Fatty Acid Oxidation

- **Fatty acid oxidation is the major source of energy for ATP synthesis specially during fasting .**
- **The body oxidizes more fatty acids each day than any other fuel ; 540 calories are used in a 12-hour period in the basal state versus 280 calories of glucose or 80 calories of amino acids .**

Turnover of Fuels in Blood[a]

Fuel	Amount in the Circulation (blood, extracellular fluid) g	Amount in the Circulation (blood, extracellular fluid) Cal	Amount Used (12 hr, basal state) g	Amount Used (12 hr, basal state) Cal
Fatty acids	0.3	3	60	540
Glucose	20	80	70	280
Amino acids	0.3	1	20	80

- **During fasting , adipose triglycerides (stored fat) are mobilized by a process known as Lipolysis ; triglycerides are hydrolyzed by the enzyme hormone–sensitive lipase into free fatty acids & glycerol which are released into the blood . The hormones glucagon , epinephrine & ACTH activate this enzyme while it is inhibited by insulin . Thus , lipolysis is accelerated during starvation and in uncontrolled diabetes mellitus .**

- **The fatty acids released during fasting spare glucose for use by brain and other glucose-dependent tissues .**

- **Fatty acid oxidation is aerobic process and are oxidized mainly in mitochondria by a process known as <u>β-oxidation</u> (major pathjway) . This process generates acetyl CoA and energy (ATP) ; oxidation of the acetyl**

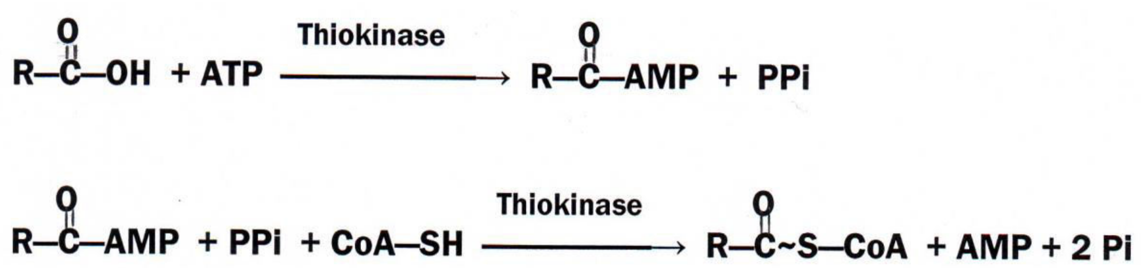
CoA in the TCA cycle produces additional ATP .

● The liver during fasting , only **partially oxidize** most of the fatty acids into acetyl CoA to obtain energy ; much of the acetyl CoA is then converted within the mitochondria to the ketone bodies which are released into the blood .

■ <u>β−oxidation of saturated fatty acids</u> : involves 3 steps :

I. <u>Activation</u> :

● Fatty acids must be activated before they can be oxidized ; they are activated by ATP in two step reaction catalyzed by the enzyme **thiokinase** to form fatty acyl CoA ; two ATP are consumed in the activation process .



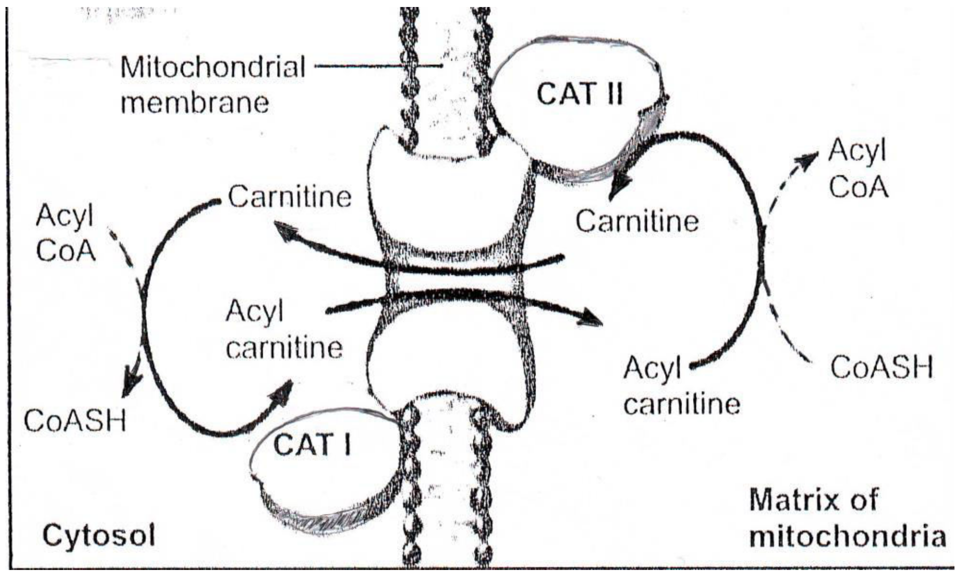
II. <u>Transport into mitochondria (Carnitine cycle)</u> :

