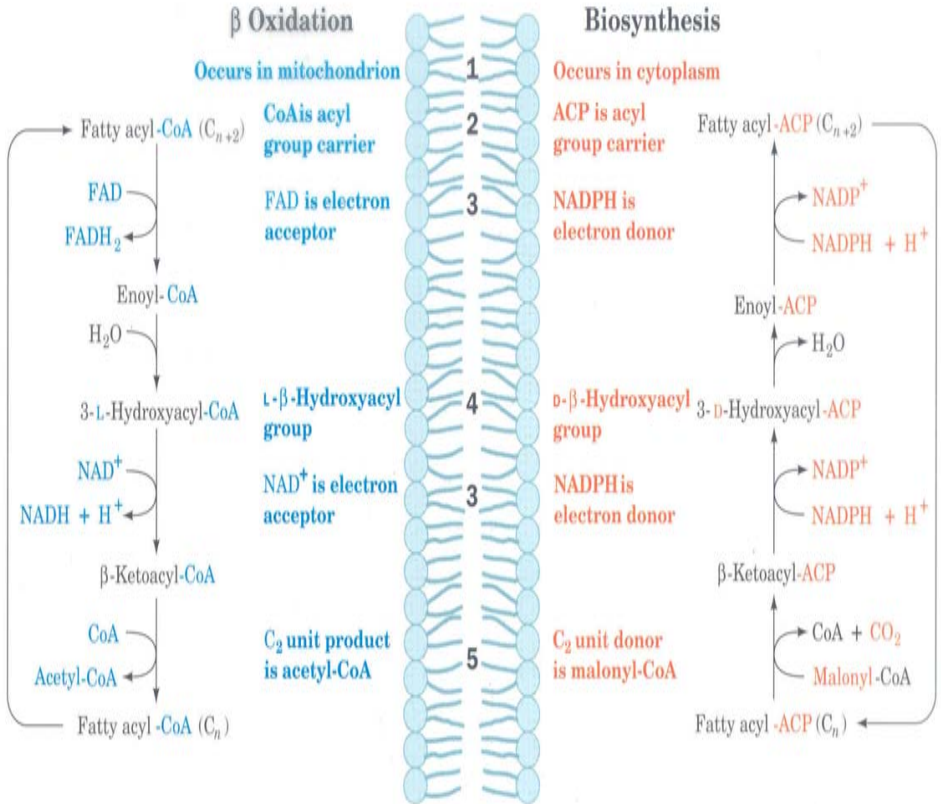
Lipid Metabolism

- Lipid nomenclature
- Oxidation of Fatty acids
- β-oxidation
- Ketone Bodies



Lipid nomenclature

- **Fatty acids**
- **triacylglycerols: know structure**
- **phospholipids**
- **waxes**
- **sphingolipids**
- **Glycosphingolipids**
- **Isoprenoids**
- **Steriods**
- **Nomenclature**
- **saturated: palmitate, stearate, no double bonds**
- **unsaturated: palmitoleate, Oleate: double bond at cis 9 position**
- **polyunsaturated**
- **Melting points: saturated vs unsaturated**

