

BCMB 3100 - Introduction to Coenzymes & Vitamins

- **Cofactors**
 - **Essential ions**
 - **Coenzymes**
 - **Cosubstrates**
 - **Prosthetic groups**
- **Coenzymes structure/function/active group**
- **Vitamins**

1

Coenzymes

Some enzymes require _____ for activity

(1) _____ (mostly metal ions)

(2) _____ (organic compounds)

Apoenzyme + **Cofactor** → **Holoenzyme**

(protein only)

(active)

(inactive)

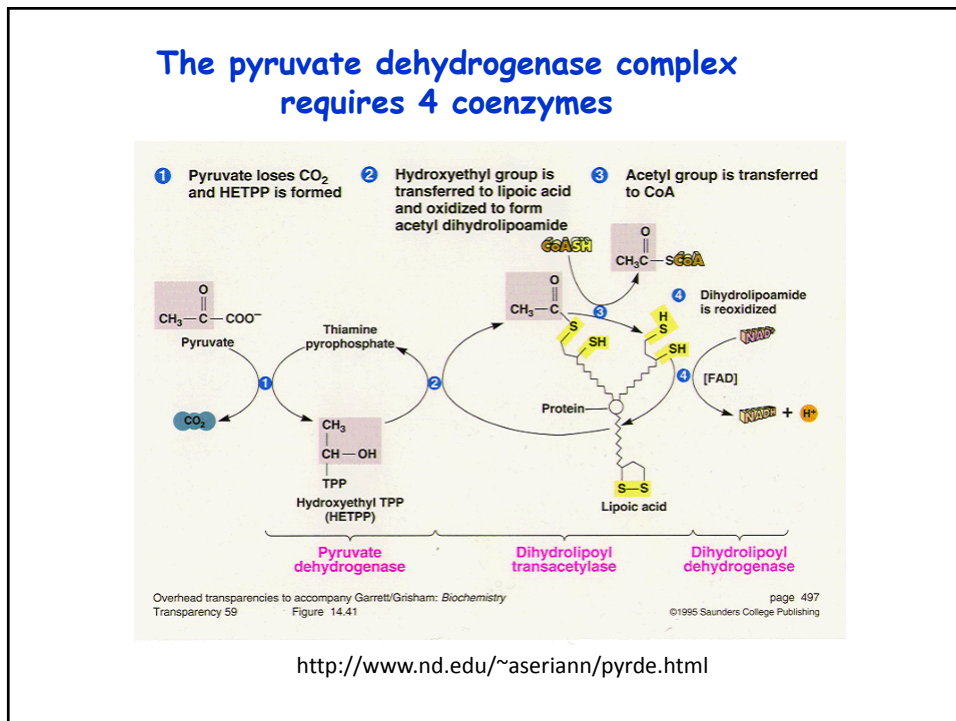
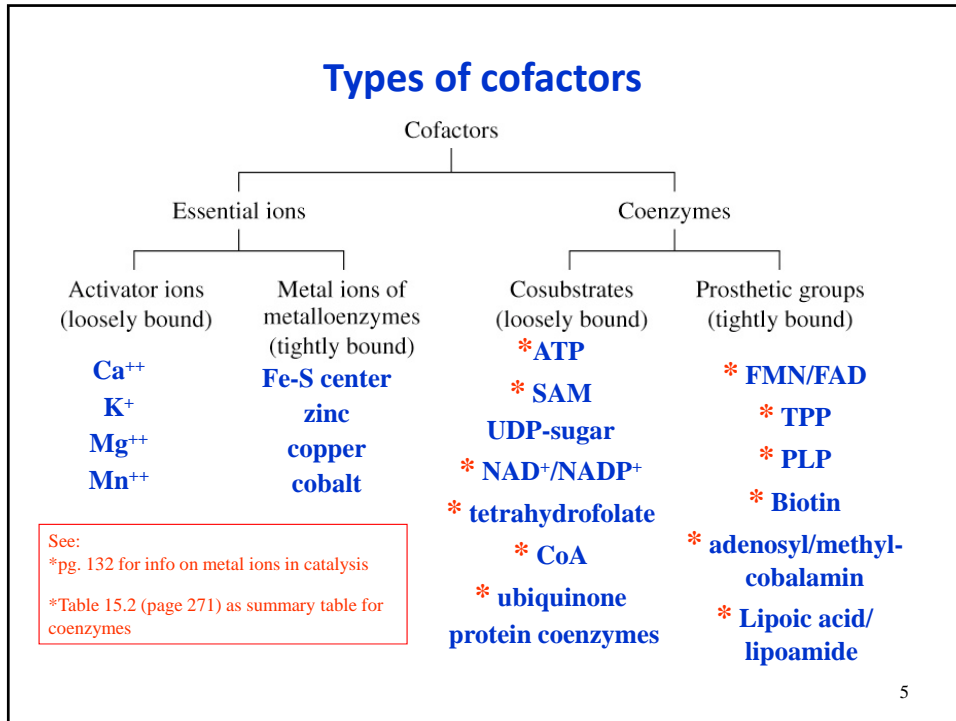
Metal ions have diverse functions in enzymes

