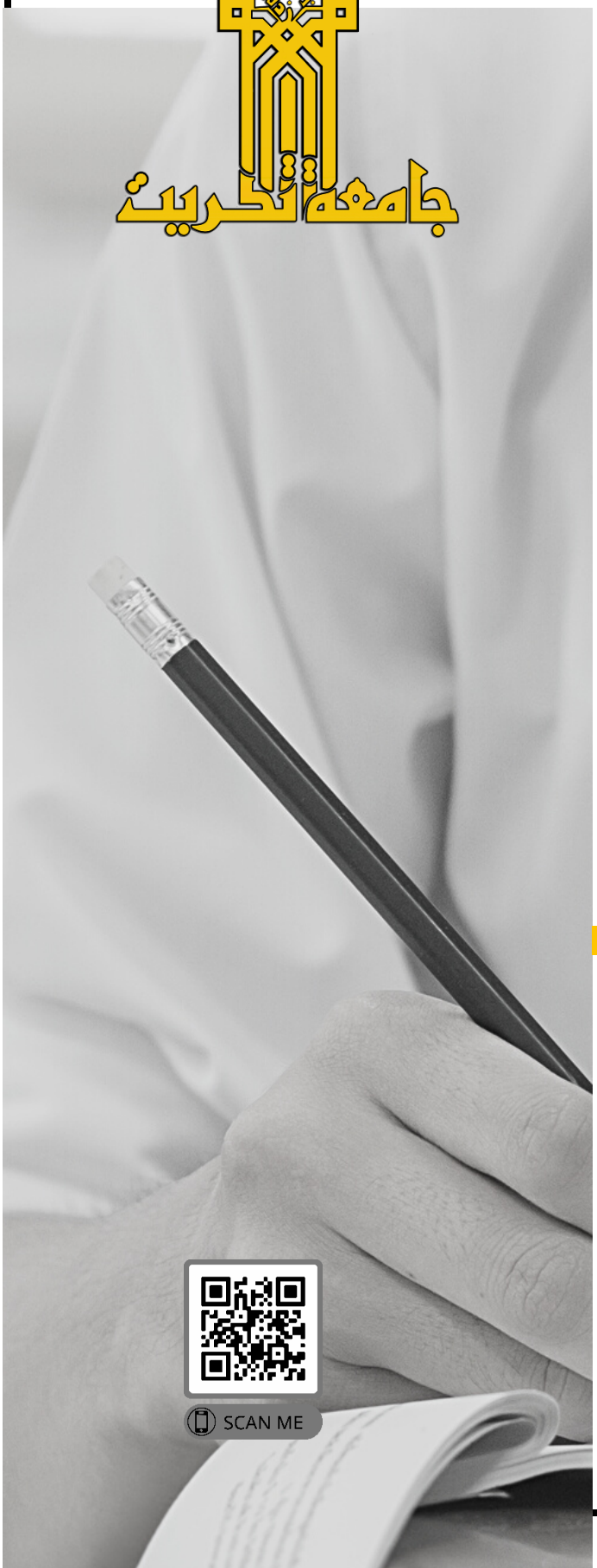

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B oxidation fatty a

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Beta-oxidation of Fatty Acid

Beta-oxidation is the catabolic process by which **fatty acid** molecules are broken down in the cytosol in prokaryotes and in the mitochondria in eukaryotes to generate acetyl-CoA.

- This results in the sequential **removal of** a two carbon fragment, **acetyl CoA**.
- Acetyl-CoA enters the **citric acid cycle** while NADH and FADH2, which are co-enzymes, are used in the electron transport chain. It is referred as "beta oxidation" because the beta carbon of the fatty acid undergoes oxidation .

