

Lipid Metabolism:



**Lipid Metabolism:**

# Topic outline:



- ❧ What is a Lipid?
- ❧ What are the functions of Lipid?
- ❧ Types of Lipid
- ❧ Digestion and Absorption of Lipids
- ❧ Catabolism of Lipids
- ❧ Fatty Acid Beta-oxidation

# What is a Lipid?

- ∞ These are nonpolar organic compounds
- ∞ Generally insoluble to water, but soluble to nonpolar solvent like;
  - chloroform
  - acetone
  - ether
  - benzene
- ∞ It contains a carbonyl group (-COOH)

# What are the functions of lipids?

- ❧ As membrane structural component.
- ❧ As intracellular storage depot of metabolic fuel.
- ❧ As transport form of metabolic fuel.
- ❧ As protective form of the cells of many bacteria, leaves of higher plants, exoskeleton of insects and the skin of vertebrates.
- ❧ A regulatory substances.
- ❧ As transport form of some neurotransmitters.
- ❧ As receptors in nerve ending membranes.
- ❧ As determinants of immunological specificity.
- ❧ Enzyme co-factors

# Types of Lipids

☞ The four main groups of lipids include:

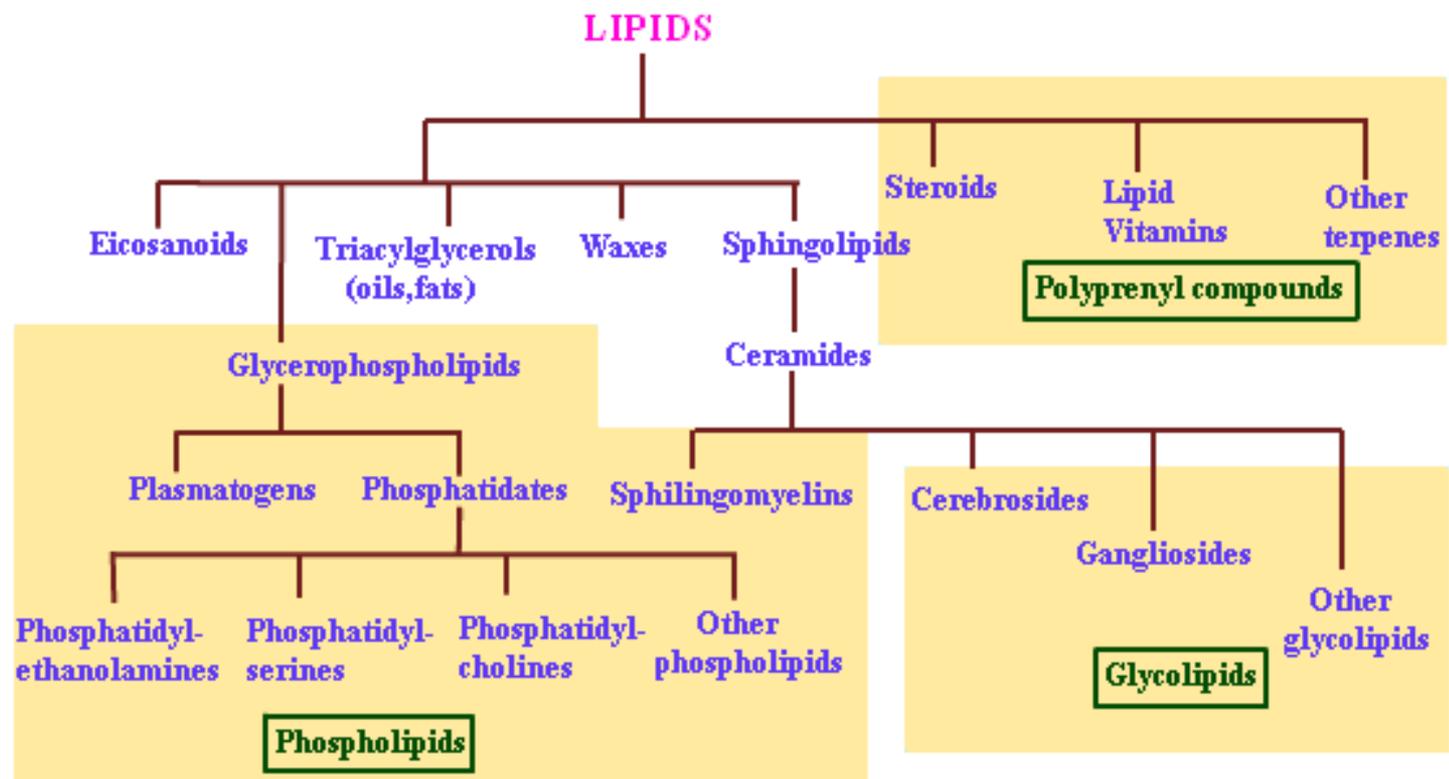
1. Fatty acids (saturated and unsaturated)
2. Glycerides (glycerol-containing lipids)
3. Nonglyceride lipids (sphingolipids, steroids, waxes)
4. Complex lipids (lipoproteins, glycolipids)

# Different Types of Lipids

The classification of lipids can be structural based or based on their functions. **Mainly lipids are classified in five types.**

- Fatty acyl (FA)
- Glycerolipids (GL)
- Glycerophospholipids (GP)
- Sterol lipids (ST)
- Sphengolipids (SP)

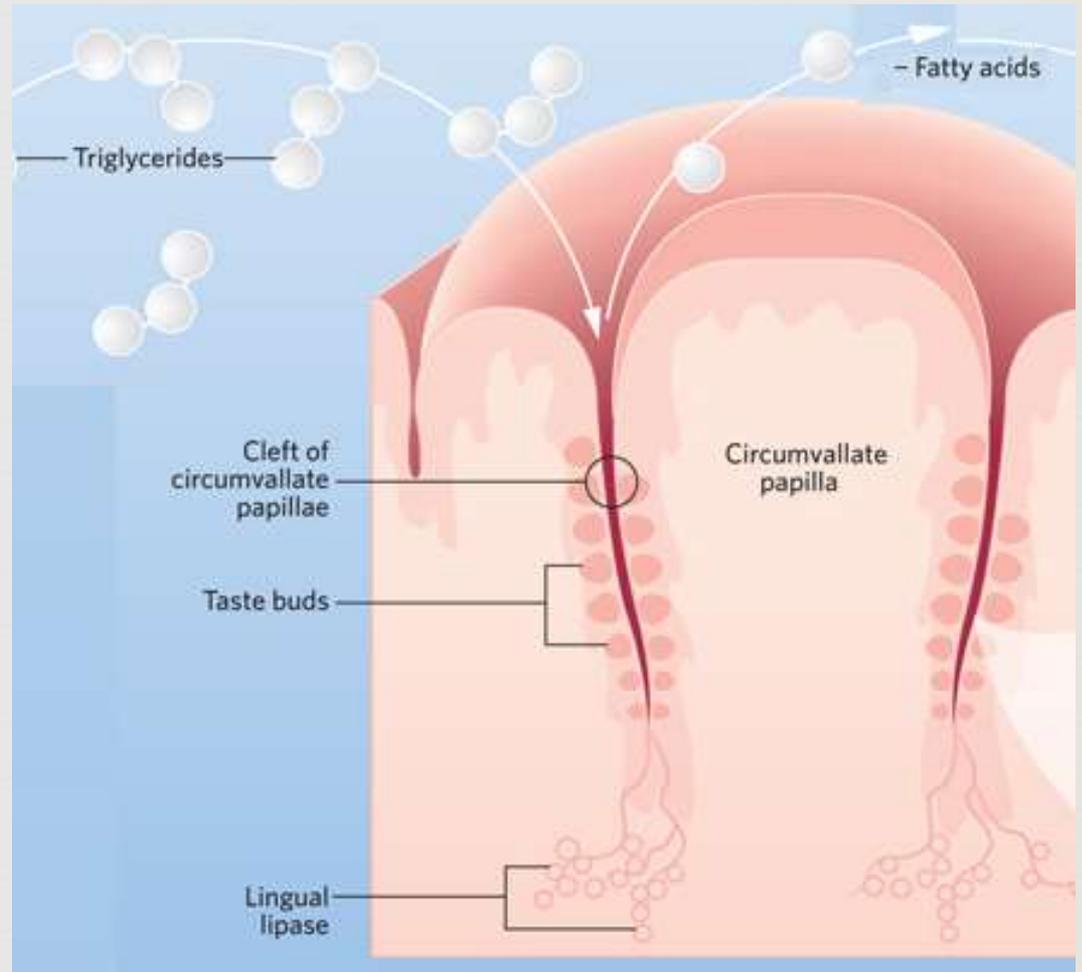
The relation between different types of lipids is as follows.



