

# Lipid Metabolism

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## Aim

**Aim of this lecture to understand the ways of energy storage in the body and to understand the lipids structure and metabolism.**

## Reading:

Marks' Essentials of Medical Biochemistry, Chapter 17.

Medical Biochemistry, Baynes and Dominiczak Chapter 37



# Classes of lipids

Are of 3 types

## 1. Fatty acid derivatives:

- Fatty acids – fuel molecules.
- Triacylglycerols – fuel storage
- Phospholipids – components of membranes and plasma lipoproteins
- Eicosanoids – local mediators

## 2. Hydroxy-methyl-glutaric acid derivatives (C6 compound):

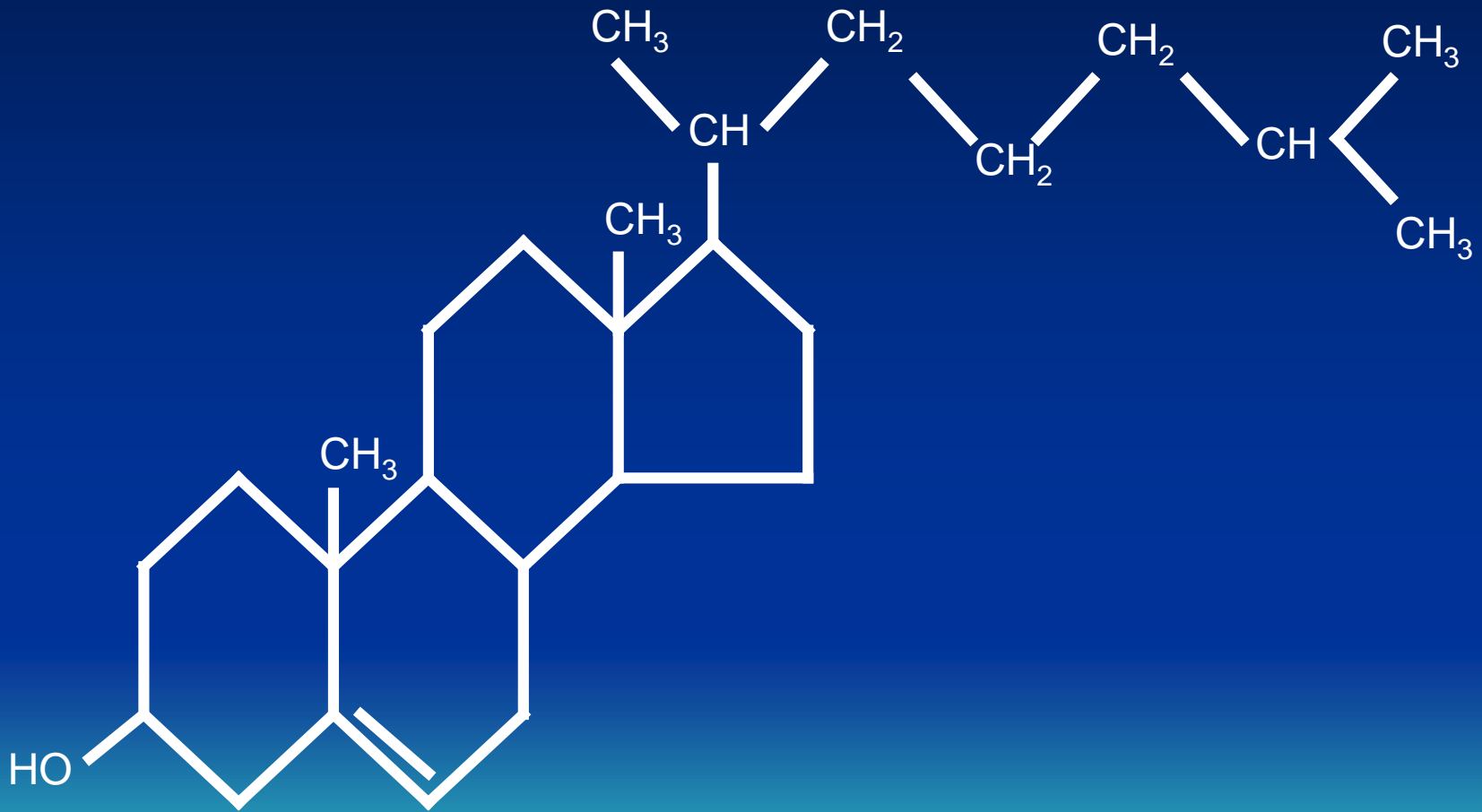
- Ketone bodies (C4) – **water soluble** fuel molecules
- Cholesterol (C27) – membranes and steroid hormone synthesis
- Cholesterol esters – cholesterol storage
- Bile acids and salts (C24) – lipid digestion

## 3. Vitamins

- A, D, E and K.

