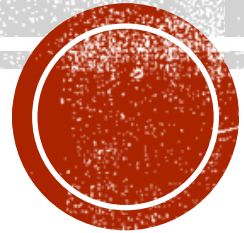
Adipose tissue metabolism (II. Lipolysis)



Students Learning Outcomes

❖ **By the end of this lecture, the students should be able to:**

1. Discuss the process of breakdown of TG (Lipolysis) and its products.
2. Identify the enzymes involved in lipolysis.
3. Demonstrate the fate of FA and glycerol after lipolysis.
4. Summarize the steps of B oxidation of Fatty acid
5. Calculate the energy produced by B oxidation of Fatty acid

Content

I. Forms of lipid in the body

II. Dynamic state of adipose tissue

III. Lipolysis & oxidation of fatty acids

IV. B oxidation of FA

LIPOLYSIS

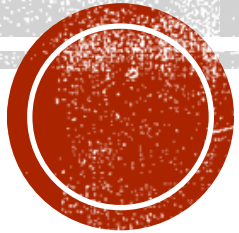
1. Definition
2. Site
3. Phases (Steps)
4. Products
5. Importance
6. Regulation

Dynamic state of adipose tissue:

- The TGs of adipose tissue are continually undergoing hydrolysis (Lipolysis) and re-esterification (lipogenesis).
- The results of these two processes determines the amount of FFA released from adipose tissue into blood.
- When the rate of lipolysis > the rate of lipogenesis, FFA accumulates and diffuses into the plasma with ↑ their level.
- Many of the nutritional, metabolic and hormonal factors regulate both of the two mechanisms

Lipolysis

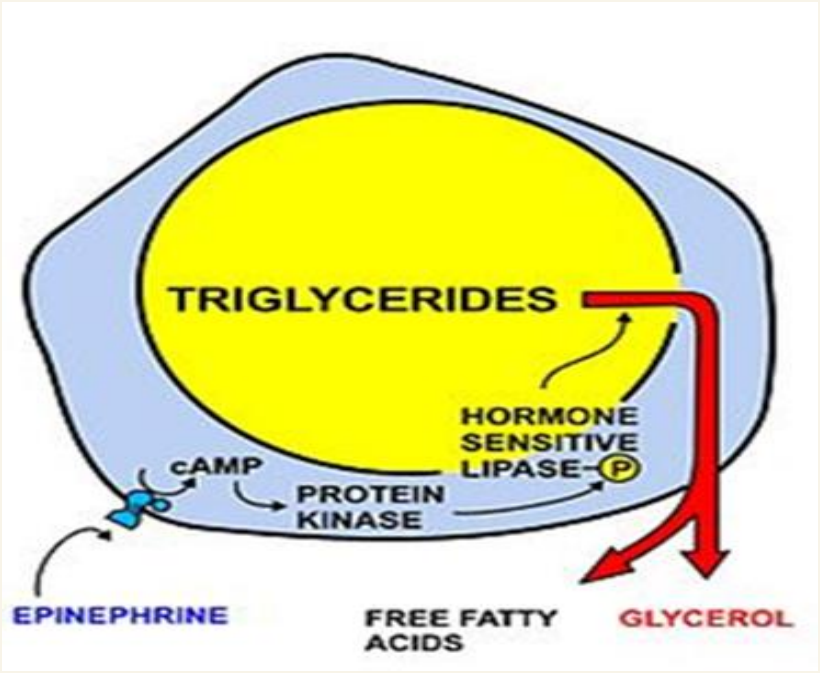
1. Definition
2. Site
3. Significance
4. Mechanism
5. Products & fate



Lipolysis

Definition:

It is the hydrolysis (breakdown) of triacylglycerol (TGs) into glycerol and free FAs



Site :

Cytoplasm of adipose tissue cells

Significance in:

