B-COMPLEX VITAMINS

BIOTIN

Vitamin B_7

Chemistry

- Heterocyclic monocarboxylic acid, $C_{10}H_{16}O_3N_2S$
- Hexahydro-2-oxo-1-thieno-3, 4 imidazole-4 valeric acid
- Sulphur containing vit., 2 fused rings, 1 imidazole, 1 thiophene derivative

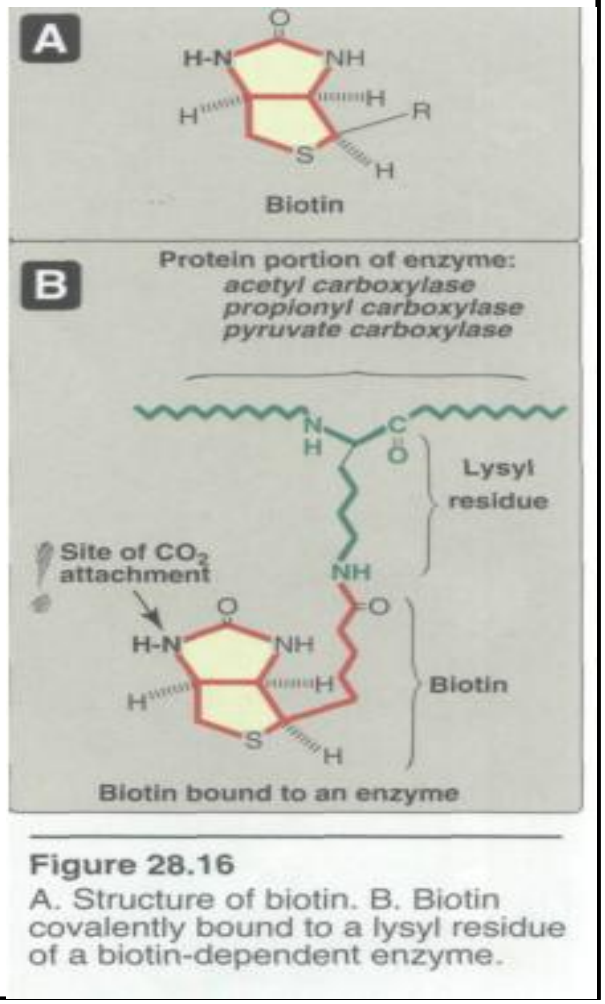

Figure 28.16
A. Structure of biotin. B. Biotin covalently bound to a lysyl residue of a biotin-dependent enzyme.

- Two active forms:

1. α-biotin (egg yolk)
2. β-biotin (liver)

(differ in nature of side chain)

- Present both as free or bound forms

Bound forms: biocytin, desthiobiotin, oxybiotin

Biocytin (ε-N-biotinyl-lysine): Biotin attach to lysine residue of tissue proteins by amide bond.

Biosynthesis/RDA

Bacteria, yeast, fungi, plants can synthesize

HUMANS: cannot synthesize, intestinal bacteria can

RDA: Adults 25-50 µg/day

RDA: Children 20-40 µg/day

Requirement increase in oral antibiotics intake, pregnancy, lactation

- Storage: May be stored in limited extent in liver & kidneys.

- Excretion:
- Urine: 10-180 µg daily
- Faeces: 15-200 µg daily

Occurrence & Sources

- Widely distributed in animals & plants
- Animal sources: liver, kidney, egg yolk, milk, milk products
- Plants sources: vegetables, legumes, grains

Metabolic role

- Biotin – prosthetic group of certain enzymes that catalyze CO_2 transfer reactions (CO_2-fixation OR Carboxylation reaction)

Conversion of pyruvate to oxaloacetate

PYRUVATE CARBOXYLASE

Step:1 CO_2-biotin complex

Step:2 CO_2 transferred to substrate (pyruvate)

