Digestion Of Lipids

Action Of Specific Lipid Digesting Enzymes in Small Intestine

- **Digestion of Lipids** is **cleavage of Ester bonds** present in their structures.

- Dietary forms of Lipids are digested:
  - By action of **specific Lipid digesting enzymes of**
  - **Pancreatic and intestinal juice**

Digestion Of Triacylglycerol (TAG) By Enzyme Pancreatic Lipase

- **Dietary** Fat/Oil which is chemically **TAG** is **predominant ingested Lipid form.**
- **TAG** is **significantly digested in small intestine**
- **After process of Emulsification.**

Action of Pancreatic Lipase

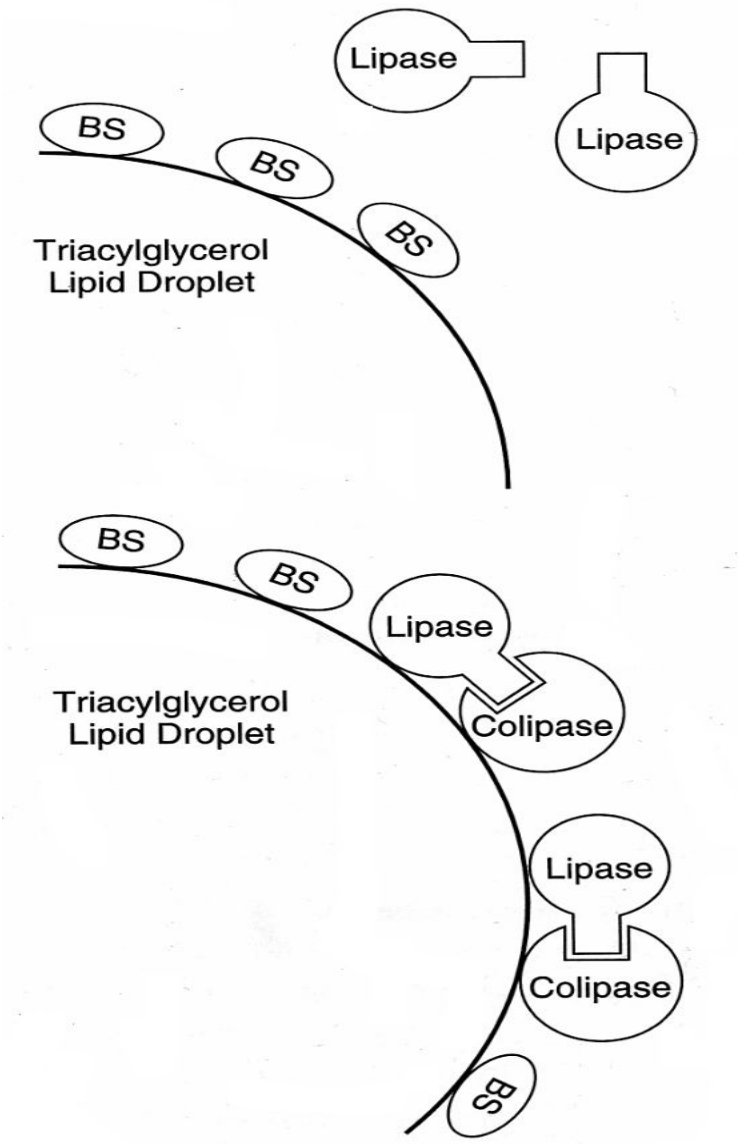
- **Pancreatic Lipase** **specifically Digests Triacylglycerol** by **cleaving ester bonds** present in its structure.

Colipase Facilitates

Pancreatic Lipase Activity

Role Of Pancreatic Colipase

- **Procolipase** secreted from Pancreas as
- **Activated to Colipase by Trypsin**



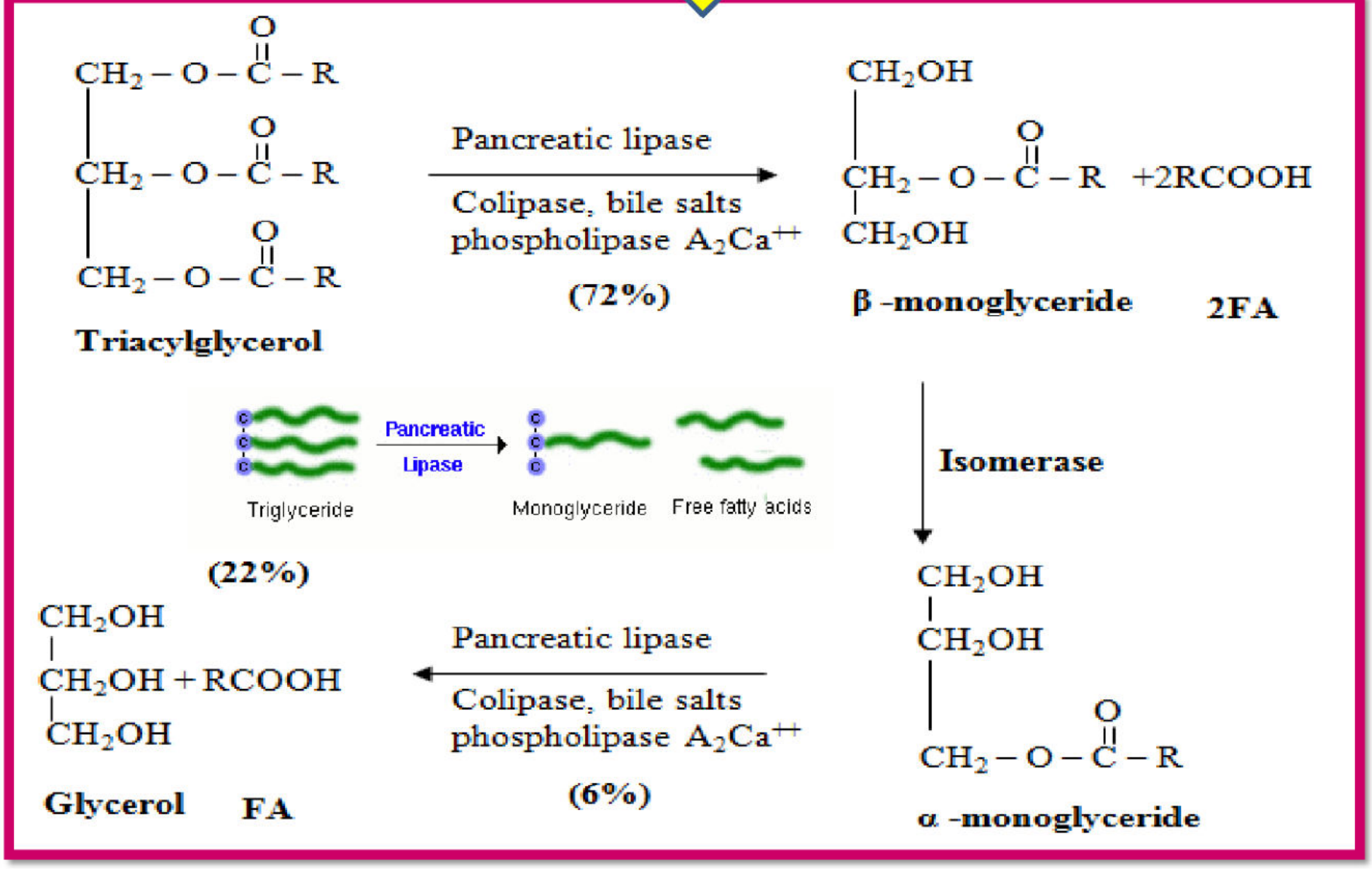
- **Colipase anchors Lipase to an Emulsion.**
  - One Colipase to one Lipase (i.e., 1:1 ratio)

- **Pancreatic Colipase**

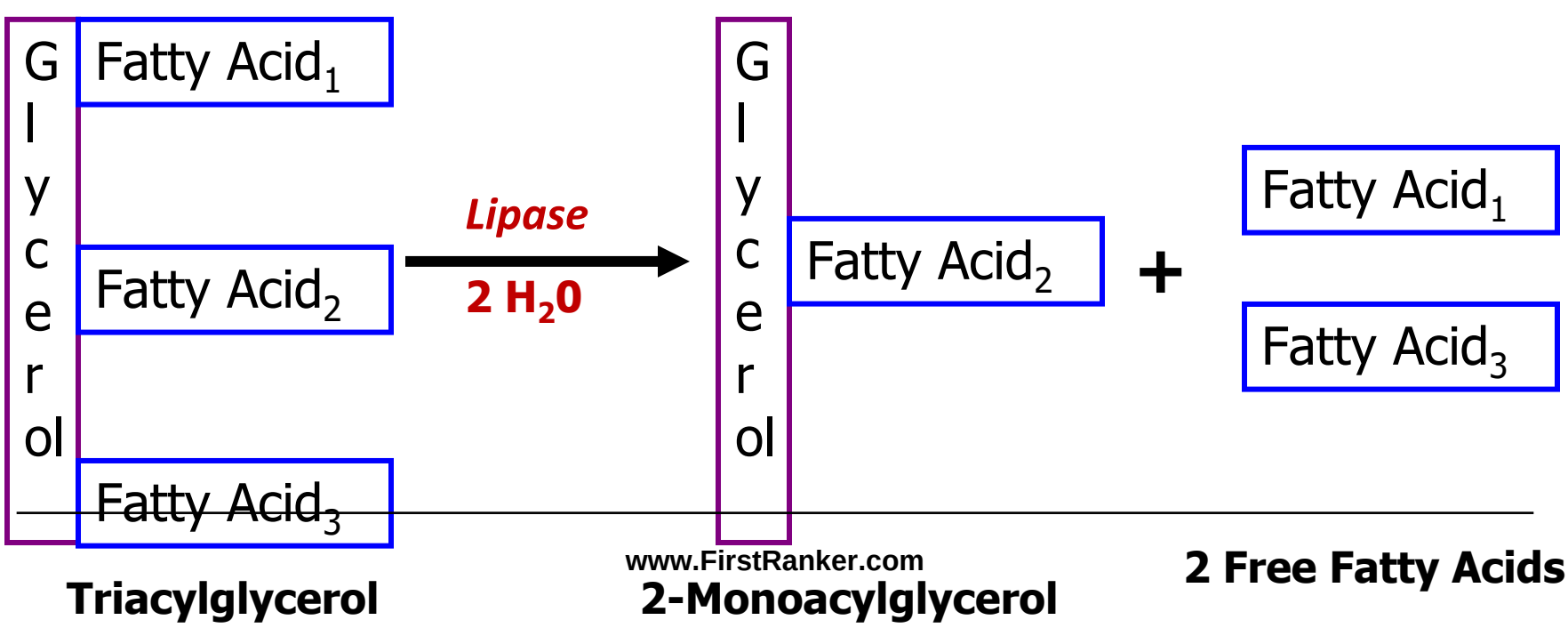
–Colipase interacts with Pancreatic Lipase to:

- **Displace Bile to allow recycling**
- **Improve activity of Pancreatic Lipase**
- Interact PL with Triacylglycerol

3- Pancreatic lipase



- **Pancreatic Lipase attack TAG at 1 and 3 positions of Ester bonds.**



Triacylglycerol

Colipase **Pancreatic Lipase**

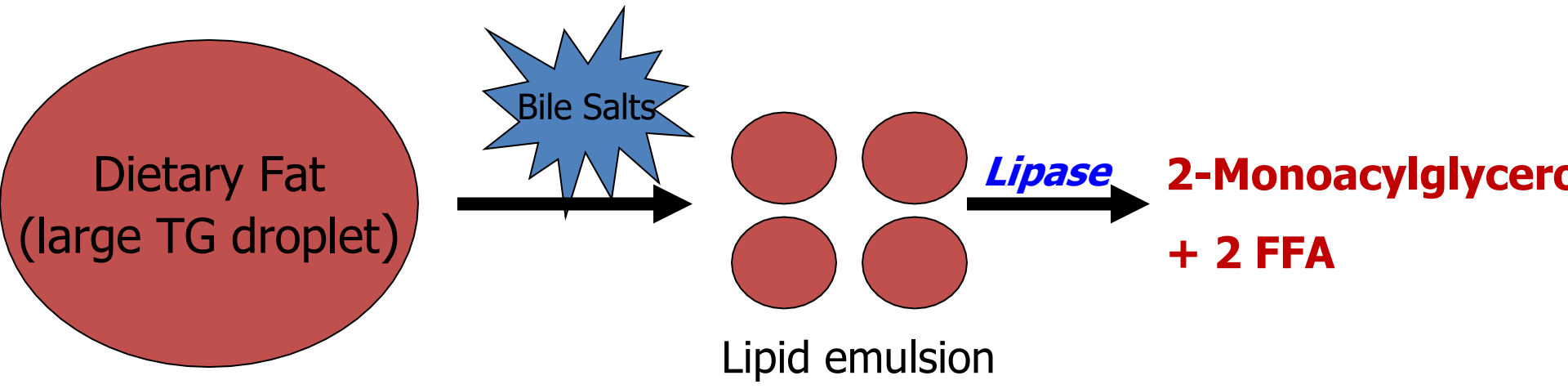
Optimum PH 8

Cleaves 1st and 3 rd ester bond of TAG

Free Fatty acids + 2-Monoacylglycerol

(Fatty acid esterified at C2 of Glycerol)

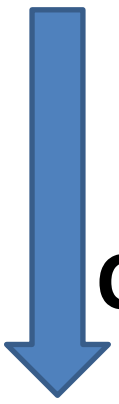
- **Pancreatic Lipase** digest TAG
- By **specifically cleaving first** and **third ester bonds of TAG structure**.



- The **products of TAG digestion**
- By **Pancreatic Lipase** activity are:
  - **Free Fatty acids**
  - **Monoacylglycerol** (2-MAG)

Action of Non Specific Lipid Esterases Of Intestinal Juice

2-Monoacylglycerol



Non Specific Esterase

Cleaves Ester bond at C2

Free Fatty acid + Glycerol

4- Intestinal lipase

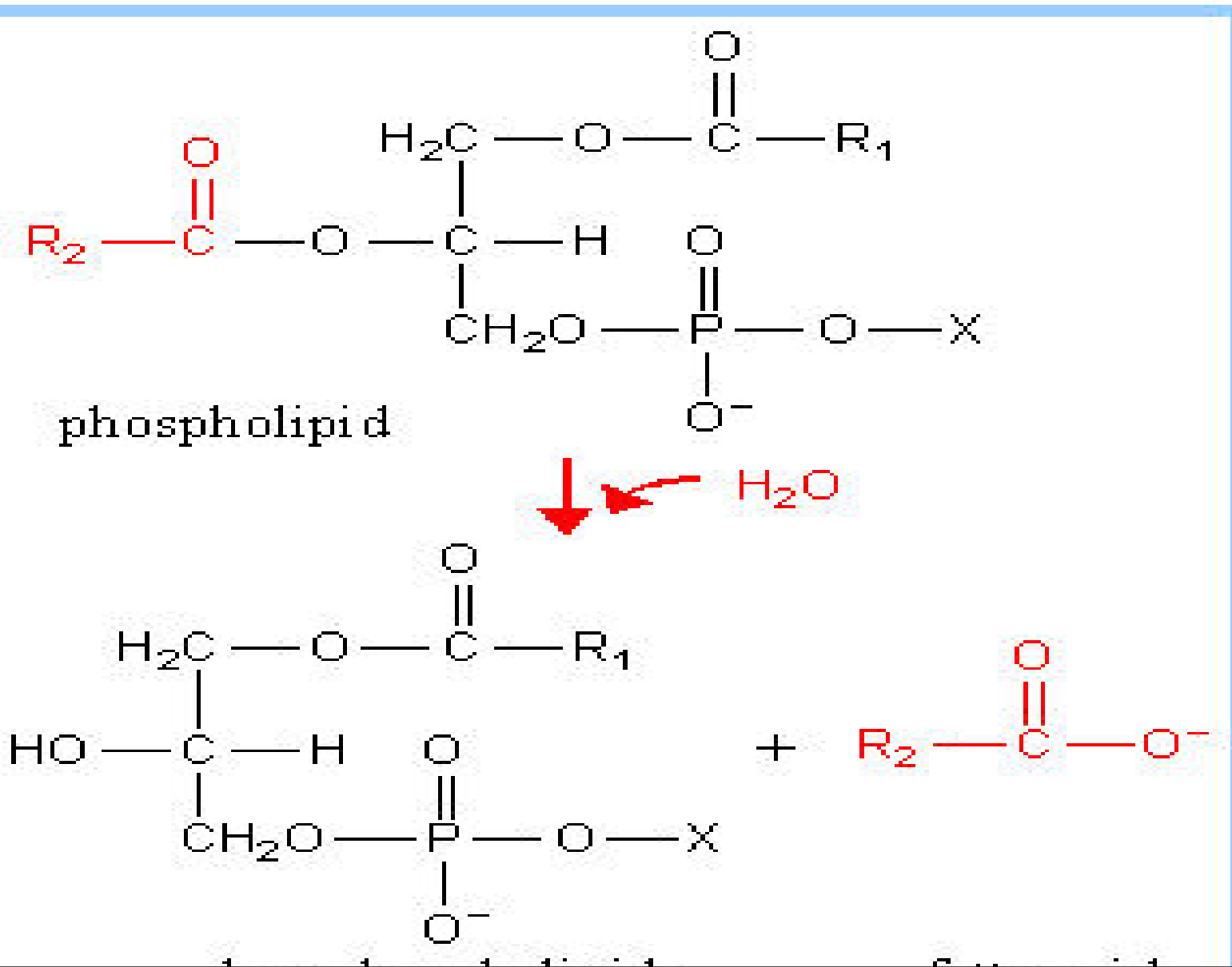
✓ **Act within intestinal mucosal cells → hydrolyse the absorbed primary (α) monoglycerides forming glycerol and FFA**

- **Non specific Lipid Esterases** act on **2-MAG /Retinol Ester**.

- It cleaves ester bonds and releases **Free Fatty acid** and **Glycerol/Retinol** respectively.

Digestion Of Phospholipids by Pancreatic Enzymes

Action of Phospholipase A2 and Lysophospholipase



Phospholipid

↓

Phospholipase A2

Cleaves Ester bond at C2 of PL

Lysophospholipid+ Free Fatty acid

Lysophospholipid

↓

Lysophospholipase

Cleaves Ester bond at C1

Glycerophosphorylcholine+ Free Fatty acid

- Pancreatic juice enzymes **Phospholipase A2** and **Lysophospholipase** digests dietary Phospholipids.