Fasting, starvation & low carbohydrate diet, for **energy** production

Lipolysis

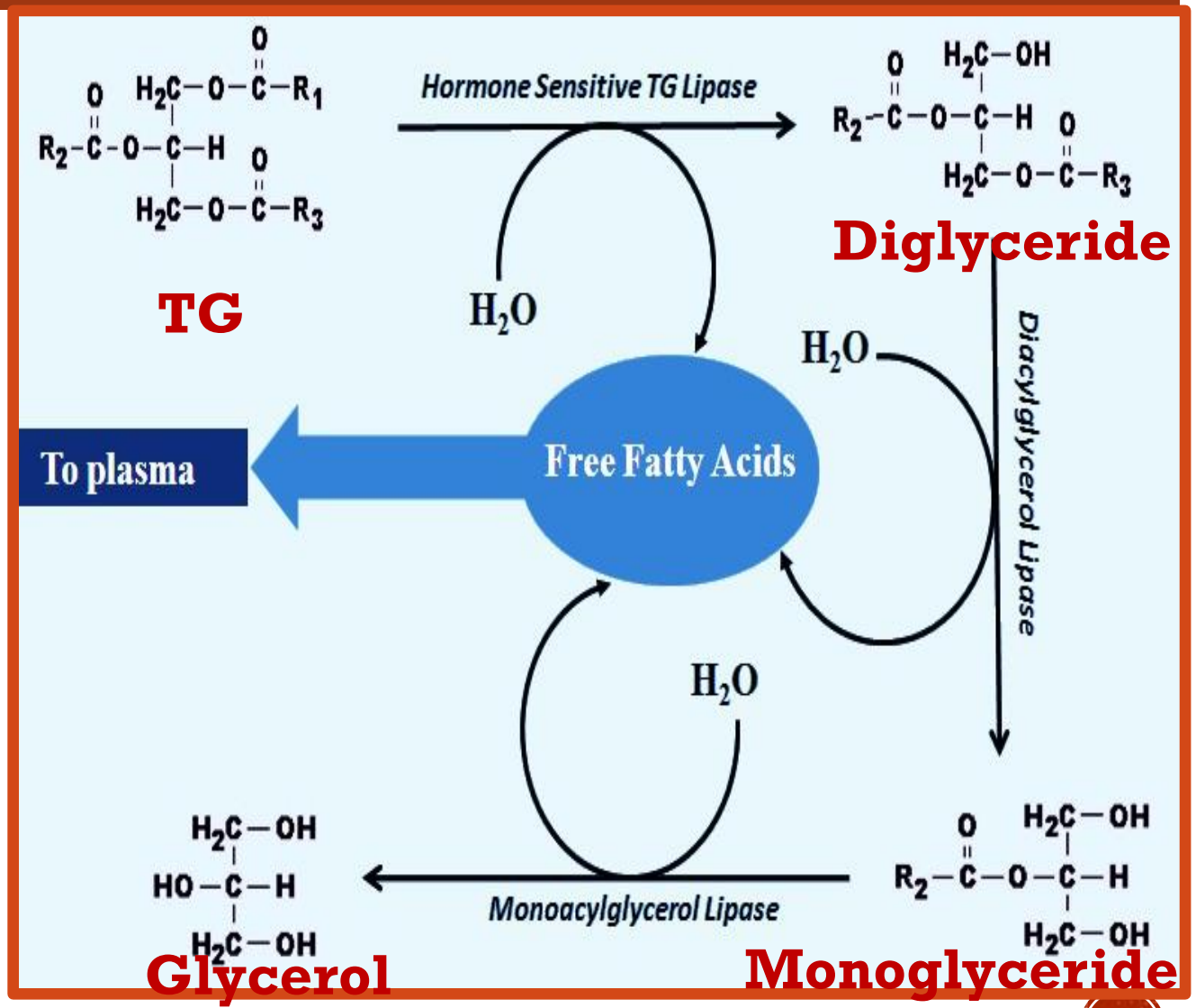
Mechanism

- ✓ 3 enzymes are involved

1- Hormone Sensitive Lipase.

2- Diglyceride Lipase

3- Monoglyceride Lipase



Lipolysis

Products and fate of lipolysis

1- Glycerol: released from adipose tissue→ blood→ directly to tissue (liver & kidney)→ used for **gluconeogenesis**→ synthesis of glucose.

2- Free fatty acids: released from adipose tissue→ blood--> carried by **albumin** in the blood→ uptaken by the tissue (especially liver) → undergo **B oxidation of FAs.** → energy & ATP production

B oxidation of FAs

1. Definition
2. Site
3. Significance
4. Steps

B oxidation of FAs

Definition:

It is the oxidation of long chain FA at **B carbon** (carbon no 3) by removal of **2 carbons** at a time in the form of **acetyl CoA.**

Site :

- Mitochondria of many tissues especially liver.
- Never occur in the RBCs or the brain (as the long chain FA not pass BBB, so not reaching the brain).

