University of Al-Ameed

Faculty of Nursing

Biochemistry

Lec.4

Chemistry of Lipids (part 2)

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Lecture Objectives

By the end of this lecture, students will be able to:

1. Describe the process of lipogenesis (fatty acid synthesis).
2. Explain the process of lipolysis (fatty acid breakdown).
3. Identify the types of lipoproteins and their role in lipid transport.

Lipid metabolism

Lipid metabolism

Lipogenesis: is the metabolic process through which fatty acids are synthesized to form triglycerides, the primary storage form of fat in adipose tissue,

Stimulated by insulin and high carbohydrate intake.

Lipolysis: is the metabolic process through which triacylglycerols (TAGs) break down by hydrolysis into their constituent molecules: glycerol and free fatty acids (FFAs).

Stimulated by hormones like glucagon and epinephrine during fasting or exercise.

Lipogenesis: Fatty Acid Synthesis

Carbohydrates and proteins obtained from the diet in **excess** of the body's needs for these nutrients can be converted to **fatty acids** which are stored as triacylglycerols , de novo fatty acid synthesis occurs primarily in **cytosol** of the liver and adipose tissue.

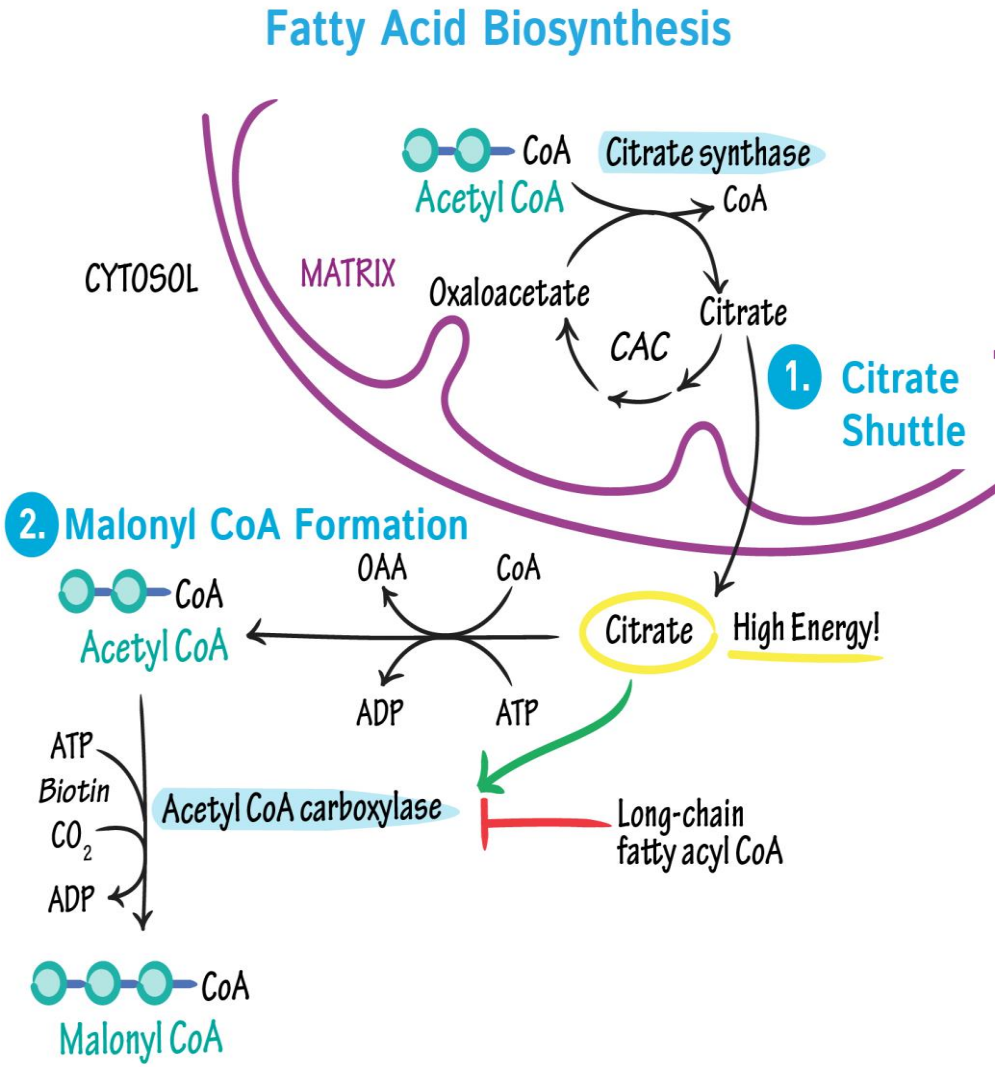
- The process takes place in three major steps: the citrate shuttle, acetyl-CoA carboxylase **(the rate-limiting step)** and fatty acid synthase complex.

Step1 :Synthesis of Acetyl-CoA and Citrate shuttle

Acetyl-CoA is generated from carbohydrates (e.g., glucose) through metabolic pathway. Acetyl-CoA cannot directly cross the mitochondrial membrane, so it is converted into citrate, which can exit the mitochondria. **Once in the cytoplasm, citrate is converted back into acetyl-CoA and oxaloacetate.**

Step 2: Acetyl CoA carboxylation to malonyl CoA

Acetyl-CoA is carboxylated to form malonyl-CoA by the enzyme acetyl-CoA carboxylase (ACC). **This step is rate-limiting step in fatty acid synthesis.**



Step3: **Fatty Acid Synthase Complex (FAS)**

The multi-enzyme complex responsible for synthesizing fatty acids.