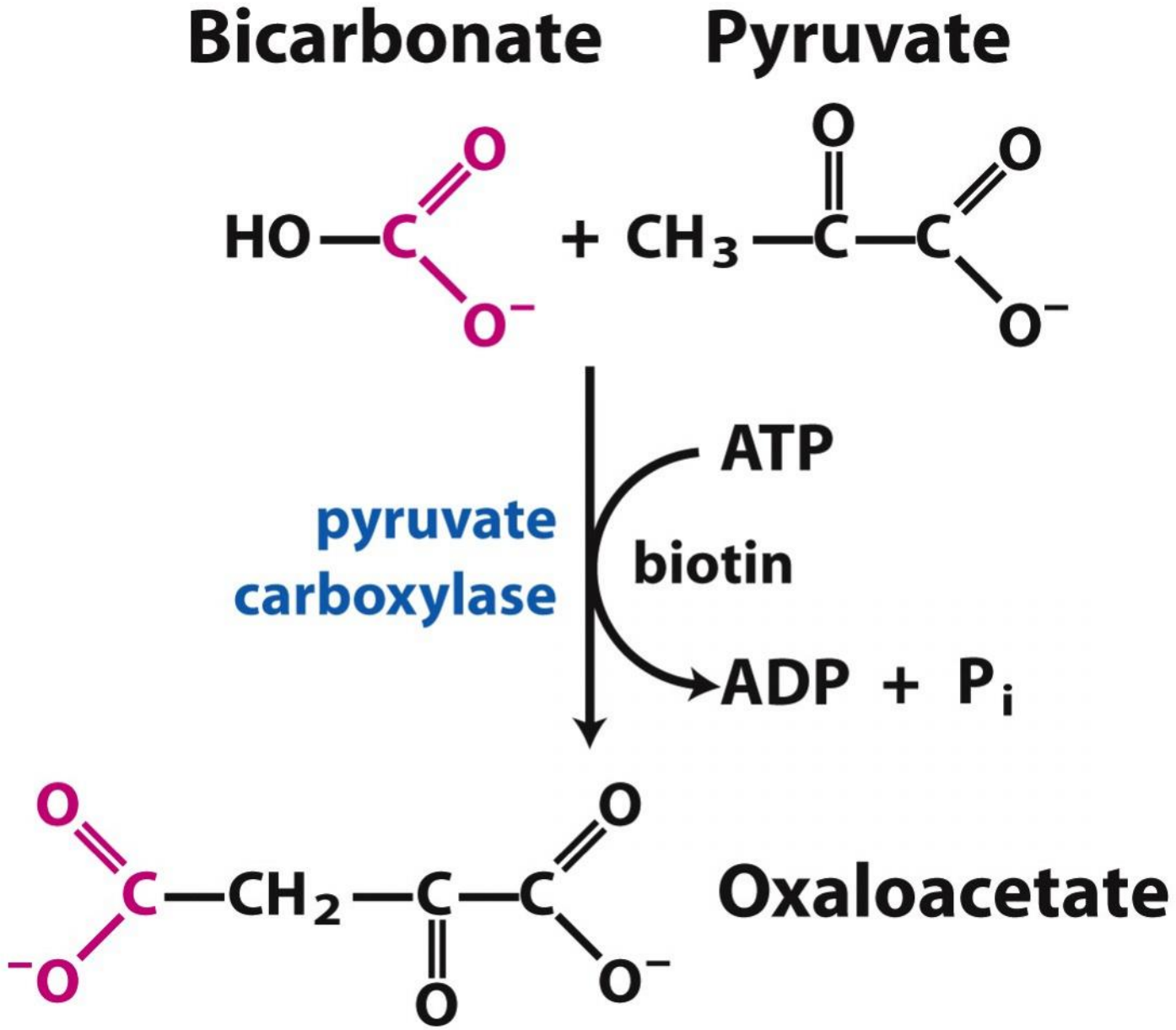

Figure 14-17a
Lehninger Principles of Biochemistry, Fifth Edition

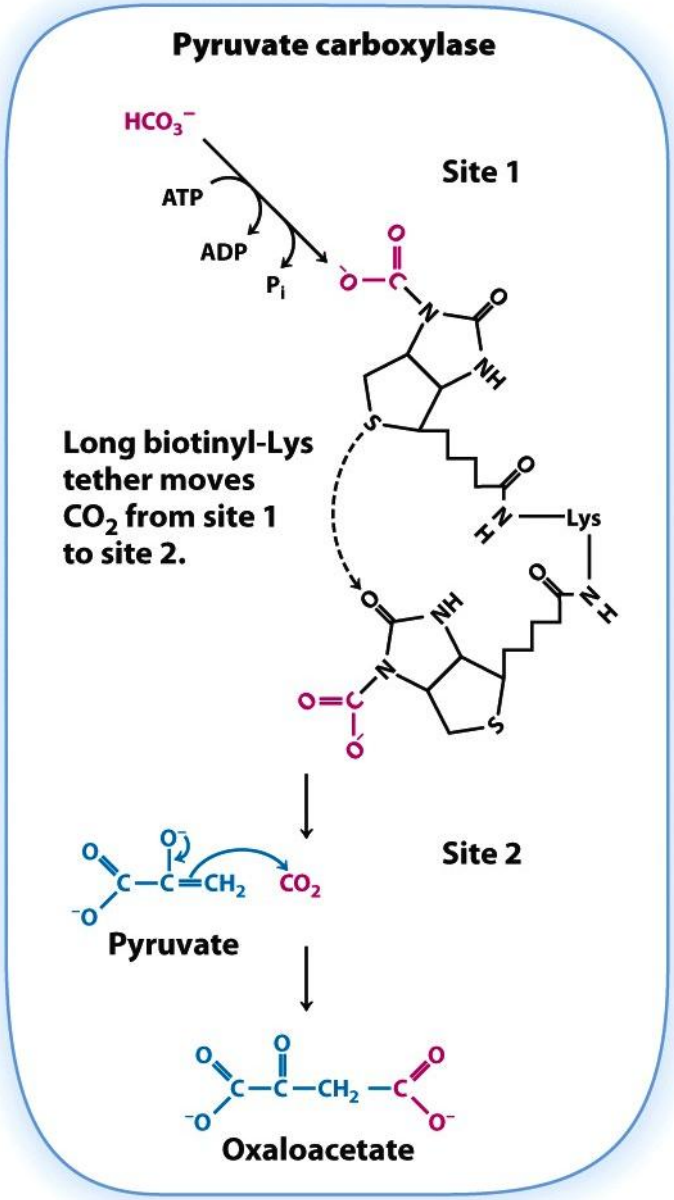

Figure 14-18
