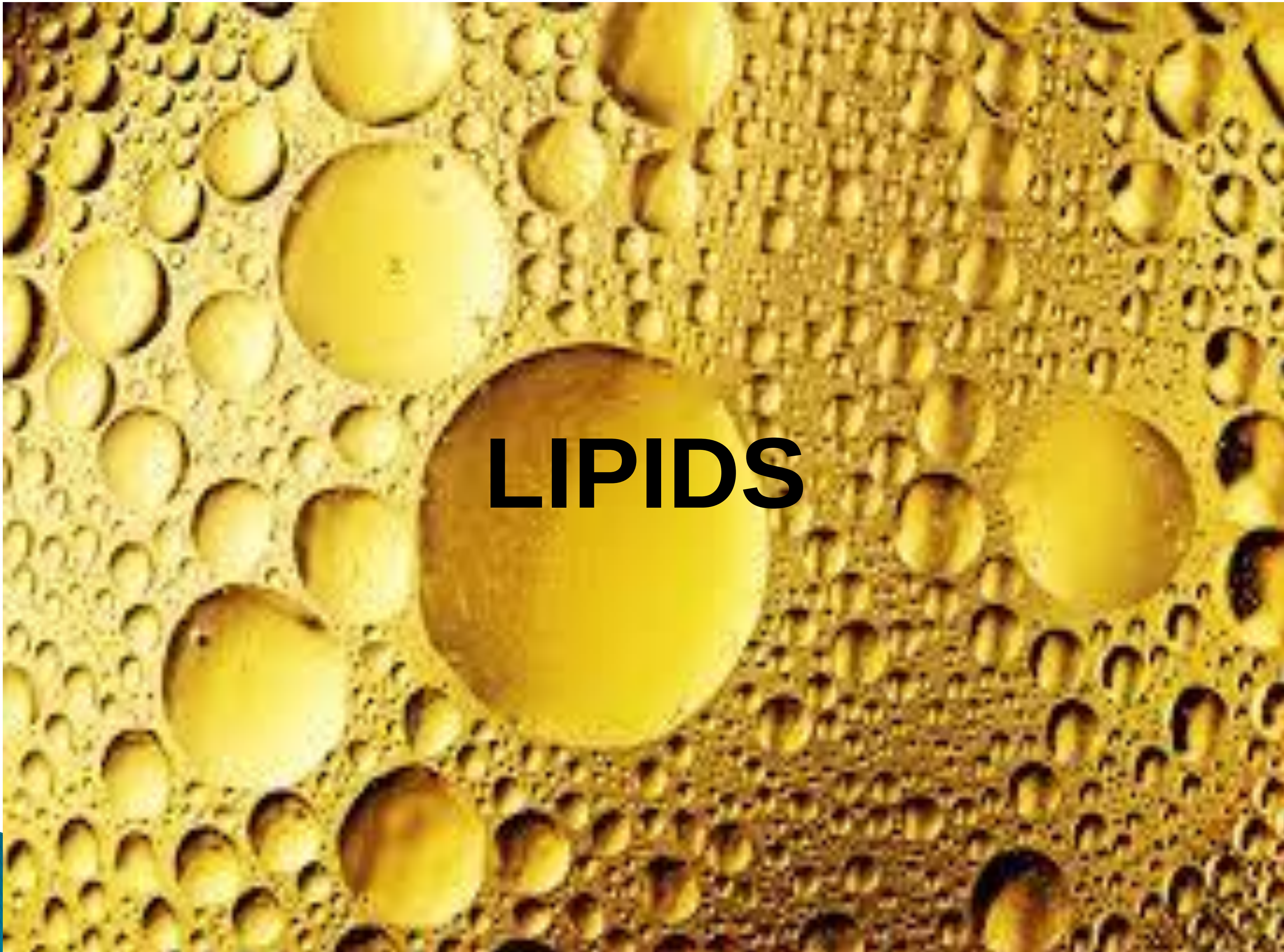
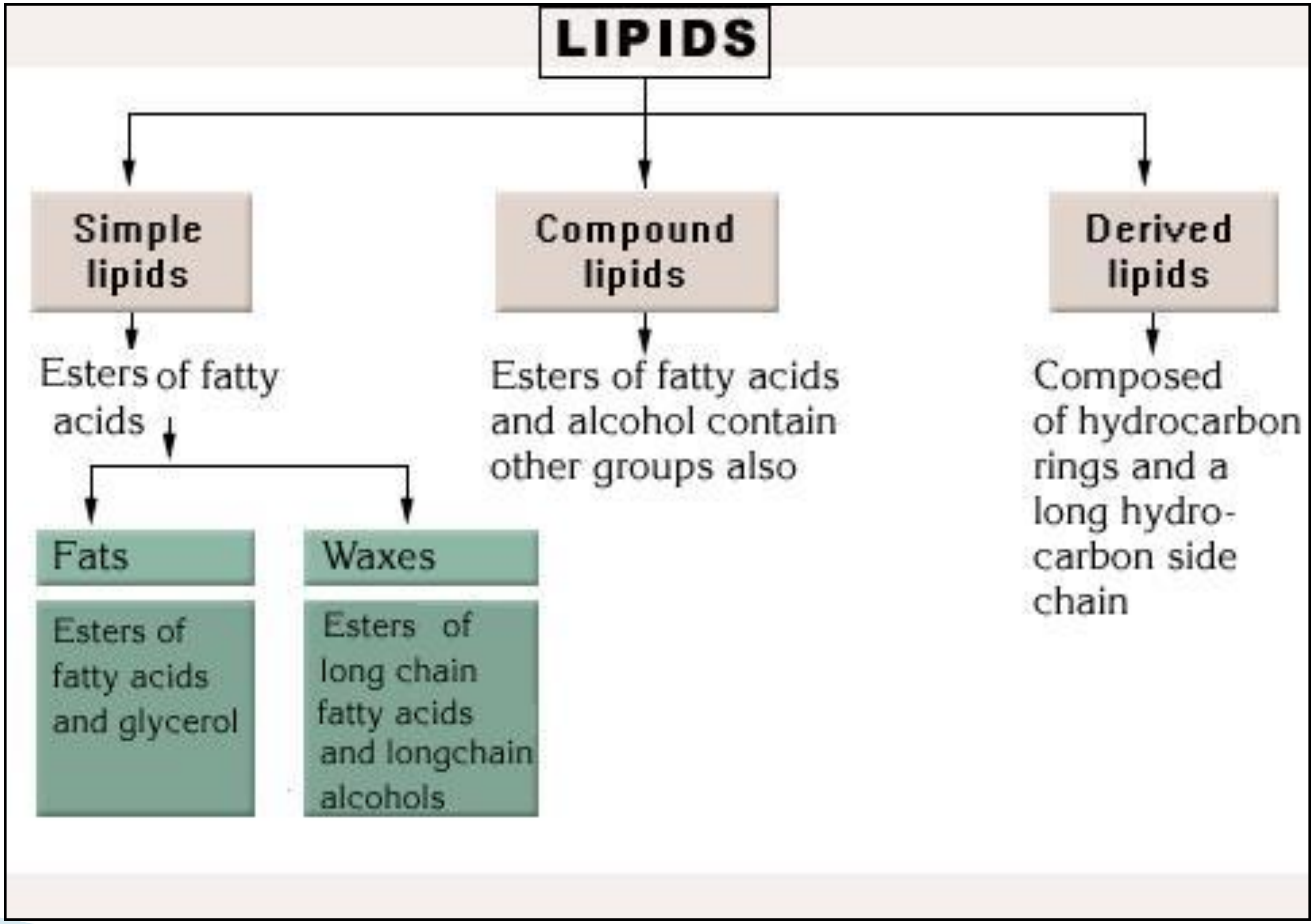
LIPIDS



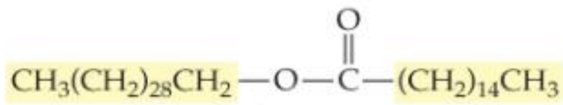
Lipids

- Heterogeneous compounds
- Insoluble in water
- Soluble in organic solvents like ether
- Esters of Fatty acids with alcohol

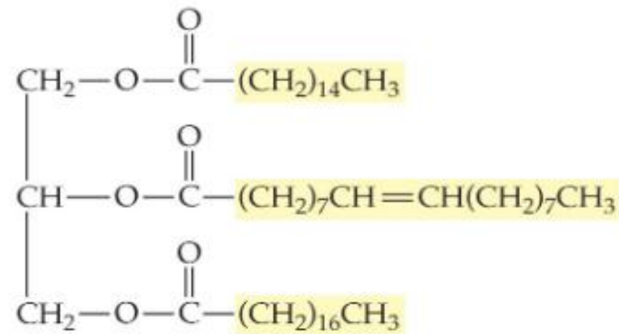
Classification of Lipids



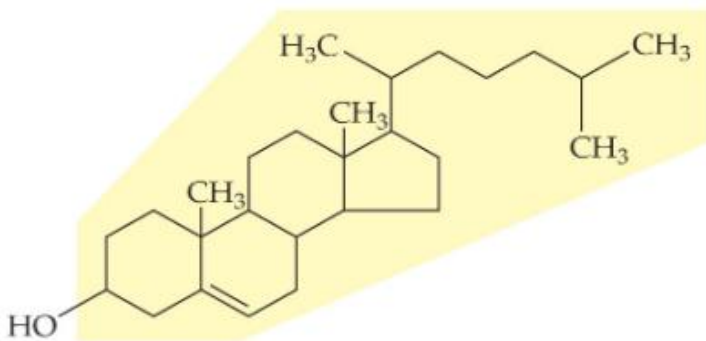
A few representative lipid structures are shown below.