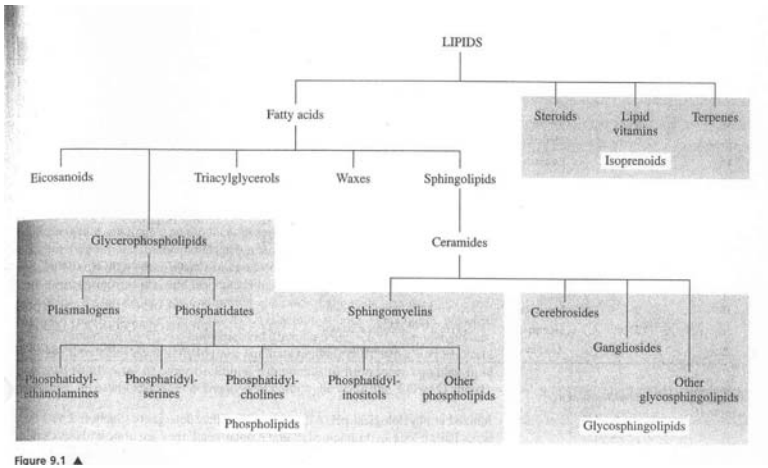


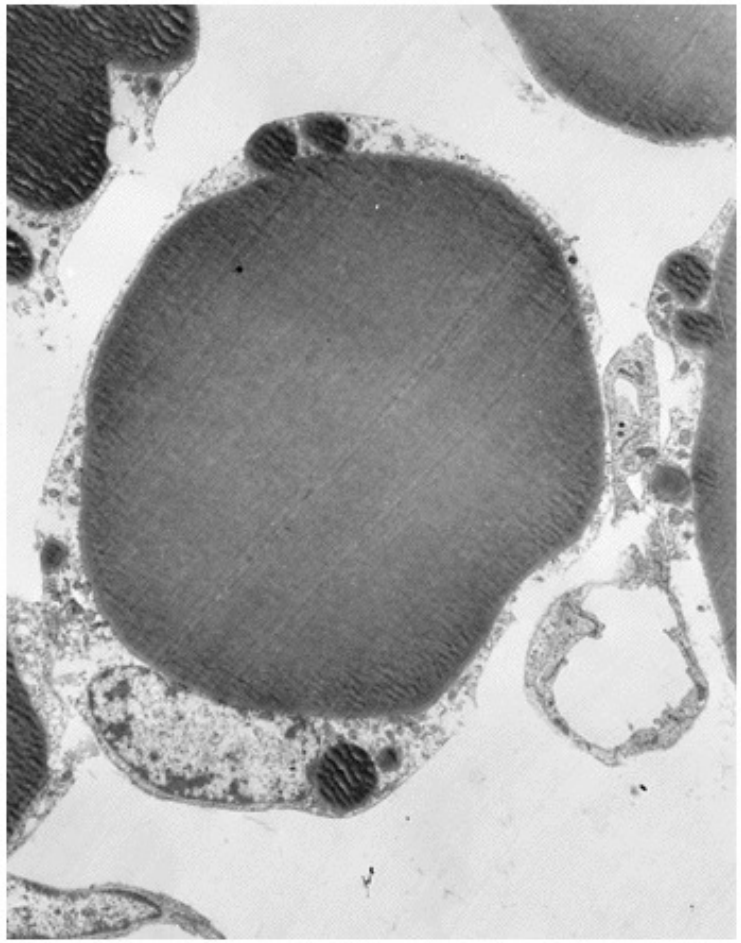
Figure 9.1 ▲

TABLE 9.1 Some common fatty acids (anionic forms)

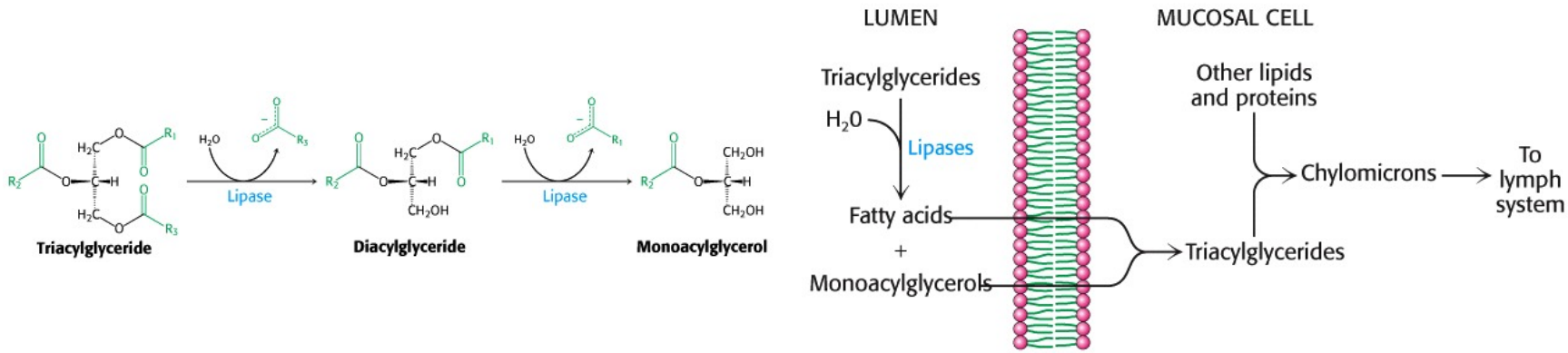
Number of carbons	Number of double bonds	Common name	IUPAC name	Melting point, °C	Molecular formula
12	0	Laurate	Dodecanoate	44	$CH_3(CH_2)_{10}COO^{\ominus}$
14	0	Myristate	Tetradecanoate	52	$CH_3(CH_2)_{12}COO^{\ominus}$
16	0	Palmitate	Hexadecanoate	63	$CH_3(CH_2)_{14}COO^{\ominus}$
18	0	Stearate	Octadecanoate	70	$CH_3(CH_2)_{16}COO^{\ominus}$
20	0	Arachidate	Eicosanoate	75	$CH_3(CH_2)_{18}COO^{\ominus}$
22	0	Behenate	Docosanoate	81	$CH_3(CH_2)_{20}COO^{\ominus}$
24	0	Lignocerate	Tetracosanoate	84	$CH_3(CH_2)_{22}COO^{\ominus}$
16	1	Palmitoleate	*cis*-Δ^9-Hexadecenoate	−0.5	$CH_3(CH_2)_5CH{=}CH(CH_2)_7COO^{\ominus}$
18	1	Oleate	*cis*-Δ^9-Octadecenoate	13	$CH_3(CH_2)_7CH{=}CH(CH_2)_7COO^{\ominus}$
18	2	Linoleate	*cis*, *cis*-$\Delta^{9,12}$-Octadecadienoate	−9	$CH_3(CH_2)_4(CH{=}CHCH_2)_2(CH_2)_6COO^{\ominus}$
18	3	Linolenate	all *cis*-$\Delta^{9,12,15}$-Octadecatrienoate	−17	$CH_3CH_2(CH{=}CHCH_2)_3(CH_2)_6COO^{\ominus}$
20	4	Arachidonate	all *cis*-$\Delta^{5,8,11,14}$-Eicosatetraenoate	−49	$CH_3(CH_2)_4(CH{=}CHCH_2)_4(CH_2)_2COO^{\ominus}$

