatty acids into mitochondria. (True)

(D) Refsum disease is caused by a defect in branched-chain fatty acid oxidation. (True)

(E) Gaucher disease is an inborn error of lipid metabolism. (False)

(4) Regarding Inborn Errors of Lipid Metabolism?

(A) Niemann-Pick disease involves sphingomyelin accumulation. (True)

(B) Zellweger syndrome is caused by peroxisomal defects. (True)
(C) Fabry disease is inherited in an X-linked recessive manner. (False)
(D) Tay-Sachs disease results from a deficiency of hexosaminidase A. (True)
(E) Adrenoleukodystrophy involves the accumulation of very-long-chain fatty acids. (True)

(5) Regarding Inborn Errors of Lysosome Metabolism?

(A) Lysosomal storage diseases result in the accumulation of undegraded macromolecules. (True)
(B) Gaucher disease is caused by a deficiency of beta-glucocerebrosidase. (True)
(C) Fabry disease involves the accumulation of ceramide trihexoside. (True)
(D) Hurler syndrome is caused by a deficiency of alpha-iduronidase. (True)
(E) Niemann-Pick disease is caused by a defect in mitochondrial function. (False)

(6) Regarding Inborn Errors of Lysosome Metabolism?

(A) Mucopolysaccharidoses involve defective degradation of glycosaminoglycans. (True)
(B) Krabbe disease results from the accumulation of galactosylceramide. (True)
(C) I-cell disease involves defective trafficking of lysosomal enzymes. (True)
(D) Pompe disease is a glycogen storage disease with lysosomal involvement. (True)
(E) Lysosomal storage diseases are inherited in an autosomal dominant manner. (False)

(7) Regarding Inborn Errors of Porphyrin Metabolism?

(A) Porphyria are inherited disorders of heme biosynthesis. (True)
(B) Acute intermittent porphyria results from a deficiency of porphobilinogen deaminase. (True)
(C) Heme biosynthesis occurs entirely in the cytoplasm. (False)
(D) Porphyria cutanea tarda is the most common porphyria. (True)
(E) Ferrochelatase deficiency results in erythropoietic protoporphyria. (True)

(8) Regarding Inborn Errors of Porphyrin Metabolism?

(A) Lead poisoning inhibits delta-aminolevulinic acid synthase. (False)
(B) Congenital erythropoietic porphyria is caused by a deficiency of uroporphyrinogen III synthase. (True)
(C) Acute intermittent porphyria is associated with neurovisceral symptoms. (True)
(D) Heme oxygenase is involved in the breakdown of heme. (True)
(E) All porphyria present with photosensitivity. (False)

(9) Regarding Inborn Errors of Mineral Metabolism?

(A) Wilson's disease is caused by a defect in copper transport. (True)
(B) Menkes disease is caused by defective copper absorption. (True)
(C) Hemochromatosis leads to excessive iron absorption. (True)
(D) Hypoparathyroidism results in hypercalcemia. (False)
(E) Vitamin D-resistant rickets is caused by a defect in renal phosphate reabsorption. (True)

(10) Regarding Inborn Errors of Mineral Metabolism?

(A) Calcitriol promotes calcium absorption in the gut. (True)
(B) PTH increases serum calcium and decreases serum phosphate. (True)
(C) Hypophosphatasia is due to a deficiency of alkaline phosphatase. (True)
(D) Excess zinc interferes with copper absorption. (True)
(E) Magnesium deficiency does not affect PTH secretion. (False)

(11) Regarding Errors of Purine Metabolism?

(A) Lesch-Nyhan syndrome is caused by hypo-xanthine-guanine phosphoribosyltransferase (HGPRT) deficiency. (True)
(B) Adenosine deaminase deficiency leads to severe combined immunodeficiency (SCID). (True)
(C) Xanthine oxidase deficiency results in decreased uric acid production. (True)
(D) Gout is caused by the accumulation of inosine. (False)
(E) Allopurinol inhibits xanthine oxidase. (True)

(12) Regarding Errors of Purine Metabolism?

(A) PRPP synthetase is overactive in gout. (True)
(B) Purine nucleoside phosphorylase deficiency results in T-cell immunodeficiency. (True)
(C) Hypoxanthine is converted to IMP by HGPRT. (True)
(D) Salvage of purines prevents their excessive degradation to uric acid. (True)
(E) Gout is associated with calcium pyrophosphate crystal deposition. (False)

(13) Regarding Inborn Errors of metabolism?

(A) Glycogen storage diseases are inherited in an autosomal dominant manner. (False)
(B) Medium-chain acyl-CoA dehydrogenase deficiency causes fasting hypoglycaemia. (True)
(C) Niemann-Pick disease involves the accumulation of sphingomyelin. (True)
(D) Acute intermittent porphyria is caused by a defect in delta-aminolaevulinic acid synthase. (False)
(E) Wilson's disease causes copper accumulation in the liver. (True)

(14) Regarding Inborn Errors of metabolism?

(A) Hurler syndrome involves a defect in mucopolysaccharide degradation. (True)
(B) G6PD deficiency leads to haemolytic anaemia under oxidative stress. (True)
(C) Hyperuricemia is a hallmark of Lesch-Nyhan syndrome. (True)
(D) Pompe disease involves lysosomal acid maltase deficiency. (True)
(E) Hypocalcaemia is common in hyperparathyroidism. (False)

(15) Regarding Inborn Errors of metabolism?

(A) MCAD deficiency is a defect in mitochondrial fatty acid oxidation. (True)
(B) Gaucher disease involves the accumulation of glucocerebrosides. (True)
(C) Xanthine oxidase deficiency causes xanthinuria. (True)
(D) Acute intermittent porphyria presents with photosensitivity. (False)
(E) Galactosemia is due to a deficiency of galactose kinase. (False)

Inborn errors of metabolism

Tutorial 02

Carbohydrate metabolism, Lipid metabolism, Porphyrin metabolism, Purine metabolism

(1) There are many forms of disorders of carbohydrate metabolism.

(1.1.)

(1.1.1.) State the commonest disorder of carbohydrate metabolism. (05 Marks)

……

(1.1.2.) List three (03) disorders of galactose metabolism (15 Marks)

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(1.2.)

(1.2.1.) State the enzyme that is deficient in Hereditary Fructose Intolerance (HFI). (05 marks)

……

(1.2.2.) List signs and symptoms of the above condition. (15 Marks)

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(1.2.3.) State the reason(s) that lead to above signs and symptoms listed above. (20 Marks)

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(1.3.) Write a short note on Pyruvate dehydrogenase deficiency. (50 Marks)

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(Total 100 Marks)

(2) Disorders of lipid and lipoprotein metabolism are primarily linked to atherogenesis, which is associated with coronary heart disease and peripheral vascular diseases.

(2.1.)

(2.1.1.) Define "Dyslipidaemia". (05 Marks)

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(2.1.2.) List four (04) factors responsible for dyslipidaemias. (10 Marks)

……

……

(2.1.3.) List four (04) examples of primary disorders of plasma lipoproteins. (10 Marks)

……

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(2.1.4.) List biochemical markers that can be used to diagnose disorders of plasma lipoproteins.

(10 Marks)

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(2.2.)

(2.2.1.) Define the term "Porphyria". (20 Marks)

……

……

(2.2.2.) List three (03) categories of porphyria based on the clinical manifestation. (15 Marks)

……

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(2.2.3.) List four (04) major signs and symptoms of porphyria (10 Marks)

……

……

(2.2.4.) Briefly describe the reasons for the signs and symptoms listed above. (20 Marks)

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Tutorial 02

Carbohydrate metabolism, Lipid metabolism, Porphyrin metabolism, Purine Metabolism-Answers

(1) There are many forms of disorders of carbohydrate metabolism.

(1.1.)

(1.1.1.) State the commonest disorder of carbohydrate metabolism. (05 Marks)

Diabetes mellitus

(1.1.2.) List three (03) disorders of galactose metabolism. (15 Marks)

1. Galactokinase deficiency
2. Galactose-1-phosphate uridyl transferase deficiency
3. UDP galactose-4-epimerase deficiency

(1.2.)

(1.1.1.) State the enzyme that is deficient in Hereditary Fructose Intolerance (HFI). (05 marks)

Aldolase B

(1.1.2.) List signs and symptoms of the above condition. **(15** Marks)

severe hypoglycaemia, vomiting, jaundice, bleeding, hepatomegaly and hyperuricaemia.

(1.1.3.) State the reason(s) that leads to above signs and symptoms listed above. (20 Marks)

Phosphorylated intermediates get accumulated in this condition. Fructose-1-phosphate is an example for a phosphorylated intermediate and this product get accumulated in liver, kidney and small intestine.

(1.2.)

(1.2.1.) Write a short note on Pyruvate dehydrogenase deficiency. (50 Marks)

A deficiency in the E1 component of the PDH complex, although rare, is the most common

biochemical cause of congenital lactic acidosis. This enzyme deficiency results in an inability to convert pyruvate to acetyl CoA, causing pyruvate to be shunted to lactic acid via lactate dehydrogenase. This causes particular problems for the brain, which relies on the TCA cycle for most of its energy, and is particularly sensitive to acidosis. Symptoms are variable and include neurodegeneration, muscle spasticity and, in the neonatal onset form, early death. The E1 defect is X-linked, but because of the importance of the enzyme in the brain, it affects both

males and females. Therefore, the defect is classified as X-linked dominant. There is no proven treatment for pyruvate dehydrogenase deficiency: however, dietary restriction of carbohydrate and supplementation with TPP may reduce symptoms in select patients.

(100 Marks)

(2) Disorders of lipid and lipoprotein metabolism are primarily linked to atherogenesis, which is associated with coronary heart disease and peripheral vascular diseases.

(2.1)

(2.1.1) Define "Dyslipidaemia". (05 Marks)

Dyslipidaemia refers to abnormal amount of lipids such as triglycerides and cholesterol in the blood.

(2.1.2) List four (04) factors responsible for dyslipidaemias. (10 Marks)

Diet, exercise, obesity,
genetic polymorphism of enzymes, structural protein and receptors of lipoprotein metabolism.

(2.1.3) List four (04) examples for primary disorders of plasma lipoproteins (Dyslipoproteinemias) (10 Marks)

Hypolipoproteinaemia/ Abetalipoproteinemia
Familial alpha-lipoprotein deficiency
Hyperlipoproteinemia
Familial hypercholesterolemia
Familial type III hyperlipoproteinemia
Familial hypertriacylglycerolemia
Familial hyperalphalipoproteinaemia
Hepatic lipase deficiency
Familial lecithin: cholesterol acyltransferase (LCAT) deficiency

(2.1.4) List biochemical markers that can be used to diagnose disorders of plasma lipoproteins. (10 Marks)

Total cholesterol
Triglyceride
HDL
LDL
VLDL

(2.2)

(2.2.1) Define the term "Porphyria". (20 Marks)

Porphyria is rare, inherited (or occasionally acquired) defects in heme synthesis, resulting in the accumulation and increased excretion of porphyrins or porphyrin precursors.

(2.2.2) List three (03) categories of porphyria based on the clinical manifestation. (15 Marks)

Chronic hepatic porphyria
Acute hepatic porphyria's
Erythropoietic porphyria's

(2.2.3) List four (04) major signs and symptoms of porphyria (20 Marks)

Anaemia, abdominal pain, neuropsychiatric symptoms, Photosensitivity

(2.2.4) Briefly describe the reasons for the signs and symptoms listed above. (20 Marks)

Anaemia Decreased heme synthesis, haemolysis, and oxidative damage to red blood cells.
Abdominal pain Neurotoxicity of ALA and PBG affecting autonomic nerves in the gastrointestinal tract.
NeuropsychiatricALA and PBG disrupt neurotransmitters and cause oxidative stress in the nervous system.
Photosensitivity Porphyrins in the skin generate reactive oxygen species when exposed to sunlight.

(Total 100 Marks)

BIOCHEMISTRY MOCK PAPERS AND ANSWERS-CAT 2

CAT- 2 (BATCH 1) MOCK MCQ

CONTINUOUS ASSESSMENT 2 – 2023/2024 BATCH
(MOCK TEST)
BIOCHEMISTRY
MULTIPLE CHOICE QUESTIONS
Time: 1 hour
This paper consists of 10 True or False questions and 10 Single Best Answer questions.
True or False type Questions

(1) True or false regarding tricarboxylic acid (TCA) cycle TCA and oxidative phosphorylation?
(A) High NADH: NAD+ ratio shifts pyruvate dehydrogenase equilibrium towards acetyl CoA.
(B) The TCA cycle generates one molecule of GTP through substrate-level phosphorylation.
(C) 2,4-DNP dissipates the pH gradient of a mitochondrial membrane.
(D) NADH and NADPH act as electron donors of the complex in oxidative phosphorylation.
(E) The cofactor of succinate dehydrogenase donates electrons to the electron transport chain.

(2) True or false regarding glucose-6-phosphate dehydrogenase deficiency?
(A) It is a x-linked recessive disorder.
(B) It causes impact generation of reduced glutathione.
(C) It makes red cells resistant to plasmodium.
(D) It decreases ribose-5-phosphate synthesis.
(E) It enhances the activity of mitochondrial HMG-CoA reductase.

(3) Which of the following criteria are used to confirm the presence diagnosis of diabetic mellitus?
(A) HbA1C ≥>= 10.5%
(B) Random blood sugar level ≥=> 200mg/dl
(C) Fasting blood sugar level ≥>200mg/dl
(D) Plasma glucose 2 hours after oral glucose tolerance test >200mg/dl
(E) Postprandial blood glucose level is >140mg/dl

(4) Regarding amino acids,
(A) Cystine has more solubility than cysteine in an aqueous medium.
(B) Asparagine is derived from the amidationamination of aspartate.
(C) Histidine amino acid in haemoglobin helps in the buffering activity.
(D) Urea with Ninhydrin gives a blue colour under a minor aciduria condition.
(E) Proline is an amino acid.

(5) Which of the following are phosphatide derivatives?
(A) Cardiolipins
(B) Triacylglycerol
(C) Platelet-activating factors

(D) Phosphatidylcholine
(E) Sphingomyelin

(6) True regarding nucleotide metabolism,
(A) Dietary purines are metabolized in the salvage pathway.
(B) Phosphoribosyl Diphosphate (PRPP) synthase is subjected to feedback inhibition.
(C) PRPP aminotransferase is deficient in the human brain.
(D) Inosine-5′-monophosphate (IMP) dehydrogenase deficiency results in gout.
(E) Folic acid derivatives provide two carbon atoms for the purine structure.

(7) Unconjugated Bilirubin is?
(A) Transport in blood bound to serum albumin.
(B) Able to cross the blood-brain barrier.
(C) Increased in serum in common bile duct stones.
(D) Degraded by phototherapy in physiological jaundice.
(E) Soluble in direct van den Bergh test

(8) True regarding the cell cycle?
(A) Centriole separation happens in the G2 phase.
(B) Histone protein synthesis takes place in the S phase.
(C) CDK regulates progression through the cell cycle checkpoints.
(D) Methotrexate stops the cell cycle at the S phase.
(E) Liver cells are capable of entering G1 from G0 upon stimulation.

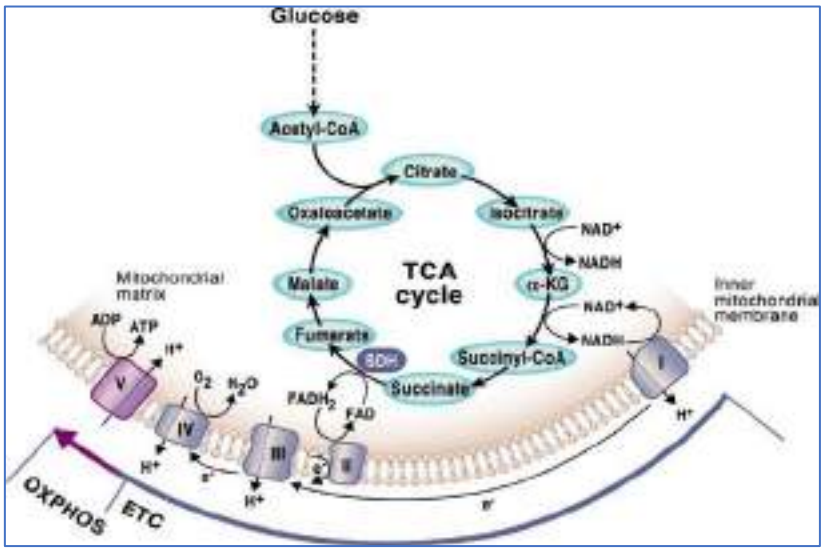
(9) Consequences of Von Gierke's disease are?
(A) fasting hypoglycaemia
(B) Hyperbilirubinemia
(C) Hyperuricemia
(D) Homocysteinemia
(E) Lactic acidosis

(10) True regarding telomerase and topoisomerase?
(A) Telomerases are active in the replication of DNA in stem cells.
(B) Telomerases unwind supercoils.
(C) Telomerase has reverse transcriptase activity.
(D) Prokaryotic telomerase is known as DNA gyrases.
(E) Eukaryotic topoisomerases are inhibited by fluoroquinolones.

CAT- 2 (BATCH 1) MOCK MCQ ANSWERS

MOCK MCQ Answer Guide
Semester 2

(1) True or False regarding TCA and oxidative phosphorylation?



https://www.nature.com/articles/s41467-019-13668-3

(A) True – High NADH: NAD+ ratio inhibits pyruvate dehydrogenase, reducing acetyl CoA formation.

(B) True – One molecule of GTP is generated during substrate-level phosphorylation in the TCA cycle.

(C) True – 2,4-DNP dissipates the proton gradient, uncoupling oxidative phosphorylation.

(D) False – NADH, not NADPH, donates electrons to Complex I in oxidative phosphorylation.

(E) True – Succinate dehydrogenase transfers electrons from FADH2 to the electron transport chain.

(2) Regarding glucose-6-phosphate dehydrogenase deficiency?

(A) True – It is an X-linked recessive disorder.

(B) True – Deficiency leads to impaired reduced glutathione generation, increasing oxidative stress.

(C) True – Confers resistance to Plasmodium falciparum due to oxidative stress in red cells.