- Participate in _____, generally tightly bound to enzyme, function e.g. as electrophilic catalysts or aid in generating a nucleophile
- Participate in _____ at the active site

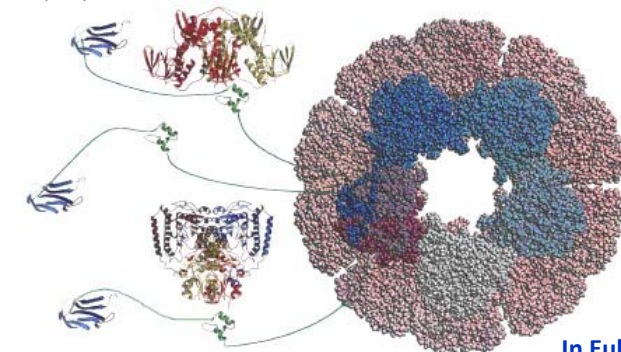
Coenzymes

- Coenzymes act as group-transfer reagents
- Hydrogen, electrons, or other groups can be transferred
- Two types of coenzymes:

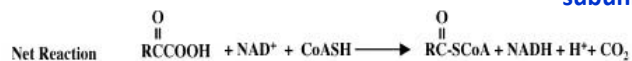
• _____



Schematic model of 3D structure (bigger than a ribosome) of **pyruvate dehydrogenase complex** of *Bacillus stearothermophilus*. The E2 chain has 3 domains: lipoyl, peripheral subunit-binding and acetyltransferase. Active sites of E1, E2 and E3 are coupled by the swinging lipoyl domain. Only one trimer of icosahedral (60-mer) E2 core is shown and only one E1(a2b2, lower) and one E3 (a2, upper) component is shown attached, for simplicity.



In Eukaryotes this complex has 102 subunits!! (30+60+12)!



<http://www.bioc.cam.ac.uk/uto/perham.html>

Table 6.2 Enzyme cofactors

Cofactor	Enzyme*
Coenzyme[†]	
Thiamine pyrophosphate (TPP)	Pyruvate dehydrogenase
Flavin adenine nucleotide (FAD)	Monoamine oxidase
Nicotinamide adenine dinucleotide (NAD ⁺)	Lactate dehydrogenase
Pyridoxal phosphate (PLP)	Glycogen phosphorylase
Coenzyme A (CoA)	Acetyl CoA carboxylase
Biotin	Pyruvate carboxylase
6'-Deoxyadenosyl cobalamin	Methylmalonyl mutase
Tetrahydrofolate	Thymidylate synthase
Metal	
Zn ²⁺	Carbonic anhydrase
Mg ²⁺	EcoRV
Ni ²⁺	Urease
Mo	Nitrogenase
Se	Glutathione peroxidase
Mn ^{2+/-3+}	Superoxide dismutase
K ⁺	Acetoacetyl CoA thiolase

*The enzymes listed are examples of enzymes that employ the indicated cofactor.

[†]Often derived from vitamins, coenzymes can be either tightly or loosely bound to the enzyme.

Table 6.2
Biochemistry: A Short Course, Second Edition
© 2013 W. H. Freeman and Company

8

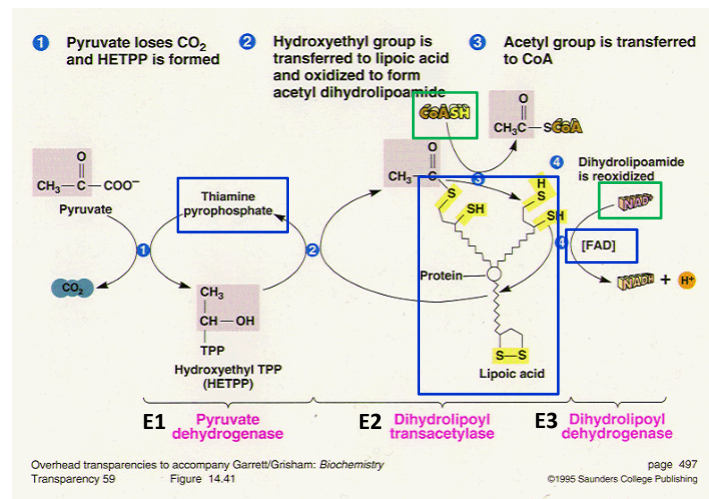
Coenzyme Classification

- There are two classes of coenzymes
- (1) _____ are altered during the reaction and regenerated by another enzyme
- (2) _____ remain bound to the enzyme during the reaction, and may be covalently or tightly bound to enzyme