Oxidation of Fatty acids

- **Know equation for palmitate: $C_{16}H_{32}O + O_2 \rightarrow CO_2 + H_2O$**
- **Comparison of glucose with palmitate for ATP production and energy yield**
- **Mobilization of Triacylglycerols from adipose tissue**
  - **hormonal control: glucagon, epinephrine**
  - **lipases**
  - **transport by lipoproteins**
  - **fate of glycerol**
- **transport into cytoplasm of cell**



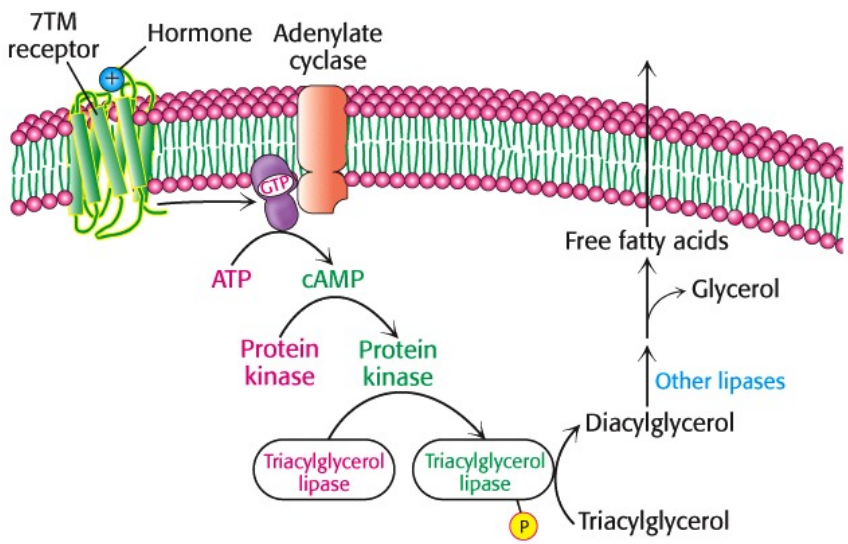
Digestion of lipid in diet



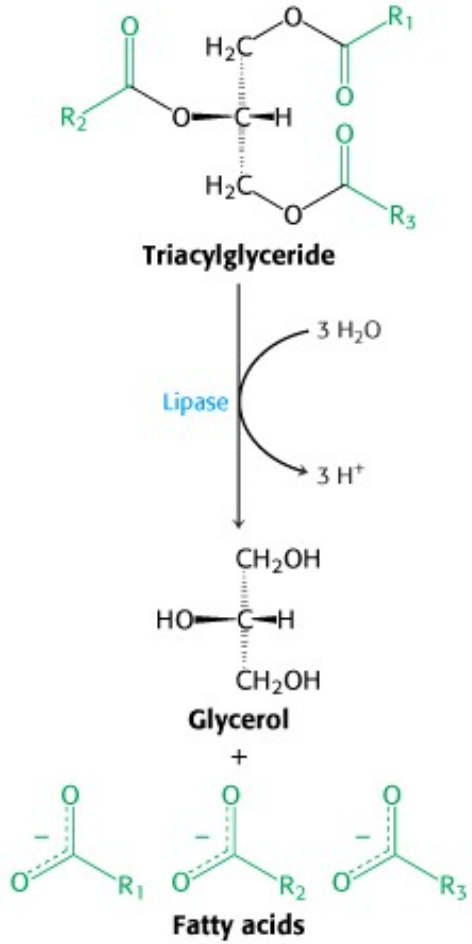
- **Triacylglycerols from diet**
- **broken down in small intestine**
- **lipases**
- **bile salts**
- **transport to adipose tissue**