# Digestion and Absorption of Lipids

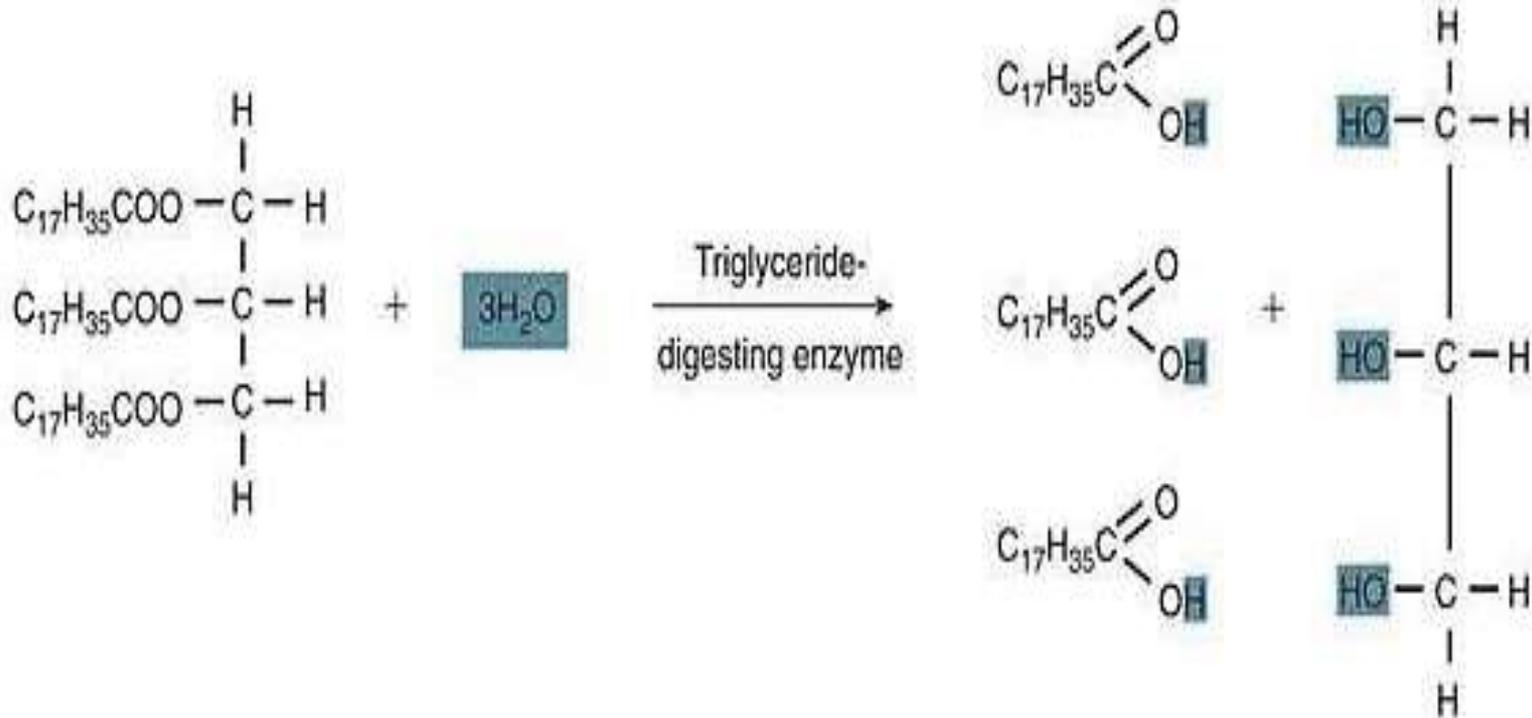
∞ Digestion of lipids initially starts in the mouth

The dietary lipid like the triglycerides will activate the taste buds connecting to the Von Ebner's gland will secrete the enzyme called the **lingual lipase**



# Triglyceride degradation

Lipid



Fat

+

Water



Fatty acids

+

Glycerol

Triglycerides are degraded by **lipases** to form **free fatty acids and glycerol**

*Lingual lipase*

Von Ebner's  
glands

-Hydrolysis of TG  
present in food  
-Perception of fat taste

*Gastric Lipase*

Fundic gastric  
chief cells

Hydrolysis of  
TG from food

*Pancreatic Triglyceride Lipase*

Pancreatic acinar  
cells

Hydrolysis of  
TG from food

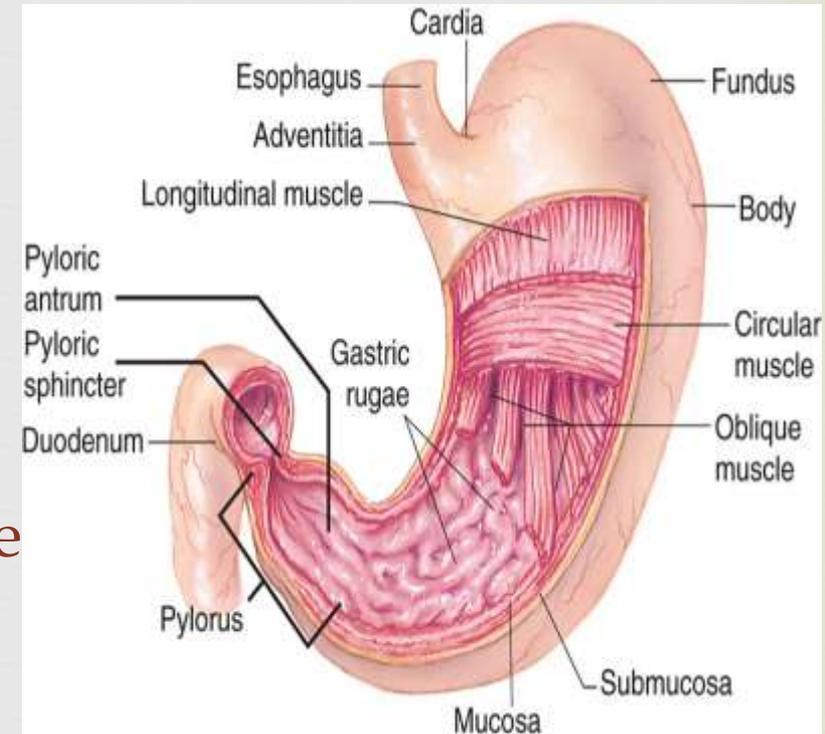
*Carboxyl Ester Lipase*

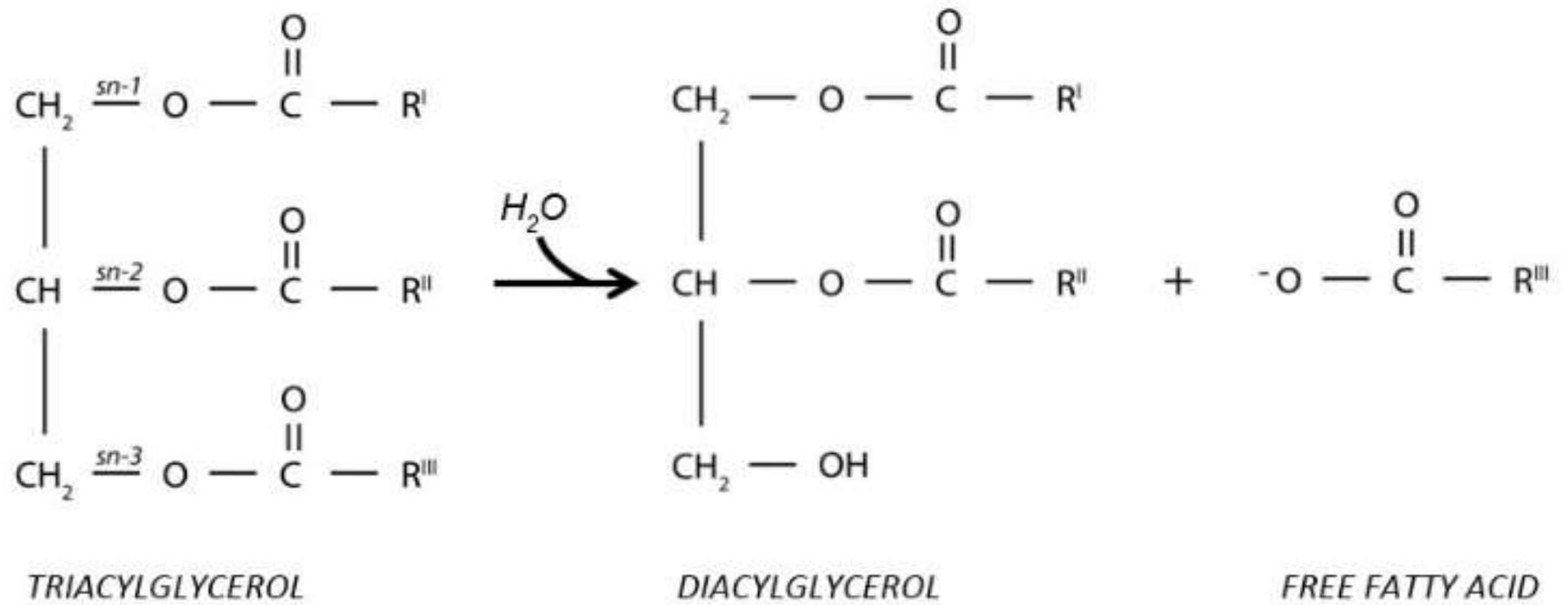
Pancreatic acinar  
cells

Hydrolysis of TG, CE,  
MG, phospholipids,  
lysophospholipids and  
ceramides

# Digestion in Stomach

- ❑ Gastric Lipase- secreted in small quantities
- ❑ More effective at alkaline p H (Average p H 7.8)
- ❑ Requires the presence of  $\text{Ca}^{++}$
- ❑ Less effective in stomach due to acidic p H except when intestinal contents are regurgitated in to the gastric lumen
- ❑ Not effective for long chain fatty acids, most effective for short and medium chain fatty acids
- ❑ Milk, egg yolk and fats containing short chain fatty acids are suitable substrates for its action





**Figure** shows the breakdown of triacylglycerols (TAGs) into Diacylglycerol (DAG) and one Free Fatty Acid (FFA) initiated by the gastric lipase.