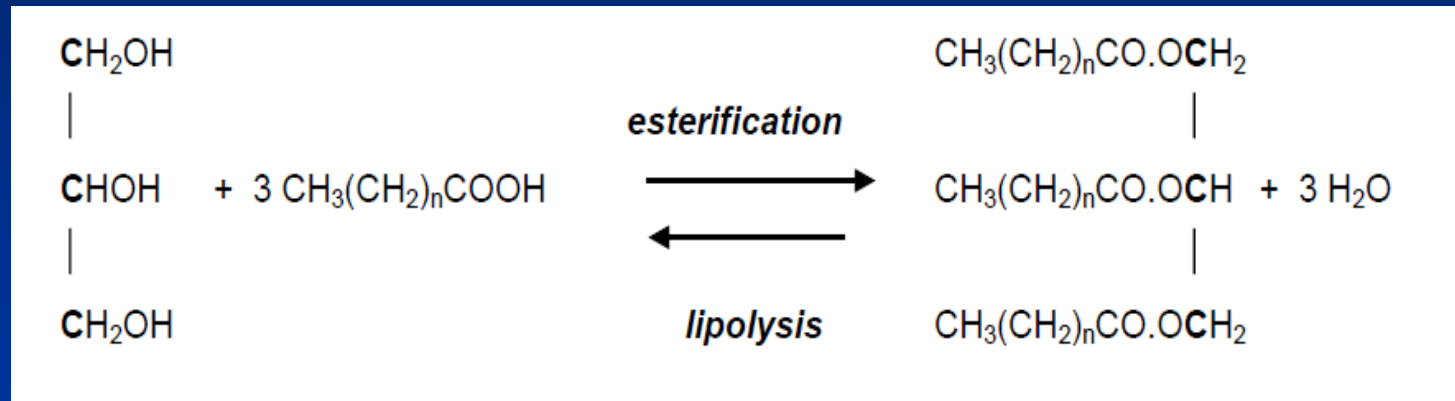


# Cholesterol



# Triacylglycerols

Triacylglycerols are the major dietary and storage lipid in the body. They consist of three fatty acids (usually long chain  $n=16$ ) esterified to glycerol:



## Stage 1 metabolism of triacylglycerols

The major dietary lipids are triacylglycerols (butter, ghee, margarine, vegetable oils).

These are hydrolysed by pancreatic lipase in the small intestine to release glycerol and fatty acids.