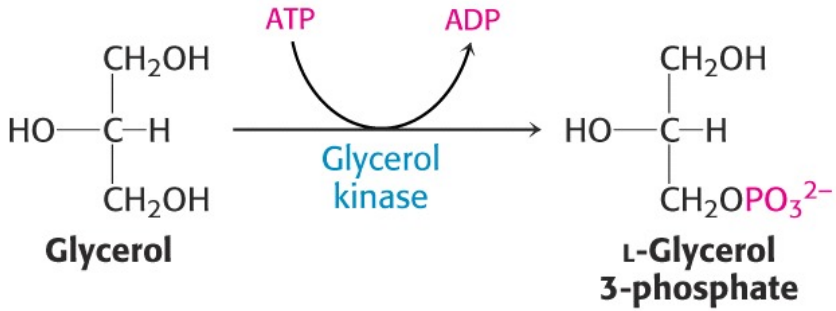
Mobilization of Triacylglycerols

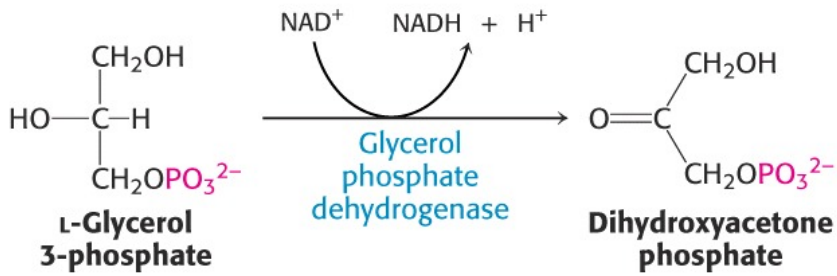
- hormonal control of lipolysis: glucagon, epinephrine
- lipases
- transport by lipoproteins
- transport into cytoplasm of cell
- Insulin inhibits lipolysis