# Role of fats in gastric emptying

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- ❑ Fats delay the rate of emptying of stomach
- ❑ Action is brought about by secretion of Enterogastrone
- ❑ Enterogastrone inhibits gastric motility and retards the discharge of bolus of food from the stomach.
- ❑ Thus fats have a high satiety value.

# Significance of Lingual and Gastric Lipases



- ❑ Play important role in lipid digestion in **neonates** since milk is the main source of energy
- ❑ Important digestive enzymes in pancreatic insufficiency such as **Cystic fibrosis or other pancreatic disorders**
- ❑ Lingual and gastric lipases can degrade triglycerides with short and medium chain fatty acids in patients with pancreatic disorders despite a near or complete absence of pancreatic lipase

# In the intestine



*Pancreatic Triglyceride Lipase*

Pancreatic acinar  
cells

Hydrolysis of  
TG from food

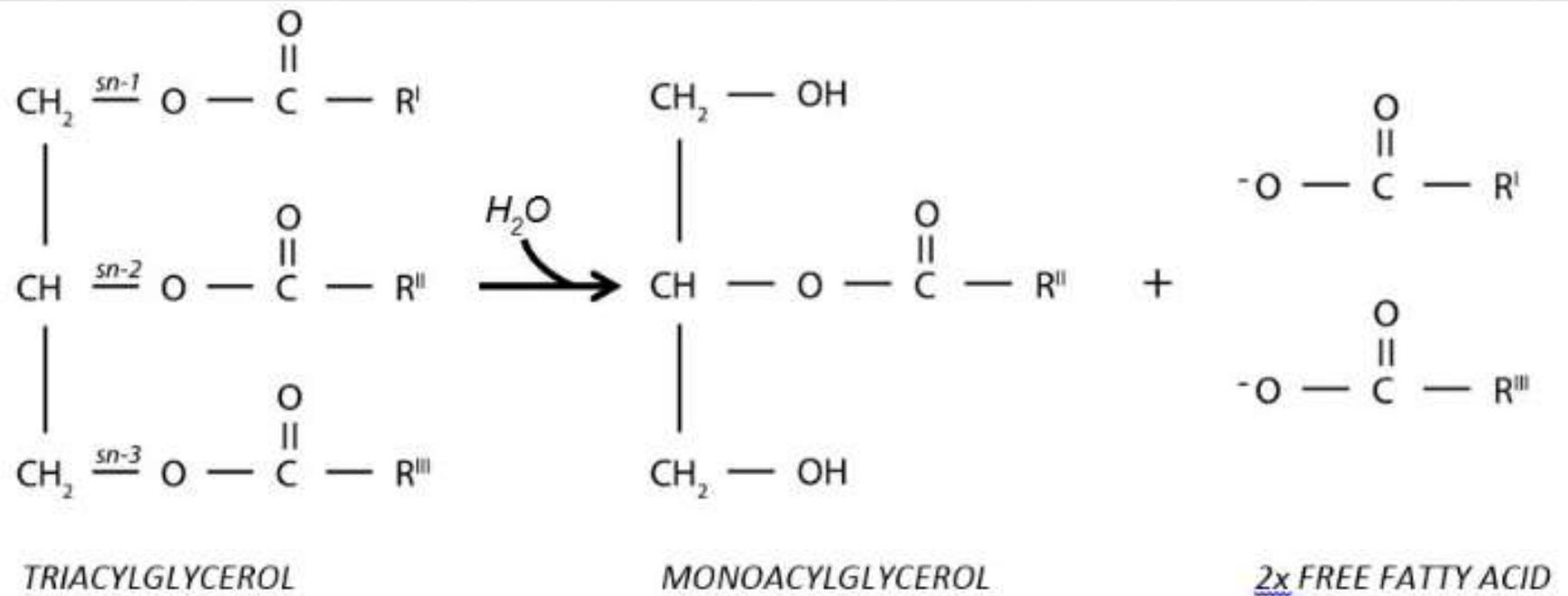
*Carboxyl Ester Lipase*

Pancreatic acinar  
cells

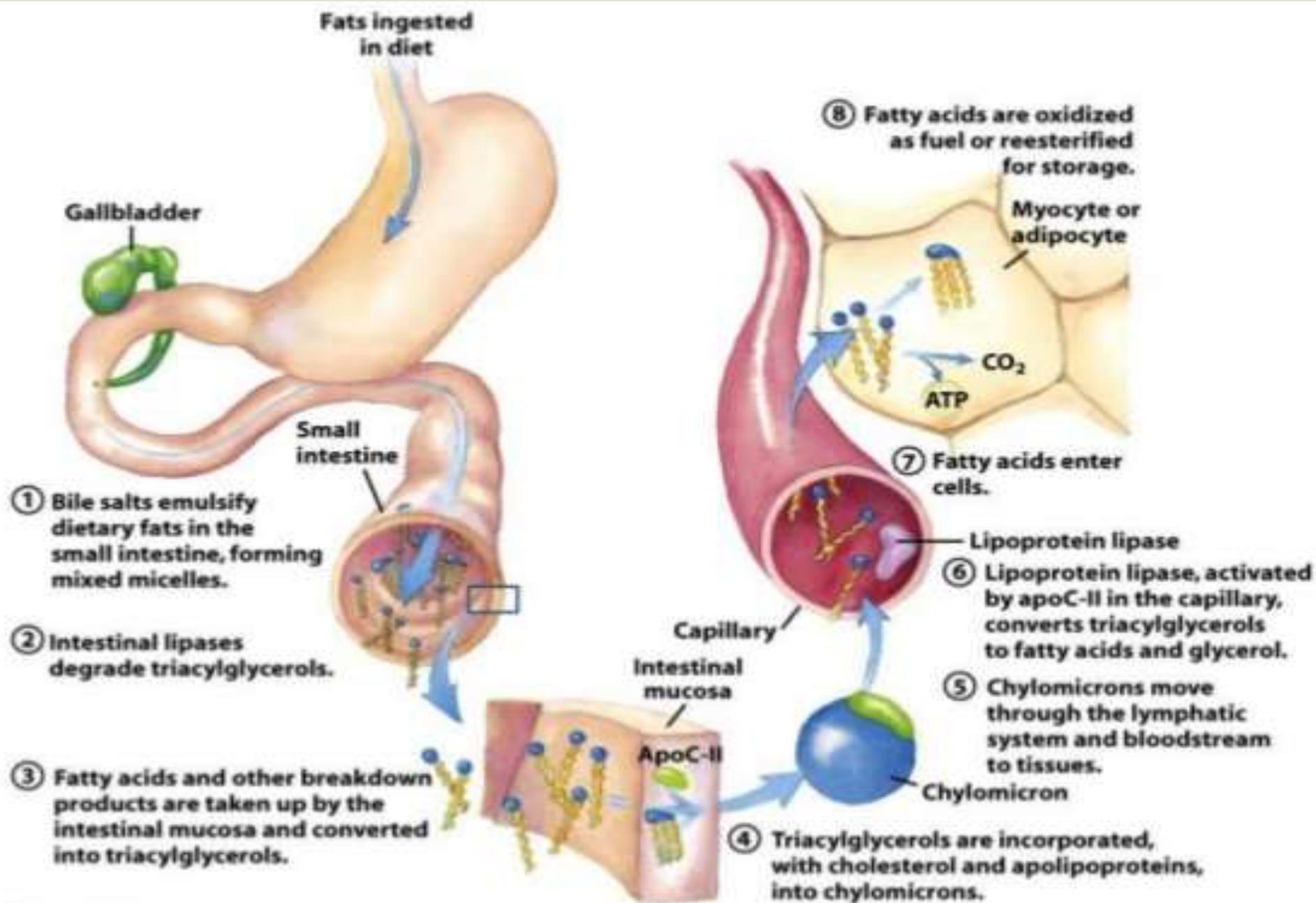
Hydrolysis of TG, CE,  
MG, phospholipids,  
lysophospholipids and  
ceramides

## Table 1. Steps of lipid digestion and absorption

Step	Location	Enzymes
1. Minor digestion (TAGs → DAGs + FFA)	mouth and stomach	lingual/ gastric lipase
2. Major digestion (all) TAG → MAG + 2FFA (PL) CE → chol. + ester (CE) PL → FA + lysoPL (PLA)	lumen of the small intestines	pancreatic lipase (+colipase) cholesterol esterase phospholipase A <sub>2</sub>
3. Formation of mixed micelles (uses bile salts as biological detergent)	lumen of the small intestines	N/A
4. Passive absorption of lipolytic products	into intestinal epithelial cell	N/A
5. Assembly and export of chylomicrons	from intestinal cells to the lymphatics	N/A



