8

Metabolism

Q 1. Define metabolism. Give its importance.

Metabolism

Metabolism is a process in which number of biochemical changes occurs in a body and helps in exchange of matter and energy between cell and its environment.

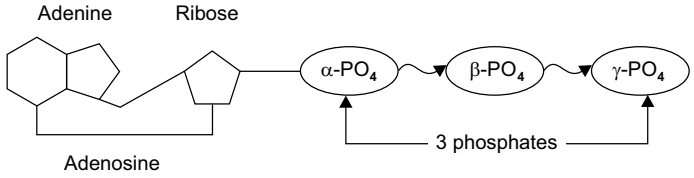
Importance of Metabolism

i. Chemical energy is obtained.
ii. Dietary nutrients are used for synthesis of new molecules.
iii. New molecules unite to form proteins, nucleic acids, etc.

Q 2. Define the terms.

i. *Catabolism*: It is the degradative phase of metabolism which provides metabolic fuel and building blocks for the cell.
ii. *Anabolism*: It is the process by which the absorbed food helps in the formation of new cells, new molecules and structural and functional units of cell and essential metabolites, is known as anabolism.
iii. *Abnormal metabolism*: The metabolic process where there is deficiency of enzymes, produces inborn errors of metabolism. This is called abnormal metabolism.
   • *Reasons for abnormal metabolism*
   i. Genetic defect, ii. Dietary deficiencies, iii. Diseased condition.

Q 3. What is ATP? Give its role in biological systems.

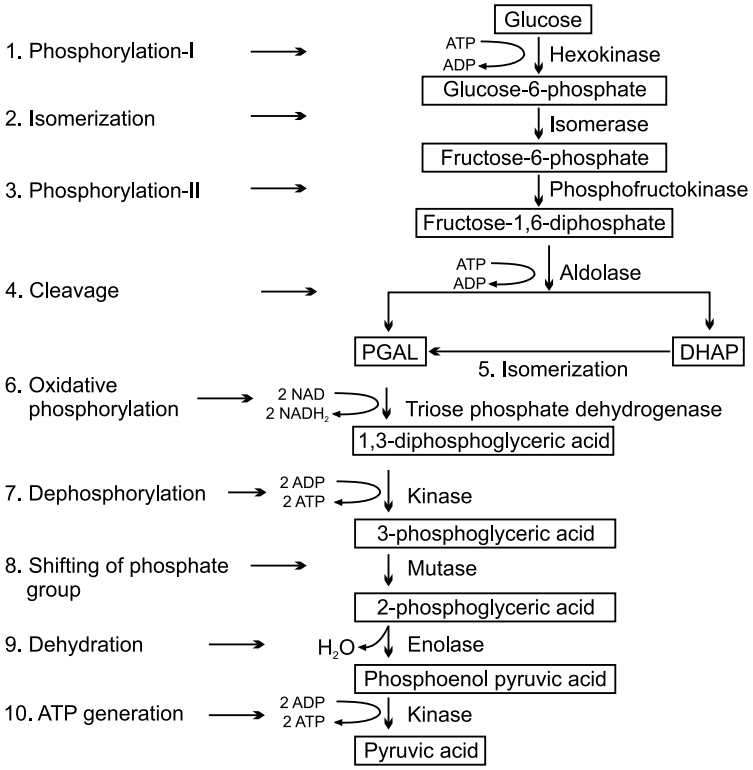


- ATP is adenosine triphosphate.
- It is a complex compound consisting of purine base-adenine, a 50 carbon sugar—the ribose, and three molecules of phosphate.
- ATP is a high energy releasing compound.

Importance of ATP

1. ATP provides energy for the synthesis of carbohydrases.
2. ATP is the main source of energy for various metabolic activities.

Q 4. Give the schematic representation of glycolysis/EMP pathway.



Glycolysis/EMP pathway

Glucolysis

Explanation

Glycolysis is the pathway in which glucose is broken down through a series of chemical reactions leading to formation of pyruvic acid.

