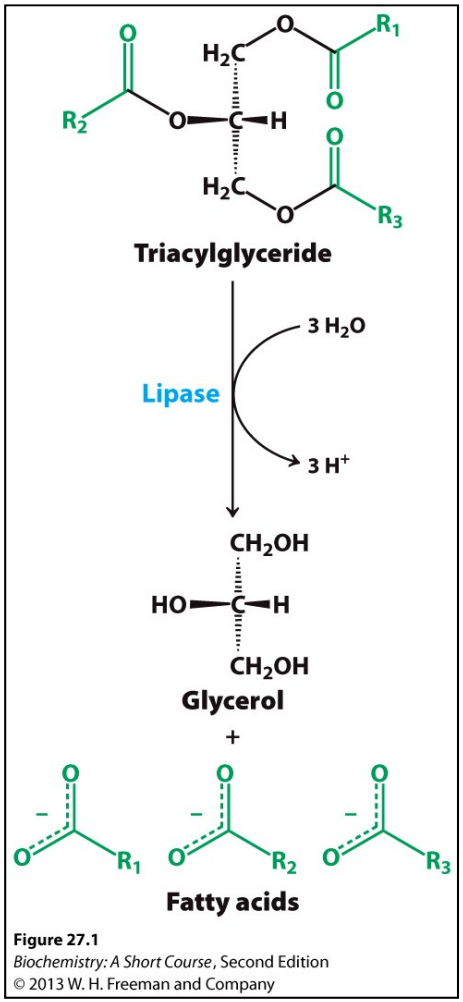
CHAPTER 27: Fatty Acid Degradation

(Problems: 1,6,8,9,11,12,14,17-21,23,31)

27.1: Fatty Acids are Processed in Three Stages

1. Mobilization of lipids. Degradation of TAGs to FAs and glycerol.
2. Activation of Fas.
3. Oxidation of FAs to acetyl-CoA, and processing by CAC.

Lipase Hydrolysis of TAGs



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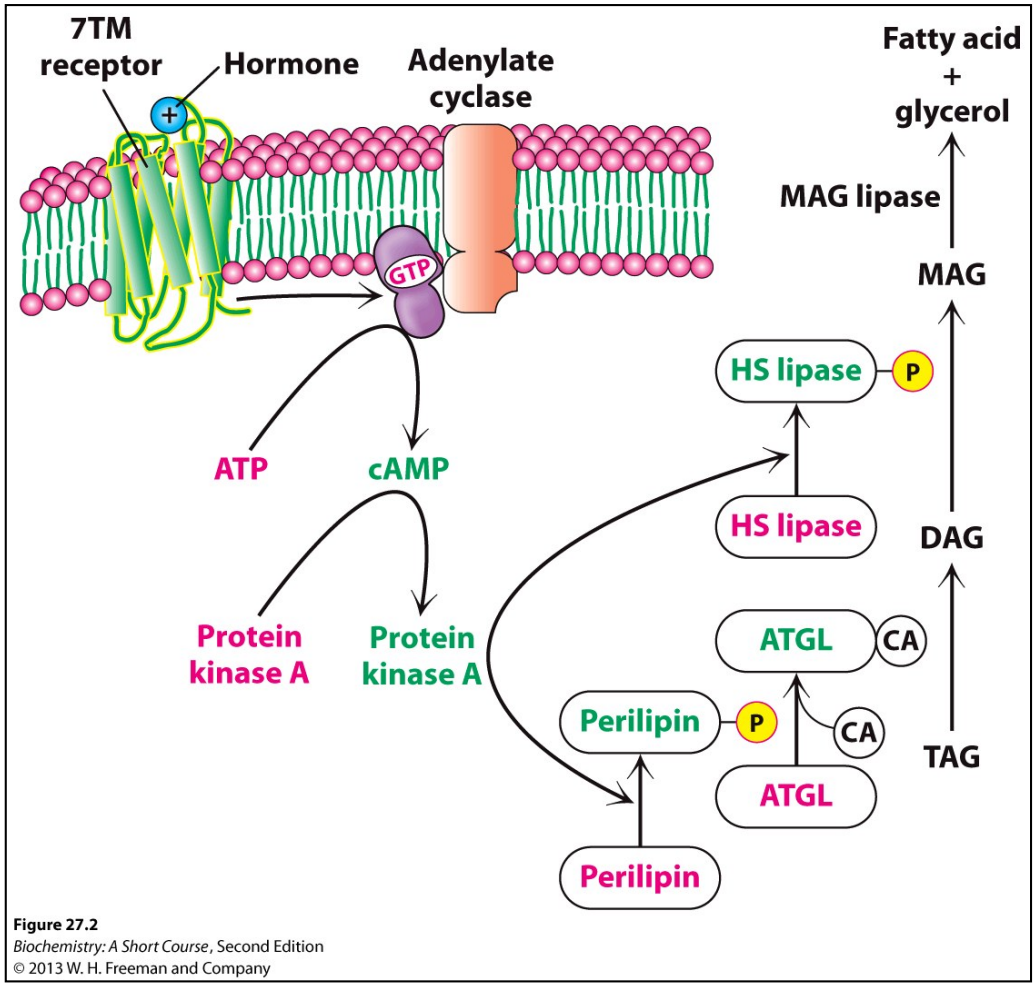