- **Initiation:**

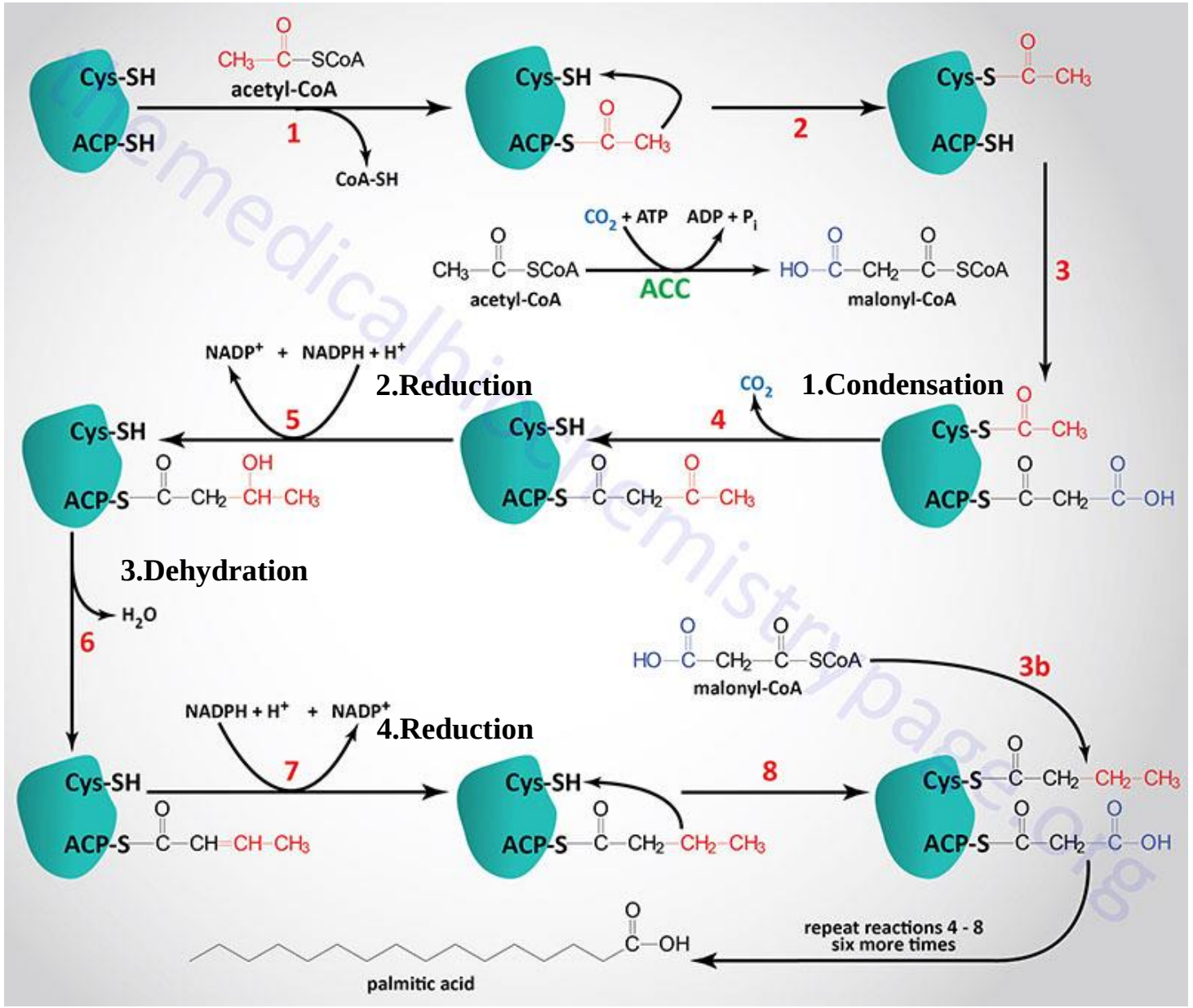
The FAS complex has two essential arms: **Cys-SH** (belonging to the amino acid Cysteine) and **ACP-SH**(Acyl Carrier Protein). The process begins by attaching an Acetyl to the Cys-SH arm, while a Malonyl is added to the ACP-SH arm

➢ Elongation Cycle:

- ❖ Condensation Reaction: A condensation reaction occurs, releasing CO_2 and forming a four-carbon intermediate.
- ❖ Reduction: The four-carbon compound undergoes reduction using NADPH,
- ❖ Dehydration: A dehydration reaction removes H2O, forming a double bond.
- ❖ Second Reduction: Another reduction step converts any double bonds back to single bonds using NADPH.