(D) False – Ribose-5-phosphate synthesis is not significantly decreased in this disorder.

(E) False – No direct link with mitochondrial HMG-CoA reductase activity.

(3) Diabetes mellitus criteria?

(A) False – HbA1c ≥6.5% is diagnostic, not 10.5%.

(B) True – Random plasma glucose ≥200 mg/dL confirms diabetes.

(C) False – Fasting glucose ≥126 mg/dL is diagnostic, not >200 mg/dL.

(D) True – Plasma glucose ≥200 mg/dL after OGTT confirms diabetes.

(E) False – post-prandial blood glucose ≥140 mg/dL is borderline but not diagnostic.

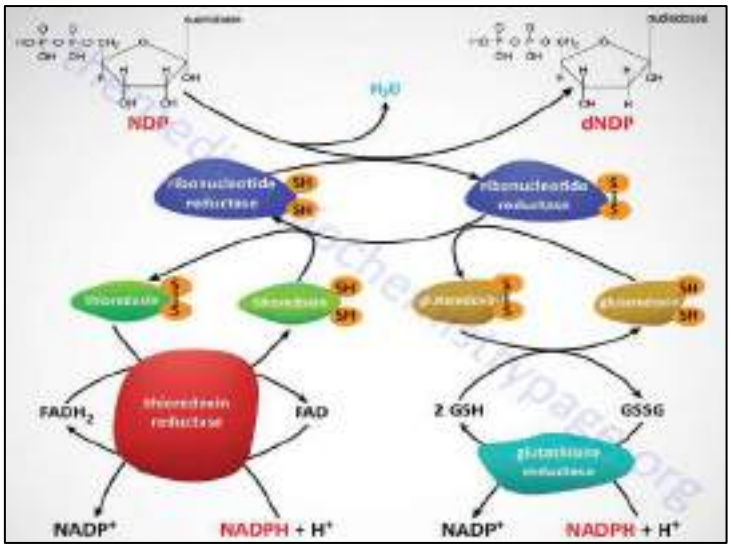
(4) Regarding amino acids?

(A) False – Cystine is less soluble than cysteine.
(B) True – Asparagine is derived from amidation of aspartate.
(C) True – Histidine in haemoglobin assists in buffering activity.
(D) False – Urea does not give a blue colour with ninhydrin.
(E) True – Proline is classified as an amino acid.

(5) Phosphatidate derivatives?

(A) True – Cardiolipins are derived from phosphatidate.
(B) True – Triacylglycerol is derived from phosphatidate.
(C) True – Platelet activating factors are derived from phosphatidate.
(D) True – Phosphatidylcholine is derived from phosphatidate.
(E) False – Sphingomyelin is not derived from phosphatidate.

(6) True regarding nucleotide metabolism?



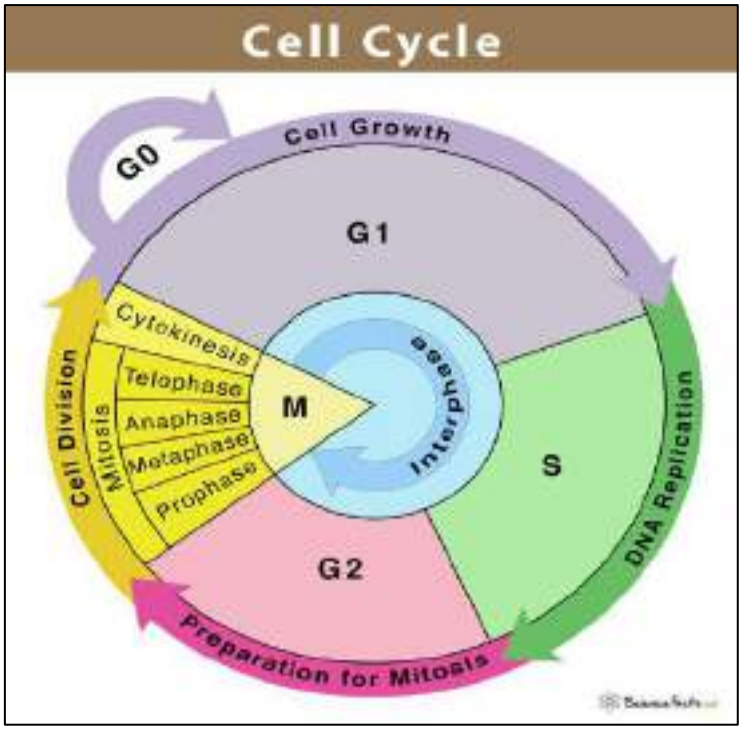
https://themedicalbiochemistrypage.org/nucleotides-biosynthesis-catabolism/

(A) False – Dietary purines are metabolized to uric acid, not salvaged.
(B) True – PRPP synthase is regulated by feedback inhibition.
(C) False – PRPP aminotransferase is present in all tissues, including the brain.
(D) False – IMP dehydrogenase deficiency does not cause gout; hyperactivity does.
(E) True – Folic acid derivatives contribute to purine biosynthesis.

(7) Unconjugated bilirubin?

(A) True – Transported in blood bound to albumin.
(B) True – Can cross the blood-brain barrier.
(C) False – Common bile duct stones cause conjugated hyperbilirubinemia.
(D) True – Degraded by phototherapy in neonatal jaundice.
(E) False – Insoluble in direct van den Bergh test.

(8) True regarding the cell cycle?



https://www.sciencefacts.net/cell-cycle.html

(A) False – Centriole separation occurs during mitosis, not the G2 phase.
(B) True – Histone protein synthesis occurs in the S phase.
(C) True – Cell cycle progression is regulated by CDKs.
(D) True – Methotrexate inhibits DNA synthesis in the S phase.
(E) True – Liver cells can re-enter the cell cycle from G0 upon stimulation.

(9) Consequences of Von Gierke's disease?

(A) True – Fasting hypoglycaemia is a key feature.
(B) False – Hyperbilirubinemia is not typically seen.
(C) True – Hyperuricemia occurs due to impaired gluconeogenesis.
(D) False – Homocysteinemia is unrelated.
(E) True – Lactic acidosis is a hallmark feature.

(10) True regarding telomerase and topoisomerase?

(A) True – Telomerase is active in stem cells.
(B) False – Telomerases do not unwind supercoils; topoisomerases do.
(C) True – Telomerase has reverse transcriptase activity.
(D) False – DNA gyrase is a type of prokaryotic topoisomerase, not telomerase.
(E) False – Fluoroquinolones inhibit bacterial, not eukaryotic, topoisomerases.

CAT- 2 (BATCH 1) MOCK SEQ

BIOCHEMISTRY
MOCK Structured Essay Paper

Semester 02
Answer all questions
Duration -: 01 hour

(1) A 3-year-old boy is brought to the emergency department after several episodes of vomiting and lethargy. His paediatrician has been concerned about his failure to thrive and possible hepatic failure along with recurrent episodes of vomiting and lethargy. After a careful history is taken, you observe that these episodes occur after ingestion of certain types of food, especially high in fructose. His blood sugar was checked in the emergency department and was extremely low.

(1.1.)

(1.1.1.) What is the probable diagnosis? (5 marks)

(1.1.2.) What is the enzyme deficient? (5 marks)

(1.1.3.) Describe the role of Glucokinase in maintaining blood glucose level.

(1.1.4.) Describe the reason for hyperuricemia in Von Gierke disease. (20 marks)

(1.2.) Briefly describe the steps in the initiation of prokaryotic DNA replication. (20 marks)

(1.2.1.) Characteristics of genetic code. (15 marks)

(1.2.2.) Explain the effects of substitutional point mutations. (15 marks)

(2)

(2.1.)

A 42-year-old woman with type 2 diabetes mellitus, who underwent a health checkup, was found to have an increased risk of heart disease, with hypercholesterolemia and hypertension. She is referred to a dietician for necessary dietary advice. Her weight and height measurements are 80 kg and 1.5m, respectively. She consumes a mixed diet.

Safe level of protein intake for an individual = 0.75 g/kg/day Digestibility of proteins in a mixed diet = 80%

(2.1.1.) Calculate the BMI of the above individual. Comment on the value. (20 marks)

(2.1.2.) Calculate the safe level of dietary protein intake for the above patient. (20 marks)

(2.1.3.) Explain the main considerations in planning a diet for the above patient. (10 marks)

(2.2.)

A 56-year-old male previously diagnosed with alcoholic cirrhosis presented to the hospital with acute onset blood vomiting (hematemesis). On examination, he was icteric and had ascites and bilateral ankle oedema. His liver function test results are given below:

Test Value Reference Level
Total Bilirubin 16.4 0.2 – 1.2 mg/dL
Serum Albumin 30 35 – 55 g/L
Alkaline Phosphatase (ALP) 224 20 – 70 IU/L
Serum Aspartate
Aminotransferase (AST)
210 10 – 40 IU/L
Serum Alanine
Aminotransferase (ALT)
101 5 – 30 IU/L

Explain the biochemical basis for the changes in the following parameters in the above patient:

(2.2.1.) Total bilirubin (10 marks)
(2.2.2.) ALT (10 marks)
(2.2.3.) ALP (10 marks)

(2.3.) Briefly explain the digestion and absorption of proteins. (20 marks)

CAT-2 (BATCH 1) MOCK SEQ ANSWERS

MOCK SEQ Answer Guide
Semester 2

1.1

1.1.1 Hereditary Fructose Intolerance

1.1.2 Aldolase B

1.1.3

- Glucokinase has a high Vmax and high Km value.
- High Km suggests that it needs high glucose for half-saturation.
- So glucokinase has a lower affinity to glucose.
- Glucokinase is located in liver parenchymal cells and pancreatic beta cells.
- It functions as a glucose sensor, determining the threshold for insulin secretion.

Glucokinase in maintaining blood glucose levels,

- Insulin maintains blood glucose concentration in hyperglycaemic situations.
- Glucokinase phosphorylates glucose only at higher glucose concentrations.
- Therefore, it acts as the threshold for insulin secretion in pancreatic beta cells.
- Glucokinase has high Vmax, allowing the liver to remove the flood of glucose delivered by portal blood.
- This prevents large amounts of glucose from entering systemic circulation following a carbohydrate meal, minimizing hyperglycaemia during the absorptive period.

1.1.4

- Von Gierke Disease: Glucose 6-phosphatase deficiency.
- This enzyme is present in the liver and kidney.
- It is involved in both gluconeogenesis and glycogenolysis.
- During starvation, gluconeogenesis and glycogenolysis are increased.
- When Glucose 6-phosphatase is deficient, Glucose 6-phosphate accumulates.
- Accumulated Glucose 6-phosphate is metabolized through the pentose phosphate pathway,

increasing ribulose 5-phosphate production.

- Purine synthesis is increased, and excess purines are degraded into uric acid, leading to hyperuricemia.
- Additionally, Glucose 6-phosphate undergoes glycolysis, producing pyruvate.
- Pyruvate is converted to lactate, causing lactic acidosis.
- Lactate and uric acid are excreted through a common channel in nephrons, so lactic acidosis impairs uric acid excretion, further increasing hyperuricemia.

1.2

1.2.1

- Initiation involves recognizing the starting site and preparing DNA for replication.
- Replication begins at an AT-rich region called the “origin of replication” (Ori).
- In E. coli, the Ori is called OriC.

- At OriC, parental strands separate to create two replication forks, where new polynucleotides form.
- Replication forks move bidirectionally from the origin.
- Initiator proteins (DnaA) recognize and bind to OriC.
- DNA helicase (DnaB) binds to DnaA, unwinds the double helix, and requires ATP.
- Each parent strand (ssDNA) serves as a template.
- Primase synthesizes a short RNA primer complementary to the template strand.
- Unwinding creates supercoils, which topoisomerase relaxes in prokaryotes.

1.2.2 Characteristics of Genetic Code:

- Degenerative (Redundant): One amino acid can be encoded by more than one codon.
- Specific (Unambiguous): Each codon specifies only one amino acid.
- Non-overlapping: Each base is read only once.
- Non-punctuated (Comma-less): Codons are read continuously until a stop codon.
- Universal: The specificity of the genetic code is conserved across organisms.

1.2.3

- A single nucleotide change in mRNA can result in:
- Silent Mutation: The codon codes for the same amino acid (e.g., wobble hypothesis).
- Missense Mutation: The codon codes for a different amino acid.
- Nonsense Mutation: The codon becomes a termination codon, leading to premature

translation termination.

Examples:

- Missense mutations can be:
- Acceptable (e.g., Hb Hikari disease).
- Partially acceptable (e.g., sickle cell disease).
- Unacceptable (e.g., HbM Boston).

2.1

2.1.1

BMI = Weight (kg) ÷ Height² (m²) = 80 ÷ (1.5 × 1.5) = 35.5 kg/m²

As her BMI is 35.5 kg/m², she is categorized as obese.

2.1.2

Safe protein intake = 0.75 × 80 = 60 g (assuming 100% digestibility).

If digestibility is 80%, required intake = 60 × 100 / 80 = 75 g.

2.1.3 Main dietary considerations:

- Lifestyle changes to reduce cardiovascular risk and diabetes.
- Consume Fiber-rich food.
- Avoid high-fat snacks and sugary foods.
- Include a low-carbohydrate, high-fat ketogenic diet.

- Incorporate antioxidants and foods rich in polyunsaturated fatty acids (PUFAs).
- Minimize saturated fat intake.

2.2

2.2.1 Total Bilirubin:

- Elevated bilirubin indicates impaired liver function due to alcoholic cirrhosis.
- The liver fails to conjugate unconjugated bilirubin, increasing total bilirubin levels.

2.2.2 ALT:

- ALT is a liver-specific enzyme involved in amino acid metabolism.
- In hepatocellular damage (e.g., cirrhosis), ALT leaks into the bloodstream.

2.2.3 ALP:

- ALP is located in the liver, bone, and bile duct epithelia.
- In cirrhosis, biliary obstruction increases ALP levels in the blood.

2.3 Digestion and Absorption of Proteins:

- Digestion begins in the stomach with pepsin, activated from pepsinogen by HCl.
- HCl denatures proteins and inactivates salivary amylase.
- In the small intestine, zymogens (e.g., trypsinogen) are activated by enterokinase, forming
- active enzymes like trypsin and chymotrypsin.
- Endopeptidases (e.g., trypsin) cleave internal peptide bonds, while exopeptidases (e.g. carboxy peptidase) cleave terminal bonds.
- Products include amino acids and oligopeptides.
- Absorption occurs in the duodenum and jejunum through Na^+/H^+ symport systems.
- Di- and tripeptides are hydrolysed into free amino acids in enterocytes.
- Amino acids are released into the bloodstream via facilitated diffusion.

CAT- 2 (BATCH 1) MOCK OSPE

01.

A patient visited the clinic due to the presence of ulceration on his foot and weight loss. He is also suffering from polydipsia and polyphagia. Glucose in high levels were found in his urine.



1. Identify the condition that the special is suffering from.
2. State the cause for the above condition.
3. Explain the reasons for Polydipsia and polyphagia.
4. State 2 tests that could be done to confirm the above condition.

02.



This patient presented with acute gouty arthritis and self-mutilating behaviors such as lip and finger biting and head banging. Additional symptoms include voluntary muscle moments and neurological impairment.

1. Identify the disease condition seen in this patient.
2. What is the enzyme deficiency scene in this patient?
3. State the basis of gout in such patients.

03.

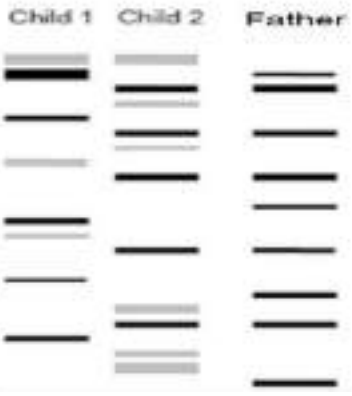


The Fouchet's test was performed on a urine sample obtained from an icteric patient. The above result was obtained. He had been diagnosed with cancer in the head of the pancreas a few months ago. He also stated that he is tools appeared clay colored.

1. What does your observation indicate?
2. What are the clinical symptoms that can be seen in an icteric patient?
3. What type of Jaundice is this likely to be?
4. What is the reason for clay-coloured stools?
5. Why doesn't UCB appear in urine?

04.

After 30 years of suspicion and much doubt, after the passing of his wife, a father of two sons wanted to have a covert DNA paternity test. The father suspected that early on in his marriage an affair had taken place and potentially one or both of his sons were not his. The father provided the investigator with 2 beer bottle samples with his son's DNA and a DNA cheek swab with his DNA. The DNA profiling thus created is given below.



1. What is the initial test carried out once the DNA samples were acquired? (3 marks)
2. Comment on the paternity of child 1 and child 2. (3 marks)
3. What is the technique used here for paternity testing? (2 marks)
4. What is a tandem repeat? (2 marks)

05.



The about diagram shows the electrophoretic pattern of lipoproteins.

1. Name A, B, C, and D.
2. Arrange A, B, C, and D in decreasing order of density.
3. State the function of each of the above lipoproteins

06.





A patient presents to the clinic with dark spots in the eyes and ears (as seen in the picture: ochronosis) With passages of dark-coloured urine.

1. What is the clinical condition?
2. What is the reason for dark-coloured urine?
3. What is the enzyme deficiency?
4. Give another complication of this condition.

07.

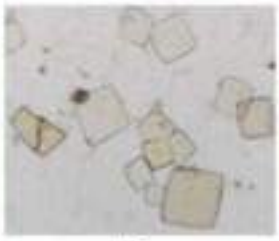
A healthy male table of hemolysis and jaundice following a prophylactic dose of Premaquin.

1. What is the most likely enzyme deficiency?
2. What is the inheritance of the enzyme deficiency mentioned above?
3. Write the biochemical reaction catalyzed by the enzyme mentioned in above(1).
4. What is the reason for hemolysis? Explain.
5. Write 2 other causes that could precipitate similar symptoms in an individual with the mentioned enzyme deficiency.

08.



A.



B.



C.