- **Phospholipase A2** cleaves **second position ester bond** of Phospholipid to form **Lysophospholipid** and Free Fatty acid.
- Lysophospholipid is then acted by **Lysophospholipase** which **cleaves ester bond at C1** to generate: **Glycerophosphorylcholine and Free Fatty acids.**

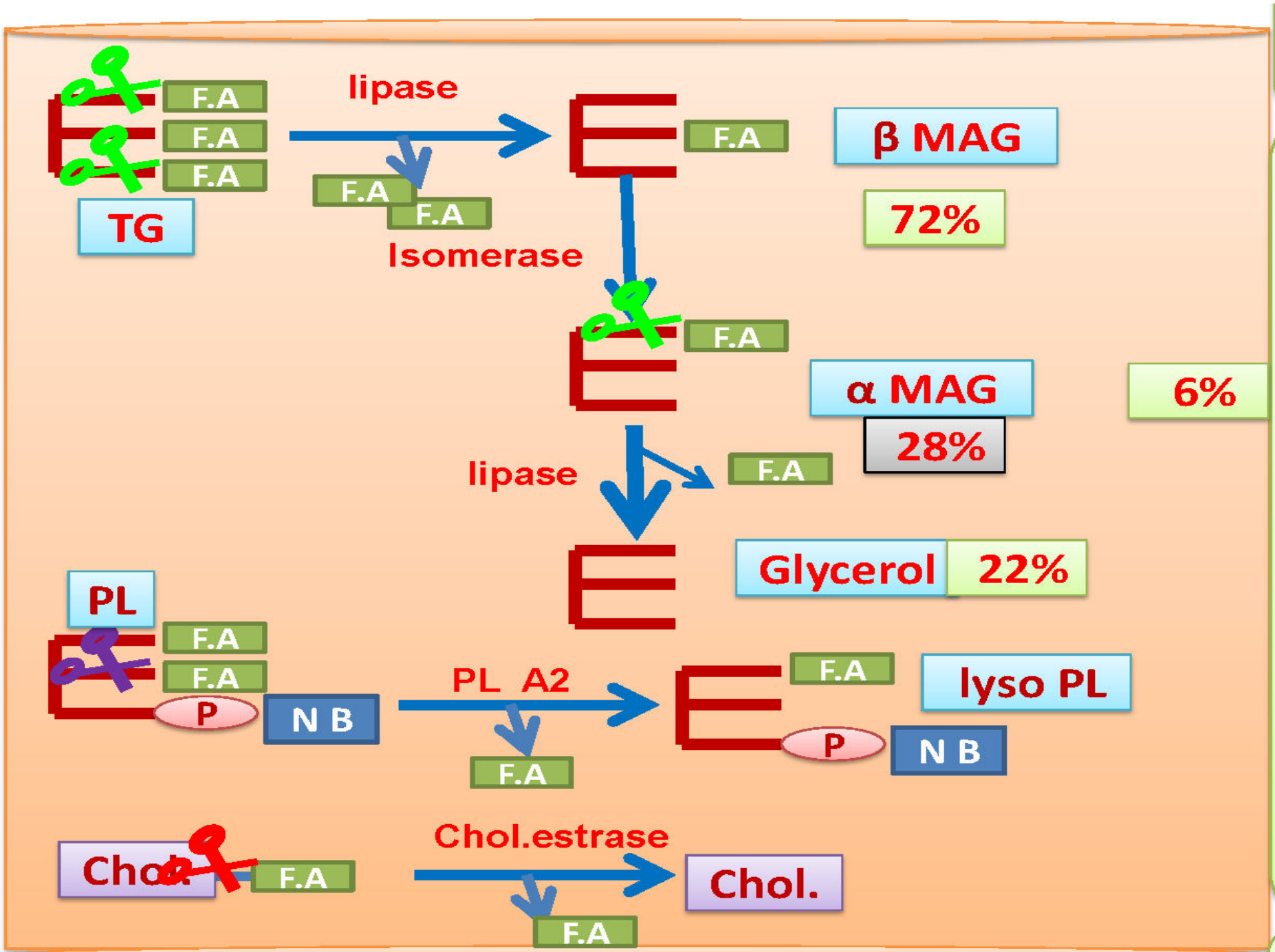
Digestion Of Cholesterol Ester By Cholesterol Esterase

Cholesterol Ester

Cholesterol Esterase

Cleaves Ester bond at C3

Free Cholesterol+ Free Fatty acid



End Products Of Lipid Digestion

- **5 Simple Forms as End products of Lipid Digestion**

1. **Free Fatty acids**
2. **Glycerol**
3. **2-Monoacylglycerol (2-MAG)**
4. **Glycerophosphoryl-Choline**
5. **Free Cholesterol**

Absorption of Dietary End Products Of Lipid Digestion

Absorption of Dietary Lipids

- End products of Lipid digestion **simple and absorbable forms**
- Get absorbed In **small intestine**

- **Rate of absorption** of different types of **Lipids differ**.
  - **Pork fat** is **almost absorbed completely.**
  - **Castor oil** is **not at all absorbed.**

Theories Of Lipid Absorption

- Absorption of Lipids is a **complex mechanism** and **various theories** are proposed to explain its mechanism.
  - **Lipolytic Theory**
  - **Partition Theory**
  - **Bergstorm Theory**

(Most Recent and accepted one)

Important Role Of Bile Salts In Both Lipid Digestion and Absorption

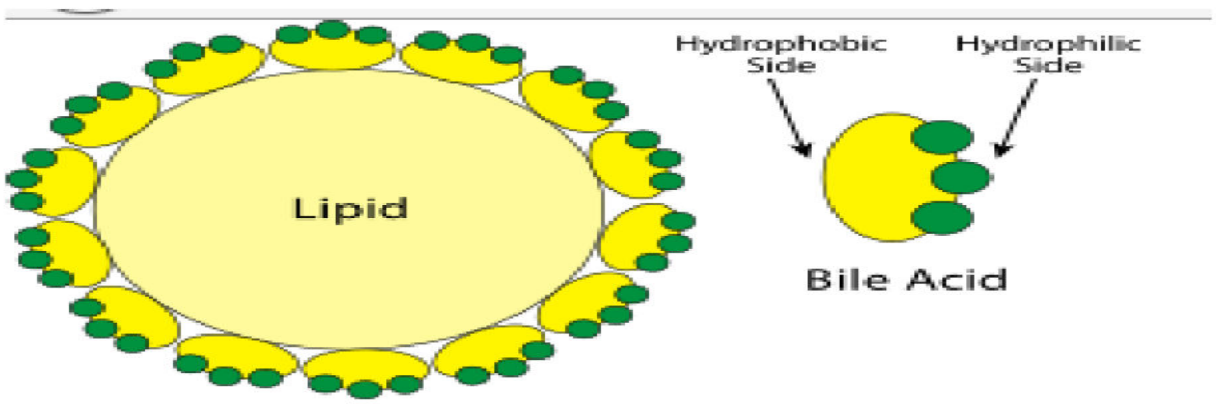
- Bile Salts in intestine helps in **Emulsification of dietary Lipids** to **form Emulsions** and **Facilitates Lipid Digestion.**

- Later Bile Salts **form Mixed Micelles** and **facilitates the absorption** of digestive end products **Lipids**.

Role Of Bile Salts In Lipid Absorption

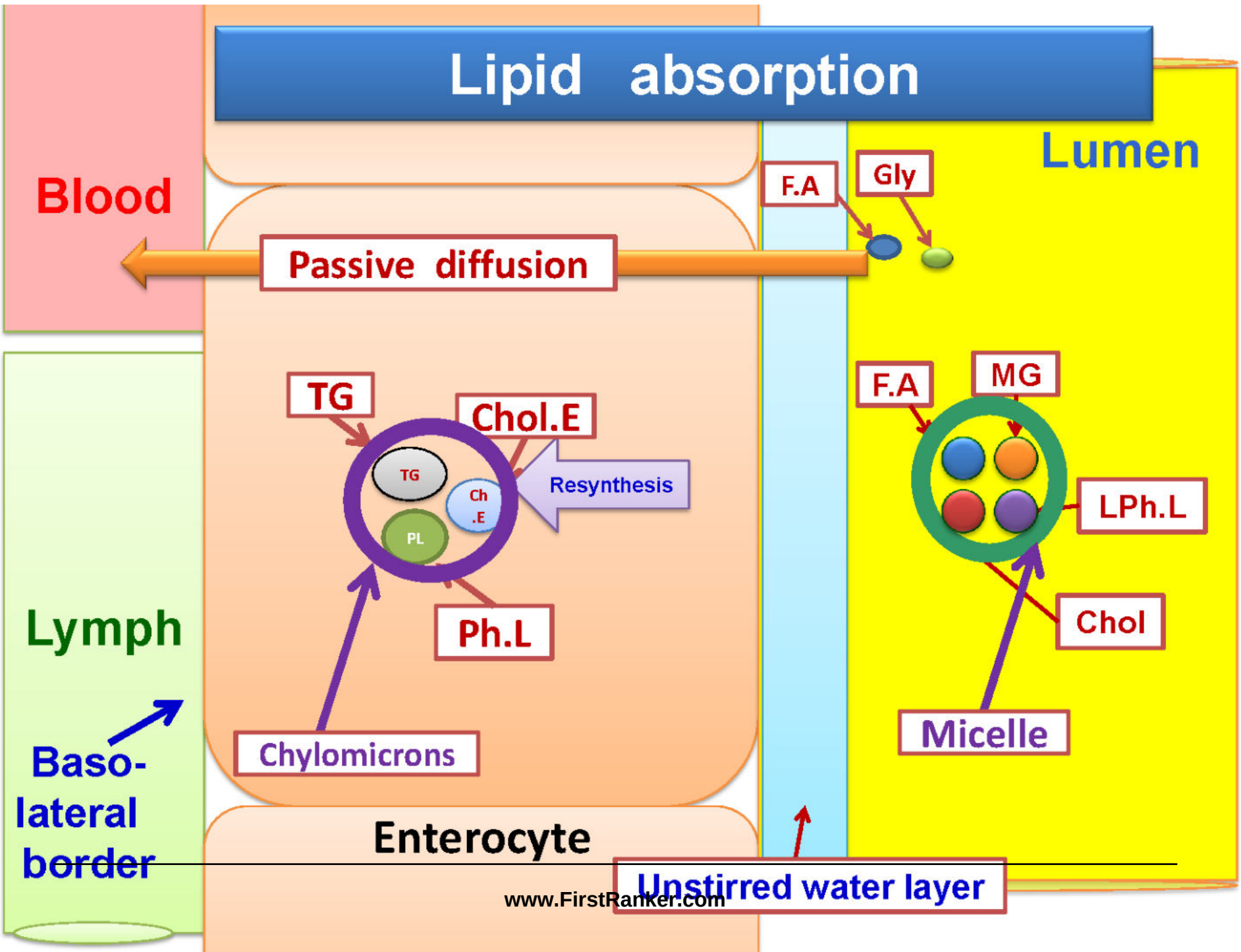
How ?

- **Bile salts surround these component (by their unpolar end while their polar endings directing outward) → water soluble micelles (0.1 –0.5 µ in diameter)**

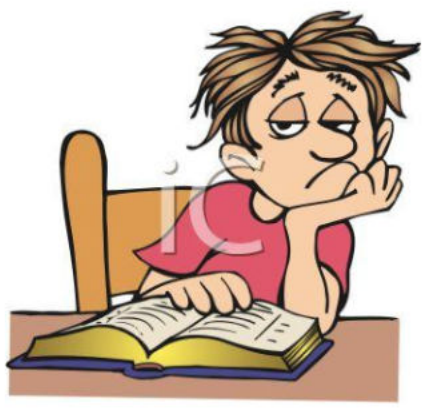


How ?

- Micelles soluble in water, enter microvilli of mucosal cells by endocytosis where fat digestion may be completed through action of intestinal lipase:



- The triglycerides, phospholipids & cholesterol bind with a protein (Apolipoprotein B_{48}) forming chylomicrons ➡ lacteals & pass with lymphatic drainage ➡ the thoracic duct ➡ systemic circulation.



Mechanism Of Lipid Absorption

- **Bile Salts play an important role in absorption** of digestive end products of dietary Lipids.

- **Bile salts help in formation** of **Mixed micelles**.

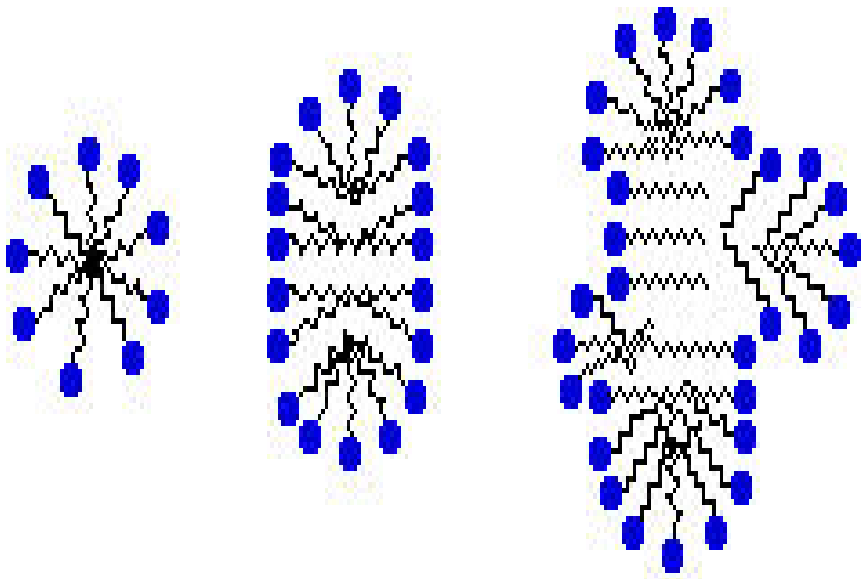
- **Mixed Micelle** is **aggregation of**

- **digestive end products** of **dietary Lipids** with a **peripheral layer of Bile Salts**.

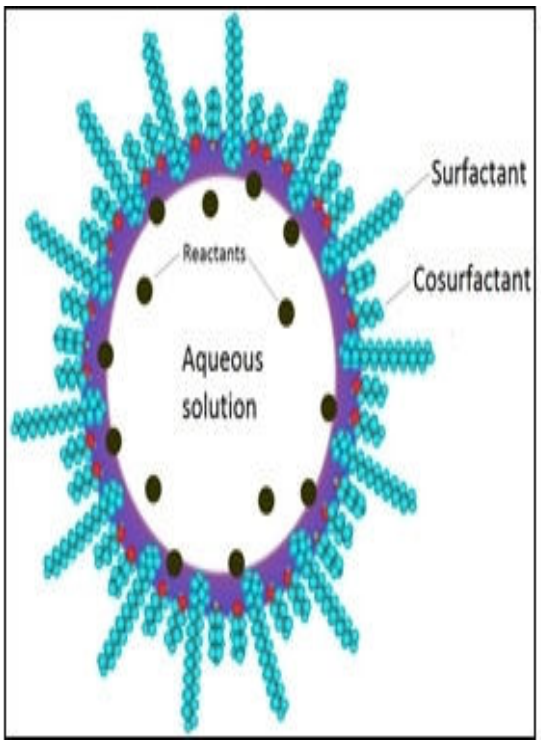
- **An efficiency of Lipid absorption depends upon:**
  - **Quantity of Bile salts**
  - **Which solubilizes and form Mixed Micelles**.

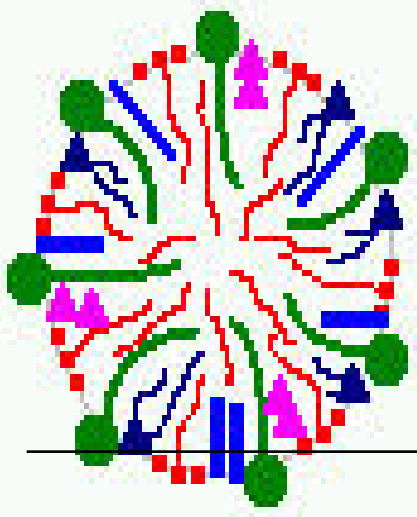
Mixed Micelle Formation

- **Mixed Micelle** is a **complex of Lipid materials and Bile salts** soluble in water
  - It contains Bile salts, end products of Phospholipids & Cholesterol at **periphery** of a **Mixed Micelles.**
  - 2-Monoacylglycerol, Free fatty acids and fat-soluble Vitamins in **center** of **Mixed Micelles.**



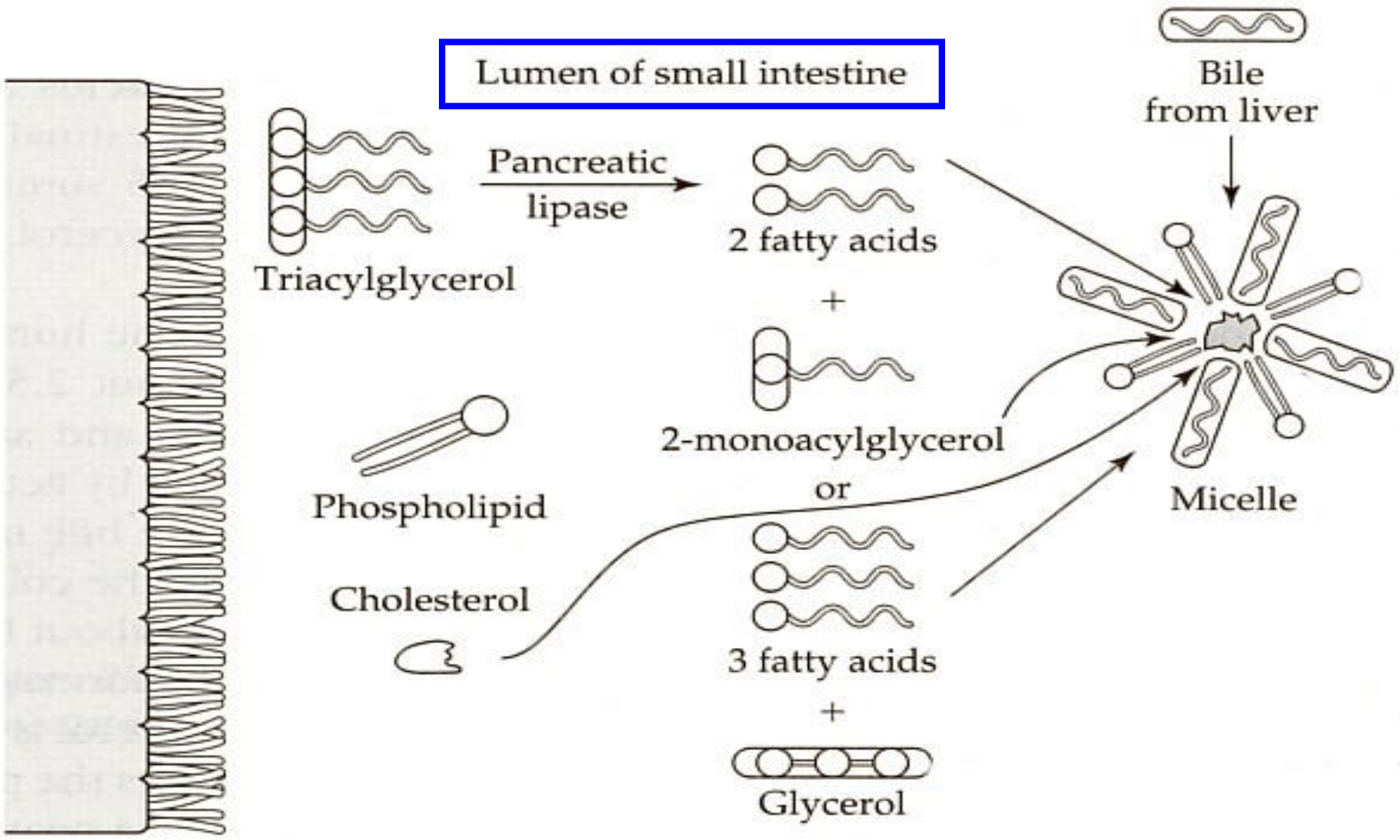
micelle assemblies of amphiphiles





Bile salts
Monoglyceride
Fatty acids
Phospholipids
Cholesterol

Mixed Micelle Formation



- In Mixed Micelle **non polar long chain fatty acids are at the center**

- At **periphery** are **Amphipathic Lipid moieties and Bile salts.**

- **Bile salts and Amphipathic Lipids** of Mixed Micelle

- **Exert a solubilizing effect on non polar Lipid** moieties and **help in their absorption.**

- **Mixed Micelles** then **get attached to an Enterocytes cell membrane.**

- This help **Lipid end products to slowly cross the mucosal membrane and get internalized.**

- **Bile salts of Mixed Micelles do not cross intestinal mucosal cell membrane.**

- They get **retained in intestinal lumen** and **later get recycled.**

- Bile salts are **reabsorbed further down the Gastrointestinal** tract (In ileum)

- **Bile salts are transported back to the Liver through enterohepatic circulation**

- Finally **recycled and secreted back into the digestive tract**

Re-Esterification of Simple Lipids
OR
Resynthesis Of Complex Forms Of Lipids
In Intestinal Mucosal Cells

- Once **simpler forms of Lipids enter** the intestinal mucosal cells/**Enterocytes**

- They are **resynthesized into complex forms** of Lipids inside intestinal mucosal cells.

Resynthesis Of Complex Lipids In Enterocytes

- Free Fatty acid (FFA) + Glycerol → Monoacylglycerol
- MAG +FFA → Diacylglycerol
- Diacylglycerol + FFA → Triacylglycerol
- Glycerophosphorylcholine + FFAs → Phospholipid
- Cholesterol +FFA → Cholesterol Ester

- Note **resynthesized complex Lipids** in intestinal mucosal cells

- Are **usually different from** those ingested through diet.