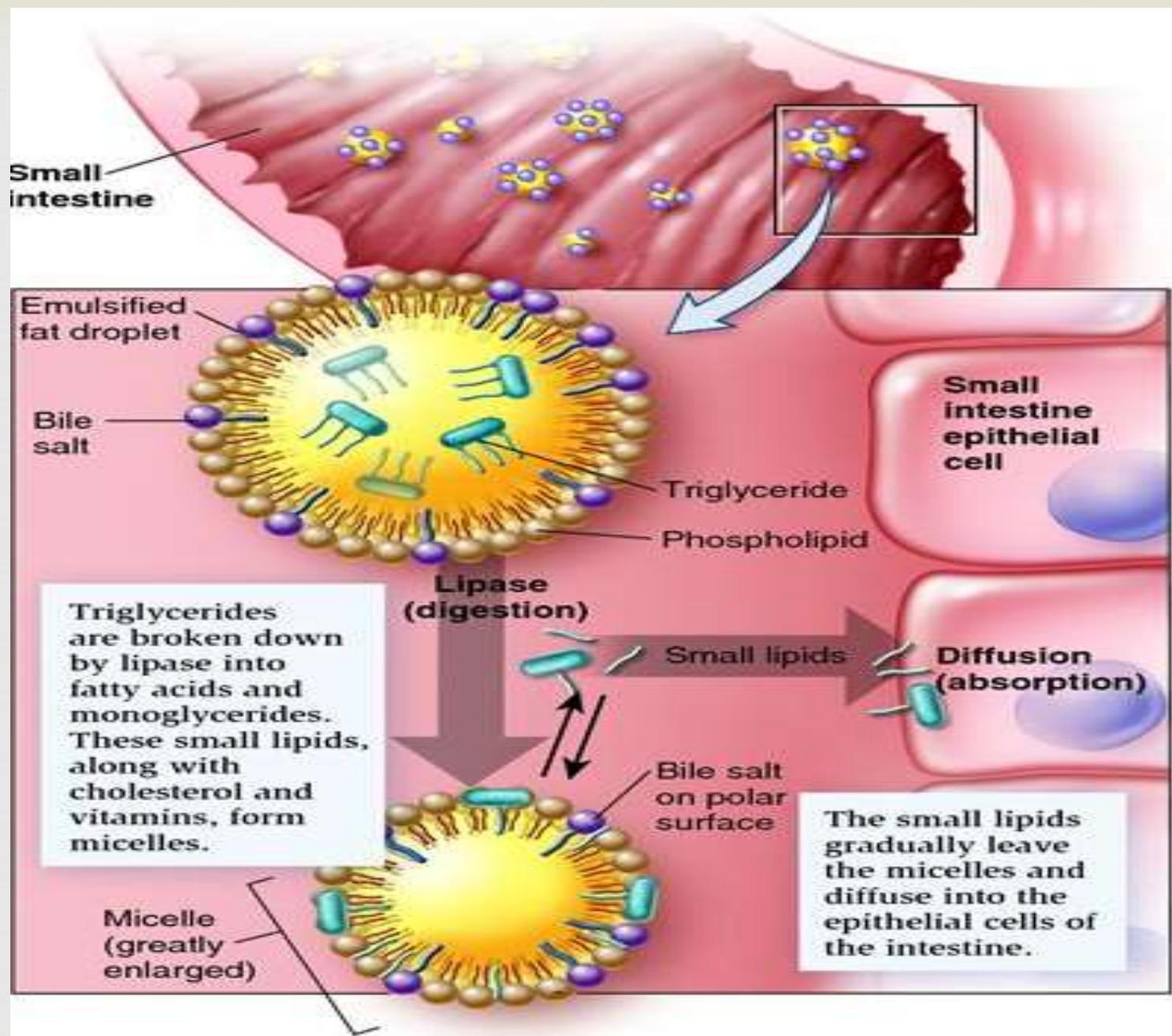
**Figure** shows the breakdown of triacylglycerols (TAGs) into Monoacylglycerol (MAG) and two Free Fatty Acids (FFA) initiated by the pancreatic lipase



**Figure 17-1**

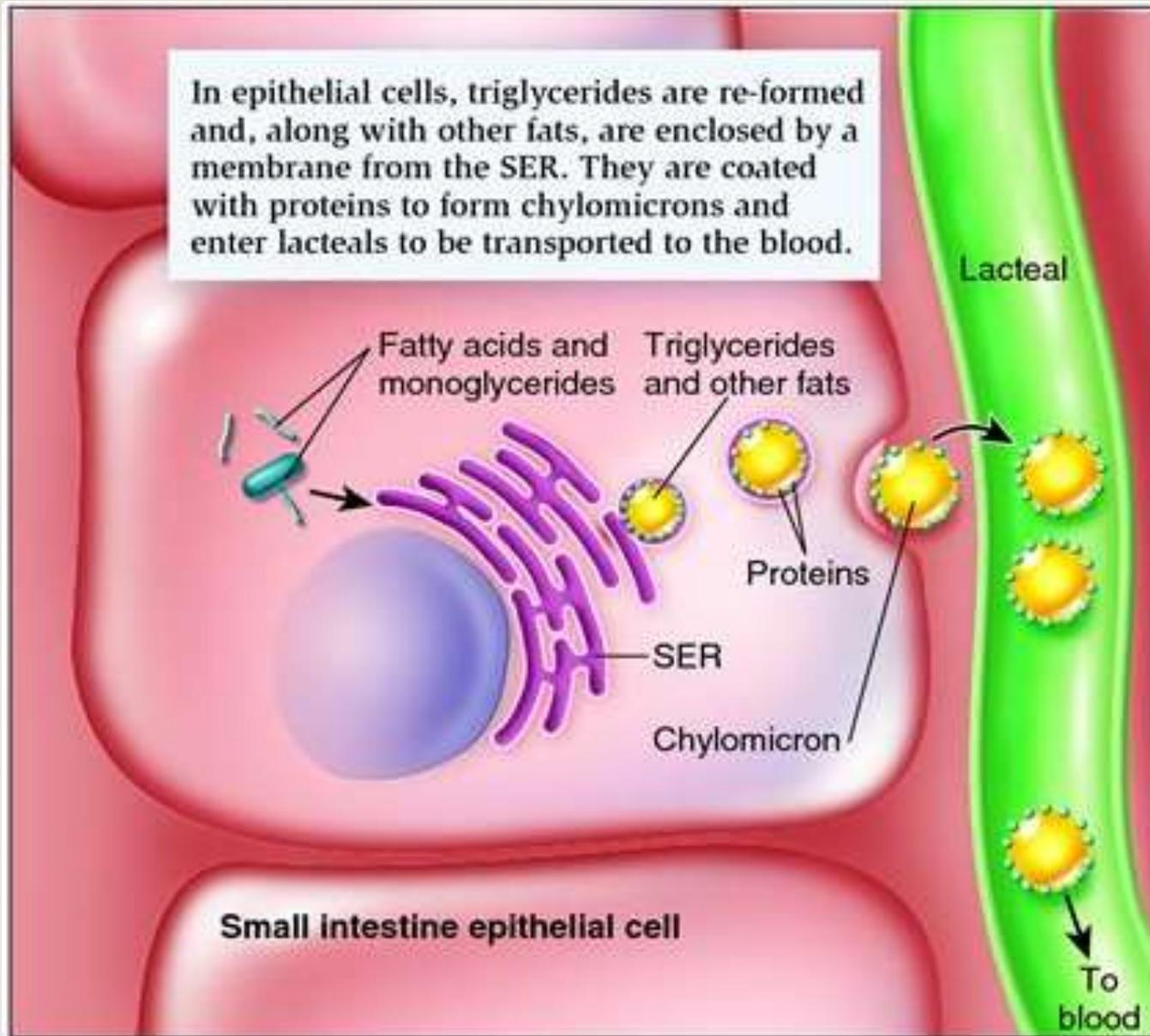
*Lehninger Principles of Biochemistry, Fifth Edition*