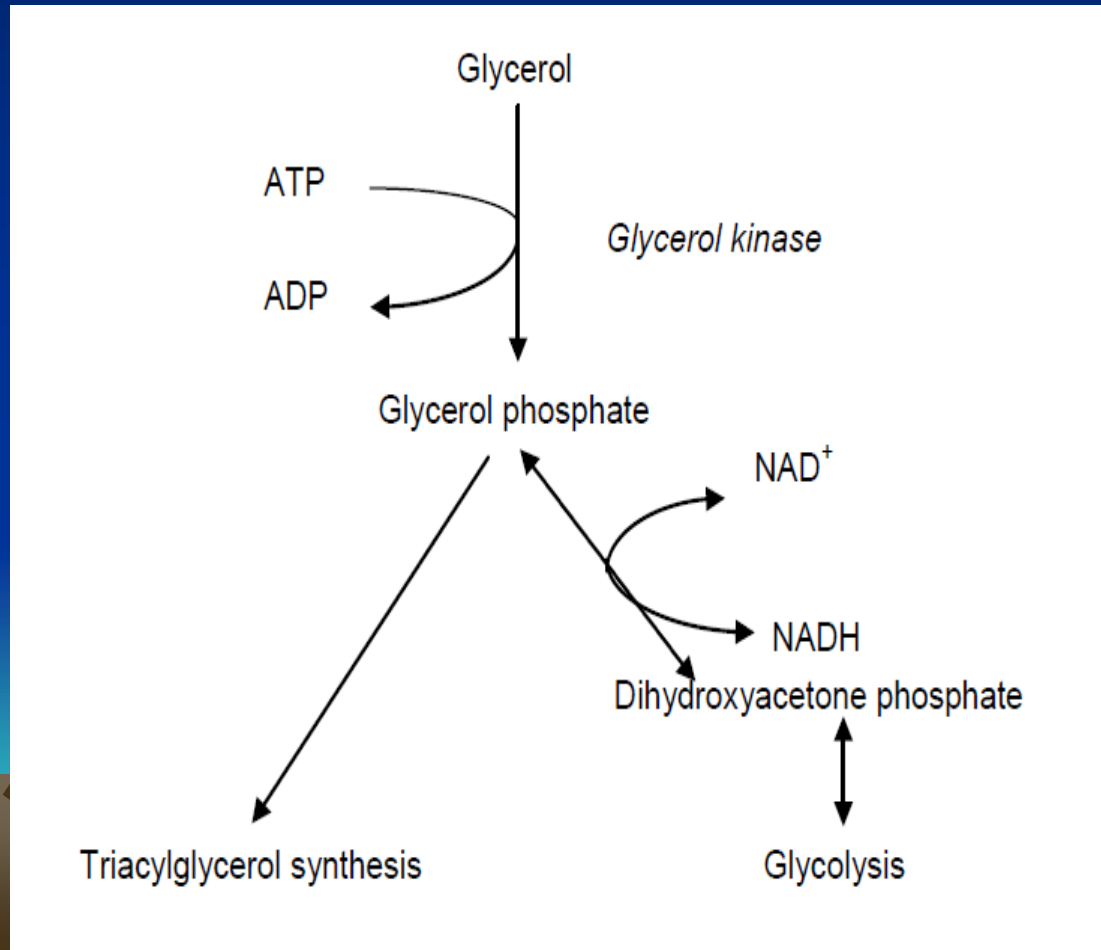
This is a complex process that requires bile salts and a protein factor called colipase.



# Glycerol metabolism

triacylglycerols hydrolysis  $\longrightarrow$  Glycerol

and enters the blood stream and is transported to the liver where it is metabolised:



# Fatty acids

The most common fatty acids in the body are long-chain molecules that contain an even number of C atoms:  $\text{CH}_3(\text{CH}_2)_n\text{COOH}$  ( $n = 14$  to  $18$ ).

They may be saturated or unsaturated (contain  $\text{C}=\text{C}$  double bonds).

- \* The saturated fatty acids are non-essential components of the diet .
- \* Certain polyunsaturated fatty acids ( $>1$  double bond) are essential components of the diet . Arachidonic acid ( $\text{C}_{20:4}$ ) is an important polyunsaturated fatty acid as it is the starting point for the synthesis of the eicosanoids (prostaglandins).



- **Stage 2 catabolism of fatty acids**

When the body is subjected to stress situations (aerobic exercise, starvation, lactation) adipose tissue triacylglycerols are hydrolysed by the enzyme hormone-sensitive lipase to release fatty acids and glycerol that diffuse from the tissue. This process is known as **lipolysis**.

It is activated by adrenaline, glucagon, growth hormone, cortisol and thyroxine and inhibited by insulin. Why?



The fatty acids are carried to tissues via the blood stream bound non-covalently to albumin. The albumin-bound fatty acids are variously called free fatty acids (FFA).

The glycerol is transported in the blood to the liver where it may be oxidised, converted to glucose or used in the synthesis of triacylglycerols.

Many tissues including liver, heart muscle and skeletal muscle can use fatty acids as a source of energy.

The process by which fatty acids are oxidised to release energy is known as  $\beta$ -oxidation and it occurs in mitochondria. Thus, cells such as red blood cells, central nervous system (brain and spinal cord), cannot oxidise fatty acids.