● Activated long chain fatty acids (Acyl CoA) require **Carnitine** to be transported into mitochondria for oxidation .

● The enzyme <u>carnitine acyltransferase-I</u> (**CAT-I**) present on the outer surface of the mitochondrial membrane , transfers acyl group of activated fatty acids (acyl CoA) to carnitine forming **acyl carnitine** .

● <u>**Translocase**</u> (a mitochondrial membrane protein) carry the **acyl carnitine** across the inner membrane into the matrix .

- **carnitine acyltransferase-II** (**CAT-II**) present in the matrix transfers the acyl group from acyl carnitine and acyl CoA is reformed ; carnitine returns to the cytosol by the same translocase .



- Carnitine cycle -

III. <u>Reactions of β–oxidation</u> :

- Beta oxidation involves **repeated rounds** (**spirals**) of **<u>four</u>** metabolic reaction steps . In each round of four reactions , two carbons are removed from the carboxyl end and released as acetyl CoA .

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- The acetyl CoA molecules produced during β-oxidation may enter the citric acid cycle and oxidized completely to generate ATP .
- **β–oxidation** is so named since the pathway involves oxidation of the β-carbon (carbon 3) of the fatty acid chain to a keto group .

<u>1st reaction : first oxidation</u> :

- One molecule of $FADH_2$ produced .

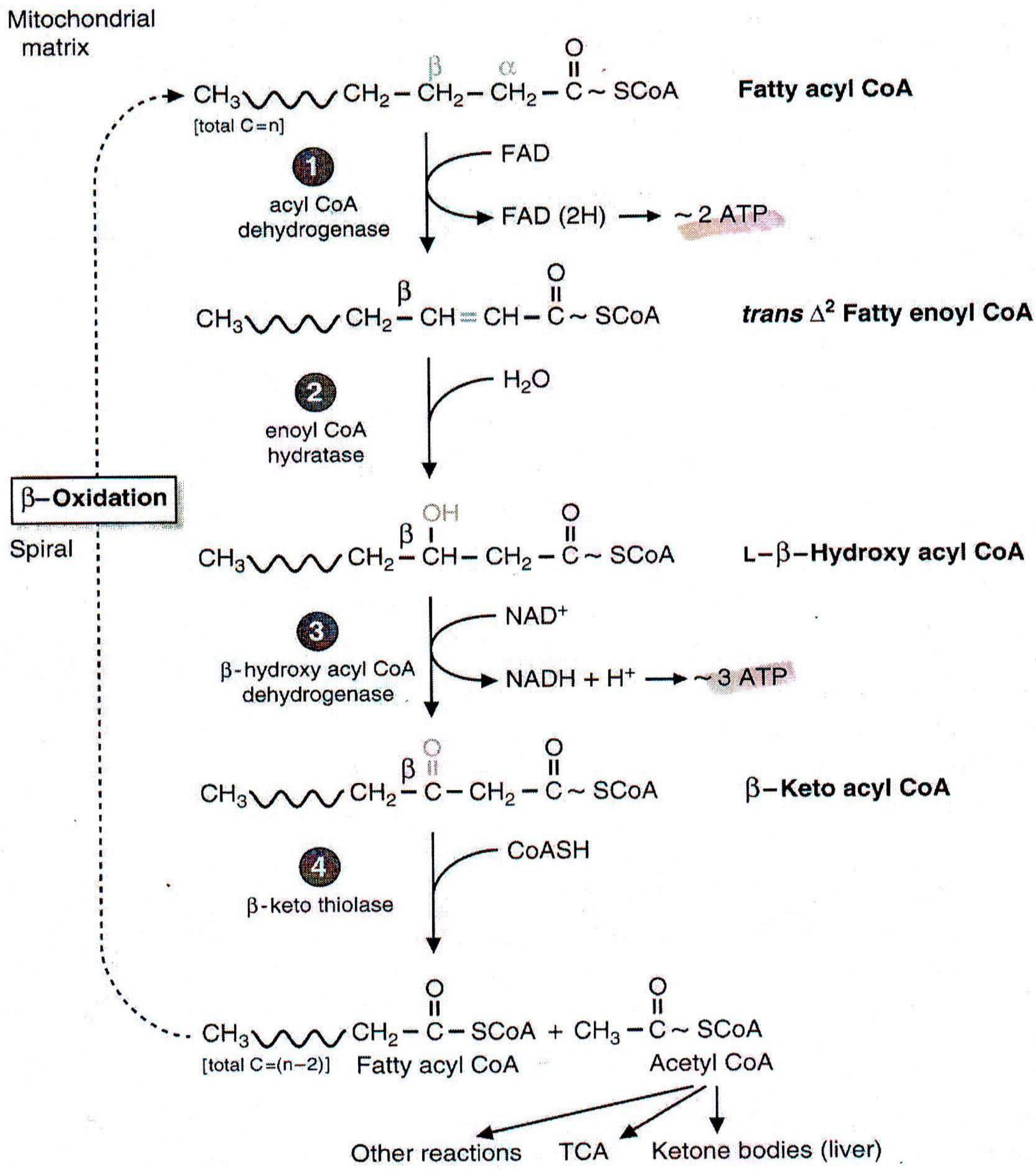
2nd reaction : hydration :

