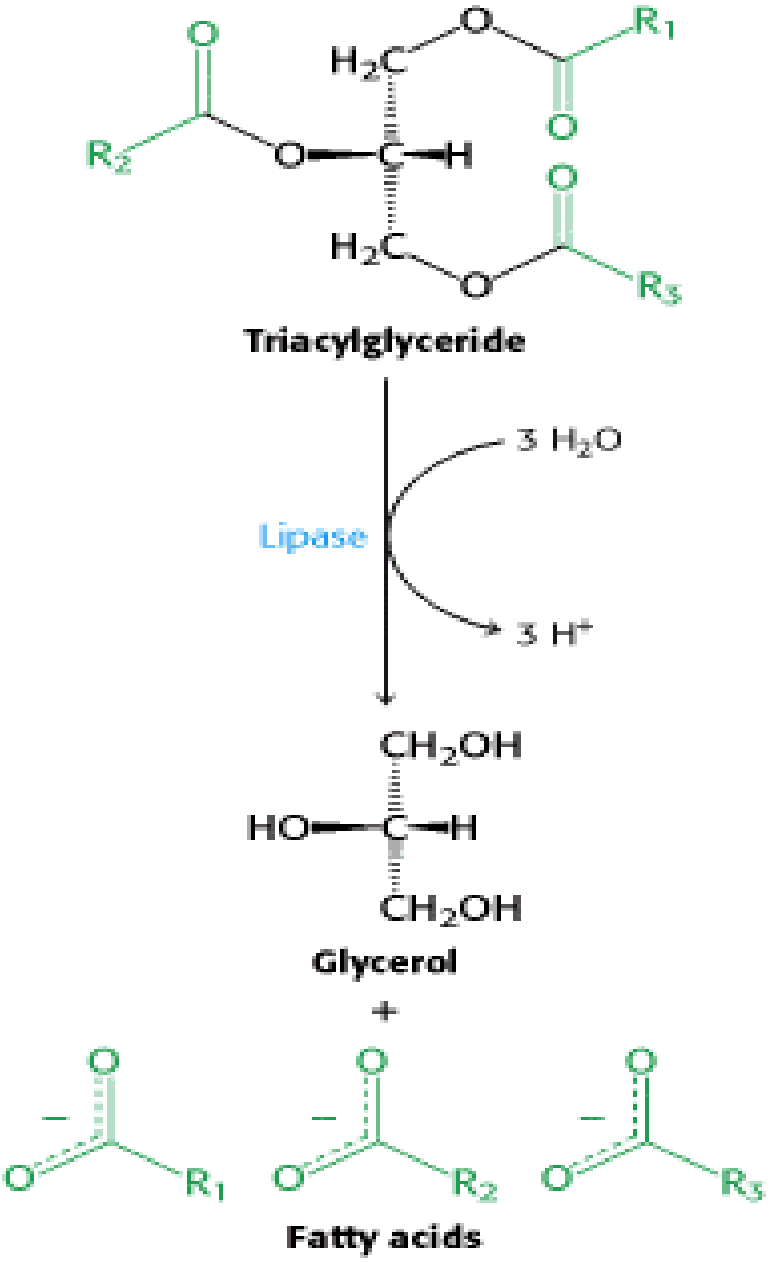
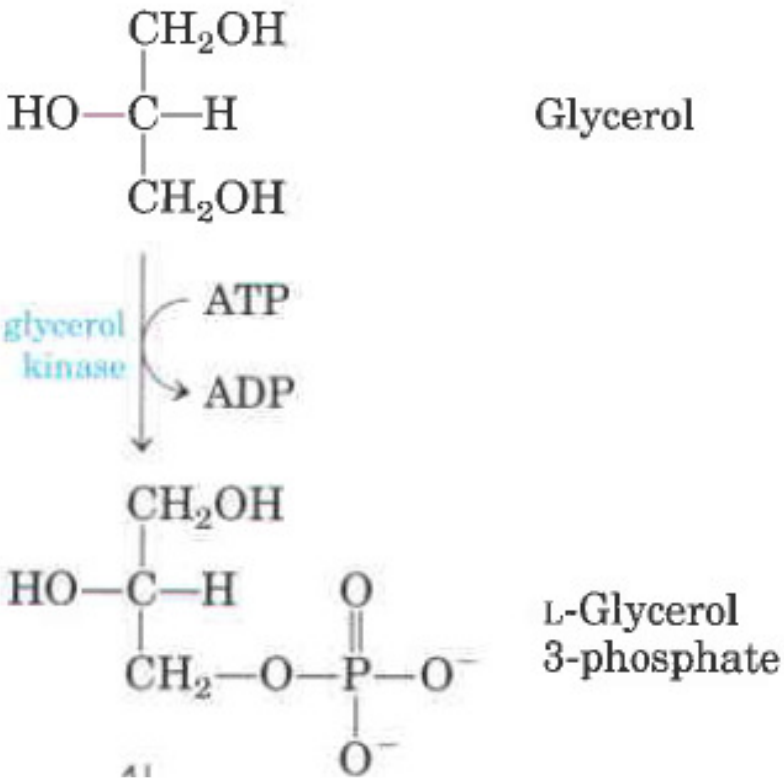