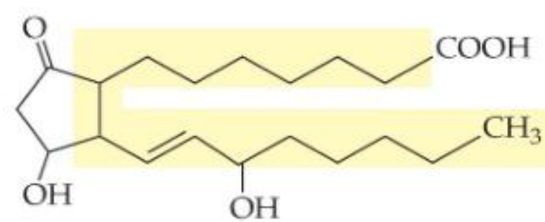
A wax



A triacylglycerol

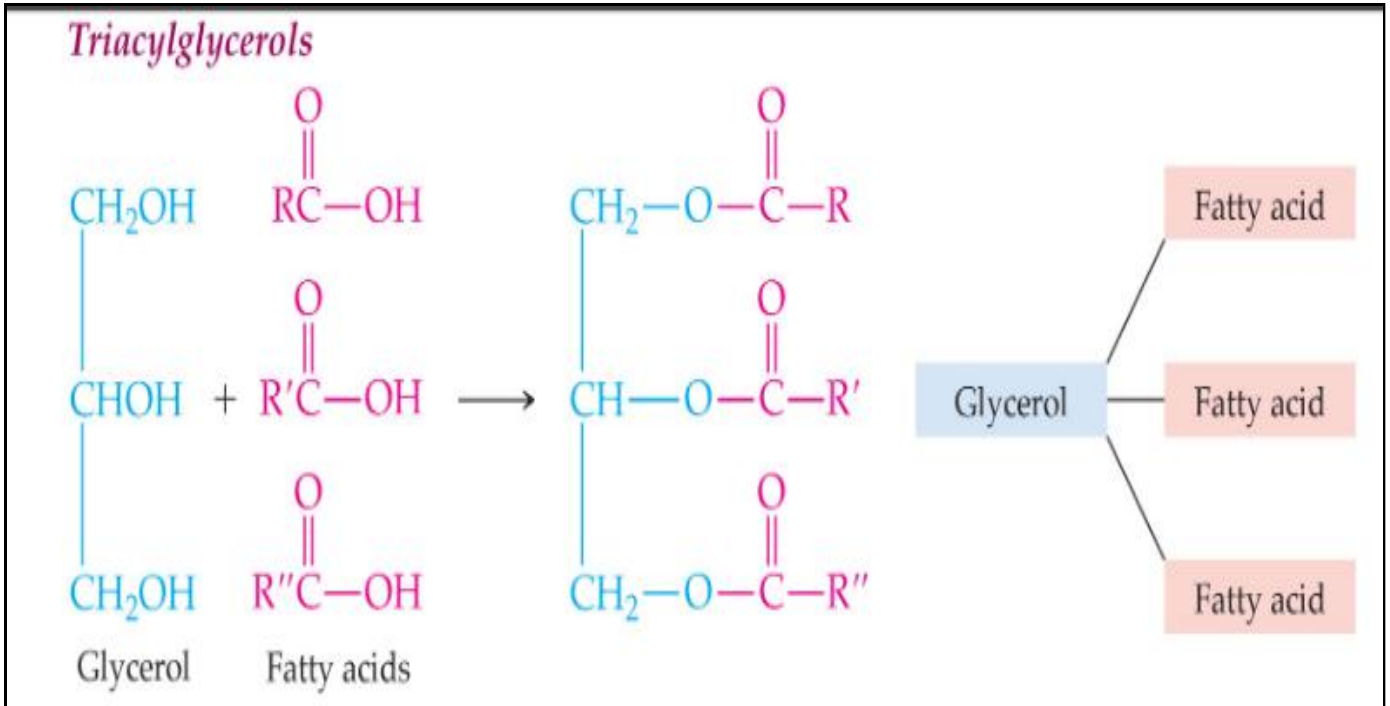


Cholesterol, a steroid

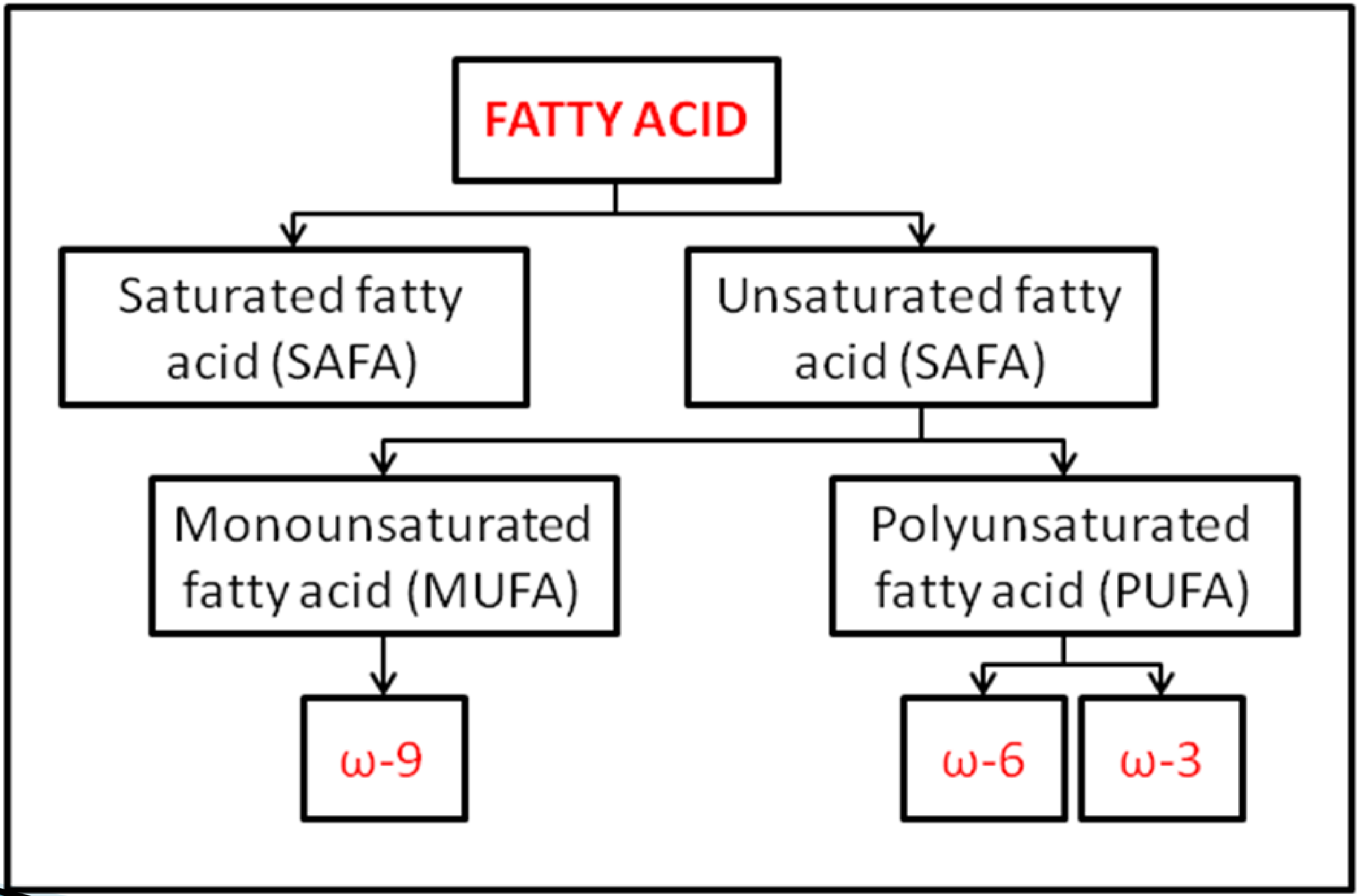


A prostaglandin

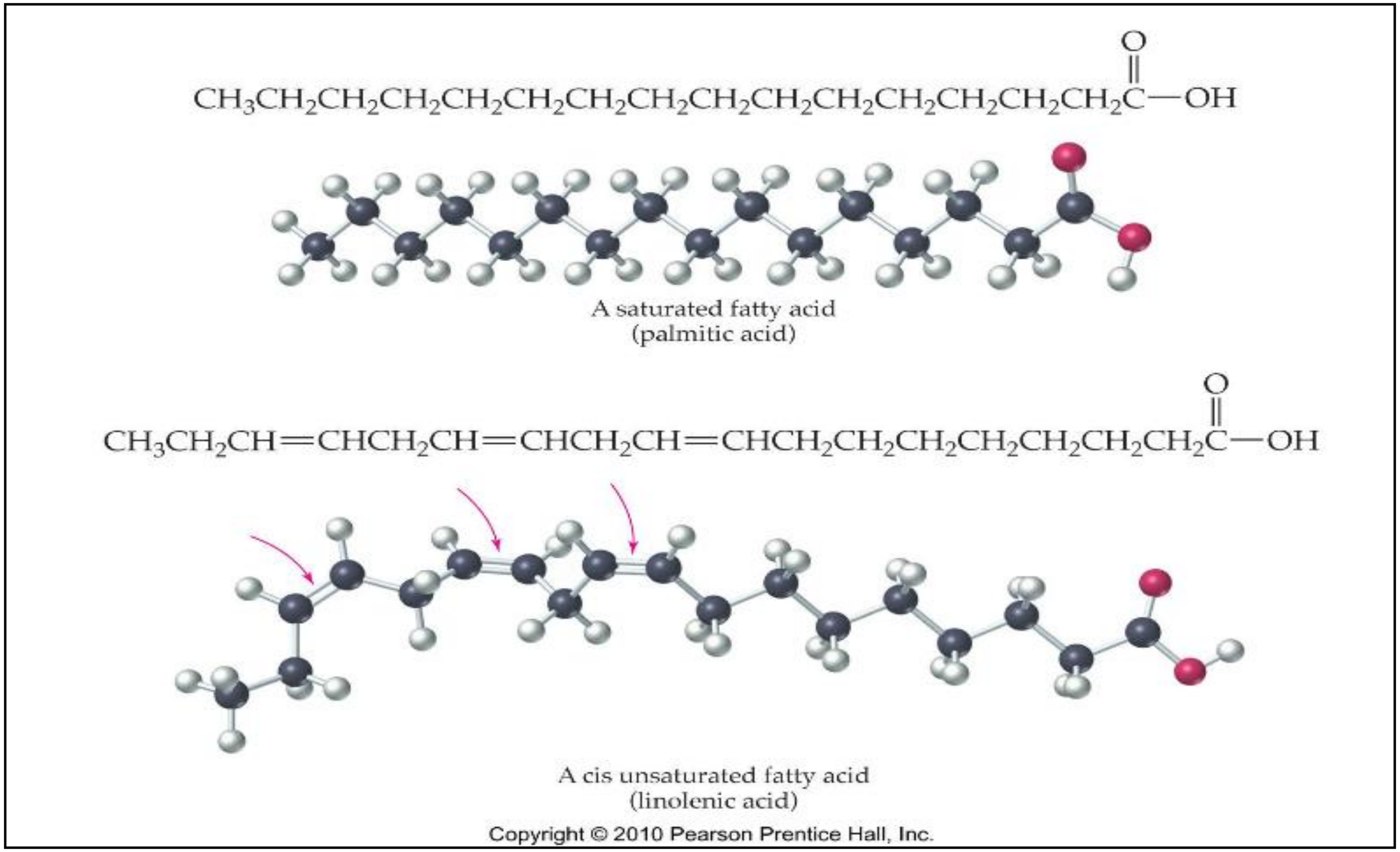
Formation of Fat



Classification of Fatty Acids



Classification of Fatty Acids



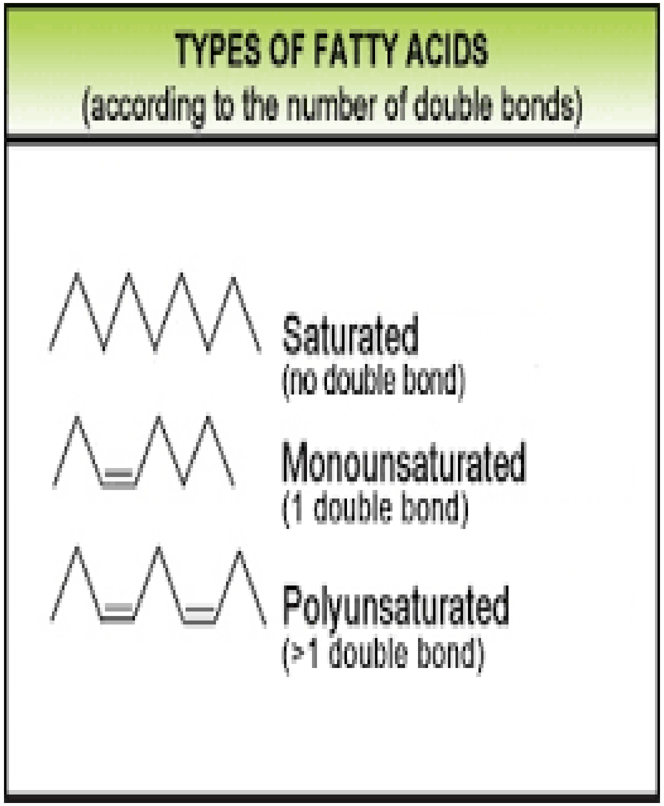
A saturated fatty acid
(palmitic acid)

A cis unsaturated fatty acid
(linolenic acid)