Reactions involved in glycolysis are as follows:

1. *Phosphorylation-I*: In this reaction, glucose is converted into glucose-6-phosphate in the presence of enzyme hexokinase. At this stage one ATP is converted into ADP.
2. *Isomerization*: In this reaction, glucose-6-phosphate is converted into fructose-6-phosphate in the presence of isomerase enzyme.
3. *Phosphorylation-II*: Fructose-6-phosphate undergoes phosphorylation with ATP and forms fructose-1,6-diphosphate in the presence of enzyme phosphofructokinase.
4. *Cleavage*: In this reaction, fructose-1,6-diphosphate splits into phosphoglyceraldehyde (PGAL) and dihydroxy acetone phosphate (DHAP) in the presence of enzyme aldolase.
5. *Isomerization*: DHAP is further undergoes isomerization to form PGAL.
6. *Oxidative phoshorylation*: PGAL is converted into 1,3-diphosphoglyceric acid in the presence of enzyme triose phosphate dehydrogenase. At this stage, 2 NAD is converted into 2 $NADH_2$.
7. *Dephosphorylation*:In this reaction, 1,3-diphosphoglyceric acid is converted into 3-phosphoglyceric acid by removal of one phosphate group.
   In this stage, 2 ADP are converted into 2 ATP.
8. *Shifting of phosphate group*: In this reaction, phosphate group from 3-phosphoglyceric acid is shifted to carbon number 2 in the presence of enzyme mutase.
9. *Dehydration*: 2-phosphoglyceric acid after dehydration produces phosphoenol pyruvic acid in the presence of enzyme enolase.
10. *Formation of pyruvic acid*: Phosphoenol pyruvic acid is converted into pyruvic acid in the presence of enzyme kinase. At this stage, 2 ATP molecules are synthesized.

Energetics of Glycolysis

Reaction	*ATP formed*
1. Oxidative phosphorylation	06
2. Dephosphorylation	02
3. Phosphoenol pyruvic acid to pyruvic acid	02
Total	10 ATP

ATP consumed in:	
1. Phosphorylation-I	01
2. Phosphorylation-II	01
Total	02 ATP

Thus, in glycolysis (10 – 2 = 08) ATPs are synthesized.

Q 5. Define the terms.

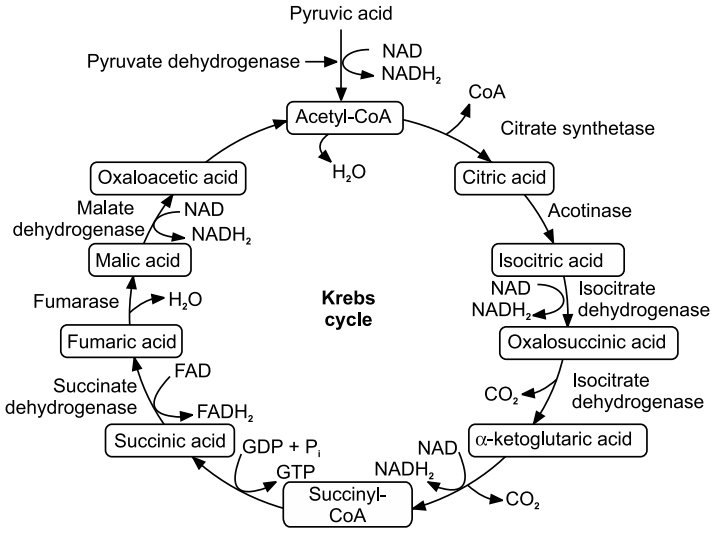
i. *Glycogenesis*: It is the process of conversion of glucose into glycogen in the liver.
ii. *Glycogenolysis*: It is the process of breakdown of glycogen into glucose in the liver.
iii. *Gluconeogenesis/neoglucogenesis*: It is the process of synthesis of glucose from noncarbohydrate sources such as amino acids, lactic acid, glycerol, etc.
iv. *Glycolysis*: It is the pathway in which glucose is broken down through a series of chemical reactions leading to formation of pyruvic acid.

Q 6. Write a note on Krebs cycle/TCA cycle/citric acid cycle.

Definition

The cycle of reactions involved in the oxidation of acetyl-CoA into CO_2 and H_2O are collectively called Krebs cycle, as it is discovered by Sir Hans Krebs.

In this cycle, different tricarboxylic acids are formed, hence called as tricarboxylic acid cycle (TCA cycle).