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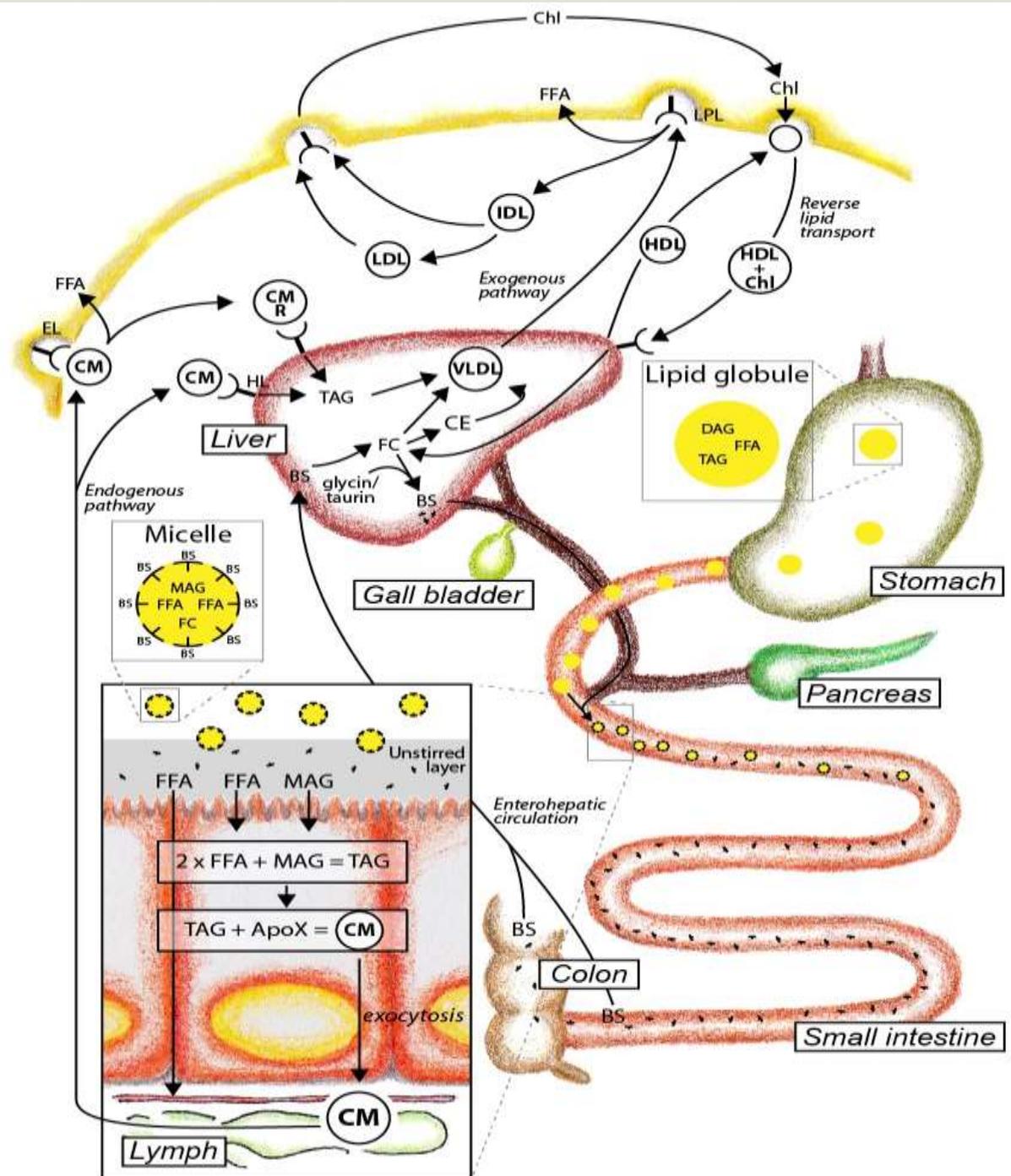


**(a) Digestion of emulsified fats into small lipids, and absorption into intestinal cells**

In epithelial cells, triglycerides are re-formed and, along with other fats, are enclosed by a membrane from the SER. They are coated with proteins to form chylomicrons and enter lacteals to be transported to the blood.



**(b) Synthesis of triglycerides and the formation and release of chylomicrons**



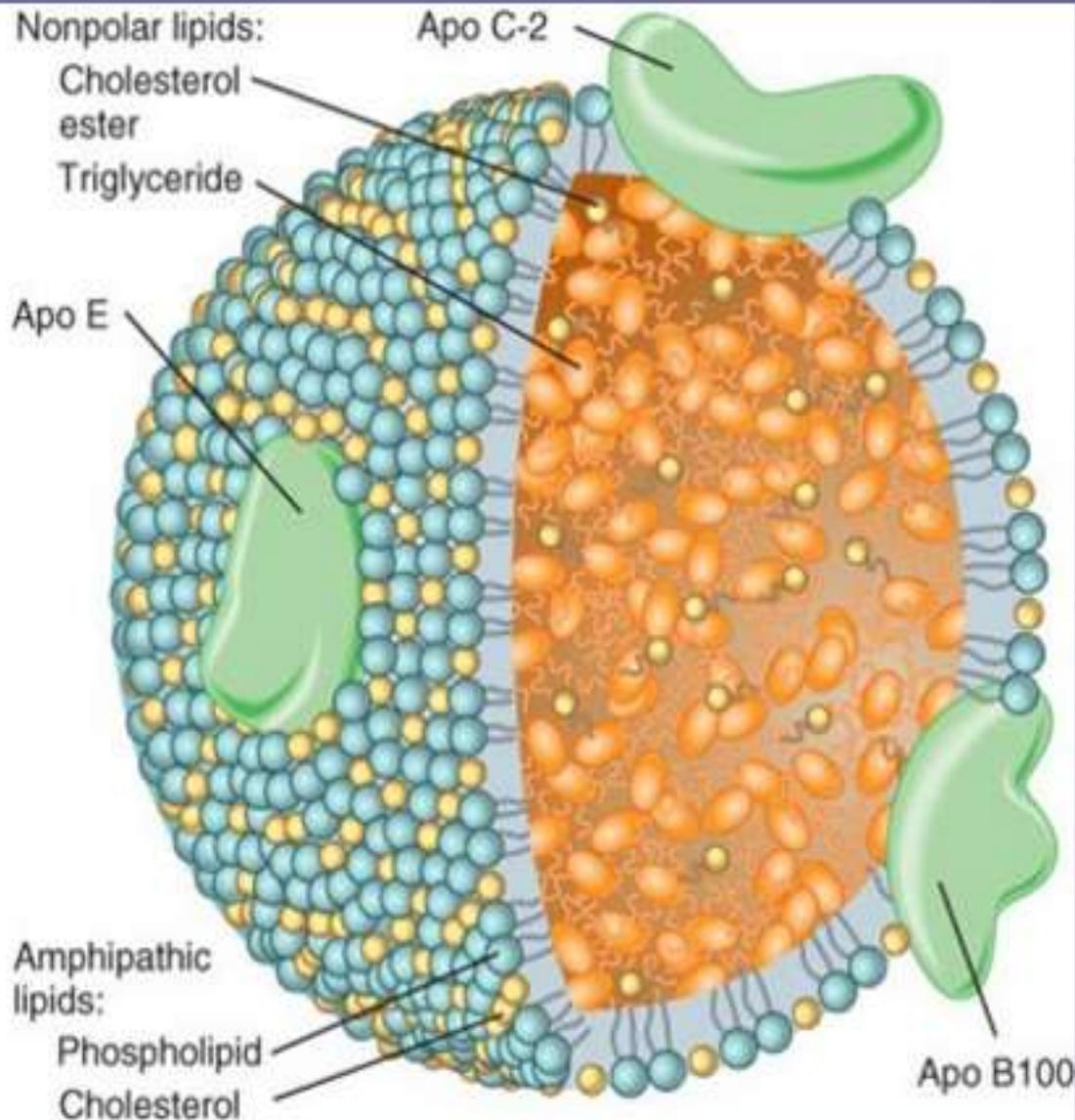
# Digestion and absorption of lipids includes 6 steps

- ✚ *Minor digestion* of triacylglycerols in mouth by lingual lipase
- ✚ *Major digestion* of all lipids in the lumen of the duodenum /jejunum by **Pancreatic lipases**
- ✚ *Bile acid* facilitated formation of mixed micelles that present the lipolytic products to the mucosal surface, followed later by **enterohepatic** bile acid recycling
- ✚ *Passive absorption* of the lipolytic products from the mixed micelle into the intestinal epithelial cell , **Glycerol & FAs  $\leq 12$  carbons in length pass thru the cell into the blood without modification. 2-monoacylglycerols and FAs  $> 12$  carbons in length are re-synthesized into TGs in the endoplasmic reticulum TGs then form large lipid globules in the ER called chylomicrons . Several apolipoproteins are required**
- ✚ *Re-esterification* of 2-monoacylglycerol, lysolecithin , and cholesterol with free fatty acids inside the intestinal **enterocyte**
- ✚ *Assembly and export* from intestinal cells to the lymphatics of **chylomicrons** coated with Apo B48 and containing triacylglycerols, cholesterol esters and phospholipids

# Lipoproteins

- *Chylomicrons* form in small intestinal mucosal cells and contain exogenous (dietary) lipids. They enter villi lacteals, are carried into the systemic circulation into adipose tissue where their triglyceride fatty acids are released and stored in the adipocytes and used by muscle cells for ATP production.
- *VLDLs* contain endogenous triglycerides. They are transport vehicles that carry triglycerides synthesized in hepatocytes to adipocytes for storage. VLDLs are converted to LDLs.
- *LDLs* carry about 75% of total blood cholesterol and deliver it to cells throughout the body. When present in excessive numbers, LDLs deposit cholesterol in and around smooth muscle fibers in arteries.
- *HDLs* remove excess cholesterol from body cells and transport it to the liver for elimination.

# Transport of Lipids by Lipoproteins



Four classes of lipoproteins are *chylomicrons*, *very low-density lipoproteins (VLDLs)*, *low-density lipoproteins (LDLs)*, and *high-density lipoproteins (HDLs)*.

# Lipid Catabolism

∞ **Catabolism** – refers to several reactions that produce energy

- it is a breakdown of complex organic compounds into a simpler compounds.

∞ It is related to carbohydrate metabolism because the carbohydrates will turn into fats. The glycerol will participate is glycolysis.