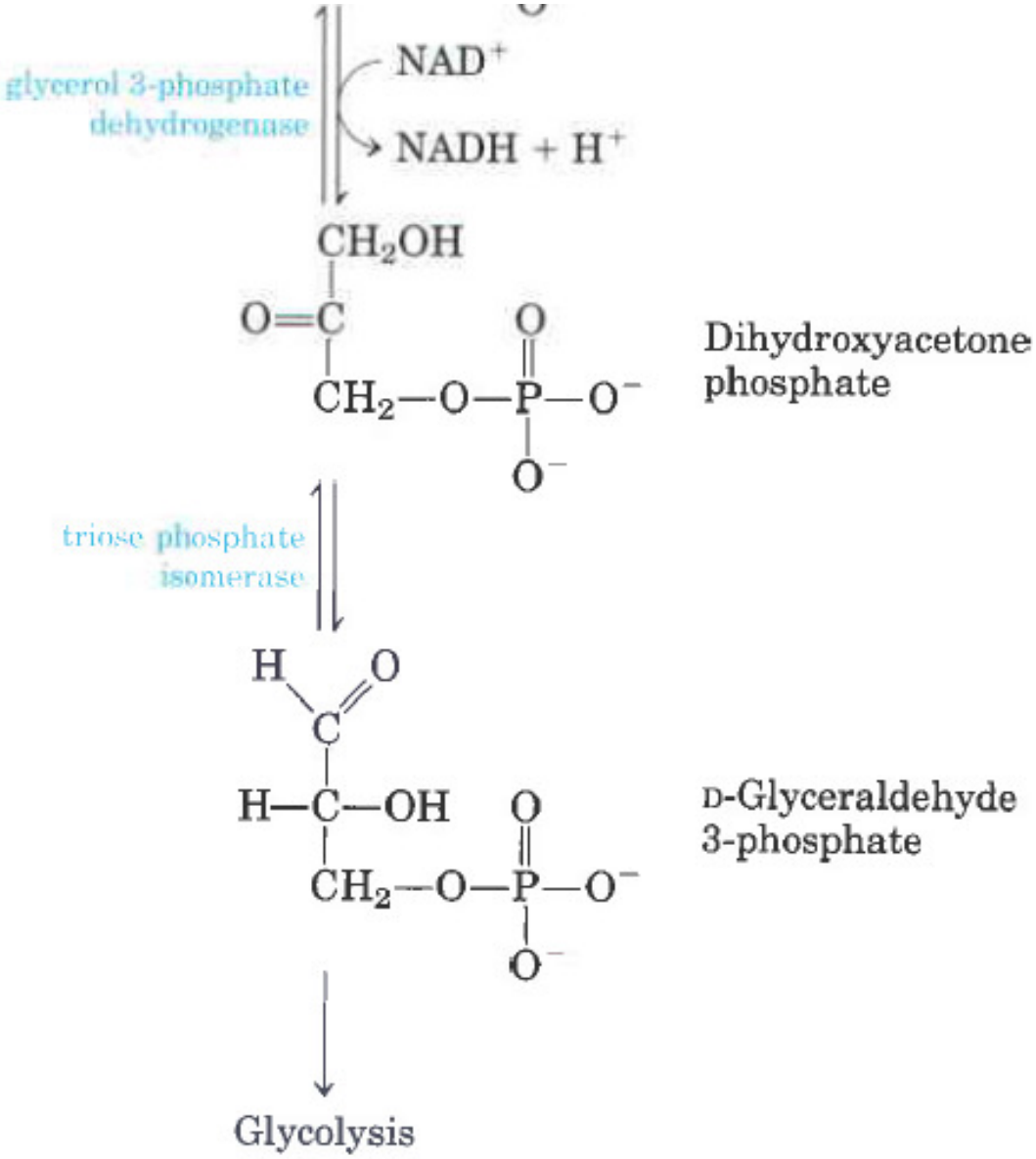
BETA OXIDATION/LIPIDS/ UG SEM 3 HONS/SDG