9

The pyruvate dehydrogenase complex requires 5 coenzymes

Cosubstrates
Prosthetic groups



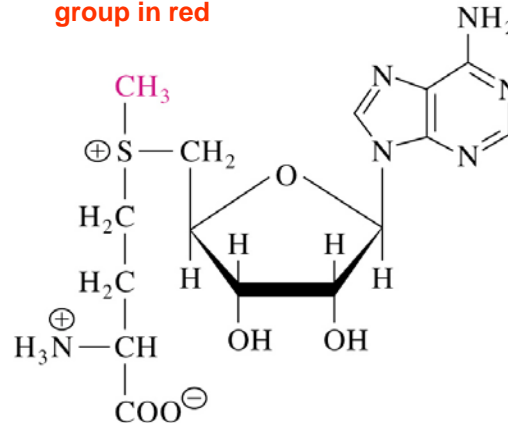
<http://www.nd.edu/~aseriann/pyrde.html>

One example of a cosubstrate coenzyme

S-Adenosylmethionine (SAM)

SAM is the donor of methyl groups for most biosynthetic reactions

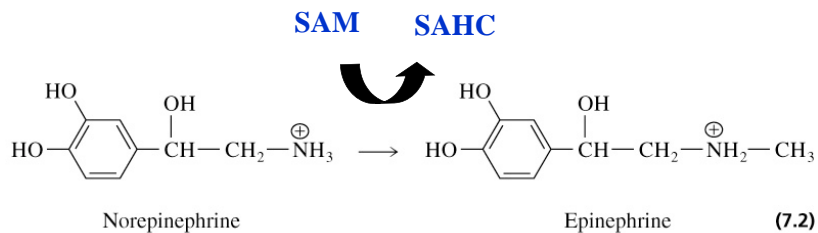
Activated methyl group in red



11



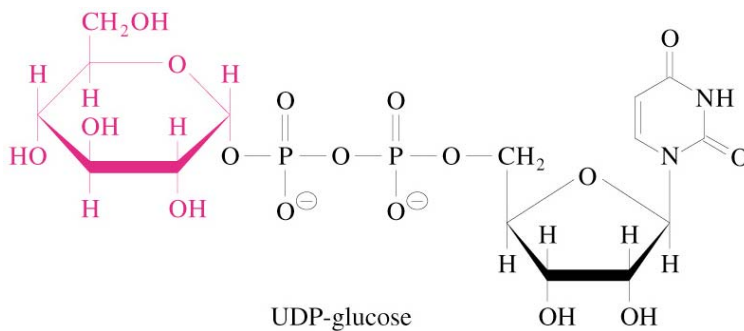
Example: SAM donates the methyl group for the synthesis of the hormone epinephrine from norepinephrine



12

A second example of a cosubstrate coenzyme

UDP-sugar: activated form of sugars used as substrate in many biosynthetic reactions



Nucleotide-sugars are cosubstrates in many glycosylation reactions

13

A third example of a cosubstrate coenzyme

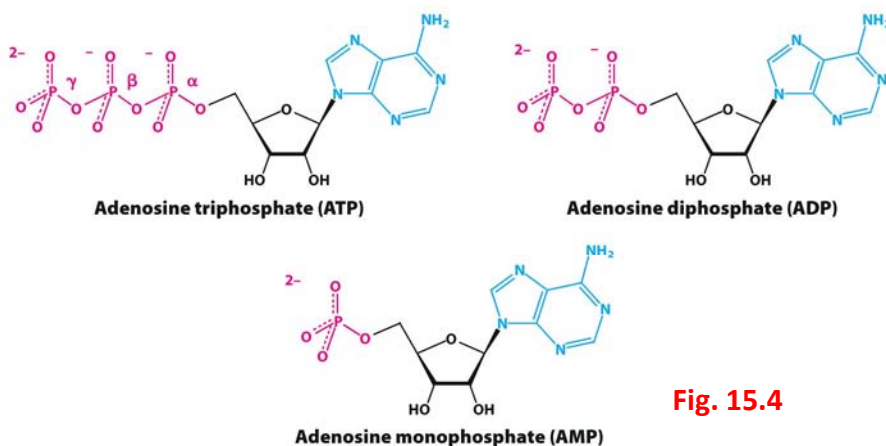


Figure 15.3
Biochemistry: A Short Course, Second Edition
© 2013 W. H. Freeman and Company

Some coenzymes require vitamins as part of their structure

_____ : organic substance required in trace amounts for a number of essential biochemical reactions

Not all vitamins are part of coenzymes; only some are

Table 15.4 Noncoenzyme vitamins

Vitamin	Function	Deficiency
A	Roles in vision, growth, reproduction	Night blindness, cornea damage, damage to respiratory and gastrointestinal tracts
C (ascorbate)	Antioxidant	Scurvy (swollen and bleeding gums, subdermal hemorrhaging)
D	Regulation of calcium and phosphate metabolism	Rickets (children): skeletal deformities, impaired growth Osteomalacia (adults): soft, bending bones
E	Antioxidant	Inhibition of sperm production; lesions in muscles and nerves (rare)
K	Blood coagulation	Subdermal hemorrhaging