- **Dietary absorbed Lipids** in intestinal mucosal cells/Enterocytes are then **mobilized out as Lipoproteins**.

Formation Of Lipoprotein Chylomicrons

In Intestinal Mucosal Cells For Transportation Of Dietary Lipids

- Lipids of dietary origin present in intestinal mucosal cells are mostly **non polar** (TAG) and **hydrophobic** in nature.

- T**ransport** of these dietary Lipids through aqueous phase of lymph and blood is

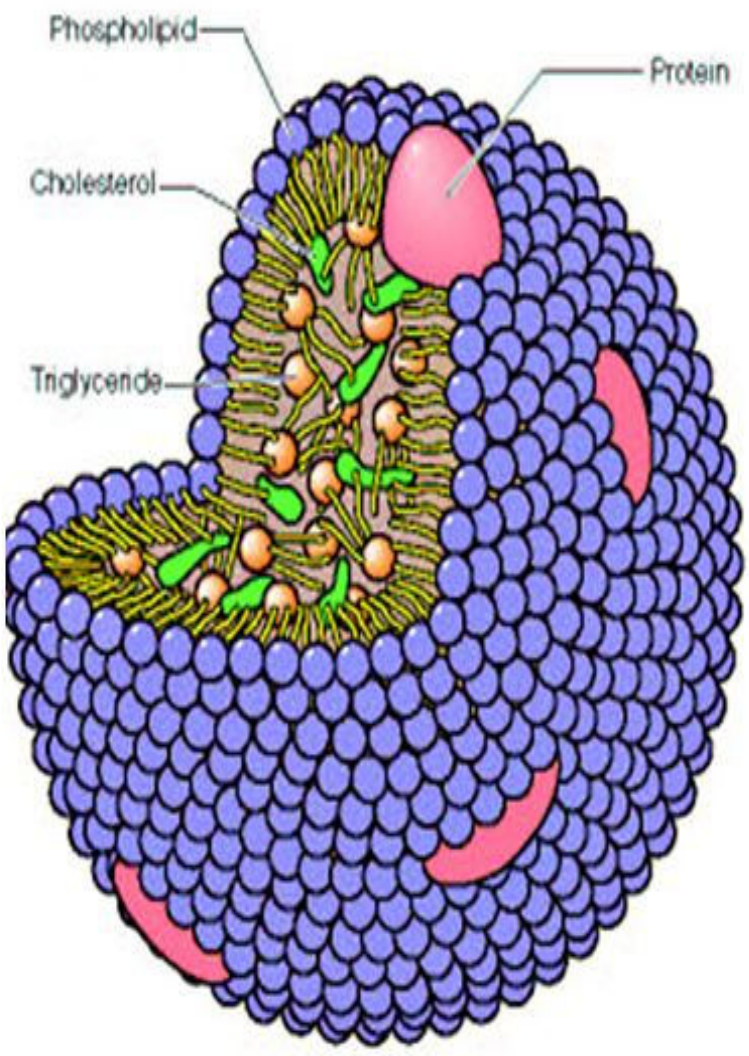
- **Facilitated through** formation of a **Lipoprotein -Chylomicron** in intestinal mucosal cells.

- **Lipoprotein Chylomicron** is **synthesized in intestinal mucosal cells/Enterocytes** by
- Aggregation of **dietary ingested, digested and absorbed Lipids** and **Apoprotein (ApoB48).**

- **Chylomicron** structure has the **non polar Lipids aggregated at center**, the **Amphipathic Lipids and Apoproteins at periphery.**

Chylomicrons

- Synthesized in small intestine (mucosal cells)
- To mobilize dietary lipids
- Transport dietary lipids
- 98% lipid, large sized, lowest density
- Apo B-48
  - Receptor binding
- Apo C-II
  - Lipoprotein lipase activator
- Apo E
  - Remnant receptor binding

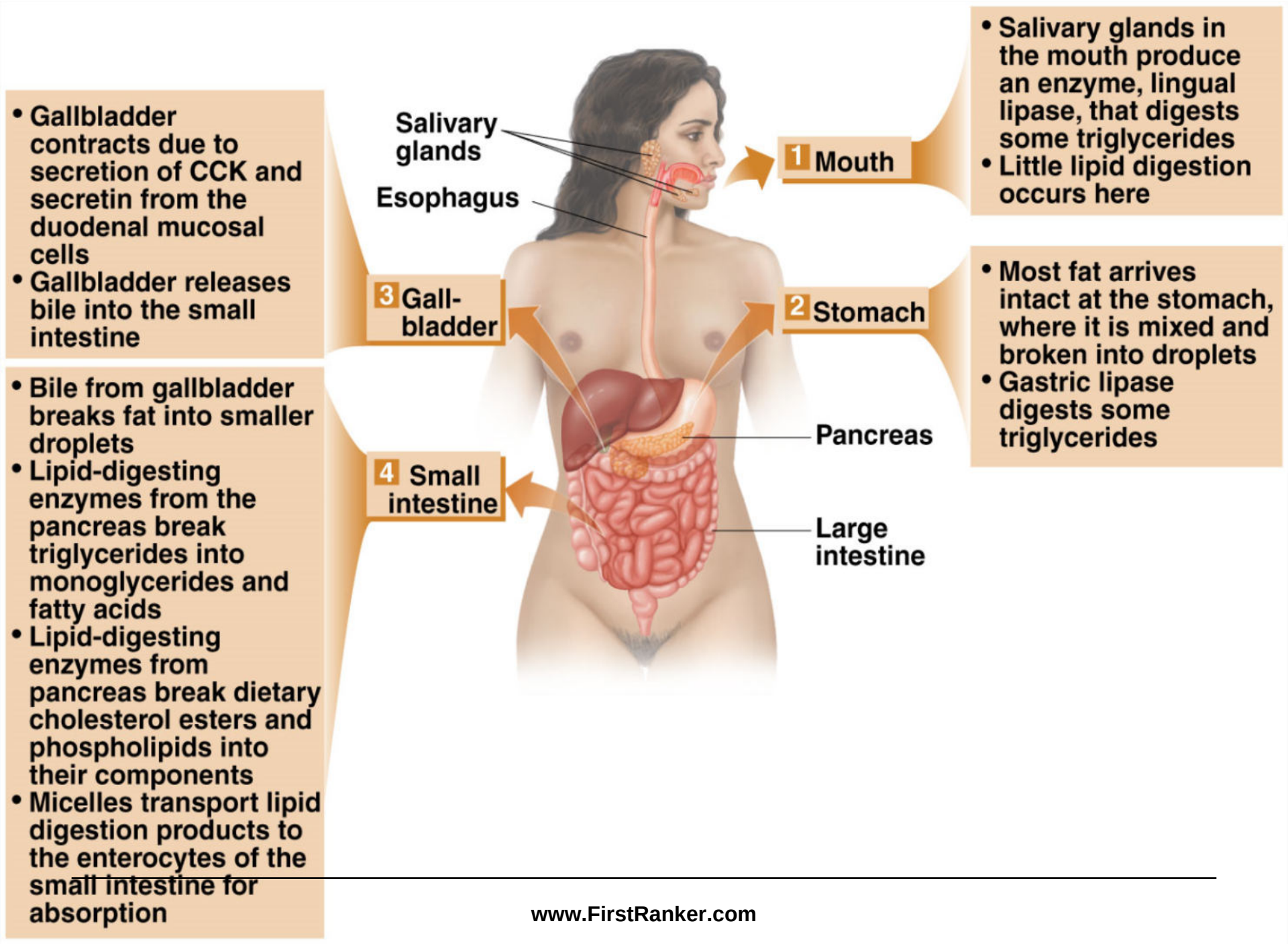


- Chylomicron has 98% of TAG (dietary origin)
- 1% other Lipids and
- 1% Proteins.

- Chylomicrons from intestinal mucosal cells are **first released in Lacteals (Lymph vessels) of Lymphatic system**
- Which then enters the **systemic blood circulation via Thoracic duct (Lymphatic duct).**

- Thus **Chylomicron serve as a vehicle for transporting the exogenous forms of dietary Lipids**

- **From Small intestine to Liver** via aqueous phase of **Lymph and Blood.**



Lipid Digestion Absorption and Transport

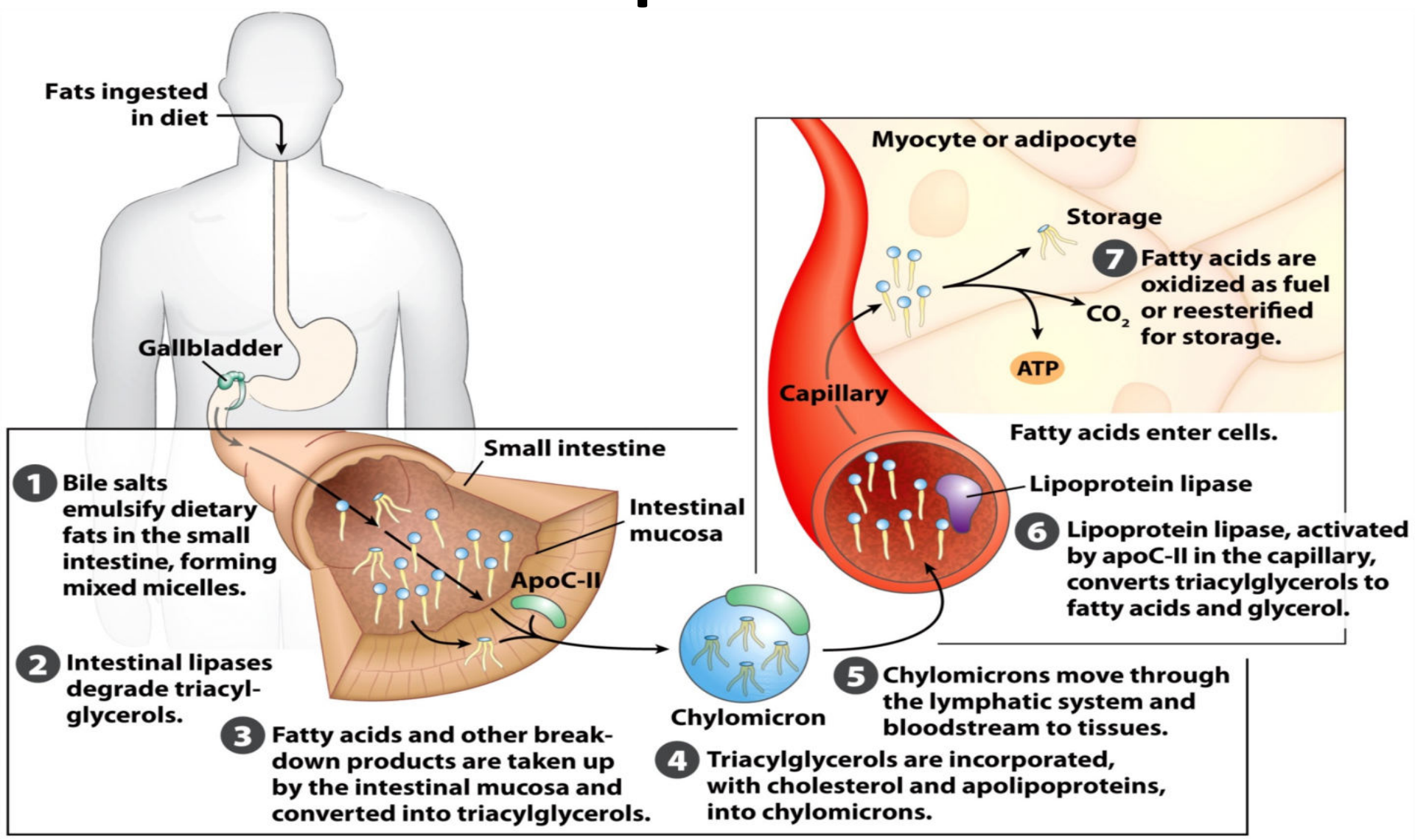
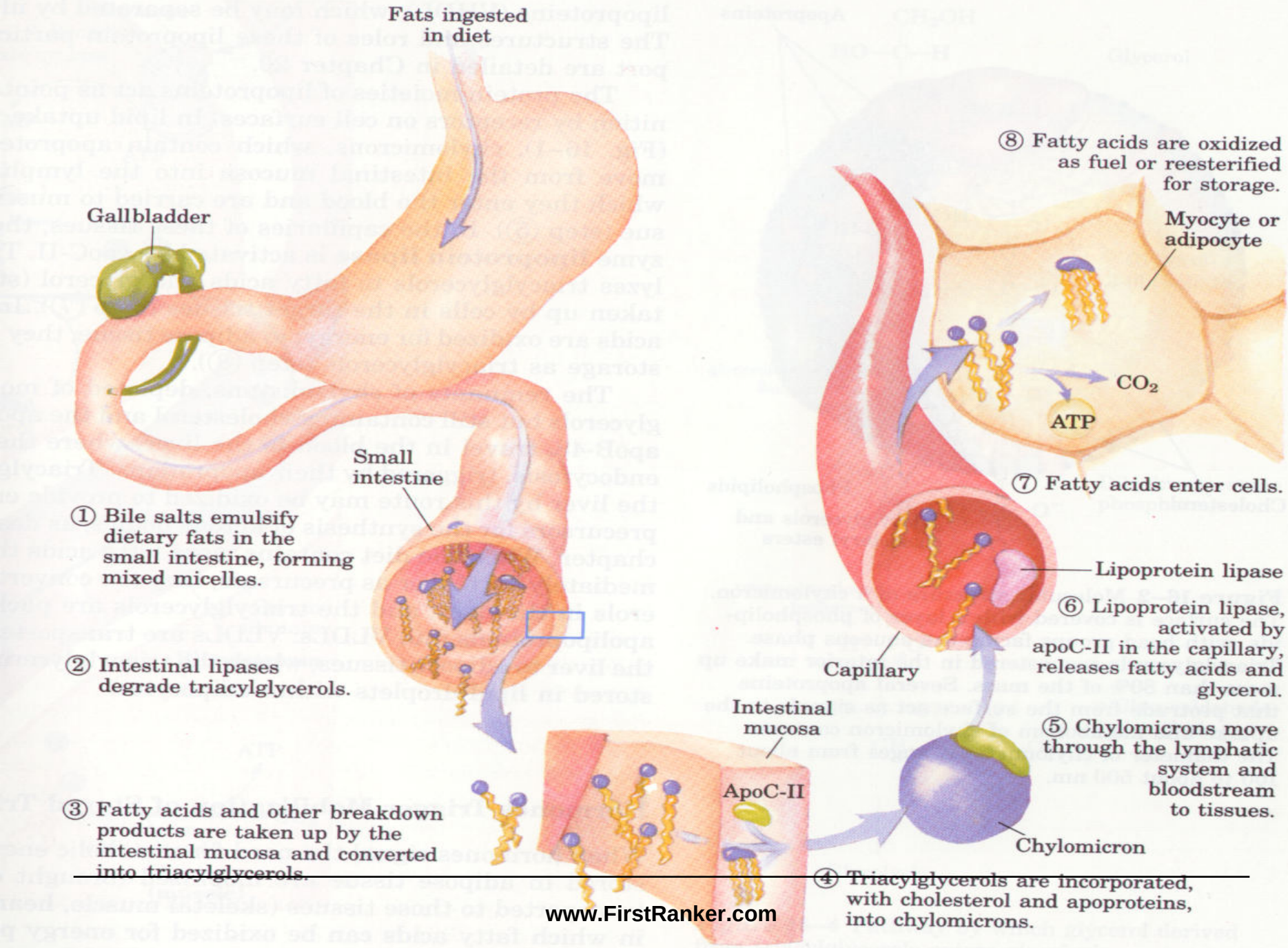
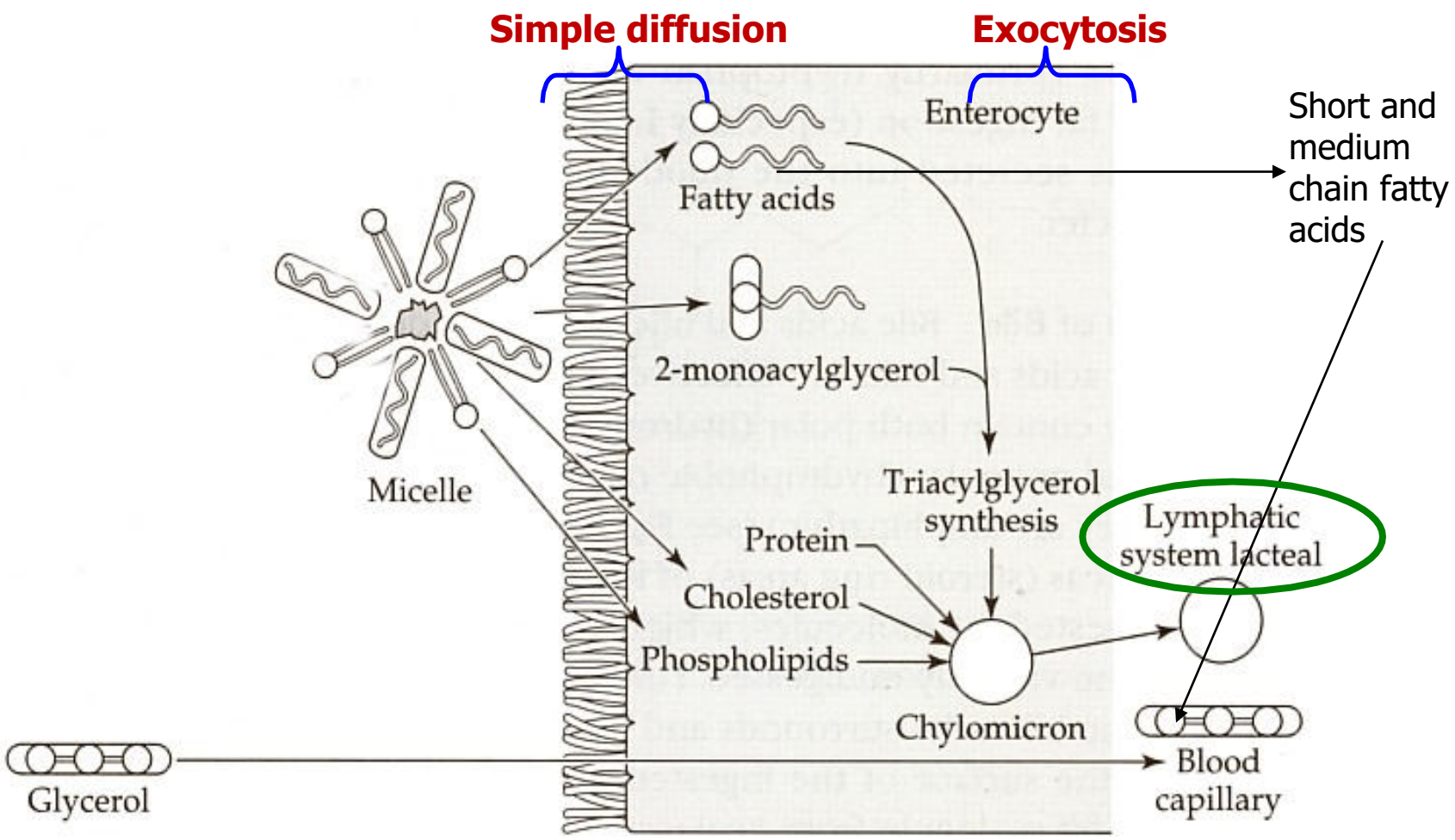
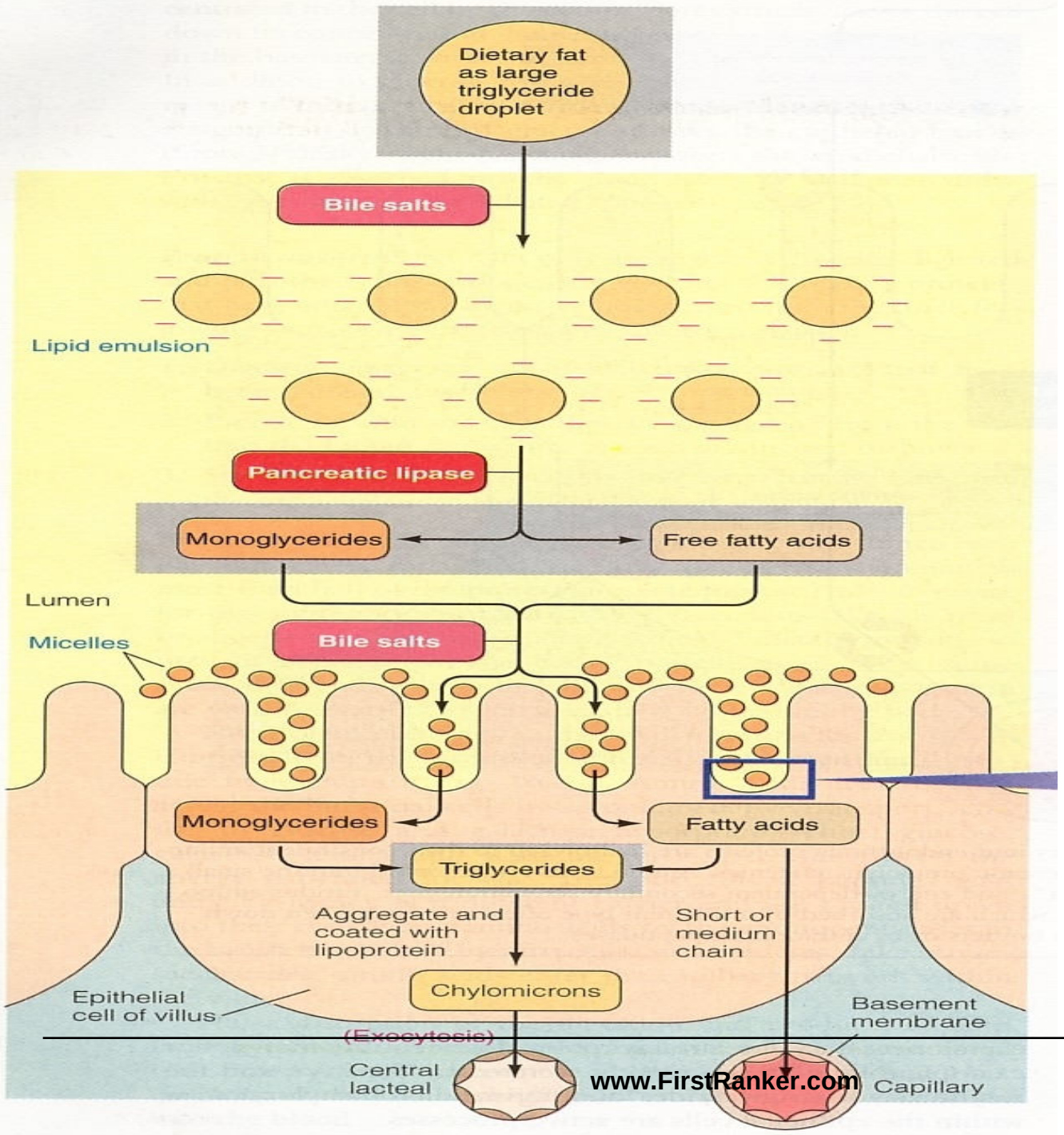