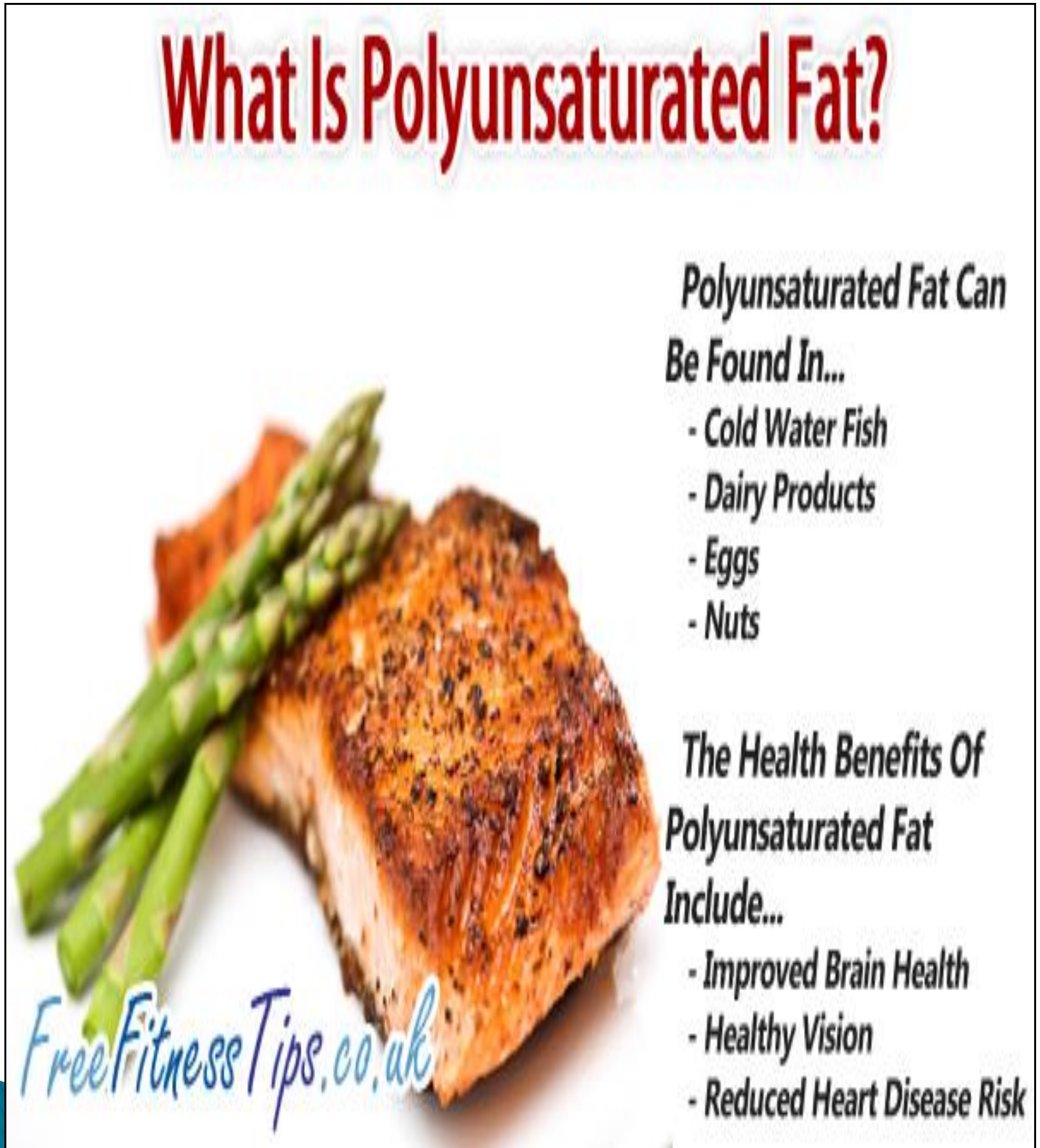
Structures of Some Common Fatty Acids

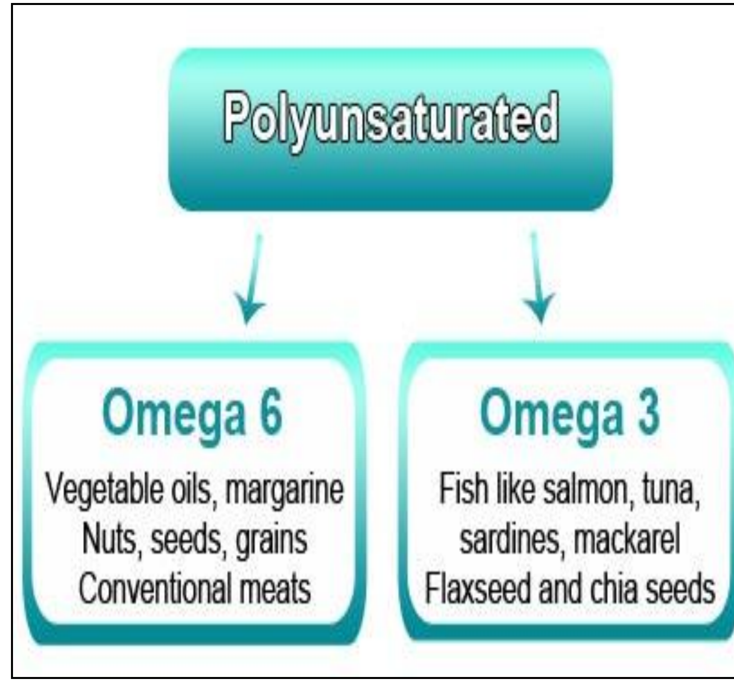
NAME	TYPICAL SOURCE	NUMBER OF CARBONS	NUMBER OF DOUBLE BONDS	CONDENSED FORMULA	MELTING POINT (°C)
Saturated					
Lauric	Coconut oil	12	0	$CH_3(CH_2)_{10}COOH$	44
Myristic	Butter fat	14	0	$CH_3(CH_2)_{12}COOH$	58
Palmitic	Most fats and oils	16	0	$CH_3(CH_2)_{14}COOH$	63
Stearic	Most fats and oils	18	0	$CH_3(CH_2)_{16}COOH$	70
Unsaturated					
Oleic	Olive oil	18	1	$CH_3(CH_2)_7CH{=}CH(CH_2)_7COOH$(cis)	4
Linoleic	Vegetable oils	18	2	$CH_3(CH_2)_4CH{=}CHCH_2CH{=}CH(CH_2)_7COOH$(all cis)	−5
Linolenic	Soybean and canola oils	18	3	$CH_3CH_2CH{=}CHCH_2CH{=}CHCH_2CH{=}CH(CH_2)_7COOH$(all cis)	−11
Arachidonic	Lard	20	4	$CH_3(CH_2)_4(CH{=}CHCH_2)_4CH_2CH_2COOH$(all cis)	−50

MUFA & PUFA


TYPES OF FATTY ACIDS
(according to the number of double bonds)
Saturated
(no double bond)
Monounsaturated
(1 double bond)
Polyunsaturated
(>1 double bond)

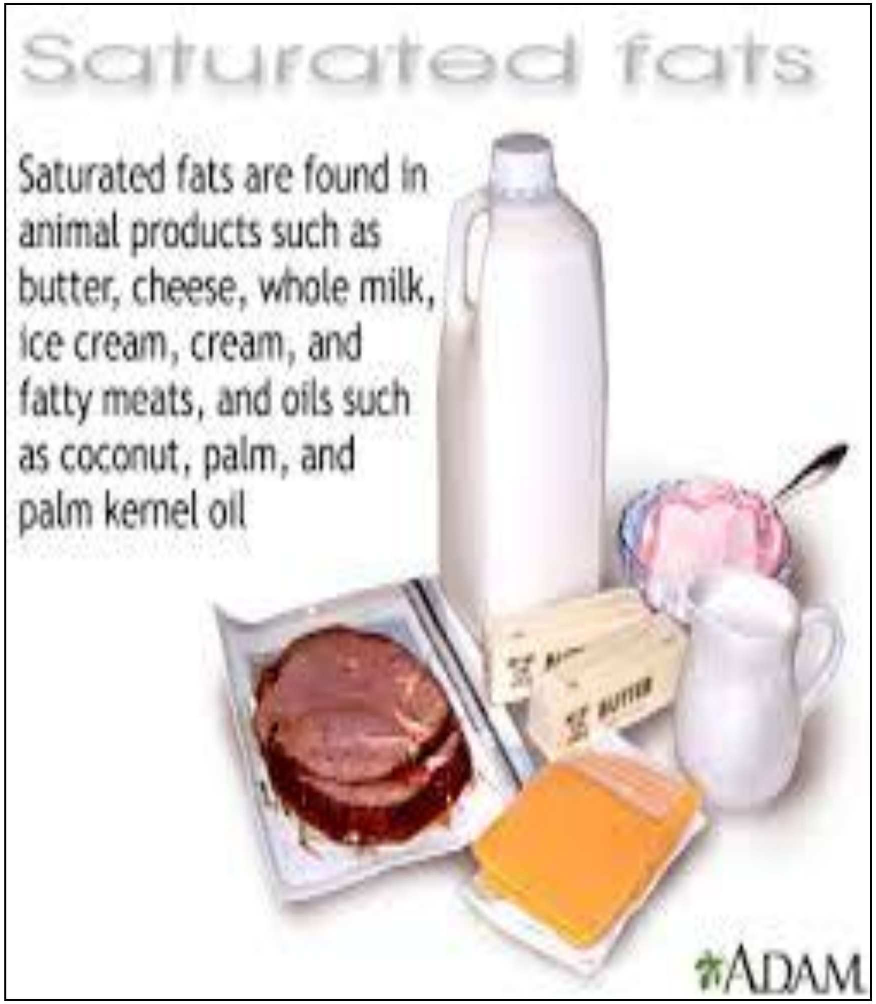

What Is Monounsaturated Fat?
Monounsaturated Fat Can Be Found In...
- Avocados
- Almonds
- Brazil Nuts
- Olive Oil
The Health Benefits Of Monounsaturated Fat Include...
- Enhanced Blood Glucose Control
- Improved Blood Cholesterol Levels
- Reduced Cancer Risk
- Reduced Inflammation
FreeFitnessTips.co.uk





Promote inflammation

Reduce inflammation



Saturated Fat content of Dietary Fats

Canola/Sunola	8%	Diet margarine	8%
Sunflower oil	11%	Poly margarine	13%
Corn/Olive oil	14%	Mono marg.	20%
Soy bean oil	14%	Chicken fat	30%
Peanut oil	20%	Dairy blend	40%
Cottonseed	25%	Lard	40%
Palm oil (red)	50%	Beef tallow	50%
Palm Kernel	90%	Butter	57%
Coconut oil	95%	vegie shortening	>50%

The Biologic Importance of Saturated Fat

CELL MEMBRANES Require (50%) saturated fatty acids to be "waterproof" and function properly

HEART Prefers saturated long-chain 16-carbon palmitic and 18-C stearic acid (over carbohydrates) for energy

BONES Need saturated fats to assimilate calcium effectively

LIVER They protect it from the adverse effects of alcohol and medications like acetaminophen

LUNGS Lung surfactant, which prevents asthma and other breathing disorders, is composed entirely of 16-C palmitic acid

HORMONES They function as signaling messengers for hormone production

IMMUNE SYSTEM Saturated fats play an important role here. They--

Prime white blood cells to destroy invading bacteria, viruses and fungi, and to fight tumors

And medium-chain 12-C lauric acid and 14-C myristic acid (in butter) kill bacteria and candida in the gut

SIGNAL SATIETY So you eat less, lose fat, and maintain a normal weight

GENERAL HEALTH Eating saturated fats lowers consumption of health-damaging carbohydrates and polyunsaturated vegetable oils

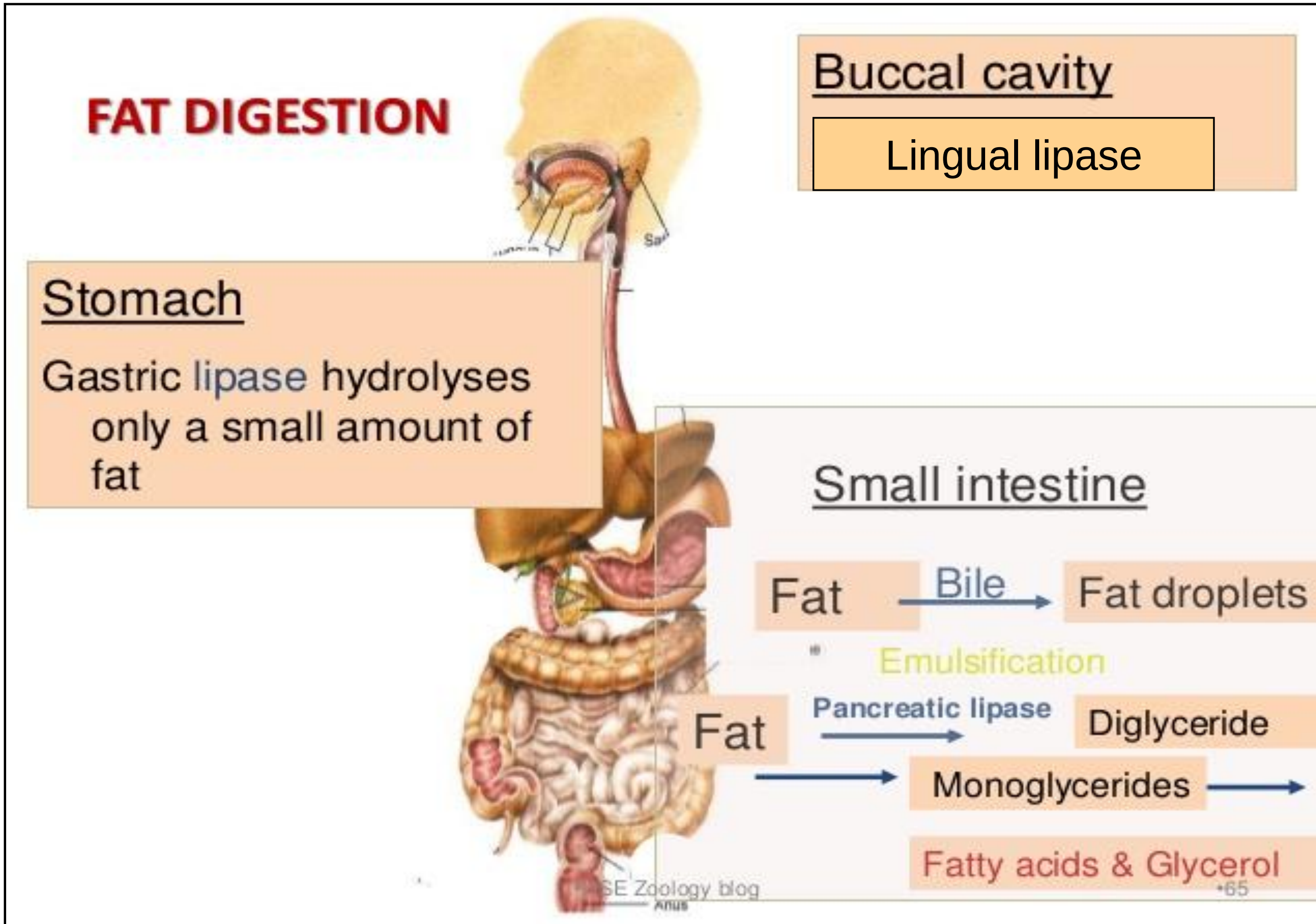
Detrimental effect: Raises blood cholesterol level

Fats & Oils

- **Oil:** A mixture of triacylglycerols that is liquid because it contains a high proportion of unsaturated fatty acids.
- **Fat:** A mixture of triacylglycerols that is solid because it contains a high proportion of saturated fatty acids.

Function of Fat

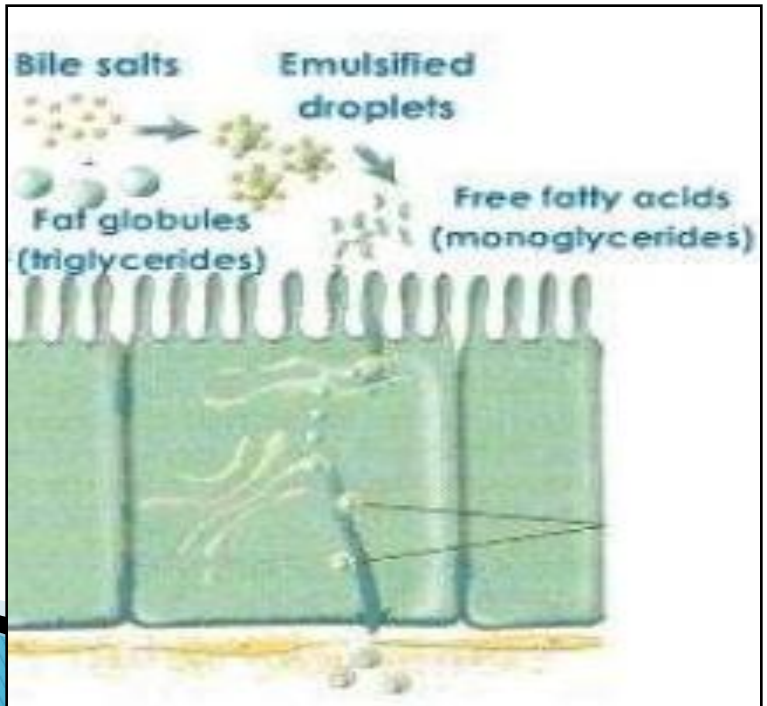
- Energy source
- They are stored in adipose tissue
- Essential nutrients
- Components of biological membranes
- Many hormones are lipids (e.g. testosterone, cortisol etc)
- Receptor, antigens and membrane anchors
- Reducing the loss of body heat (Insulator)
- Electrical insulator of axon of neurons
- Facilitate the digestive process by depressing gastric secretion
- Bile salts solubilize phospholipids and cholesterol
- Pheromones


FAT DIGESTION
Buccal cavity
Lingual lipase
Stomach
Gastric lipase hydrolyses only a small amount of fat
Small intestine
Fat
Bile
Fat droplets
Emulsification
Fat
Pancreatic lipase
Diglyceride
Monoglycerides
Fatty acids & Glycerol
Zoology blog
Anus

