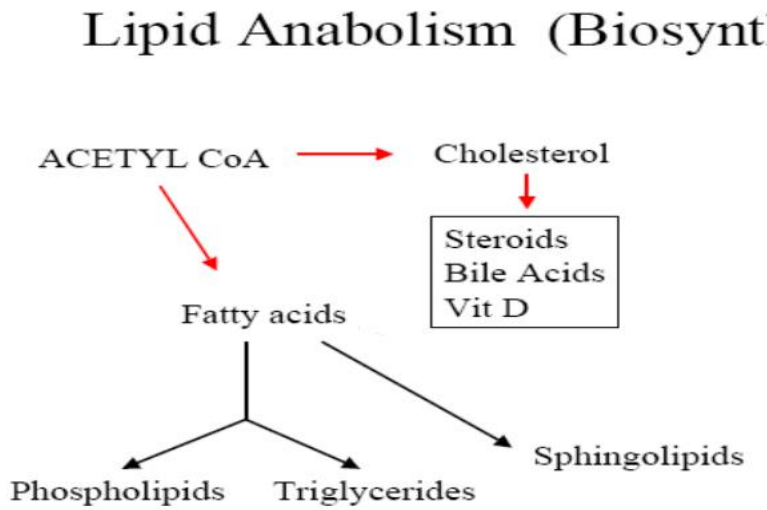
EIGHTH CHAPTER: Lipids metabolism (Part 2)

II. Lipid biosynthesis

In humans, the majority of fatty acids are exogenous, however most tissues are capable of synthesis from acetyl CoA (liver, kidneys, adipose tissue, lungs, mammary glands).

Lipid anabolism (lipogenesis) is synthesis from amino acids which are converted to acetyl-CoA and from glucose into glyceraldehyde 3-phosphate. Both of acetyl-CoA and glyceraldehyde 3-phosphate converted into triglycerides.



II.1. Fatty acid biosynthesis

The synthesis of FA is endergonic and reductive. It requires the following 3 elements:

- ATP: source of energy;
- Acetyl-CoA: precursor: it has Triple origin:
    - Glycolysis giving pyruvate which under the action of pyruvate dehydrogenase gives acetyl-CoA.
    - The catabolism of amino acids.
    - β-oxidation of fatty acids.
- $NADPH,H^+$: reductant (proton source).

The precursor for fatty acids is acetyl-CoA and it occurs in the cytosol of the cell. Lipogenesis allows the synthesis of saturated fatty acids by condensation of acetate molecules (2 Carbons).

The entire synthesis is carried out at the level of a multi-enzyme complex called fatty acid synthase.

The overall net reaction, using palmitate (16:0) as a model substrate is:

8 Acetyl-coA + 7 ATP + 14 NADPH + 6H+ → palmitate + 14 NADP+ + $6H_2O$ + 7ADP + 7P¡

The elongation of saturated fatty acids beyond 16 carbon atoms is carried out in the endoplasmic reticulum and the mitochondrion. In the first case, elongation involves fatty acid elongases. In the second case, elongation paradoxically involves certain lipolysis enzymes

The synthesis of unsaturated fatty acids from saturated fatty acids takes place at the levels of the endoplasmic reticulum membrane by fatty acid desaturases. Desaturation consumes molecular oxygen (O2) and uses NAD as a cofactor:

$$\text{Stearic acid} + 2\text{NADH},H^+ + O_2 \rightarrow \text{Oleic acid} + NAD^+ + 2H_2O$$

II.2. Membrane lipid biosynthesis

There are two major classes of membrane lipids: glycerophospholipids and sphingolipids. Although many different membrane lipids are synthesized in our body, pathways share the same pattern. The first step is synthesizing the backbone (sphingosine or glycerol), the second step is the addition of fatty acids to the backbone to make phosphatidic acid. Phosphatidic acid is further modified with the attachment of different hydrophilic head groups to the backbone. Membrane lipid biosynthesis occurs in the endoplasmic reticulum membrane.

II.3. Triglyceride biosynthesis

The phosphatidic acid is also a precursor for triglyceride biosynthesis. Phosphatidic acid phosphotase catalyzes the conversion of phosphatidic acid to diglyceride, which will be converted to triglycerides by acyltransferase. Triglyceride biosynthesis occurs in the cytosol.

II.4. Cholesterol biosynthesis

Cholesterol can be made from acetyl-CoA through a multiple-step pathway known as isoprenoid pathway. Cholesterols are essential because they can be modified to form different hormones in the body such as progesterone. 70% of cholesterol biosynthesis occurs in the cytosol of liver cells.