Figure 17-1

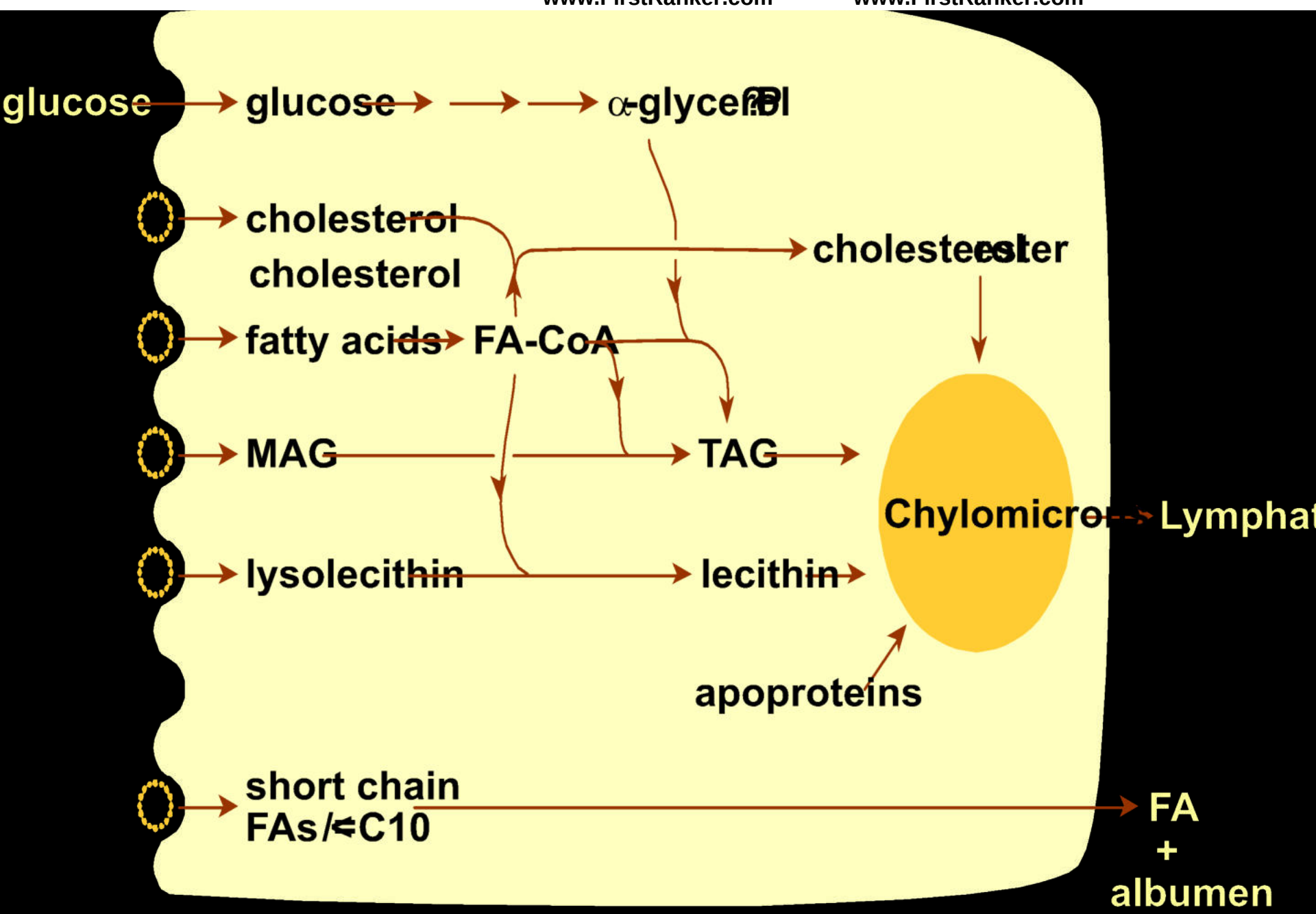


Mechanism Of Lipid Absorption





Overview of Lipid Digestion and Absorption

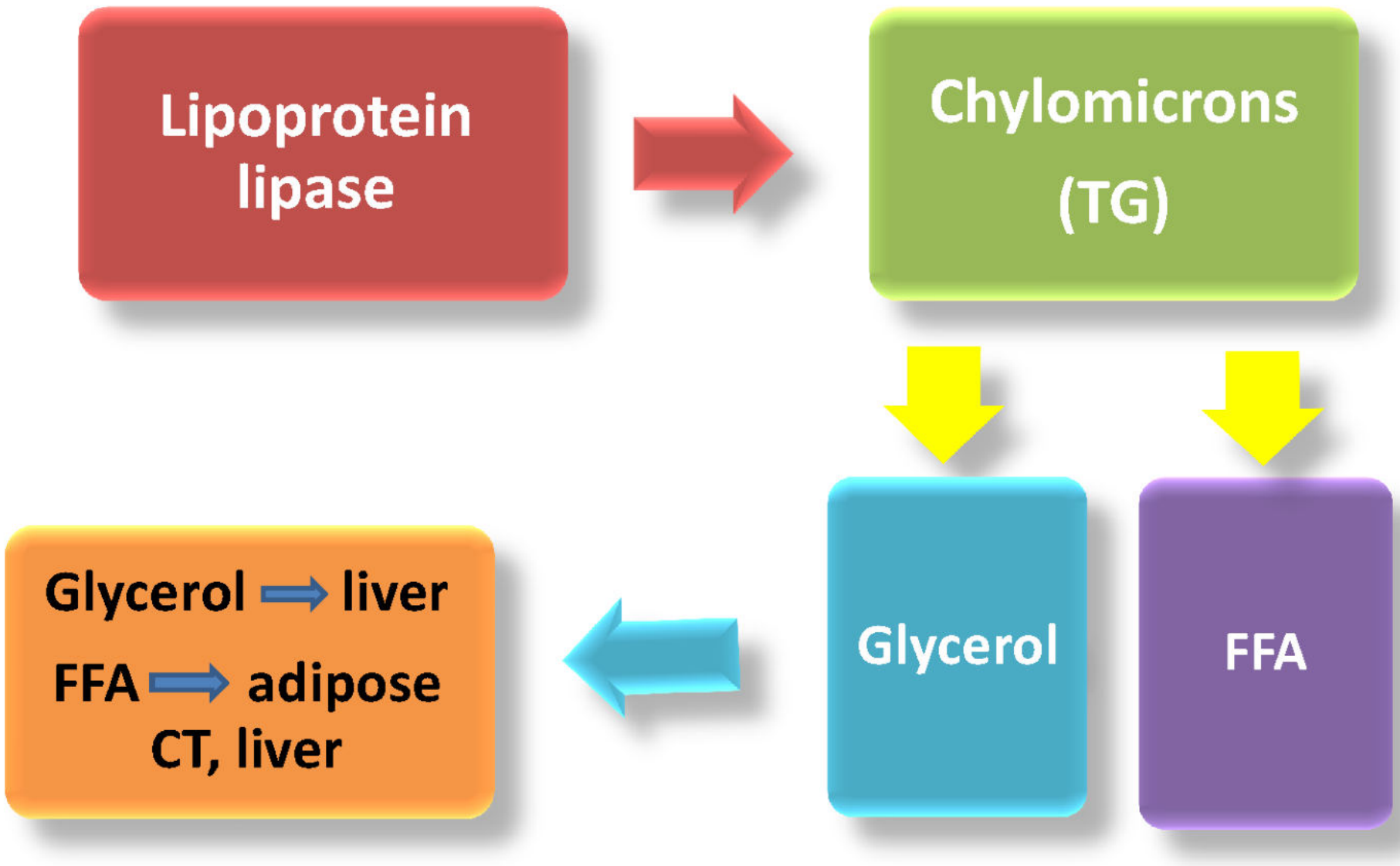


Transportation Of Chylomicrons Through Blood Circulation

Fate of absorbed lipids

- Immediately after absorption of lipids there is turbidity of plasma due to circulating chylomicrons (appear in plasma 2 hours after meals)
- This turbidity is soon cleared by lipoprotein lipase enzyme (clearing factor)

Action OF Enzyme Lipoprotein Lipase On Lipoproteins (Chylomicrons and VLDL)

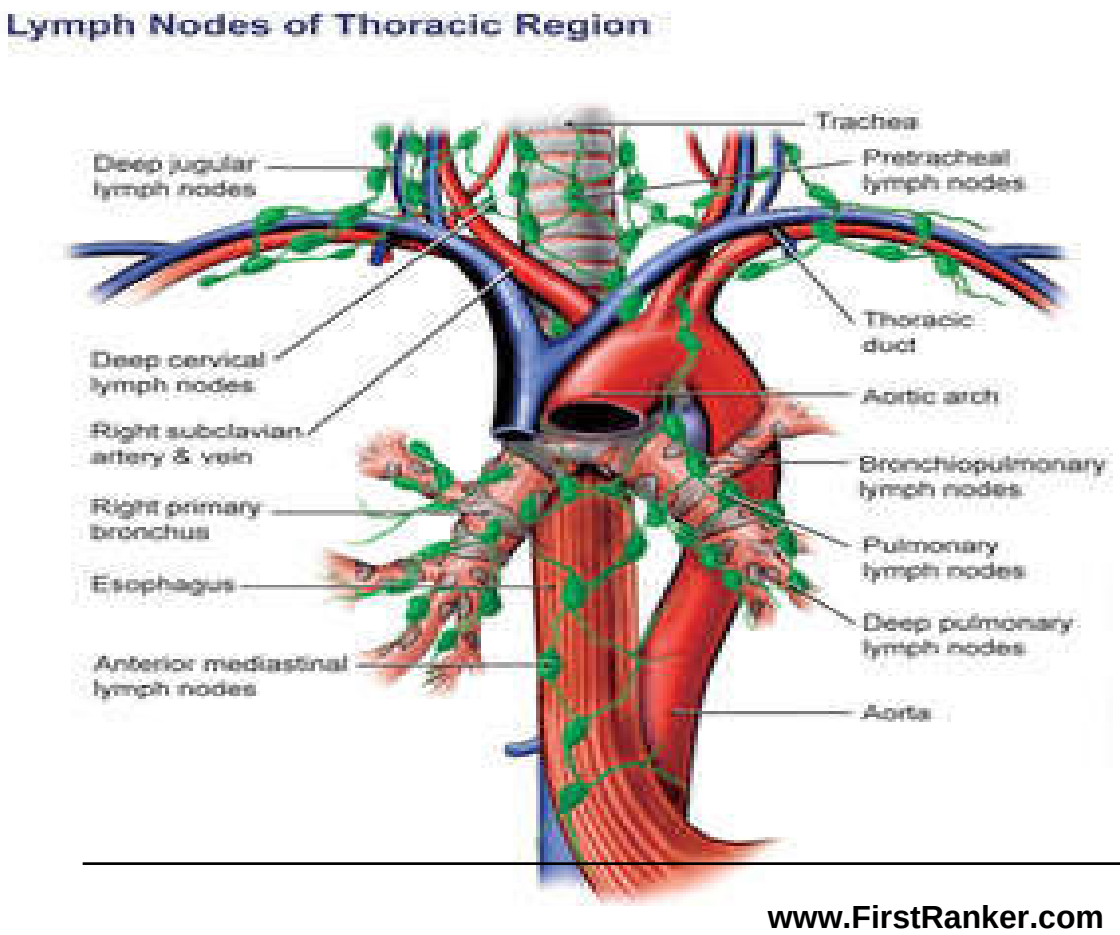


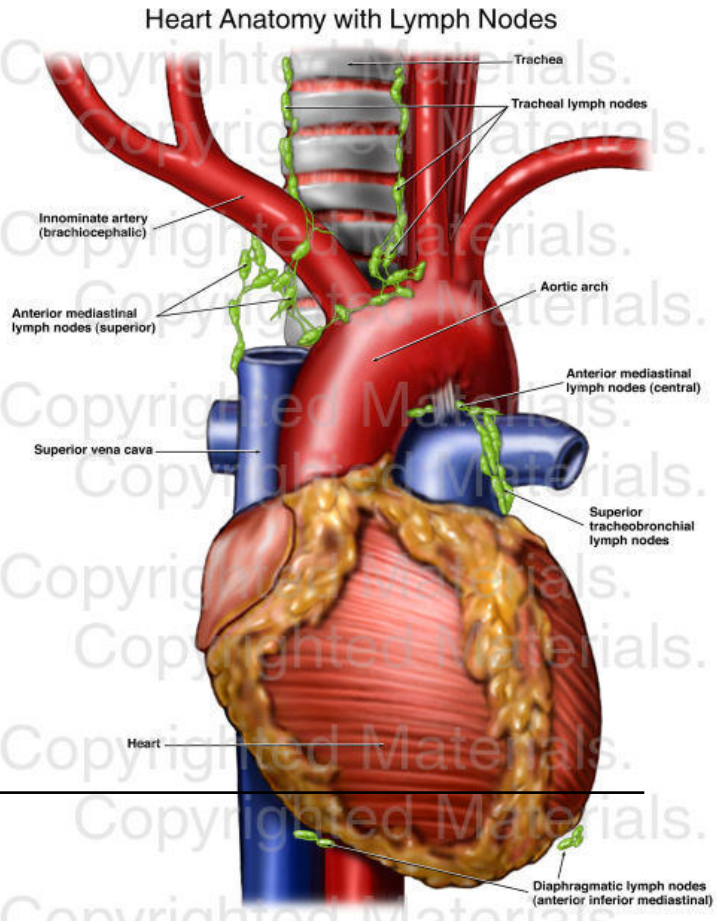
Plasma Lipid Clearance OR Role Of Clearing Factor

- Most of absorbed Lipids from GIT mucosal cells **do not** directly enter the blood stream.

- Instead, they are packaged into **Chylomicrons** and first released into the lymph.

- Lymph dumps **into Aortic arch** (via **Thoracic duct** connection with **left Sub Clavian vein enter systemic blood circulation**) .





LPL Clears Chylomicrons from Blood

- Chylomicrons transported through blood stream are **cleared by LPL activity and taken up by:**
  - **Adipocytes (Store House Of TAG)**
  - **Muscle**
  - **Liver**

Lipids are Not Carried through Enterohepatic Circulation

- **Since Liver is not the store house of Lipids.**

Liver is not a Storage house for TAG

- Unlike **Carbohydrates (Glucose) and Protein (Amino acids)** who **use enterohepatic circulation to reach first to Liver.**

- Most **Lipids carried through lymphatic and systemic circulatory system to reach Liver lastly.**

- This allows **Lipids to be cleared by the whole body** and **avoids overwhelming of Lipids to Liver .**

- Clearance of Lipoproteins from circulation
- Is mediated by an enzyme **Lipoprotein Lipase (LPL) acting upon TAG of Lipoproteins.**

- **Nascent (New) Chylomicrons** released from intestinal mucosal cells are circulated **first through lymph** and **then in systemic blood circulation**.

- **Nascent Chylomicrons** in blood circulation **get matured**

- After the receipt of **Apo C II and ApoE from HDL.**

- **Apo C II** of Mature Chylomicron then **stimulates an enzyme Lipoprotein Lipase (LPL)**

- **LPL associated in endothelial lining of Blood vessels,** of **Adipose, Heart, Skeletal Muscles** as well as in **Lactating Mammary glands.**

- Stimulated **Lipoprotein Lipase** then acts **upon the TAG** of Lipoproteins (Chylomicron and VLDL).
- Lipoprotein Lipase **hydrolyze the TAG** of Lipoproteins to **Free Fatty acids and Glycerol.**
- Released **Glycerol and Free Fatty acids enter the adjacent** Adiposecytes.

- Glycerol and FFAs entered in Adipocytes are **transformed into TAG.**
  - **TAG is storage form of Fatty acids**
  - **TAG** serve **as a reserve source of energy.**

Liver Internalizes Only Chylomicron Remnants

- **LPL by its activity on Chylomicrons reduces its content of TAG.**

- **Chylomicrons with Maximally reduced TAG content** and now termed as **Chylomicron Remnant.**

- **Chylomicron remnant** in comparison to Nascent Chylomicron is

- **Smaller in size**, and has very **less percentage of dietary TAG**, associated to it.

- **Chylomicron remnants** get fixed to their **specific receptors** present on **Hepatocytes and get internalized.**

- The internalized Chylomicron remnants inside the Liver gets further **metabolized.**

- **Thus Lipoprotein Lipase is also termed as Clearing Factor**

- Since Lipoprotein Lipase clears Lipaemic sera(Chylomicrons) in post absorptive phase.