After the second reduction, the growing fatty acid chain moves from the ACP-SH arm back to the Cys-SH arm, making the ACP-SH arm free to accept a new malonyl group for the next cycle

This cycle repeats, adding two carbon units in each turn



*Cys=Cysteine

*ACP= Acyl carrier protein

Step3: Fatty Acid Synthase Complex (FAS

Lipolysis :Fatty acid oxidation (B-oxidation)

- The major pathway for catabolism of fatty acids is a mitochondrial pathway called **β-oxidation**, producing **acetyl CoA, NADH, and FADH2.**
- **Beta-oxidation** of fatty acids occurs primarily in the **mitochondria** of cells, This process typically takes place **during periods of fasting, prolonged exercise, or when carbohydrate intake is low, as the body relies on fat stores for energy**.

the main steps Lipolysis (fatty acids oxidation)

Step **I** :Activation of Fatty acid

Step **II** : Transport of fatty acyl CoA into mitochondria

Step **III** : Beta- oxidation (Consists of 4 reactions)

1-Dehydrogenation (FAD-dependent)

2- Hydration

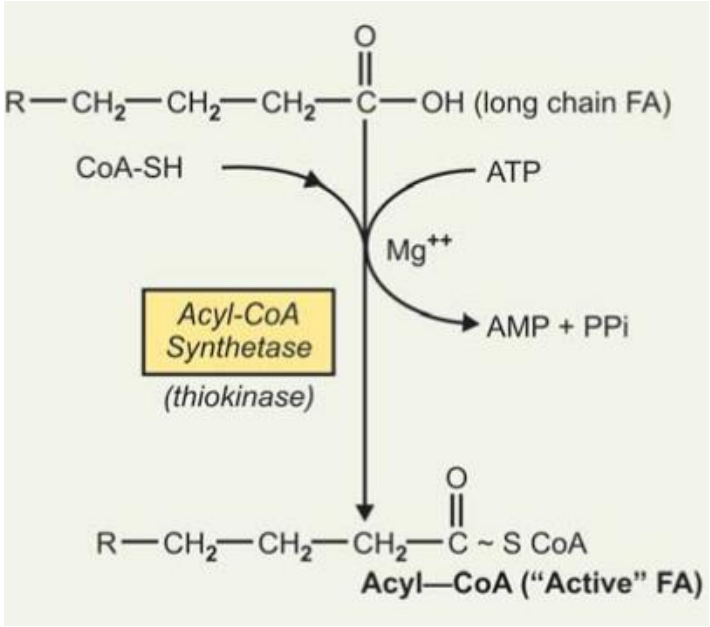
3-Dehydrogenation (NAD-dependent)

4-Cleavage (Remove 2C as acetyl CoA)

Step I: Activation of fatty acid

Fatty acid is converted to fatty acyl CoA by **thiokinase or acyl CoA synthetase**.