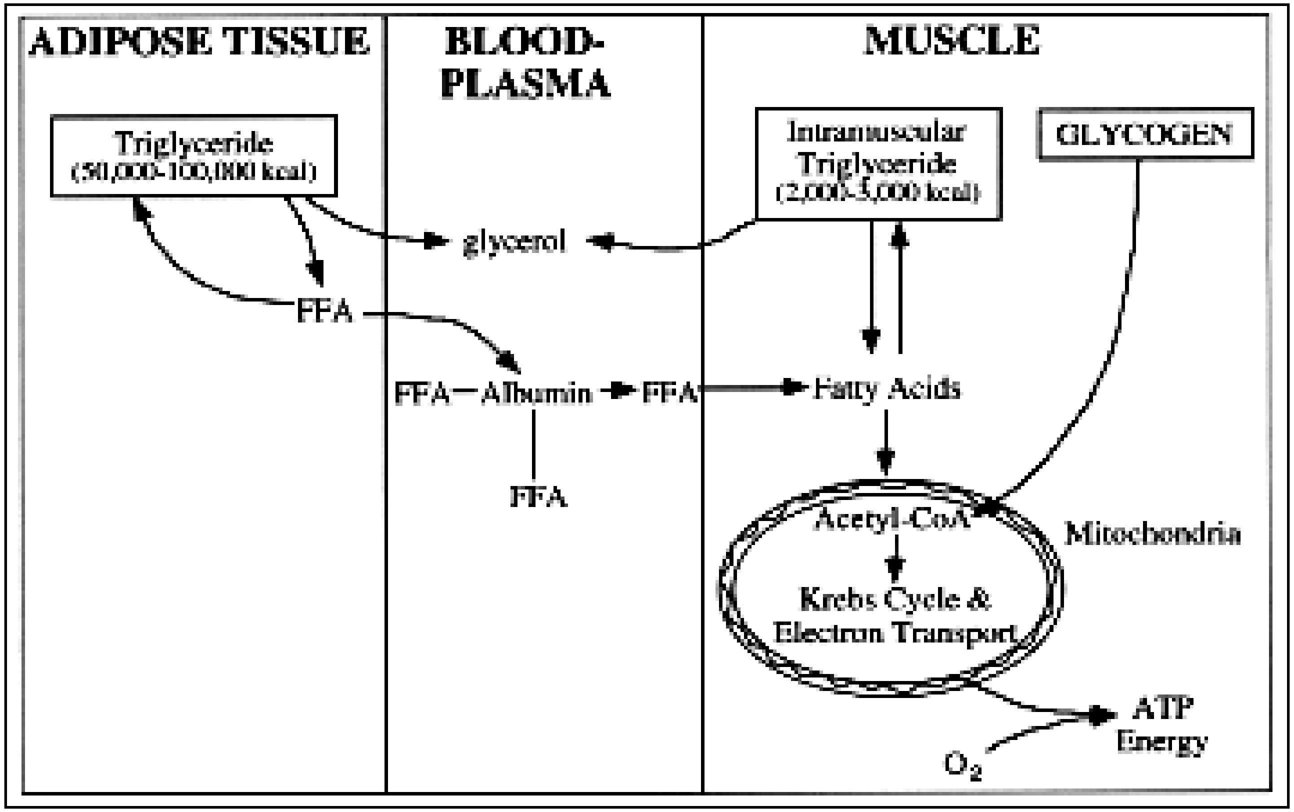
ABSORPTION OF FAT

- Fatty acids and glycerol insoluble in water so they cannot be absorbed directly from the lumen of the intestine.
- With the help of bile salts & phospholipids the fatty acids and glycerol are converted into small spherical water soluble droplets called **micelles.**

Micelles are reformed into very small protein coated fat globules called chylomicrons. Which are transported in to the lymph vessels (lactales)in the villi.



Storage & Utilization of Fats



- Triglyceride from adipose tissue can be broken down to glycerol and free fatty acids (FFA).
- The fatty acids have two fates -- they can also be released into circulation or they can be re-esterified back into triglycerides.
- FFA can be mobilized by binding to plasma albumin for transportation in the circulation to skeletal muscle and other tissues.
- Intramuscular triglyceride can also be broken down to glycerol and fatty acids, which enter the mitochondria for oxidation during exercise.

Fatty Acid Oxidation

TYPES OF FATTY ACID OXIDATION

Fatty acids can be oxidized by-

1) **Beta oxidation-** Major mechanism, occurs in the mitochondria matrix. 2-C units are released as acetyl CoA per cycle.

2) **Alpha oxidation**- Predominantly takes place in brain and liver, one carbon is lost in the form of CO_2 per cycle.

3) **Omega oxidation-** Minor mechanism, but becomes important in conditions of impaired beta oxidation

4) **Peroxisomal oxidation-** Mainly for the trimming of very long chain fatty acids.

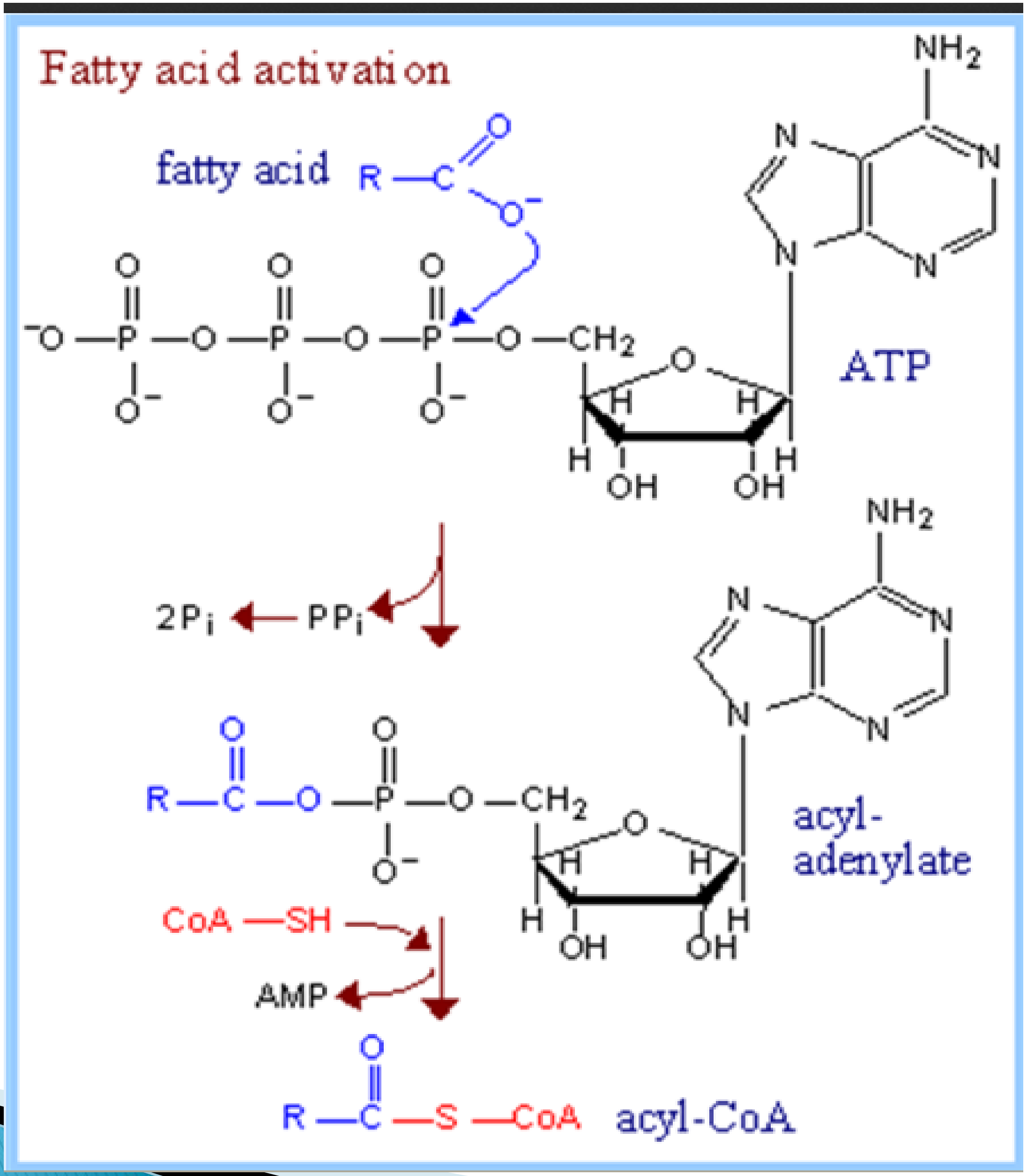
Fatty acid oxidation

- Site : all tissues , prominent in liver and skeletal muscle.
- Intracellular location: mitochondria.
- Substrate: fatty acids.
- Product: acetyl CoA, NADH, FADH2

Steps in fatty acid oxidation

- Activation of fatty acids
- Transport of fatty acids across mitochondrial membranes into mitochondrial matrix
- Beta oxidation of fatty acids.

Activation of fatty acids

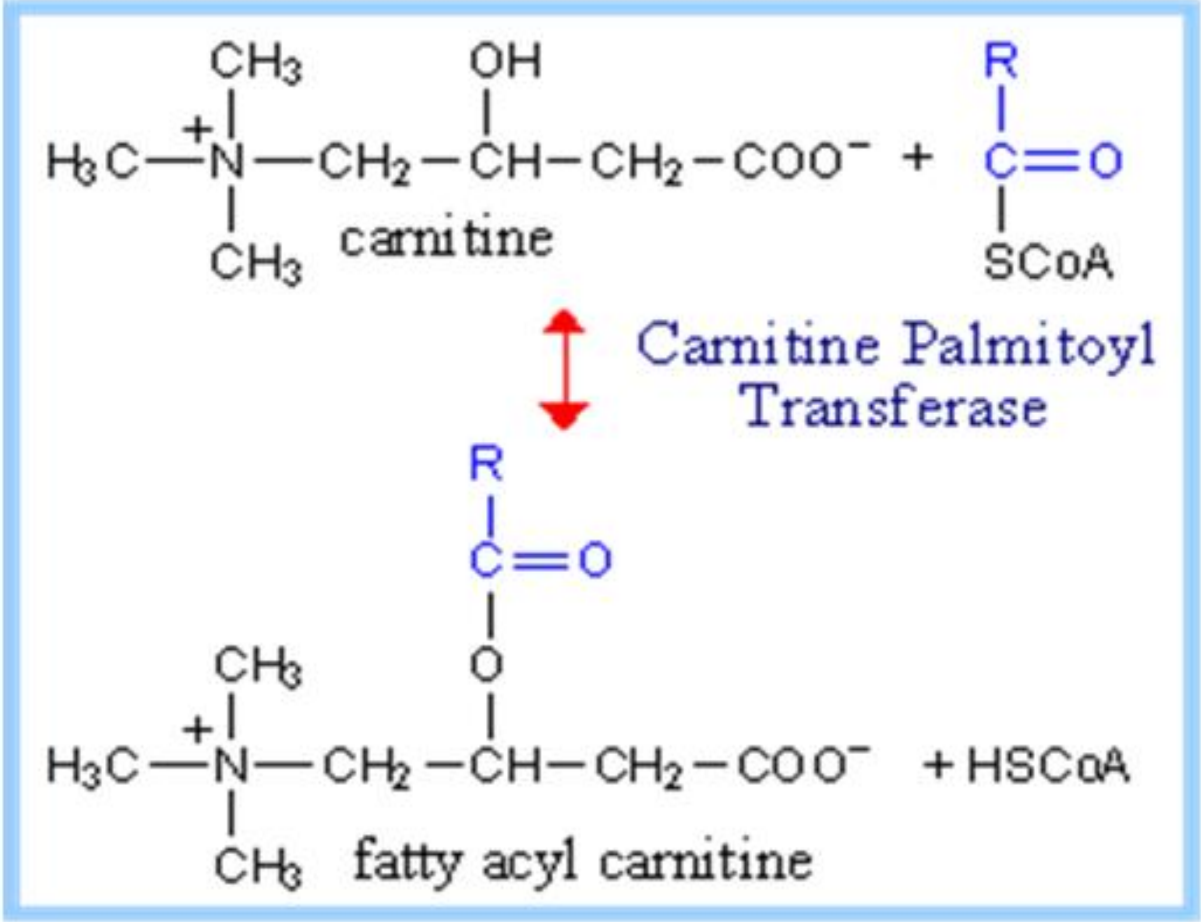


Carnitine as a Carrier

Carnitine carries fatty acyl groups across the inner mitochondrial membrane

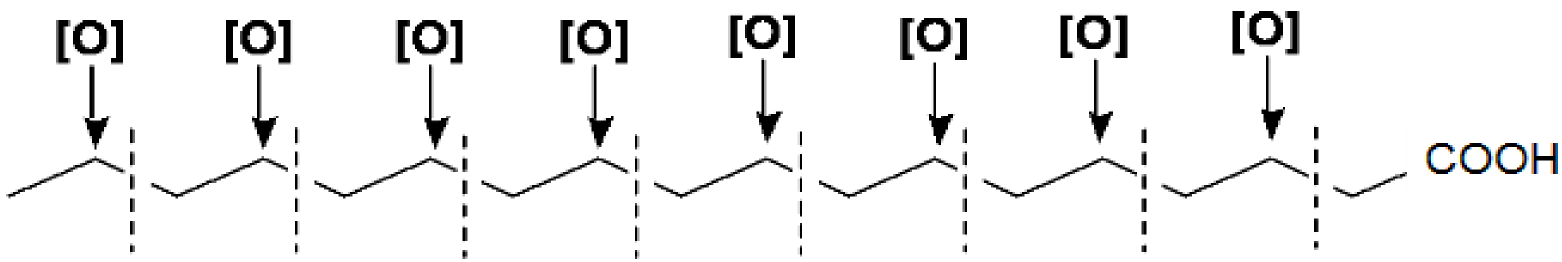
- Mitochondrial inner membrane is impermeable to bulky polar molecules like CoA.
- Hence acyl group from cytosol is carried into mitochondrial matrix by carnitine- carnitine shuttle.
- Short chain fatty acids are carried directly into the mitochondrial matrix
- Long-chain and medium chain FAs are converted to acyl carnitines and are then transported in to the mitochondria.
- Acyl-CoA are reformed inside the mitochondria