Breakdown of triacylglycerides



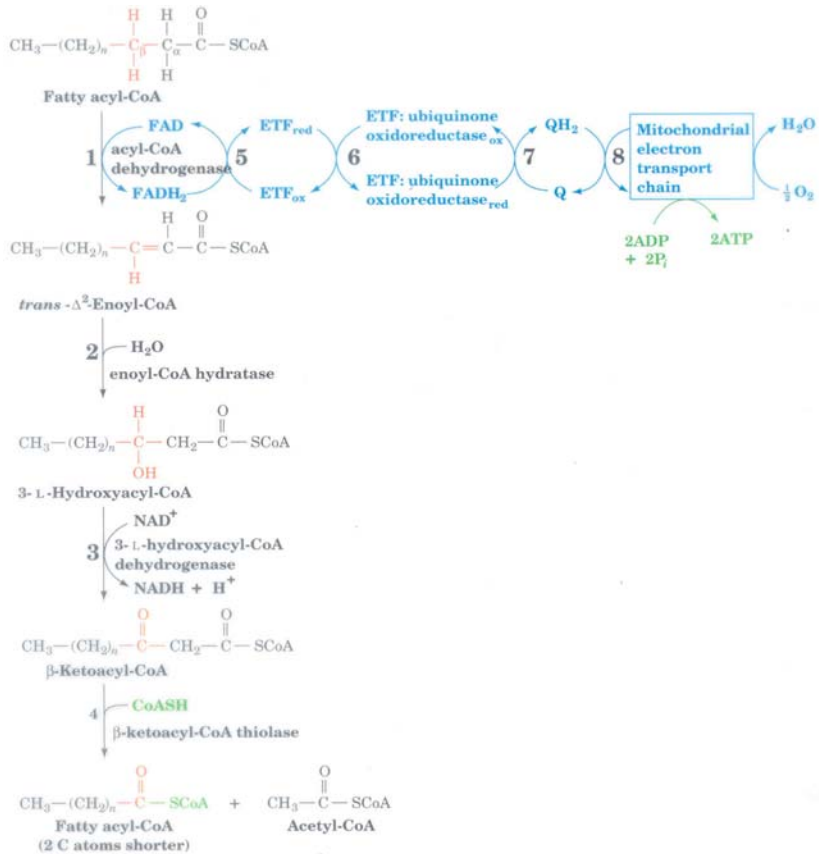




fate of glycerol

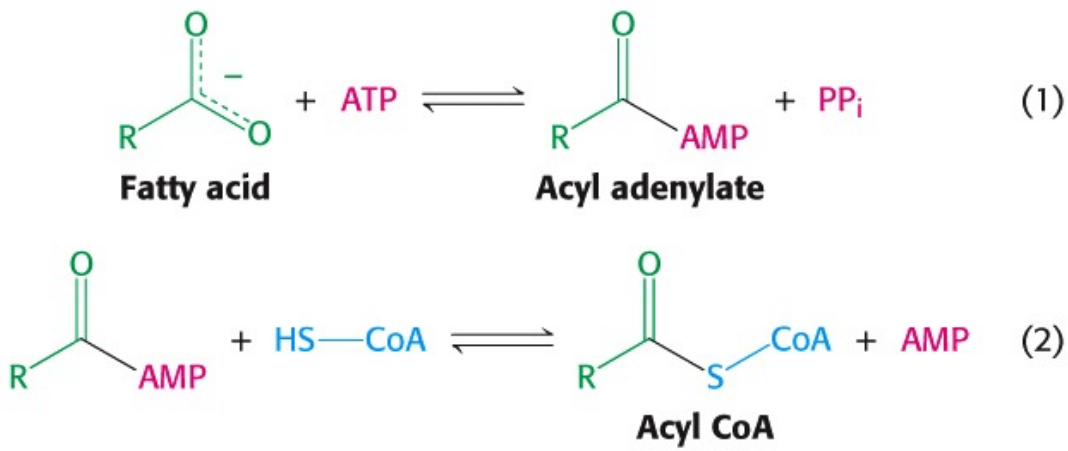
β-oxidation

- occurs in mitochondria
- uses FAD and NAD
- produces acetyl CoA



acyl CoA synthetase

- two step reaction
- ATP + FA ---> AMP-FA
- AMP-FA + CoASH ------> FA-CoA + AMP



Transport into mitochondria

- Carnitine shuttle
- CAT I/II
- Translocase reaction

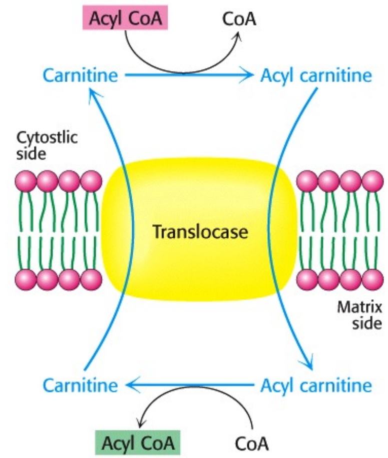
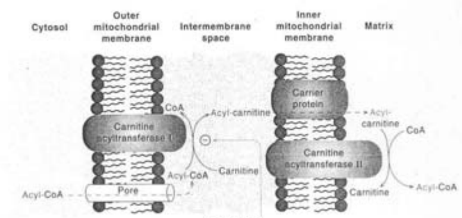


Figure 18.21

Acyl-CoA is not transported across the inner membrane of the mitochondrion. Instead, the acyl-CoA reacts with carnitine to yield the acyl-carnitine derivative. This reaction is catalyzed by carnitine acyltransferase I, which is located on the outer mitochondrial membrane. The acyl-carnitine is transported across the inner membrane by a specific carrier protein. Once inside the matrix of the mitochondrion, the acyl-carnitine is converted back to its acyl-CoA derivative, the substrate for the start of β oxidation. This reaction catalyzed by carnitine acyltransferase II, which is located on the mitochondrial inner membrane. Note that acyltransferases I and II oriented in their respective membranes so that the reactions they catalyze occur in intermembrane space and the mitochondrial ma respectively. The carnitine is also transferred by the carrier prote



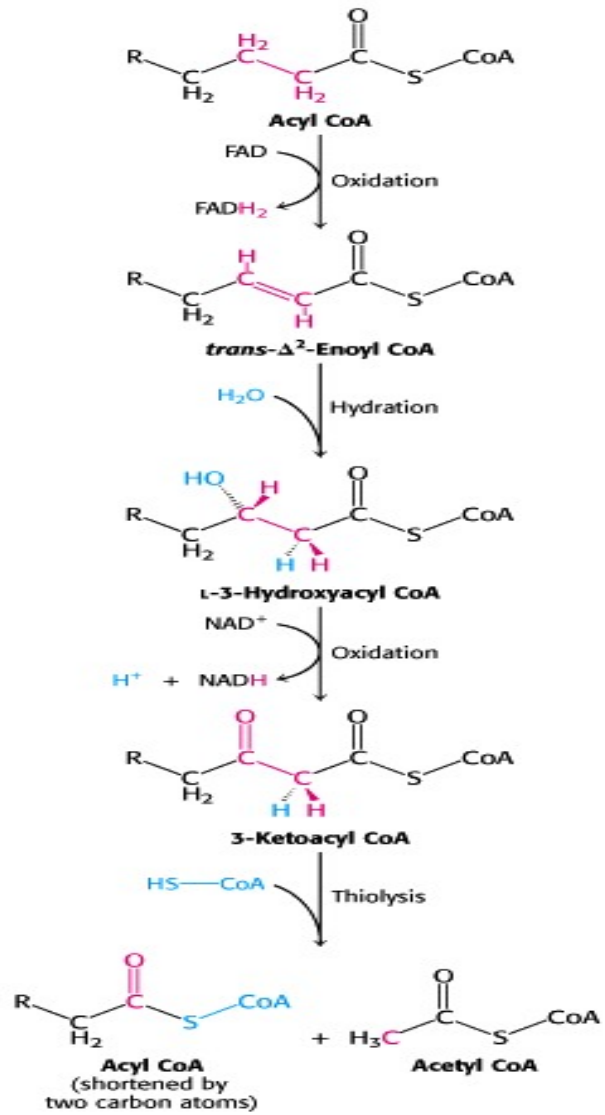
$$RCOCoA + (CH_3)_3N^+{-}CH_2\underset{\substack{|\\ OH}}{C}HCH_2COO^- \rightleftharpoons$$