1. Identify the crystals A and B.
2. Write the shapes of the crystals indicated above.
3. Mention a disease in which 'B' can appear in urine.
4. Identify the type of urinary cast indicated by C.
5. Name a pathological condition in which this type of cast can appear in urine

09.

A patient admitted to the clinic had elevated phenylalanine and phenyl ketones in body fluids. He was diagnosed to be having phenylketonuria(PKU)

1. What is the most likely enzyme deficiency?
2. Write the biochemical reaction catalyzed by the enzyme mentioned above.
3. What is the reason for elevated serum phenyl ketone levels? Write 3 examples of phenyl ketones.
4. What are the clinical features of a patient with PKU? Melanin synthesis is impaired in PKU patients. What is the reason for this?
5. What territory advice would you give a patient with PKU?

10.

An elderly patient with familial combined hyperlipidemia was identified to have a potential risk of myocardial infarction.

1. What is the defect seen in the above-mentioned type of hyperlipidemia?
2. State the elevated lipoprotein pattern seen in the above patient.
3. He was prescribed a long-term dose of Aspirin by his doctor. Explain the basis of the above method of treatment to minimize the risk of MIs.

CAT- 2 (BATCH 1) MOCK OSPE ANSWERS

MOCK OSPE ANSWER GUIDE

Semester 2

01.

(1) Diabetic mellitus (1 mark)
(2) Insulin deficiency of insulin resistance (1 mark)
(3) Polydipsia – in the presence of diabetes blood glucose level increases. Plasma osmolality increases. More water is dragged into plasma from the cells which results in the increase of water loss. Therefore, thirst increases.
(4) Polyphagia – glucose cannot enter the cells of the satiety centre hence feeding Centre is not inhibited so this results in the increase of appetite. (4 marks)
(5) Fasting blood sugar (FBS) – if it is more than 126mg/dl on two occasions, oral glucose tolerance test (OGTT) – more than 200mg/dl after 2 hours (2 marks)
(6) Diabetic symptoms with casual Glucose level more than 200mg/dl (2 marks)

02.

(1) Lesch-Nyhan syndrome (2 marks)
(2) HGPRTase deficiency (2 marks)
(3) Due to HGPRTase deficiency, the Salvage pathway of purine synthesis (guanine and hypoxanthine) is not efficient. This causes an accumulation of PRPP, resulting in an excess production of uric acid, which causes hyperuricemia leading to the accumulation of sodium urate crystals in joints leading to gout. (6 marks)

03.

(1) The presence of bile pigments (conjugated bilirubin) in urine. Ex-bilirubin, biliverdin (1 mark)
(2) Yellowish discoloration of skin, mucus membranes, and sclera (2 marks)
(3) Post hepatic jaundice (obstructive jaundice) (1 mark)
(4) Usually, CB that enters the duodenum is converted by gut bacteria into urobilinogen and stercobilinogen (major fate). Stercobilinogen oxidizes to stercobilin which is responsible for the characteristic colour of faeces. This patient suffers from a cancer in the head of the pancreas. Therefore, CB does not reach the intestine. Due to low stercobilinogen levels in faces, stools will appear pale and clay-coloured. (4 marks)
(5) As UCB is bound to albumin it can't be filtered across the glomerular capillary membrane, so UCB does not appear in urine. (2 marks)

04.

(1) PCR (3 marks)
(2) Child 1 is not the father's child (3 marks)
(3) Restriction fragment length polymorphism (RFLP) (2 marks)
(4) Tandem repeats are short sequences of DNA scattered throughout the genome; repeated units are unique to any given person but different from person to person (2 marks)

05.

(1) A – Chylomicrons
B – LDL
C – VLDL
D – HDL (2 marks)

(2) D>B>C>A (2 marks)

(3) A – transports dietary lipids to body tissues including the liver
B – transports cholesterol to peripheral tissues
C – transports endogenous TAG from the liver to extrahepatic tissues
D – transport cholesterol from peripheral tissues back to the liver (reverse cholesterol transport) (4 marks)

(4) A – Apo B-48, Apo CII and Apo E
B – Apo B-100
C – Apo B-100, Apo CII and Apo E
D – Apo AI, reservoir for Apo CII and Apo E (2 marks)

06.

(1) Alkaptonuria (2 marks)

(2) Accumulation and excretion of homogentisic acid in urine which is oxidized to an Alkapton when exposed to air. (3 marks)

(3) Homogentisate oxidase (2 marks)

(4) Arthritis due to blackening and then destruction of cartilage and connective tissue in the spine, hips, knees, and shoulders. (3 marks)

07.

(1) Glucose-6-phosphate dehydrogenase deficiency (1 mark)

(2) X-linked recessive (1 mark)

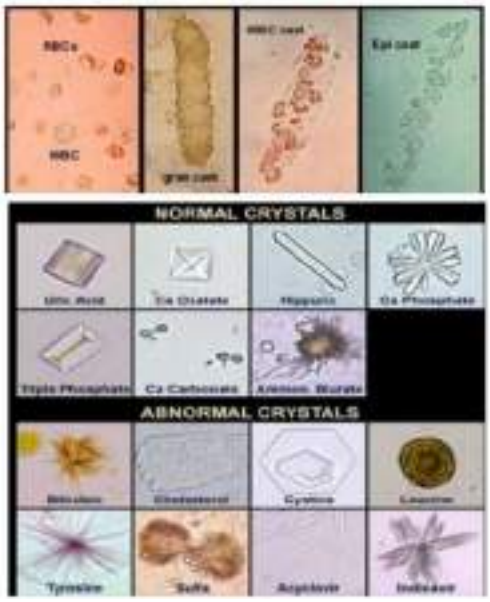
(3) Glucose 6 phosphate 

6-phosphogluconolactone (6PGL)
NADPH

(2 marks)

(4) G6PD is the key regulatory enzyme of the PPP. This is the sole pathway that synthesizes NADPH in red blood cells. NADPH is in red blood cells for the regeneration of reduced glutathione (GSH). GSH is an antioxidant essential to maintain normal red blood cell structure, keep Haemoglobin in the Fe^{+2} state, and prevent the formation of methaemoglobin. In the absence of GSH, RBC will undergo intravascular haemolysis on exposure to oxidative stress (due to the formation of methaemoglobin) resulting in jaundice. (4 marks)

(5) Favism
Exposure to certain chemicals ex – mothballs
Infections
Other drugs: Aspirin, Sulphonamides (antibiotic) (2 marks)



08.

(1) A – cholesterol crystals
B – uric acid crystals (2 marks)

(2) A – rhombic shape
B – haphazard shape (2 marks)

(3) Gout (2 marks)

(4) White blood cell cast (2 marks)

(5) Infections (2 marks)

09.

(1) Phenylalanine hydroxylase (1 mark)

(2) Phenylalanine $\xrightarrow{\text{phenylalanine hydroxylase}}$ Tyrosine (1 mark)

(3) Phenylalanine accumulates in body fluids and is metabolized into phenyl ketones such as phenylpyruvate, phenylacetate, and phenyl lactate. (3 marks)

(4) Brain damage, learning difficulties, epilepsy
Reason for impaired melanin synthesis: elevated Phe competitively inhibits tyrosinase enzyme.
Tyrosine -> DOPA -> Melanie (3 marks)

(5) Consume a diet low in Phe, and avoid aspartame (an artificial sweetener) (2 marks)

10.

(1) Due to overproduction of apo B containing lipoproteins by the liver (type IIb) (2 marks)

(2) Elevated LDL and VLDL (2 marks)

(3) Aspirin is a nonselective COX inhibitor (NSAID)
It irreversibly inhibits both COX 1 and Cox 2 enzymes.
COX 1: mainly found in platelets, produces thromboxane A2 (TXA_2). TXA_2 promotes platelet aggregation and vasoconstriction.
COX 2: mainly found in endothelial cells, produces prostacyclin - inhibits platelet aggregation, and stimulates vasodilation.
Platelet: lack a nucleus, unable to synthesize new Cox 2 enzyme once inhibited (takes around 4 days for new platelets to enter circulation)
Endothelial cells: contain nuclei, and are capable of producing new Cox 2 enzymes by gene expression.
The net effect of using aspirin – inhibits platelet aggregation and stimulates vasodilation
(6 marks)

BIOCHEMISTRY CONTINUOUS ASSESSMENT-2

2022/2023 (FIRST BATCH)

CAT- 2 (BATCH 1) MCQ PAPER

Uva Wellassa University

UVA WELLASSA UNIVERSITY
FACULTY OF MEDICINE

Continuous Assessment 02
March 2025
2022/2023 (01st) Batch
BIOCHEMISTRY (MCQ)

Time: 10.00 a.m. – 11.00 a.m. (01 hr.) **Date: 03.03.2025**

Please do not attempt or promote copying. No textbooks, notes, mobile phones, smart watches, or any other electronic communication devices are allowed.

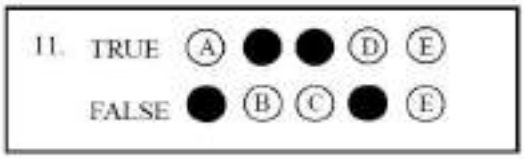
Please read the following instructions before marking responses on your answer sheets

1. Check that your question paper has total **06 pages** including the front page, which you are reading now.
2. **A single answer sheet is provided**. Please write your index number in the given space.
3. Read each question carefully before answering.
4. Mark the correct response as a **heavy black mark filling the relevant circle completely**, using a black lead pencil (6B or above grade).
5. Mark no stray marks on the answer sheet. In case of an error, erase cleanly.
6. Your final answer should be a densely colored circle through which the underlying letter is not visible.
7. Marking using any other method (e.g., mark the circle with a cross) is not valid.

TEN (10) TRUE/FALSE TYPE QUESTIONS (Pages 1 to 3)

1. Mark whether each response is true or false.
2. Given below is an example of how to mark a true/false type question.

1. Woman has
   - A. one ovary.
   - B. one nose
   - C. two ears
   - D. one eye
   - E. two hairs



A correct response will get +1 mark
An incorrect response will get -1 mark
No response will get zero mark
Negative marks will not be carried over

TEN (10) SINGLE BEST CHOICE TYPE QUESTIONS (Pages 4 to 6)

1. Mark the best response. Only one response per question should be marked.
2. If you mark the correct response, you will get the full marks for the question.
3. If you mark an incorrect response, fail to mark any response, select more than one response, or mark your response unclearly, you will not receive any marks for that question.
4. Given below is an example of how to mark a single best response type question.

16. Speaking is a unique ability observed in humans. Which of the following body parts is primarily used for speech production?

   - A. Tongue
   - B. Hands
   - C. Feet
   - D. Ears
   - E. Nose



Question numbers 01 to 10 are True or False type questions. Mark your answer each of the 5 responses (A to E).

1. True or false regarding glucokinase?
   A. In pancreatic β cells, glucokinase acts as the glucose sensor.
   B. It has a much lower K_m value than hexokinase.
   C. It is an isoenzyme of the hexokinase group.
   D. It is the predominant enzyme for glucose phosphorylation in the liver.
   E. The lower V_{max} of the enzyme minimizes hyperglycaemia during the absorptive perio

2. Activators of pyruvate dehydrogenase (PDH) complex includes
   A. acetyl CoA
   B. ATP
   C. insulin
   D. Mg^{2+}
   E. NADH

3. Substrates for the reaction catalysed by alanine aminotransferase includes
   A. alanine
   B. ammonia
   C. glutamate
   D. pyruvate
   E. α-ketoglutarate

4. Which of the following enzymes of the urea cycle is/are located in mitochondria?
   A. Arginase
   B. Argininosuccinate synthase I (ASSI)
   C. Arginosuccinate lyase
   D. Carbamoyl phosphate synthetase I (CPS I)
   E. Ornithine transcarbamoylase

5. Which of the following amino acids is/are converted to metabolites that serve as vasodila
   A. Arginine
   B. Glycine
   C. Histidine
   D. Phenylalanine
   E. Tyrosine

6. Which of the following is/are bile salts?
   A. Bilirubin
   B. Glucuronic acid
   C. Glycocholic acid
   D. Stercobilinogen
   E. Taurochenodeoxycholic acid

7. Which of the following is/are energy donors in biochemical reactions?
   A. Adenosine triphosphate
   B. Coenzyme A
   C. Flavin adenine dinucleotide
   D. Guanosine triphosphate
   E. Nicotinamide adenine dinucleotide

8. Which of the following amino acids is/are required for **both** purine and pyrimidine synthesis?
   A. Aspartic acid
   B. Glutamine
   C. Glycine
   D. Phenylalanine
   E. Tryptophan

9. Which of the following cells remain in the G1 phase of the life cycle?
   A. Cardiomyocytes
   B. Fibroblasts
   C. Hematopoietic stem cells
   D. Skeletal muscle cells
   E. Nerve cells

10. Which of the following statements is/are true regarding applications of gene therapy?
   A. Introducing a functional copy of the mutated gene is used to correct genetic defects.
   B. Heritable genetic changes are caused by somatic gene therapy.
   C. CRISPR-Cas9 is a genome-editing tool.
   D. It is applied to reprogram immune responses to prevent self-attack in autoimmune diseases.
   E. Viral vectors are used for gene delivery.

Questions number 11 to 20 are Single Best Response (SBR) type. Select the best response to each question.

11. A 25-year-old male presented to the emergency department with complaints of fatigue, and passing dark-coloured urine (tea-coloured urine) which started two days after taking an antibiotic for a respiratory tract infection. On examination, he was pale and icteric, with mild splenomegaly.
Laboratory investigations revealed haemoglobin of 8 g/dL, elevated lactate dehydrogenase (LDH), increased indirect bilirubin, and the presence of Heinz bodies on peripheral blood smear.

Which of the following deficiency best explains the underlying mechanism causing his symptoms?
A. Glucose 6-phosphate
B. NADPH
C. Reduced form of glutathione
D. Ribose 5-phosphate
E. Ribulose 5-phosphate

12. A 3-day-old newborn was brought to the emergency department with vomiting, poor feeding, and lethargy. On physical examination, the baby was jaundiced with hepatomegaly.
Laboratory investigations showed hypoglycaemia, elevated liver enzymes, and metabolic acidosis. Urinalysis showed the presence of reducing substances. Further inquiry revealed that the baby was started on formula feeding shortly after birth.

Which of the following is the most likely enzyme deficiency responsible for this condition?
A. Aldolase reductase
B. Galactokinase
C. Galactose-1-phosphate uridyltransferase (GALT)
D. UDP-Glucose pyrophosphorylase
E. UDP-Hexose 4-epimerase

13. A 52-year-old man with a 15-year history of poorly controlled type 2 diabetes mellitus presented to the clinic with complaints of swelling in his ankles and frothy urine.
Laboratory investigations revealed elevated serum creatinine, reduced estimated glomerular filtration rate (eGFR), and significant proteinuria (>3.5 g/day).

Which of the following biochemical process mostly contributes for the above-mentioned signs and symptoms?
A. Accumulation of advanced glycation end-products (AGEs)
B. Activation of protein kinase C (PKC)
C. Activation of the hexosamine pathway
D. Increased aldose reductase activity (polyol pathway)
E. Increased synthesis of mevalonate

14. A 5-day-old full-term newborn was brought to the clinic due to yellowish discoloration of the skin and eyes for the last two days. The baby had been delivered vaginally without complications. He had been breastfeeding well and had normal urine output and bowel opening.
On examination, he was active with no signs of lethargy, hypotonia, or poor feeding. Jaundice was noted up to the chest (Kramer zone 3). Vital signs were stable, and no hepatosplenomegaly was detected.

Which of the following is the most likely cause?

A. Biliary atresia
B. Congenital hypothyroidism
C. Haemolytic disease of the newborn (HDN)
D. Neonatal sepsis
E. Physiological jaundice of the newborn

15. A 25-year-old woman with a history of type 1 diabetes mellitus presented to the emergency department with nausea, vomiting, rapid breathing, and abdominal pain. On examination, she was dehydrated and had a fruity odour on her breath.
Laboratory tests revealed hyperglycaemia, metabolic acidosis with an increased anion gap, and positive serum ketones.

Which of the following biochemical process is primarily responsible for her ketoacidosis?
A. Accumulation of triglycerides in liver cells, causing liver dysfunction.
B. Excessive glycogenolysis that leads to ketone accumulation.
C. Increased hepatic gluconeogenesis depleting oxaloacetate, promoting ketogenesis.
D. Increased lipolysis leading to elevated free fatty acids.
E. Tissue hypoperfusion leading to lactic acidosis.

16. A 45-year-old man with a strong family history of premature heart disease presented for evaluation of chest discomfort during exertion.
His lipid profile showed total cholesterol of 280 mg/dL (< 200 mg/dL), triglyceride of 140 mg/dL (<150 mg/dL), and LDL cholesterol of 250 mg/dL (<150 mg/dL), despite maintaining a healthy diet and aerobic exercise routine.

What is the most likely biochemical defect contributing to his condition?

A. Decreased clearance of LDL from blood
B. Elevated chylomicrons due to impaired lipoprotein lipase activity
C. Excessive secretion of very low-density lipoproteins
D. Impaired fatty acid oxidation due to mitochondrial dysfunction
E. Increased reverse cholesterol transport

17. A 10-year-old boy presented with progressive myopia, intellectual disability, and frequent thrombotic events. On examination, he had lens dislocation (downward), tall stature, long limbs, and pectus excavatum. Laboratory tests showed elevated plasma homocysteine and methionine levels.

Which of the following is the most likely enzyme deficiency responsible for his condition?
A. Branched-chain α-ketoacid dehydrogenase
B. Cystathionine β-synthase (CBS)
C. Homogentisate oxidase
D. Phenylalanine hydroxylase
E. Tyrosinase

18. A newborn is being screened for sickle cell anaemia due to a family history of the disease. The physician recommends a molecular diagnostic test using restriction fragment length polymorphism (RFLP) analysis.

Which of the following feature of RFLP helps in identifying sickle cell anaemia?