Reactions

1. Formation of acetyl-CoA
2. Formation of isocitric acid
3. Formation of oxalosuccinic acid
4. Formation of α-ketoglutaric acid
5. Formation of succinyl-CoA
6. Formation of succinic acid
7. Formation of fumaric acid
8. Formation of malic acid
9. Formation of oxaloacetic acid.

Krebs Cycle

1. *Formation of acetyl-CoA*: Pyruvic acid is decarboxylated to acetyl-CoA for its entry into citric acid cycle. In this stage, NAD is converted into $NADH_2$.
2. *Formation of isocitric acid*: Acetyl-CoA is converted into citric acid which further converted into isocitric acid in the presence of enzyme acotinase.
3. *Formation of oxalosuccinic acid*: Isocitric acid gets converted into oxalosuccinic acid in the presence of enzyme isocitrate dehydrogenase.
4. *Formation of α-ketoglutaric acid*: Oxalosuccinic acid is converted into α-ketoglutaric acid in the presence of isocitrate dehydrogenase.
5. *Formation of succinyl-CoA*: α-ketoglutaric acid is converted into succinyl-CoA.
6. *Formation of succinic acid*: Succinyl-CoA is converted into succinic acid.
7. *Formation of fumaric acid*: Succinic acid is converted into fumaric acid in the presence of succinate dehydrogenase.
8. *Formation of malic acid*: Fumaric acid is converted into malic acid in the presence of enzyme fumarase.
9. *Formation of oxaloacetic acid*: Malic acid is converted into oxaloacetic acid in the presence of enzyme malate dehydrogenase.This oxaloacetic acid again enters into the cycle and gets converted into acetyl-CoA.

Energetics of Citric Acid Cycle

Reactions	*ATP molecules formed*
1. Pyruvic acid → Acetyl-CoA	03
2. Isocitric acid → Oxalosuccinate	03
3. α-ketoglutaric acid → Succinyl-CoA	03
4. Succinyl-CoA → Succinic acid	01
5. Succinic acid → Fumaric acid	02
6. Malic acid → Oxaloacetic acid	03
Total	15 ATP

One molecule of glucose gives two molecules of pyruvic acid, therefore, total number of ATP formed in citric acid cycle = 15 × 2 = 30 ATP

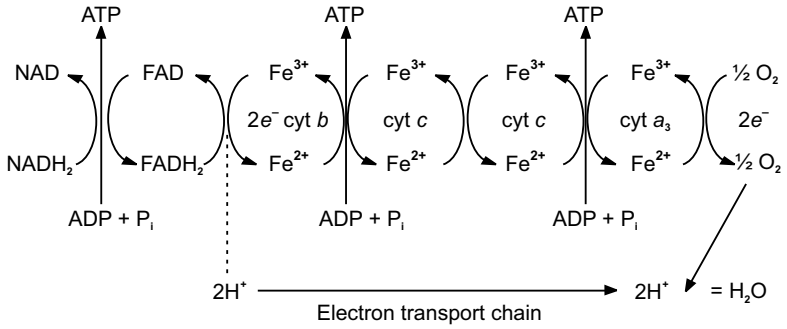
Total number of ATP formed in aerobic oxidation are:
a. From TCA cycle—30
b. From glycolysis—08

Total = 38 ATP

Q 7. Write a note on electron transport chain (ETC/ETS)./What is 'terminal oxidation'?

ETS

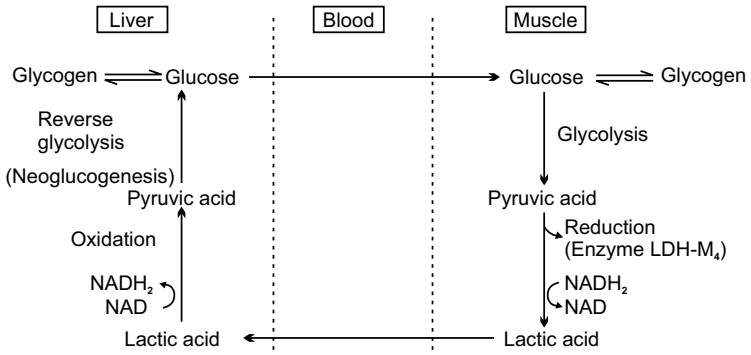
The process of oxidation of reduced coenzymes ($NADH_2$ and $FADH_2$) and different electron, carries through various enzyme systems, is called *electron transport system* or terminal oxidation. In this process, the hydrogen from ETS is transferred to molecular oxygen. This is known as terminal oxidation.