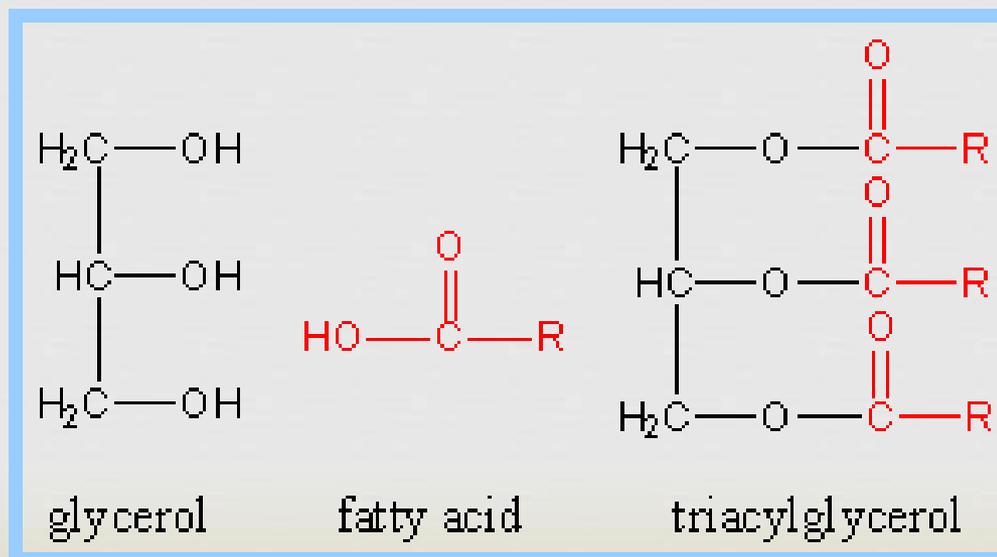
∞ It is important process because the produced Fatty acids will participate in fatty acid oxidation.

∞ Energy is produced through a process called lipogenesis

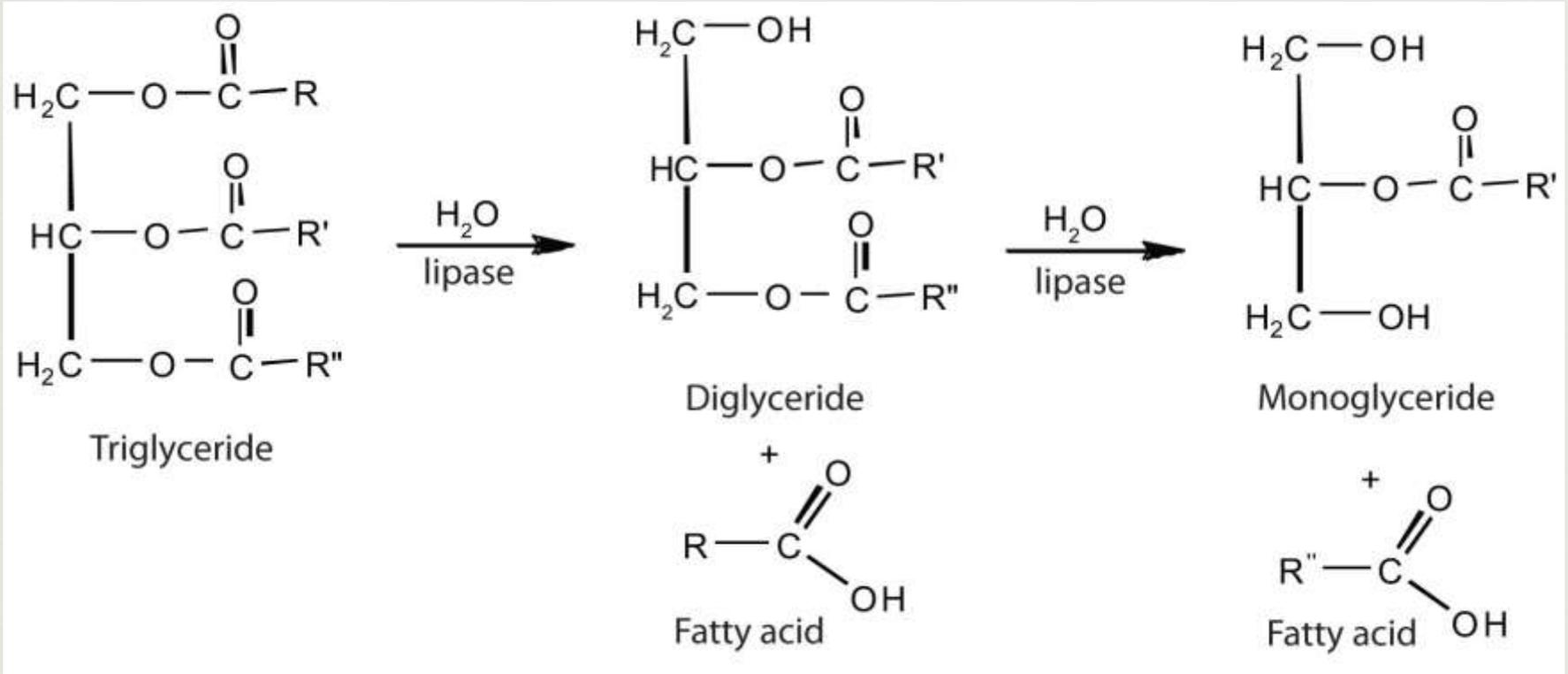
# 1. Lipolysis- splitting of fat, stimulated by : epinephrine, norepinephrine and cortisol

∞ **Triacylglycerols** (triglycerides) are the most abundant dietary lipids

- Each triacylglycerol has a **glycerol** backbone to which are esterified **3 fatty acids**. Most triacylglycerols are "mixed." The three fatty acids differ in chain length and number of double bonds



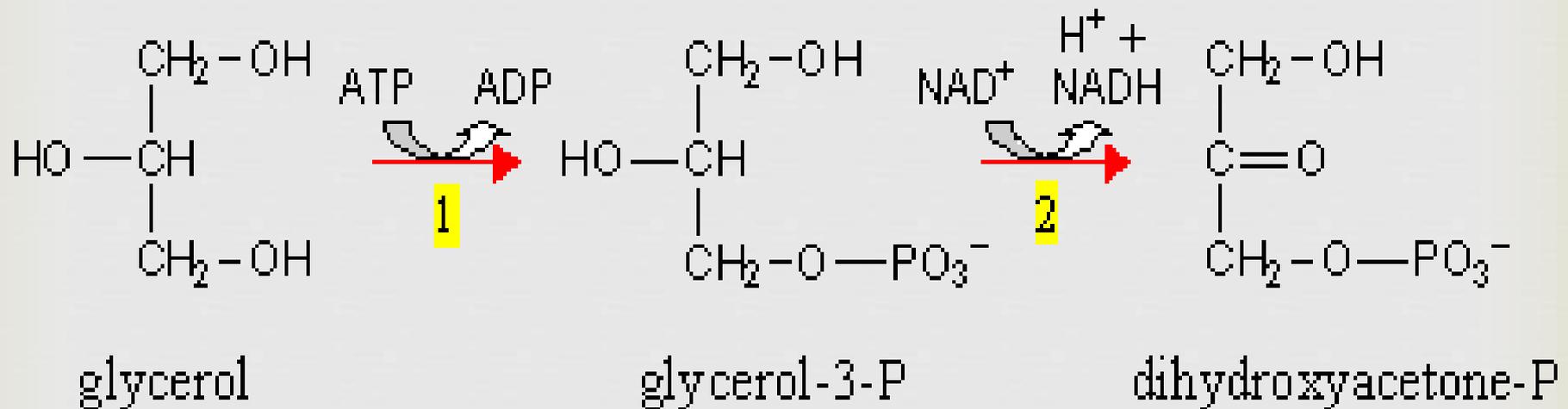
# Stage 1. Lipid catabolism (Lipolysis)

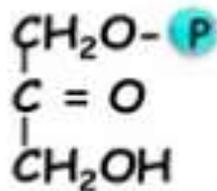


**Lipases** hydrolyze triacylglycerols, releasing one fatty acid at a time, producing diacylglycerols, and eventually glycerol. .

The end of the process 3 fatty acids and 1 glycerol.

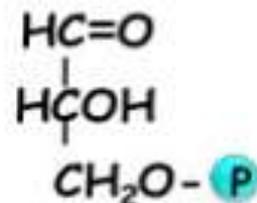
- ∞ **Glycerol** arising from hydrolysis of triacylglycerols is converted to the **Glycolysis** intermediate **dihydroxyacetone phosphate**, by reactions catalyzed by:
- (1) Glycerol Kinase
  - (2) Glycerol Phosphate Dehydrogenase.