Fatty acid oxidation—stages:-

The β-oxidation of fatty acids involves three stages

I. Activation of fatty acids occurring in the cytosol

II. Transport of fatty acids into mitochondria

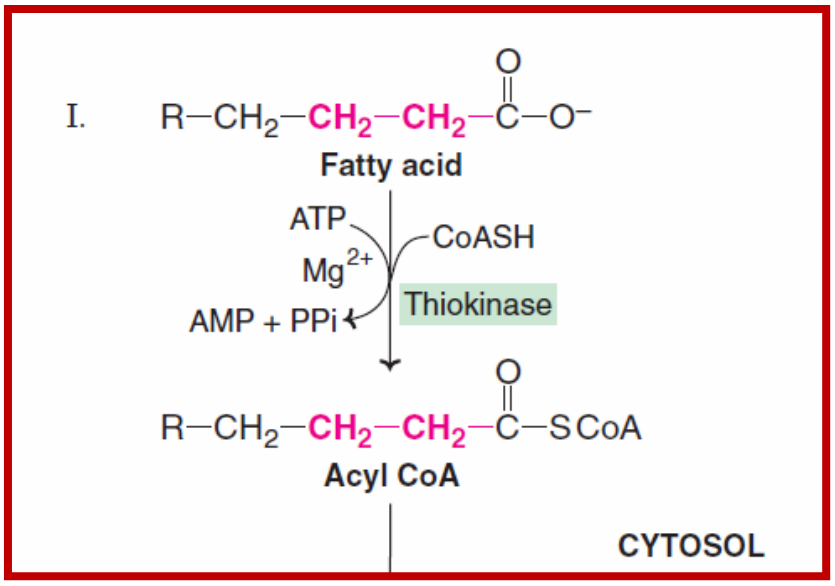
III. β -Oxidation proper in the mitochondrial matrix.

- Fatty acids are oxidized by most of the tissues in the body. However, **brain, erythrocytes and adrenal medulla cannot utilize fatty acids for energy requirement**.

A. Activation of fatty acids

1. In the cytosol of the cell, long-chain fatty acids are activated by ATP and coenzyme A, and fatty **acyl-CoA** is formed. Short-chain fatty acids are activated in mitochondria.

2. The ATP is converted to AMP and pyrophosphate (PPi), which is cleaved by pyrophosphatase to two inorganic phosphates (2 Pi). Because two high-energy phosphate bonds are cleaved, the equivalent of **two** molecules of ATP is used for fatty acid activation.



B. Transport of fatty acyl-CoA from the cytosol into mitochondria

*** Fatty acyl-CoA from the cytosol reacts with carnitine in the outer mitochondrial membrane, forming fatty acylcarnitine. The enzyme is carnitine acyltransferase I (CAT I), which is also called carnitine palmitoyl l transferase I (CPT I). Fatty acyl carnitine passes to the inner membrane, where it re-forms to fatty acyl-CoA, which enters the matrix. The second enzyme is carnitine acyl transferase II (CAT II).