Significance in:

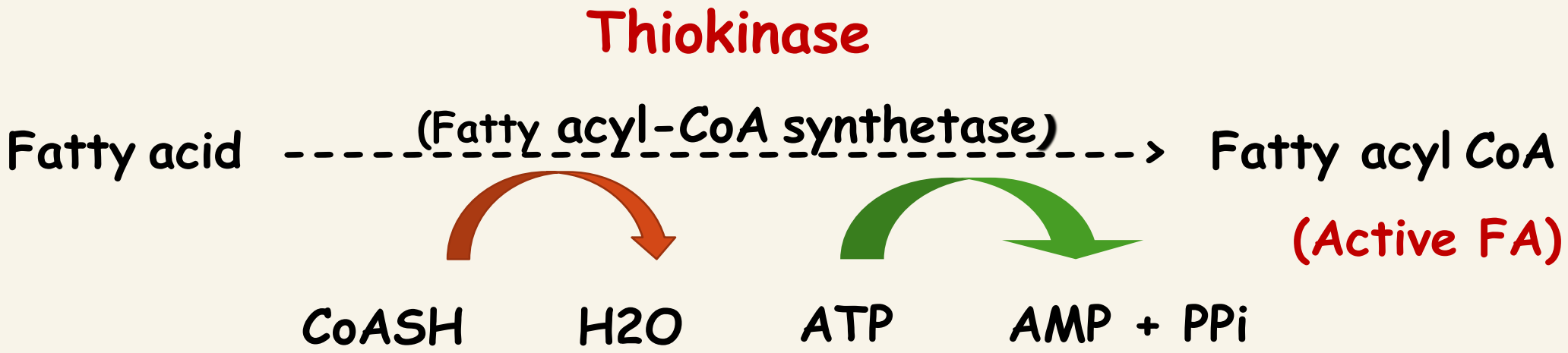
Fasting, starvation & low carbohydrate diet, for **energy** production.

B oxidation of FAs

Steps

1. Activation of long chain fatty acids inside the cytoplasm
2. Transport of active fatty acids into the mitochondria
3. B oxidation of active fatty acid inside the mitochondria

1. Activation of long chain fatty acids in the cytoplasm



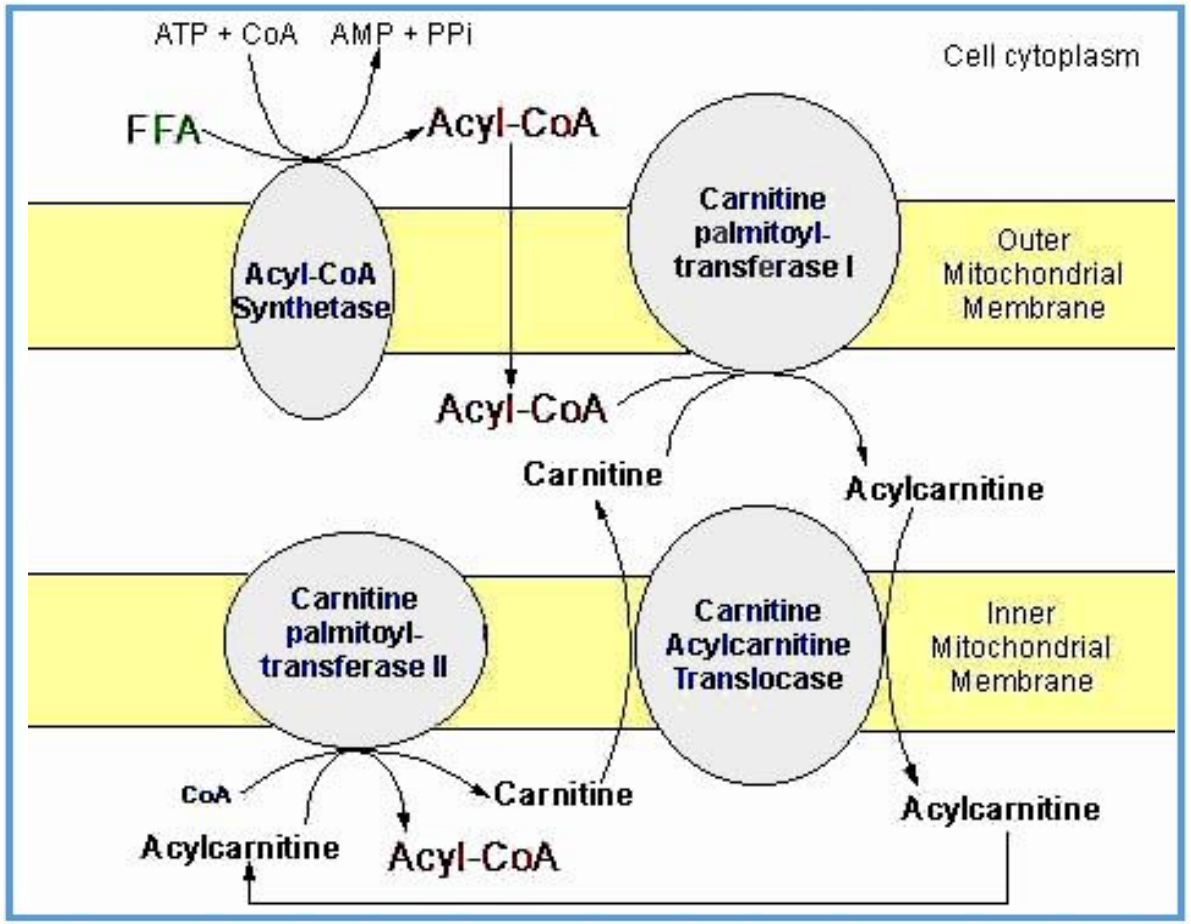
- Catalyzed by thiokinase (in outer mitochondrial membrane)
- Loss of **2 high energy** P bonds which are equivalent to **2 ATP**