The initial event in the utilization offat as an energy source is the hydrolysis of triacylglycerols by lipases, an event referred to as ***lipolysis***.



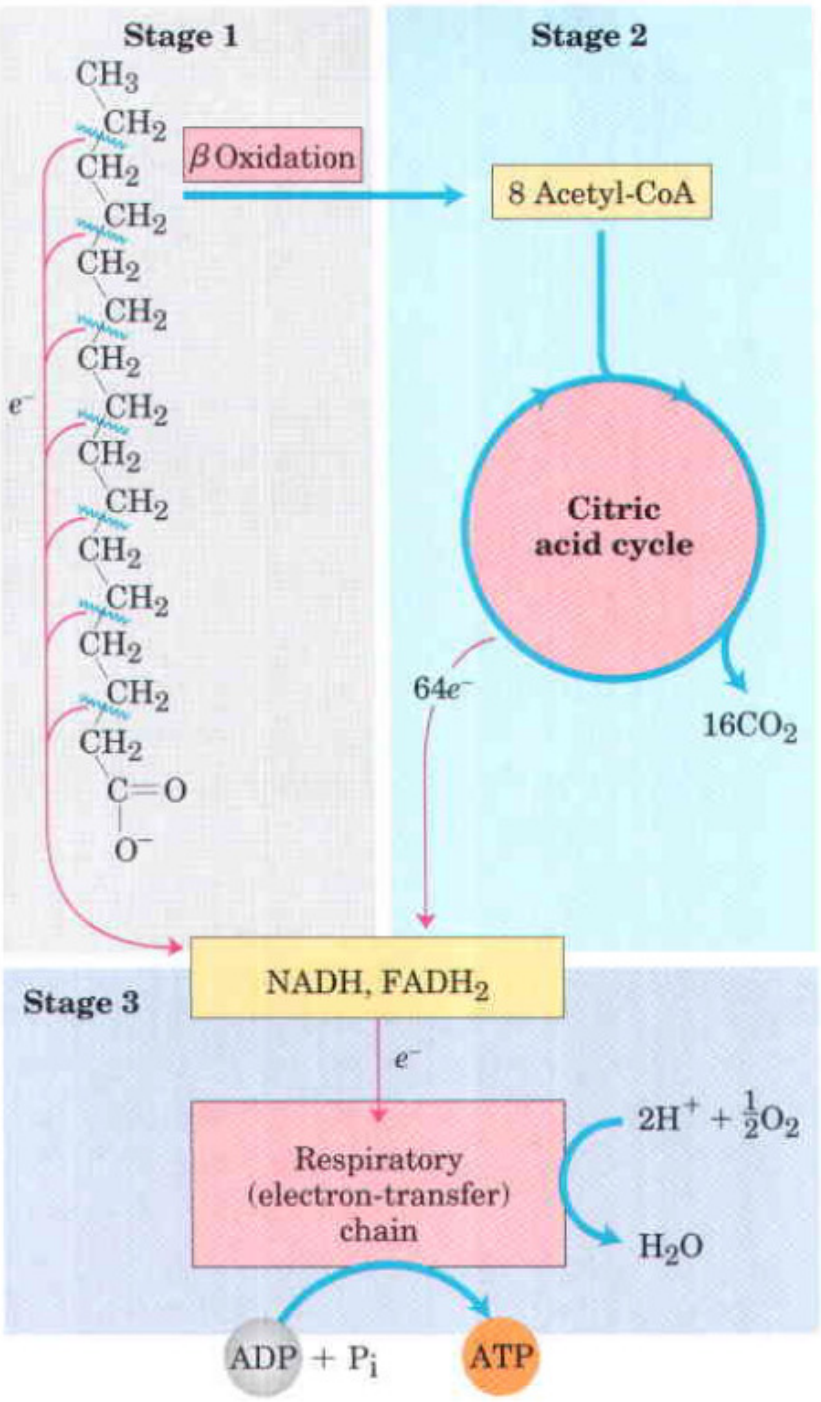


Entry of glycerol into the glycolytic pathway



Glycerol formed by lipolysis is absorbed by the liver and phosphorylated, oxidized to dihydroxyacetone phosphate, andthen isomerized to glyceraldehyde 3-phosphate.