This reaction occurs in **cytoplasm** and activated by ATP and coenzyme A

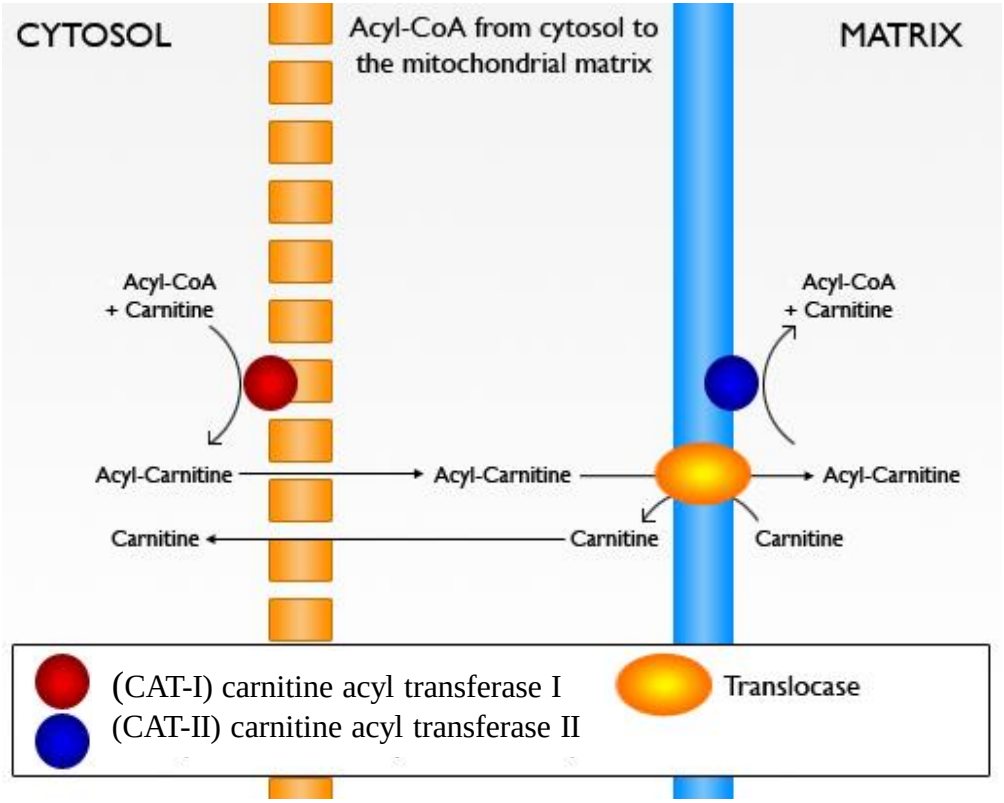


Step II: Transport of acetyl CoA into mitochondria

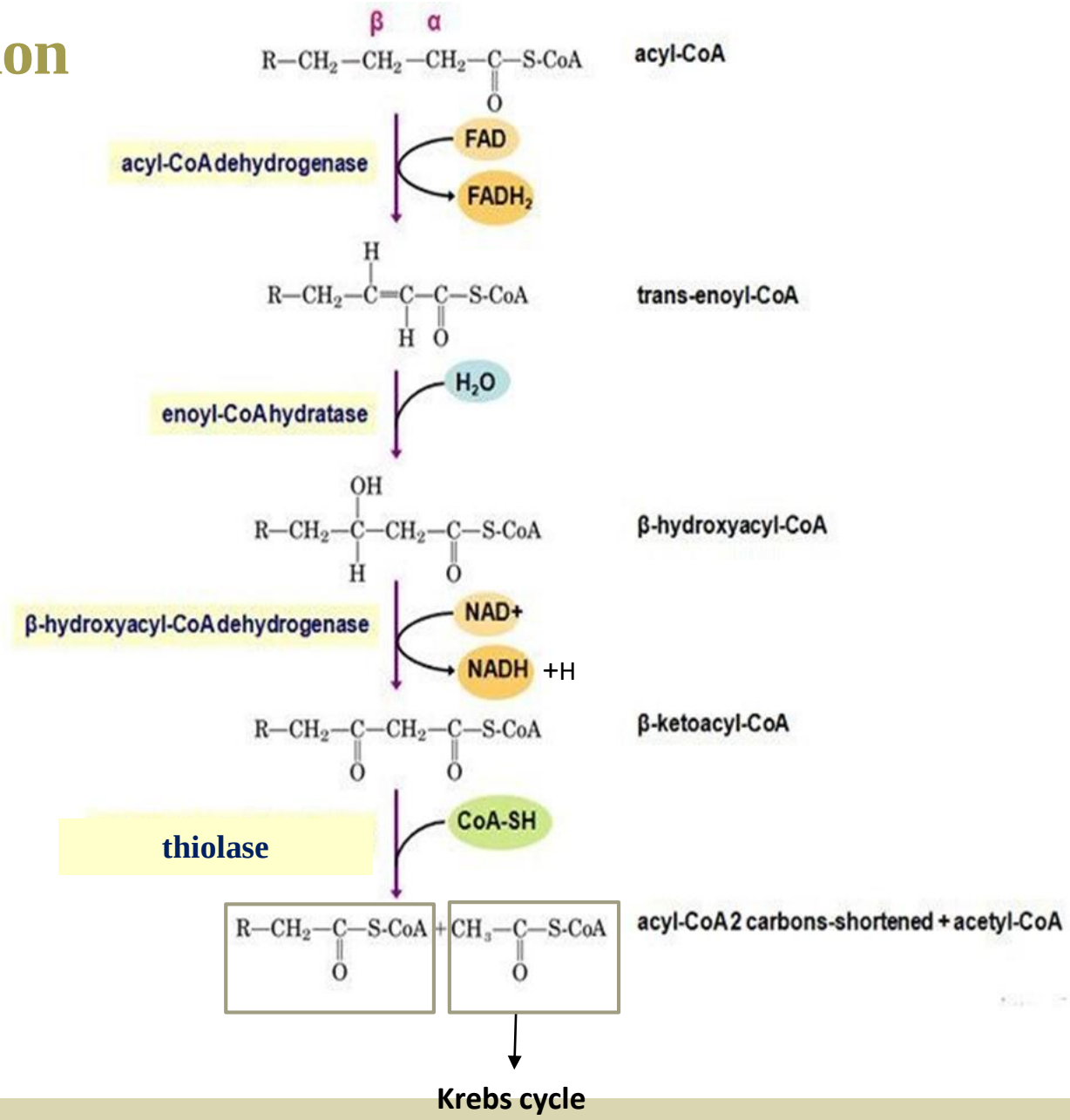
The inner mitochondrial membrane doesn't permit fatty acids to pass through it. But The activated FA(fatty acyl CoA) enter mitochondria through Carnitine shutter.

First, the acyl group is transferred from CoA to carnitine to form acyl carnitine. This is catalyzed by enzyme **carnitine acyl transferase (CAT-I)** on outer surface of mitochondria. Second, acyl carnitine enters into matrix by translocase. acyl carnitine is converted into acyl CoA by an enzyme **carnitine acyl transferase II (CAT-II)** an enzyme of the inner mitochondrial membrane,

The carnitine return to cytosol for re-use.



Step III: Beta-oxidation



Step III: reactions of Beta-oxidation

1. Dehydrogenation (formation of double bond)

Acyl-CoA is oxidized by the enzyme acyl-CoA dehydrogenase. This creates a double bond between the alpha (C2) and beta (C3) carbons, producing trans-enoyl-CoA. This step uses FAD and produces $FADH_2$, which enters the Electron Transport Chain (ETC) to generate ATP

2. Hydration

The enzyme enoyl-CoA hydratase adds a water molecule (H2O) across the double bond of trans-enoyl-CoA.This forms β-hydroxyacyl-CoA ,where the hydroxyl group (-OH) is attached to the beta carbon (C3).