Carnitine as a Carrier

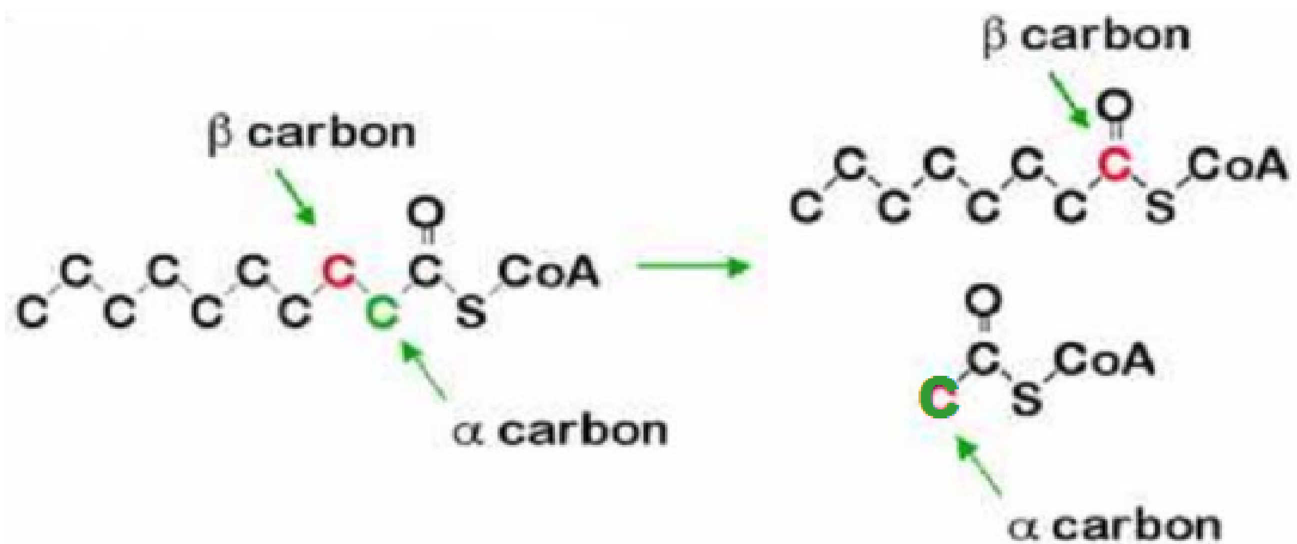


Beta Oxidation

- **Oxidation of fatty acids to acetyl CoA**



In this process the β carbon is oxidised via a ketone intermediate to a thioester

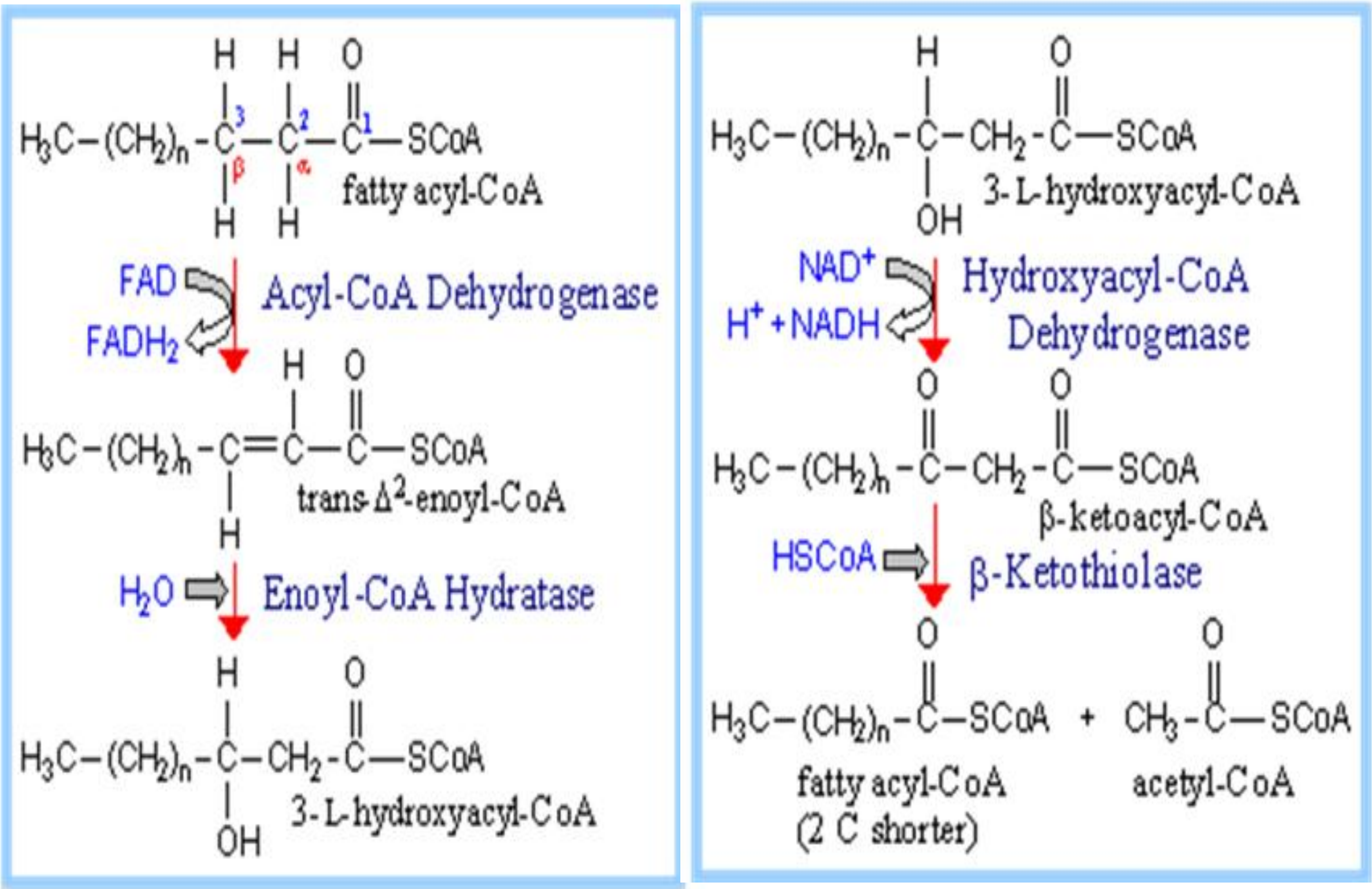


Beta-oxidation

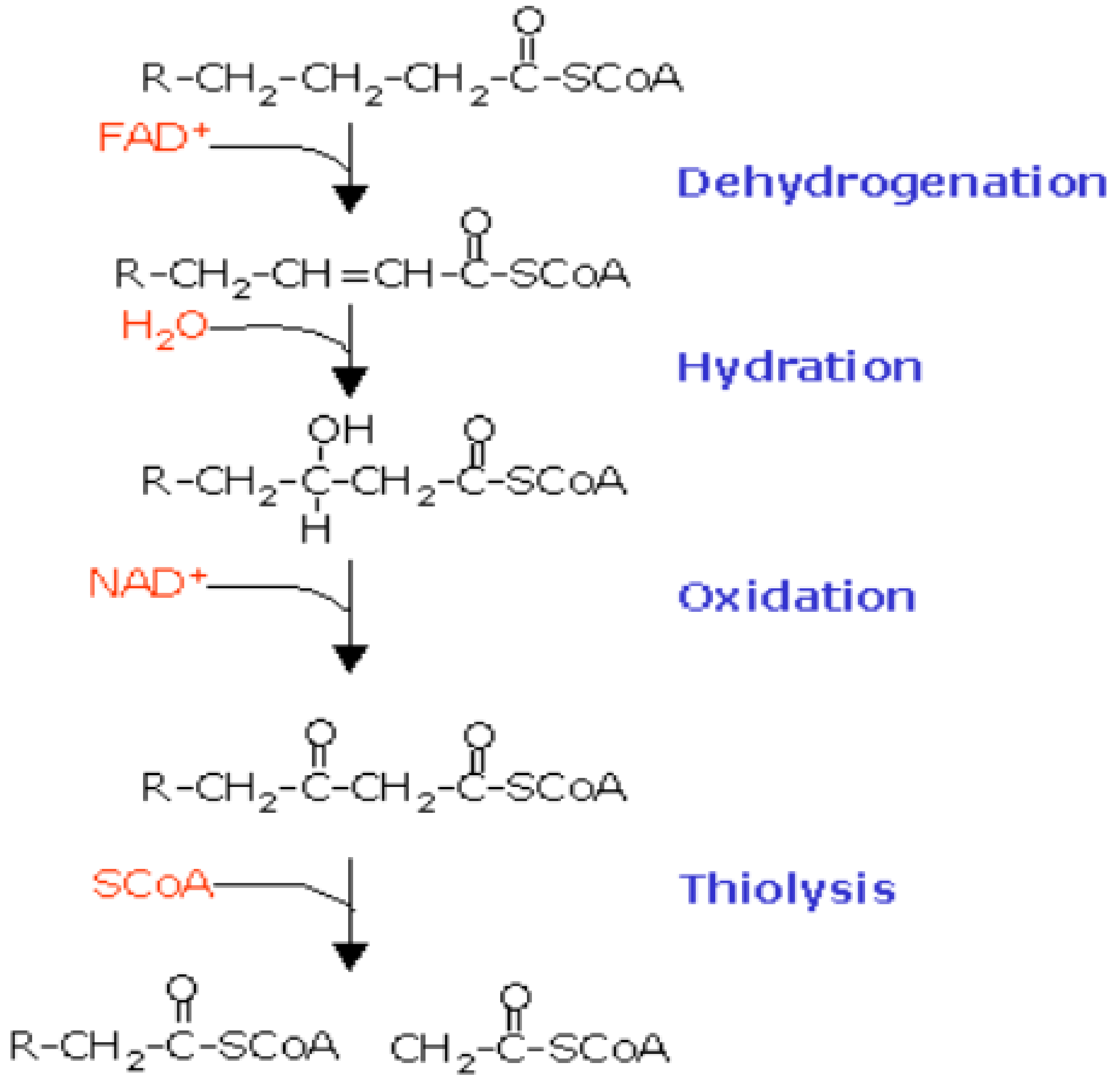
<u>Four enzymatic reactions</u>:

- **1.Dehydrogenation** between alpha and beta carbons(C2 and C3) in a FAD-linked reaction.
- **2.Hydration** of the double by enoyl CoA hydratase.
- **3.A second dehydrogenation** in a NAD-linked reaction.
- **4.Thiolytic cleavage** of the thioester by beta-ketoacyl CoA thiolase.
- This sequence of reactions <u>repeated</u> until the fatty acyl chain is completely degraded to acetyl CoA.\

Beta – oxidation of fatty acids



Beta – oxidation of fatty acids



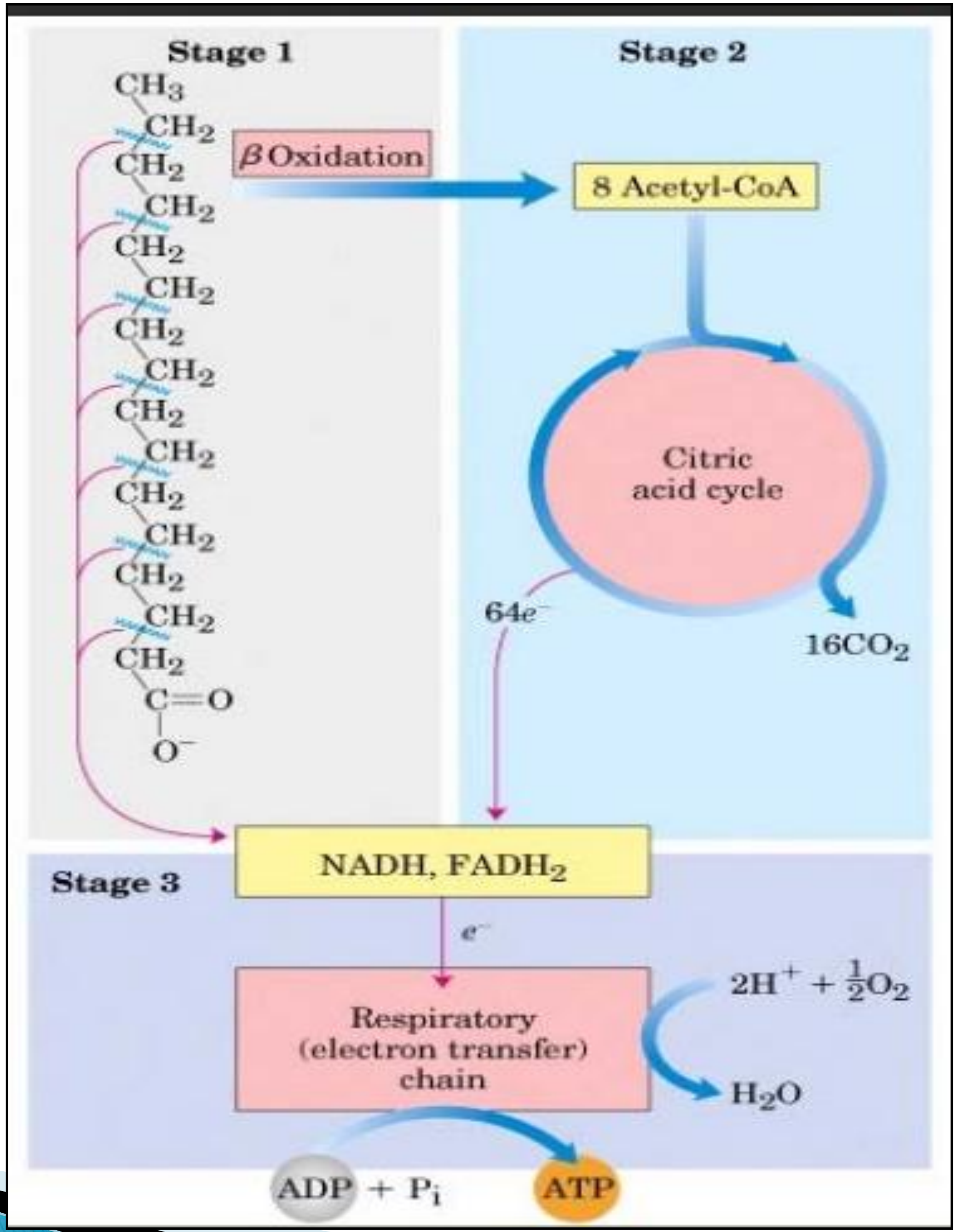
Complete Beta Oxidation of Palmitoyl CoA