A. Its ability to detect abnormal haemoglobin protein structure using electrophoresis
B. Its ability to detect the loss of restriction site due to Glu → Val mutation in β globin gene (HBB)
C. Its ability to amplify the β-globin gene using PCR and sequences the mutation directly
D. Its ability to quantify haemoglobin fractions to distinguish HbS from HbA
E. Its ability to use fluorescent probe to hybridize the site of mutation

19. A 04 month-old baby was brought to the clinic with poor feeding, irritability, and a musty body odour. On examination, the baby had fair skin, and eczema and delayed development milestones. Laboratory tests showed elevated serum phenylalanine levels.

Which of the following enzyme deficiency is responsible for this condition?
A. Tyrosine aminotransferase
B. Dihydropteridine reductase
C. Homogentisate oxidase
D. Phenylalanine hydroxylase
E. Fumarylacetoacetate hydrolase

20. Urea cycle defects (UCDs) are inherited metabolic disorders characterized by the impaired ability to detoxify ammonia.

Which of the following biochemical abnormality is the most characteristic of urea cycle defects (UCDs)?
A. Hyperammonaemia with elevated lactate and pyruvate
B. Hyperammonaemia with elevated orotic acid in urine
C. Hyperammonaemia with hyperglycaemia and increased ketone bodies
D. Hyperammonaemia with metabolic acidosis and ketosis
E. Hyperammonaemia with increased blood urea nitrogen (BUN)

CAT- 2 (BATCH 1) MCQ ANSWERS

(1) True or false regarding glucokinase?

(A) In pancreatic β cells, glucokinase acts as the glucose sensor – **True,** regulates insulin secretion in response to blood glucose.
(B) It has a much lower Km value than hexokinase – **False,** glucokinase has a higher Km than hexokinase.
(C) It is an isoenzyme of the hexokinase group – **True,** glucokinase is hexokinase IV.
(D) It is the predominant enzyme for glucose phosphorylation in the liver – **True,** main hepatic enzyme after meals.
(E) The lower Vmax of the enzyme minimizes hyperglycaemia during the absorptive period – **False,** glucokinase has a high Vmax.

(2) Activators of pyruvate dehydrogenase (PDH) complex?

(A) Acetyl CoA – **False,** end-product inhibitor of PDH.
(B) ATP – **False,** high-energy state inhibits PDH.
(C) Insulin – **True,** activates PDH phosphatase.
(D) Mg^{2+} – **True,** required for PDH phosphatase activity.
(E) NADH – **False,** product inhibition of PDH.

(3) Substrates for alanine aminotransferase?

(A) Alanine – **True,** amino group donor in transamination.
(B) Ammonia – **False,** not used in transamination reactions.
(C) Glutamate – **False,** product not substrate of ALT.
(D) Pyruvate – **True,** keto-acid partner of alanine.
(E) α-Ketoglutarate – **True,** amino group acceptor forming glutamate.

(4) Urea cycle enzymes located in mitochondria?

(A) Arginase – **False,** cytosolic enzyme.
(B) Argininosuccinate synthase I – **False,** cytosolic enzyme.
(C) Argininosuccinate lyase – **False,** cytosolic enzyme.
(D) Carbamoyl phosphate synthetase I – **True,** mitochondrial enzyme.
(E) Ornithine transcarbamoylase – **True,** mitochondrial enzyme.

(5) Amino acids converted to vasodilator metabolites?

(A) Arginine – **True,** forms nitric oxide.
(B) Glycine – **False,** no vasodilator metabolite.
(C) Histidine – **True,** forms histamine.
(D) Phenylalanine – **False,** no vasodilator product.
(E) Tyrosine – **False,** catecholamines are mainly vasoconstrictors.

(6) Bile salts?

(A) Bilirubin – **False,** bile pigment.
(B) Glucuronic acid – **False,** conjugates bilirubin, not bile acids.
(C) Glycocholic acid – **True,** conjugated bile salt.

(D) Stercobilinogen – **False,** faecal bile pigment.
(E) Taurochenodeoxycholic acid – **True,** conjugated bile salt.

(7) Energy donors in biochemical reactions?
(A) Adenosine triphosphate – **True,** universal energy donor.
(B) Coenzyme A – **False,** transfers acyl groups.
(C) Flavin adenine dinucleotide – **False,** electron carrier.
(D) Guanosine triphosphate – **True,** energy donor in specific reactions.
(E) Nicotinamide adenine dinucleotide – **False,** redox carrier.

(8) Amino acids required for both purine and pyrimidine synthesis?
(A) Aspartic acid – **True,** contributes atoms to both.
(B) Glutamine – **True,** nitrogen donor in both pathways.
(C) Glycine – **False,** required only for purines.
(D) Phenylalanine – **False,** not involved.
(E) Tryptophan – **False,** not involved.

(9) Cells remaining in G1 (G0) phase?
(A) Cardiomyocytes – **True,** permanent cells.
(B) Fibroblasts – **False,** capable of division.
(C) Hematopoietic stem cells – **False,** actively dividing.
(D) Skeletal muscle cells – **True,** permanent cells.
(E) Nerve cells – **True,** permanent cells.

(10) Applications of gene therapy?
(A) Introducing a functional copy of the mutated gene – **True,** corrects genetic defects.
(B) Heritable genetic changes by somatic gene therapy – **False,** affects only somatic cells.
(C) CRISPR-Cas9 is a genome-editing tool – **True,** enables targeted gene editing.
(D) Reprogramming immune responses in autoimmune diseases – **True,** immunomodulatory applications exist.
(E) Viral vectors used for gene delivery – **True,** common method in gene therapy.

(1) **Best answer: C. Reduced form of glutathione**
Reason: G6PD deficiency → ↓ NADPH → ↓ reduced glutathione, causing oxidative damage, Heinz bodies, and haemolysis after drugs.

(2) **Best answer: C. Galactose-1-phosphate uridyltransferase (GALT)**
Reason: Classic galactosaemia presents after milk feeding with jaundice, hepatomegaly, hypoglycaemia, and reducing substances in urine.

(3) **Best answer: A. Accumulation of advanced glycation end-products (AGEs)**
Reason: AGEs cause basement membrane thickening and glomerulosclerosis leading to diabetic nephropathy and proteinuria.

(4) **Best answer: E. Physiological jaundice of the newborn**
Reason: Day 3–5 jaundice, healthy baby, no hepatosplenomegaly, due to immature UDP-glucuronyl transferase.

(5) **Best answer: C. Increased hepatic gluconeogenesis depleting oxaloacetate, promoting ketogenesis**
Reason: In DKA, oxaloacetate is diverted to gluconeogenesis, acetyl-CoA enters ketone body formation.

(6) **Best answer: A. Decreased clearance of LDL from blood**
Reason: Very high LDL with normal triglycerides suggests familial hypercholesterolaemia due to LDL receptor defect.

(7) **Best answer: B. Cystathionine β-synthase (CBS)**
Reason: Homocystinuria causes lens dislocation (downward), marfanoid habitus, thrombosis, ↑ homocysteine and methionine.

(8) **Best answer: B. Loss of restriction site due to Glu → Val mutation in β-globin gene**
Reason: Sickle cell mutation abolishes a restriction enzyme site, detected by RFLP.

(9) **Best answer: D. Phenylalanine hydroxylase**
Reason: Classic PKU presents with musty odour, fair skin, eczema, developmental delay, ↑ phenylalanine.

(10) **Best answer: B. Hyperammonaemia with elevated orotic acid in urine**
Reason: In UCDs (especially OTC deficiency), excess carbamoyl phosphate enters pyrimidine synthesis → ↑ orotic acid.

CAT- 2 (BATCH 1) SEQ PAPER

UVA WELLASSA UNIVERSITY
FACULTY OF MEDICINE

Continuous Assessment 02
March 2025
2022/2023 (01st) Batch
BIOCHEMISTRY (SEQ)

Time: 11.15 a.m. – 12.15 p.m. (01 Hour) Date: 03.03.2025

Index (MED) Number: .....

Instructions to candidates:

- This paper consists of two (02) Structured Essay Questions
- Answer all questions
- Write the answers in the space provided
- Write your index number in the space provided on each answer sheet
- Start each question on a new page

Q.1

1.1

a. List **four** gluconeogenic precursors. (10 marks)

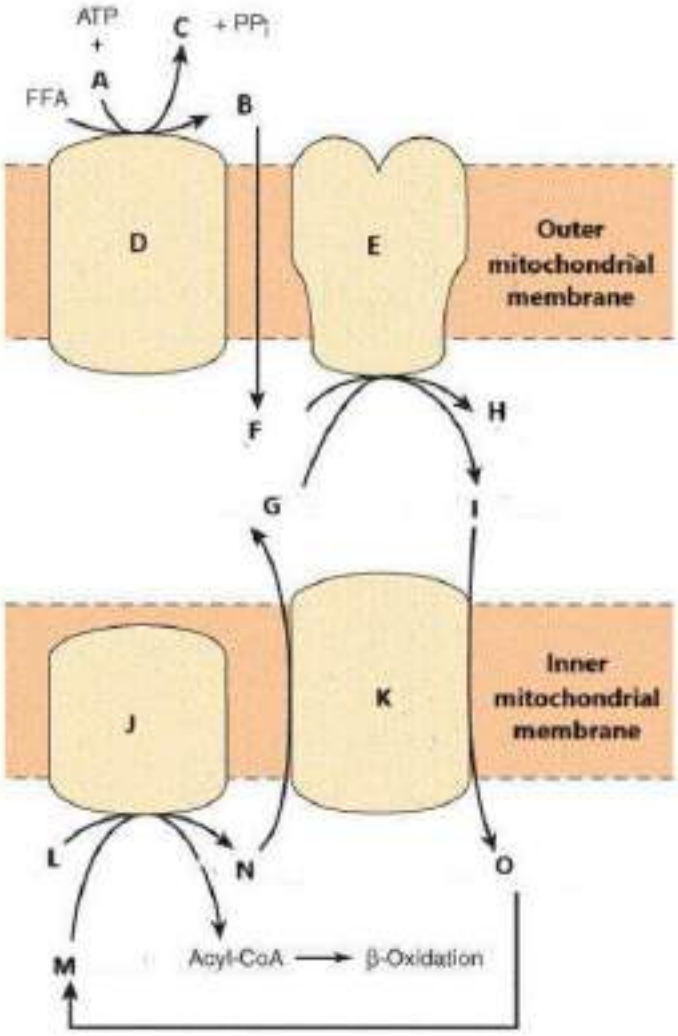
b. List **three** hormones which are antagonistic to insulin. (10 marks)

c. Outline the carbohydrate metabolism during fasting. (20 marks)

1.2.

a. Briefly illustrate (with a diagram) and outline the hormonal regulation of lipolysis in adipocytes. (30marks)

b. An illustration outlining the main steps of transport of long-chain fatty acids across the inner mitochondrial membrane is given. Identify the molecules/ enzymes denoted by letters A to O. (30 marks)



Q2. 2.1 Briefly explain the fate of heme molecules released from broken down red cells after completing their life span. (35 Marks)

2.2

a. Define porphyria. (10 Marks)

b. List **three** biochemical investigations for screening porphyria. (15 Marks)

2.3. Outline how the major metabolic pathways are integrated in the liver during the post-absorptive state. (40 Marks)

CAT -2 (BATCH 1) SEQ ANSWERS

UVA WELLASSA UNIVERSITY
FACULTY OF MEDICINE

Continuous Assessment 02
March 2025
2022/2023 (01st) Batch
BIOCHEMISTRY (SEQ)

Time: 11.15 a.m. – 12.15 p.m. (01 Hour) Date: 03.03.2025

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Q.1

1.1

a. List **four** gluconeogenic precursors. (10 marks)

2.5- Lactate, pyruvate, glycerol, α-ketoacids, propionate, fatty acids

01 – glutamine, amino acids,

b. List **three** hormones which are antagonistic to insulin. (10 marks)

Epinephrine, norepinephrine, cortisol, growth hormone, thyroid hormone

c. Outline the carbohydrate metabolism during fasting. (20 marks)

1*20 2*10

The liver first uses glycogen degradation and then gluconeogenesis to blood glucose levels to sustain energy metabolism of the brain and other glucose-requiring tissues in the fasted (postabsorptive) state.

1. **Increased glycogen degradation**

- During the brief absorptive period, ingested glucose is the major source of blood glucose.
- Several hours later, blood glucose levels have declined sufficiently to cause

increased secretion of glucagon and decreased release of insulin.

- The increased glucagon to insulin ratio causes a rapid mobilization of liver glycogen stores (which contain about 80 g of glycogen in the fed state) due to phosphorylation (activation) of glycogen phosphorylase
- liver glycogen is nearly exhausted after 10–18 hours of fasting
- therefore, hepatic glycogenolysis is a transient response to early fasting.

2. Increased gluconeogenesis

- The synthesis of glucose and its release into the circulation are vital hepatic functions during fasting
- The carbon skeletons for gluconeogenesis are derived primarily from glucogenic amino acids and lactate from muscle and glycerol from adipose.
- Gluconeogenesis, favored by activation of fructose 1,6-bisphosphatase (due to a drop in its inhibitor, fructose 2,6-bisphosphate) and by induction of phosphoenolpyruvate (PEP) carboxykinase by glucagon begins 4–6 hours after the last meal and becomes fully active as stores of liver glycogen are depleted
- Gluconeogenesis plays an essential role in maintaining blood glucose during both over night and prolonged fasting.

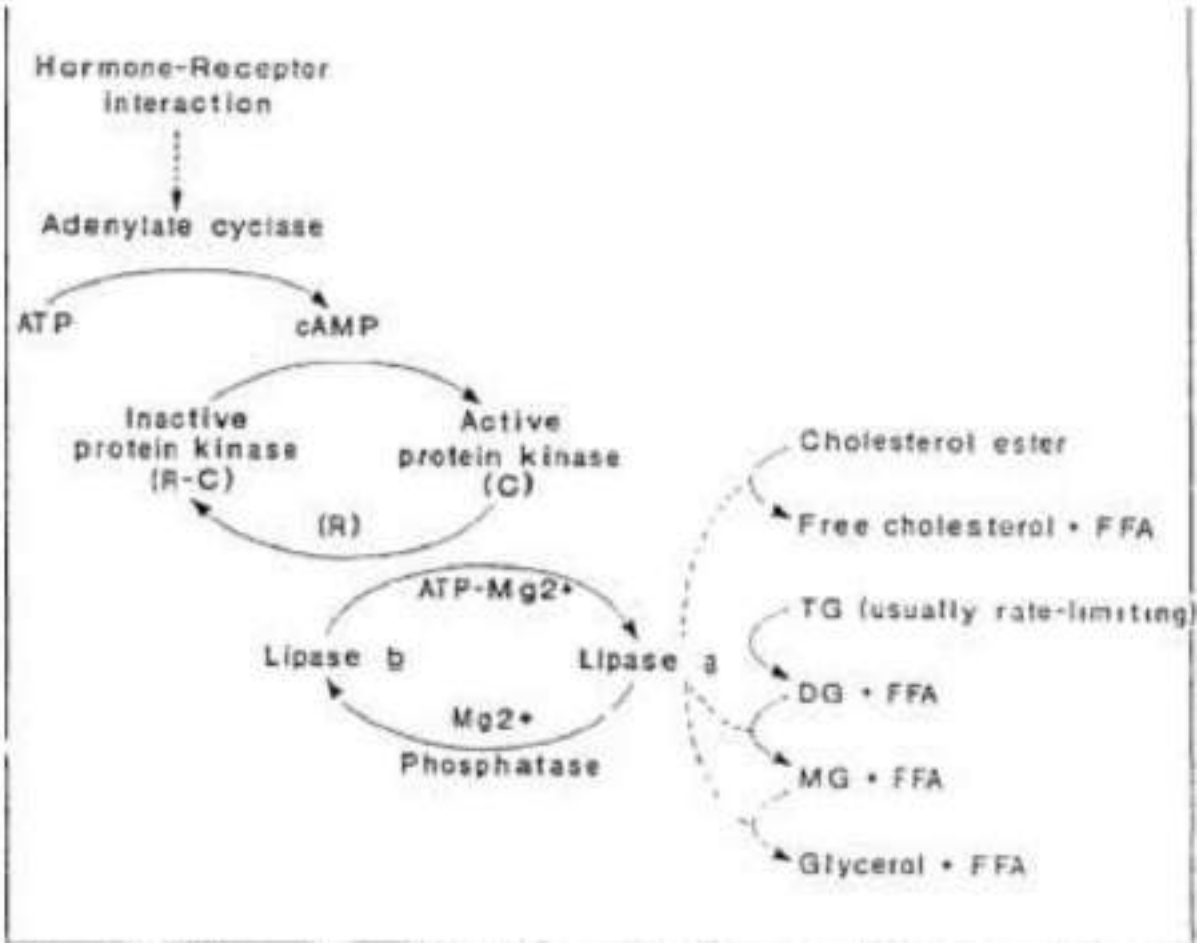
1.2.

a. Briefly illustrate (with a diagram) and outline the hormonal regulation of lipolysis in adipocytes. (30marks)