3. Second Dehydrogenation:

the hydroxyl group in C3 of B-hydroxyacyl CoA is oxidized by NAD+ in a reaction that is catalyzed by B-hydroxyacyl-CoA dehydrogenase. The end products are ß- ketoacyl CoA and NADH + H,the NADH will enter the electron transport chain produce ATP

4. Thiolysis (Cleavage)

Finally, β-ketoacyl-CoA is cleaved by the thiol thiolase. The cleavage occurs between C2 and C3. The products are one molecule of Acetyl-CoA (containing the original C1 and C2) and an Acyl-CoA chain that is two carbons shorter than the original chain

The number of ATP produced from the breakdown of fatty acid contains (14 C)

14-carbon fatty acid undergoes 6 cycles of beta-oxidation (since each cycle removes 2 carbons).

Each cycle produces:
1 FADH2
1 NADH

14 C
↓
12C (2C Acetyl COA) Krebs cycle
↓
10C (2C Acetyl COA) Krebs cycle
↓
8C (2C Acetyl COA) Krebs cycle
↓
6C (2C Acetyl COA) Krebs cycle
↓
4C (2C Acetyl COA) Krebs cycle
↓
2C 2C 2(2C Acetyl COA) Krebs cycle

7 Krebs Cycle =7*10=70 ATP
6 NADH=6*2.5=15 ATP
6 FADH2=6*1.5=9 ATP

94 -2= **92 ATP**

***Activation Cost: -2 ATP**

Conclusion

The length of fatty acid determines the number of beta-oxidation cycles and the number of Acetyl-CoA molecules produced

Carbons in Fatty Acid	Acetyl CoA C/2	β-oxidation cycles (C/2) -1
12	6	5
14	7	6
16	8	7
18	9	8

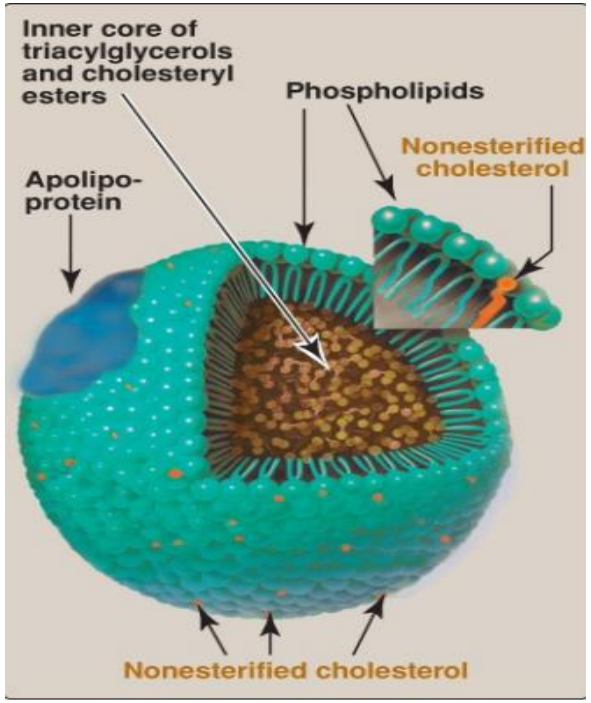
Lipoproteins

lipoproteins

- The plasma lipoproteins are spherical

macromolecular complexes of lipids and proteins (apo-protein)

- Lipoproteins function both to keep their component lipids soluble as they transport them in the plasma and to provide an efficient mechanism for transporting their lipid contents to (and from) the tissues



Types of Lipoproteins

Lipoproteins are classified based on their density, which is determined by the ratio of lipid to protein content.

1. Chylomicrons

Function: Transport dietary triglycerides and cholesterol from the intestines to other tissues.

Characteristics: **Largest and least dense** lipoproteins; primarily composed of triglycerides

2. Very-Low-Density Lipoprotein (VLDL):

Function: Transports endogenous triglycerides synthesized in the liver to peripheral tissues.

Characteristics: Rich in triglycerides and some cholesterol ; converted into LDL after delivering triglycerides.

3. Low-Density Lipoprotein (LDL):

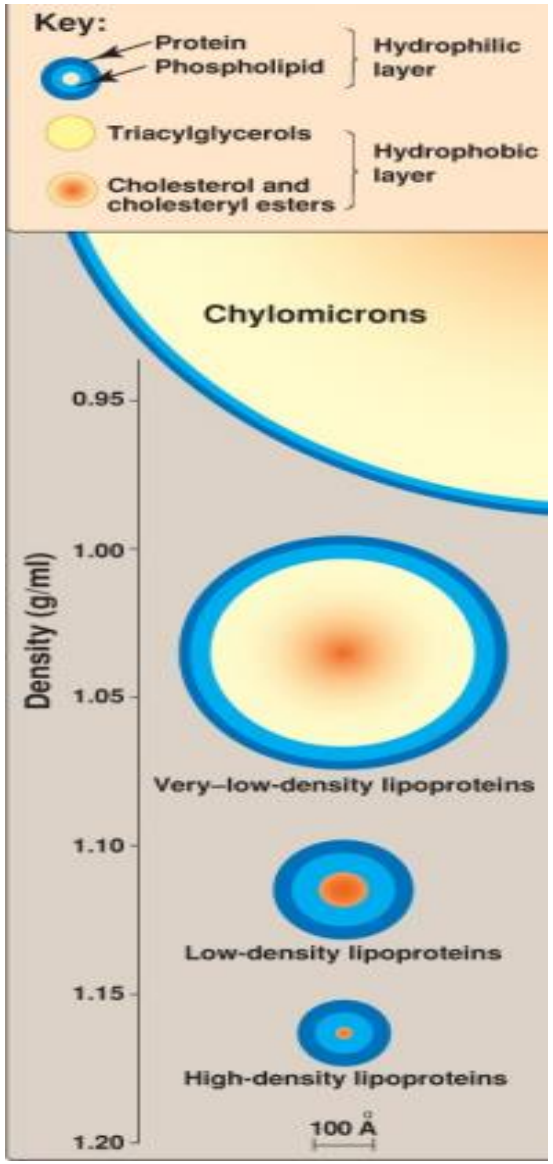
Function: Often referred to as "bad cholesterol" LDL carries cholesterol from the liver to cells throughout the body.