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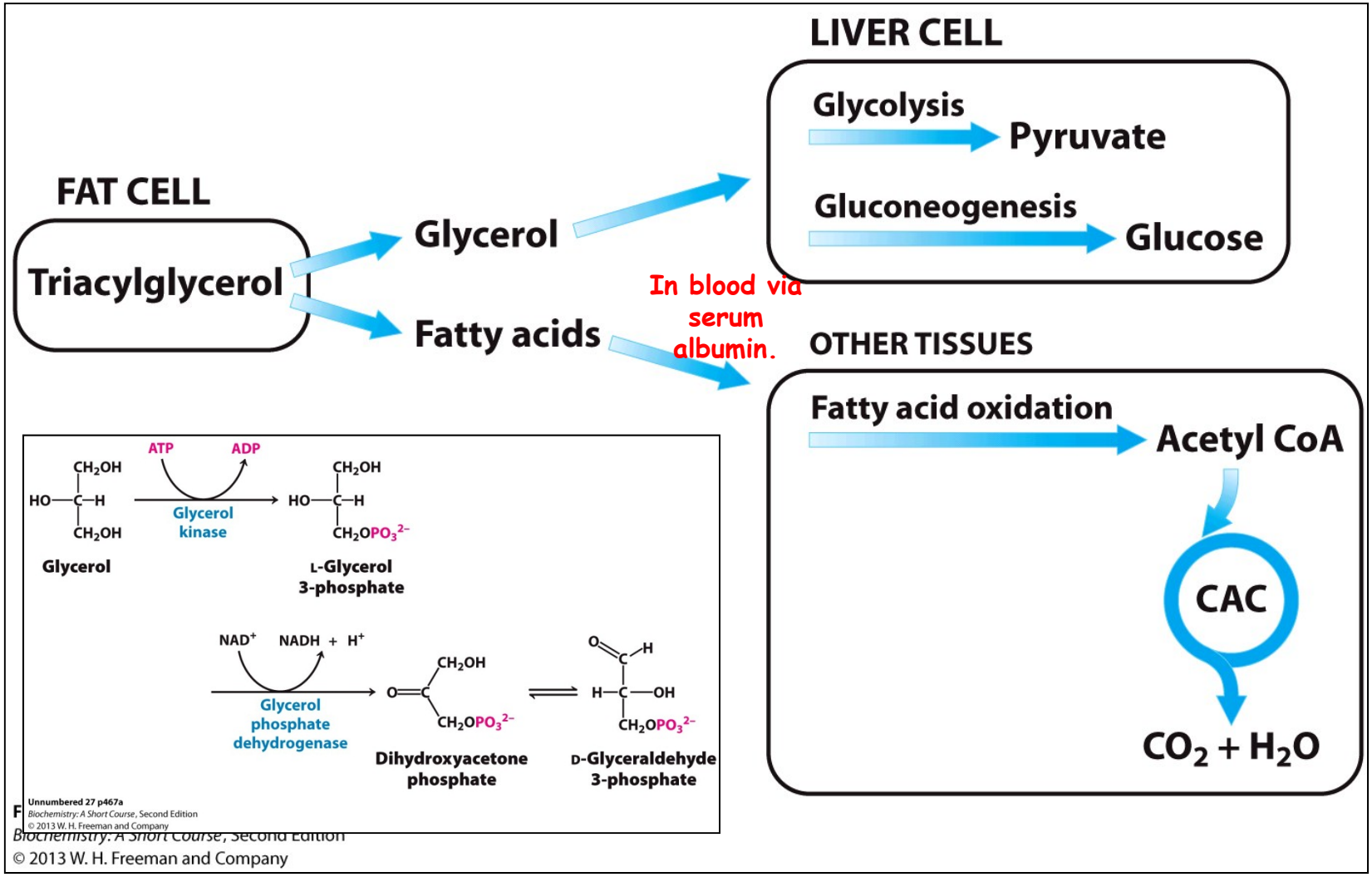
Perilipin: mobilization of TAGs, and release of ATGL co-activator (CA).

ATGL: Adipose triglyceride lipase. Hydrolysis of one FA from TAG to produce DAG + FA.

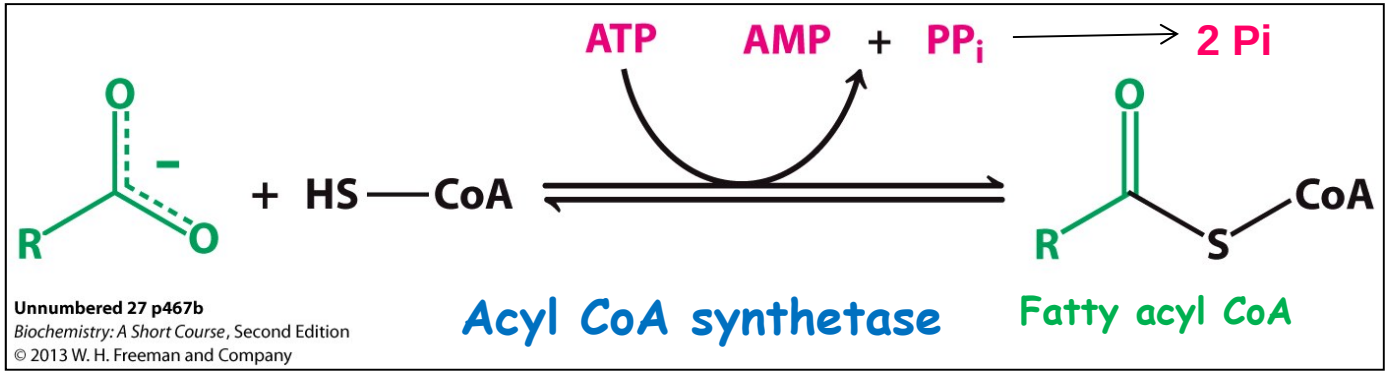
HS-lipase: Hormone sensitive lipase. Hydrolysis of FA from DAG to produce MAG + FA.