Table 15.4
Biochemistry: A Short Course, Second Edition
© 2013 W. H. Freeman and Company

Table 15-4

Some vitamins are _____

- Four lipid vitamins: A, D, E, K
- All contain rings and long, aliphatic side chains
- All are highly hydrophobic
- The lipid vitamins differ widely in their functions

Vitamin-Derived Coenzymes

- **Vitamins:** required for synthesis of some coenzymes, must be obtained from nutrients
- Animals rely on plants, meat, & microorganisms for vitamin sources
- Most vitamins must be enzymatically transformed to make the coenzyme (e.g. some water soluble vitamins)
- **BE SURE TO LEARN WHICH VITAMINS ARE PART OF WHICH COENZYMES (Tables 15.2 & 15.3)**

Vitamins, nutritional deficiency diseases

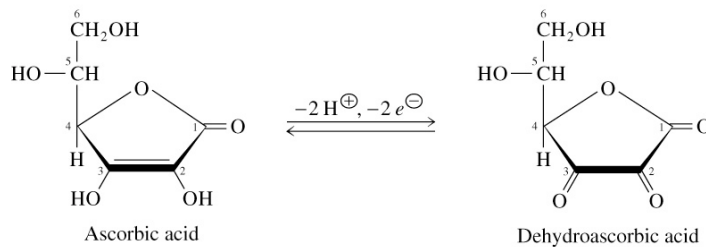
(see Table 15.3 and Appendix D)

<u>Vitamin</u>	<u>Disease</u>
Ascorbate (C)	Scurvy
Nicotinic acid (B₃)	Pellagra
Riboflavin (B ₂)	Growth retardation
Pantothenate (B₅)	Dermatitis in chickens
Thiamine (B ₁)	Beriberi
Pyridoxal (B ₆)	Dermatitis in rats
Biotin	Dermatitis in humans
Folate	Anemia, spina bifida
Cobalamin (B ₁₂)	Pernicious anemia

19

Vitamin C: a vitamin but not a coenzyme

- A reducing reagent for hydroxylation of collagen
- Deficiency leads to the disease scurvy
- Most animals (not primates) can synthesize Vit C



20

You must learn to recognize the major coenzymes

Group Activity on Coenzymes

Be sure to read through “Hints for learning coenzymes” as you prepare and teach your coenzymes to your group.

Be sure to work in your groups to learn the co-enzymes over the next week.