Q 8. What is Cori cycle? Explain.

Cori Cycle

The conversion of lactate to glucose takes place entirely in the liver and its re-entry into the muscle, is called Cori cycle.



- This cycle is discovered by scientistco Carl Ferdinand Cori, hence named as Cori cycle.
- It is a cyclic process by which lactic acid is converted into glucose in the liver and after that glucose appears in muscle where glucose can be converted to glycogen and stored in muscles.
- Cori cycle is designed for recycling of lactic acid.
- During vigorous muscular activity, glycogen in muscle is converted in glucose. Then glucose is converted into pyruvic acid by glycolysis.
- Muscles under such condition do not receive sufficient oxygen for normal and complete oxidation of pyruvic acid.
- Now, alternatively pyruvic acid is reduced to the lactic acid by enzyme LDH-M_4 and in presence of $NADH_2$ as hydrogen donor. So, $NADH_2$ is oxidised to NAD.
- Lactic acid if accumulates in muscles, it can result in toxicity of damaging the muscles so via circulating blood, lactic acid from muscles is taken to liver cells. In the liver cells, lactic acid is oxidised to pyruvic acid.
- Finally, pyruvic acid is converted into glucose, actually by reverse glycolysis mechanism also called *neoglucogenesis*.
- Glucose thus generated, thereafter can be converted to glycogen and stored in liver.
- Whenever necessary glycogen can be converted to glucose again by the action of hormone glucogen. Then glucose via bloodstream can be brought to muscles to repeat with same Cori cycle mechanism.

Significance of Cori Cycle

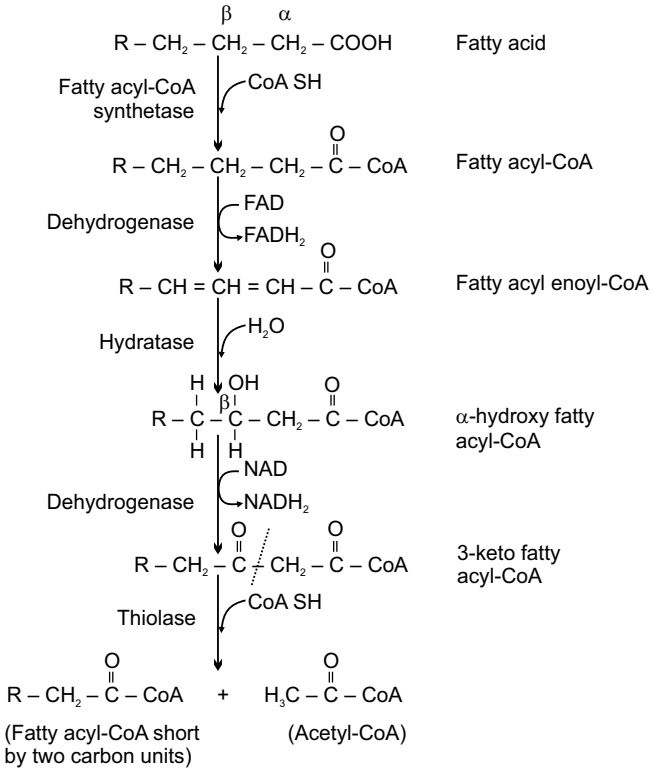
1. It allows proper cycling of lactic acid, so as to avoid toxicity of muscles due to lactic acid accumulations.
2. This mechanism allows skeletal muscles to work without any significant additional supply of oxygen to the muscles.
3. Same mechanism allows conversion of lactic acid to glucose and by proper glucose circulation, it can allow normal operation of energy metabolism in muscles.

Q 9. Write a note on b-oxidation of fatty acids.

β-oxidation of Fatty Acids

β-oxidation is a sequential removal of two carbon units as acetyl-CoA from carboxyl terminal of fatty acids by oxidation.