# Fatty acid transport into mitochondria

Net effect: Long-chain fatty acyl CoA is transported from the outside to the inside of mitochondria

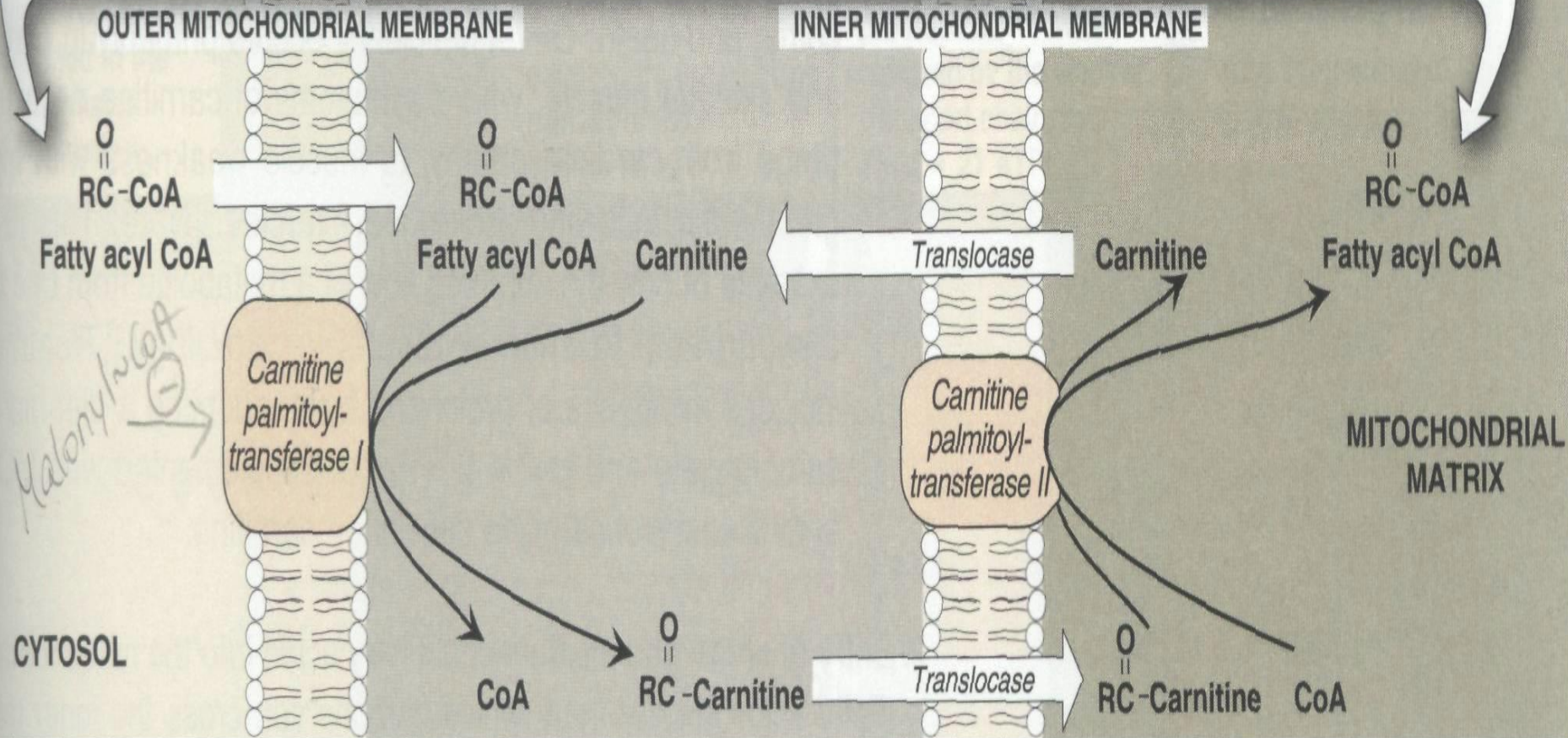
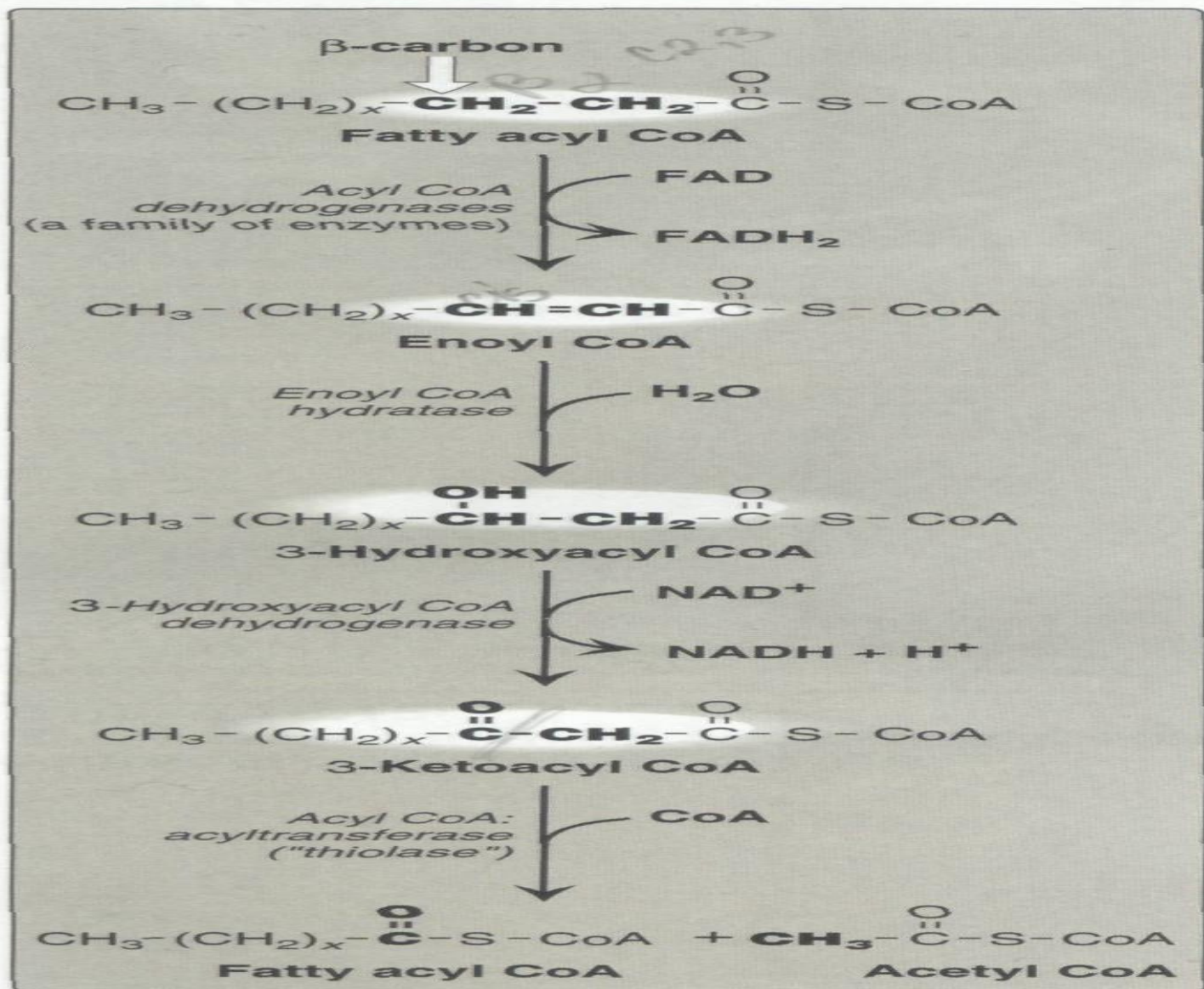