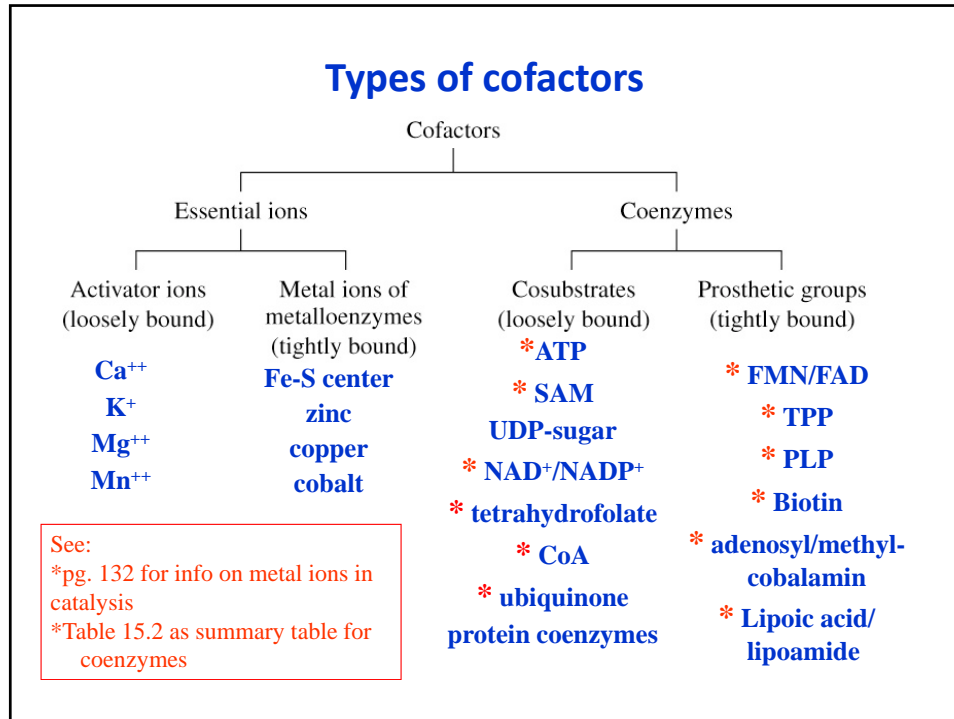


Table 15.2 Some activated carriers in metabolism

Carrier molecule in activated form	Group carried	Vitamin precursor
ATP	* Phosphoryl	
NADH and NADPH 2 electrons	Electrons	Nicotinate (niacin)
FADH ₂ 1 or 2 electrons	Electrons	Riboflavin (vitamin B ₂)
FMNH ₂ 1 or 2 electrons	Electrons	Riboflavin (vitamin B ₂)
Coenzyme A	Acyl	Pantothenate
Lipoamide	Acyl	
Thiamine pyrophosphate <small>2 carbon groups containing carbonyl</small>	Aldehyde	Thiamine (vitamin B ₁)
Biotin	CO ₂ <small>ATP-dependent carboxylation</small>	Biotin
Tetrahydrofolate	One-carbon units	Folate
S-Adenosylmethionine	Methyl	
Uridine diphosphate glucose	Glucose	
Cytidine diphosphate diacylglycerol	Phosphatidate	
Nucleoside triphosphates	Nucleotides	

Note: Many of the activated carriers are coenzymes that are derived from water-soluble vitamins.

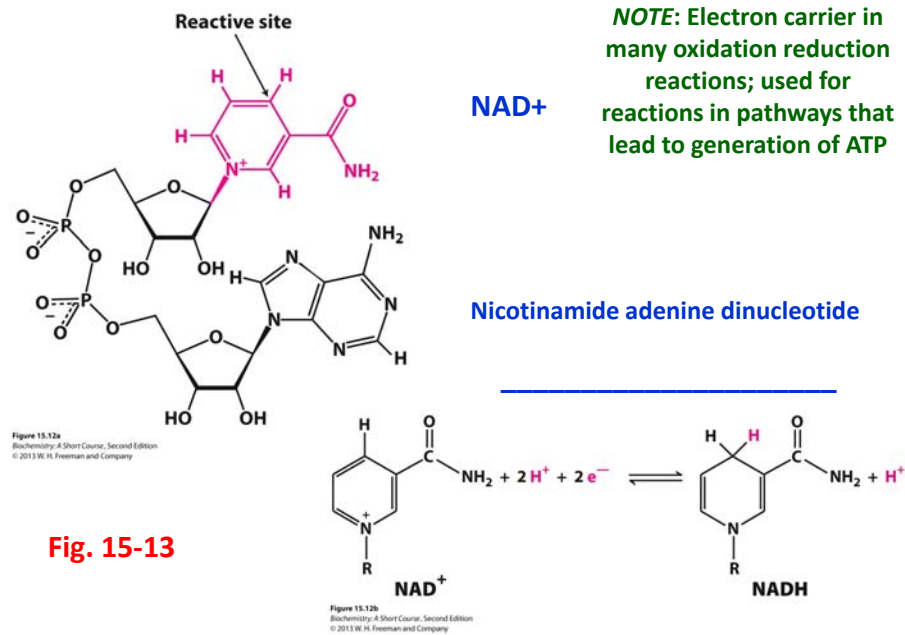
Table 15.2
 Biochemistry: A Short Course, Second Edition
 © 2013 W. H. Freeman and Company