Characteristics: contain high proportion of cholesterol compared to VLDL; elevated levels are associated with an increased risk of atherosclerosis and cardiovascular disease.

3. High-Density Lipoprotein (HDL):

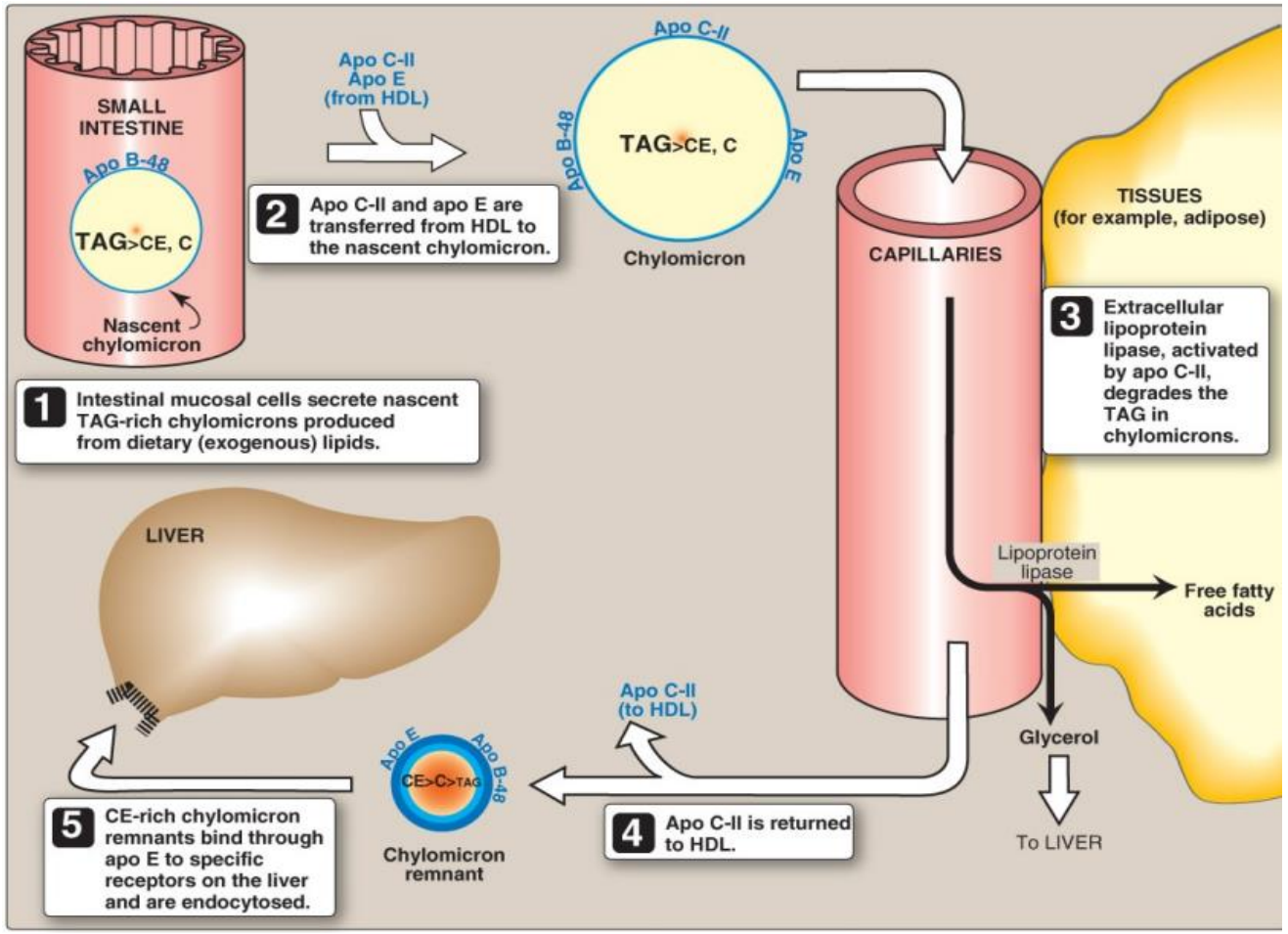
Function: Known as "good cholesterol" HDL helps transport excess cholesterol from tissues back to the liver for excretion or recycling.

Characteristics: Smallest and most dense lipoprotein; higher levels are generally associated with a lower risk of heart disease.