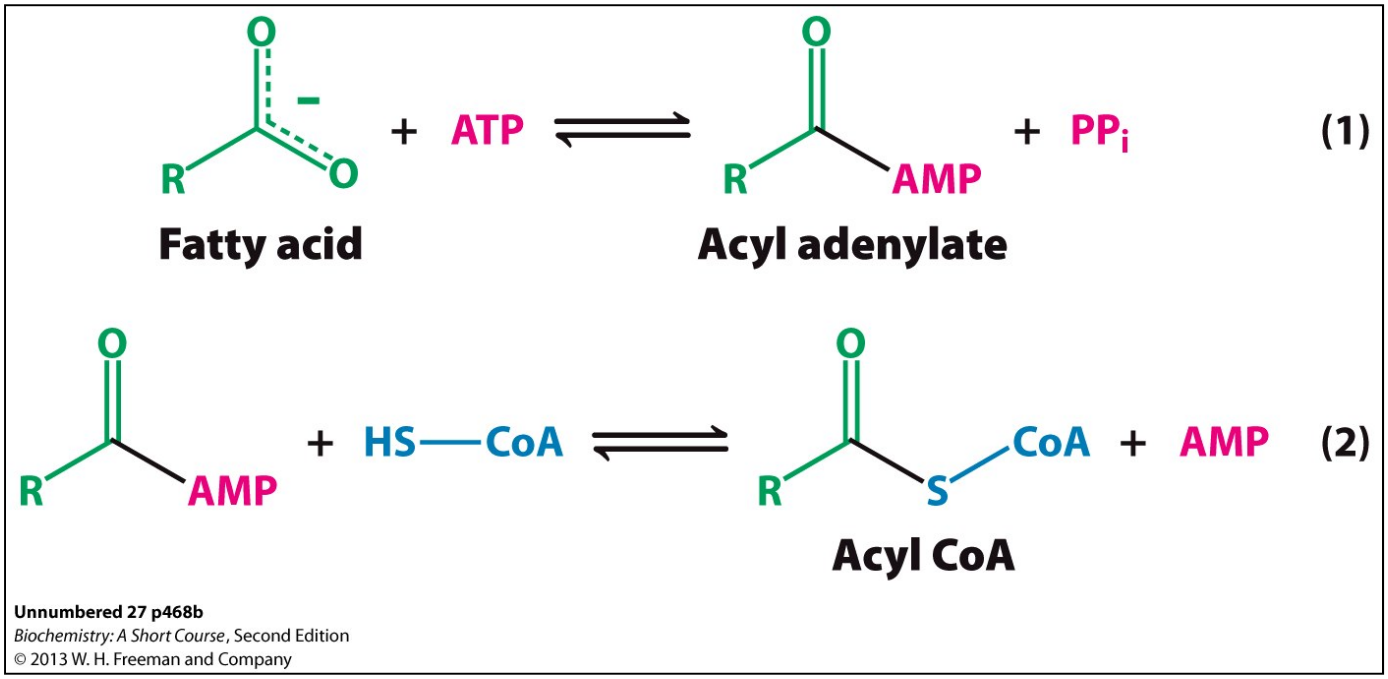
MAG lipase: Hydrolysis of remaining FA from MAG to produce glycerol and FA.