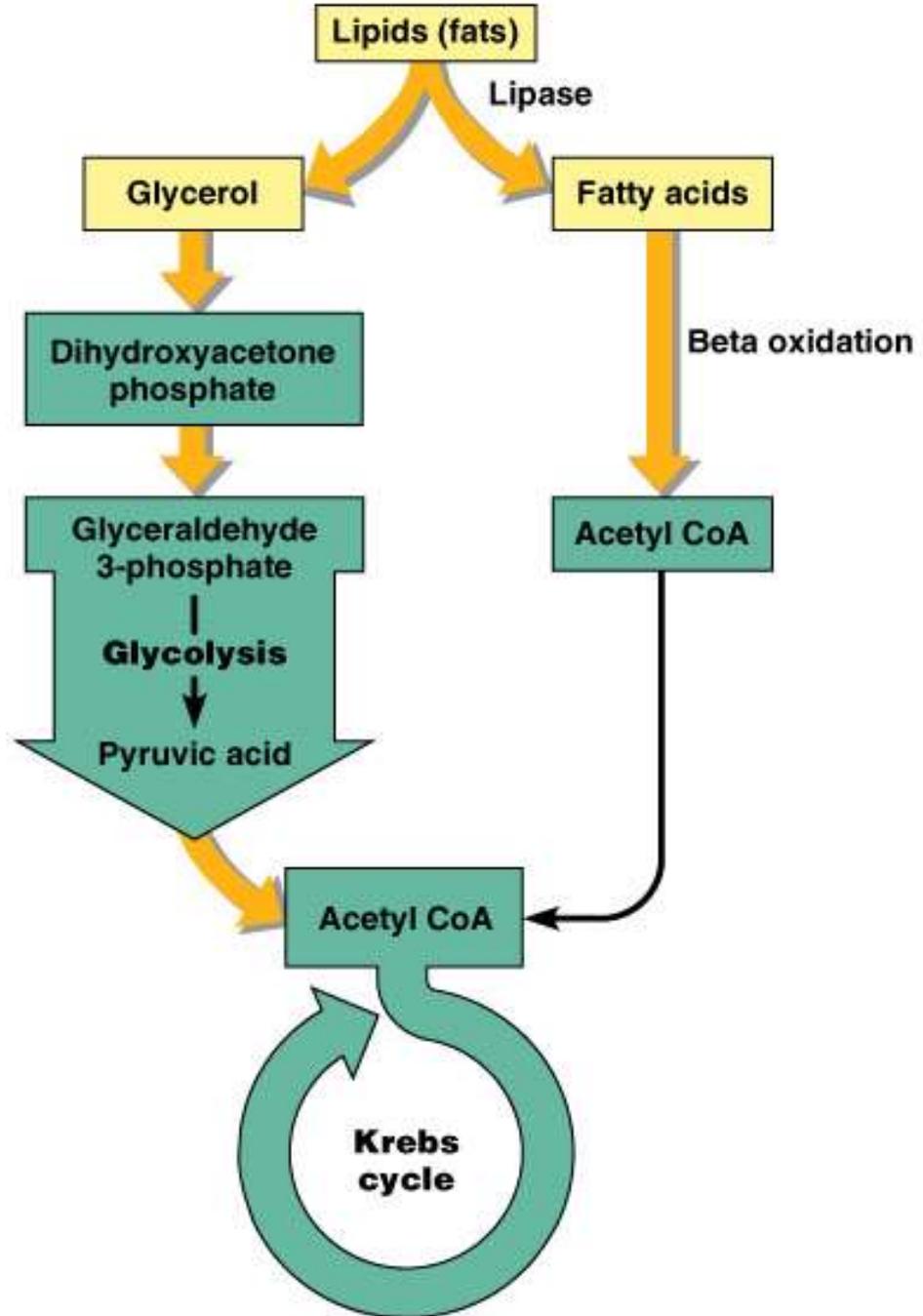
Dihydroxyacetone  
phosphate

**Phosphotriose  
isomerase**



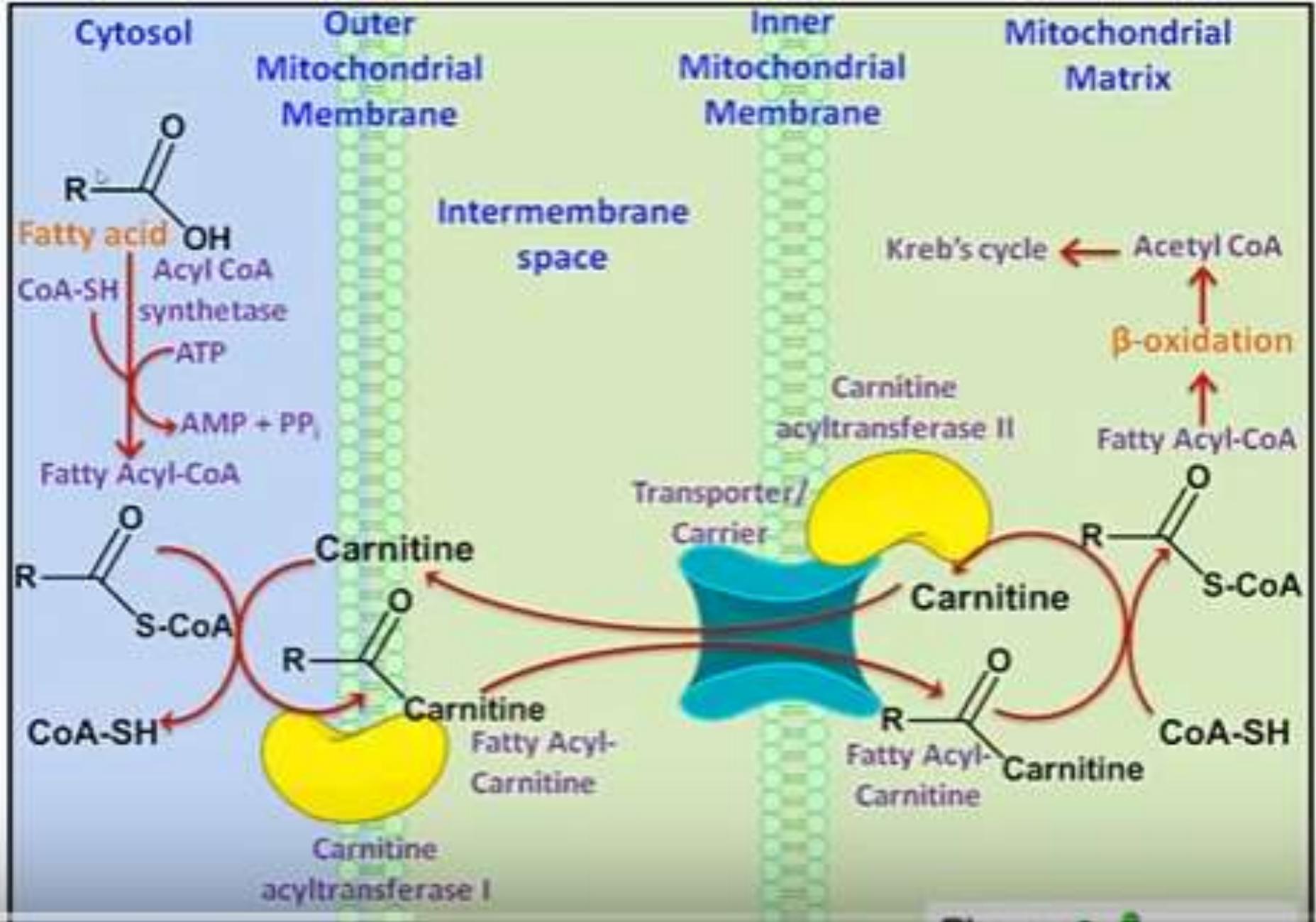
Glyceraldehyde  
3-phosphate

- ⌘ Dihydroxyacetone phosphate is isomerised to glyceraldehyde 3-phosphate by the enzyme Phosphotriose isomerase.
- ⌘ In this reaction, 2 molecules of glyceraldehyde 3-phosphate are formed.
- ⌘ Glyceraldehyde 3-phosphate can also be synthesized from glycerol (fats) by phosphorylation.
- ⌘ This is reversible reaction.



# Beta Fatty Acid Oxidation

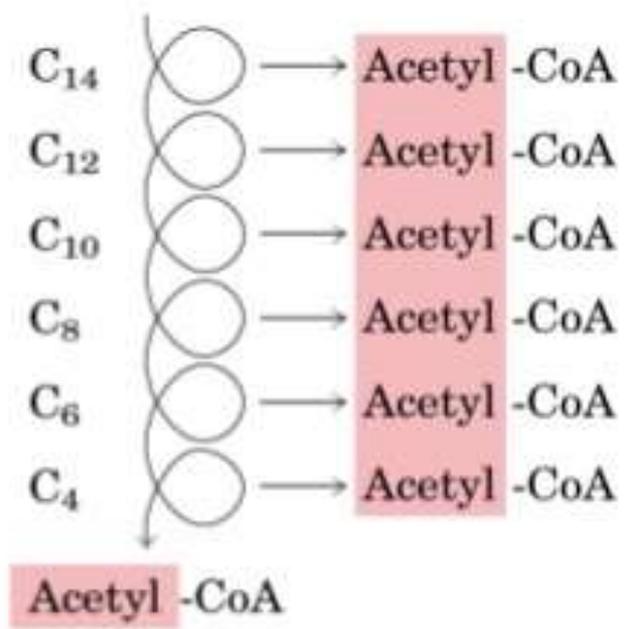
- ☞ The end product of each cycle is the **fatty acid** shortened by 2 carbons and acetyl CoA.
- ☞ The series of reactions is also **known as the beta-oxidation** pathway because the major reaction site is the **beta-carbon** or #3 carbon from the thioester carbon.
- ☞ Happens in the mitochondrial membrane
- ☞ The fatty acids must be activated and turned into acetyl-CoA