Reactions of β-oxidation of Fatty Acids



The steps involved in β-oxidation of fatty acids are as follows:

1. *Activation of fatty acid*: In this stage, fatty acid gets converted into an active fatty acyl-CoA in the presence of fatty acyl-CoA synthetase.
2. *Formation of unsaturated acyl-CoA*: The hydrogens from fatty acyl-CoA are taken up by FAD of the enzymes and thus unsaturated acyl-CoA is formed.
3. *Formation of β-hydroxyl acyl-CoA*: In this stage, one water molecule is added to produce β-hydroxy fatty acyl-CoA.
4. *Formation of 3-keto fatty acyl-CoA*: The hydrogens from β-hydroxyl acyl-CoA are taken up by NAD of the enzyme and thus 3-keto fatty acyl-CoA is formed.
5. *Thiolytic cleavage of 3-keto fatty acyl-CoA*: 3-keto fatty acyl-CoA undergoes thiolytic cleavage forms acetyl-CoA and active fatty acid containing two carbons less than original.

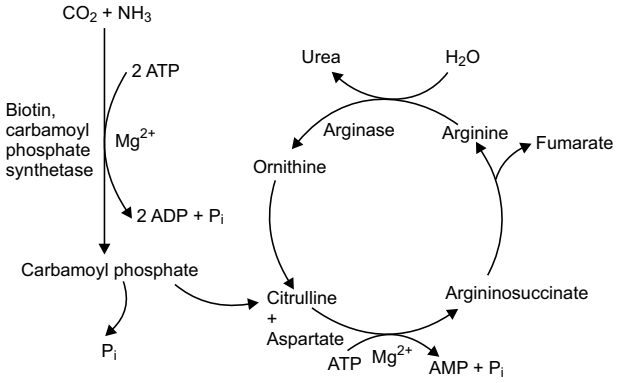
Energetics of Palmitic Acid Oxidation

Mechanism	*ATP yield*
I. **β-Oxidation (7 cycles)**	
7 $FADH_2$ [oxidized by electron transport chain (ETC), each $FADH_2$ gives 2 ATP]	14
7 NADH (oxidized by ETC, each NADH liberates 3 ATP)	21
II. **From 8 acetly-CoA**	
Oxidized by citric acid cycle, each acetyl-CoA provides 12 ATP	96
Total energy from one mole of palmitoyl-CoA	131
Energy utilized for activation (formation of palmitoyl-CoA)	–2
Net yield of oxidation of one molecule of palmitate	129

Q 10. Describe the chemical reactions involved in the formation of urea in the body./Write a note on urea cycle.

Urea Cycle

Ammonia is combined with CO_2 and forms a urea by various reactions catalysed by the enzymes present in the liver mitochondria through urea cycle.



Reactions Involved in Urea Cycle

1. *Formation of carbamoyl phosphate*: Ammonia combines with CO_2 to form carbamoyl phosphate in the presence of biotin and 2 molecules of ATP.
2. *Formation of citrulline*: Citrulline is formed by the transfer of carbamoyl group–$CONH_2$ from carbamoyl to ornithine.
3. *Formation of argininosuccinate*: Amino group of aspartase condenses with citrulline to form argininosuccinate. This reaction is catalysed by argininosuccinate synthetase and requires a molecule of ATP.

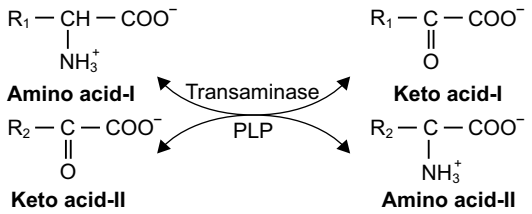
4. *Formation of arginine*: Reversible cleavage of argininosuccinate takes place to form arginine and fumarate.
5. *Formation of urea*: It is the last reaction of urea cycle which generates ornithine from arginine for its re-entry in the cycle.

Q 11. What is transamination? Give salient features of transamination./Write a note on transamination.

Transamination

Definition: The transfer of an amino ($-NH_2$) group from an amino acid to a keto acid is known as transamination.

- The transamination process involves the interconversion of a pair of amino acids and a pair of keto acids, catalysed by a group of enzymes called transaminases (i.e. amino transferases).
- Transamination reaction is as follows:



Transamination reaction

- Salient features of transamination are:
  1. All transaminases require pyridoxal phosphate (PLP), a coenzme derived from vitamin B_6.
  2. There is no free NH_3 liberated, only the transfer of amino group occurs.
  3. Transamination is ***reversible***.
  4. It involves both catabolism (degradation) and anabolism (synthesis) of amino acids. Transamination is ultimately responsible for the synthesis of nonessential amino acids.
  5. Transamination diverts the excess amino acids towards ***energy generation***.
  6. The amino acids undergo transamination to finally concentrate nitrogen in glutamate. **Glutamate** is the only amino acid that undergoes oxidative deamination to a significant extent to liberate free NH_3 for urea synthesis.
  7. All amino acids except lysine, threonine, proline and hydroxyproline participate in transamination.