Carnitine

$$(CH_3)_3N^+{-}CH_2CHCH_2COO^- + CoA \quad (4)$$

β-oxidation

- Acyl CoA dehydrogenase
- enoyl-CoA hydratase
- L-hydroxyacyl dehydrogenase
- ketoacyl-CoA thiolase
- Repeat steps



Summary of Reactions

TABLE 22.1 **Principal reactions in fatty acid oxidation**

Step	Reaction	Enzyme
1	Fatty acid + CoA + ATP $\rightleftharpoons$ acyl CoA + AMP + PP_i	Acyl CoA synthetase [also called fatty acid thiokinase and fatty acid:CoA ligase (AMP)]
2	Carnitine + acyl CoA $\rightleftharpoons$ acyl carnitine + CoA	Carnitine acyltransferase (also called carnitine palmitoyl transferase)
3	Acyl CoA + E-FAD $\longrightarrow$ *trans*-Δ^2-enoyl CoA + E-$FADH_2$	Acyl CoA dehydrogenases (several isozymes having different chain-length specificity)
4	*trans*-Δ^2-Enoyl CoA + H_2O $\rightleftharpoons$ L-3-hydroxyacyl CoA	Enoyl CoA hydratase (also called crotonase or 3-hydroxyacyl CoA hydrolyase)
5	L-3-Hydroxyacyl CoA + NAD^+ $\rightleftharpoons$ 3-ketoacyl CoA + NADH + H^+	L-3-Hydroxyacyl CoA dehydrogenase
6	3-Ketoacyl CoA + CoA $\rightleftharpoons$ acetyl CoA + acyl CoA (shortened by C_2)	β-Ketothiolase (also called thiolase)

Energy production

- NADH and FADH from B-oxidation
- TCA cycle from acetyl CoA
- Total net yield is minus 2 ATP from activation

Table 18-1 The Yields of ATP in the Oxidative Steps during Oxidation of One *Molecule of Palmitoyl-CoA to* $CO_2 + H_2O$

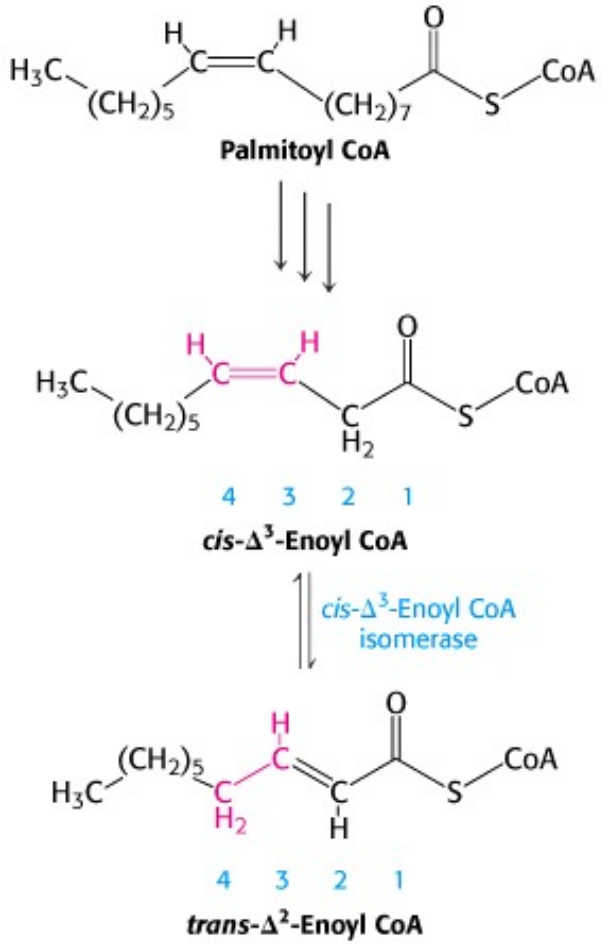
	NAD-linked *steps*	FAD-linked *steps*	ATP
Acyl-CoA dehydrogenase		7	14
3-Hydroxyacyl-CoA dehydrogenase	7		21
Isocitrate dehydrogenase	8		24
α-Ketoglutarate dehydrogenase	8		24
Succinyl-CoA synthetase†			8
Succinate dehydrogenase		8	16
Malate dehydrogenase	8		24
Total ATP formed			131

† Assuming that the GTP formed reacts with ADP to yield ATP.