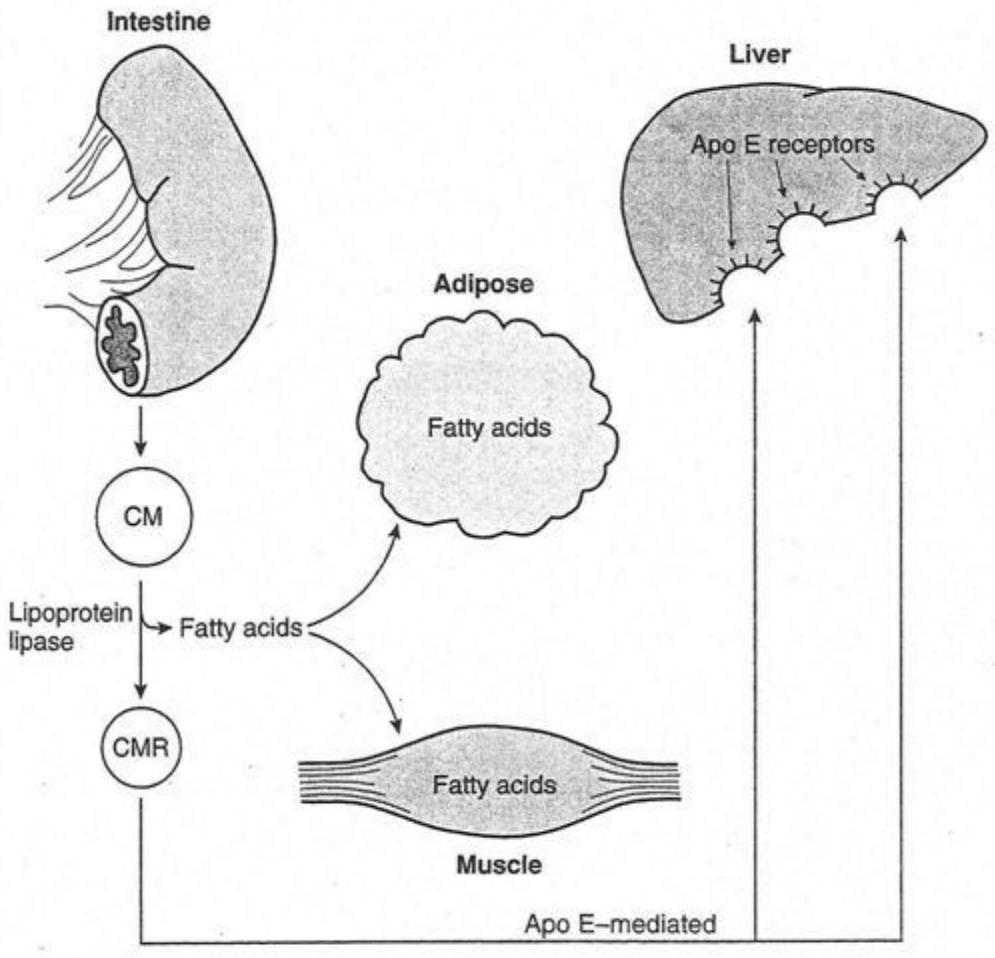
LPL Activity On Chylomicrons

- In **Post absorptive phase** most of the **blood Chylomicrons** are transformed to **Chylomicron remnants**
- By the **Lipoprotein Lipase activity**,
- The released moieties from Chylomicrons are **internalized by Adiposecytes and Hepatocytes**
- This **clears the circulating Chylomicrons from blood.**

Chylomicron Metabolism

figure 19-3

- Nascent chylomicron (B-48)
- Mature chylomicron (+apo C & apo E)
- Lipoprotein lipase
- Chylomicron remnant
  - Apo C removed
  - Removed in liver

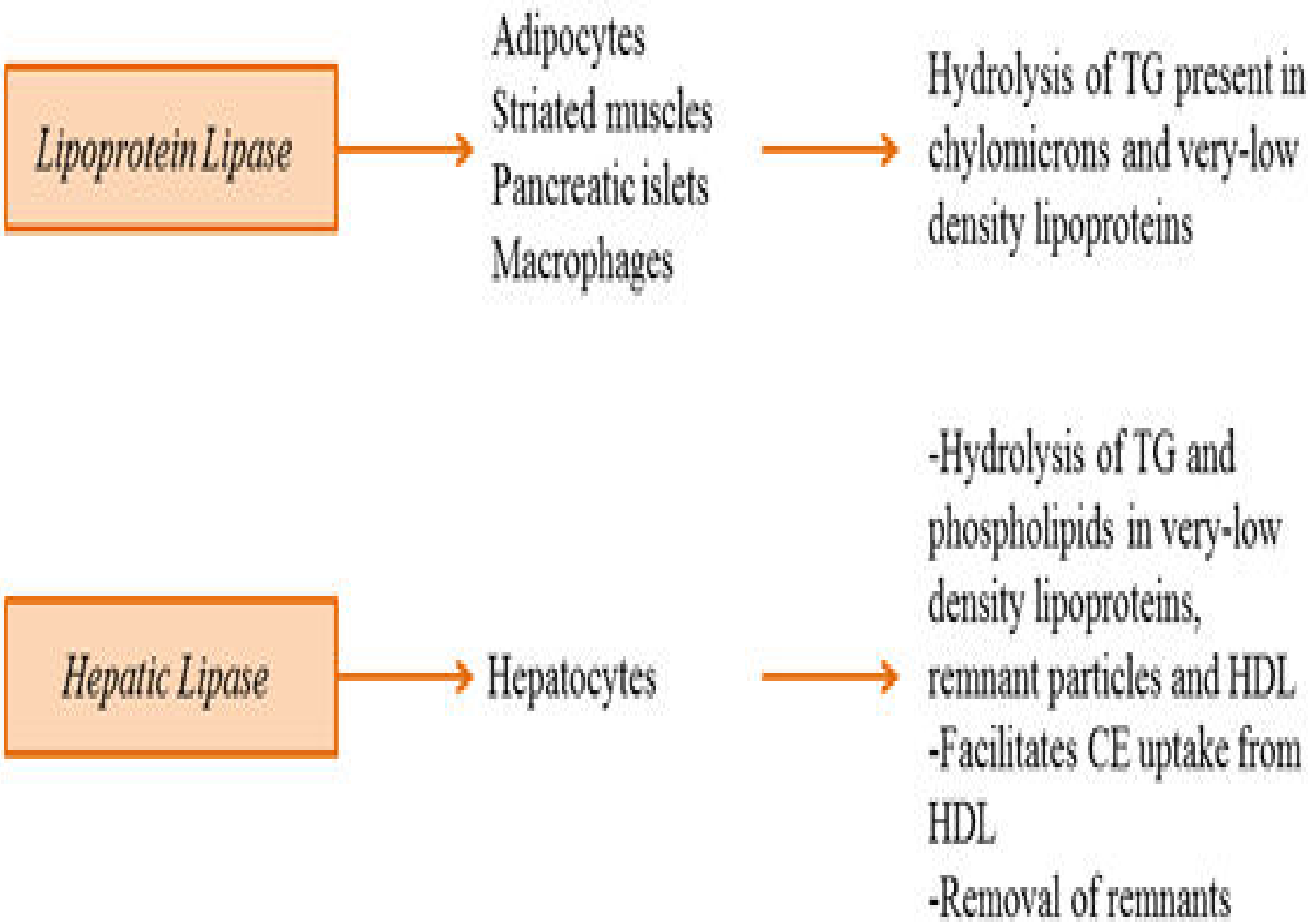


❖ **Defect In Lipoprotein Lipase**
Do not clear blood Lipoproteins

Accumulates Chylomicrons and VLDL in blood circulation

Heparin Is a Coenzyme For Lipoprotein Lipase

- **MI patients** are administered with **Heparin injections**
- Which may **stimulate Lipoprotein Lipase activity**
- And **clear blood with elevated Chylomicrons and VLDL**.



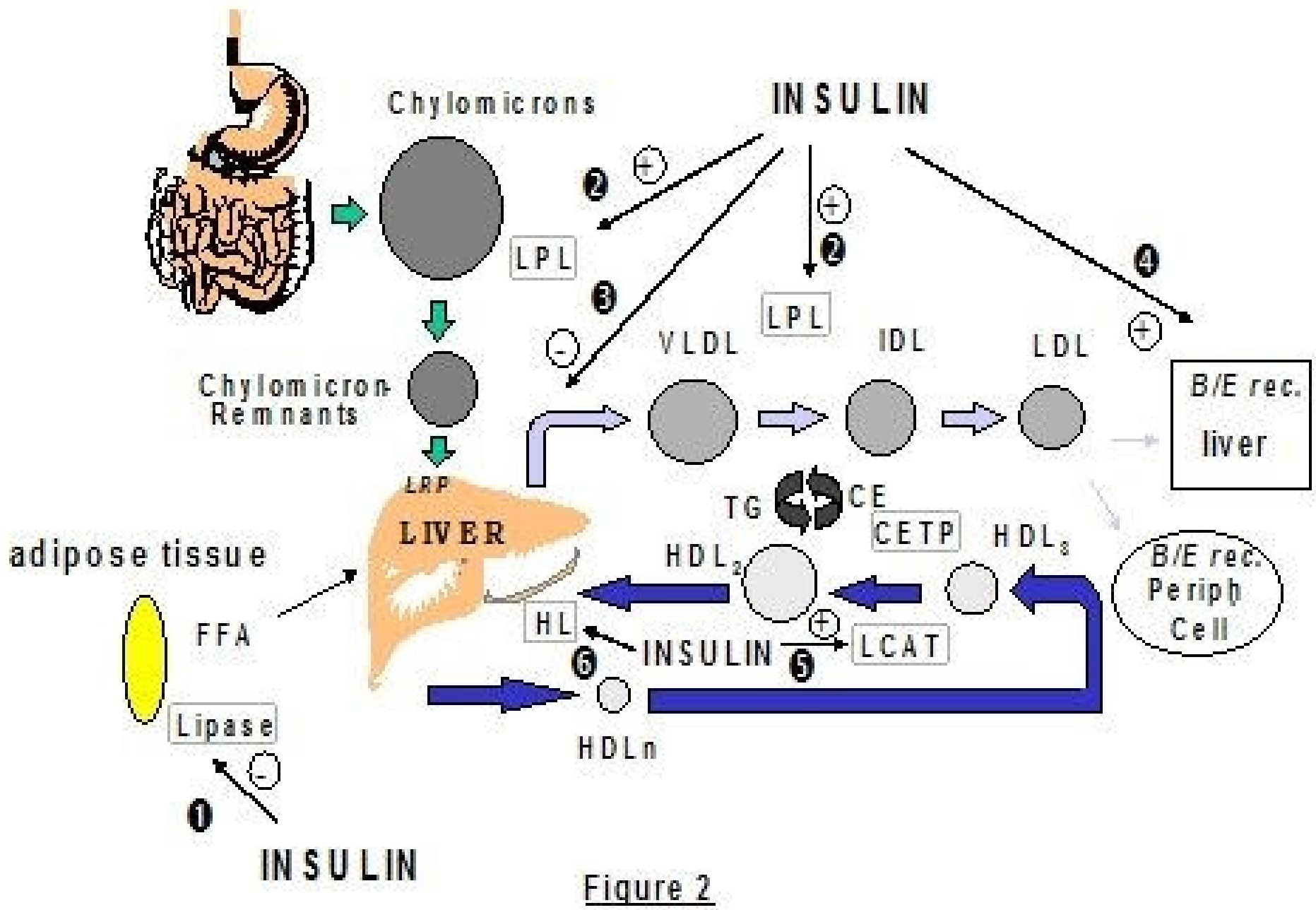
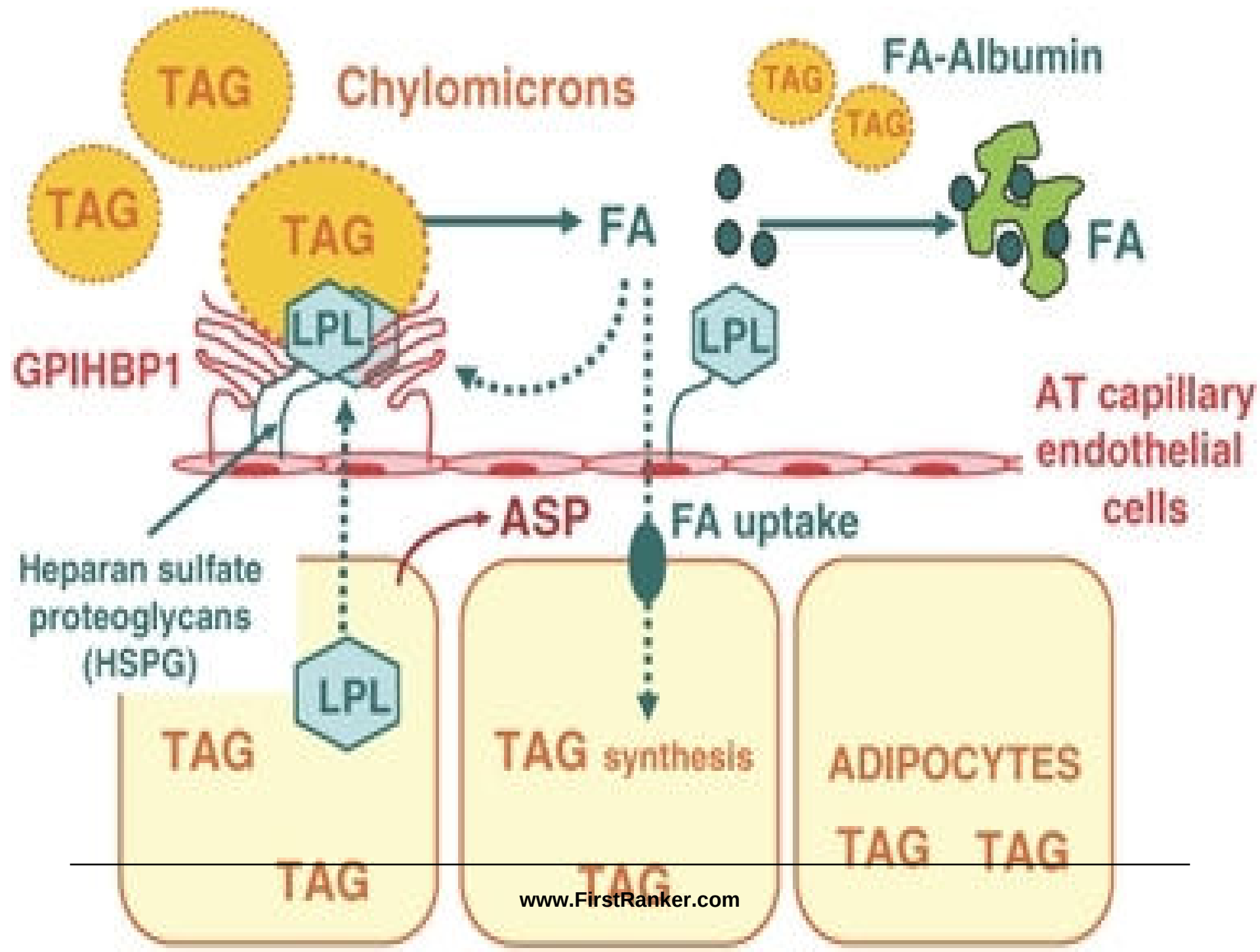


Figure 2



Transport of Short Chain Fatty Acids And Medium Chain Fatty Acids Is Different From

Long Chain Fatty Acids

Absorption of lipids

- The end products of lipid digestion are : monoglycerides, FA, glycerol, cholesterol & lysophospholipids

1- Glycerol and short chain FA :

water soluble → carried through portal circulation

2- Long chain FA, monoglycerides,cholesterol & lysophospholipids :

need bile salts to be absorbed

- **Transport of Short and Medium chain Fatty acids**

–These **enter portal blood directly from enterocytes**

–Transported after bound to Albumin in blood

- **Albumin–FFA complex**

–FFA are then internalized in Liver

- Oxidized to liberate ATPs

OR

- Elongated and used for TAG formation

- **Long-chain Fatty acids**
  - –Transported in form of **Chylomicrons**
  - –Drain into Lymphatics via Lacteals
  - –Enter blood stream at **Thoracic duct**

Defective Lipid Digestion and Absorption

Leads To

Steatorrhoea

Steatorrhoea

- **Steatorrhoea** is a **Lipid Malabsorption condition**
- Where there is **no digestion** and **no absorption** of **dietary Lipids from GIT**
- Dietary **ingested Lipids** are **excreted out** through **feces as it is.**
- Steatorrhoea leads to **Fatty stools**
- **Characteristic whitish/greyish,greasy Stool**

Causes Of Steatorrhoea

- The basic cause to suffer from Steatorrhoea is:
  - **Absence of emulsifying agents- Bile salts** in **small intestine.**
  - **Absence of specific Enzymes for Lipid digestion.**

Any Condition Affecting, Synthesis, Secretion and Transport of Bile to Intestine

Biliary Insufficiency

leads to Steatorrhoea

- Extensive **Liver damage** affects Bile Synthesis.
- **Celiac Diseases**:
  - –Sprue **(Intestinal Disorder)**
  - –Crohn's Disease **(Inflammatory Bowl Disease)**

- **Surgical removal of intestine**

- **Obstructive Jaundice**
  - –Obstruction due to narrowing of bile duct after surgeries
  - –Obstruction of CBD due to Gall Stones
- **Chronic Pancreatic Diseases**

Biochemical Alterations in Steatorrhea

Excretes Lipids > 6gm/day

- No/Less **Bile and Bile Salts** in small intestine
- No/Less **Emulsification** of dietary Lipids
- No/Less **Emulsions** formed
- No/Less **Contact of Lipids with Lipases**

- No/Less **digestion** of dietary Lipids
- No/Less **formation of Mixed Micelles**
- No/Less **absorption** of dietary Lipids
- **More excretion of dietary Lipids through feces**.
- Whitish and greasy stools.

Consequences Of Steatorrhea

- In Steatorrhoea person suffers from **deficiency of essential Fatty acids and Fat Soluble Vitamins.**

- Body **lacks exogenous TAG as secondary source of Energy.**

- **Body lacks** from Exogenous source of **Phospholipids and Cholesterol**.

Diagnosis OF Steatorrhoea

- **Determination Of Fecal Fat**

- **Microscopically** (Fat Globules present)
- **Quantitatively** (Gravimetric Method)

Abnormalities of lipid digestion due to impaired lipolysis

Type of Defect	Biochemical Disturbance	Examples of Disease States
Rapid gastric emptying	Reduction in the efficiency of lipid interaction with bile and pancreatic secretions	Gastrectomy, as in treatment of ulcer or in neoplasms of stomach
Acidic duodenal pH	Inactivation of pancreatic lipase and decreased ionization of bile acids	Zollinger-Ellison's syndrome
Decreased CCK release	Deficiency of bile and pancreatic secretions	Disorders associated with mucosal destruction; regional enteritis, gluten enteropathy
Congenital lipase or colipase deficiency	Defective lipolysis	
Pancreatic insufficiency	Defective lipolysis	Chronic pancreatitis, pancreatic duct obstruction (e.g., cystic fibrosis)
Absence or decreased bile salts	Decreased lipolysis due to impaired micelle formation	(Next Table)

Abnormalities of maldigestion/malabsorption

- The main causes of malabsorption (**STEATORRHEA**) under 3 catagories:

1. Disorders of intraluminal digestion:

a) Altered gastric function	Post gastrectomy syndrome
b) Pancreatic insufficiency	Chronic pancreatitis Cystic fibrosis Pancreatic cancer
c) Bile acid deficiency	Disease/resection of terminal ileum Small bowel bacterial over growth.

2.Disorders of transport into mucosal cells:

a) Generalised disorders due to reduction in absorptive surface area.	Celiac disease Tropical sprue
b) Specific disorders	Hypolactasia Vit B12 in pernicious anemia Zn in acrodermatitis enteropathica

Chyluria

- **Chylomicrons in Urine** is termed as Chyluria.
- Abnormal condition where **lymphatic drainage system opens in urinary tract**.
- **Urine appears milky**
- **Chyluria occurs in Filariasis.**

Chylothorax

- **Chylomicrons in Pleural fluid** is termed as Chylothorax.
- Abnormally **Thoracic duct opens in pleural cavity**.