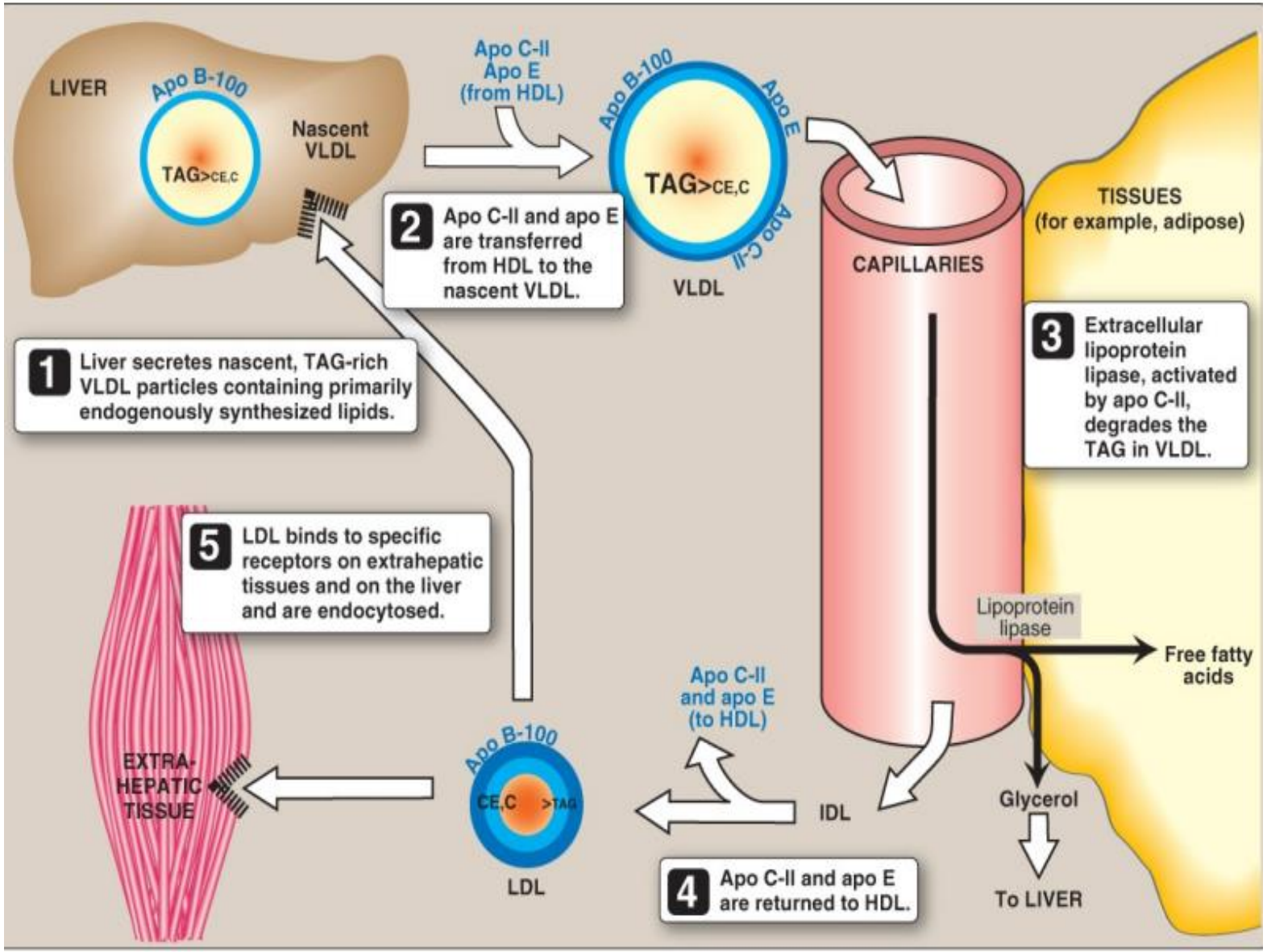


Plasma lipoprotein (sizes and densities)