This molecule is an intermediate in both theglycolytic and the gluconeogenic pathways.


Stage 1
Stage 2
CH_3
CH_2
β Oxidation
8 Acetyl-CoA
e^-
Citric acid cycle
$64e^-$
$16CO_2$
C=O
O^-
NADH, $FADH_2$
Stage 3
e^-
$2H^+ + \frac{1}{2}O_2$
Respiratory (electron-transfer) chain
H_2O
ADP + P_i
ATP

β-OXIDATION OF FATTY ACIDS

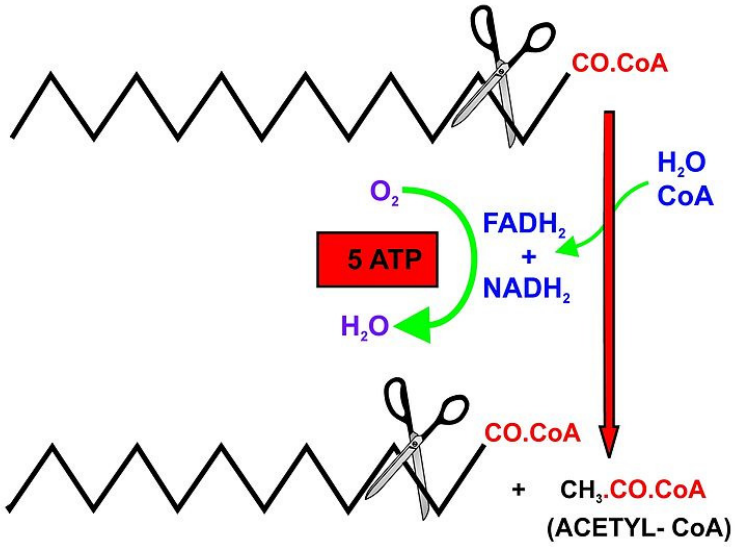
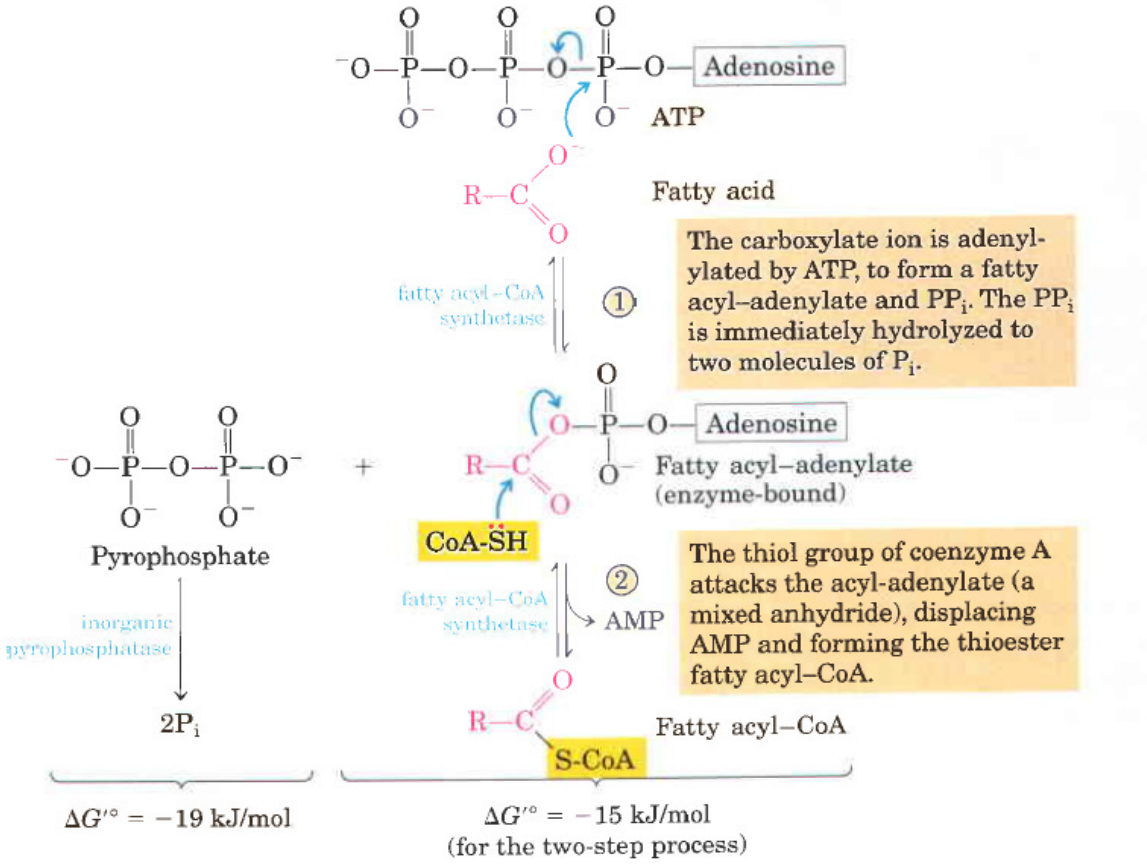