Q 12. What is deamination? Explain oxidative and non-oxidative deamination./Write a note on 'deamination of amino acids'.

Deamination

Definition: The removal of amino group from the amino acids as NH_3 (ammonia) is known as deamination.

- Deamination results in liberation of ammonia for urea synthesis.
- Deamination may be oxidative or non-oxidative.

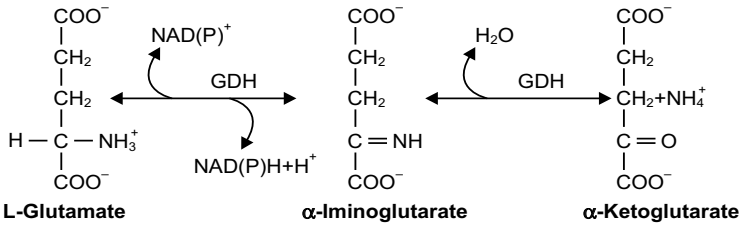
A. Oxidative Deamination

- Oxidative deamination is the liberation of free ammonia from the amino group of amino acids coupled with oxidation.
- This takes place mostly in liver and kidney.
- The purpose of oxidative deamination is to provide NH_3 for urea synthesis and α-keto acids for a variety of reactions including energy generation.

Examples

1. *Oxidative deamination by glutamate dehydrogenase (GDH):*

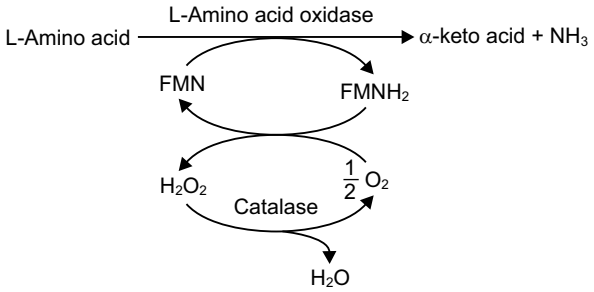
- In this reaction, glutamate rapidly undergoes oxidative deamination catalysed by glutamate dehydrogenase (GDH) to liberate ammonia.
- The conversion of glutamate to α-ketoglutarate occurs through the formation of an intermediate α-aminoglutarate.



Oxidation of glutamate by glutamate dehydrogenase (GDH)

2. *Oxidative deamination by amino acid oxidases:*

- L-amino acid oxidase and D-amino oxidase are flavoproteins, possessing FMN and FAD, respectively.
- They act on the corresponding amino acids (L or D) to produce α-keto acids and NH_3.
- In this reaction, oxygen is reduced to H_2O_2 which is later decomposed by catalase.

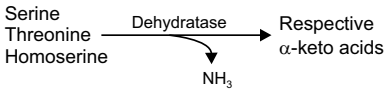


Oxidative deamination of amino acids

B. Non-oxidative Deamination

Some of the amino acids can be deaminated to liberate NH_3 without undergoing oxidation.

a. **Amino acid dehydrases:** Serine, theronine and homoserine are the hydroxy amino acids. They undergo non-oxidative deamination catalysed by PLP-dependent dehydrases (dehydratases).

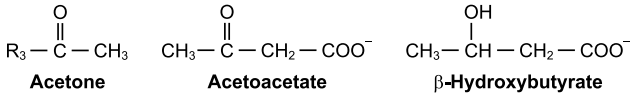


b. **Deamination of histidine:** The enzyme histidase acts on histidine to liberate NH_3 by a non-oxidative deamination process.

Q 13. What are ketone bodies? Write a note on ketogenesis.