10*2 Marks

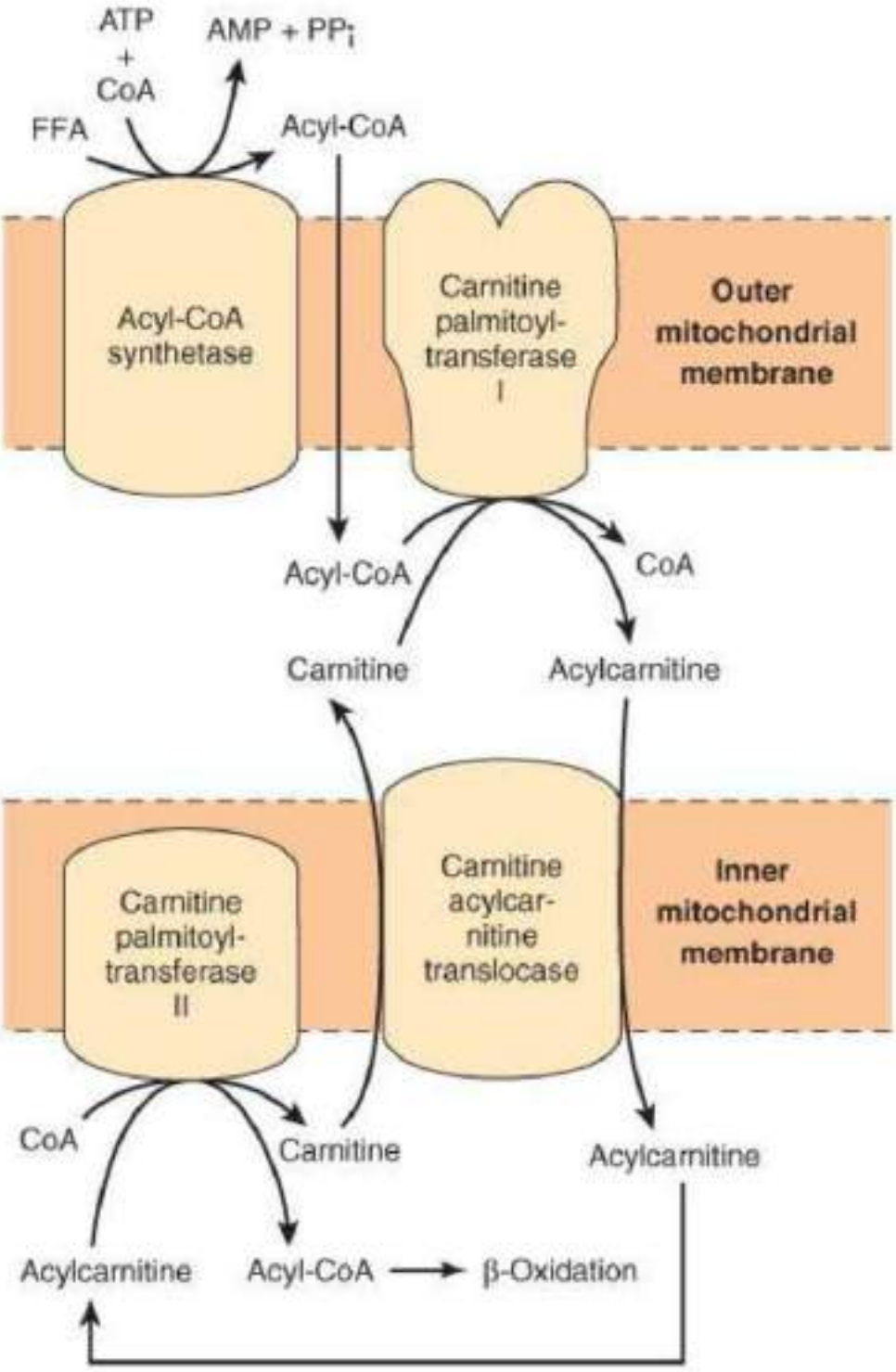
- (Activation of hormone-sensitive lipase (HSL)
- This enzyme is activated when phosphorylated by a 3 ',5 '-cyclic AMP(cAMP)–dependent protein kinase.
- 3',5'-Cyclic AMP is produced in the adipocyte when one of several hormones (such as epinephrine or glucagon) binds to receptors on the cell membrane, and activates adenylyl cyclase
- Because acetyl CoA carboxylase is inhibited by hormone-directed phosphorylation when the cAMP-mediated cascade is activated, fatty acid synthesis is turned off when TAG degradation is turned on.
- In the presence of high plasma levels of insulin and glucose, HSL is dephosphorylated, and becomes inactive.

For a meaningful clear illustration 10 marks


Hormone-Receptor
interaction
Adenylate cyclase
ATP
cAMP
Inactive
protein kinase
(R-C)
Active
protein kinase
(C)
(R)
ATP-Mg2+
Lipase b
Lipase a
Mg2+
Phosphatase
Cholesterol ester
Free cholesterol + FFA
TG (usually rate-limiting)
DG + FFA
MG + FFA
Glycerol + FFA

b. An illustration outlining the main steps of transport of long-chain fatty acids across the inner mitochondrial membrane is given. Identify the molecules/ enzymes denoted by letters A to O. (30 marks)

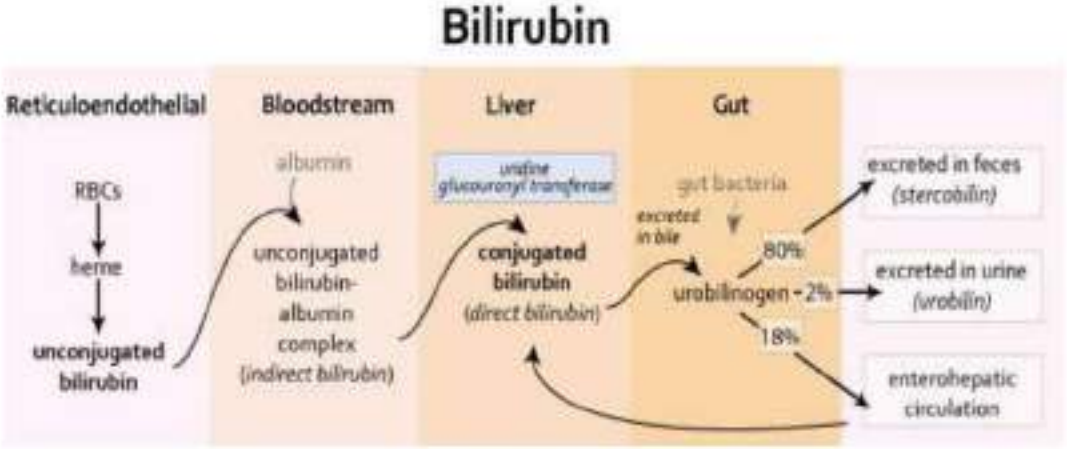
A. CoA
B. Acetyl CoA
C. AMP
D. Acyl-CoA synthetase
E. Carnitine palmitoyl-transferase I
F. Acetyl CoA
G. Carnitine
H. CoA
I. Acylcarnitine
J. Carnitine palmitoyl-transferase II
K. Carnitine acylcarnitine translocase
L. CoA
M. Acylcarnitine
N. Carnitine
O. Acylcarnitine


ATP
+
CoA
AMP + PPi
FFA
Acyl-CoA
Acyl-CoA synthetase
Carnitine palmitoyl-transferase I
Outer mitochondrial membrane
Acyl-CoA
CoA
Carnitine
Acylcarnitine
Carnitine palmitoyl-transferase II
Carnitine acylcar-nitine translocase
Inner mitochondrial membrane
CoA
Carnitine
Acylcarnitine
Acylcarnitine
Acyl-CoA
β-Oxidation

Q2. 2.1 Briefly explain the fate of heme molecules released from broken down red cells after completing their life span. (35 Marks)

22*1.5 Marks (2*16)+3

- breakdown of heme to bilirubin in macrophages of the reticuloendothelial system
- unconjugated bilirubin transported to the liver through blood bound to albumin
- bilirubin is taken up via facilitated diffusion (03 marks) by the liver
- conjugated with glucuronic acid
- active secretion of conjugated bilirubin in to bile
- secretion in to the intestine
- removal of glucuronic acid by the bacteria in the intestine
- conversion of bilirubin in to urobilinogen
- reabsorption of some of the urobilinogen from the gut
- enters portal blood
- a portion of urobilinogen participate in the **enterohepatic urobilinogen cycle**
- The remainder of the urobilinogen is transported by the blood to the kidney
- is converted to yellow urobilin and **excreted, giving urine** its characteristic color.
- Urobilinogen is oxidised to brown stercobilin by intestinal bacteria, **excreted in feces**



2.2

a. Define porphyria. (10 Marks)

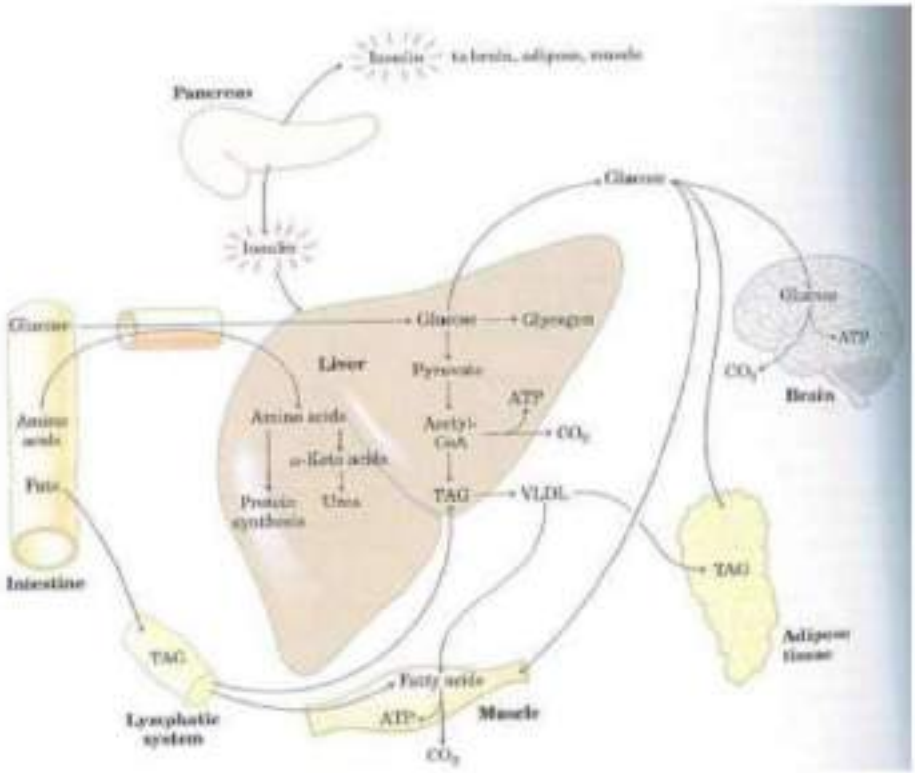
Porphyrias are rare, inherited (or occasionally acquired)
defects in heme synthesis,
resulting in the accumulation and increased excretion of porphyrins or porphyrin precursors

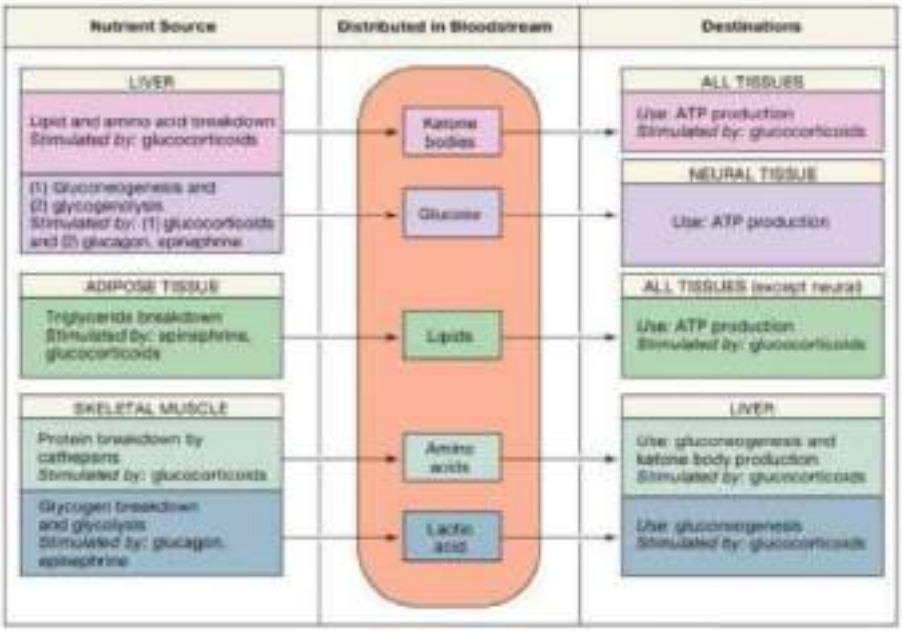
b. List **three** biochemical investigations for screening porphyria. (15 Marks)

δ-aminolevulinic acid (ALA)
porphobilinogen (PBG)
uroporphyrins
coproporphyrins
porphyrins

2.3. Outline how the major metabolic pathways are integrated in the liver during the post-absorptive state. (40 Marks)

16*2.5





- The **post-absorptive state** (4–12 hours after a meal) is characterized by a decline in blood glucose levels as dietary sources are depleted.
- The liver plays a central role in maintaining energy homeostasis by integrating several metabolic pathways

1. Glycogenolysis (Breakdown of Glycogen)

- The liver breaks down stored **glycogen** into glucose-6-phosphate.
- Glucose-6-phosphate is converted to free **glucose**, which is released into the bloodstream to maintain blood glucose levels.
- This process is stimulated by **glucagon** and **epinephrine** while **insulin** levels drop.

2. Gluconeogenesis (Synthesis of Glucose)

- As glycogen stores are depleted (after ~12 hours), the liver synthesizes glucose from:
    - **Amino acids** (from muscle protein breakdown)
    - **Lactate** (from anaerobic glycolysis in muscles and red blood cells)
    - **Glycerol** (from triglyceride breakdown in adipose tissue)
- This process is stimulated by **glucagon** and **cortisol**.

3. Lipid Metabolism (Fat Utilization)

- The liver increases **fatty acid oxidation**, breaking down fatty acids from adipose tissue.

- Fatty acids provide **acetyl-CoA**, which enters the **TCA cycle** for ATP production.
- When acetyl-CoA accumulates, the liver converts it into **ketone bodies** (ketogenesis), which serve as an alternative energy source for the brain and muscles.

4. Protein Metabolism

- Muscle proteins are broken down into **amino acids**, which enter the liver for gluconeogenesis.
- The liver removes excess nitrogen via the **urea cycle**, preventing ammonia toxicity.

5. Ketogenesis (Ketone Body Production)

- As fasting continues, **acetyl-CoA** from fatty acid oxidation is converted into **ketone bodies** (β-hydroxybutyrate, acetoacetate).
- Ketone bodies are released into circulation for energy use by the brain, muscles, and heart.

Metabolic Regulation in the Post-Absorptive State

- **Glucagon:** Stimulates glycogenolysis, gluconeogenesis, and lipolysis.
- **Epinephrine:** Enhances glycogen breakdown and fat mobilization.
- **Cortisol:** Promotes protein breakdown and gluconeogenesis.

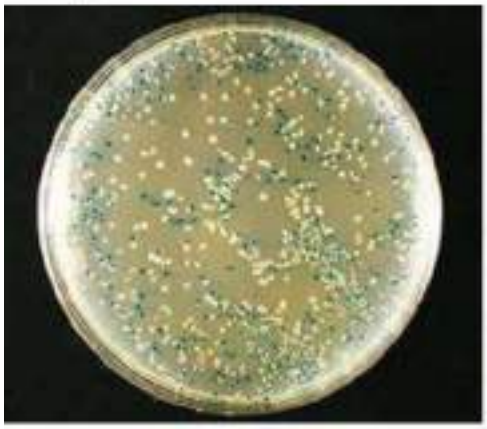
(Total 100 Marks)

CAT -2 (BATCH 1) OSPE PAPER

Continuous Assessment 2 (CAT 2)
MBBS-Academic year 2024-2025
Biochemistry
OSPE questions
Batch 01
Faculty of Medicine
Uva Wellassa University of Sri Lanka

Question 01

The diagram depicts a petri dish containing bacterial colonies grown on LB agar supplemented with ampicillin, X-gal, and IPTG. The bacteria were transformed using a pUC19 vector containing a foreign DNA insert.



a. State the role of **lacZ gene** (2.5 Marks)

b. Differentiate between recombinant and non-recombinant colonies on the plate. (2.5 Marks)

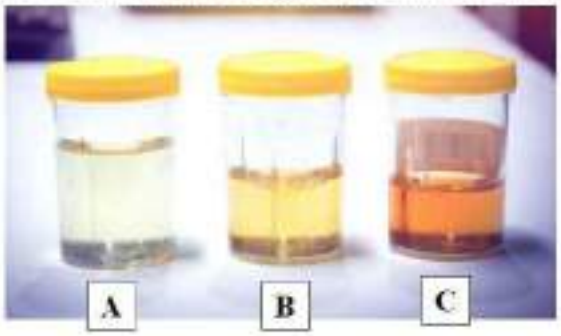
c. State the reason for including ampicillin in the medium. (2.5 Marks)

d. State a possible reason for the presence of only blue colonies. (2.5 Marks)

(Total: 10 Marks)

Question 02

You have provided 03 urine samples from 03 different subjects labeled A, B, and C. Report the appearance of each sample and comment about the hydration status of each subject.



Sample	Appearance	Hydration status
A		
B		
C		

(Total: 10 Marks)

Question 03

A urine sample from a 50-year-old patient presented with jaundice, dark-colored urine, and light-colored stools was sent to the laboratory. A 5 mL of the urine sample was taken and 1 mL of barium chloride (10%) reagent was added. The mixture was filtered to collect the precipitate and 1–2 drops of a solution of ferric chloride in trichloroacetic acid were added.



a. Observe the colour change. Based on this observation, what was the test most likely performed? (2.5 Marks)

b. Interpret the results. (2.5 Marks)

c. Name two diseases that give similar results that you observed. (5.0 Marks)

(Total: 10 Marks)

Question 04

Based on the provided information, identify the medical condition and answer the questions that follow.

A 3-year-old girl was presented with the symptoms including lethargy, vomiting, irritability, poor appetite, and seizures after meals. It was informed that she has a cousin with a metabolic disorder.

Lab Results:

- Serum ammonia : 200 µmol/L (Normal: 11 to 32 µmol/L)
- Urine Orotic Acid : Elevated
- Amino Acid Profile : low citrulline & arginine, high glutamine

a. What is the most likely medical condition affecting this subject? (5.0 Marks)

b. What is the primary cause for this condition? (5.0 Marks)

(Total: 10 Marks)

Question 05

A urine sample from a patient was tested using Rothera's test. The result showed a purple-colored ring at the junction of the liquids.



a. What is the purpose of Rothera's test? (2.5 Marks)

b. Which compound is responsible for the coloured ring? (2.5 Marks)

c. Name two conditions where this test is likely to give a positive result. (5.0 Marks)

(Total: 10 Marks)

Question 06

A 5-year-old boy was brought to the clinic due to concerns about his very light skin, white hair, and pale blue eyes since birth. His parents mention he often squints in bright light and has blurry vision. There's no known family history of similar conditions. On examination, he shows signs of photophobia and reduced visual acuity.