FIGURE 17–7 Stages of fatty acid oxidation. Stage 1: A long-chain fatty acid is oxidized to yield acetyl residues in the form of acetyl-CoA. This process is called β oxidation. Stage 2: The acetyl groups are oxidized to CO_2 via the citric acid cycle. Stage 3: Electrons derived from the oxidations of stages 1 and 2 pass to O_2 via the mitochondrial respiratory chain, providing the energy for ATP synthesis by oxidative phosphorylation.

Fatty Acids Are Activated and Transported into Mitochondria

- Fatty acid + CoA + ATP $\rightleftharpoons$ fatty acyl–CoA + AMP + PP_i



The overall reaction is

$$\text{Fatty acid} + \text{CoA} + \text{ATP} \longrightarrow \text{fatty acyl–CoA} + \text{AMP} + 2P_i \qquad (17\text{–}1)$$
$$\Delta G'^\circ = -34 \text{ kJ/mol}$$

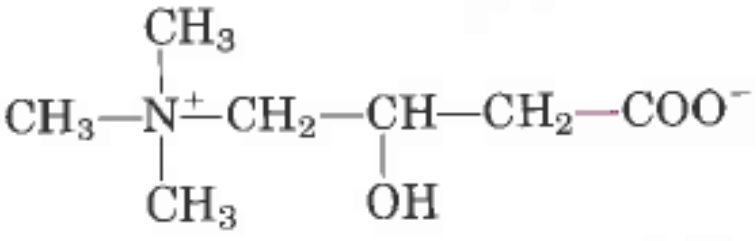
Activated fatty acids are oxidized in the mitochondrial matrix.