Ketone Bodies

- The compounds, namely acetone, acetoacetate, and β-hydroxybutyrate are known as ketone bodies.
- Ketone bodies are water-soluble and energy yielding.
- Structures of ketone bodies:



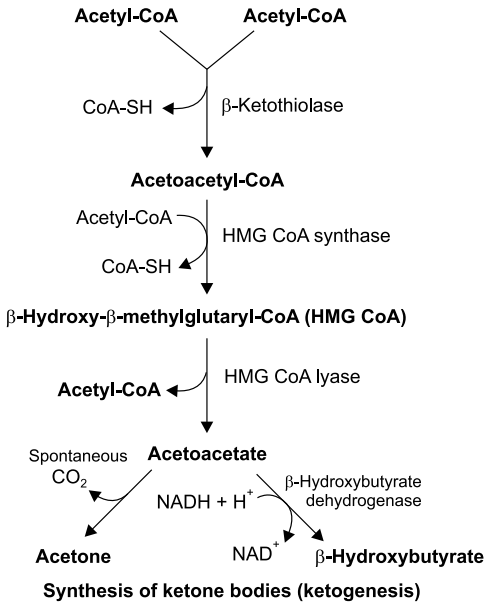
Structures of ketone bodies

Ketogenesis

The process of formation/synthesis of ketone bodies is known as ketogenesis.

- Ketogenesis occurs in the liver.
- The enzymes for ketone body synthesis are located in the mitochondrial matrix.
- Acetyl-CoA, formed by oxidation of fatty acids, pyruvate or some amino acid, is the precursor for ketone bodies.

- The reaction of ketogenesis is as follows:



Synthesis of ketone bodies (ketogenesis)

Explanation of Ketogenesis Reactions

1. Two moles of acetly-CoA condense to form acetoacetyl-CoA. This reaction is catalysed by thiolase.
2. Acetoacetyl-CoA combines with another molecule of acetyl-CoA to produce β-hydroxy-β-methyl glutaryl-CoA (HMG CoA). ***HMG CoA synthase***, catalysing this reaction, ***regulates the synthesis of ketone bodies***.
3. HMG CoA lyase cleaves HMG CoA to produce acetoacetate acetly-CoA.
4. Acetoacetate can undergo spontaneous decarboxylation to form acetone.
5. Acetoacetate can be reduced by a dehydrogenease to β-hydroxy-butyrate.

The carbon skeleton of some amino acids (ketogenic) is degraded to acetoacetate or acyl-CoA and, therefore to ketone bodies, e.g. leucine, lysine, phenylalanine etc.

Significance of Ketogenesis

1. Ketogenesis is a mechanism that allows the liver to oxidise increasing quantities of fatty acids within a tightly coupled system of oxidative phosphorylation without increasing its total energy expenditure.
2. Acetoacetate and β-hydroxybutyrate are normal fuels of respiration.

3. Glucose is the major fuel for the brain and red blood cells. But, in prolonged starvation, 75% of the fuel needs of the brains are met by acetoacetate, reducing its needs for glucose.
4. Acetoacetate can be regarded as water soluble transportable form of acetyl unit.
5. Acetoacetate also has a regulatory role in lipid metabolism.

Q 14. What is ketolysis? Explain utilization of ketone bodies.

Ketolysis

Ketolysis is the opposite process to ketogenesis that aims to regain energy via oxidation of ketone bodies which takes place in the mitochondria.

Utilization of Ketone Bodies (Ketolysis)

- The ketone bodies are utilized by extrahepatic tissues as 'fuel'.
- The ketone bodies, being water-soluble, are easily transported from the liver to various tissues.
- The two ketone bodies—acetoacetate and β-hydroxybutyrate serve as an important source of energy for the peripheral tissues such as skeletal muscle, cardiac muscle, renal cortex, etc.
- The production of ketone bodies and their utilization become more significant when glucose is in short supply to the tissues, as observed in: a. Starvation, b. Diabetes millitus
- During prolonged starvation, ketone bodies are the major fuel source for the brain and other parts of the central nervous system.

Q 15. What do you mean by ketoacidosis?

Ketoacidosis

- Ketosis produces metabolic acidosis known as ketoacidosis.
- Increased utilization of fats for energy causes metabolic acidosis, due to release of ketoacids such as acetic acid, β-hydroxybutyric acid into the plasma more rapidly that can be taken up and oxidized by the tissue cells. As a result, these moderately strong acids are buffered when present in blood or other tissues and that lead to a loss of buffer cation (HCO_3^-), that progressively depletes the alkali reserve, causing ketoacidosis.
- Ketoacidosis is partly compensated by hyperventilation with reduction of PCO_2 and therefore, reduction of H_2CO_3 concentration.
- Both acetoacetate and β-hydroxybutyrate are strong acids and increase in their concentration in the blood would cause acidosis.
- Diabetic ketoacidosis is dangerous—may result in coma and even death; if not treated.