Lehninger Principles of Biochemistry, Fifth Edition

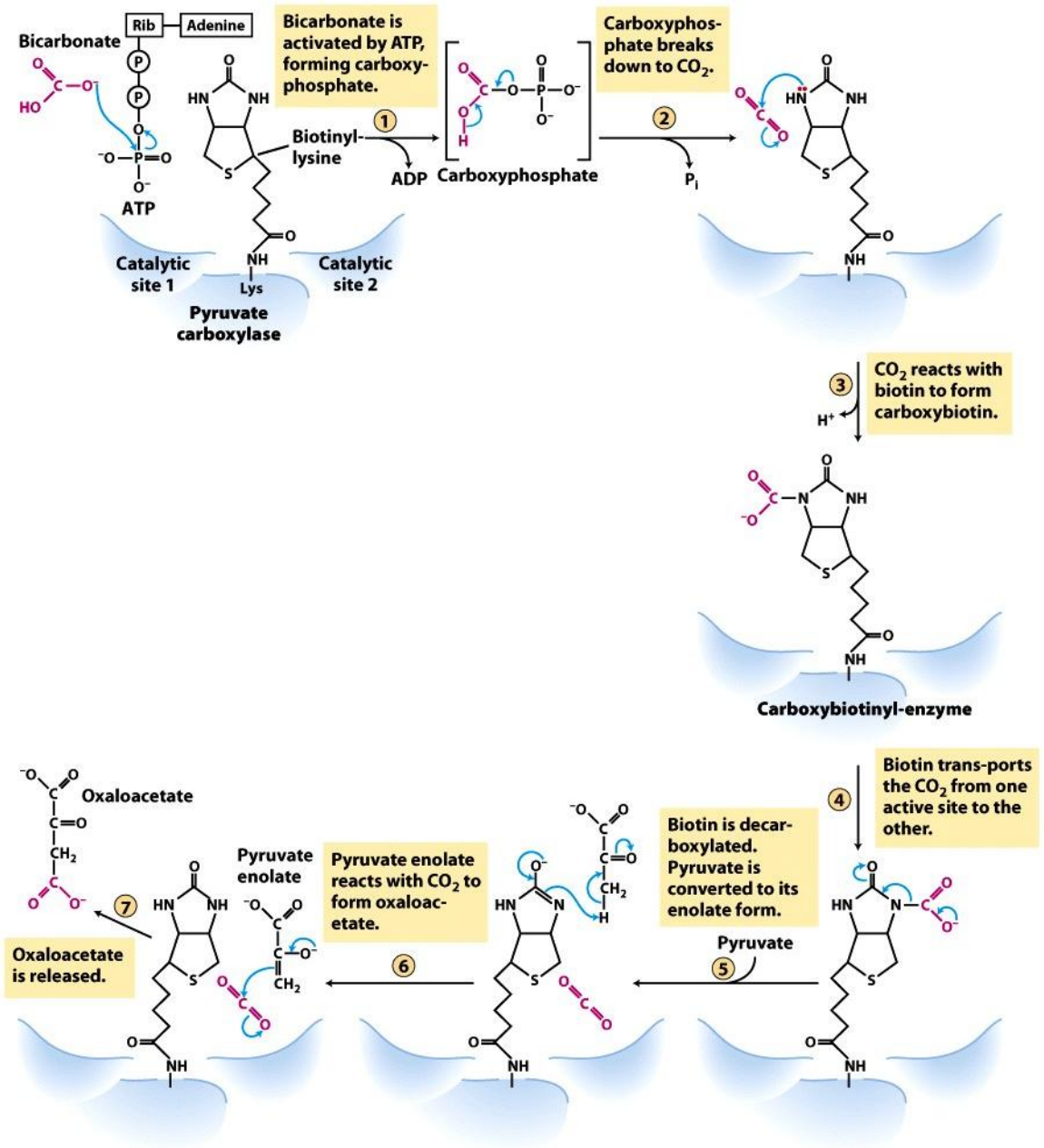

Figure 16-16

Lehninger Principles of Biochemistry, Fifth Edition

- **Conversion of acetyl-CoA to malonyl-CoA**
  Extra-mitochondrial de Novo FA synthesis

Acetyl-CoA Carboxylase

Step:1 CO_2-biotin complex

Step:2 CO_2 transferred to substrate (acetyl-CoA)