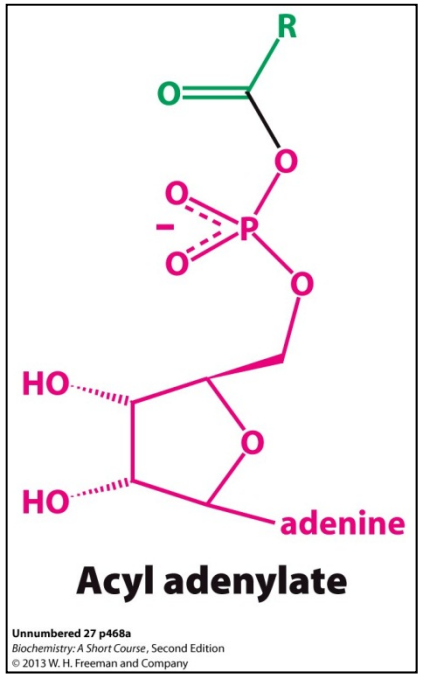
Distribution of FAs and Glycerol



Activation of FAs

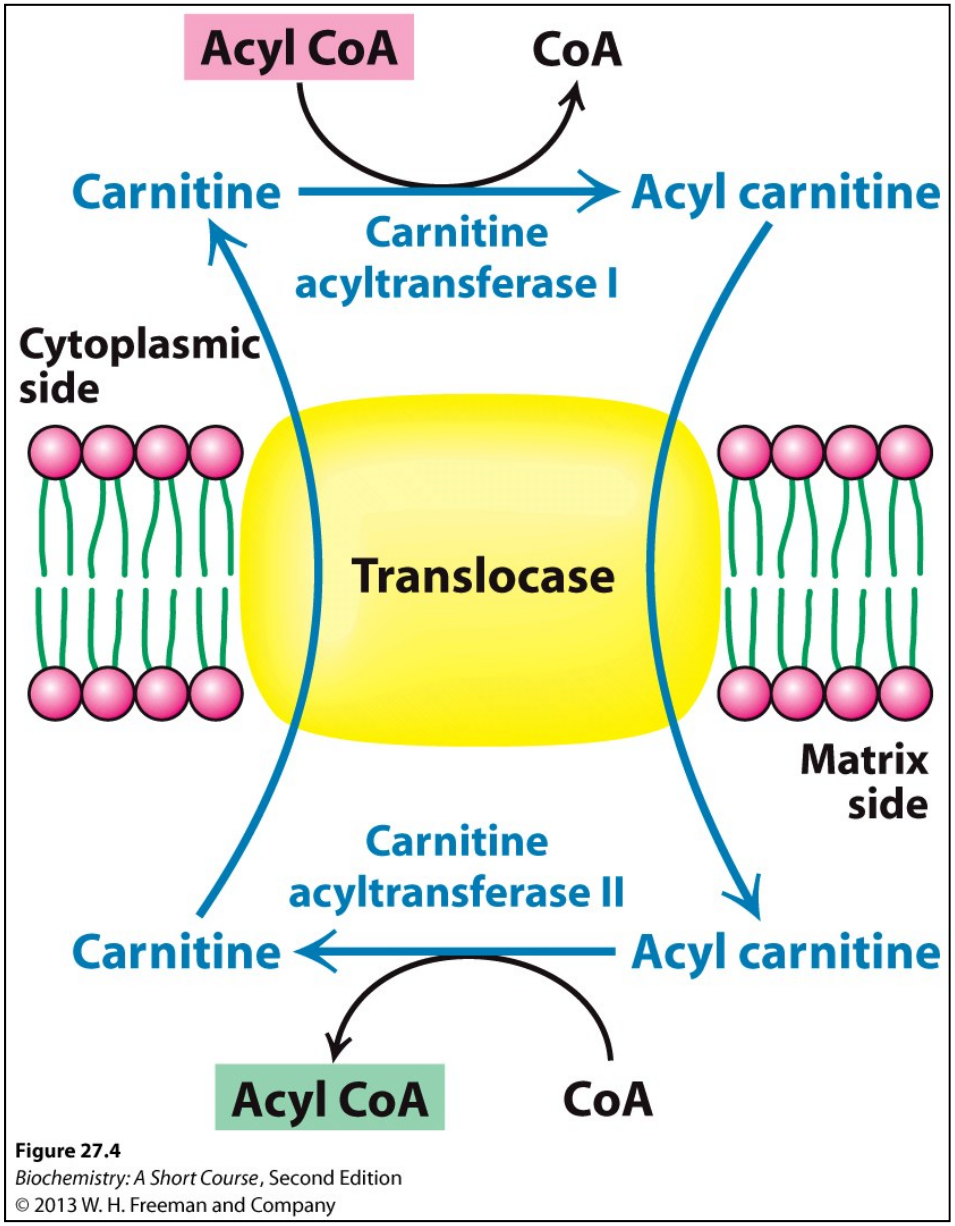






Equivalent to the hydrolysis of 2 ATP.

Transport to Mitochondria



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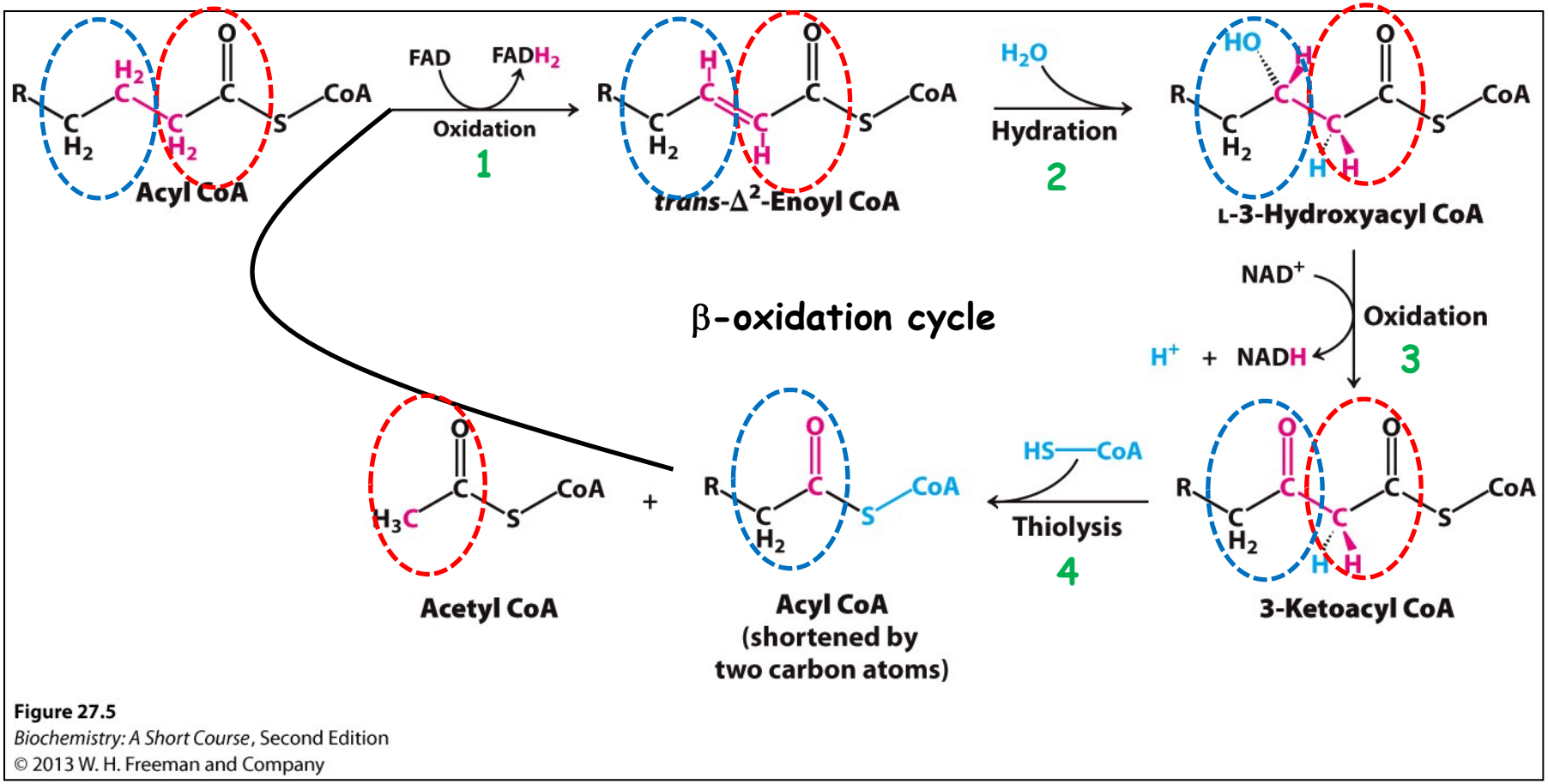
Fatty Acid Oxidation