2. Transport of active fatty acids into the mitochondria (carnitine shuttle)

- ✓ **Long chain active FA (Acyl CoA) cannot penetrate the mitochondrial membrane for B oxidation except after combination with carnitine.**

- ✓ **3 enzymes are important for carnitine shuttle:**

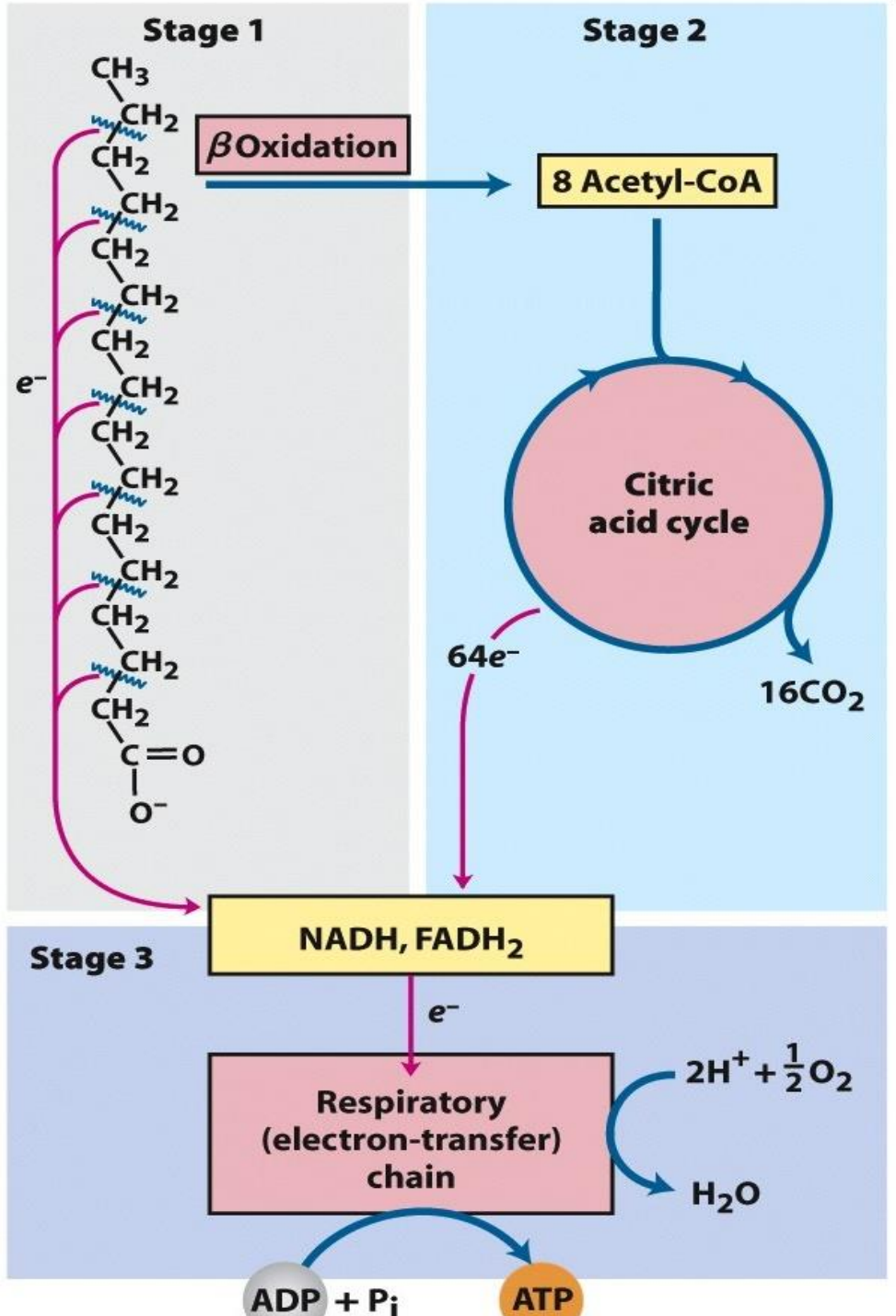
1. **Carnitine acyl transferase I (CPT I)**
2. **Carnitine acyl CarnitineTranslocase**
3. **Carnitine acyl transferase II (CPT II)**