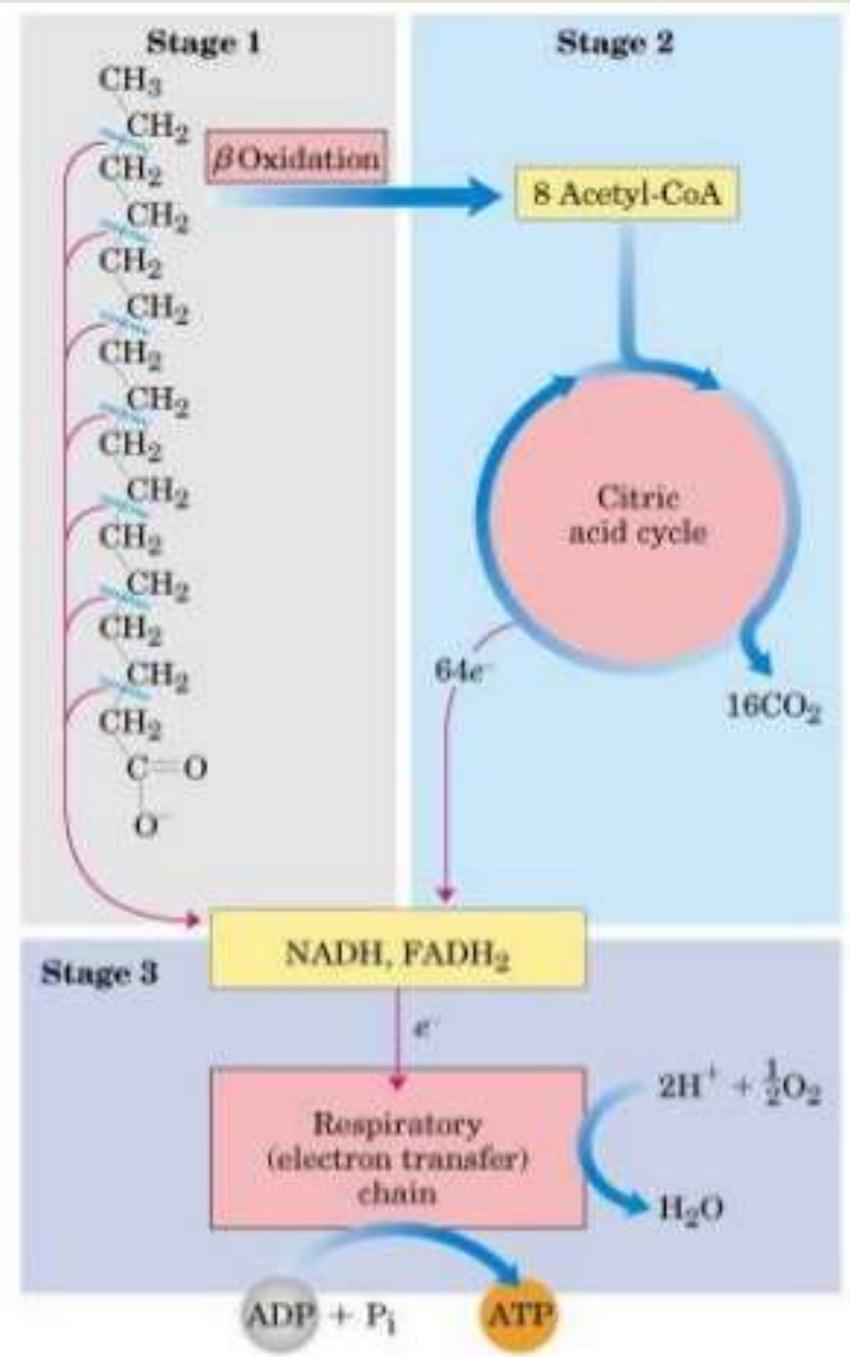
## Activation and Transported to Mitochondria

- $\text{FA} + \text{CoA} + \text{ATP} \rightarrow \text{fatty acyl-CoA} + \text{AMP} + 2\text{P}_i$
- Coupled to the cleavage of ATP
- **AcylCoASynthetase**— a family of isozymes specific for short, medium and long chain FA that catalyze production of fatty acyl-CoA
- Transported through inner mitochondrial membrane via **carnitine**
  - uses specific acylcarnitine transporter

# $\beta$ -oxidation – first of three stages of fatty acid oxidation



(b)



# 4 Steps of $\beta$ -oxidation

1. Dehydrogenation of the fatty acyl-CoA to make a trans double bond between  $\alpha$  and  $\beta$  carbon.

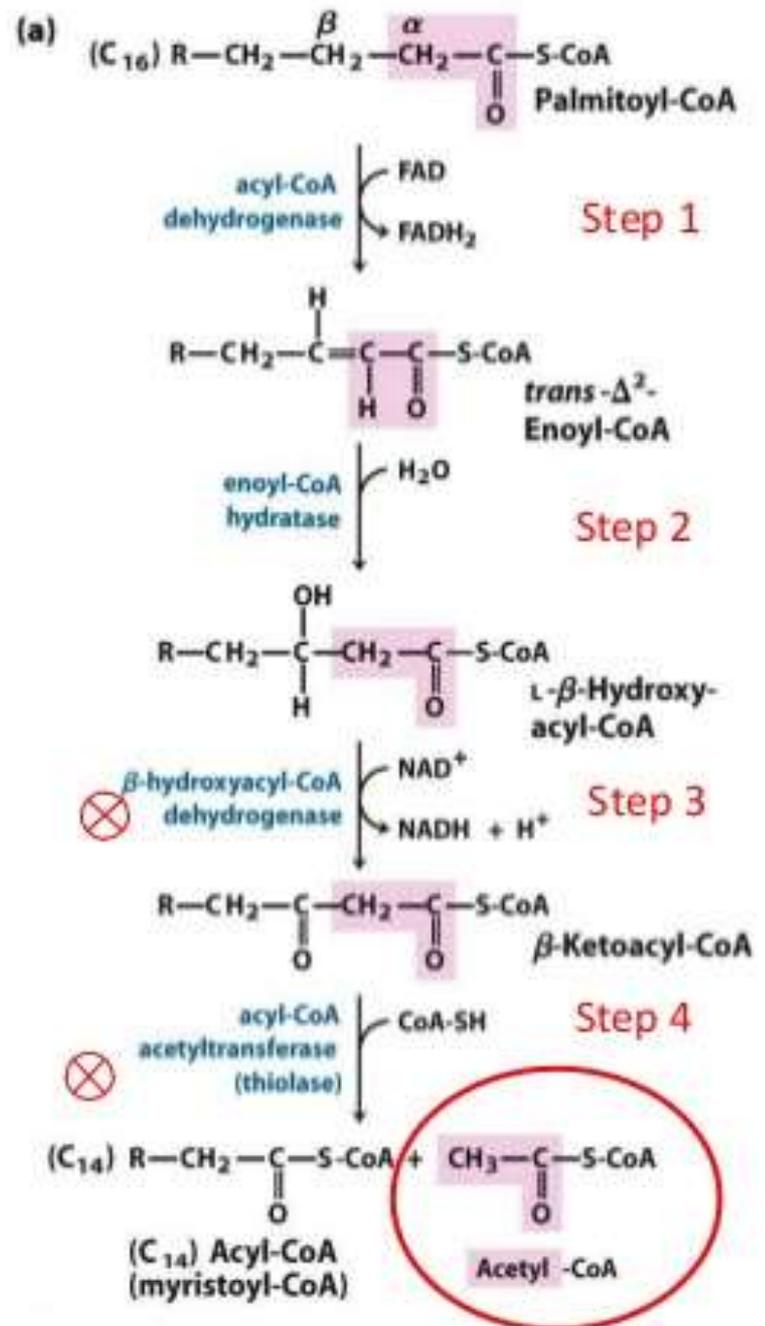
- Short, medium, and long chain acyl-CoA dehydrogenases
- $e^-$  removed transferred to FAD

2. Hydration of the double bond

1. Dehydrogenation of the  $\beta$ -hydroxyl group to a ketone

-  $e^-$  removed transferred to  $NAD^+$

1. Acylation – addition of CoA and production of acetyl-CoA



# Energy Yield from $\beta$ -Oxidation

- Yield of ATP per mole of stearic acid ( $C_{18}$ ).

Step	Chemical Step	Happens	ATP
1	<b>Activation</b> (stearic acid $\rightarrow$ stearyl CoA)	Once	-2
2	<b>Oxidation</b> (acyl CoA $\rightarrow$ trans-enoyl CoA) produces $FADH_2$	8 times	16
4	<b>Oxidation</b> (hydroxy-acyl CoA to ketoacyl CoA) produces $NADH + H^+$	8 times	24
	<b>Oxidation</b> of acetyl CoA by the common metabolic pathway, etc.	9 times	108
	<b>TOTAL</b>		<b>146</b>

# New research examines p-synephrine's role in burning fat during rest and exercise

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## Abstract

Lipolysis of white adipose tissue triacylglycerol stores results in the liberation of glycerol and nonesterified fatty acids that are released into the vasculature for use by other organs as energy substrates. In response to changes in nutritional state, lipolysis rates are precisely regulated through hormonal and biochemical signals. These signals modulate the activity of lipolytic enzymes and accessory proteins, allowing for maximal responsiveness of adipose tissue to changes in energy requirements and availability. Recently, a number of novel adipocyte triacylglyceride lipases have been identified, including desnutrin/ATGL, greatly expanding our understanding of adipocyte lipolysis. We have also begun to better appreciate the role of a number of nonenzymatic proteins that are critical to triacylglyceride breakdown. This review provides an overview of key mediators of lipolysis and the regulation of this process by changes in nutritional status and nutrient intakes.

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Thank you 😊