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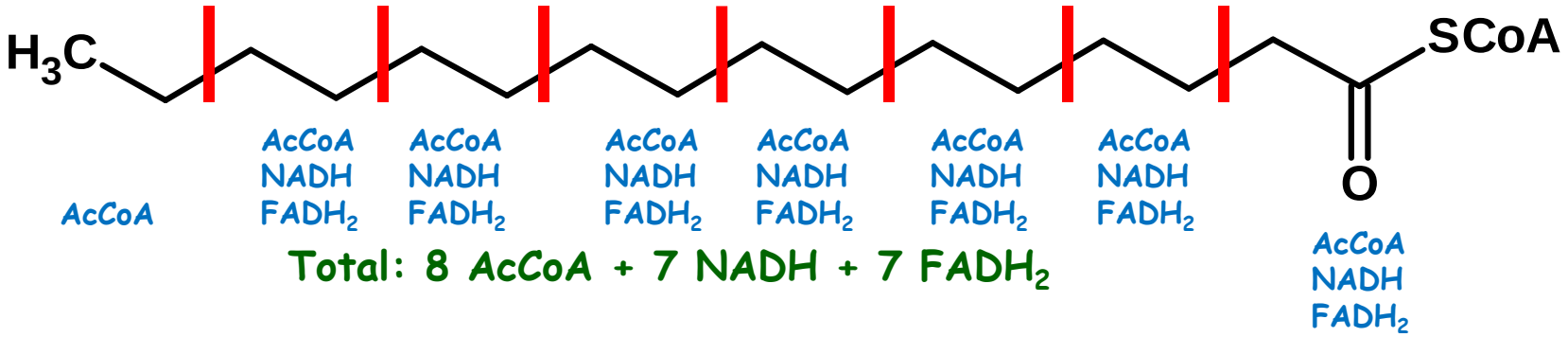

Total: 8 AcCoA + 7 NADH + 7 $FADH_2$

Table 27.1 Principal reactions required for fatty acid degradation

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

*An AMP-forming ligase.

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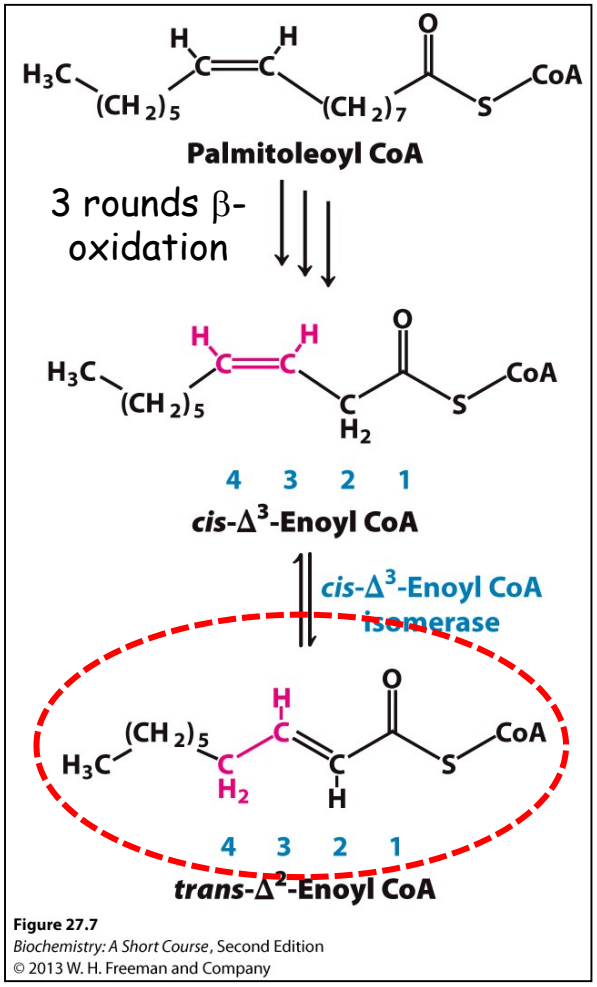
Net yield of ATP per palmitate oxidized to 16 CO_2

	ATP generated
8 acetyl CoA	80
7 QH_2	10.5
7 NADH	17.5
	108 ATP
ATP expended to activate palmitate	-2
Net yield:	106 ATP

Glc (6 C) = 32 ATP which is 5.33 ATP/C

PA (16 C) = 106 ATP which is 6.88 ATP/C

27.2: Degradation of Unsaturated and Odd-Chain Fatty Acids



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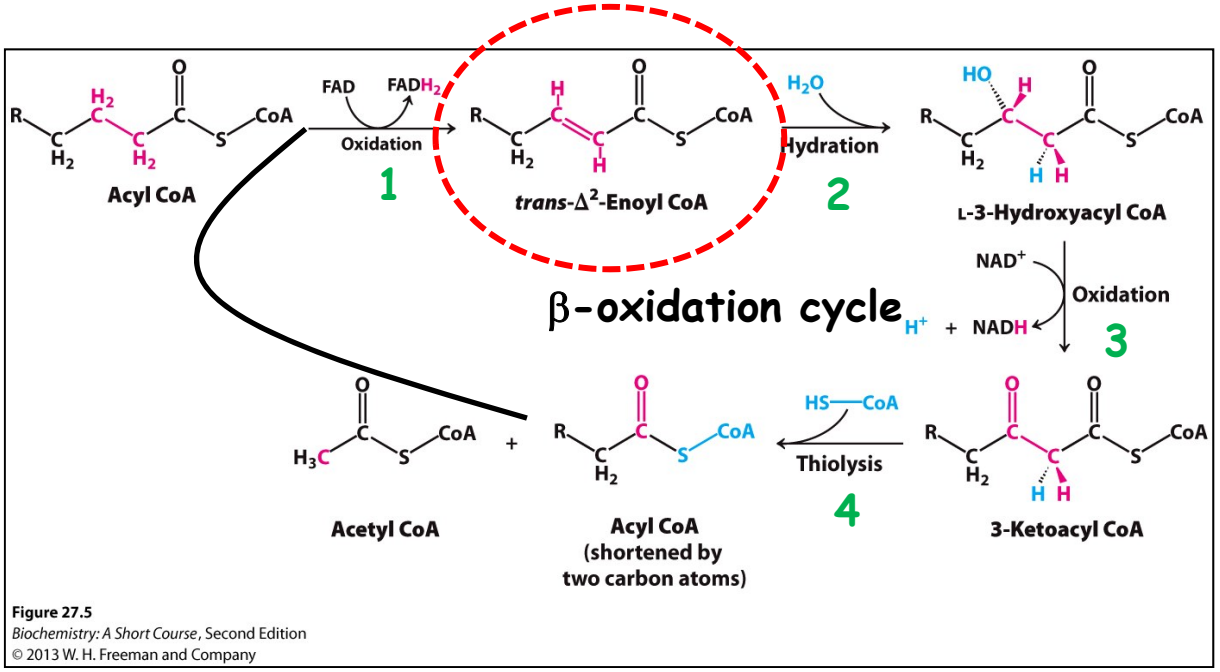
Unsaturated Fatty Acids