Q 16. Write a note on 'fatty liver'.

Fatty Liver

- Fatty liver is the condition where there is an excessive accumulation of fat primarily neutral fat, triacylglycerol in the liver parenchymal cells.
- The normal concentration of lipid in the liver is around 5%.
- Liver is not a storage organ for fat.
- In pathological conditions, the fat level in the liver is increased up to 25 to 30% and is known as fatty liver or fatty infiltration of liver.

Causes of Fatty Liver

1. Increased synthesis of triglycerides.
2. Impairment in lipoprotein synthesis.
3. Fatty liver occurs in conditions in which there is an imbalance between hepatic triacylglycerol synthesis and the secretion of VLDL.

Classification of Fatty Liver

1. *Physiological fatty liver*: It is associated with increased levels of plasma-free fatty acids from the diet (high fat diet) or from the adipose tissue during starvation.
2. *Pathological fatty liver*: It occurs due to an impairment in the biosynthesis of plasma lipoproteins, which in turn impair the transport of triacylglycerol from liver, thus allowing triacylglycerol to accumulate in the liver.

Conditions that Cause Fatty Liver

- High fat diet
- Starvation or insulin insufficiency
- Alcoholism
- Dietary deficiency of lipotropic factors, essential fatty acids, etc.
- High cholesterol diet
- Use of certain chemicals.

Q 17. What is hypercholesterolemia? Explain.

Hypercholesterolemia

- Increase in plasma cholesterol (>250 mg/dl) concentration is known as hypercholesterolemia.
- It is also associated with atherosclerosis and coronary heart disease.
- Hypercholesterolemia is observed in many disorders like:
  a. *Diabetes mellitus*: Due to increased cholesterol synthesis since the availability of acetyl-CoA is increased.

b. *Hypothyroidism* (*myxoedema*): This may be due decrease in the HDL receptors on hepatocytes.
c. *Obstructive jaundice*: Due to an obstruction in the excretion of cholesterol through bile.
d. *Nephrotic syndrome*: Increase in plasma globulin concentration is the characteristic feature of nephrotic syndrome.

Causes of Hypercholesterolemia

- Poor diet
- Junk food, fast food
- Alcoholism
- Dialysis therapy
- Cushing's syndrome
- Anorexia nervosa

Complications due to Hypercholesterolemia

- Thrombosis
- Atherosclerosis
- Embolism
- Cardiovascular and coronary heart diseases.
- Heart attack
- Coronary thrombosis
- Fat embolism

Objective Questions with Answers in Bold Letters

1. **Catabolism** is the degradative phase of metabolism which provides metabolic fuel and the building blocks for the cell.
2. **ATP** is a high-energy releasing compound.
3. The process of conversion of glucose into glycogen in the liver is called **glycogenesis**.
4. **Glycogenolysis** is the process of breakdown of glycogen into glucose in the liver.
5. The process of synthesis of glucose from non-carbohydrate source is known as **gluconeogenesis/neoglucogenesis**.
6. The pathway of breakdown of glucose into pyruvic acid is known as **glycolysis**.
7. In glycolysis, total **8 ATP** molecules are synthesized.
8. Krebs cycle/citric acid cycle/TCA cycle involves **oxidation of acetyl-CoA**.
9. Total number of ATPs formed in Krebs cycle is **30**.
10. The total number of ATPs formed in aerobic oxidation of glucose is **38**.
11. **ETC** means electron transport chain and also known as terminal oxidation.
12. The conversion of lactate to glucose takes place entirely in the liver and its re-entry into the muscle is called **Cori cycle**.
13. **Cori cycle** is designed for recycling of lactic acid.
14. **β-oxidation** is a sequential removal of two carbon units as acetyl-CoA from carboxyl terminal of fatty acids by oxidation.
15. **Insulin** is a peptide which plays an important role in glucose metabolism.
16. HMP-pathway means **hexose monophosphate shunt**.