Carnitine Shuttle

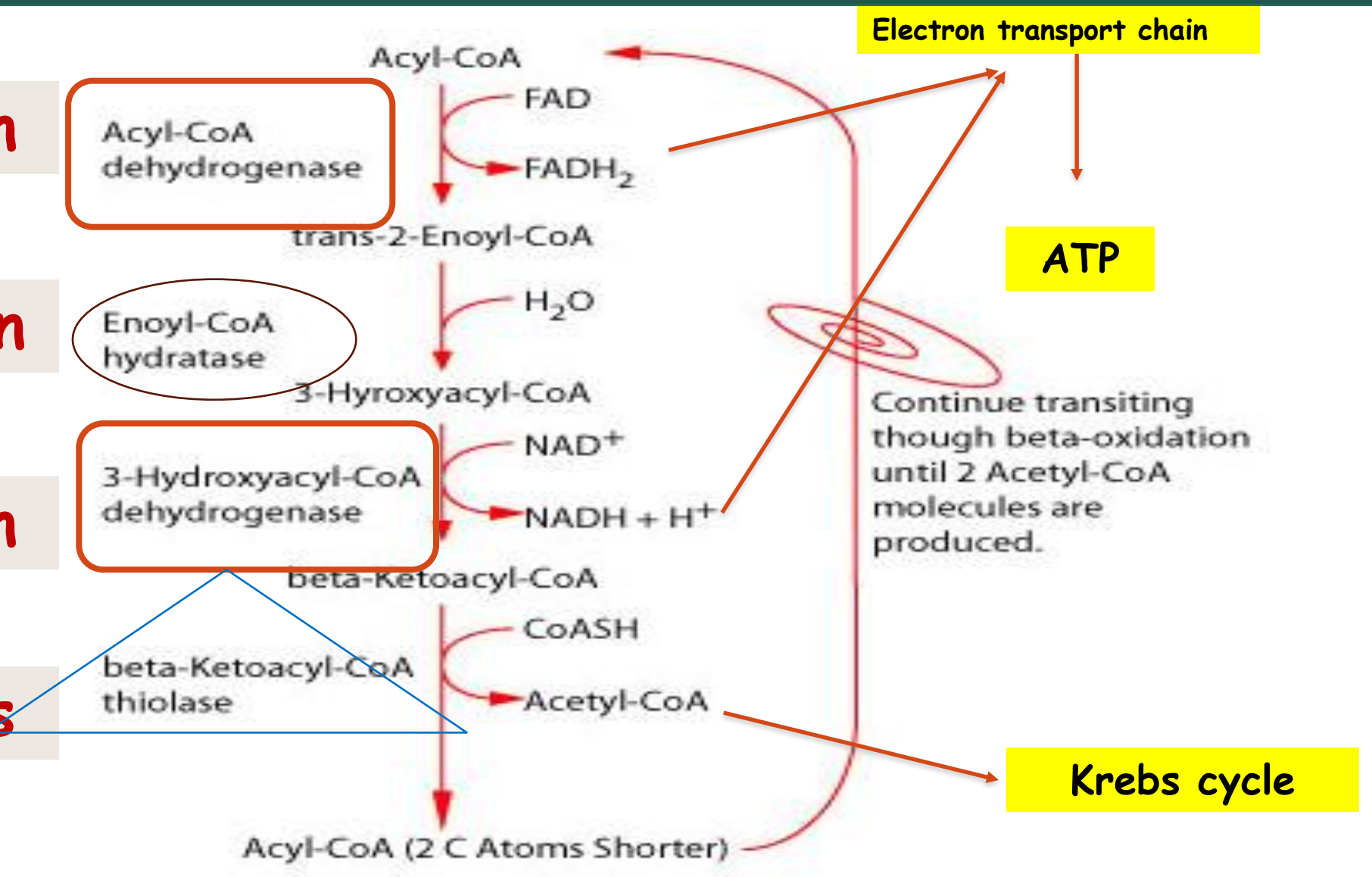
3. Steps of B oxidation of active fatty acid inside the mitochondria