CH_3CH_2-CH_2CH_2-CH_2CH_2-CH_2CH_2-CH_2CH_2-CH_2CH_2-CH_2CH_2-$CH_2COSCoA$

$$\xrightarrow{\text{7 Cycles}}$$

$$8\ CH_3COSCoA + 7\ FADH_2 + 7\ NADH + 7\ H^+$$

Oxidation of 8 acetyl-CoA in TCA cycle will produce 8 ATPs, 8 $FADH_2$, 24 NADH


Stage 1
Stage 2
CH_3
CH_2
β Oxidation
8 Acetyl-CoA
Citric acid cycle
$64e^-$
$16CO_2$
$C=O$
O^-
Stage 3
NADH, $FADH_2$
e^-
Respiratory (electron transfer) chain
$2H^+ + \frac{1}{2}O_2$
H_2O
ADP + P_i
ATP

Energy yield from palmitic acid

		ATP
• **From palmitoyl CoA to acetyl CoA**:		
Acyl CoA dehydrogenase	7 $FADH_2$	14
Beta-OH dehydrogenase	7 NADH	21
• **From 8 acetyl CoA**		96
• Total energy yield		131
ATP are used for activation of FA		-2
Hence net gain of ATP		**129**

Regulation of fatty acid oxidation

•**CPT-1 is the rate determining step**. It is allosterically inhibited by malonyl CoA

•Starvation/Hypoglycemia increases β oxidation.

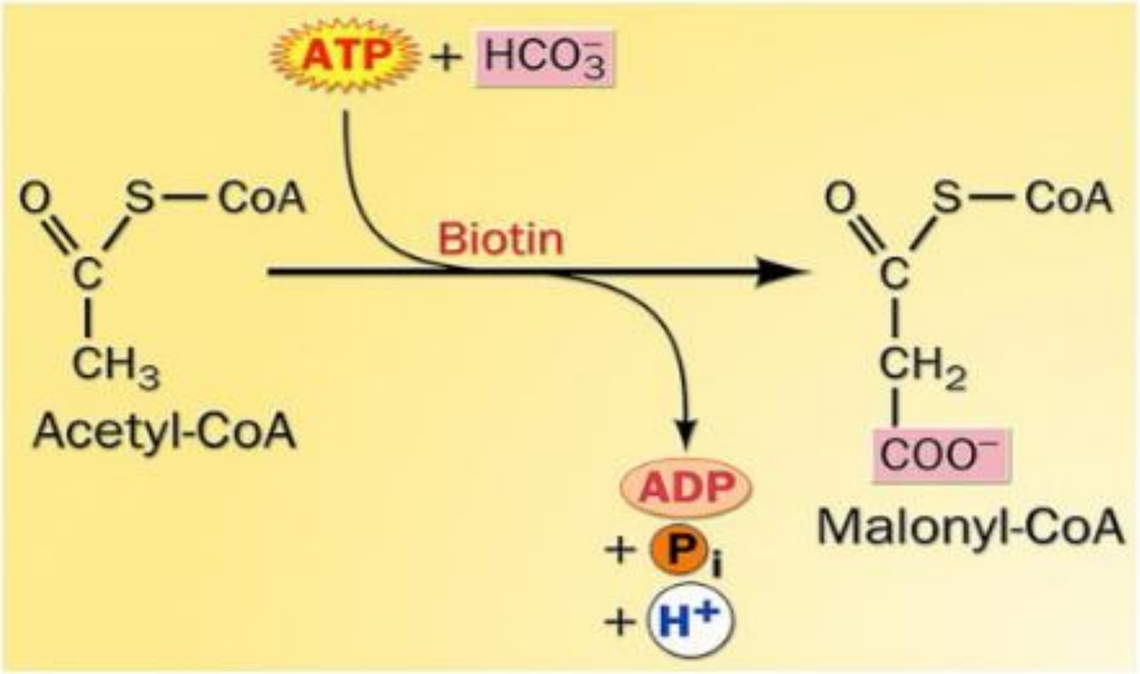
•Malonyl CoA inhibits β oxidation

•β oxidation yields Acetyl CoA, NADH & FADH requiring the respiratory chain for further metabolism.

•Fatty acids cannot be used as an energy source in the absence of O_2

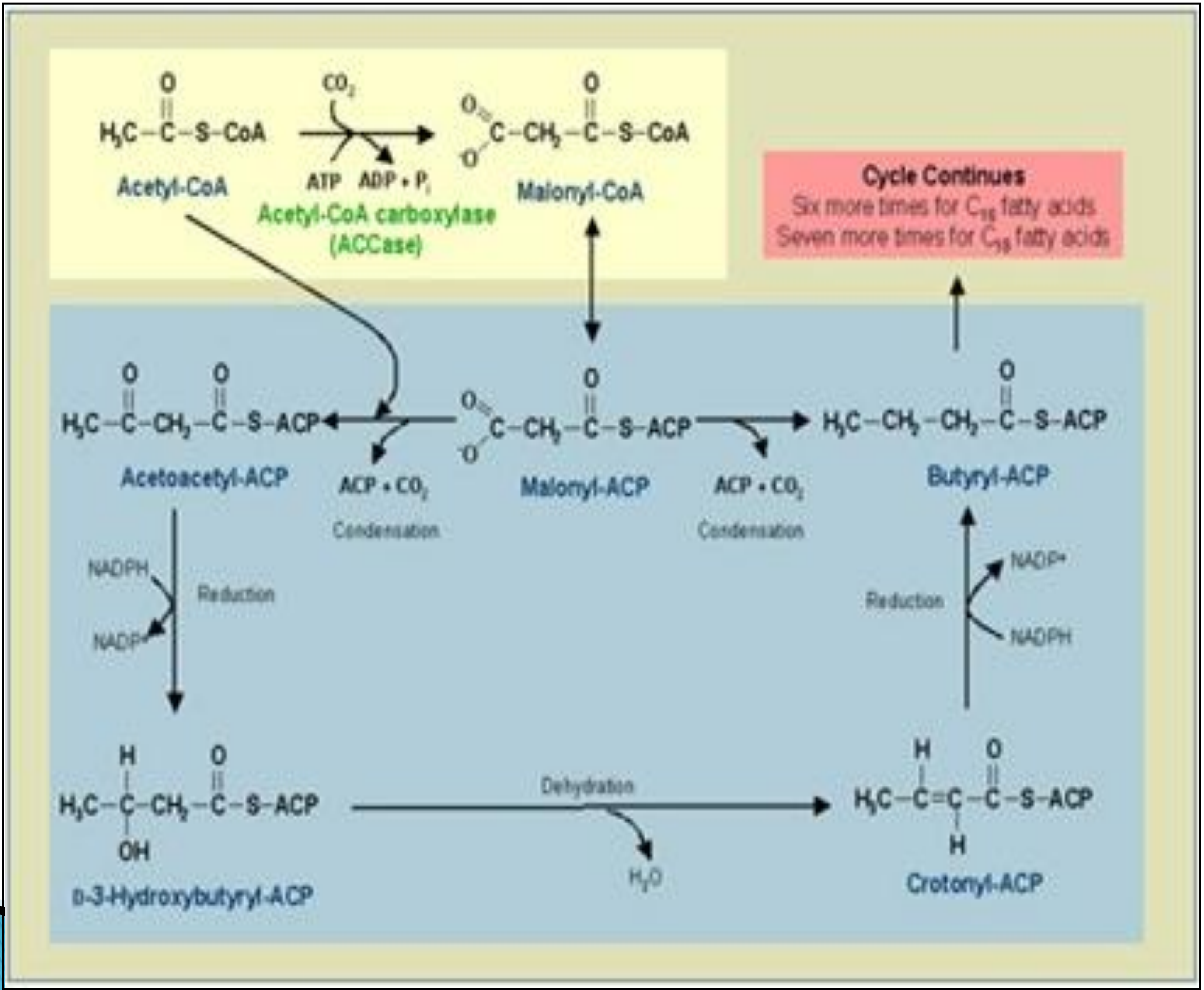
Fatty Acid Synthesis

Reaction catalyzed by Acetyl CoA Carboxylase



Activation of acetate : Acetyl-CoA to malonyl CoA

Fatty Acid Synthesis



Stoichiometry of the reaction

The stoichiometry of the synthesis of palmitate is:

$$\text{Acetyl CoA} + 7\ \text{malonyl CoA} + 14\ \text{NADPH} + 20\ H^+ \longrightarrow \text{palmitate} + 7\ CO_2 + 14\ \text{NADP}^+ + 8\ \text{CoA} + 6\ H_2O$$

The equation for the synthesis of the malonyl CoA used in the preceding reaction is:

$$7\ \text{Acetyl CoA} + 7\ CO_2 + 7\ \text{ATP} \longrightarrow 7\ \text{malonyl CoA} + 7\ \text{ADP} + 7\ P_i + 14\ H^+$$

Hence, the overall stoichiometry for the synthesis of palmitate is:

$$8\ \text{Acetyl CoA} + 7\ \text{ATP} + 14\ \text{NADPH} + 6\ H^+ \longrightarrow \text{palmitate} + 14\ \text{NADP}^+ + 8\ \text{CoA} + 6\ H_2O + 7\ \text{ADP} + 7\ P_i$$

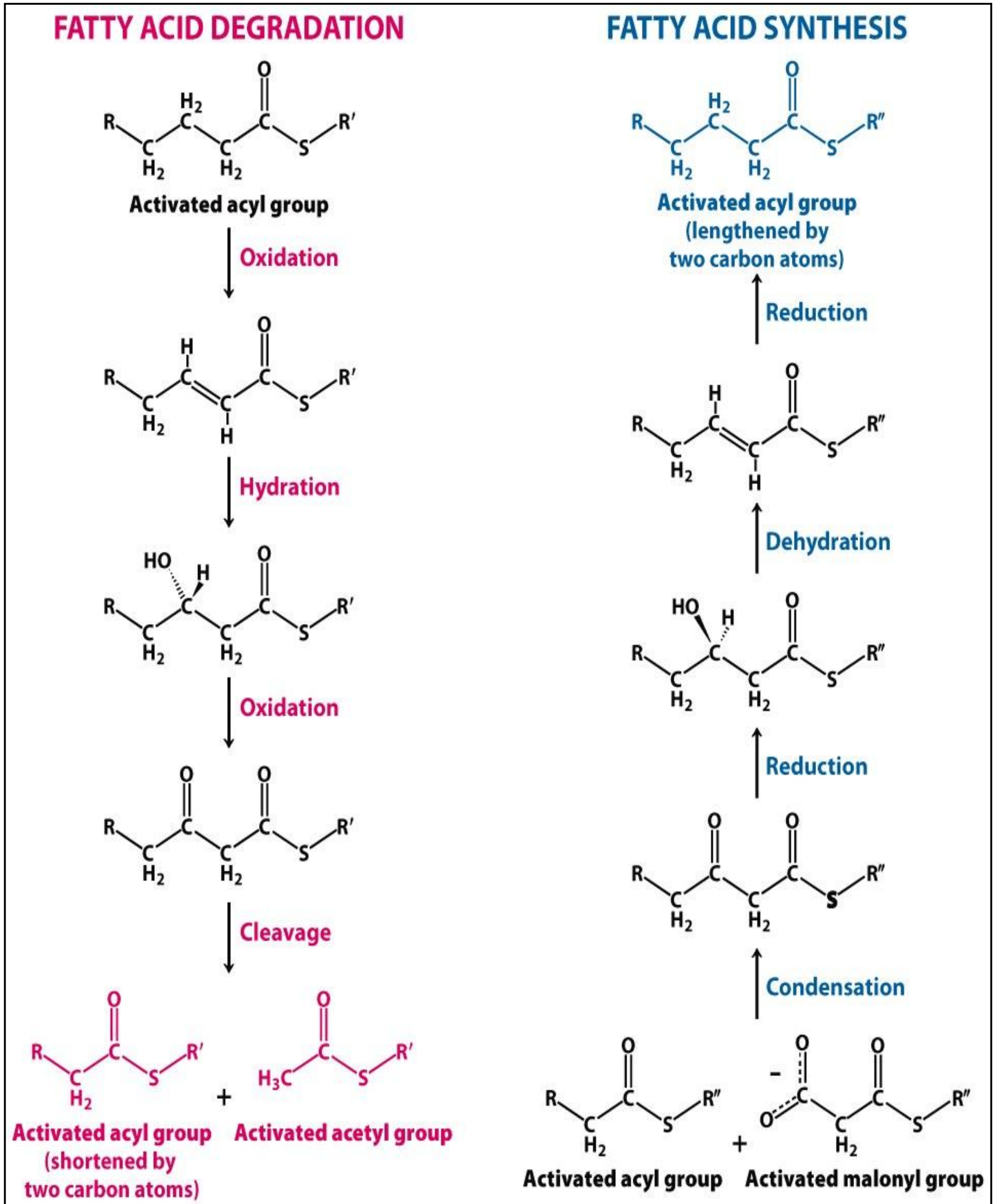


Figure 22.2
Biochemistry, Seventh Edition

Differences between FA degradation and synthesis

Characteristic	Degradation	Synthesis
Location	Mitochondrial Matrix	Cytosol
Activated intermediates	Thioesters of CoA	Thioesters of ACP
Enzymes	4 distinct, nonassociated enzymes	FAS is a multienzyme complex
Process	2-Carbon fragments removed as acetyl CoA	2-Carbon elongation using malonyl CoA
Direction	Starts at carboxyl end	Starts at methyl end
Fatty acid size	All sizes are degraded	Only Palmitate is made
Redox reaction cofactors	FAD/FADH2 and NAD+/NADH	NADP+/NADPH
Major tissue site	Muscle and liver	Liver
Nutritional status	In starvation	After carbohydrate-rich meal
Hormonal regulation	Low insulin / glucagon ratio	High insulin/glucagon ratio
Activator	FFA generated by hormone-sensitive lipase	Citrate
Inhibitor	Malonyl CoA (inhibits carnitine acyl transferase)	Fatty acyl CoA (inhibits acetyl CoA carboxylase)

Allosteric regulation

•Acetyl CoA carboxylase is the rate limiting step. It is allosterically inhibited by palmitoyl CoA and activated by citrate.