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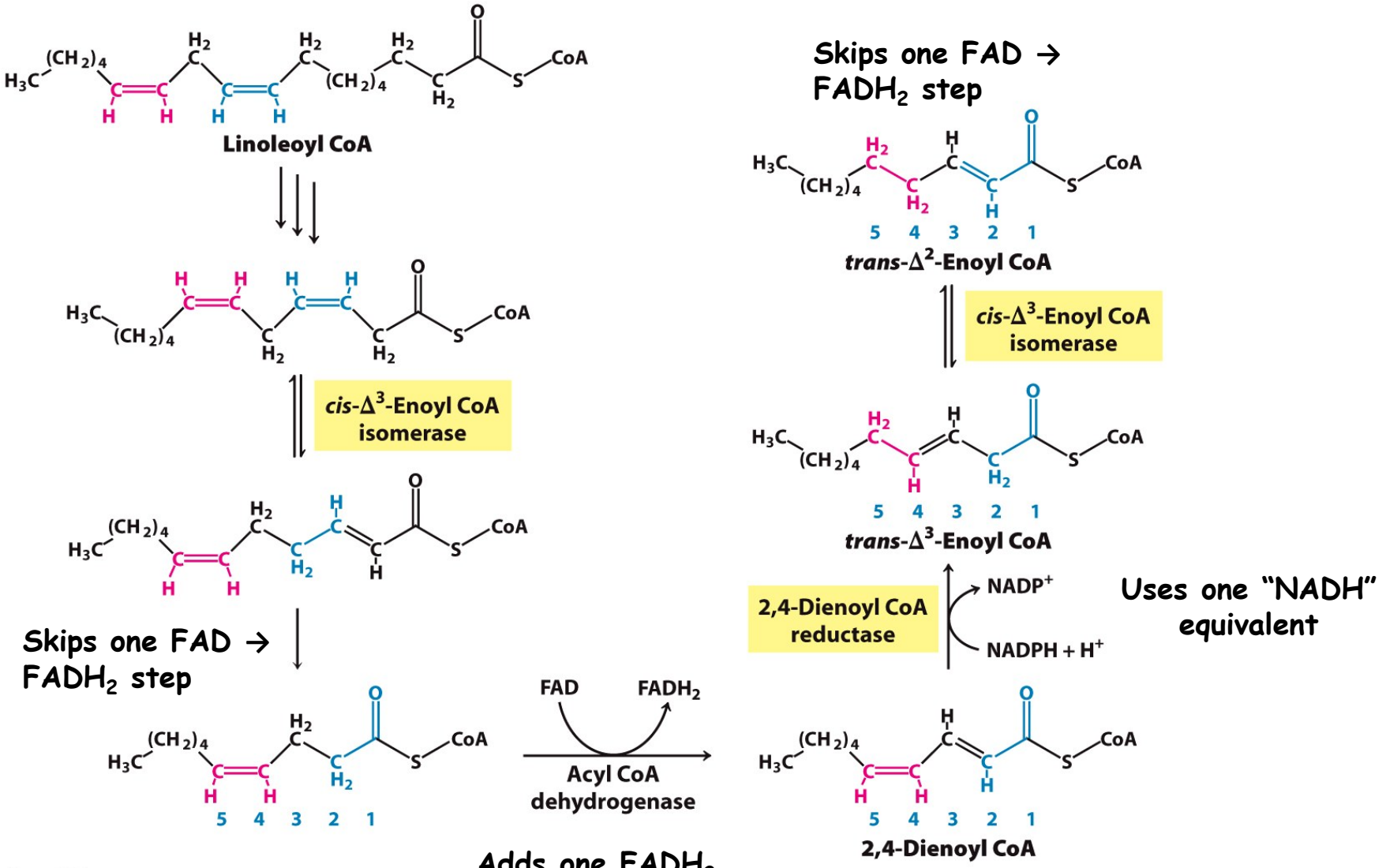
Skips one FAD → $FADH_2$ step



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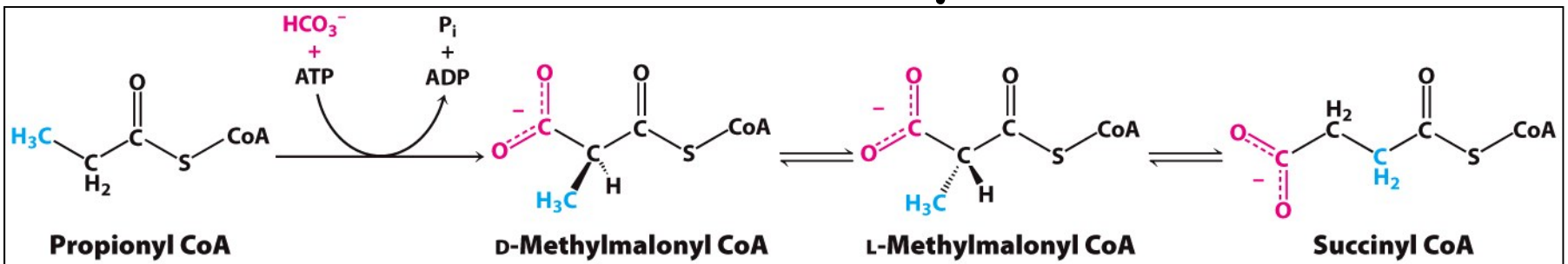
Summary: -1 $FADH_2$, -1 NADH