- **It occurs in the form of repeated cycles, in each cycle:**
  - **An acetyl CoA (2C) is released from the FA (FA become shorter by 2C) → enter Kreps cycle**
  - **FADH2 + NADH+H are produced → enter Electron transport chain**



3. Steps of B oxidation of active fatty acid inside the mitochondria

1. Oxidation
2. Hydration
3. Oxidation
4. Thiolysis



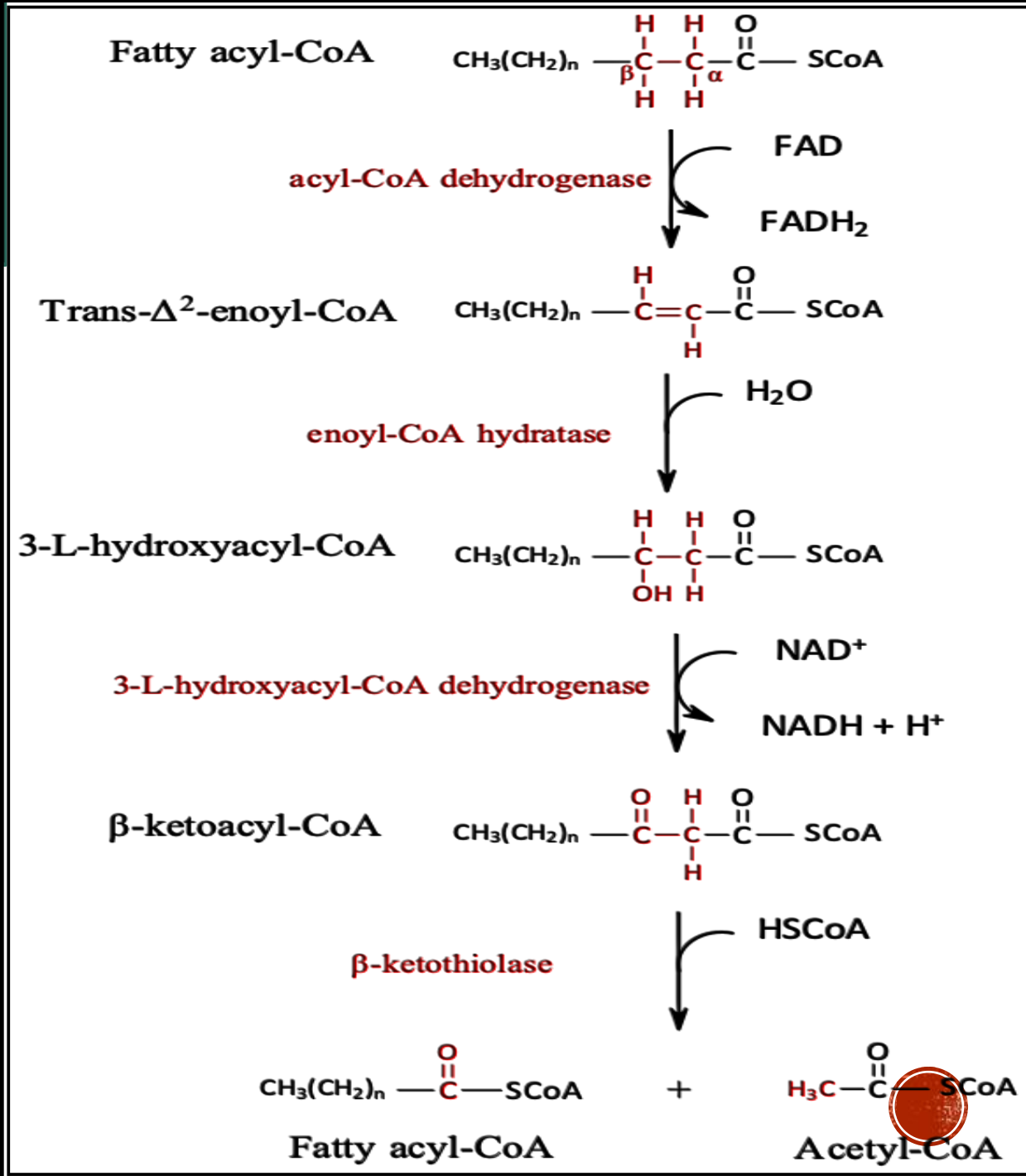
3. Steps of B oxidation of active fatty acid inside the mitochondria