Questions

1. What is the most likely medical condition? (5.0 Marks)
2. What is the underlying cause of this condition? (5.0 Marks)

(Total: 10 Marks)

Question 07

A 5-year-old boy presented with recurrent episodes of lethargy, vomiting, and dizziness, especially after consuming fruits, honey, or sweets. Occasional hypoglycaemic episodes. He has an older sibling with a history of intolerance to fruity foods.

Lab Results:

- Urine Reducing Sugars : Positive
- Urine Glucose (Dipstick Test) : Negative
- Seliwanoff's Test : Positive
- Benedict's Test : Positive

a. What is the most likely medical condition affecting this child? (2.5 Marks)

b. Which biochemical tests help to differentiate between glucose, fructose, and galactose in urine? (2.5 Marks)

c. What is the enzymatic defect responsible for this condition? (2.5 Marks)

d. What dietary advice would you give to manage this disorder? (2.5 Marks)

(Total: 10 Marks)

Question 08

A 52-year-old male subject attended the family physician complaining of fatigue, occasional chest pain, and a family history of cardiovascular disease. He leads a sedentary lifestyle and frequently consumes fatty foods.

Physical Examination: BMI: 30 kg/m^2 ,Blood Pressure: 150/95 mmHg
Lab Results (Lipid Profile):

- Total Cholesterol : 280 mg/dL (Normal < 200 mg/dL)
- Triglycerides : 250 mg/dL (Normal <150 mg/dL)
- HDL-Cholesterol : 35 mg/dL (Normal >45 mg/dL)
- LDL-Cholesterol : 190 mg/dL (Normal <150 mg/dL)

a. What is the most likely medical condition? (5.0 Marks)

b. What lifestyle modifications would you recommend to manage his condition? (5.0 Marks)

(Total: 10 Marks)

Question 09

A 48-year-old female subject presented with increased thirst, frequent urination, fatigue, and unintentional weight loss over the past three months. She has a family history of type 2 diabetes mellitus.

Physical Examination: BMI: 32 kg/m², Blood Pressure: 145/90 mmHg
Lab Results:

- Fasting Plasma Glucose (FPG) : 160 mg/dL (Normal <100 mg/dL)
- HbA1c : 8.5% (Normal ≤ 6.5%)
- Urine Ketones : Negative

a. What is the most likely medical condition affecting this subject? (2.5 Marks)

b. How does HbA_{1c} help in assessing glycaemic control? (5.0 Marks)

c. What laboratory tests are used for monitoring diabetes complications? (2.5 Marks)

(Total: 10 Marks)

Question 10

A 45-year-old man presented with complaints of increased thirst, frequent urination, and fatigue for the past six months. He has a sedentary lifestyle and a family history of diabetes.
Physical Examination: BMI: 29 kg/m² (Overweight), Blood Pressure: 140/88 mmHg
Oral Glucose Tolerance Test (OGTT) Results:

- Fasting Plasma Glucose (FPG) : 105 mg/dL (Normal <100 mg/dL)
- 1-hour Plasma Glucose : 175 mg/dL (Normal <180 mg/dL)
- 2-hour Plasma Glucose : 160 mg/dL (Normal <140 mg/dL)
- Urine Glucose (2-hour sample) : Positive

a. What is the interpretation of this subject's OGTT results? (2.5 Marks)

b. What is the significance of the 'lag curve' in OGTT? (2.5 Marks)

c. What is the difference in the glucose metabolism between a normal subject and a person producing a lag curve? (2.5 Marks)

d. What is renal glycosuria, and how does it differ from diabetes-related glycosuria? (2.5 Marks)

(Total: 10 Marks)

CAT -2 (BATCH 1) OSPE ANSWERS

Question 01 – Blue-white screening (pUC19)

a. Role of lacZ gene

- Encodes β-galactosidase enzyme
- Enables blue-white screening by hydrolysing X-gal

b. Recombinant vs non-recombinant colonies

- Recombinant colonies: White (lacZ disrupted by foreign DNA insert)
- Non-recombinant colonies: Blue (intact lacZ gene → β-galactosidase produced)

c. Reason for including ampicillin

- Selects bacteria containing the plasmid with ampicillin-resistance gene
- Kills non-transformed bacteria

d. Reason for presence of only blue colonies

- No foreign DNA insertion
- Failed ligation or vector re-circularized without insert

Question 02 – Urine samples

Sample	Appearance	Hydration status
A	Pale yellow / clear	Well hydrated
B	Dark yellow	Dehydrated
C	Very dark / amber	Severely dehydrated

Question 03 – Urine bile salt test

a. Colour change & test performed

- Emerald green colour
- Hay's sulphur test (modified bile salt test)

b. Interpretation

- Bile salts present in urine
- Suggests obstructive (cholestatic) jaundice

c. Two diseases with similar results

- Carcinoma of head of pancreas

- Gallstones (extrahepatic biliary obstruction)

Question 04 – Urea cycle disorder

a. Most likely medical condition

- Ornithine transcarboxylase (OTC) deficiency

b. Primary cause

- Defect in OTC enzyme of urea cycle
- Leads to hyperammonaemia and elevated orotic acid

Question 05 – Rothera's test

a. Purpose

- Detection of ketone bodies in urine

b. Compound responsible for coloured ring

- Acetoacetate (and acetone to lesser extent)

c. Two conditions with positive test

- Diabetic ketoacidosis
- Prolonged fasting / starvation

Question 06 – Albinism

1. Most likely medical condition

- Oculocutaneous albinism

2. Underlying cause

- Tyrosinase deficiency
- Impaired conversion of tyrosine to melanin

Question 07 – Fructose metabolism disorder

a. Most likely medical condition

- Hereditary fructose intolerance

b. Tests differentiating glucose, fructose & galactose

- Seliwanoff's test

- Benedict's test

c. Enzymatic defect

- Aldolase B deficiency

d. Dietary advice

- Avoid fructose, sucrose, and sorbitol
- Strict dietary restriction

Question 08 – Dyslipidaemia

a. Most likely medical condition

- Mixed dyslipidaemia / hyperlipidaemia

b. Lifestyle modifications

- Low-fat, low-cholesterol diet
- Regular aerobic exercise
- Weight reduction
- Smoking cessation
- Limit alcohol intake

Question 09 – Diabetes mellitus

a. Most likely medical condition

- Type 2 diabetes mellitus

b. Role of HbA1c

- Reflects average blood glucose over past 2–3 months
- Indicates long-term glycaemic control
- Not affected by daily glucose fluctuations

c. Tests for monitoring complications

- Urine microalbumin
- Serum creatinine

Question 10 – OGTT

a. Interpretation of OGTT

- Impaired glucose tolerance (prediabetes)

b. Significance of lag curve

- Delayed insulin response
- Indicates early diabetes risk

c. Difference in glucose metabolism

- Normal: rapid insulin release and glucose uptake
- Lag curve: delayed insulin secretion and prolonged hyperglycaemia

d. Renal glycosuria

- Glucose in urine with normal blood glucose
- Due to low renal threshold, unlike diabetes where hyperglycaemia causes glycosuria

2023/2024 (SECOND BATCH)

CAT- 2 (BATCH 2) MCQ PAPER

Uva Wellassa University

UVA WELLASSA UNIVERSITY
FACULTY OF MEDICINE
Continuous Assessment 02
November 2025
2023/2024 (02nd) Batch
Biochemistry
Multiple Choice Questions (MCQ) Paper

Time 10.00 am – 11.00 am (01 hour) Date of the exam: 2025.11.10

Please do not attempt or promote copying. No textbooks, notes, mobile phones, smart watches, or any other electronic communication devices are allowed.

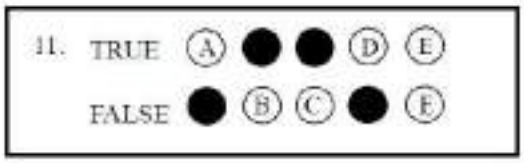
Please read the following instructions before marking responses on your answer sheets

1. Check that your question paper has a total of **06 pages**, including the front page.
2. **A single answer sheet is provided**. Please write your index number in the given space.
3. Read each question carefully before answering.
4. Mark the correct response as a **heavy black mark filling the relevant circle completely**, using a black lead pencil (6B or above grade).
5. Mark no stray marks on the answer sheet. In case of an error, erase cleanly.
6. Your final answer should be a densely coloured circle through which the underlying letter is not visible.
7. Marking using any other method (e.g., marking the circle with a cross) is not valid.

Ten (10) True or False Type Questions (Questions 1-10/Page 2-3)

1. Mark whether each response is true or false.
2. Given below is an example of how to mark a True or False type question.

Q 11. A woman has
- A. one ovary.
- B. one nose.
- C. two ears.
- D. one eye.
- E. two hairs.

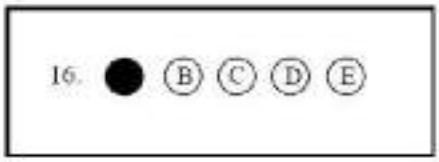


A correct response will get = +1 mark
An incorrect response will get = −1 mark
No response will get = 0 (zero) mark
Negative marks will not be carried over to the next question

Ten (10) Single Best Answer (SBA) Type Questions (Questions 11-20/ Page 4-6)

1. Mark the best response. Only one response per question should be marked.
2. If you mark the correct response, you will get the full marks for the question.
3. If you mark an incorrect response, fail to mark any response, select more than one response, or mark your response unclearly, you will not receive any marks for that question.
4. Given below is an example of how to mark a single best response type question.

Q 16. Speaking is a unique ability observed in humans. Which of the following body parts is primarily used for speech production?
- A. Tongue
- B. Hands
- C. Feet
- D. Ears
- E. Nose



1

Question no. 01 to 10 are True or False type questions. Mark your answer for each of the 5 responses (A to E).

1. True or False regarding maple syrup urine disease (MSUD)?
   A. Classic MSUD presents with symptoms in early adulthood.
   B. In dietary management, leucine should be avoided.
   C. In MSUD, the branched-chain α-keto acid dehydrogenase complex is affected.
   D. It is an autosomal recessive disorder.
   E. Nicotinamide supplementation is used as a therapy.

2. True or False regarding von Gierke's disease (glycogen storage disease type I)?
   A. It is caused by the deficiency of α-1,4-glucosidase.
   B. It leads to severe fasting hypoglycaemia.
   C. It presents with hyperuricemia.
   D. It primarily affects the skeletal muscle.
   E. There is excessive accumulation of glycogen in the liver.

3. True or False regarding homocystinuria?
   A. It increases the risk of stroke.
   B. It is an autosomal dominant disorder.
   C. It is due to a deficiency of methionine synthase.
   D. It presents with lens abnormalities.
   E. Vitamin B_3 (Niacin) supplementation is used as a treatment.

4. True or False regarding DNA Libraries?
   A. A cDNA library is constructed using tRNA as the starting material.
   B. A genomic DNA library contains both coding and non-coding sequences.
   C. cDNA libraries are useful for expressing eukaryotic proteins in bacteria.
   D. cDNA libraries contain introns and promoters.
   E. Genomic libraries are useful in studying gene regulation.

5. True or False regarding Restriction Fragment Length Polymorphism (RFLP)?
   A. It is used for DNA paternity testing.
   B. It is used to diagnose sickle cell anaemia.
   C. RFLP patterns are identical in individuals of the same family.
   D. Single-base substitutions create a restriction site.
   E. Tandem repeats cause RFLP variations.

6. True or False regarding vitamins act as coenzymes in the TCA cycle?
   A. Vitamin B_1 (Thiamine)
   B. Vitamin B_3 (Niacin)
   C. Vitamin B_5 (Pantothenic acid)
   D. Vitamin B_9 (Folic acid)
   E. Vitamin B_{12} (Cobalamin)

7. True or False regarding the end products formed at the end of one turn of the TCA cycle?
   A. CO_2
   B. $FADH_2$
   C. Lactic acid
   D. NADH
   E. Pyruvate

8. True or False regarding classic galactosemia?
   A. In this condition, glycolysis is affected.
   B. It is inherited in an autosomal recessive pattern.
   C. It leads to jaundice in neonates.
   D. It leads to the accumulation of galactitol in lens.
   E. The biochemical basis is the galactokinase deficiency.

9. Which of the following combinations of urinary biochemical findings are correctly matched with the related condition?

A.	Bile salts	- conjugated hyperbilirubinemia
B.	Bilirubin	- hemolytic jaundice
C.	Glucose	- glycosuria
D.	Monoclonal immunoglobulin light chains	- multiple myeloma
E.	Proteinuria	- renal glomerular damage

10. True or False regarding the cell cycle?
    A. During the G_1 phase DNA replication occurs.
    B. During the M phase, chromosomes are invisible under the microscope.
    C. p53 protein induce cell cycle arrest in response to DNA damage.
    D. The G_1/S checkpoint ensures that DNA replication is complete before mitosis begins.
    E. The progression through different phases of the cell cycle is regulated by Cyclin-dependent kinases (CDKs).

Question no. 11 to 20 are Single Best Answer (SBA) type. Select the best response to each question.

11. A 25-year-old male with a history of recurrent jaundice develops haemolytic anaemia after long term use of sulphonamide antibiotic.

    Which of the following best explains the underlying biochemical defect?
    A. Excess NADPH production
    B. Fructose-6-phosphate accumulation
    C. Impaired regeneration of reduced glutathione
    D. Ribose-5-phosphate deficiency
    E. Transketolase deficiency

12. A 58-year-old man with poorly controlled type 2 diabetes mellitus presents with gradual blurring of vision. He has not been taking his medication as prescribed by the clinician. Examination reveals bilateral lens opacities (cataract).

    Which of the following best explains the biochemical basis for the development of cataract in this patient?
    A. Accumulation of glycogen in the lens.
    B. Accumulation of sorbitol.
    C. Decreased activity of aldose reductase.
    D. Decreased NADH formation in the polyol pathway.
    E. Increased oxidation of fatty acids in the lens.

13. A 50-year-old woman with a family history of diabetes mellitus presents with borderline high fasting plasma glucose. The 2-hour post-load plasma glucose in OGTT is significantly elevated. Her physician also requests measurement of HbA1c.

    Which of the following best explains the biochemical basis for using HbA1c?
    A. HbA1c aids in the diagnosis of diabetic nephropathy.
    B. HbA1c assesses chronic hyperglycemia.
    C. HbA1c decreases in response to acute hypoglycemia.
    D. HbA1c measures the rate of insulin degradation.
    E. HbA1c reflects hepatic glycogen stores in diabetes mellitus.

14. A 35-year-old man presents with multiple yellowish papules over his elbows and knees and a strong family history of premature coronary artery disease. Laboratory investigations reveal markedly elevated plasma LDL-cholesterol levels, while triglycerides are normal.

    Which of the following best explains the biochemical basis of his condition?
    A. Decreased clearance of LDL due to defective LDL receptor-mediated endocytosis.
    B. Decreased secretion of VLDL by the liver.
    C. Increased activity of lipoprotein lipase in adipose tissue.
    D. Increased cholesterol excretion in bile.
    E. Increased synthesis of HDL due to enhanced Apo A-I production.

15. A 45-year-old obese woman with a history of high-fat diet presents with right upper quadrant pain after fatty meals. Ultrasound scan reveals gallstones. Laboratory investigations show normal liver enzyme levels.

Which of the following best explains the biochemical basis for gallstone formation in this patient?

A. Decreased bile pigment formation due to low bilirubin synthesis.
B. Decreased secretion of lecithin into bile.
C. Increased cholesterol secretion into bile.
D. Increased conjugation of bile acids with glycine and taurine.
E. Increased synthesis of bile salts leading to supersaturation.

16. A 20-year-old medical student skips meals for 24 hours while studying for an examination. Despite the prolonged fast, his blood glucose level remains within the normal range.

Which of the following biochemical process primarily helps maintain his blood glucose concentration during fasting?

A. Cholesterol synthesis
B. Fatty acid synthesis
C. Gluconeogenesis
D. Glycolysis
E. Utilization of ketone bodies

17. A 45-year-old man with uncontrolled type 1 diabetes mellitus presents with dehydration, deep labored breathing, and fruity odor in breath. Laboratory tests reveal hyperglycemia, ketonuria, and metabolic acidosis.

Which of the following best explains the biochemical basis for his metabolic state?

A. Decreased activity of hormone-sensitive lipase
B. Deficiency of Apo C-II
C. Increased gluconeogenesis and fatty acid oxidation
D. Increased glucose uptake in adipose and muscle tissue
E. Increased lipoprotein lipase activity

18. A 6-year-old boy presents with failure to thrive, developmental delay, and sparse (thin), depigmented, and kinky (tightly coiled) hair. His serum copper and ceruloplasmin levels are markedly reduced.

Which of the following best explains the biochemical basis of his condition?

A. Defective ceruloplasmin synthesis in the liver
B. Defective copper incorporation into cytochrome oxidase due to impaired copper transport
C. Impaired biliary copper excretion resulting in copper deposition in tissues
D. Increased copper absorption leading to hepatic accumulation
E. Overactivity of metallothionein in the liver

19. A 5-year-old boy presents with developmental delay, self-mutilating behavior, and gouty arthritis. Enzyme assay of erythrocytes reveals almost absent hypoxanthine-guanine phosphoribosyl transferase (HGPRT) activity.

Which of the following best explains the biochemical consequence of this enzyme deficiency?

A. Decreased purine synthesis due to reduced PRPP availability
B. Decreased salvage of pyrimidine bases
C. Decreased uric acid production due to reduced xanthine oxidase activity
D. Impaired conversion of uric acid to allantoin
E. Increased degradation of purines leading to uric acid overproduction

20. A researcher uses a bacterial enzyme that recognizes a specific palindromic DNA sequence at defined sites, producing fragments with "sticky ends" for insertion into a plasmid vector.

Which of the following enzyme is used in this process?

A. DNA ligase
B. DNA polymerase I
C. Restriction endonuclease
D. Reverse transcriptase
E. Topoisomerase

CAT- 2 (BATCH 2) MCQ ANSWERS

(Q1) True or False regarding maple syrup urine disease (MSUD)?