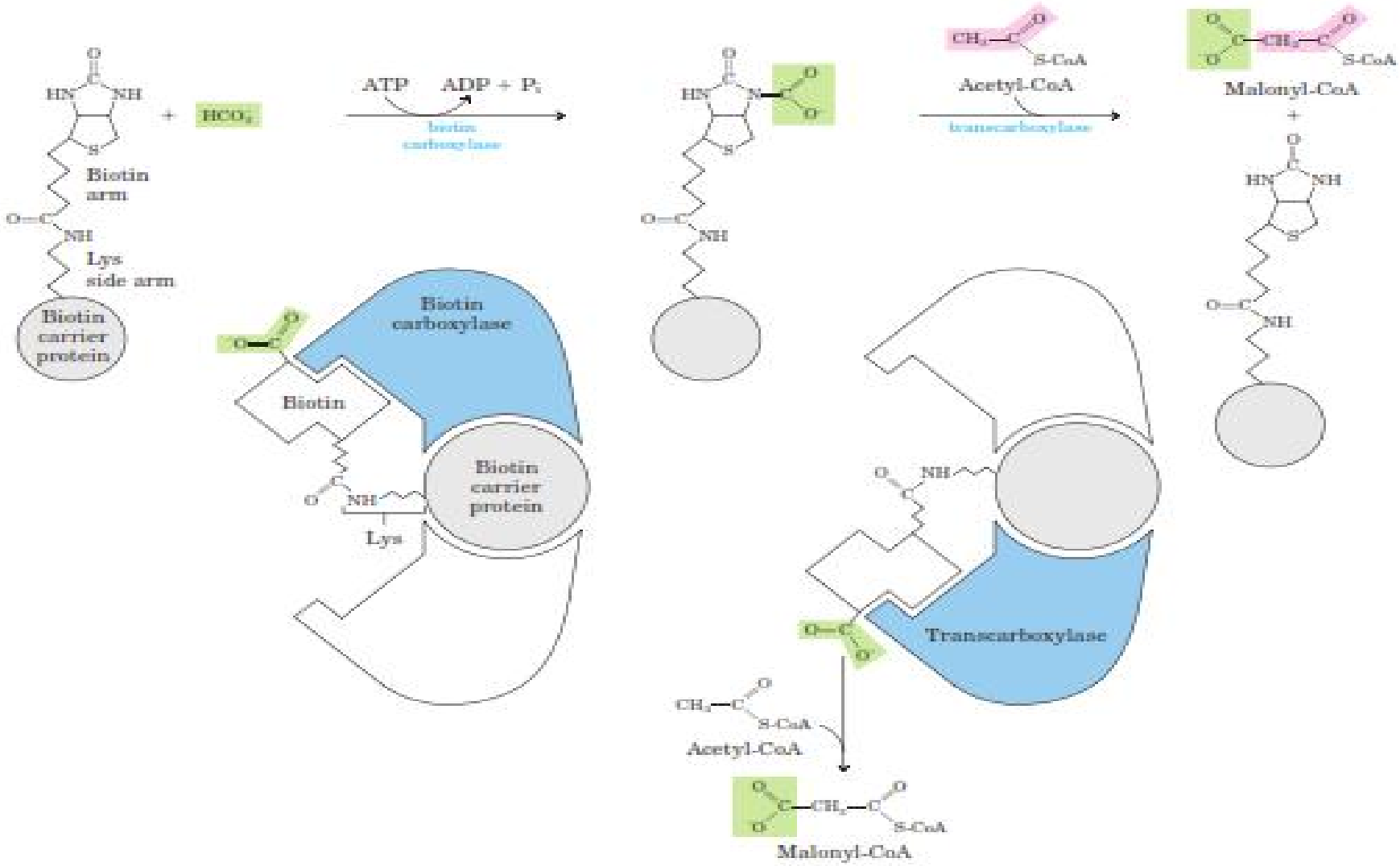

FIGURE 21–1 The acetyl-CoA carboxylase reaction. Acetyl-CoA carboxylase has three functional regions: biotin carrier protein (gray); biotin carboxylase, which activates CO_2 by attaching it to a nitrogen in the biotin ring in an ATP-dependent reaction (see Fig. 16–16); and transcarboxylase, which transfers activated CO_2 (shaded green) from biotin to acetyl-CoA, producing malonyl-CoA. The long, flexible biotin arm carries the activated CO_2 from the biotin carboxylase region to the transcarboxylase active site, as shown in the diagrams below the reaction arrows. The active enzyme in each step is shaded blue.