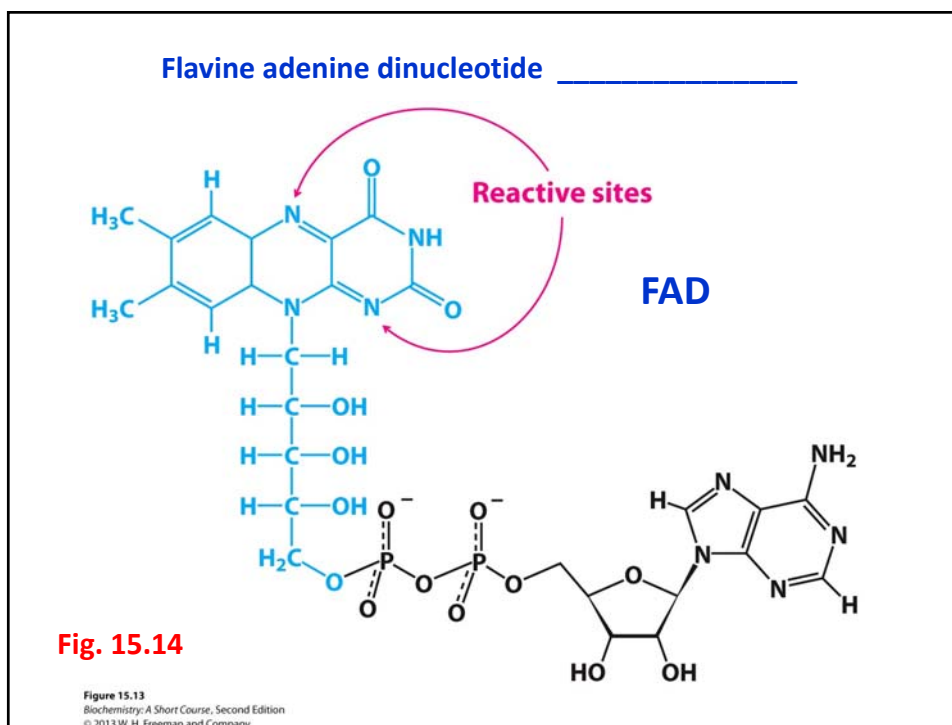
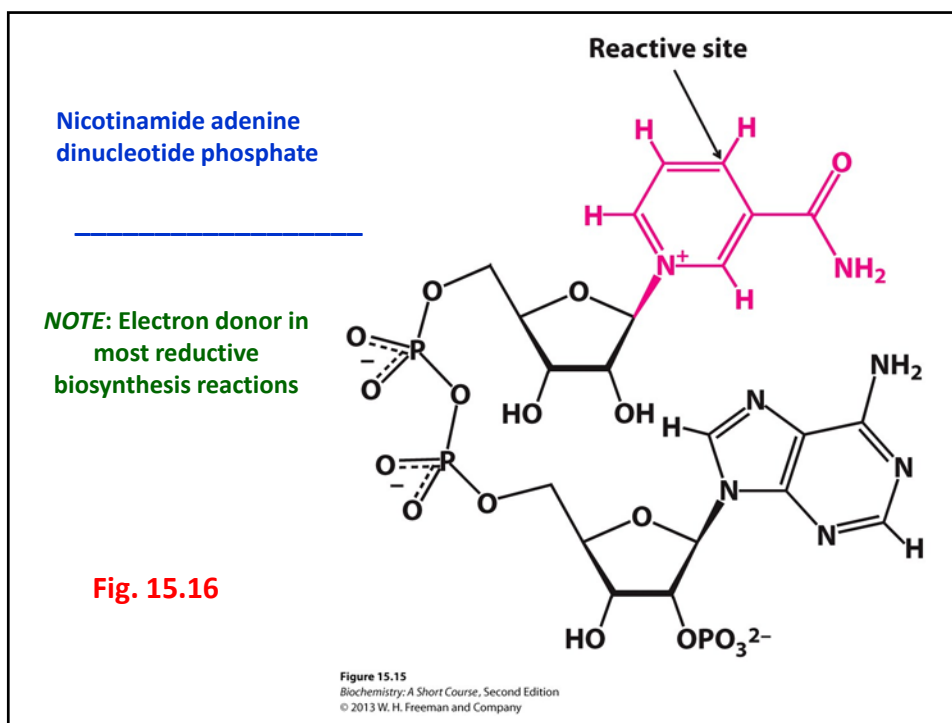
***ATP may also donate pyrophosphoryl and adenosyl groups or adenylyl groups**