- A special transport mechanism is needed to carry long-chain acyl CoA

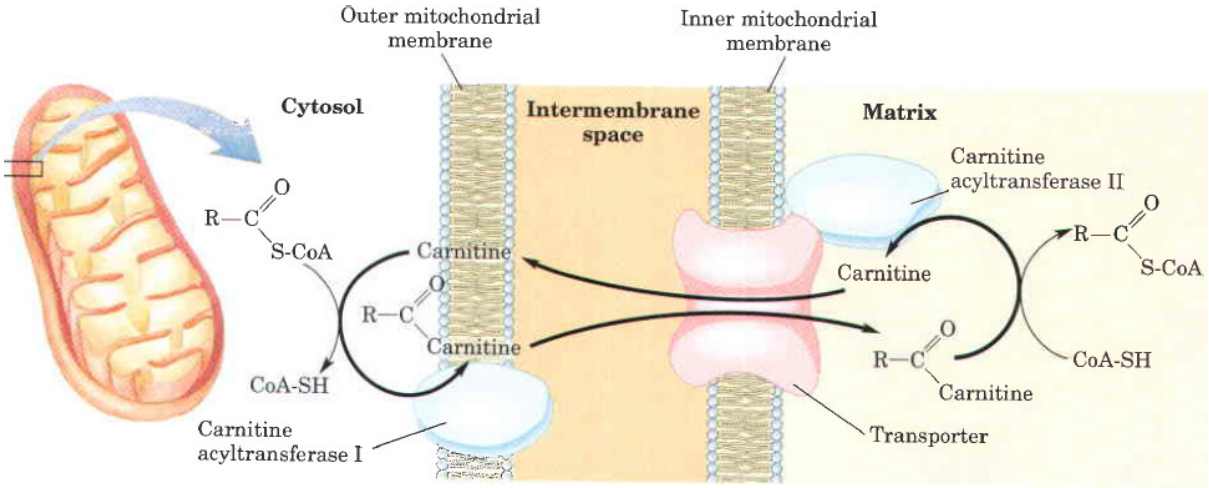
molecules across the inner mitochondrial membrane.

- Activated long-chain fatty acids are transported across the membrane by

conjugating them to *carnitine*, a zwitterionic alcohol.



Carnitine



Carnitine shuttle

Acyl carnitine is shuttled across the inner mitochondrial membrane by a translocase.

Finally, the translocase returns carnitine to the cytosolic side in exchange for an incoming acyl carnitine.

The β-oxidation pathway.