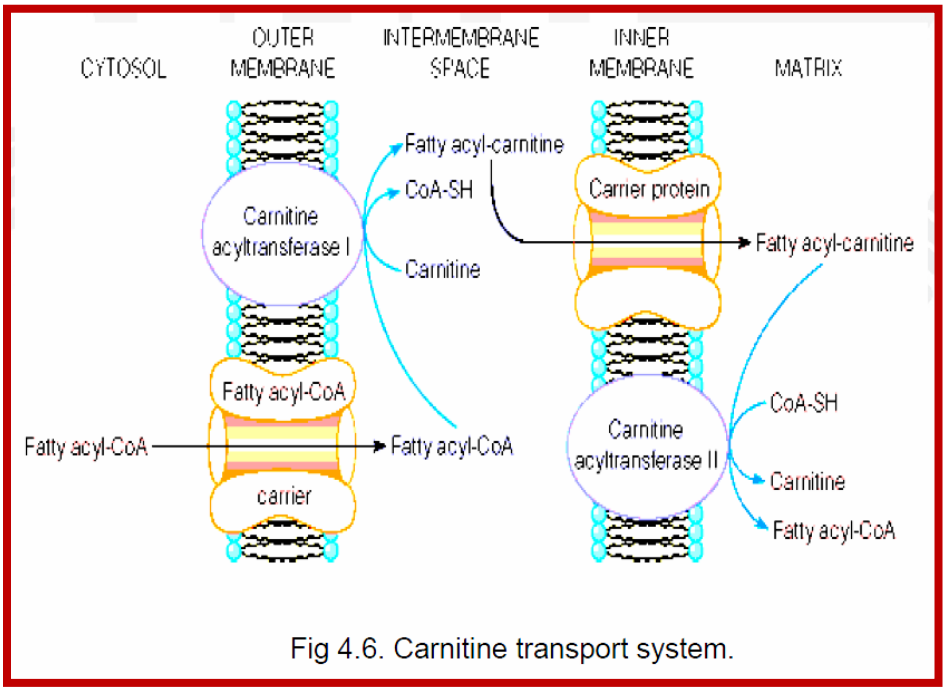


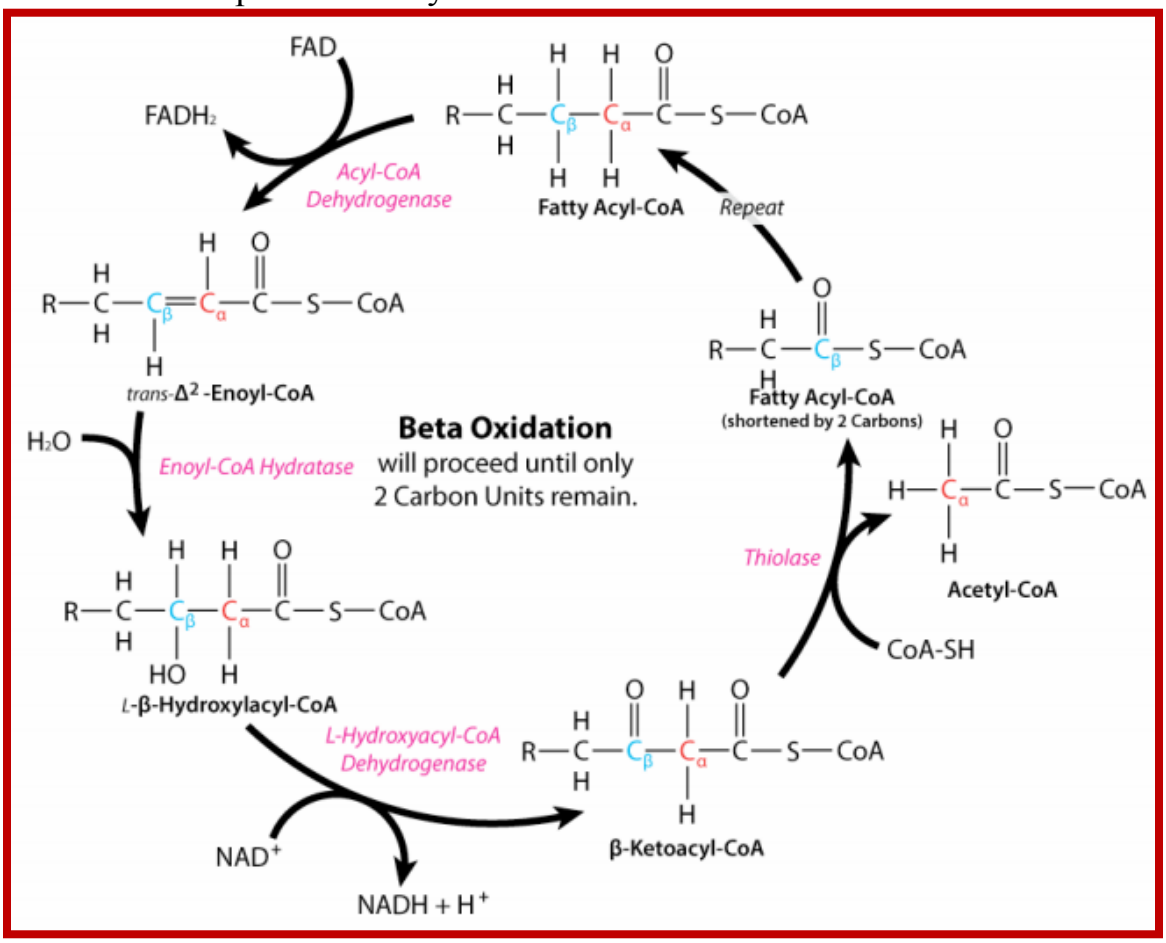
Fig 4.6. Carnitine transport system.