Overview Of Lipid Metabolism

- Lipid metabolism involves:
  - **Lipolysis**
  - **Lipogenesis**

❖**Liver and Adipose tissue** play a central role in Lipid metabolism.

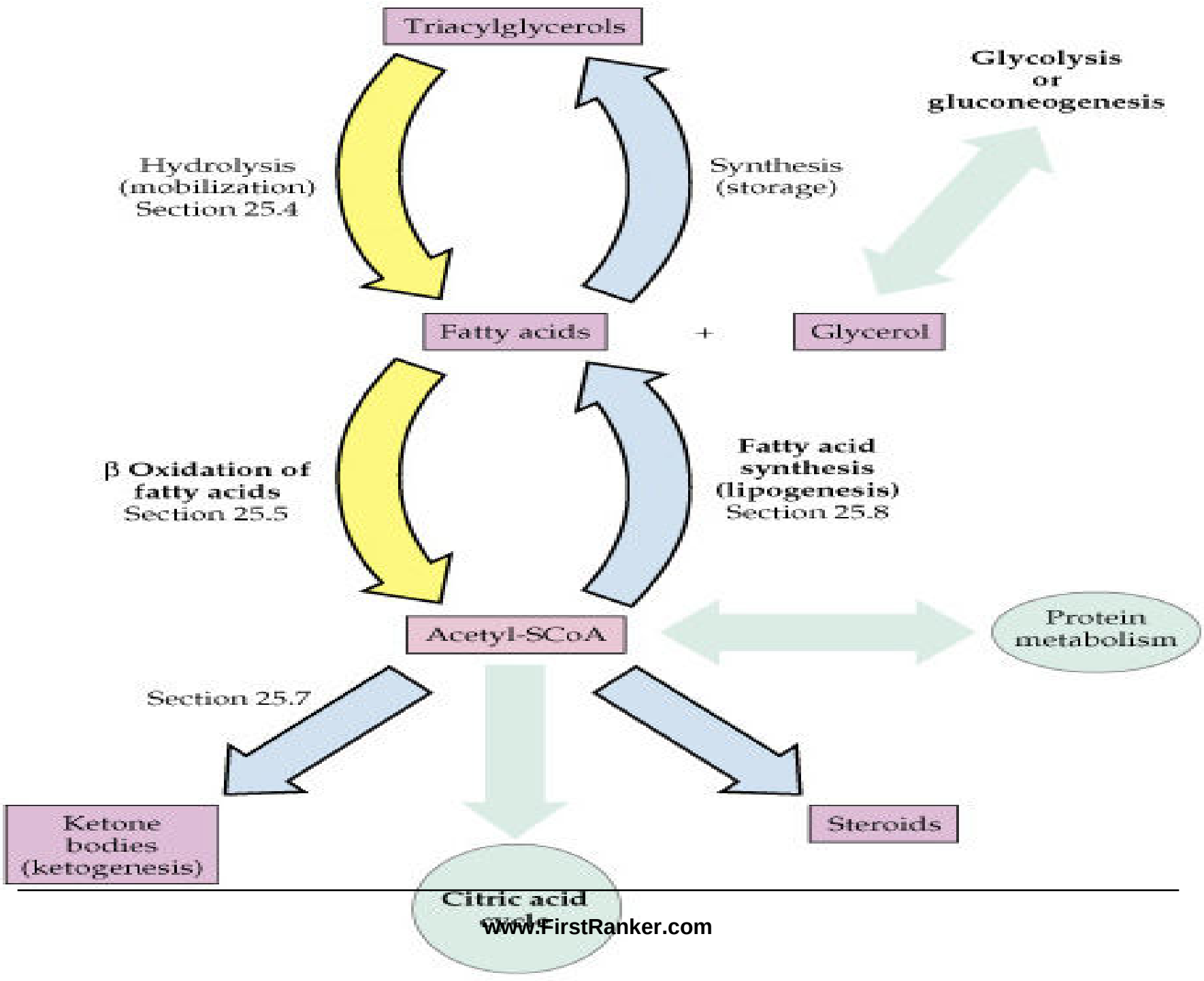
❖**Adipose tissue** is **main store house of Triacylglycerol** in the body.

Major Tissues In Lipid Metabolism

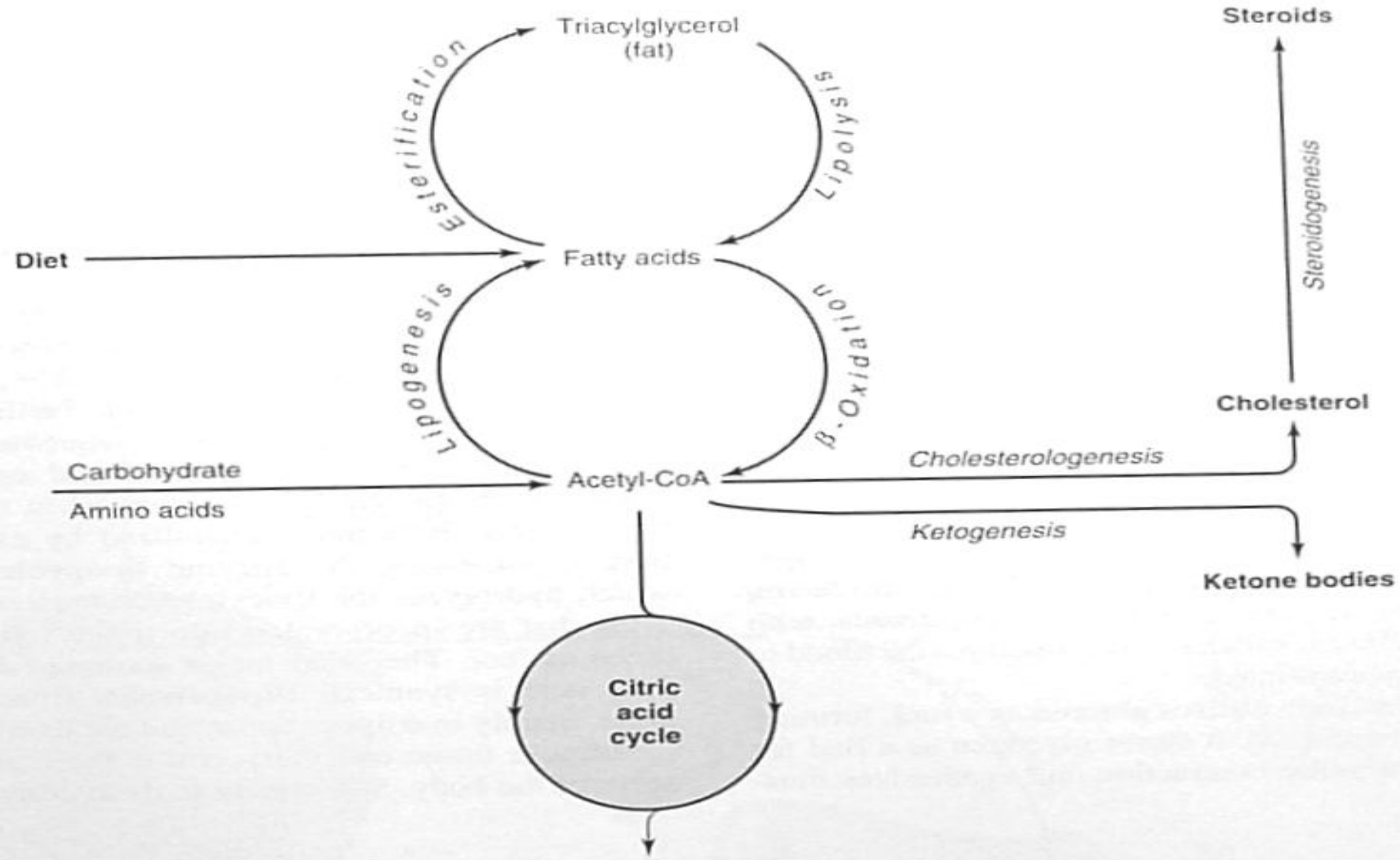
- **Adipocytes----- Lipolysis**
- **Liver---------- Lipogenesis**

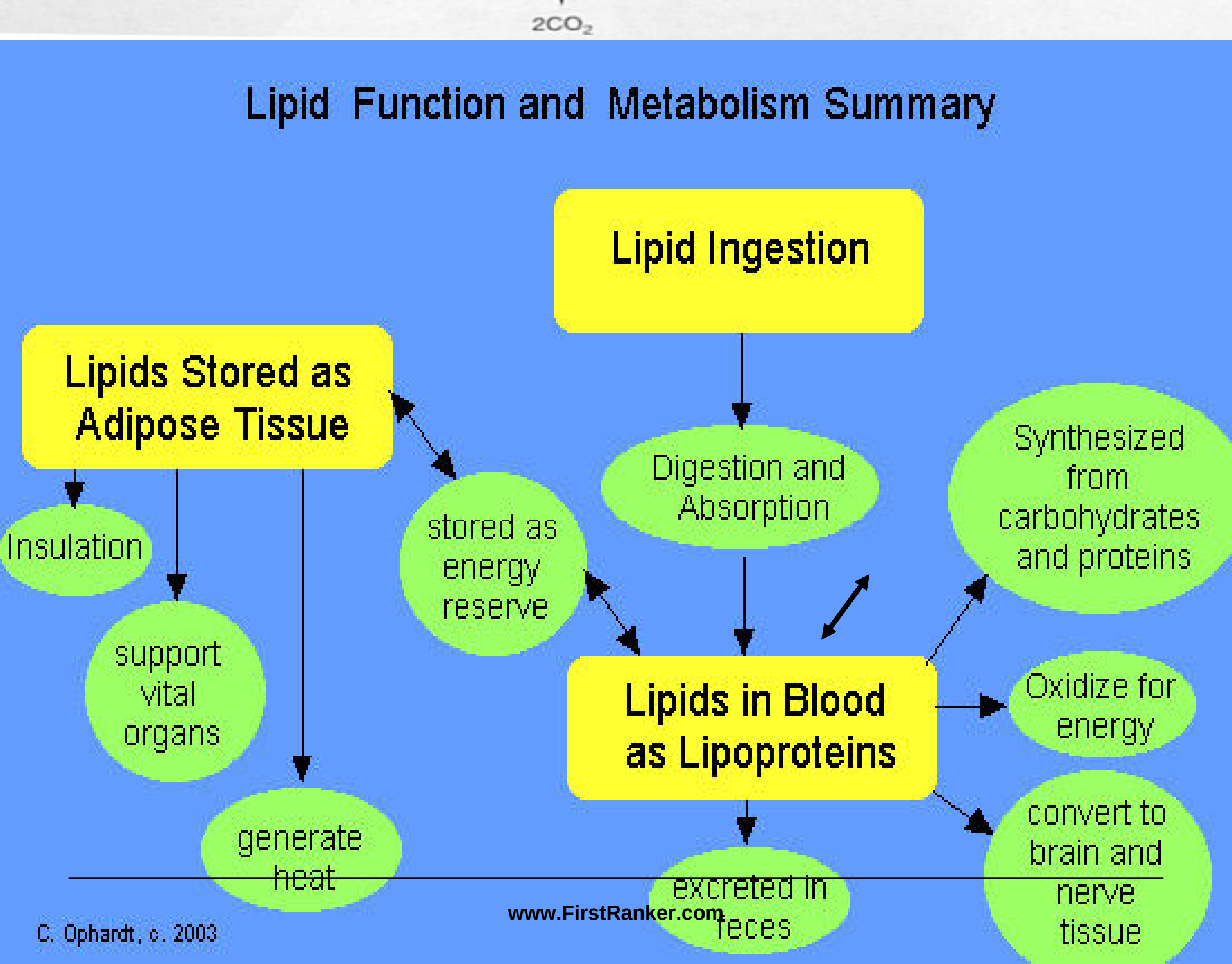
- **Fatty acids** are **highly reduced** compounds **oxidized/catabolized** to **Acetyl CoA**

- **Fatty acids are biosynthesized** using **Acetyl CoA as a precursor**.



Lipid Metabolism





What Is Lipolysis?

OR

Role Of Hormone Sensitive Lipase (HSL)

Fat Storage in White Adipose Tissue

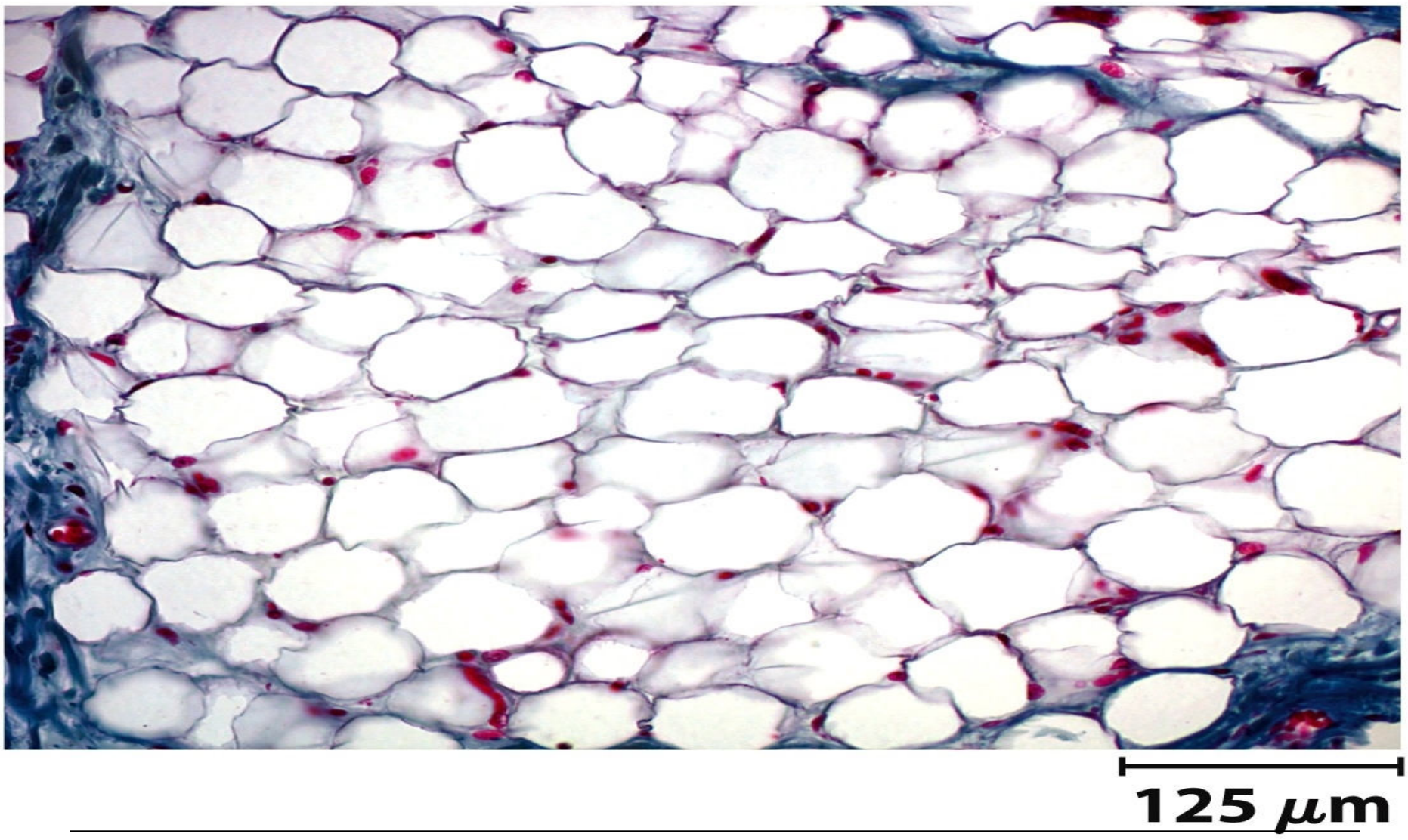


Figure 10-4a
Lehninger Principles of Biochemistry, Sixth Edition
© 2013 W. H. Freeman and Company

- In a **well fed condition** **TAG** is stored as **reserve source** of energy in **Adiposecytes.**

- **Lipolysis occurs in an emergency conditions**
  - **Fasting Phase**
  - **Between Meals**
  - **When Blood Glucose Lowers**
  - **Low Insulin High Glucagon**

Lipolysis

- **Lipolysis** is **break down of Depot Fat-**Triacylglycerol(TAG)
- Into **Free Fatty acids and Glycerol**
- By enzyme activity of **Hormone sensitive Lipase**