1. Oxidation

2. Hydration

3. Oxidation

4. Thiolysis



- **B oxidation of active fatty acids** occurs inside the mitochondria in **repetitive cycles**

- **Each cycle of β- oxidation consists of 4 reactions:**
  1) **Oxidation**: produces $FADH_2$
  2) **Hydration**
  3) **Oxidation**: produces NADH + H
  4) **Thiolysis (Cleavage):** releases **one acetyl CoA.**
- **Each cycle of β- oxidation produces FA shorter by 2 C atom.**
- **This cycle is repeated several time until complete FA oxidation, and the** final cycle produces 2 acetyl CoA for even number saturated fatty acids

- **The number of turns (cycles) of β– oxidation = (N / 2) – 1**

(N is the number of carbon atoms in the FA)

Reaction	Enzyme	Reducing equivalents produced
1. Oxidation	Acyl CoA Dehydrogenase	$FADH_2$ = 2 ATP
2. Hydration	Enoyl CoA Hydratase	-
3. Oxidation	Hydroxy Acyl CoA Dehydrogenase	$NADH+H^+$ = 3 ATP
4. Thiolysis (Cleavage)	Thiolase	-

B oxidation of FAs

Energy produced by B oxidation of FA

How many ATP produced from complete B oxidation of palmitic acid (16 carbon FA)

1- Activation of palmitic acid to palmityl CoA (active FA)

requires 2 ATP (- 2 ATP)

2- Transport inside mitochondria: not require any ATP

3- B oxidation of palmityl CoA:

B oxidation of FAs

Energy produced by B oxidation of FA

$$\left[\left(\frac{N}{2}-1\right) x\ 5\ ATP\right]+\left[\frac{N}{2} x\ 12\ ATP\right]-\ 2\ ATP$$

3- B oxidation of palmityl CoA:

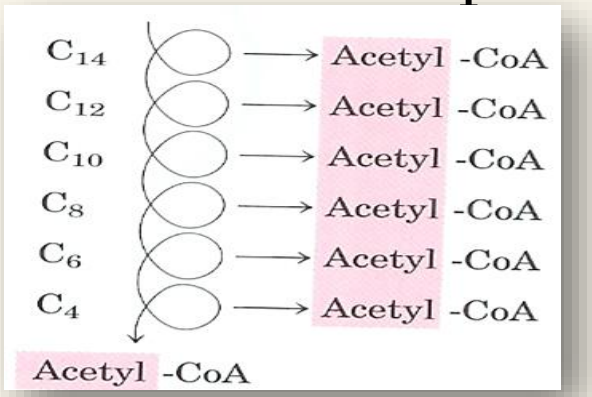
palmityl CoA has 16 Carbons, SO: β-oxidation of palmitic acid will be repeated 7 cycles (NO of cycles= N/2-1), producing 8 molecules of acetyl COA.(=N/2).