Lipoproteins Metabolism

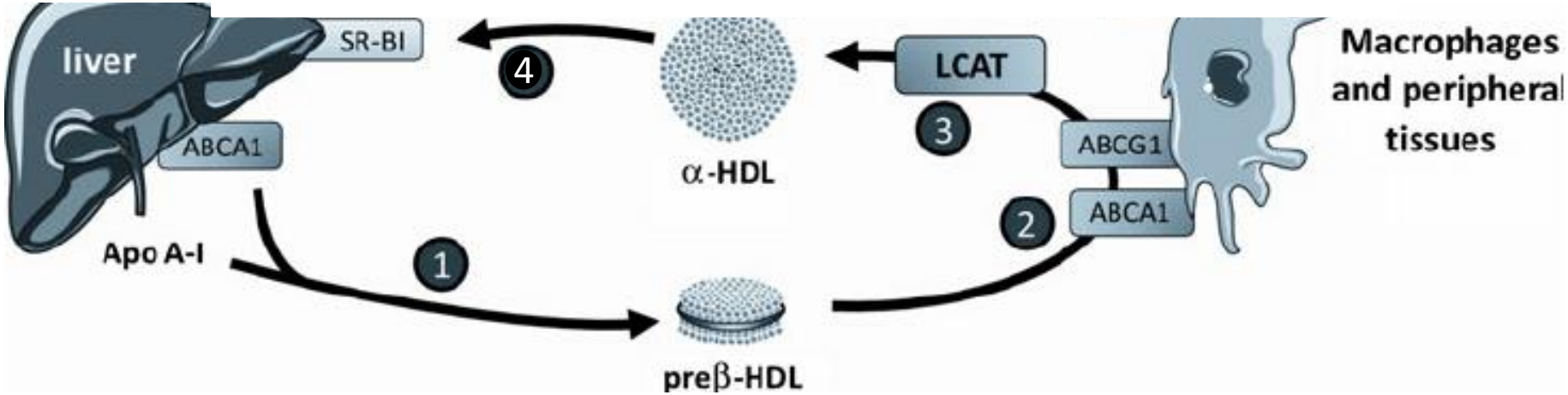


Metabolism of chylomicrons

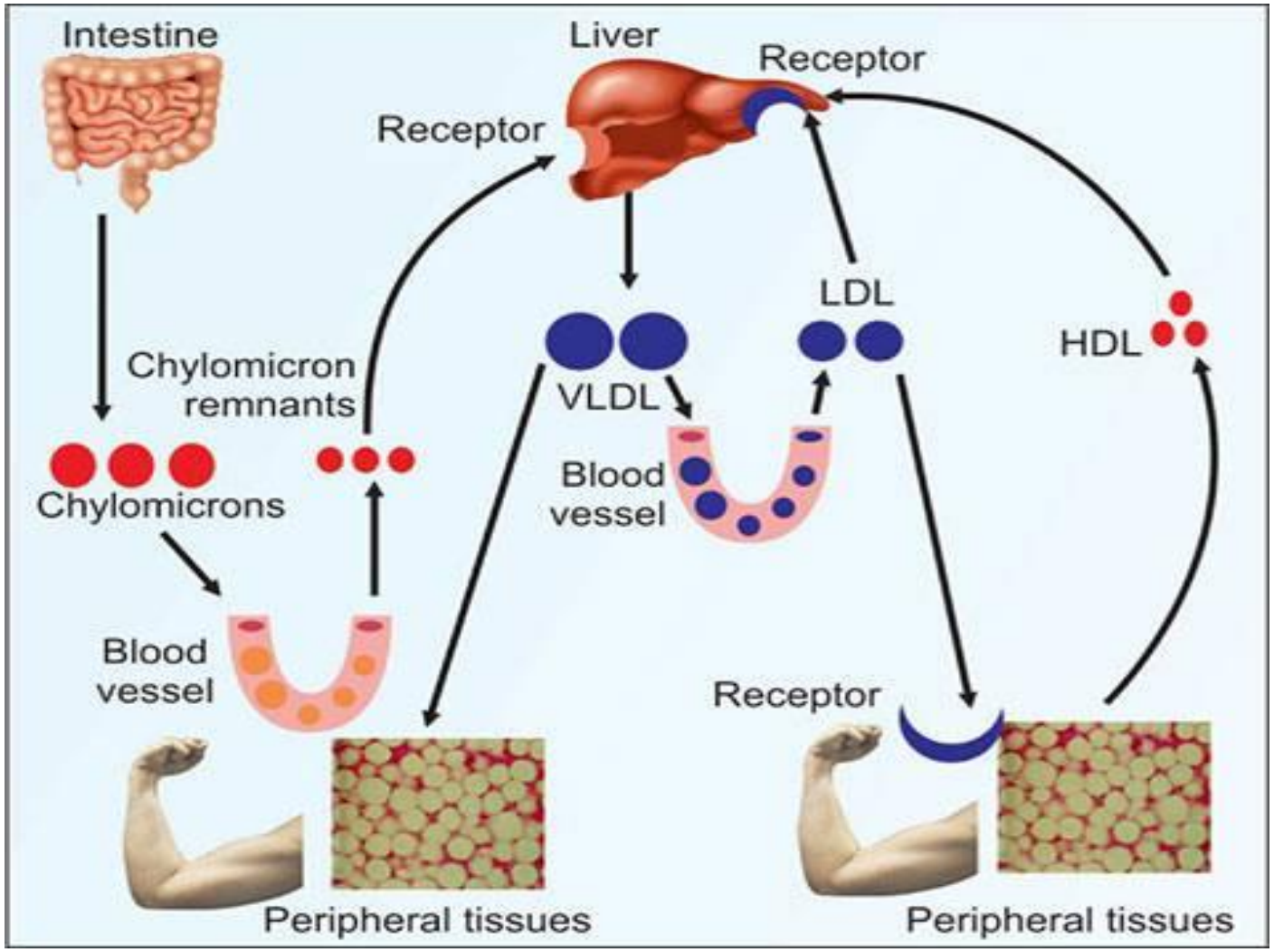


Metabolism of very–low-density lipoprotein (VLDL) and low-density lipoprotein (LDL) particles

reverse cholesterol transport pathway



*(ABCA1) ATP bindind cassette A1
*(ABCG1) (ATP-binding cassette sub-family G member 1)
*(LCAT) lecithin cholesterol acyl transferase
*(SR-B1) scavenger receptor B1



Summary of Lipoprotein Metabolism

Thank You