Triacylglycerol

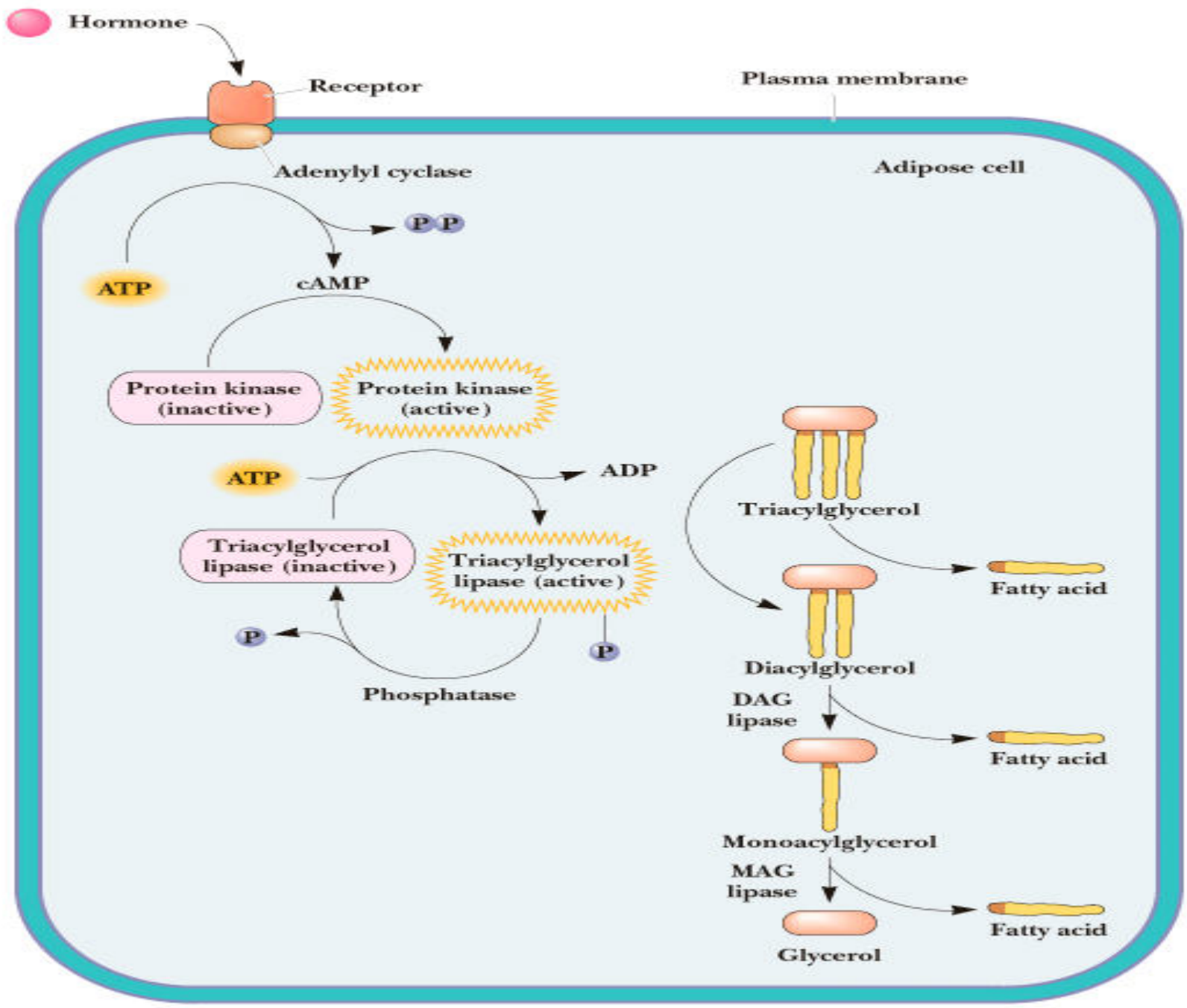
In Adipocytes

Hormone Sensitive Lipase

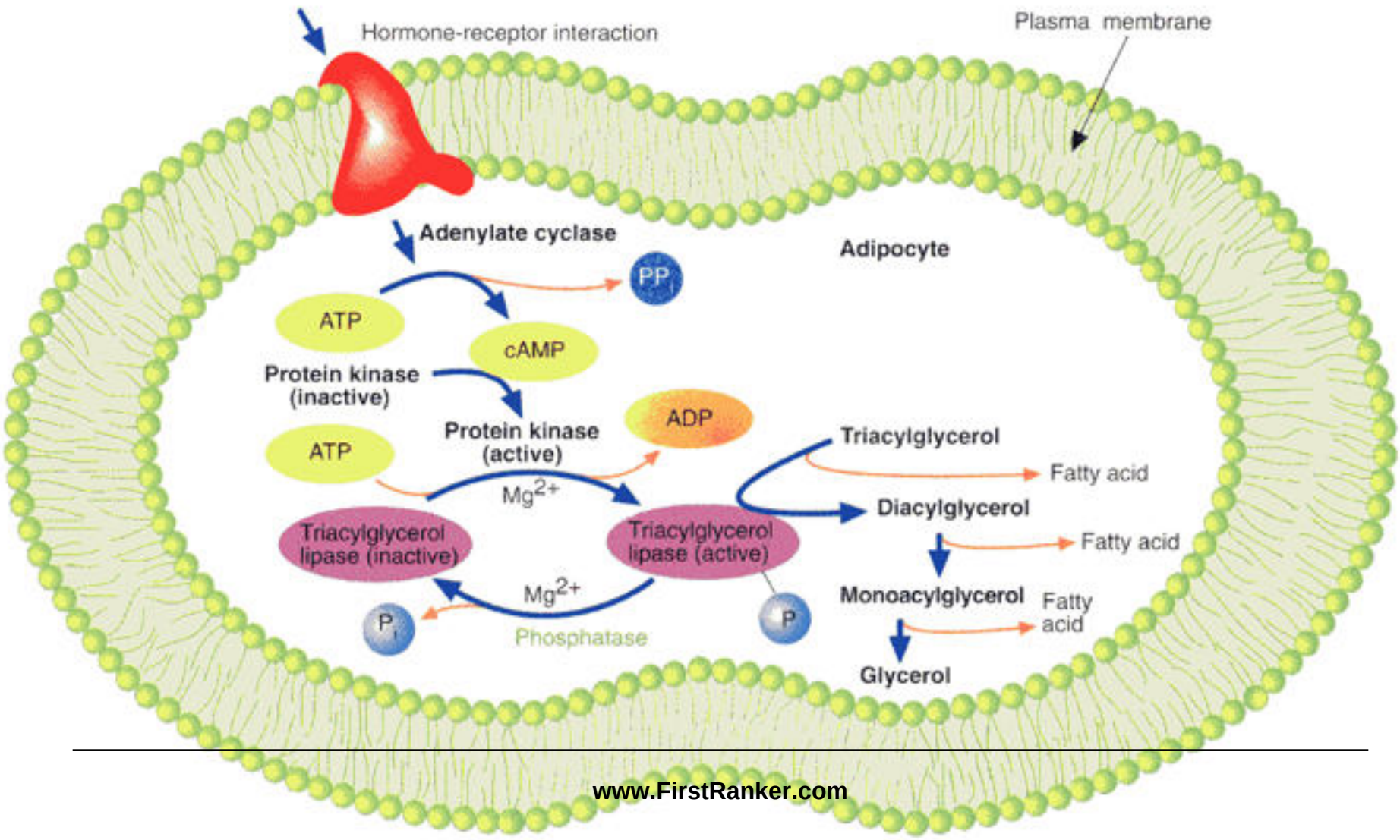
Triacylglycerol Lipase

Cleaves Ester bonds

Glycerol+ Free Fatty acid



Diagrammatic View Of Lipolysis



Significance Of Lipolysis

- During **Lipolysis** secondary source of energy **TAG**

- **Stored** as depot Fat **gets catabolized and utilized.**

Conditions Of Lipolysis

- **Lipolysis significantly and efficiently occurs :**
  - In emergency **fasting condition**
  - **In between long hours after meals**
  - When primary source of energy **Glucose go below normal range** in blood
  - **Low Insulin and high Glucagon or Epinephrine**
  - **By activity of Hormone Sensitive Lipase**

- Enzyme **Hormone Sensitive Lipase** of Adipocytes is stimulated By Hormones:
  - **Glucagon and Epinephrine mediated via cAMP cascade activity of enzymes**.

- On Lipolysis the Free **Fatty acids** and **Glycerol** are **mobilized out of adipocytes in blood circulation.**

End Products Of Lipolysis

- Free Fatty Acids
- Glycerol

Fate Of Glycerol After Lipolysis

- **Glycerol** (polar moiety)released in emergency condition during Lipolysis
- Is carried through blood and **enters in Liver and Muscles**.

Fate Of Glycerol In Muscles

(In Muscles)

Glycerol Enter into Glycolytic Pathway

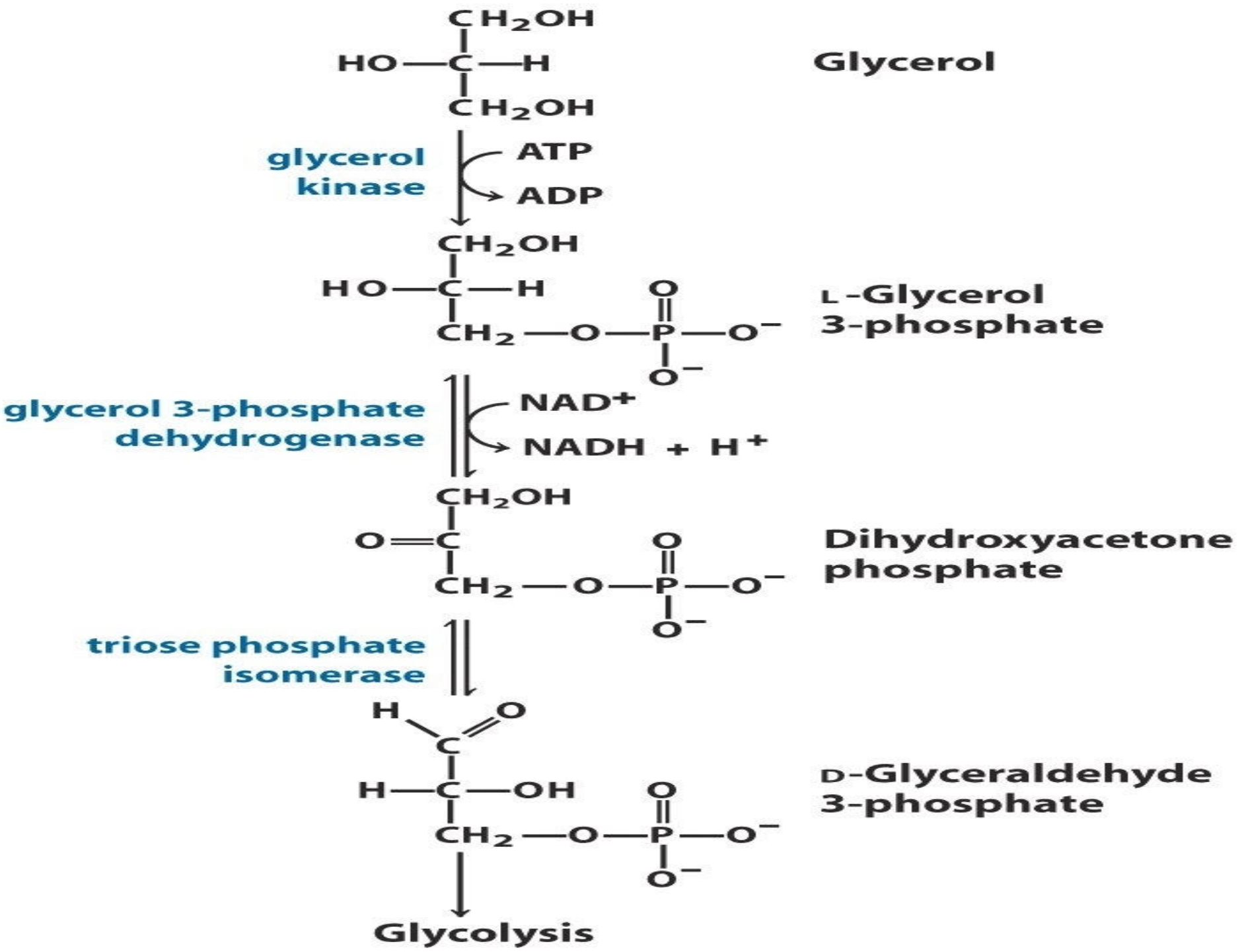
Glycerol

↓ Glycerol Kinase

Glycerol-3-Phosphate

↓

Glyceraldehyde-3-PO4



- **Glycerol** of Lipolysis is metabolized **via Glycolysis in Muscles**

- Glycerol in muscles is Phosphorylated to **Glycerol-3-PO4**

- Glycerol-3-PO4 is further oxidized to **Glyceraldehyde-3-PO4**

- Thus Glyceraldehyde-3-PO4 in **Muscles** make its **entry in Glycolysis**
- Further gets metabolized to **generate energy (ATP)** for muscle activity.

Fate Of Glycerol In Liver

(In Liver)

Glycerol Of Lipolysis

Is a Precursor For Gluconeogenesis

Glycerol Is Used For Glucose Biosynthesis In Liver

- Glycerol of Lipolysis is metabolized via **Gluconeogenesis in Liver**

- Glycerol in Liver is Phosphorylated to **Glycerol-3-PO4** by **Glycerol Kinase**

- Glycerol-3-PO4 is further oxidized to

- Glyceraldehyde-3-PO4 and isomerized to DHAP

- This then is converted to Glucose.

- Thus Glyceraldehyde-3-PO4 in **Liver** make its entry in **Gluconeogenesis** and
- Further gets metabolized to **produce Glucose.**

- **Glucose formed in Liver** is mobilized out into blood and Correct Hypoglycemia.
- Glucose supplied to Brain and Hepatocytes in **fasting condition.**

Fate Of Free Fatty Acids After Lipolysis

- **Non polar Long Chain Free Fatty acids** released **in blood circulation** after Lipolysis are not transported on its own.
- Needs the help of a polar moiety.

Polar Moiety Albumin Transports Long Chain Free Fatty Acids In Blood Released After Lipolysis

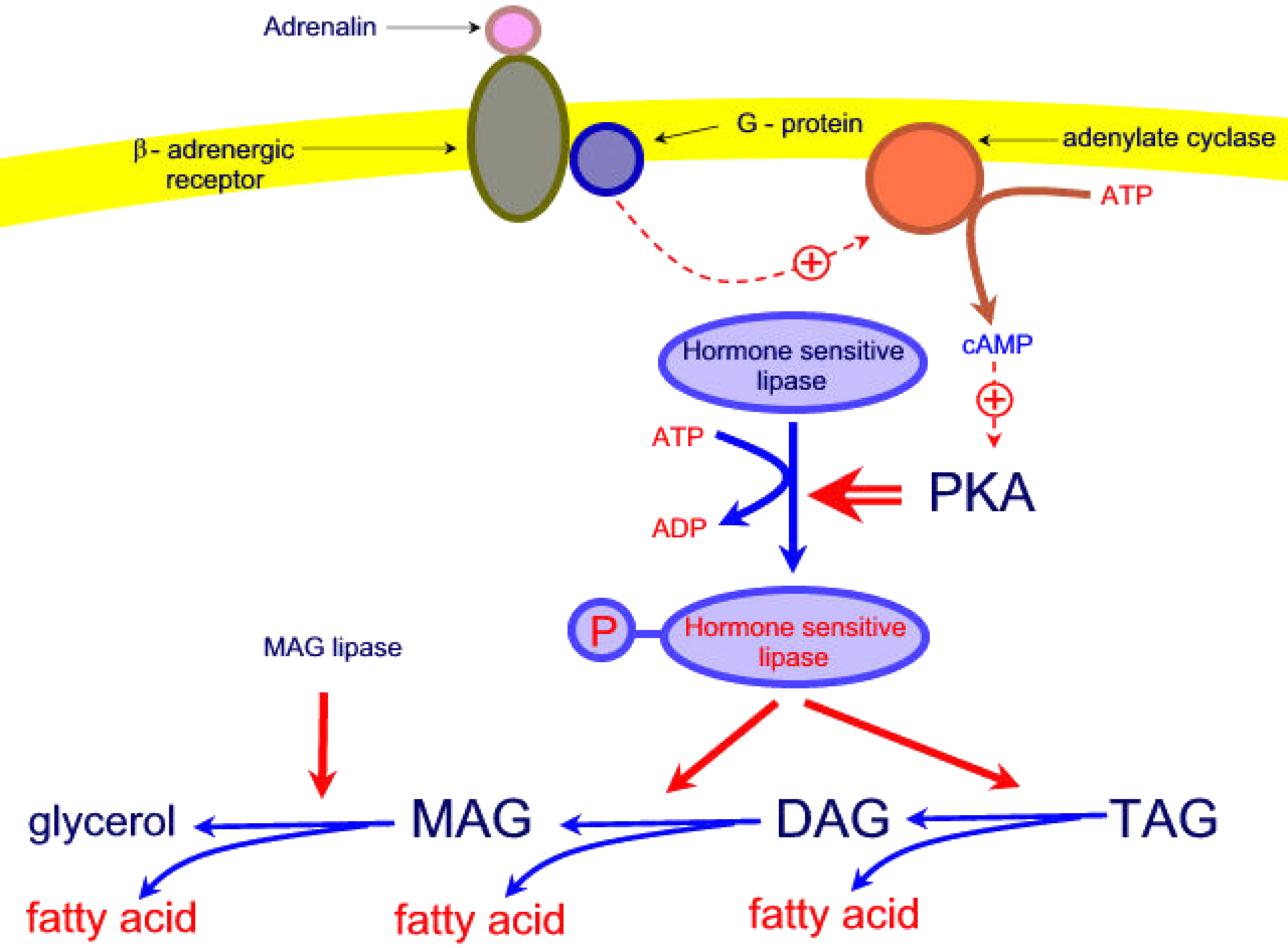
- **Long chain Free Fatty acids** are **uncharged/nonpolar/hydrophobic**
- They are linked with polar Protein moiety **Albumin**
- **FFA-Albumin complex** get transported through blood circulation.

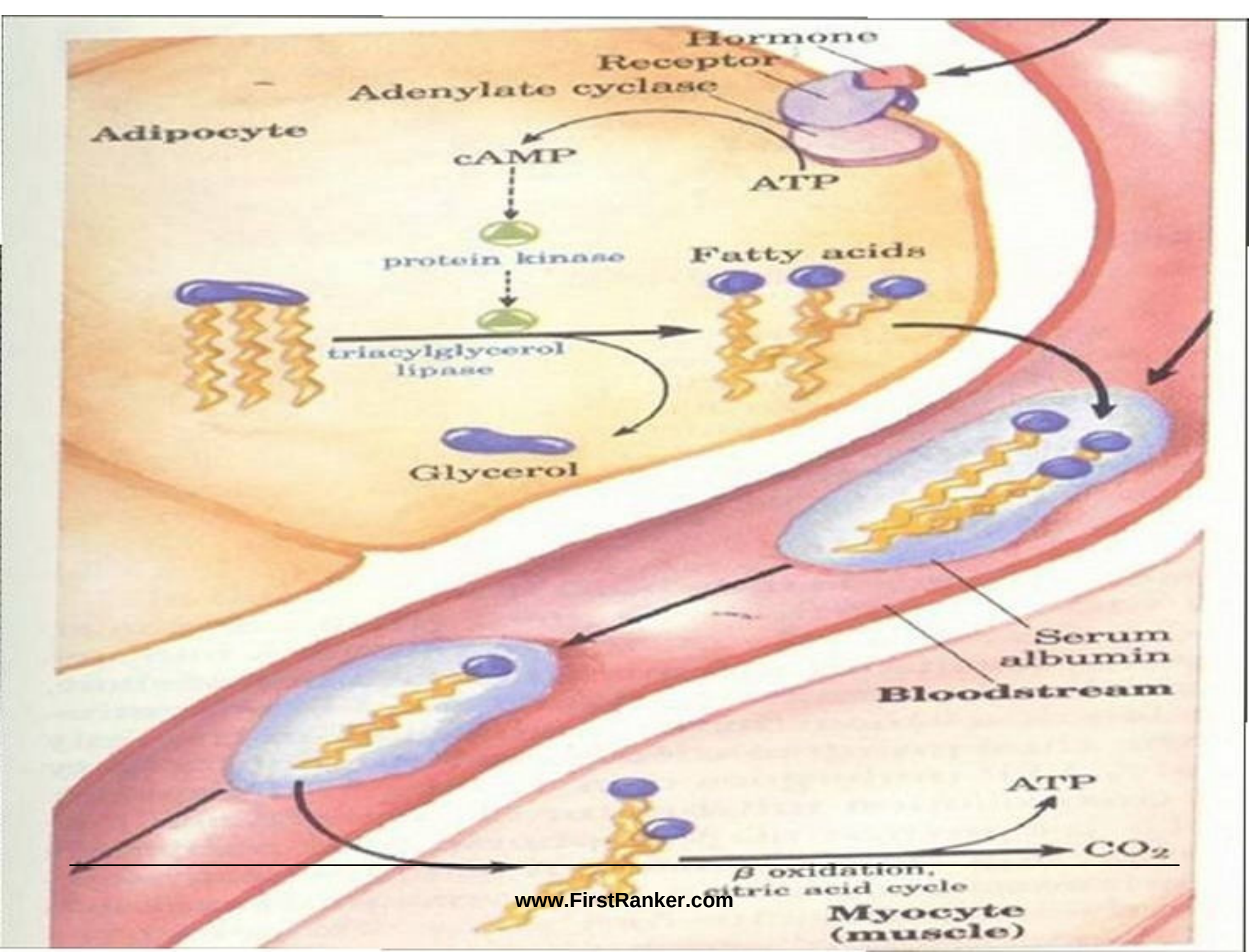
- Albumin remain in the blood circulation
- Free Fatty acids make its entry in Muscle cells.

Fatty Acids In Muscles Oxidized To Liberate Energy (ATP)

- Free Fatty acids are **highly reduced compounds.**
- **Free Fatty acids entered in Muscles** during emergency condition
- After Lipolysis, are **oxidized to liberate chemical form of energy ATP.**

- Thus after Glucose Free **Fatty acid** serve as **secondary source of energy** to body tissues.





Oxidation Of Fatty Acids

OR

Catabolism/Degradation Of Fatty Acids

How Fatty Acid Oxidation Serve As Energy Source?