Steps ;-

1. Acyl CoA dehydrogenase converts acyl CoA to acyl trans enoyl CoA

2. Hydratase converts it to 3-hydroxy acyl CoA.
3. Hydroxy acyl CoA dehydrogenase converts it to 3keto acyl CoA.
4. It is further converted to acyl CoA and acetyl CoA.by Thiolase
The cycle is repeated 7 times for palmitic acid for complete oxidation. See the figure

The FADH2 and NADH +H+ join the electron transport chain as high energy electron carriers (ETC). The latter donates its reducing equivalents (hydrogens) to NADH dehydrogenase to produce 3ATP per pair of electrons and the former produces only 2ATPS.

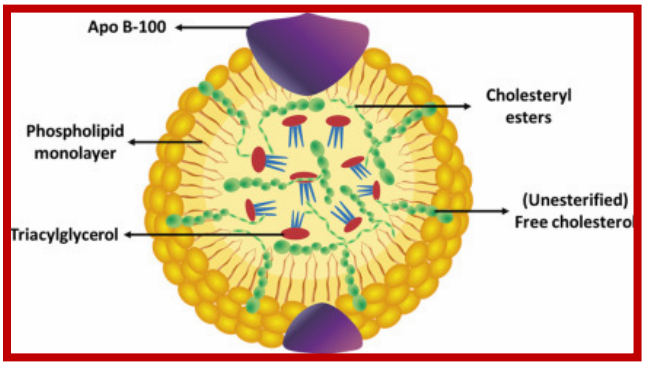


Complete oxidation of fatty acid can be divided in to two stages.
A. Formation of acetyl CoA.
B. Oxidation of acetyl CoA to CO2, water via TCA cycle.

- Palmitoyl CoA + 7FAD + 7 NAD +7CoA = 8 Acetyl CoA+7FADH2 +7 NADH+H.

Reduced equivalents enter ETC and produce energy rich phosphate bonds. Acetyl CoA release energy through TCA cycle.
7 FADH2 → 7 x 2 = 14 ATPs
7NADH+H → 7 x 3 = 21 ATPs
8 Acetyl CoA → 8 x 12 = 96 ATPs
Total ATP produced from one molecule of palmitic acid is **131**. Two ATPs (Two energy rich bonds) are utilized, during activation of fatty acid. Therefore total gain of ATPs is **129.**

Lipoproteins
Plasma lipids contain triacylglycerols, cholesterol and other polar lipids.Lipids combined with apolipoproteins to form Lipoproteins. Based on their density they are classified into four subgroups:



Chylomicrons:
These are derived from intestinal absorption of triacylglycerols and other lipids and have a very short lifespan. They have the least density and richly consist TAG. Chylomicrons transport dietary triacylglycerols and cholesterol from the intestine to the liver for metabolism.

VLDL (very low density lipoproteins):

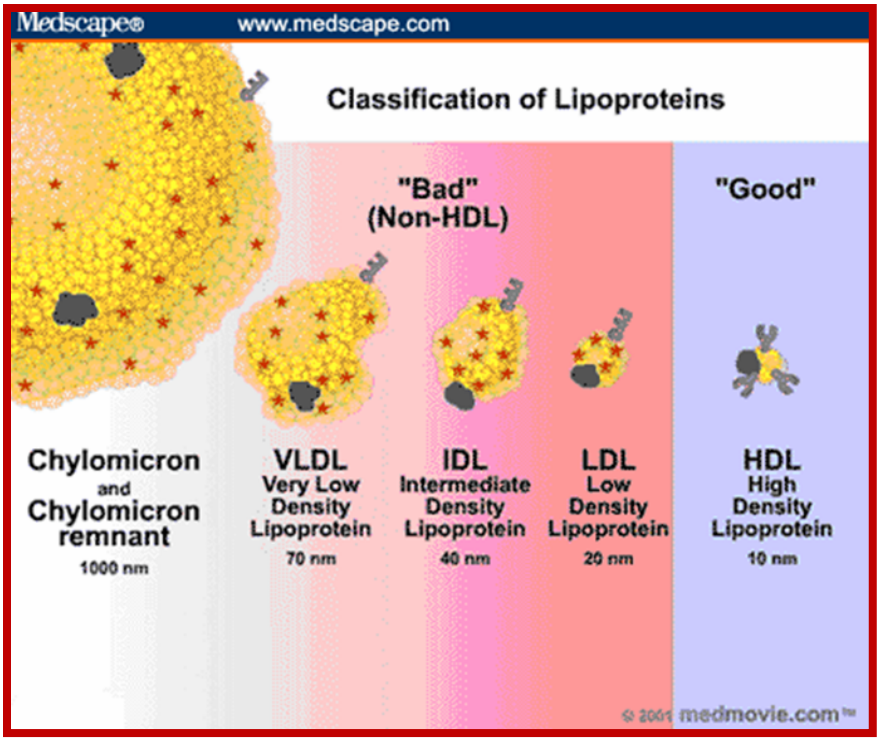
These are synthesized in the liver and used to transport triacylglycerols from the liver to extrahepatic tissues.