(A) Classic MSUD presents with symptoms in early adulthood – **False**, classic MSUD presents in the neonatal period with poor feeding and encephalopathy.

(B) In dietary management, leucine should be avoided – **True**, leucine is the most neurotoxic branched-chain amino acid and must be restricted.

(C) In MSUD, the branched-chain α-keto acid dehydrogenase complex is affected – **True**, deficiency of this enzyme complex causes accumulation of BCAAs.

(D) It is an autosomal recessive disorder – **True**, MSUD follows autosomal recessive inheritance.

(E) Nicotinamide supplementation is used as a therapy – **False**, thiamine (vitamin B_1) may help in some cases, not nicotinamide.

(Q2) True or False regarding von Gierke's disease (Glycogen storage disease type I)?

(A) It is caused by the deficiency of α-1,4-glucosidase – **False**, it is due to glucose-6-phosphatase deficiency.

(B) It leads to severe fasting hypoglycemia – **True**, inability to release free glucose causes profound fasting hypoglycemia.

(C) It presents with hyperuricemia – **True**, lactic acidosis reduces uric acid excretion leading to hyperuricemia.

(D) It primarily affects the skeletal muscle – **False**, it mainly affects the liver and kidney.

(E) There is excessive accumulation of glycogen in the liver – **True**, impaired glycogenolysis causes hepatomegaly.

(Q3) True or False regarding homocystinuria?

(A) It increases the risk of stroke – **True**, elevated homocysteine causes thrombosis and vascular events.

(B) It is an autosomal dominant disorder – **False**, classic homocystinuria is autosomal recessive.

(C) It is due to a deficiency of methionine synthase – **False**, most commonly due to cystathionine β-synthase deficiency.

(D) It presents with lens abnormalities – **True**, ectopia Lentis (downward and inward) is characteristic.

(E) Vitamin B_3 (Niacin) supplementation is used as a treatment – **False**, treatment includes vitamin B_6, folate, and vitamin B_{12}, not niacin.

(Q4) True or False regarding DNA libraries?

(A) A cDNA library is constructed using tRNA as the starting material – **False**, cDNA is synthesized from mRNA.

(B) A genomic DNA library contains both coding and non-coding sequences – **True**, it includes introns and regulatory regions.

(C) cDNA libraries are useful for expressing eukaryotic proteins in bacteria – **True**, absence of introns allows bacterial expression.
(D) cDNA libraries contain introns and promoters – **False**, cDNA contains only exons.
(E) Genomic libraries are useful in studying gene regulation – **True**, they contain promoters and regulatory elements.

(Q5) True or False regarding Restriction Fragment Length Polymorphism (RFLP)?
(A) It is used for DNA paternity testing – **True**, RFLP detects individual DNA variation.
(B) It is used to diagnose sickle cell anemia – **True**, the sickle mutation alters a restriction enzyme site.
(C) RFLP patterns are identical in individuals of the same family – **False**, patterns are similar but not identical (except identical twins).
(D) Single-base substitutions create a restriction site – **True**, point mutations may create or abolish restriction sites.
(E) Tandem repeats cause RFLP variations – **True**, variation in repeat length alters fragment size.

(Q6) True or False regarding vitamins acting as coenzymes in the TCA cycle?
(A) Vitamin B_1 (Thiamine) – **True**, thiamine pyrophosphate is a coenzyme for α-ketoglutarate dehydrogenase.
(B) Vitamin B_3 (Niacin) – **True**, NAD^+/NADH functions as an electron carrier in the TCA cycle.
(C) Vitamin B_5 (Pantothenic acid) – **True**, it forms part of Coenzyme A.
(D) Vitamin B_9 (Folic acid) – **False**, it is involved in one-carbon metabolism, not directly in the TCA cycle.
(E) Vitamin B_{12} (Cobalamin) – **False**, it is involved in methylmalonyl-CoA metabolism, not directly in the TCA cycle.

(Q7) True or False regarding the end products formed at the end of one turn of the TCA cycle?
(A) CO_2 – **True**, two molecules of CO_2 are released per turn of the TCA cycle.
(B) $FADH_2$ – **True**, one $FADH_2$ is produced during conversion of succinate to fumarate.
(C) Lactic acid – **False**, lactic acid is produced in anaerobic glycolysis, not in the TCA cycle.
(D) NADH – **True**, three molecules of NADH are generated per turn of the cycle.
(E) Pyruvate – **False**, pyruvate is converted to acetyl-CoA before entering the TCA cycle.

(Q8) True or False regarding classic galactosemia?
(A) In this condition, glycolysis is affected – **False**, the primary defect is in galactose metabolism, not glycolysis.
(B) It is inherited in an autosomal recessive pattern – **True**, classic galactosemia is autosomal recessive.

(C) It leads to jaundice in neonates – **True**, liver dysfunction causes neonatal jaundice.
(D) It leads to the accumulation of galactitol in lens – **True**, galactose is converted to galactitol causing cataracts.
(E) The biochemical basis is the galactokinase deficiency – **False**, classic galactosemia is due to galactose-1-phosphate uridyltransferase (GALT) deficiency.

(Q9) Correctly matched urinary biochemical findings with related condition?

(A) Bile salts – conjugated hyperbilirubinemia – **True**, bile salts appear in urine in obstructive (conjugated) jaundice.
(B) Bilirubin – hemolytic jaundice – **False**, unconjugated bilirubin is not excreted in urine.
(C) Glucose – glycosuria – **True**, glucose in urine defines glycosuria.
(D) Monoclonal immunoglobulin light chains – multiple myeloma – **True**, Bence Jones proteins are seen in multiple myeloma.
(E) Proteinuria – renal glomerular damage – **True**, glomerular injury increases protein leakage.

(Q10) True or False regarding the cell cycle?

(A) During the G_1 phase DNA replication occurs – **False**, DNA replication occurs in the **S phase**.
(B) During the M phase, chromosomes are invisible under the microscope – **False**, chromosomes are condensed and visible during mitosis.
(C) p53 protein induces cell cycle arrest in response to DNA damage – **True**, p53 activates DNA repair or apoptosis.
(D) The G_1/S checkpoint ensures that DNA replication is complete before mitosis begins – **False**, this is ensured by the G_2/M checkpoint.
(E) The progression through different phases of the cell cycle is regulated by cyclin-dependent kinases (CDKs) – **True**, CDKs with cyclins control cell cycle progression.

(Q11) 25-year-old male with hemolytic anemia after sulphonamide use,

Correct answer: C. Impaired regeneration of reduced glutathione

Explanation:
Sulphonamides cause oxidative stress. In **G6PD deficiency**, there is reduced NADPH production, leading to **failure to regenerate reduced glutathione**, resulting in oxidative damage to RBCs and hemolysis.

(Q12) 58-year-old diabetic with cataract,

Correct answer: B. Accumulation of sorbitol

Explanation:
In hyperglycemia, excess glucose in the lens is converted to **sorbitol via aldose reductase**.

Sorbitol accumulates (cannot diffuse out), causing osmotic damage and **cataract formation**.

(Q13) Measurement of HbA1c in diabetes,

Correct answer: B. HbA1c assesses chronic hyperglycemia

Explanation:
HbA1c reflects **average blood glucose over the previous 2–3 months**, based on non-enzymatic glycation of hemoglobin, making it a marker of long-term glycemic control.

(Q14) Xanthomas, high LDL, normal triglycerides,

Correct answer: A. Decreased clearance of LDL due to defective LDL receptor-mediated endocytosis

Explanation:
This presentation is typical of **familial hypercholesterolemia**, caused by defective LDL receptors, leading to **markedly elevated LDL cholesterol**, xanthomas, and premature coronary artery disease.

(Q15) Gallstone formation in an obese woman on a high-fat diet,

Correct answer: C. Increased cholesterol secretion into bile

Explanation:
Cholesterol gallstones form when bile becomes **supersaturated with cholesterol**, commonly due to increased hepatic cholesterol secretion (obesity, high-fat diet). This exceeds the solubilizing capacity of bile salts and lecithin.

(Q16) Maintenance of normal blood glucose after 24-hour fast,

Correct answer: C. Gluconeogenesis

Explanation:
After ~24 hours of fasting, **hepatic glycogen is depleted** and blood glucose is maintained mainly by **gluconeogenesis** from lactate, glycerol, and amino acids.

(Q17) Uncontrolled type 1 diabetes with ketoacidosis,

Correct answer: C. Increased gluconeogenesis and fatty acid oxidation

Explanation:
Insulin deficiency leads to increased **lipolysis**, fatty acid β-oxidation, and hepatic **ketone**

body production, along with increased gluconeogenesis—causing hyperglycemia and metabolic acidosis.

(Q18) Child with sparse kinky hair, low copper and ceruloplasmin,

Correct answer: B. Defective copper incorporation into cytochrome oxidase due to impaired copper transport

Explanation:
This describes **Menkes disease**, caused by impaired copper transport, leading to deficiency of copper-dependent enzymes (e.g., cytochrome c oxidase), resulting in neurodevelopmental delay and kinky hair.

(Q19) Child with Lesch–Nyhan syndrome (HGPRT deficiency),

Correct answer: E. Increased degradation of purines leading to uric acid overproduction

Explanation:
HGPRT deficiency impairs **purine salvage**, causing accumulation of PRPP and increased **de novo purine synthesis**, followed by excessive **purine degradation to uric acid**, resulting in hyperuricemia and gout.

(Q20) Enzyme producing sticky ends at palindromic DNA sequences,

Correct answer: C. Restriction endonuclease

Explanation:
Restriction endonucleases recognize **specific palindromic DNA sequences** and cleave them to produce **sticky (cohesive) ends**, facilitating insertion into plasmid vectors during recombinant DNA technology.

CAT- 2 (BATCH 2) SEQ PAPER

Uva Wellassa University

UVA WELLASSA UNIVERSITY
FACULTY OF MEDICINE
Continuous Assessment 02
November 2025
2023/2024 (02nd) Batch
Biochemistry
Structured Essay Questions (SEQ) Paper

Time 11.15 am – 12.15 pm (01 hour) Date of the exam: 2025.11.10

Index (MED) Number .....

Please do not attempt or promote copying. No textbooks, notes, mobile phones, smart watches, or any other electronic communication devices are allowed.

Instructions to Candidates

1. This paper contains two (02) Structured Essay Questions.
2. Answer all questions.
3. Write your answers in the spaces provided.
4. If additional space is required, you may use extra sheets. Ensure that the relevant question number is clearly indicated on each additional sheet.
5. Write your index number in the designated space on each answer sheet, including any extra sheets used.

Q1.

1.1.

A 3-day-old baby was brought to the neonatal intensive care unit with poor feeding, lethargy, and episodes of vomiting. His parents reported that he had been unusually sleepy since birth and had minimal interest in feeding. There were no signs of jaundice and hepatomegaly.

Laboratory findings:

- Elevated plasma ammonia levels
- Normal liver function tests
- Mild respiratory alkalosis
- Normal blood glucose
- Elevated urinary orotic acid

The paediatrician suspected a urea cycle disorder.

1.1.1. What is the biochemical significance of the urea cycle? (05 Marks)

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1.1.2. Outline the key regulatory methods of the urea cycle. (20 Marks)

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1.1.3. State the reasons for normal liver function tests results in this patient? (10 Marks)

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1.1.4. Name the enzyme most likely deficient in this child? (05 Marks)

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1.1.5. Explain the biochemical basis for elevated orotic acid levels in this child. (20 marks)

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1.2. Fructosuria occurs in essential fructoseuria an inherited disease in fructose metabolism.

1.2.1. Name the defective enzyme in essential fructoseuria. (10 Marks)

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1.2.2. Briefly outline the biochemical basis of the development of fructosuria in essential fructoseuria. (30 Marks)

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Q2.

A 45-year-old male, presented to the clinic with fatigue, mild jaundice, and generalized pruritus. He reported recent weight gain and frequent consumption of high-fat meals. There was no history of alcohol abuse. On examination, he had mild hepatomegaly, but no splenomegaly or ascites.

Laboratory findings:

- Mildly elevated serum total and conjugated bilirubin
- Elevated serum ALT and AST
- Elevated serum triglycerides and LDL-cholesterol
- Normal plasma glucose levels

The physician suspected hepatic dysfunction affecting bilirubin metabolism.

2.1. Regarding bilirubin metabolism

2.1.1. State the biochemical basis for the elevated conjugated bilirubin in this patient.

(10 Marks)

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2.1.2. Outline the key steps of bilirubin metabolism from heme breakdown to excretion.

(30 Marks)

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2.2. Regarding lipid metabolism

2.2.1. List **three** biomolecules present in the structure of the LDL-cholesterol molecule.

(15 Marks)

a. .....

b. .....

c. .....

2.2.2. What is the recent lifestyle change that would have led to the abnormal lipid profile findings of this patient? (05 Marks)

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2.2.3. Outline the reverse cholesterol transport of HDL. (25 Marks)

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2.2.4. State **two** lifestyle modifications that would improve his lipid profile findings.

(15 Marks)

a. ……

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b. ……

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(Total: 100 Marks)

CAT-2 (BATCH 2) SEQ ANSWERS

UVA WELLASSA UNIVERSITY
FACULTY OF MEDICINE
Continuous Assessment 03
November 2025
2023/2024 (02nd) Batch
Biochemistry
Structured Essay Questions (SEQ) Paper

Time 11.15 am – 12.15 pm (01 hour) Date of the exam: 2025.09.15

Index (MED) Number .....

Model Answers

Q1.

A 3-day-old was brought to the neonatal intensive care unit with poor feeding, lethargy, and episodes of vomiting. His parents reported that he had been unusually sleepy since birth and had minimal interest in feeding. There were no signs of jaundice and hepatomegaly.

Laboratory findings:

- Elevated plasma ammonia levels
- Normal liver function tests
- Mild respiratory alkalosis
- Normal blood glucose
- Elevated urinary orotic acid

The paediatrician suspected a urea cycle disorder.

1.1.

1.1.1. What is the biochemical significance of the urea cycle? (05 Marks)

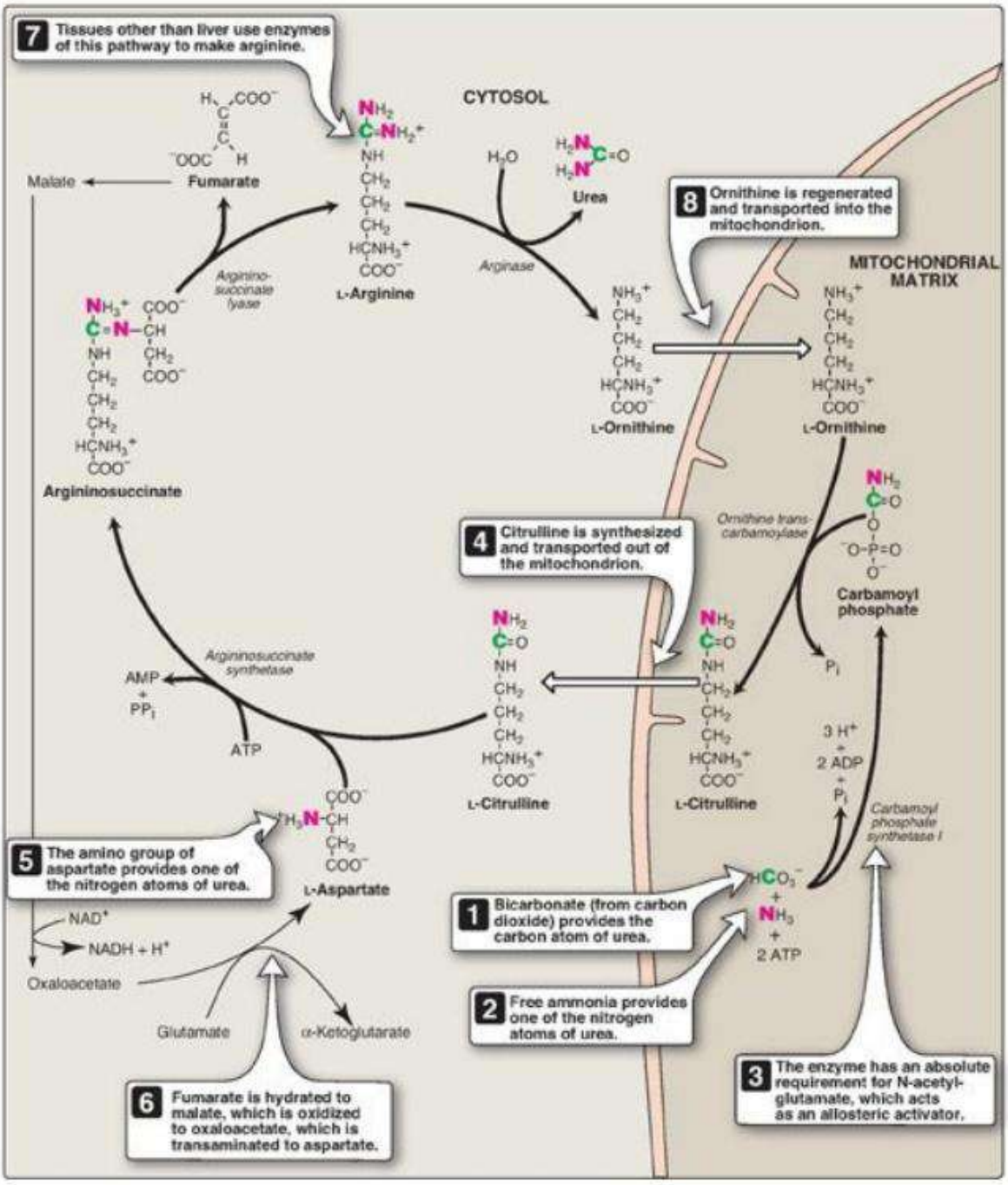
detoxification of ammonia/ sysnthsis of urea (1/2)

1.1.2. Outline the key regulatory methods of the urea cycle. (20 Marks)

- The urea cycle occurs mainly in the liver
  - partly mitochondrial
  - partly cytosolic

Figure 1. Source: Lippincott's Illustrated Reviews, Biochemistry

- Key steps:
- Formation of carbamoyl phosphate (via CPS I)
  - condensation of NH_4^+ ions with CO2 (HCO_3^-)
  - irreversible and rate-limiting step
  - requires N-acetyl glutamate.**(elaborate)**
- Arginase cleaves arginine → urea + ornithine (re-enters mitochondria).
- Urea is excreted by the kidneys.
- Deficiency of any enzyme results in ammonia accumulation.