- In each cycle FADH2 and NADH+H+ is produced and will be transported to ETC

  FADH2 ----------→ 2 ATP

  NADH+H+ ----------→ 3 ATP

  So 7 cycles 5X7=35 ATP



- **Each cycle produce 8 acetyl CoA that enter the Krebs and produces 12 ATP,**

  8X 12 = <u>96 ATP</u>

  Net ATP= - 2 ATP + 35 ATP+ 96 ATP= 129 ATP

Homework

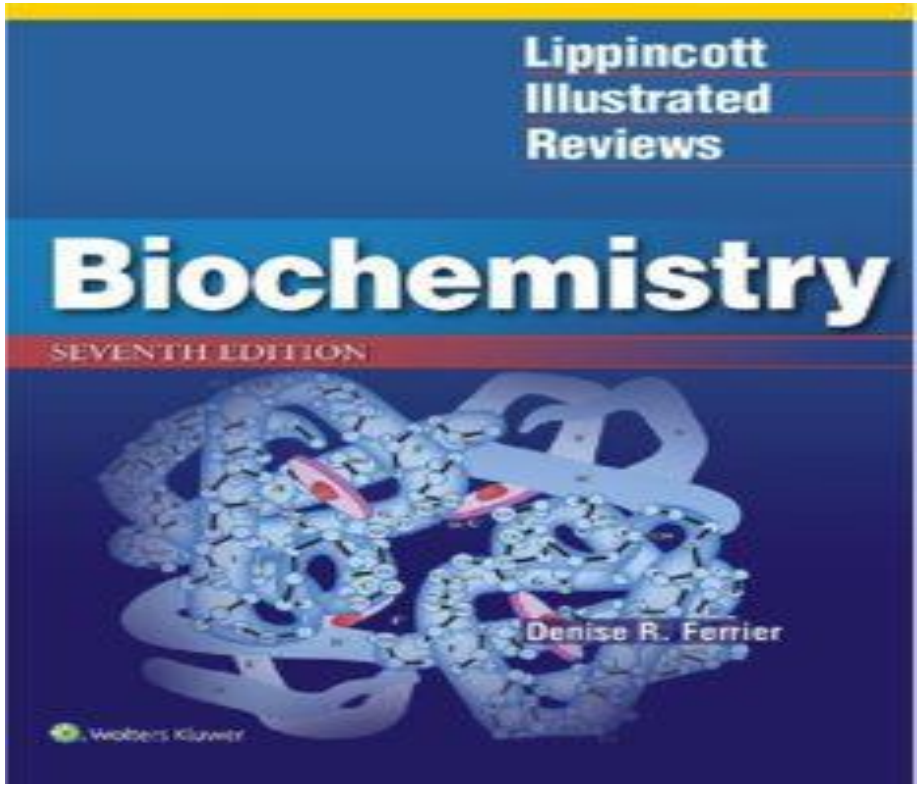
Calculate the number of ATP produced from B oxidation of

1- Stearic acid (18 carbon)

2- Stearyl CoA (18 carbon)


Life
isn't about
finding yourself.
...
Life
is about
creating yourself.

References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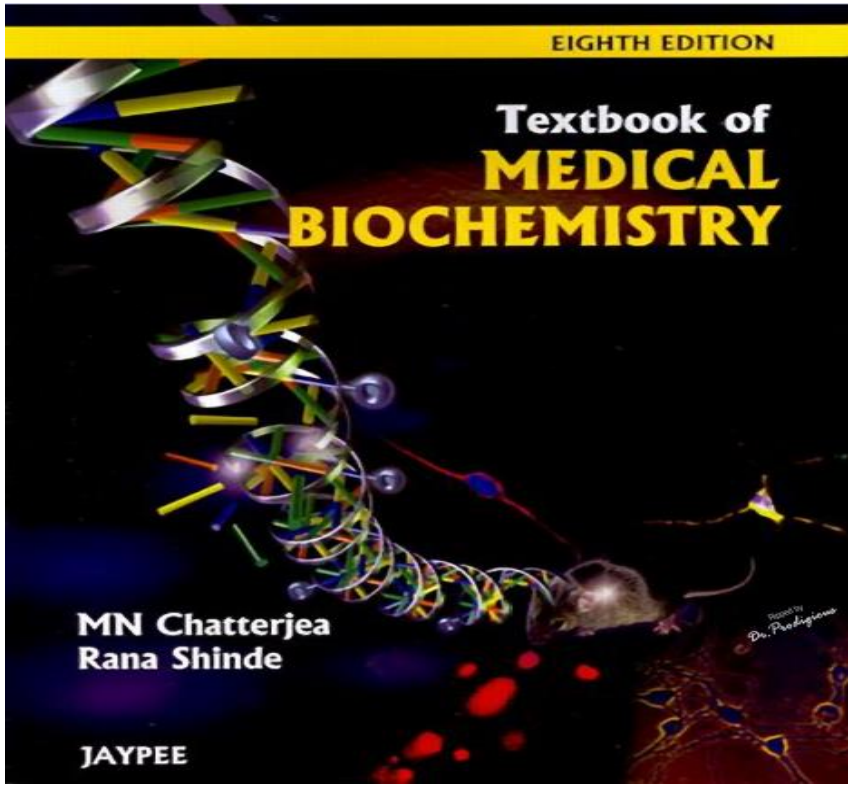
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