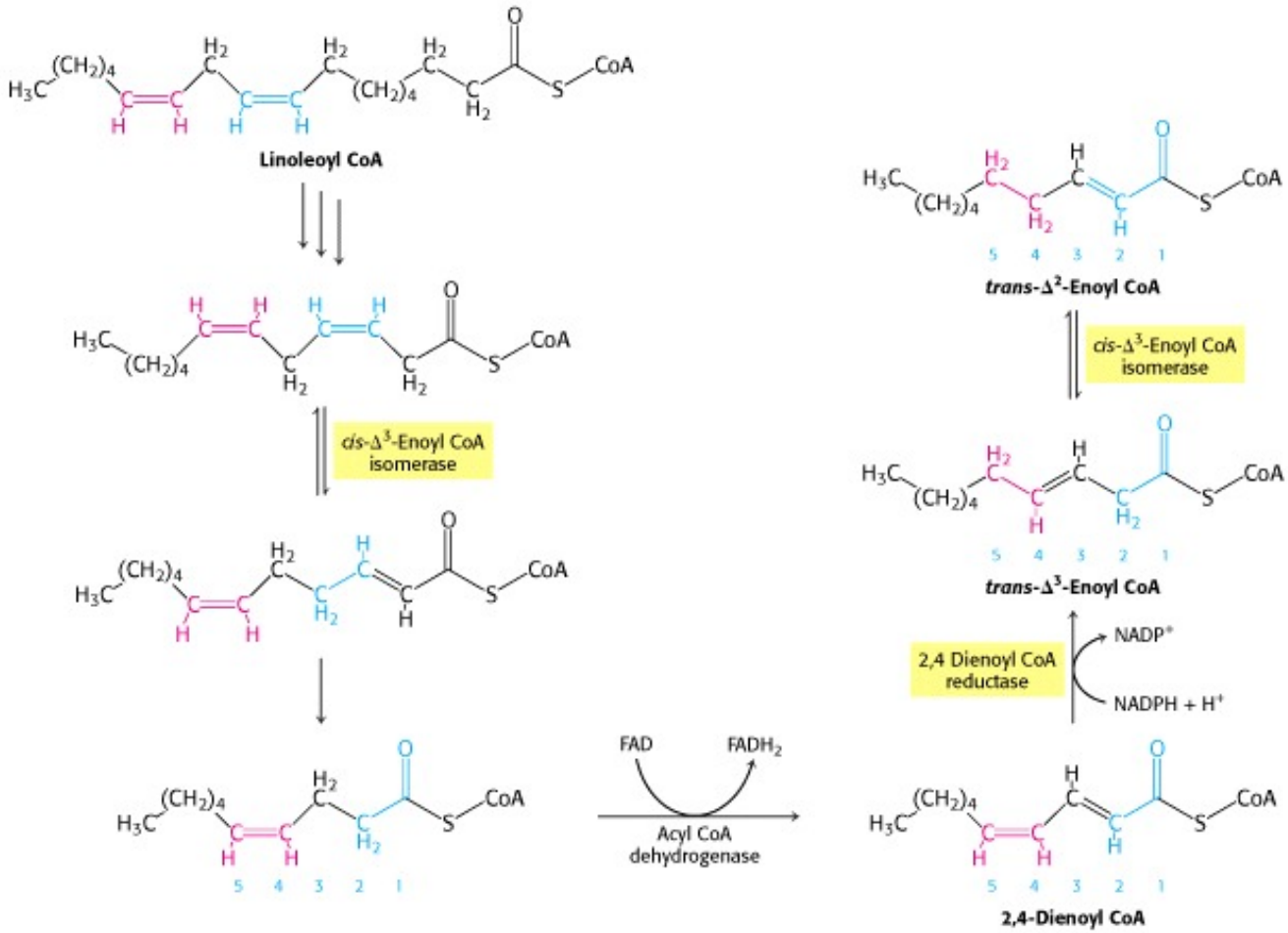
$$\text{Palmitoyl-S-CoA} + 23O_2 + 131P_i + 131\text{ADP} \longrightarrow \text{CoA-SH} + 131\text{ATP} + 16CO_2 + 146H_2O \quad (6)$$