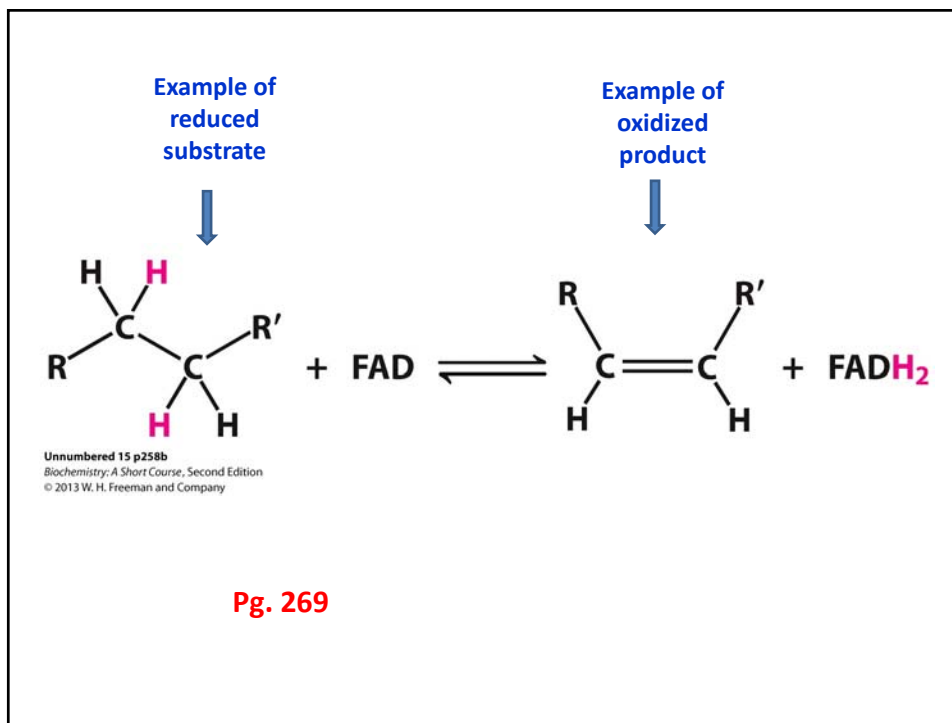
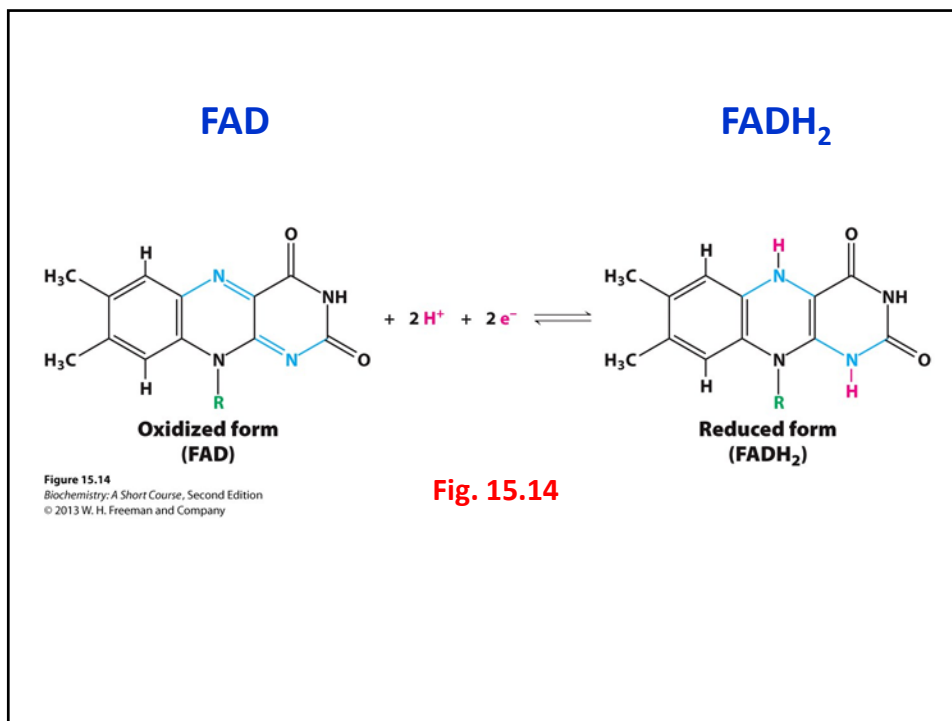
Table 15.3 The B vitamins

Vitamin	Coenzyme	Typical reaction type	Consequences of deficiency
Thiamine (B ₁)	2 carbon groups containing carbonyl Thiamine pyrophosphate	Aldehyde transfer	Beriberi (weight loss, heart problems, neurological dysfunction)
Riboflavin (B ₂)	Flavin adenine dinucleotide (FAD)	Oxidation-reduction	Cheliosis and angular stomatitis (lesions of the mouth), dermatitis
Pyridoxine (B ₆)	Pyridoxal phosphate	Group transfer to or from amino acids	Depression, confusion, convulsions
Nicotinic acid (niacin, B ₃)	Nicotinamide adenine dinucleotide (NAD ⁺)	Oxidation-reduction	Pellagra (dermatitis, depression, diarrhea)
Pantothenic acid (B ₅)	Coenzyme A	Acyl-group transfer	Hypertension
Biotin (B ₇)	Biotin-lysine adducts (biocytin)	ATP-dependent carboxylation and carboxyl-group transfer	Rash about the eyebrows, muscle pain, fatigue (rare)
Folic acid (B ₉)	Tetrahydrofolate	Transfer of one-carbon components; thymine synthesis	Anemia, neural-tube defects in development
Cobalamin (B ₁₂)	5'-Deoxyadenosyl cobalamin	Transfer of methyl groups; intramolecular rearrangements	Anemia, pernicious anemia, methylmalonic acidosis

Table 15.3
Biochemistry: A Short Course, Second Edition
 © 2013 W. H. Freeman and Company