It consists of four steps,

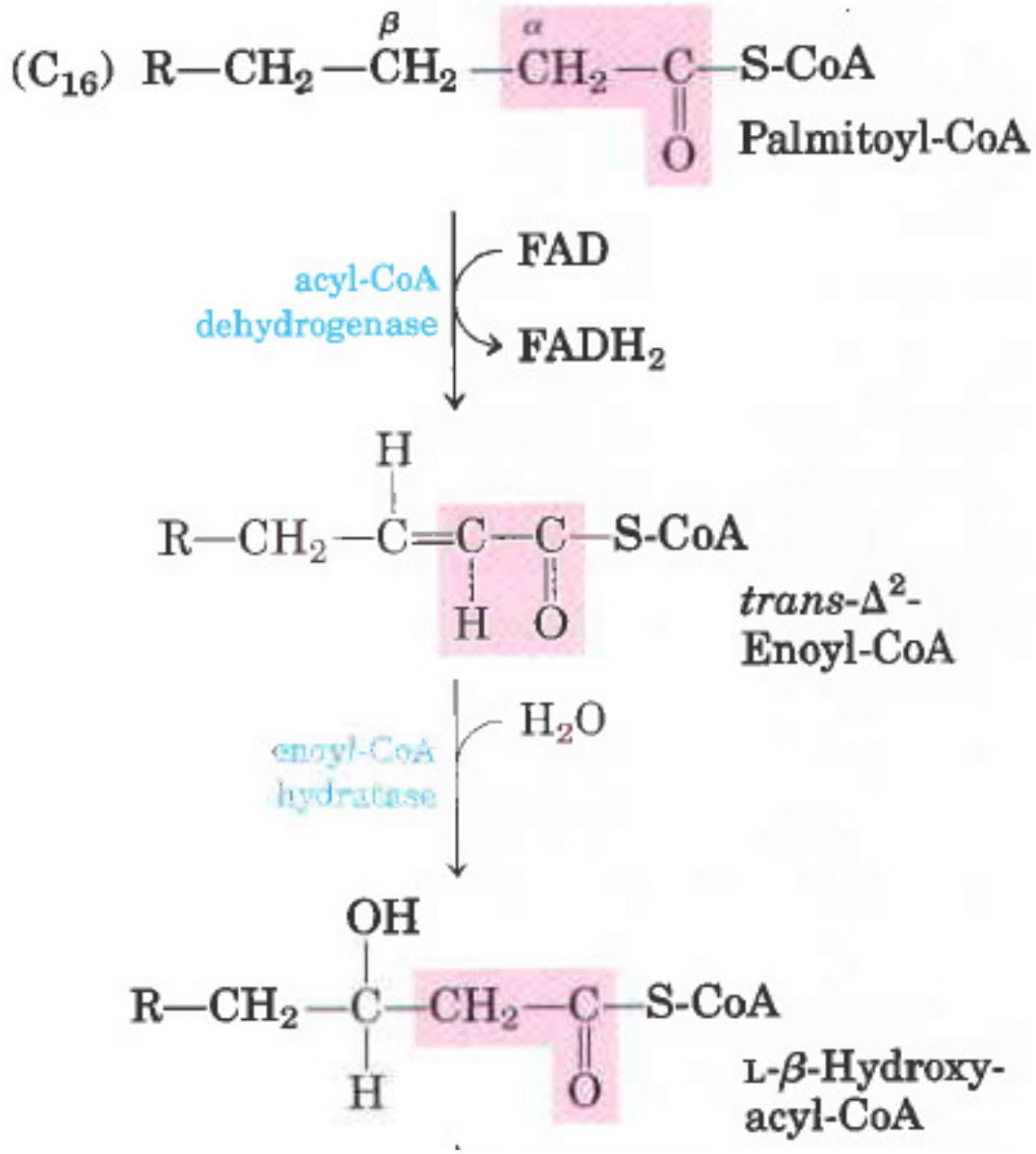
(1)dehydrogenation,

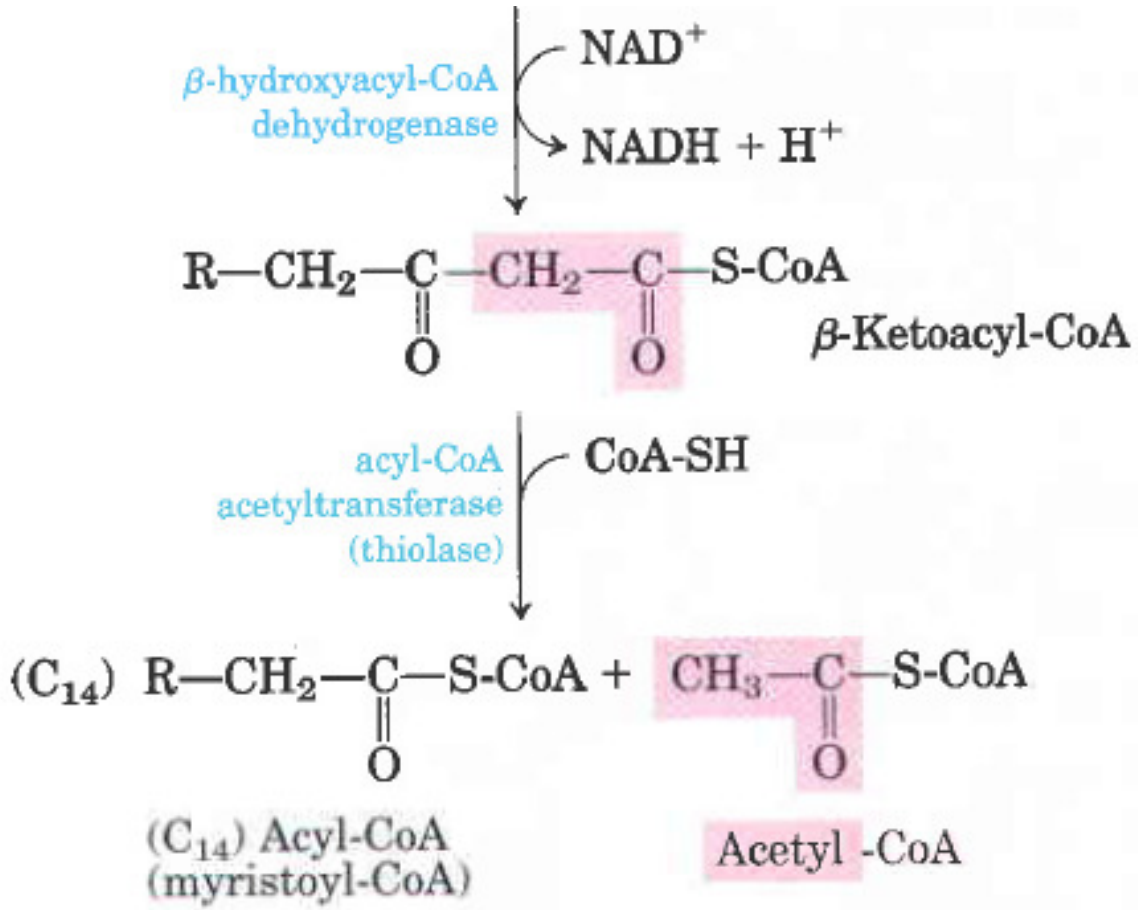
(2)addition of water to the resulting double bond,