7 Tissues other than liver use enzymes of this pathway to make arginine.
CYTOSOL
Malate
Fumarate
Argininosuccinate lyase
L-Arginine
H2O
Arginase
Urea
8 Ornithine is regenerated and transported into the mitochondrion.
MITOCHONDRIAL MATRIX
L-Ornithine
L-Ornithine
Argininosuccinate
4 Citrulline is synthesized and transported out of the mitochondrion.
Ornithine transcarbamoylase
Carbamoyl phosphate
Pi
Argininosuccinate synthetase
AMP + PPi
ATP
L-Citrulline
L-Citrulline
3 H+ + 2 ADP + Pi
Carbamoyl phosphate synthetase I
5 The amino group of aspartate provides one of the nitrogen atoms of urea.
L-Aspartate
NAD+
NADH + H+
Oxaloacetate
Glutamate
α-Ketoglutarate
1 Bicarbonate (from carbon dioxide) provides the carbon atom of urea.
HCO3− + NH3 + 2 ATP
2 Free ammonia provides one of the nitrogen atoms of urea.
3 The enzyme has an absolute requirement for N-acetylglutamate, which acts as an allosteric activator.
6 Fumarate is hydrated to malate, which is oxidized to oxaloacetate, which is transaminated to aspartate.

1.1.3. State the reasons for normal liver function tests results in this patient? (10 Marks)

The **hepatocytes are structurally intact**.
The defect is in a **specific enzyme** of the urea cycle, not hepatocellular damage.
LFTs (ALT, AST, bilirubin, albumin, PT) remain normal despite **hyperammonemia**.

1.1.4. Name the enzyme most likely deficient in this child? (05 Marks)

Ornithine transcarbamylase (OTC) deficiency → carbamoyl phosphate accumulates

1.1.5. Explain the biochemical basis for elevated orotic acid levels in this child. (20 marks)

Excess carbamoyl phosphate leaks into the cytosol and enters the pyrimidine synthesis pathway, forming orotic acid.

- Thus, orotic aciduria with hyperammonemia indicates OTC deficiency.

1.2. Regarding frutoseuria

1.2.1. Name one (01) condition that leads to the presence of fructose in urine (fructosuria). (05 Marks)

Essential Fructosuria (Benign Fructosuria)

1.2.2. Name the defective enzyme in the condition mentioned in 1.2.1. (05 Marks)

Fructokinase (Fructose kinase) deficiency

1.2.3. Briefly outline the biochemical basis of the development of fructosuria in the condition mentioned in 1.2.1. (30 Marks)

- In the liver
- fructose is normally
- phosphorylated
- by fructokinase
- to fructose-1-phosphate, using ATP.
- In Essential Fructosuria, fructokinase is deficient or inactive.
- Fructose cannot be efficiently phosphorylated
- and trapped in hepatocytes.
- As a result, fructose accumulates in the blood (fructosemia)
- and is excreted in the urine (fructosuria).
- The condition is benign and asymptomatic, since other pathways (e.g., hexokinase in extrahepatic tissues) can metabolize small amounts of fructose.

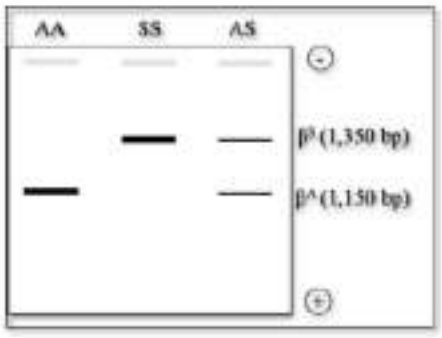
(Total:100 Marks)

CAT- 2 (BATCH 2) OSPE PAPER

Q1.

Sickle Cell Disease

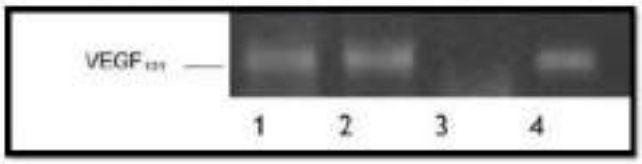
You are provided with genomic DNA samples from three individuals: a **normal individual (AA)**, a **heterozygous carrier (AS)**, and a **patient with sickle cell disease (SS)**. A molecular analysis of the **β-globin gene** was performed using a **restriction enzyme digestion**, followed by **agarose gel electrophoresis** to detect the mutation responsible for sickle cell anemia.
The gel electrophoresis results are shown below.



Q2.

Gene Expression

A lab technician wants to compare the expression of the Vascular Endothelial Growth Factor (VEGF) gene in two oral tissue samples from a normal subject (sample 3) and a patient with an oral lesion (Sample 04). RNA was extracted from both samples, converted into cDNA, and PCR was performed to detect VEGF expression. The results of gel electrophoresis is given.



2.1. Which type of molecule is used as the template to study gene expression in this experiment? (03 Marks)

2.2. What is the first step required to analyze gene expression using PCR in this experiment? (03 Marks)

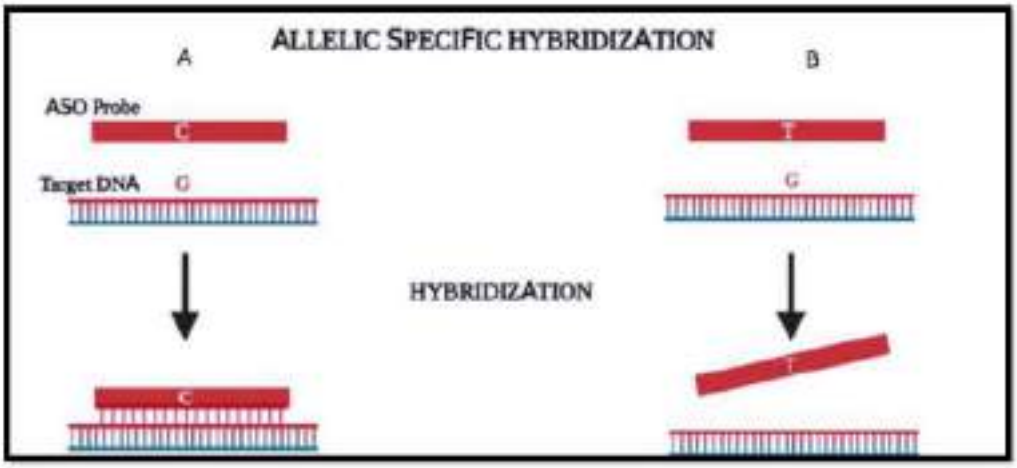
2.4. If VEGF is being expressed in a tissue, what would you expect to see on an agarose gel after PCR? (04 Marks)

(Total: 10 Marks)

Q3.

Point Mutation

A laboratory is testing a group of people for a point mutation in the CFTR gene associated with cystic fibrosis. The lab uses allele-specific oligonucleotide (ASO) probes. Two probes are used: one binds to the normal allele, and the other binds to the mutant allele.



3.1. What is the principle of ASO probe hybridization in detecting mutations? (04 Marks)

3.2. A patient shows binding only with the mutant probe. What is the genotype of the patient? (03 Marks)

3.3. A patient shows binding with both the normal and mutant probes. What is the genotype of this patient? (03 Marks)

(Total: 10 Marks)

Q4.

Sodium Hypobromite Test

A urine sample from a 45-year-old male patient was tested using the Sodium Hypobromite Test. The sample showed brisk effervescence immediately after adding the reagent.



4.1. What is the biochemical compound detected in this test? (03 Marks)

4.2. What causes the effervescence? (02 Marks)

4.3. State the biochemical basis of the presence of this compound in urine. (05 Marks)

(Total: 10 Marks)

Q5.

Urine analysis

A 7-year-old girl presents with mild periorbital puffiness and cola-colored, frothy urine for 4 days. Her mother reports that she had a sore throat about two weeks ago, which was not treated with antibiotics.

Urine dipstick shows:

Protein	: ++
Blood	: +++
Glucose	: Negative

Microscopy : Dysmorphic red blood cells (RBCs) and RBC casts are seen

5.1. What do the following urine findings indicate in this child?

Urine dipstick

5.1.1. Protein ++ (02 Marks)
5.1.2. Blood +++ (02 Marks)
5.1.3. Glucose negative (02 Marks)
5.1.4. Cola colour (02 Marks)

Microscopy

5.1.5. Dysmorphic RBC (02 Marks)

(Total: 10 Marks)

Q6.

Classic Galactosemia

A one-week-old baby presents with poor feeding, jaundice, hepatomegaly, and failure to thrive. The clinician suspects classic galactosemia.

A qualitative test on the baby's urine sample was performed and the result is given.

6.1. State the test performed on the sample of urine. (03 Marks)
6.2. Interpret the results. (03 Marks)
6.3. State the underlying metabolic defect in classic galactosemia. (04 Marks)

(Total: 10 Marks)

Q7.

Oral Glucose Tolerance Test (OGTT)

A 30-year-old pregnant woman undergoes an Oral Glucose Tolerance Test (OGTT) as a part of routine antenatal screening at 24 weeks of gestation. Plasma glucose levels were measured in fasting and 2-hour OGTT blood samples.



Laboratory Findings:

Time of Sample Collection	Plasma Glucose (mg/dL)	Reference Range (mg/dL)
Fasting	102 mg/dL	< 100 mg/dL (Normal)
2 hours after glucose load	168 mg/dL	< 140 mg/dL (Normal)

7.1. Interpret the results of this patient's OGTT. (06 Marks)

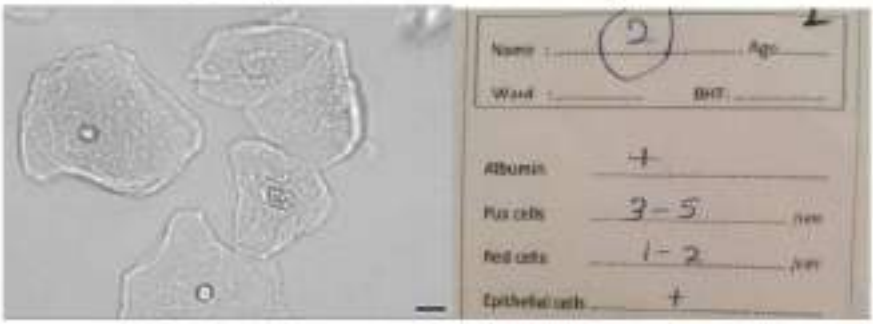
7.1. What is the condition that leads to the above biochemical findings? (04 Marks)

(Total: 10 Marks)

Q8.

Epithelial cells in Urine

A 25-year-old female presents with dysuria, frequent urination, and mild lower abdominal discomfort. A routine urinalysis is performed, and the following results are obtained.



8.1. State the test used to identify epithelial cells in the urine. (03 Marks)

8.2. Interpret the findings of epithelial cells. (03 Marks)

8.3. State **one** possible reason for the presence of epithelial cells in the urine sample of this patient. (04 Marks)

(Total: 10 Marks)

Q9.

Leucine crystals in urine



A 2-year-old child presents with hepatomegaly and developmental delay. A urinalysis is performed and leucine crystals were present in urine sample.

9.1. State the test used to identify leucine crystals in urine. (04 Marks)

9.2. State the biochemical basis of the presence of leucine crystals in urine. (04 Marks)

9.3. State the deficient enzyme that leads the biochemical abnormality mentioned in 9.2. (02 Marks)

(Total: 10 Marks)

Q10.

Lipid Profile

A 45-year-old male patient presents for a routine lipid profile. On blood collection, the serum appears **milky and turbid**.



10.1. What is the substance that gives rise to the milky and turbid appearance of this blood sample? (04 Marks)

10.2. State two (02) conditions that would lead to the appearance in this specimen. (06 Marks)

(Total: 10 Marks)

CAT-2 (BATCH 2) OSPE ANSWERS

(01)

1.1.
Restriction Fragment Length Polymorphism (RFLP) analysis using restriction enzyme digestion followed by agarose gel electrophoresis.

1.2
AA (normal individual): Only the normal β-globin allele is present, so the restriction enzyme cuts at the normal site, producing a specific fragment pattern (single or expected band).

SS (sickle cell patient): Both β-globin alleles carry the sickle mutation, which abolishes the restriction site. The enzyme cannot cut, producing a different fragment pattern (single band of larger size).
AS (heterozygous carrier): One normal allele and one mutated allele are present, so the enzyme cuts only the normal allele. This produces two DNA bands: one corresponding to the cut normal allele and one uncut mutant allele.

1.3.
Because they have one normal allele and one mutant allele, the restriction enzyme cuts only the normal allele, leaving the mutant allele uncut. This results in two different fragment sizes, which appear as two bands on the gel.

(02)

2.1.
mRNA

2.2.
Reverse transcription of RNA into complementary DNA (cDNA).

2.3. .
A visible PCR band corresponding to the VEGF gene.

(03)

3.1.
A perfect match between probe and target indicates the presence of the normal or mutant allele.

3.2.
Homozygous mutant

3.3.
Heterozygous carrier

(04)

4.1.

The compound detected is urea.

4.2.

Effervescence occurs due to the release of nitrogen gas when urea is broken down by sodium hypobromite.

4.3

Decreased urinary urea levels are seen in chronic liver disease (due to impaired urea synthesis) or renal failure (due to reduced excretion).

(05)

5.1.1. Abnormal/ indicate glomeruli damage
5.1.2. Abnormal/ indicate glomerular damage
5.1.3. normal/
5.1.4. abnormal/ presence of hemoglobin/ red cells in urine
5.1.5. abnormal/ indicate glomerular damage Presence of hemoglobin

(06)

6.1.

- Reducing sugar test (Benedict's test)
    - A qualitative test to detect reducing sugars in urine.
    - In classic galactosemia, galactose accumulates in the blood and is excreted in urine.

6.2.

- Positive Benedict's test → presence of reducing sugars in urine.
- In this infant:
    - The test would show a color change (green → yellow → brick-red) depending on the concentration of reducing sugars.
    - This indicates galactosuria, consistent with galactosemia.

6.3. Underlying metabolic defect in classic galactosemia:

Deficiency of galactose-1-phosphate uridyltransferase (GALT).
This enzyme catalyzes the conversion of galactose-1-phosphate + UDP-glucose → UDP-galactose + glucose-1-phosphate in the Leloir pathway.
Deficiency leads to accumulation of:

- Galactose-1-phosphate in liver, kidney, and other tissues.
- Galactose in blood and urine.
-

- Clinical consequences: jaundice, hepatomegaly, failure to thrive, vomiting, cataracts, risk of E. coli sepsis in neonates.

(07)

7.1.

The fasting plasma glucose level (102 mg/dL) is above the normal reference limit (≥92 mg/dL).

The 2-hour plasma glucose level (168 mg/dL) is also above the diagnostic threshold (≥153 mg/dL).

Since one or more values meet or exceed the diagnostic thresholds, this patient fulfills the criteria for Gestational Diabetes Mellitus (GDM).

7.2

Gestational Diabetes Mellitus

(08)

1. urine microscopy
2. Interpret the findings of epithelial cells.
   1.1.1. Abnormally high number of epithelial cells are present in this urine sample
   1. State the clinical significance of the presence of epithelial cells in urine
   1.1.2. Increased numbers may indicate:
   1.1.3. Urinary tract infection (UTI) / Improper sample collection

(09)

Microscopic examination of urine sediment is used to identify leucine crystals.

9.2.

- The presence of leucine crystals indicates impaired metabolism of branched-chain amino acids (BCAAs) — leucine, isoleucine, and valine.

9.3.

- This occurs due to a deficiency of branched-chain α-keto acid dehydrogenase (BCKD) complex).

(10)

10.1.

- Lipids/ chylomicrons

10.2.

- The biochemical cause is an elevated concentration of triglycerides, particularly due to accumulation of chylomicrons and/or VLDL in the plasma.
- This may occur due to:
  - Primary (genetic) hyperlipoproteinemia, such as:
    - Type I (Familial chylomicronemia) – deficiency of lipoprotein lipase (LPL) or its cofactor Apo C-II, leading to chylomicron accumulation.
    - Type V hyperlipoproteinemia – elevated chylomicrons and VLDL.
  - Secondary (acquired) causes, such as:
    - Uncontrolled diabetes mellitus – decreased insulin activity reduces LPL activity.
    - Alcohol abuse, obesity, or hypothyroidism – increase VLDL synthesis by the liver.
    - Postprandial state – transient rise in chylomicrons after a fatty meal.
- The triglyceride content in such cases usually exceeds 400 mg/dL (4.5 mmol/L), resulting in visible serum turbidity.



MESSAGE OF THE DEAN

As the Dean of the Uva Wellassa Medical Faculty, it is with deep pride and sincere enthusiasm that I introduce to you "Mastering Biochemistry–Part II: A Comprehensive Guide to MCQs, Essays, and OSPEs." This publication marks an important milestone in our continued dedication to improving the educational experience of students.

In the constantly advancing field of medicine, a strong understanding of Physiology remains fundamental to future achievements. This guide has been carefully developed to provide you with an extensive resource that not only addresses a broad spectrum of question formats including MCQs, essays, and OSPEs but also delivers detailed answers and explanations to strengthen learning.

The purpose of this book is to provide you with essential tools required to perform well in examinations and to enhance your understanding of anatomical concepts. We are confident that this guide will function as a valuable companion in your academic journey, providing clarity, confidence, and a solid framework for studies.

I convey my sincere appreciation to faculty members and contributors who have committed their knowledge and effort to bring this resource to fruition. It is our wish that you will regard this guide as a source of guidance and motivation as you progress through medical education.

Wishing you continued success in your studies and future medical profession career.

Sincerely,

Senior Professor Muditha Vidanapathirana,
MBBS (Col), DLM, MD, MA (SJP), FFFLM (UK)
Dean,
Faculty of Medicine,
Uva Wellassa University of Sri Lanka

Rs. 1500/-

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