- Conversion of propionyl-CoA to methylmalonyl-CoA

Propionyl-CoA Carboxylase

Oxidation of odd carbon fatty acids

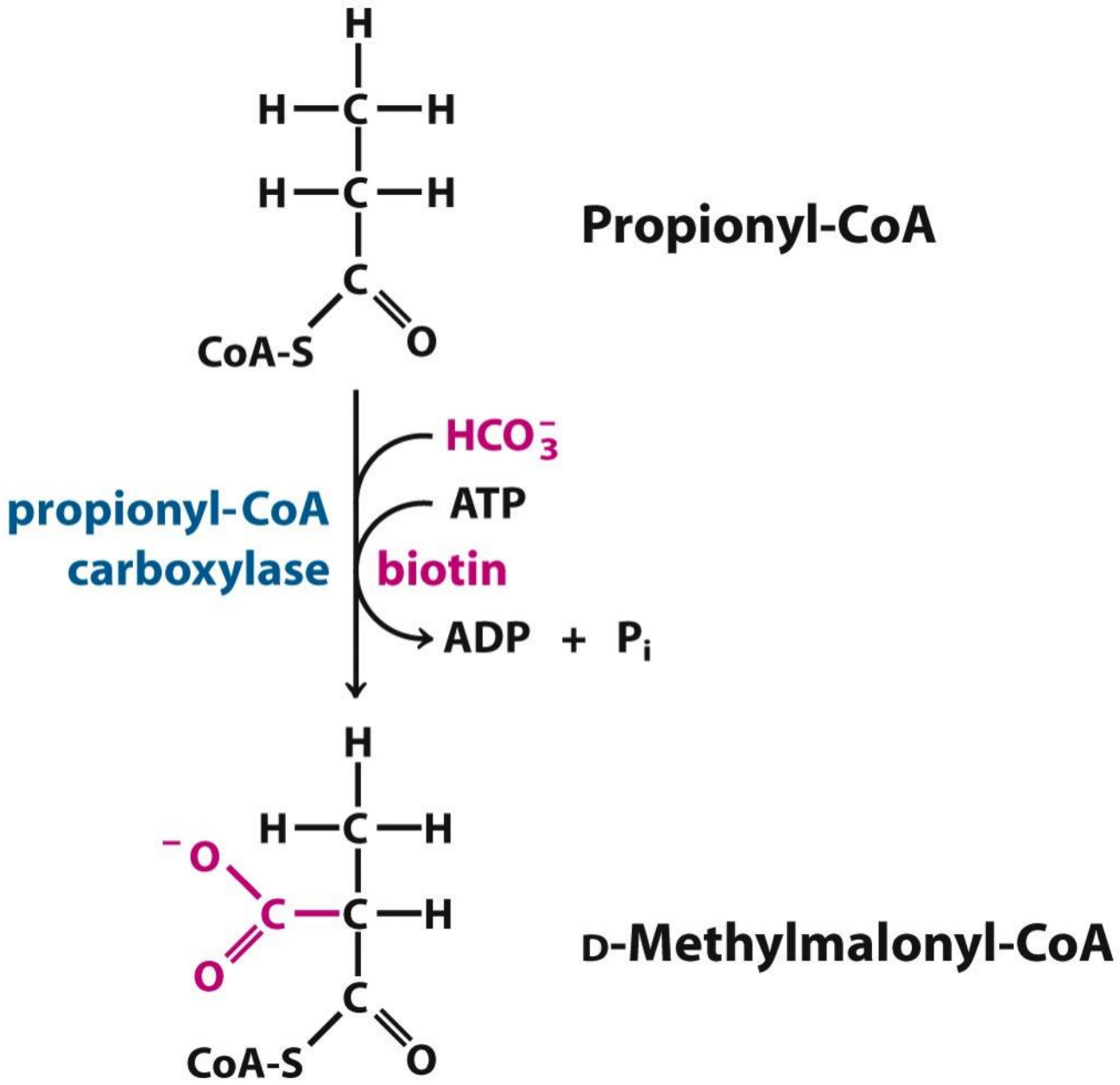

Figure 17-11 part 1
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- Other Enzyme systems

-Succinic acid dehydrogenase & decarboxylase

-Deaminases of Asp, Ser, Thr amino acids

Biological Tethers

A tether is a molecule that carries 1 or 2 carbon intermediates from one active site to another

They are used in lipid synthesis, gluconeogenesis, conversion of pyruvate into Acetyl CoA

Lipoate -lysine residue complex associated with dihydrolipoyl transacetylase, which is used for carrying hydroxyethyl from hydroxyethyl TPP. This compound forms Acetyl- CoA, a convergent molecule in metabolic pathways.

Biotin- lysine residue complex associated with pyruvate carboxylase, an enzyme which plays an important role in gluconeogenesis. It is involved in the production of oxaloacetate from pyruvate.

Synthesis of fats: β-mercaptoethylamine-pantothenate complex associated with an acyl carrier protein