Odd-Chain Fatty Acids



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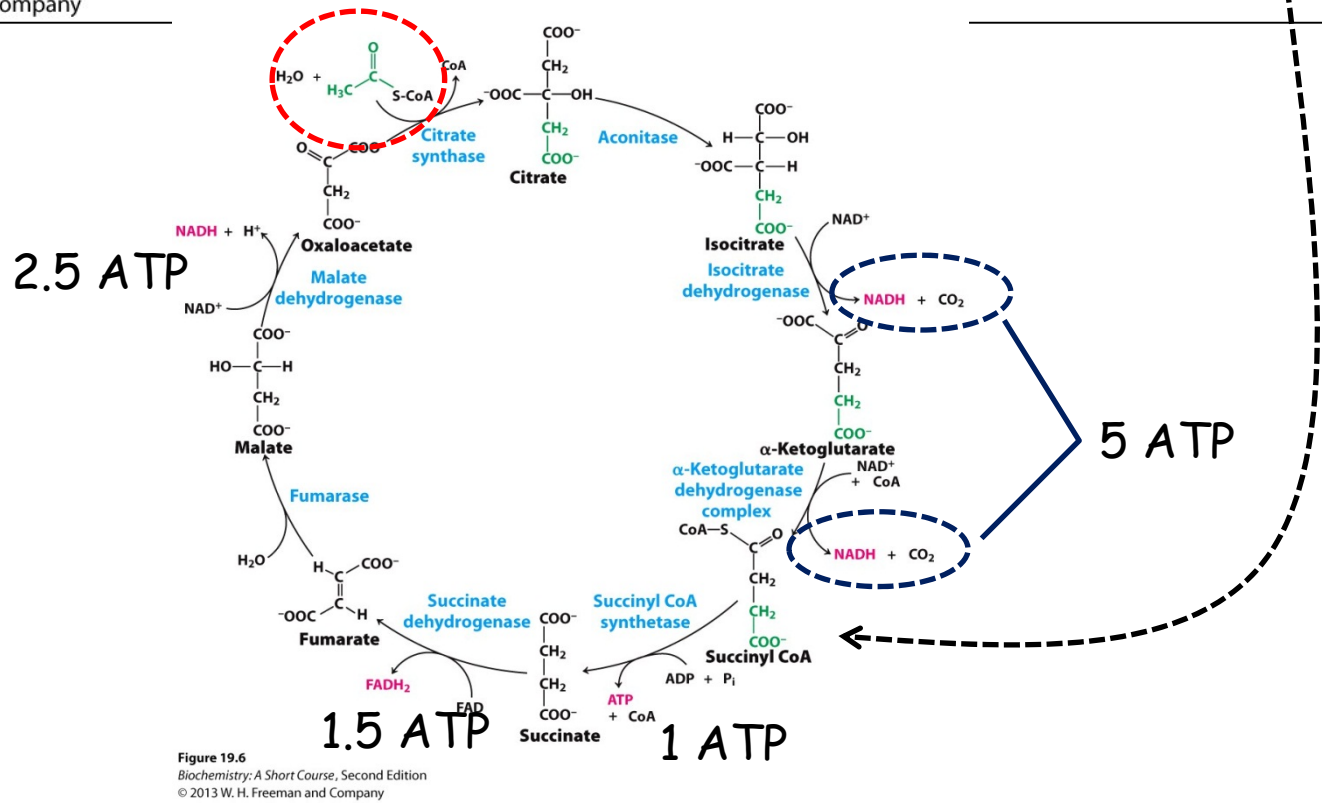

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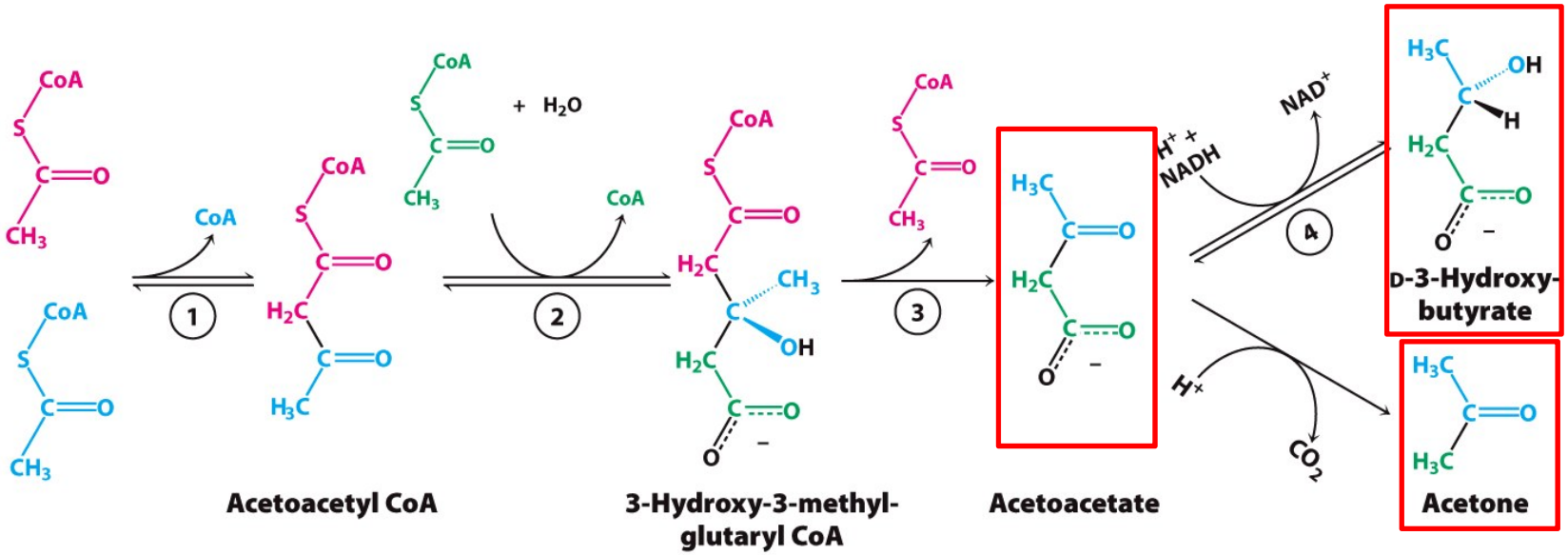
How many ATPs would result from oxidiation of heptadecanoic acid?