Figure 16.16  
Carnitine shuttle.

# $\beta$ -oxidation of fatty acids



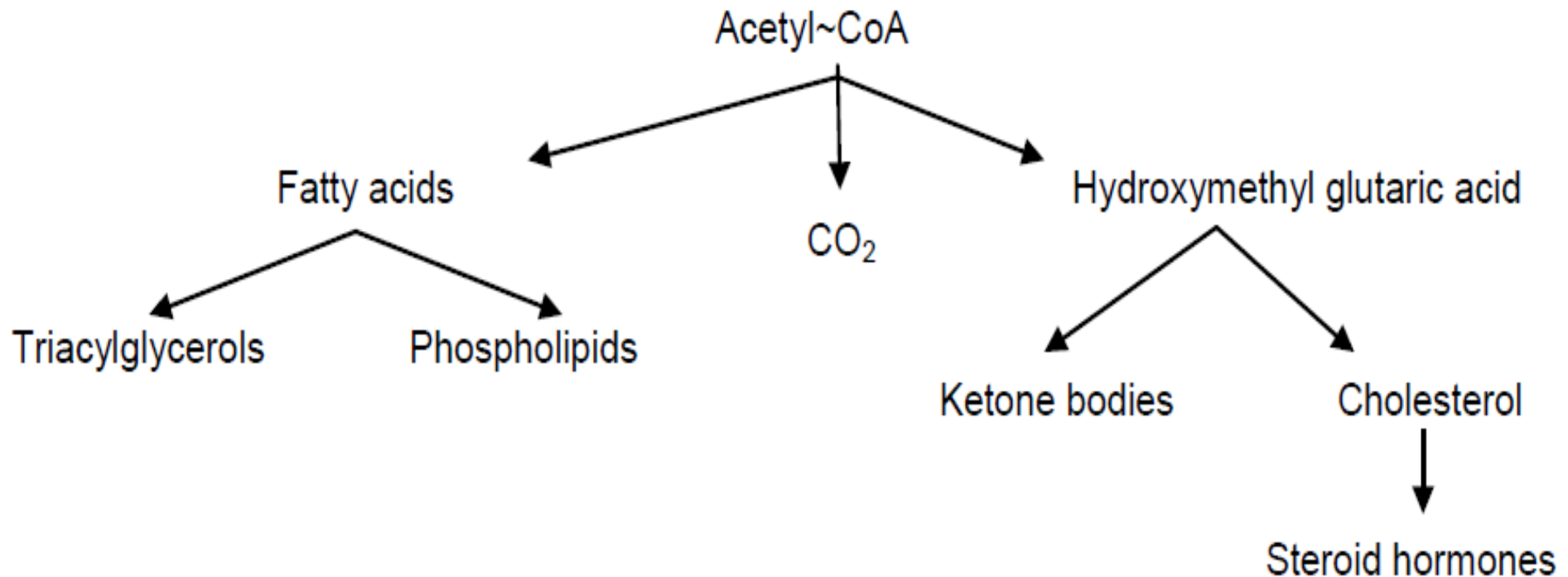
**Figure 16.17**

Enzymes involved in the  $\beta$ -oxidation of fatty acyl CoA.

# Acetyl~CoA

Acetyl~CoA is produced by the catabolism of fatty acids, sugars, alcohol and certain amino acids .

It is also an important intermediate in lipid biosynthesis. The major site of lipid synthesis in the body is the liver .



## Fatty acid synthesis (lipogenesis)

Fatty acids (e.g. palmitic acid,  $\text{CH}_3(\text{CH}_2)_{14}\text{COOH}$ ) are synthesised from acetyl~ CoA (derived from the catabolism of carbohydrate, amino acids) at the expense of ATP and NADPH. The pathway occurs in the **cytoplasm** and can be represented by the overall equation:



Malonyl~CoA is produced from acetyl~CoA by the enzyme *acetyl~CoA carboxylase* in a reaction that requires biotin:



*Acetyl~CoA carboxylase* plays an important role in controlling the rate of fatty acid synthesis.

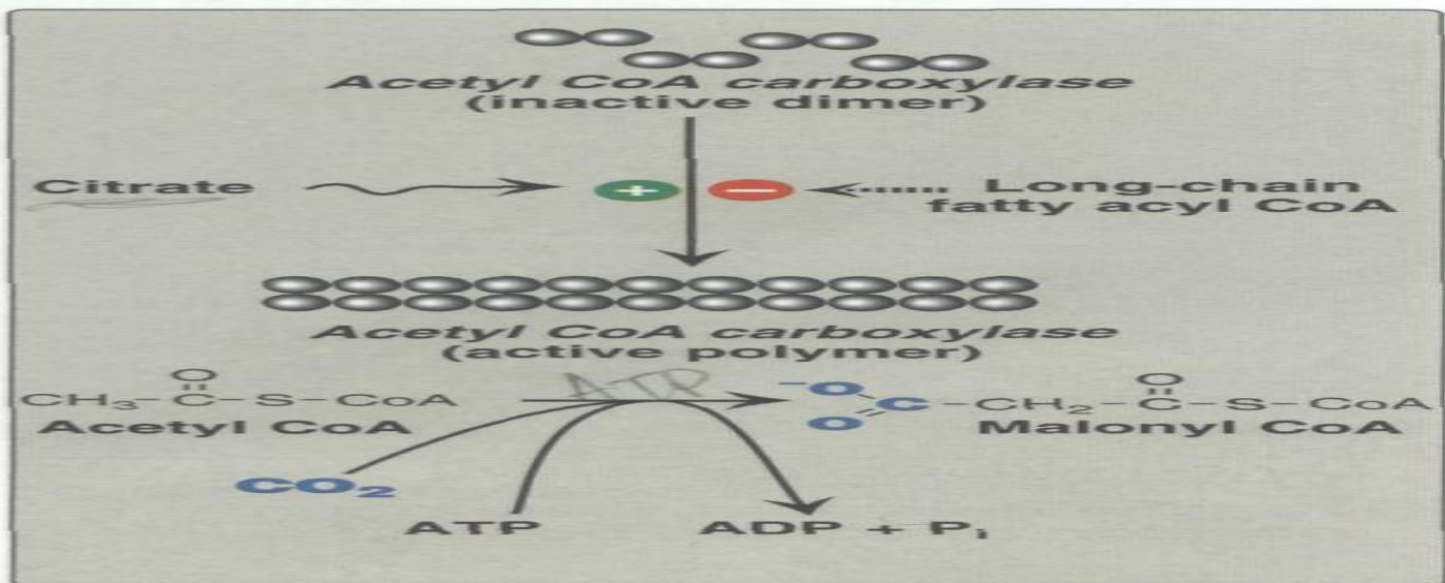
Insulin activates the enzyme by promoting its dephosphorylation while glucagon and adrenaline inhibit the enzyme by promoting its phosphorylation.