- **Fatty acids** are an important **secondary source of energy** to body.
  - As **Fatty acids** are **reduced compounds**
  - Possess **CH2-CH2** hydrocarbon **bonds with bond energy within it .**

- **Oxidation of Fatty acid /Catabolism or breakdown of Fatty acid is by:**
  - **Removal** of **Hydrogen** **from hydrocarbon chain (CH2-CH2).**
  - Which are **temporarily** **accepted by oxidized form of Coenzymes**
  - With **formation of** **reduced Coenzymes**
  - **Reoxidation of** **these** **reduced Coenzymes** **by entry** **in ETC /Oxidative Phosphorylation generates ATP.**

- **Oxidation of the Hydrocarbon bonds of fatty acid chain makes them weaker**
- **Easy Cleavage of hydrocarbon bonds** of Fatty acid
- Which helps **in shortening of the long Fatty acid chain.**

Types Of Fatty Acid Oxidation

1. Oxidation Based On Type Of Carbon Atom

- **Alpha(α) Oxidation**(Phytanic acid –Branched Chain FA)
- **Beta (β) Oxidation** **(Most Predominant)**
- **Omega(ω) Oxidation** (When defect in β Oxidation)

2.Oxidation Based On Number Of Carbon Atom

- **Beta Oxidation** of **Even Carbon Chain Fatty acid oxidation**
- **Beta Oxidation** of **Odd Chain Fatty Acid Oxidation**
- **Very Log Chain Fatty Acid** (VLCFA) Oxidation

3.Oxidation Based On Nature Of Bonds

- Oxidation of **Saturated Fatty acids**
- Oxidation of **Unsaturated Fatty acids**

4.Oxidation Based On Cellular Site

- **Mitochondrial** Fatty acid Oxidation
- **Endoplasmic Reticulum** Fatty acid Oxidation
- **Peroxisomal** Fatty acid Oxidation

How Palmitic Acid is Completely Oxidized In Human Body? Calculate Its Energetics

General Pattern To Study Metabolic Pathways

- Synonyms/Different Names of Pathway.
- What is Pathway ? (In brief)
- What type Of Pathway? (Catabolic/Anabolic)
- Where thus pathway occurs/Location? (Organ/Cellular site)
- When pathway occurs/Condition? (well fed/emergency/aerobic/anaerobic)

- Requirements for Pathway (If Anabolic Pathway)
- How pathway Occurs/Stages/Steps? (Type of Rxn , Enzymes ,Coenzymes)
- Why Pathway occurred? (Significance of Pathway)

- Precursor, intermediates, byproducts and end products of metabolic Pathway.
- Energetics of pathway/Net ATP Use and Net Generation of ATPs
- Interrelation ships with other Pathways
- Regulation of Pathway :Modes of regulation.
- Regulatory Hormone/ Regulatory Enzyme/Modulators.
- Inborn Error of the Metabolic Pathway

Beta Oxidation
Of
Even Carbon

Saturated Fatty Acid

At Mitochondrial Matrix

Historical Aspects Of Beta Oxidation of Fatty Acids

- **Albert Lehninger** showed that
- **β Oxidation of Fatty acids** occurred in the **Mitochondria.**

- **Knoop** showed that Fatty acid is **oxidized and degraded by removal of 2-C units**

- **F. Lynen and E. Reichart** showed that **2-C unit released** is **Acetyl-CoA**, but **not free Acetate.**

Beta Oxidation Of Palmitate (C16)

What Is Beta Oxidation Of Fatty Acid ?

Definition Of β Oxidation of Fatty acid

- Oxidation of a Fatty acid at **Beta Carbon atom/C3** (-**CH2)**

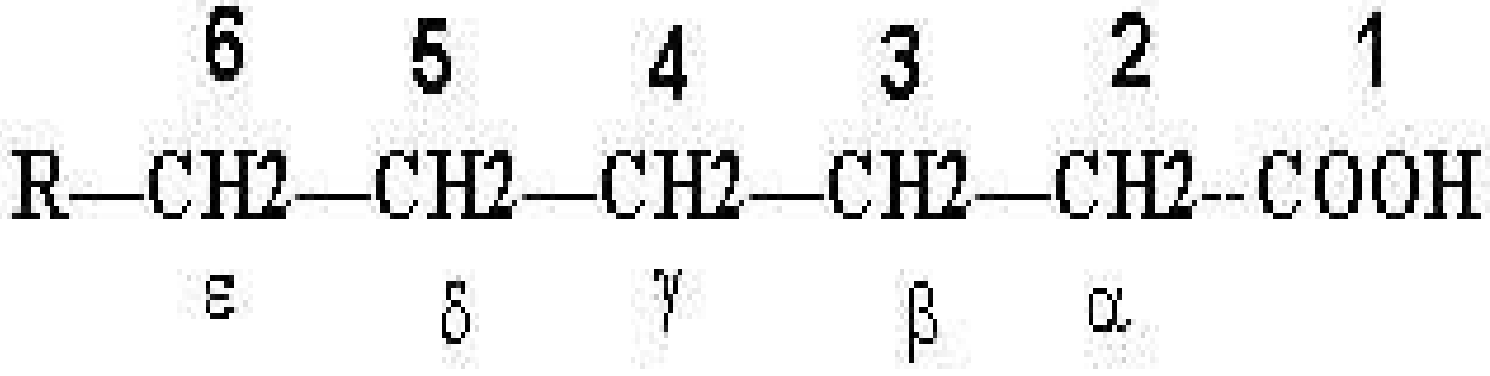
- **Beta Oxidation of Fatty Acid is most predominant type of Fatty acid oxidation.**

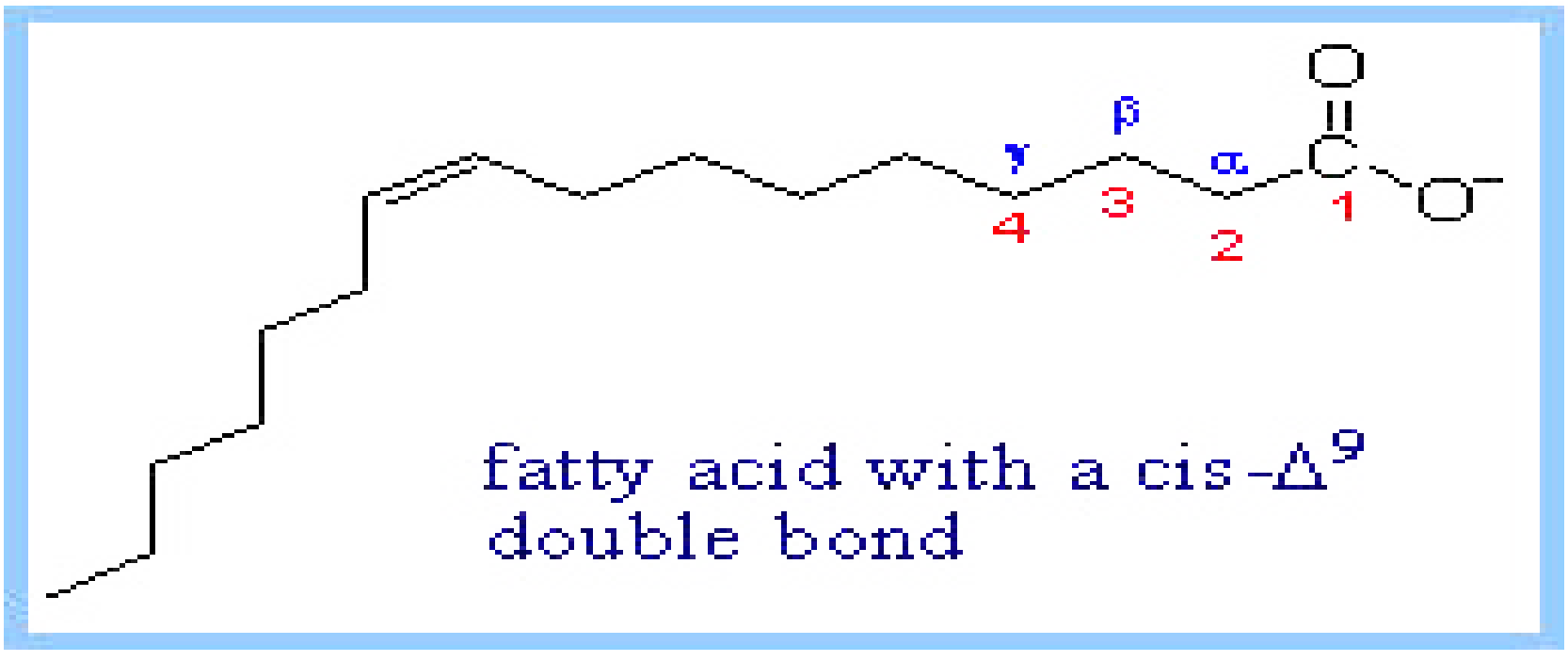
- **Most of Fatty acids in cells get oxidized and catabolized via Beta Oxidation of Fatty Acid**

β-Oxidation OF Fatty Acid

- **β-oxidation of Fatty acids is catabolic/ degradative , energy generating metabolic pathway of Fatty acids**

- It is referred as **β-oxidation** pathway, because **oxidation occurs at β-carbon (C3) of a Fatty acid.**



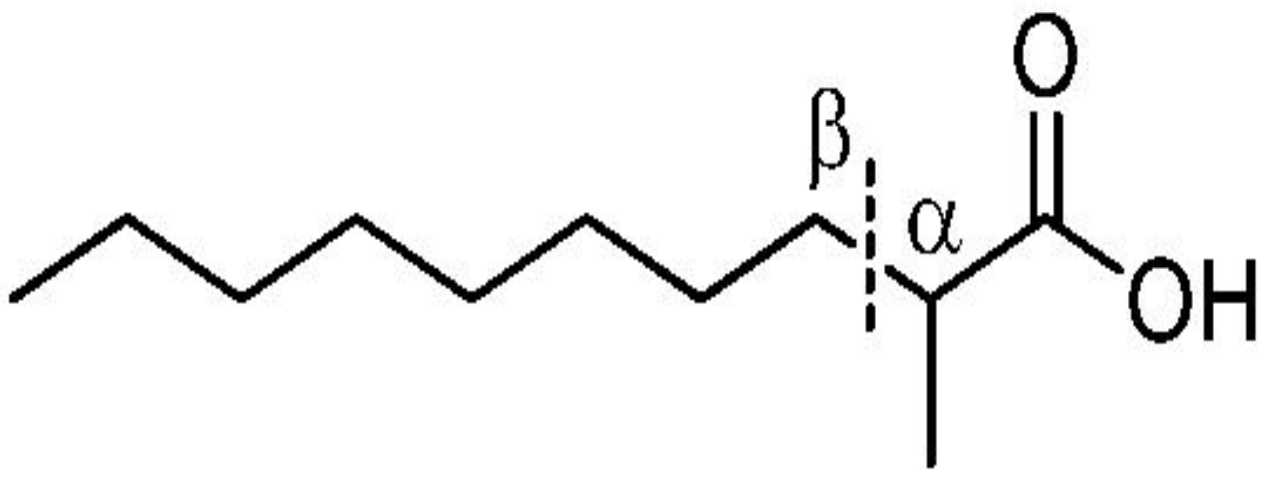


- During Beta oxidation of Fatty acid **(-CH2) of Beta position is oxidized and**
- **Transformed to Carbonyl atom (-C=O)**

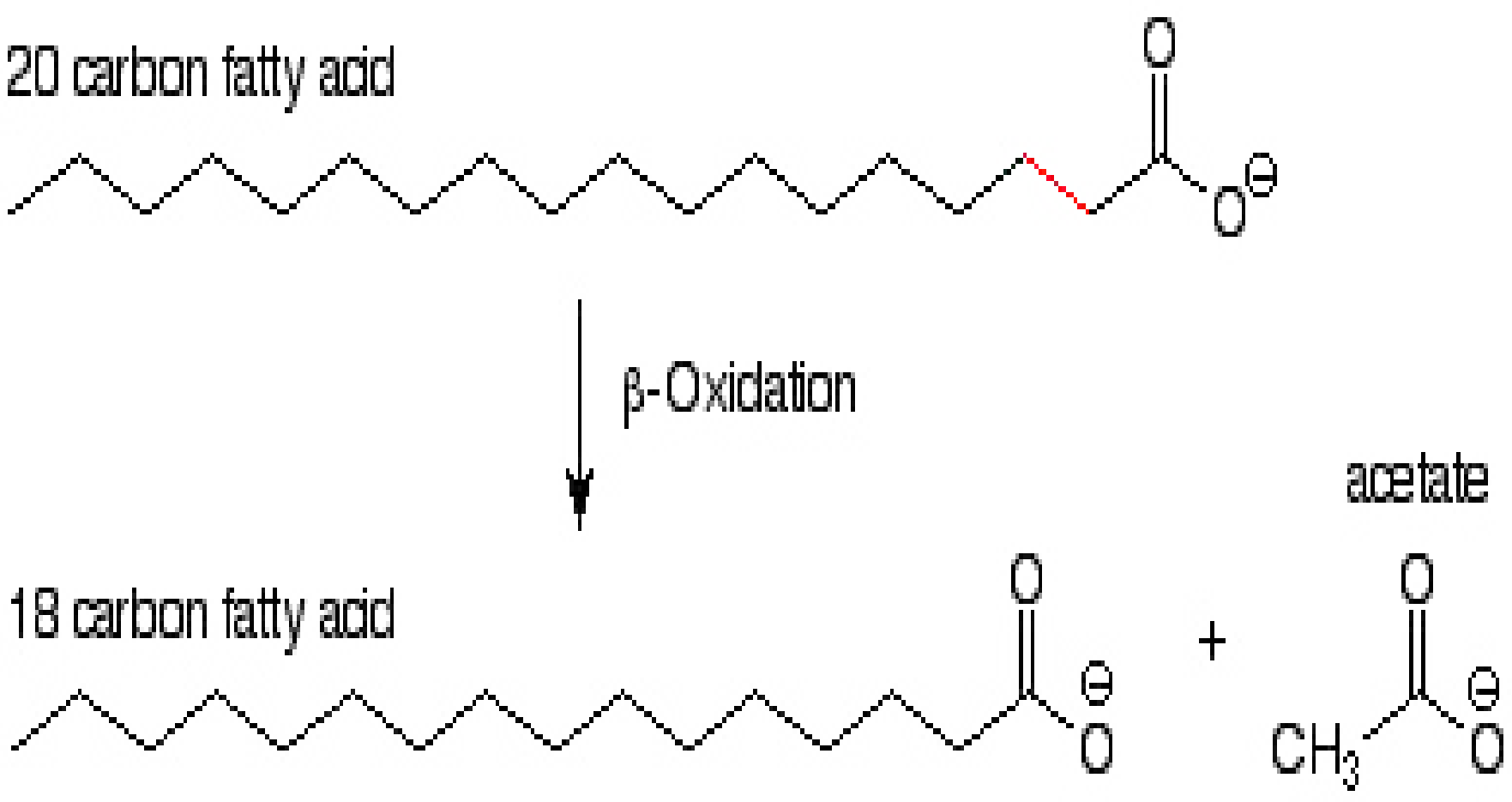
- Oxidized and transformed Beta positioned -**C-H2** to **-C=O** during steps of Beta Oxidation Proper.

- **Makes bond between Alpha and Beta Carbon atom weaker and cleavable to release 2Carbon unit Acetyl-CoA.**

The Weak bond between Alpha and Beta Carbon Atom is Cleaved to release 2Carbon Unit Acetyl-CoA



- **With a removal of 2-C units there is shortening of Fatty acid chain.**
- The **2-C units** released after steps of Beta Oxidation is **Acetyl-CoA** (active Acetate) **which enters TCA for its complete oxidation.**



β-Oxidation OF Fatty Acid Is a Catabolic Energy Producing Pathway

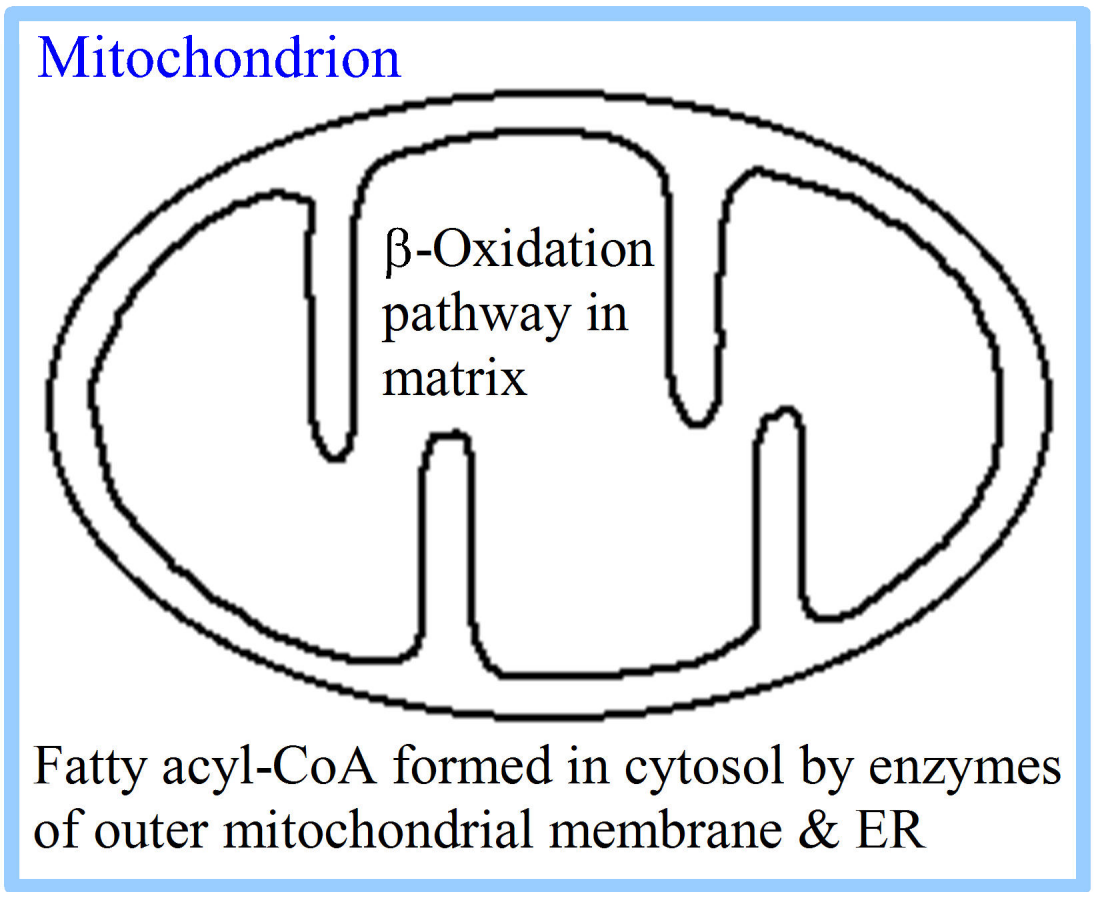
Organs Involved with Beta Oxidation Of Fatty Acid

- Skeletal Muscles
- Heart
- Hepatocytes
- Kidney

Cellular Site For Beta Oxidation Of Fatty Acid

- **Cytosol**
  (Activation of Fatty acid)

- **Mitochondrial Matrix**
  (Beta Oxidation Proper)



β-Oxidation pathway:

Fatty acids are degraded in the **Mitochondrial Matrix** via the β-Oxidation Pathway.

Organs Which Do Not Operate Beta Oxidation Of Fatty Acid

Remember In
Brain and Erythrocytes
Fatty Acids
Do Not Serve
As A Source Of Energy

- **Free Fatty acids cannot cross the blood brain barrier**
- **Hence Fatty acids do not enter Brain to get oxidized.**

- **Beta Oxidation proper** of Fatty acid **takes place in Mitochondrial matrix**
- Since mature **RBC's has no Mitochondria**
- Hence **no oxidation of Fatty acids occurs in Erythrocytes.**

- **In emergency conditions**

–**Since Brain and Erythrocytes cannot oxidize Fatty acids** and use as energy source.

–These organs **has to depend only on Glucose for getting energy for their vitality.**

Type Of Metabolic Pathway

- **Beta Oxidation Of a Fatty acid is a:**
  - –**Catabolic** Pathway
  - –**Degradative** Pathway
  - –**Energy generating** metabolic pathway in emergency phase

Condition Of Its Occurrence

- Usually Beta Oxidation of Fatty acids efficiently occurs **after Lipolysis.**
- When there is **low use of Glucose** by body cells
  - In **Fasting condition**
  - In **between Meals**
  - During **Severe Exercises** and Marathon Races
  - In Patients of **Diabetes mellitus**

Stages And Reaction Steps Of Beta Oxidation Of Fatty Acids

Three Stages Of Beta Oxidation For Fatty acid Palmitate

Stage I
Activation of Fatty acid (Acyl Chain) to Acyl-CoA In Cytosol

– Palmitate to Palmitoyl-CoA In Cytosol

Stage II

Translocation of Activated Fatty acid From Cytosol into Mitochondrial Matrix

Through The Role of Carnitine

(Carnitine Shuttle)

Stage III

Steps of Beta Oxidation Proper In Mitochondrial Matrix

- Oxidation Reaction
- Hydration Reaction
- Oxidation Reaction
- Cleavage Reaction