27.3: Ketone Bodies



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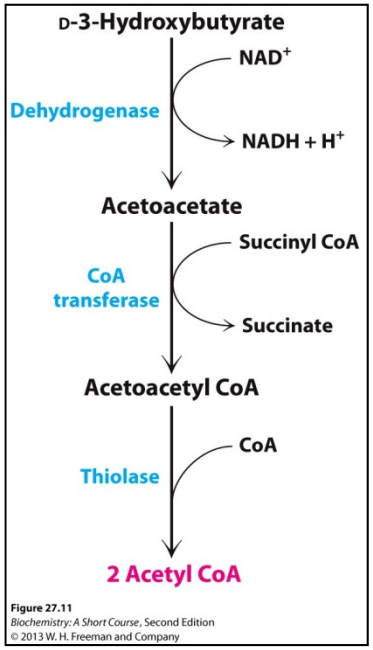
Acetoacetate
3-Hydroxybutyrate
Acetone

} **Water soluble**
Easily transportable
Synthesis in liver



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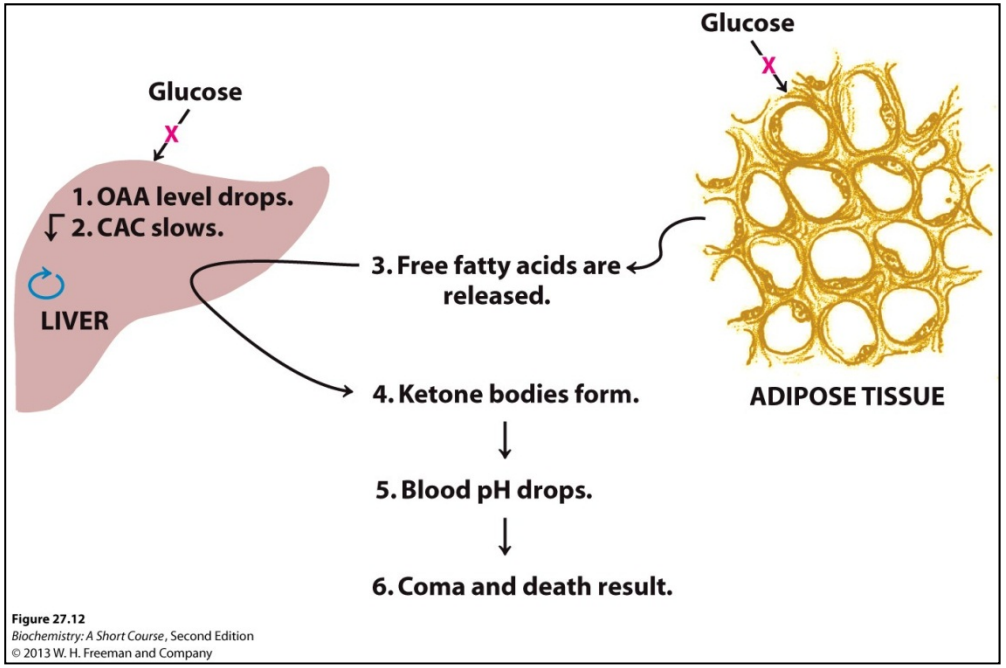
27.4: Physiological Conditions and Fatty Acid Metabolism

Diabetes



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Starvation

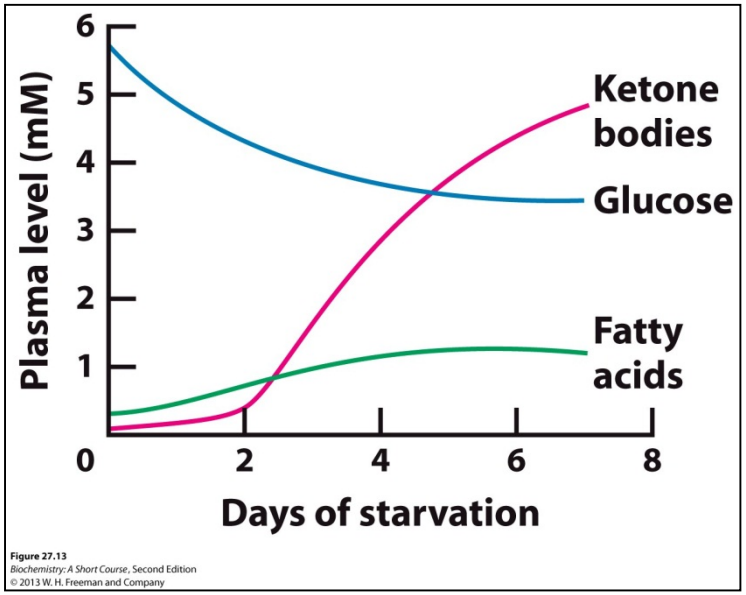

Figure 27.13
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