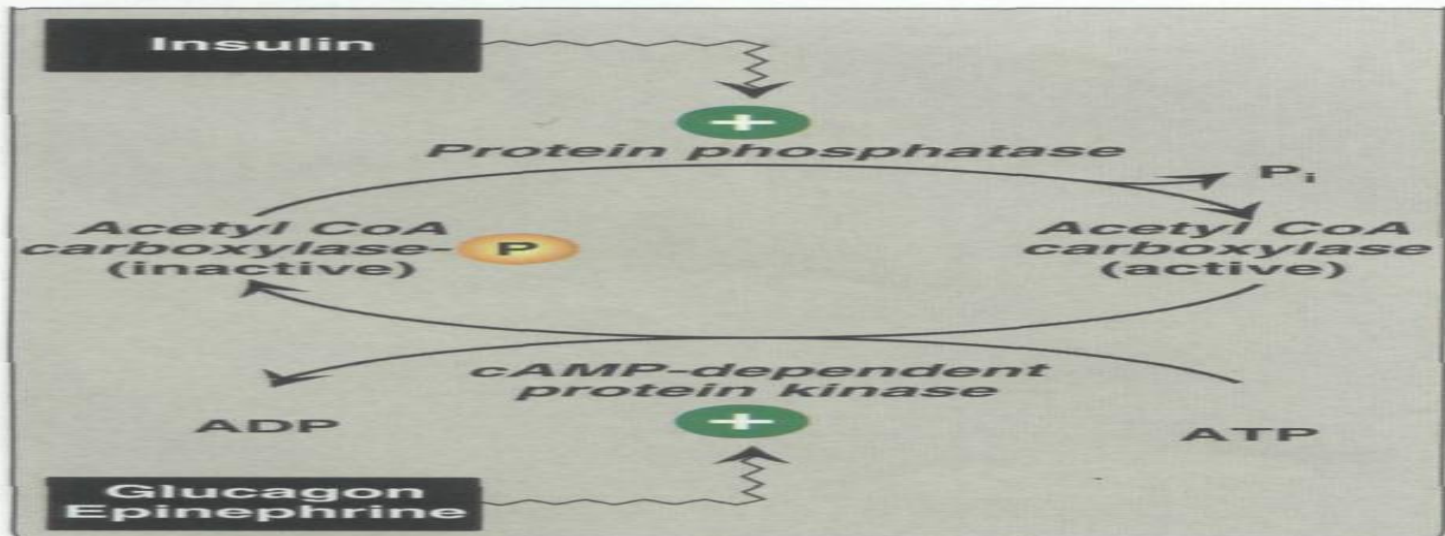
- most of the dietary carbohydrates and proteins in excess of requirement convert to fatty acids and esterified to triacylglycerols to be stored in adipose tissue.
- These processes are important clinically as excessive lipid synthesis and storage is the cause of:
  1. **obesity**
  2. **type 2 diabetes**
  3. **Atherosclerosis** (CVD)

The process is **stimulated** by **insulin** and **inhibited** by the anti-insulin hormones **glucagon** and **adrenaline**.





**Figure 16.7**  
 Allosteric regulation of malonyl CoA synthesis by *acetyl CoA carboxylase*. The carboxyl group contributed by dissolved CO<sub>2</sub> is shown in blue.



**Figure 16.8**  
 Hormone-mediated, covalent regulation of *acetyl CoA carboxylase*.



**Thank you**