LDL (Low density lipoproteins)

These are produced from the final stage in the catabolism of VLDL. They transport cholesterol synthesized in the liver to peripheral tissues. LDL is metabolized via the LDL receptor Approximately 30% of the LDL is degraded in extra hepatic tissues, rest is degraded in liver.

HDL (High Density Lipoproteins):

HDL has the highest density in this group since it contains more protein and cholesterol than triacylglycerols. It transports excess cholesterol from peripheral tissues to the liver for degradation and removal. Therefore, HDL cholesterol is good cholesterol but LDL cholesterol is called bad cholesterol. High concentration of circulating VLDL,LDL are indicative of possible atherosclerosis .Elevated HDL is a good sign which indicates less chances of atherosclerosis .There is a correlation between the incidence of coronary heart disease and low level of HDL.The higher the ratio of HDL/LDL, the less the chances of CHD .



KETONE BODIES

The compounds namely **acetone, acetoacetate** and **β-hydroxybutyrate** (or 3-hydroxybutyrate) are known as ketone bodies (**Fig.14.10**). Only the first two are true ketones while β- hydroxybutyrate does not possess a keto (C= O) group. **Ketone bodies are water-soluble** and **energy yielding**. Acetone, however, is an exception, since it cannot be metabolized. The ketone body formation (particularly overproduction) occurs primarily due to non availability of carbohydrates to the tissues. This is an outcome of excessive utilization of fatty acids to meet the energy requirements of the cells.

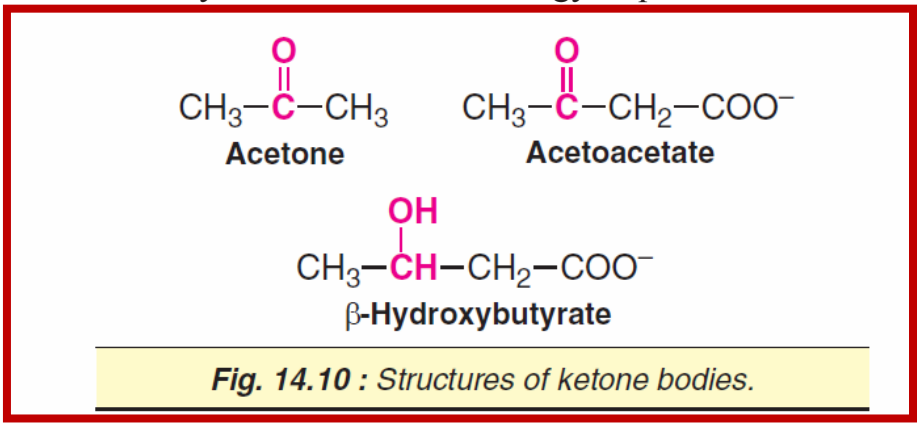


Fig. 14.10 : Structures of ketone bodies.

Utilization of ketone bodies

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 important sources of energy for the **peripheral tissues** such as skeletal muscle, cardiac muscle, renal cortex etc. The tissues which lack mitochondria (e.g. erythrocytes) however, cannot utilize ketone bodies. The production of ketone bodies and their utilization become more significant when glucose is in short supply to the tissues, as observed in **starvation**, and **diabetes mellitus**. During prolonged **starvation**, ketone bodies are the major **fuel source for the brain** and other parts of central nervous system.

- **Starvation :** Starvation is accompanied by **increased degradation of fatty acids** (from the fuel reserve triacylglycerol) to meet the energy needs of the body. This causes an overproduction ketone bodies.