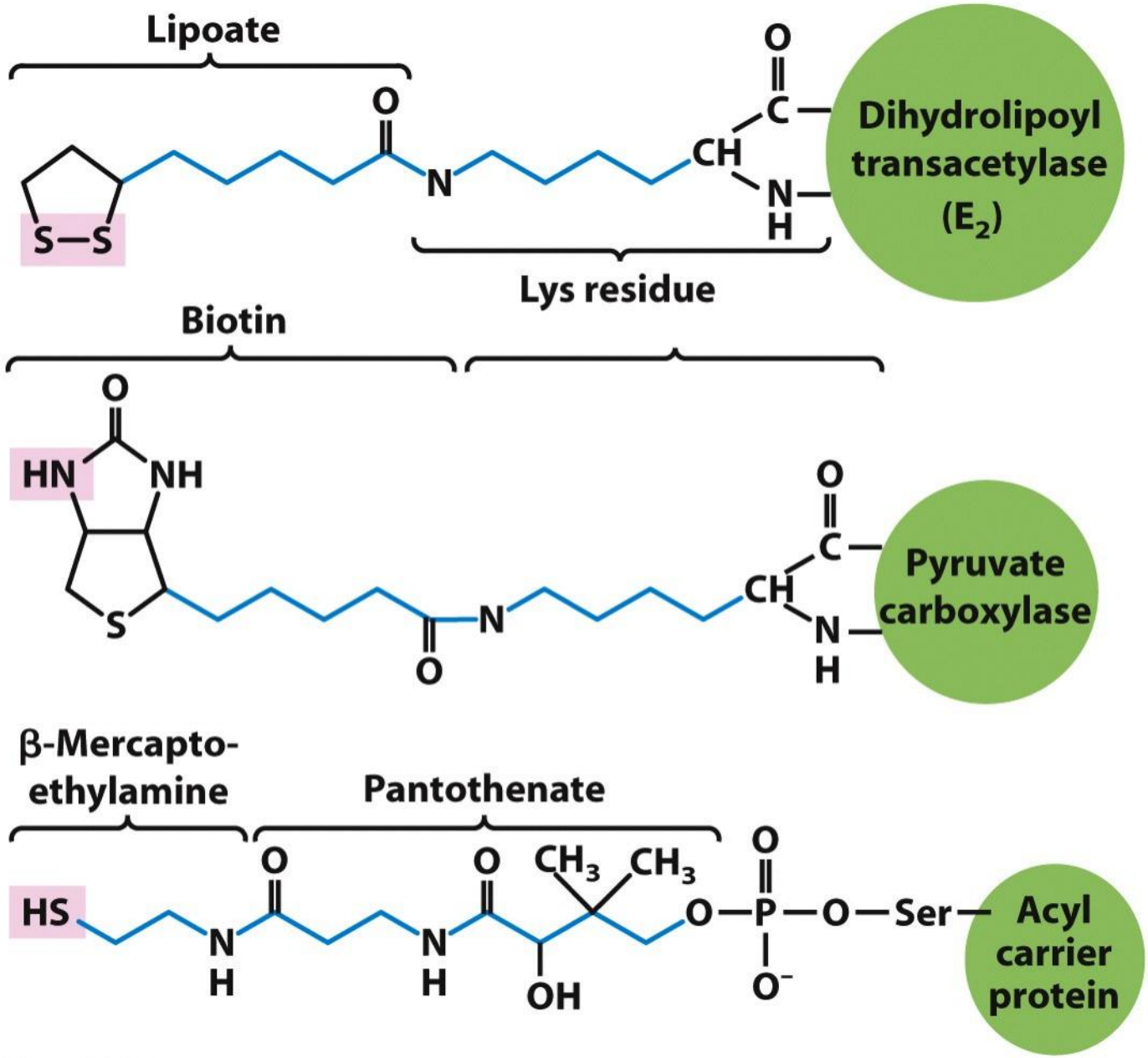

Figure 16-17
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Deficiency

- Egg-White Injury: Anti-vitamin "avidin" in egg white
- Avidin inactivate Biotin
- Biotin deficiency may be induced by excessive dietary egg white or excluding dietary biotin
- Administration of biotin cures

Clinical Aspects-Deficiency Diseases

1. Congenital:

Rare genetic deficiency of holocarboxylase synthase enzyme

- E involve in biotin metabolism
- Biotin not utilized, cause deficiency
- Dermatitis, greying of hair, lose of hair (alopecia; baldness)

2. Acquired (Leiner's disease)

- Observed in breast feeding infants in association with persistent diarrhoea
- Low biotin contents in human milk, poor absorption due to diarrhoea cause deficiency
- Administration of biotin cures

References:

- Nelson, D.L and M.M. Cox. 2013. Lehninger Principles of Biochemistry. 6th ed. Worth Publishers, NY.
- Chatterjee, M. N. and R. Shinde. 2007. Textbook of Medical Biochemistry. 7th ed (Indian edition). Jaypee Brothers, Medical Publishers (P) Ltd, New Delhi, India.