3rd reaction : second oxidation :

One molecule of NADH is produced .

4th reaction : cleavage :

The enzyme thiolase breaks the bond between α- & β- carbons . The products are acetyl CoA and a fatty acyl CoA which is two carbon shorter than the original fatty acid .



Steps of β-oxidation.

<u>ENERGETICS</u> :

<u>ATP generated from beta-oxidation of Palmitic acid (C-16)</u> :

- One molecule of **Palmitic acid** which has 16 carbons is cleaved in 7 rounds of β-oxidation producing <u>7</u> **$FADH_2$** ,<u>7</u> **NADH** and <u>8</u> **acetyl CoA** .

  7 $FADH_2$ X 2 = 14 ATP
  7 NADH X 3 = 21 ATP
  8 acetyl CoA X 12 = 96 ATP .
- One molecule of palmitic acid , therefore , generates a total of **131 ATP** .
- **Activation** of one molecule of palmitic acid require 2 high energy bond **equivalent of 2 ATP** .
- <u>Therefore</u> , the net energy yield from complete oxidation of one molecule of palmitic acid is equal to 131 – 2 = **129 ATP** .

<u>Fat versus Carbohydrate</u> :

A second advantage for the body to store excess energy as fat rather than as glycogen is that **more energy is obtained from fat oxidation than from carbohydrate (glucose) oxidation** . This is so as follows:

- Sum of <u>two</u> molecules of **<u>glucose</u>** contain same number of carbon atoms as <u>one</u> molecule of **<u>Lauric acid</u>** (12carbons) .
- β –oxidation of one molecule of **<u>lauric acid</u>** produces 6 molecules of acetyl CoA in 5 rounds and will generate a net of **95 ATP** :

  5 $FADH_2$ X 2 = 10 ATP
  5 NADH X 3 = 15 ATP
  6 acetyl CoA X 12 = 72 ATP
  Total ATP generated = **<u>97 ATP</u>**
  2 ATP used in activation
  Net yield = 97 – 2 = **95 ATP** .
- On the other hand , oxidation of one molecule of glucose generates **38 ATP**(glycolysis +TCA) .
- Oxidation of two molecules of glucose generates **<u>72 ATP</u>** .
- <u>Therefore</u> , body gets less ATP from glucose than from fat .

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