(3)oxidation of the β-hydroxyacyl-CoA to a ketone,

(4)thiolytic cleavage by coenzyme A.

An activated fatty acid is oxidized to introduce a double bond;
The double bond is hydrated to introduce an oxygen;
The alcohol is oxidized to a ketone;
Finally, the four carbon fragment is cleaved by coenzyme A to yield acetyl CoA
and a fatty acid chain two carbons shorter.


(C16) R—CH2—CH2—CH2—C—S-CoA
β
α
O
Palmitoyl-CoA
acyl-CoA dehydrogenase
FAD
FADH2
H
R—CH2—C=C—C—S-CoA
H O
trans-Δ2-Enoyl-CoA
enoyl-CoA hydratase
H2O
OH
R—CH2—C—CH2—C—S-CoA
H O
L-β-Hydroxy-acyl-CoA


β-hydroxyacyl-CoA dehydrogenase
NAD+
NADH + H+
R—CH2—C—CH2—C—S-CoA
β-Ketoacyl-CoA
acyl-CoA acetyltransferase (thiolase)
CoA-SH
(C14) R—CH2—C—S-CoA + CH3—C—S-CoA
(C14) Acyl-CoA (myristoyl-CoA)
Acetyl -CoA

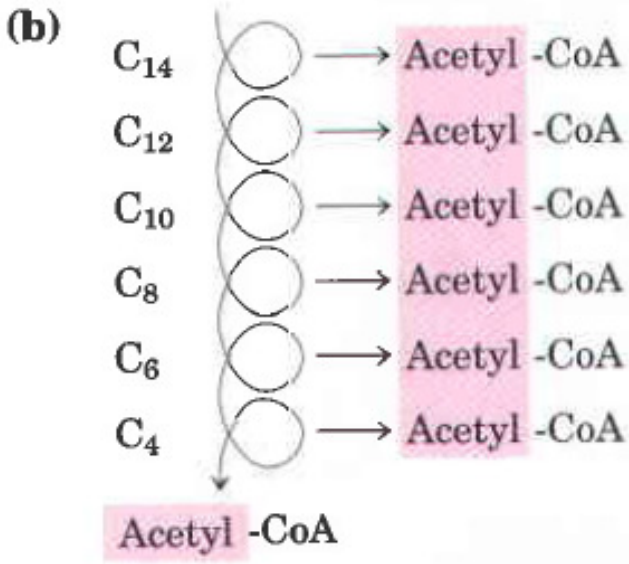


FIGURE 17–8 The β-oxidation pathway. **(a)** In each pass through this four-step sequence, one acetyl residue (shaded in pink) is removed in the form of acetyl-CoA from the carboxyl end of the fatty acyl chain—in this example palmitate (C_{16}), which enters as palmitoyl-CoA. **(b)** Six more passes through the pathway yield seven more molecules of acetyl-CoA, the seventh arising from the last two carbon atoms of the 16-carbon chain. Eight molecules of acetyl-CoA are formed in all.

$$\text{Palmitoyl-CoA} + 7\text{CoA} + 7\text{O}_2 + 28\text{P}_i + 28\text{ADP} \longrightarrow 8\ \text{acetyl-CoA} + 28\text{ATP} + 7\text{H}_2\text{O}$$