•palmitoyl CoA inhibits citrate shuttle.

•Malonyl CoA 7 acetyl CoA inhibit β oxidation.

•ATP & NADPH inhibit β oxidation.

•Hormonal regulation by Insulin & Glucagon.

Hormonal Regulation of Fatty Acid Synthesis and Breakdown

Stimulates **Glucagon**

Insulin **Stimulates**

ATP $\xrightarrow{\text{Adenylyl cyclase}}$ **cAMP** $\xrightarrow{\text{Phosphodiesterase}}$ **AMP**

Activates Protein Kinase

Inactivates Acetyl CoA carboxylase by phosphorylation

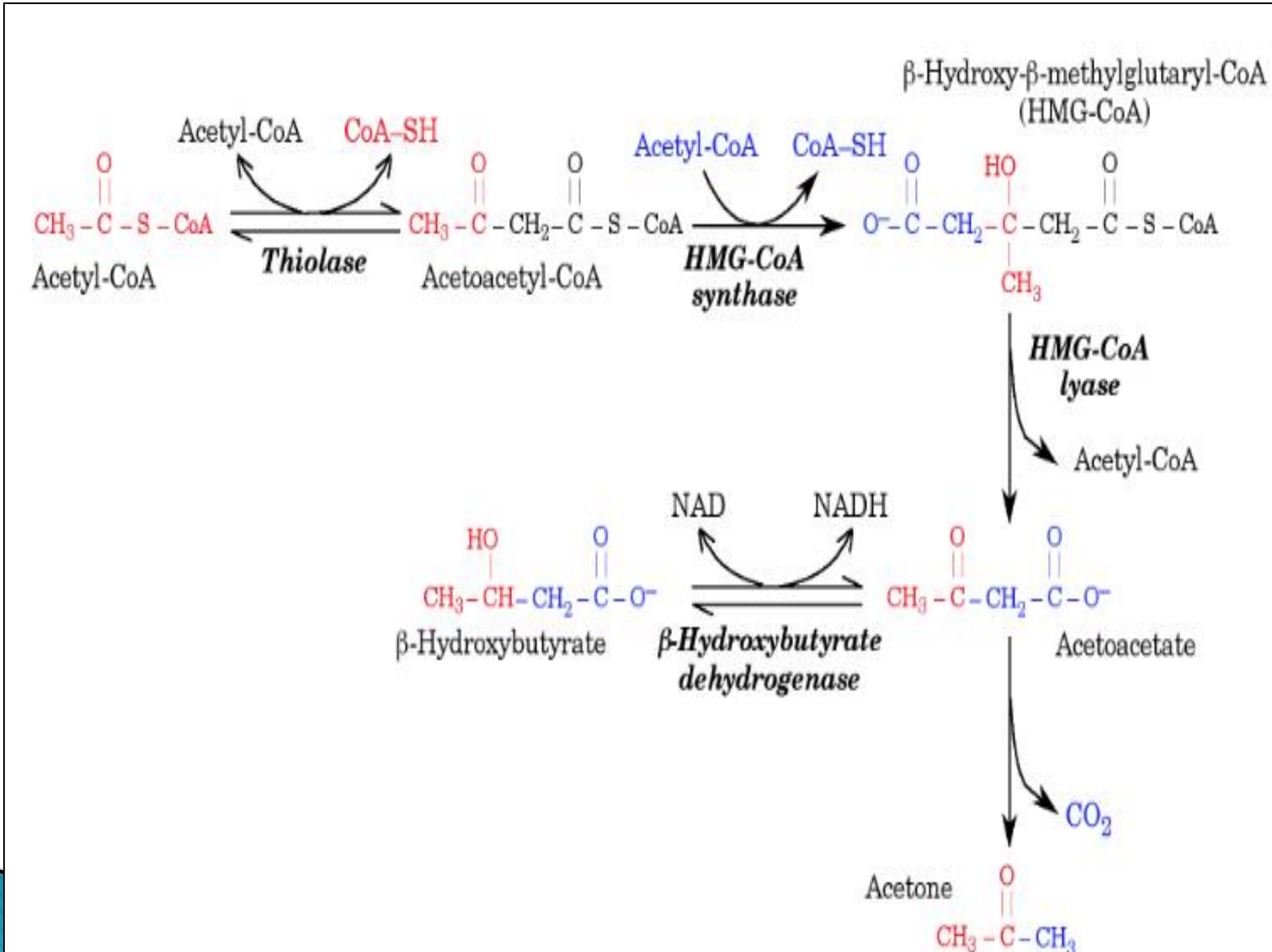
Activates lipase

Inhibition of fatty acid synthesis and increase of lipolysis and release of FFA

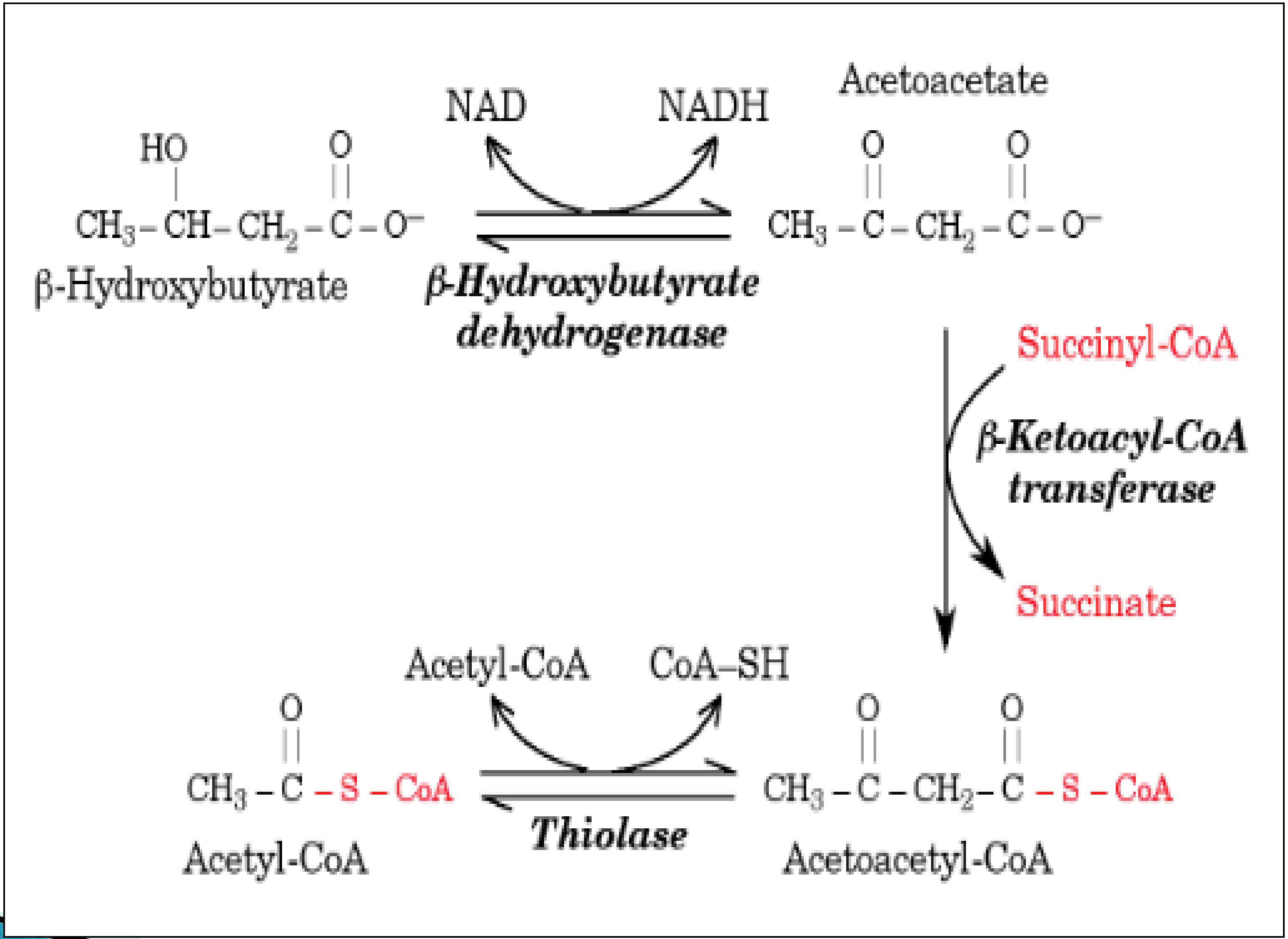
Inactivates lipase

Activate acetyl CoA carboxylase

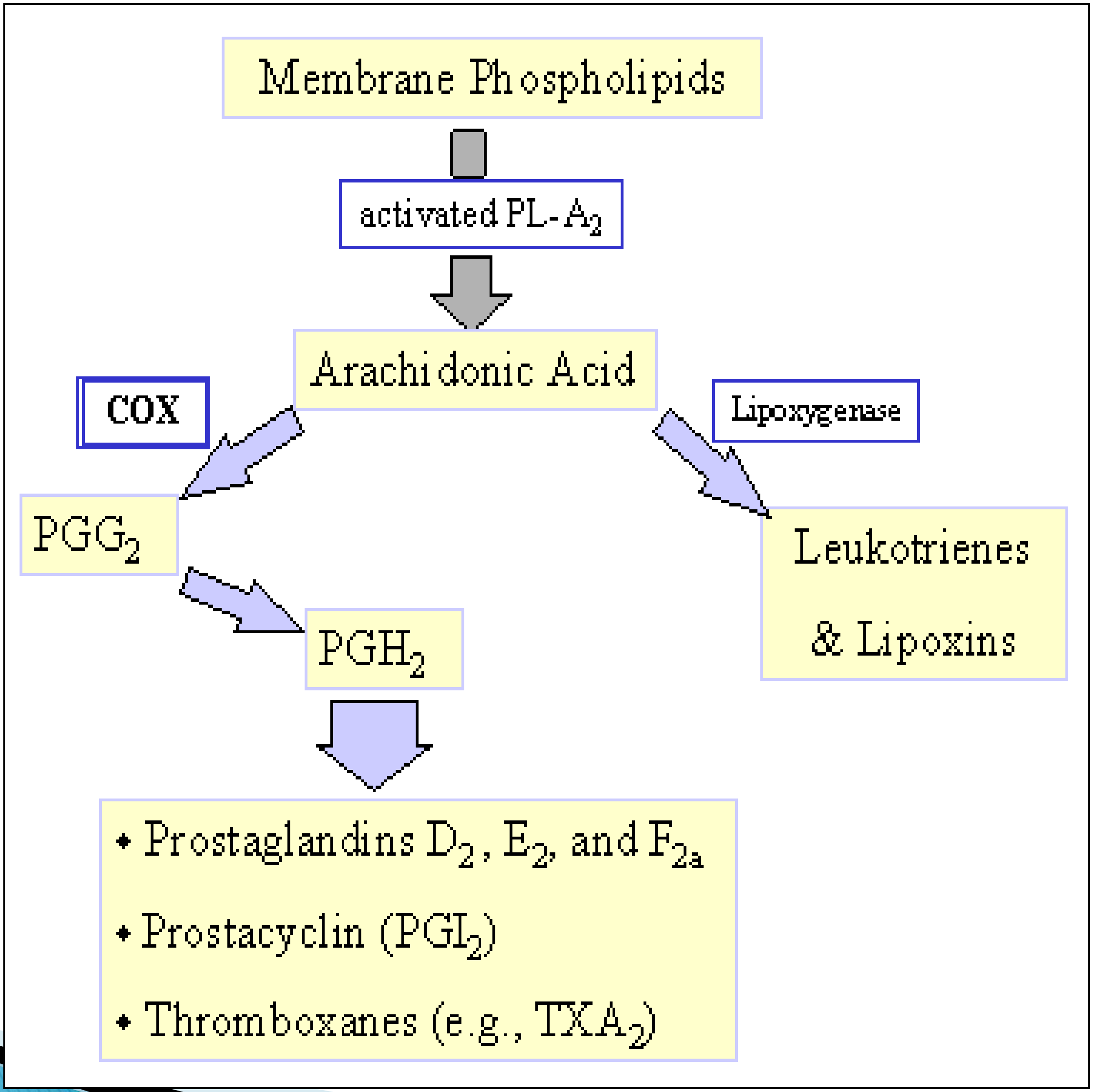
Synthesis of Ketone Bodies



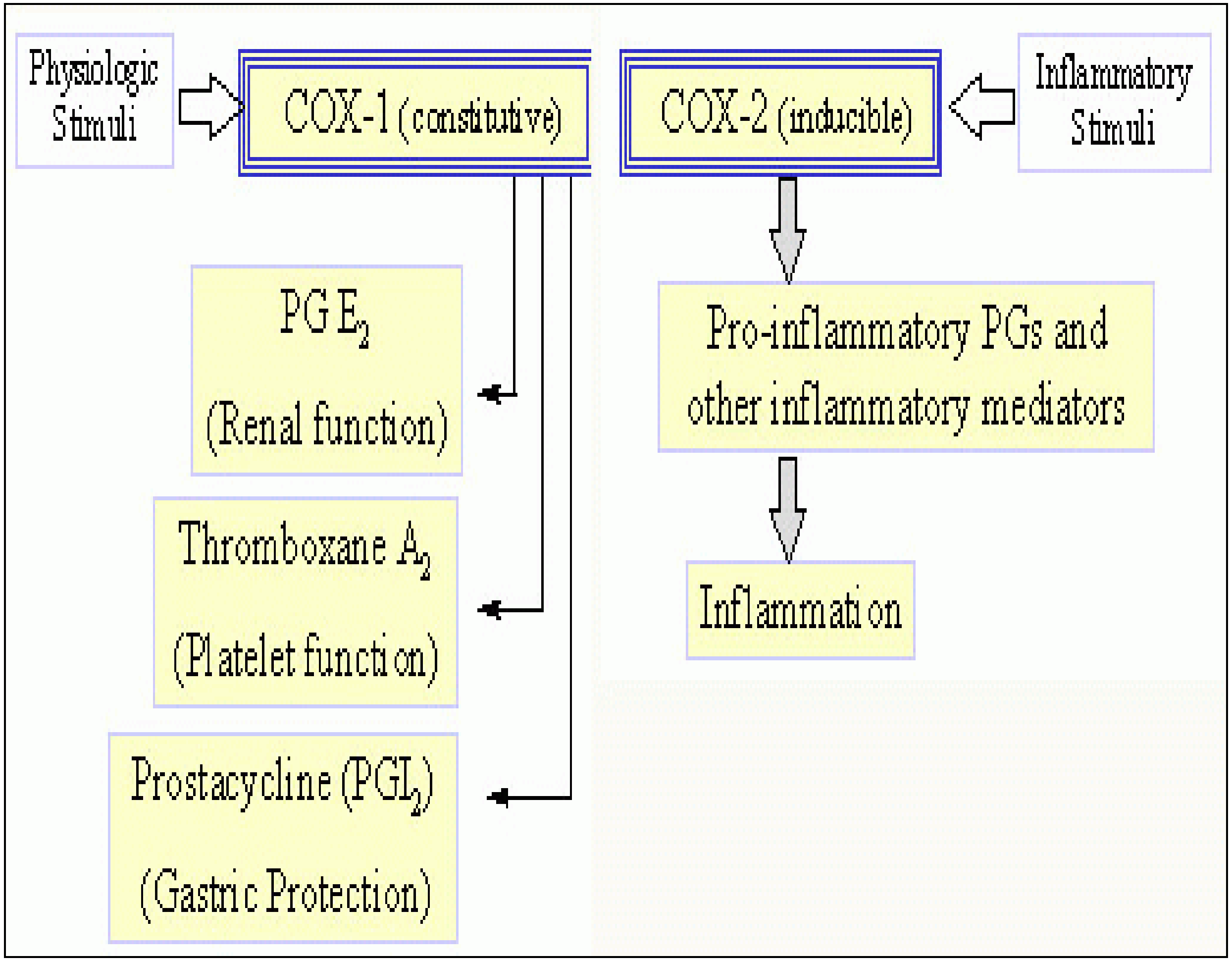
Utilization of Ketone Bodies



Biosynthesis of Prostaglandins

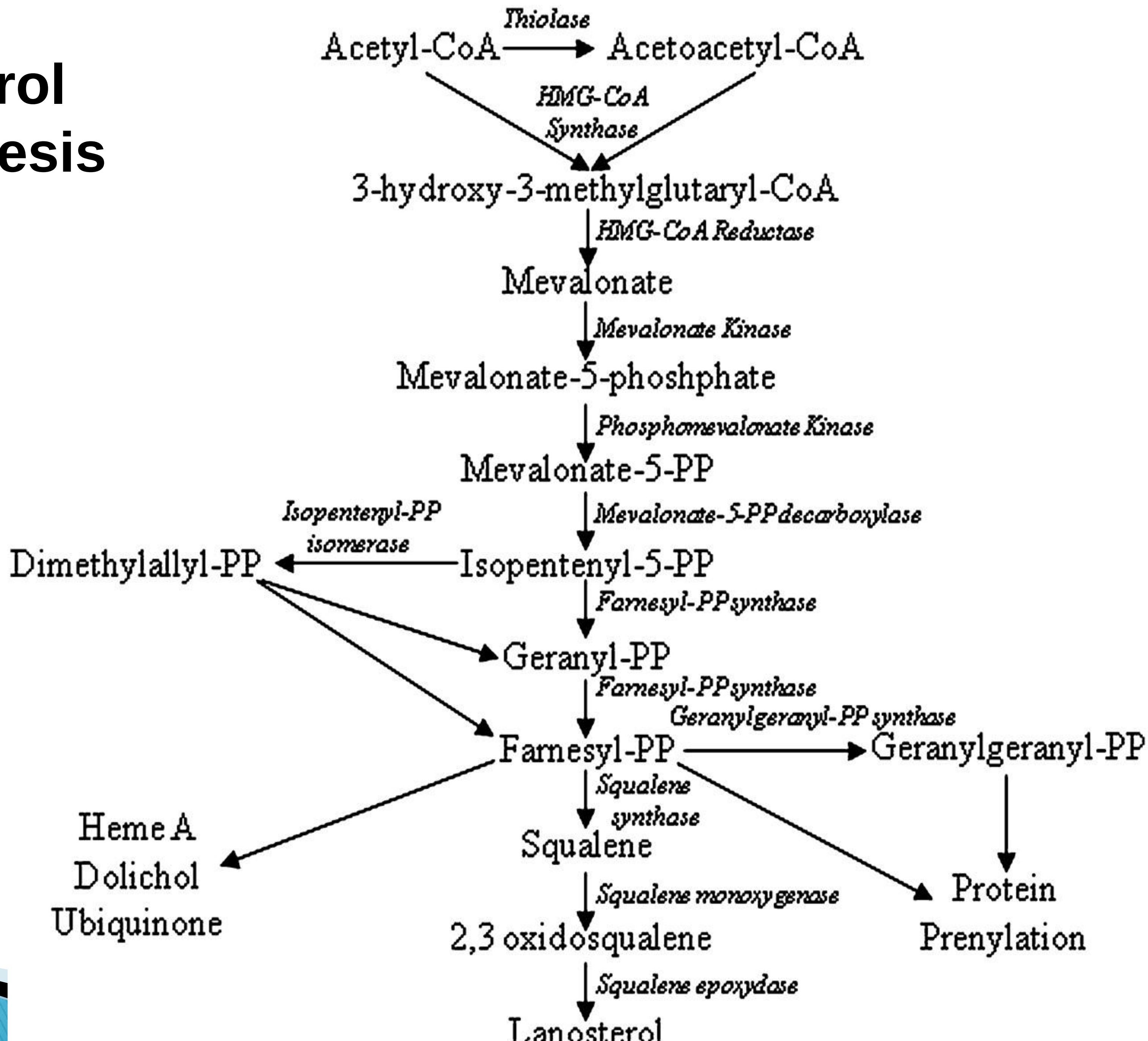


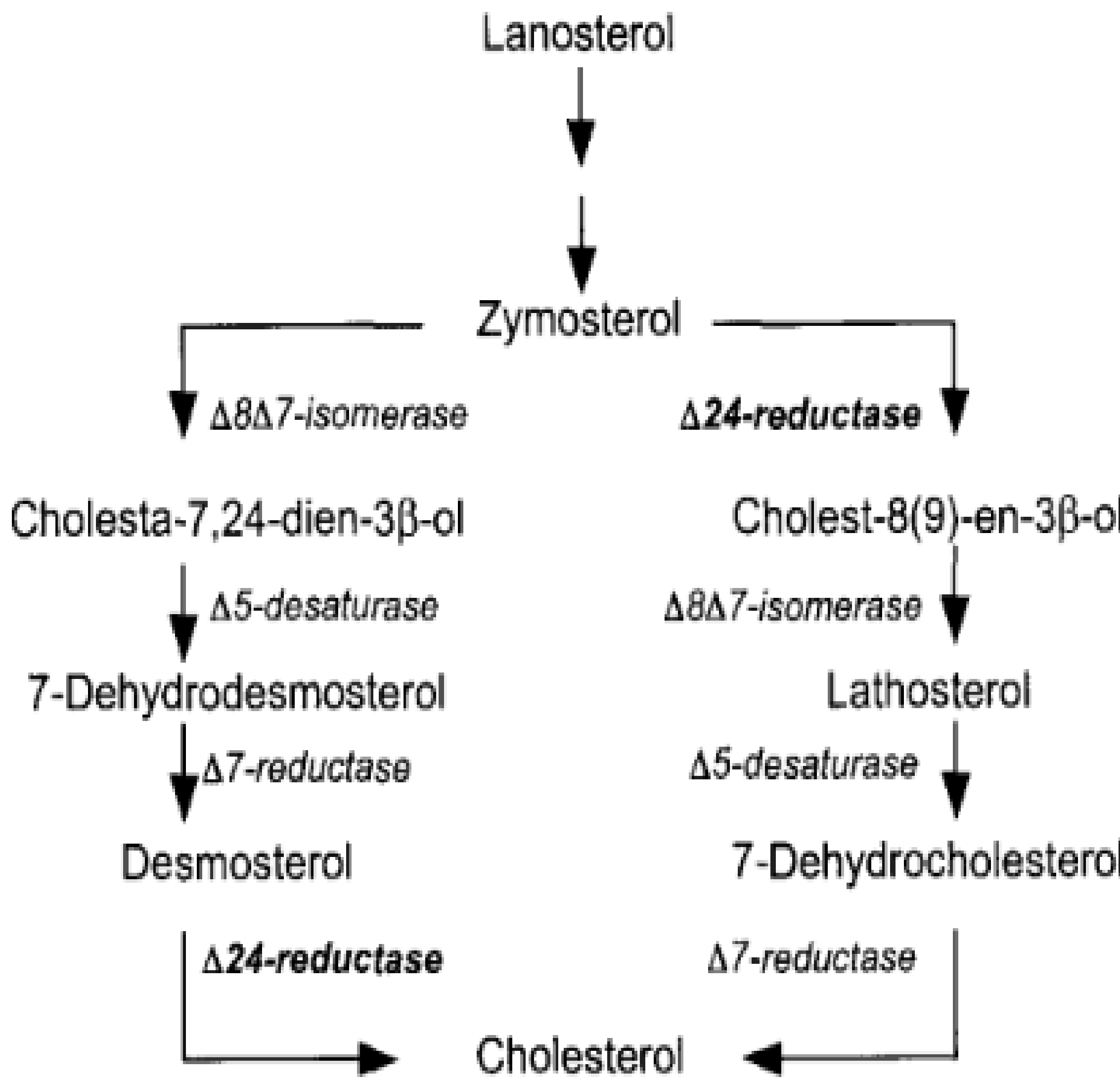
COX-I & COX-2



Physiologic Stimuli
COX-1 (constitutive)
COX-2 (inducible)
Inflammatory Stimuli
PGE2
(Renal function)
Thromboxane A2
(Platelet function)
Prostacycline (PGI2)
(Gastric Protection)
Pro-inflammatory PGs and other inflammatory mediators
Inflammation

Cholesterol Biosynthesis




Lanosterol
Zymosterol
Δ8Δ7-isomerase