Oxidation of Unsaturated Fatty acids

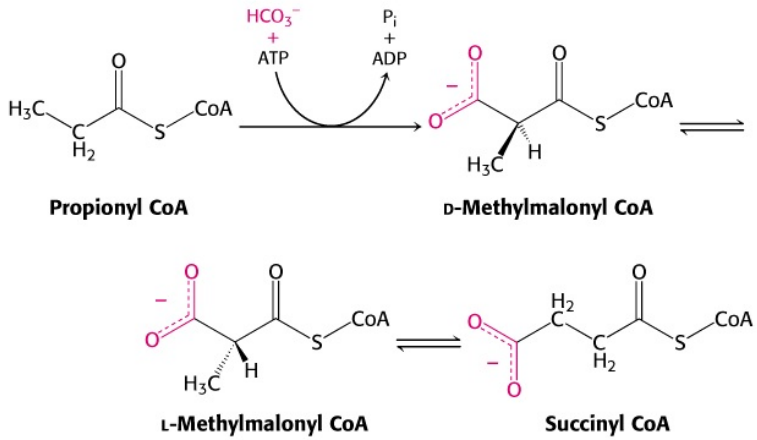
- New enzymes
- enoyl CoA isomerase
- 2,4 dienoyl-CoA reductase



Unsaturated Fatty acids

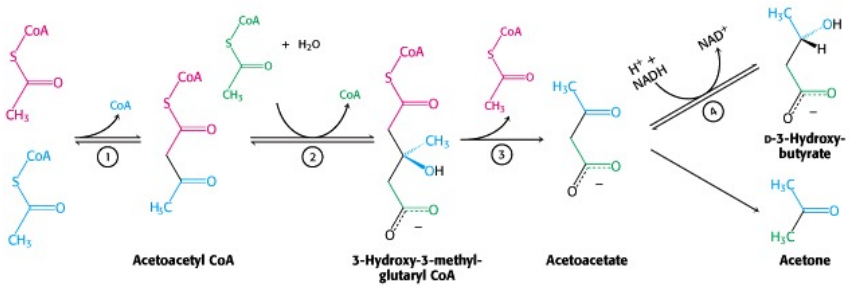


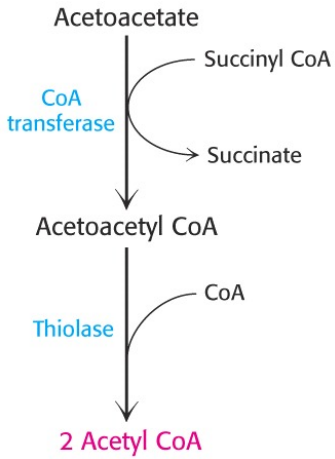
Oxidation of odd chain fatty acids



- form propionyl CoA
- produce succinyl CoA

Ketone Bodies





- Acetoacetate
- Acetone
- B-hyroxybutyrate
- HMG CoA synthase

Ketone bodies and diabetes

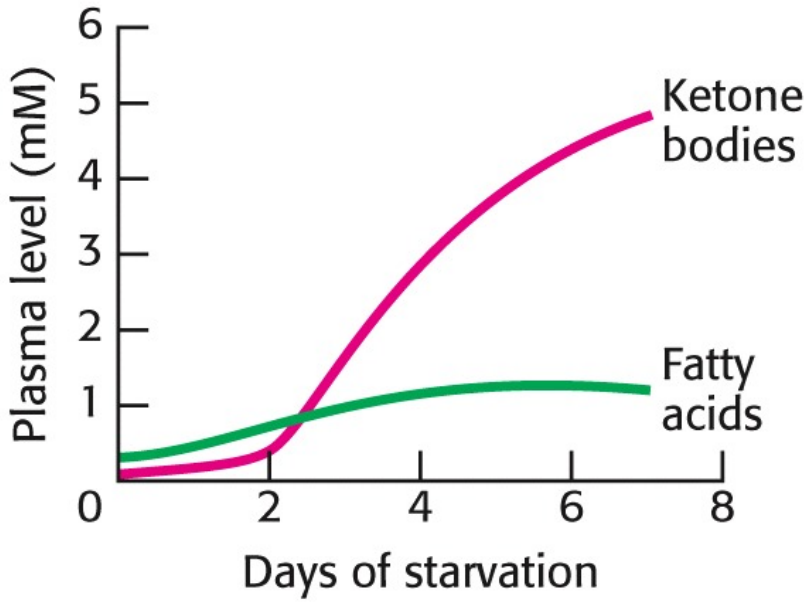


Table 16–2 Ketone body accumulation in diabetic ketosis

	Urinary excretion (mg/24 h)	Blood concentration (mg/100 mL)
Normal	≤125	<3
Extreme ketosis (untreated diabetic)	5,000	90