Δ24-reductase
Cholesta-7,24-dien-3β-ol
Cholest-8(9)-en-3β-ol
Δ5-desaturase
Δ8Δ7-isomerase
7-Dehydrodesmosterol
Lathosterol
Δ7-reductase
Δ5-desaturase
Desmosterol
7-Dehydrocholesterol
Δ24-reductase
Δ7-reductase
Cholesterol

Regulation of Cholesterol Biosynthesis

Short-term regulation

•HMG-CoA Reductase is inhibited by phosphorylation by AMP-Dependent protein Kinase

Long-term regulation

•Regulated proteolysis of HMG-CoA Reductase

•Regulated Transcription

The Utilization of Cholesterol

•Cholesterol is transported in the plasma predominantly as cholesteryl esters associated with lipoproteins.

•Dietary cholesterol is transported from the small intestine to the liver within chylomicrons.

•Cholesterol synthesized by the liver, as well as any dietary cholesterol in the liver that exceeds hepatic needs, is transported in the serum within LDLs.

•The liver synthesizes VLDLs and these are converted to LDLs through the action of endothelial cell-associated lipoprotein lipase.

•**Reverse cholesterol transport** allows peripheral cholesterol to be returned to the liver in LDLs.

•Ultimately, cholesterol is excreted in the bile as free cholesterol or as bile salts following conversion to bile acids in the liver.

•Cholesterol metabolism is via the cytochrome P450 pathway.