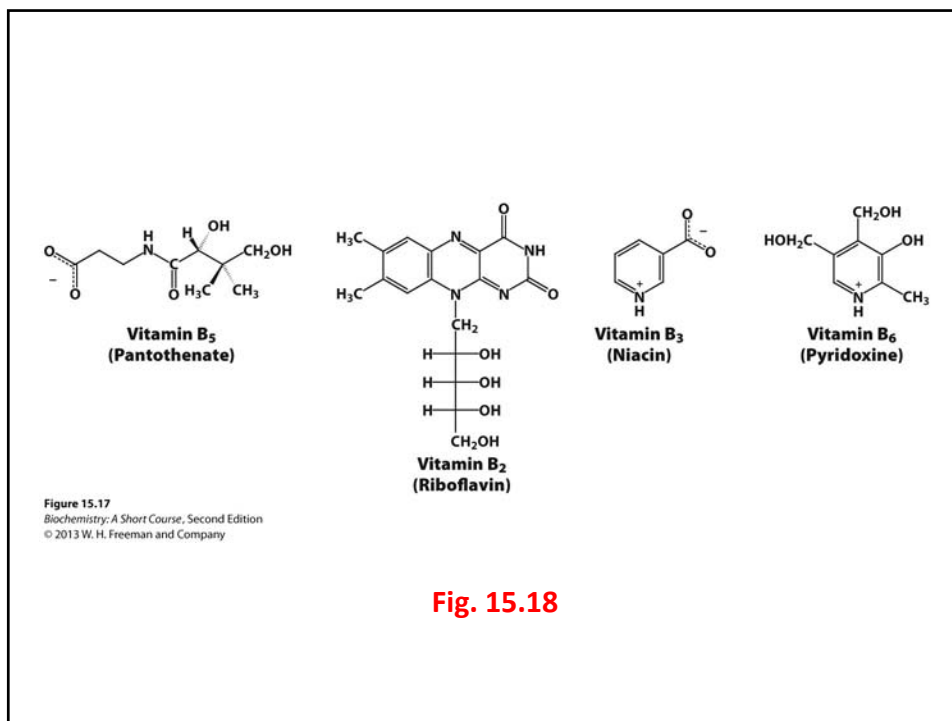


Fig. 15.18

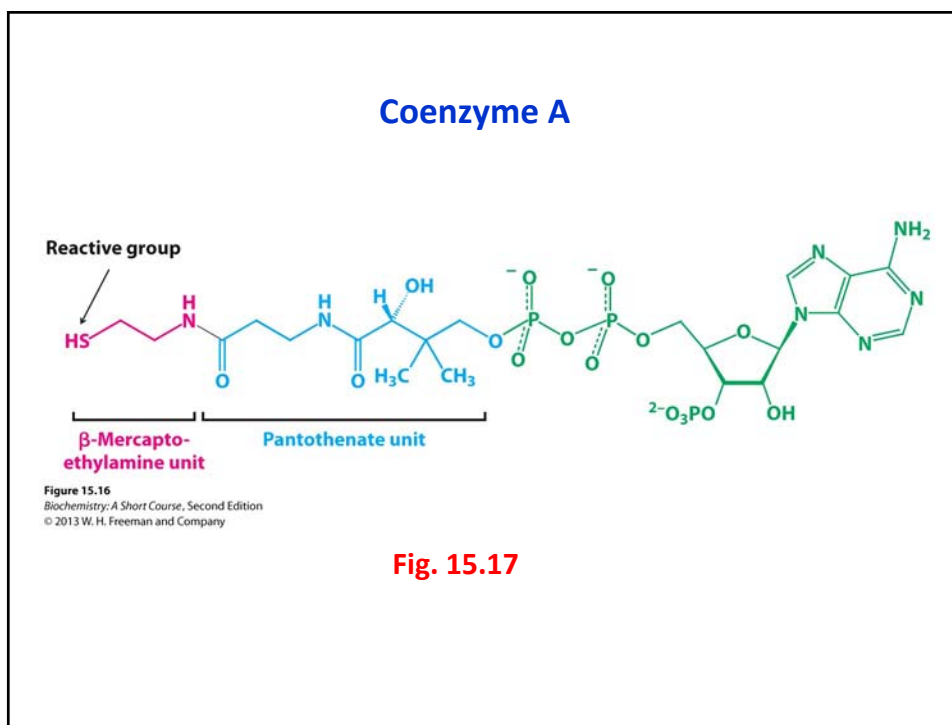


Fig. 15.17

Coenzyme A

(carrying an acetyl group during a reaction)

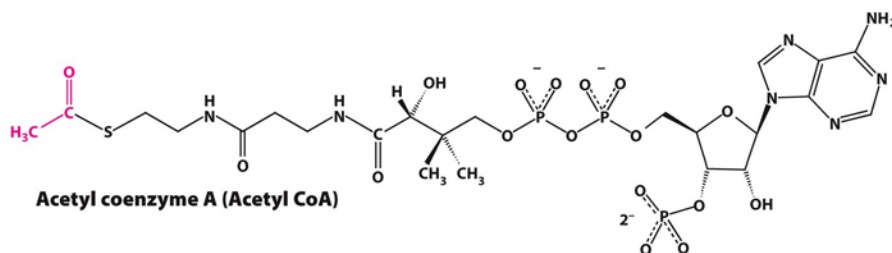
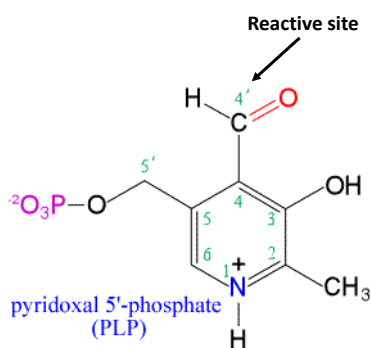


Figure 18.1
Biochemistry: A Short Course, Second Edition
 © 2013 W. H. Freeman and Company

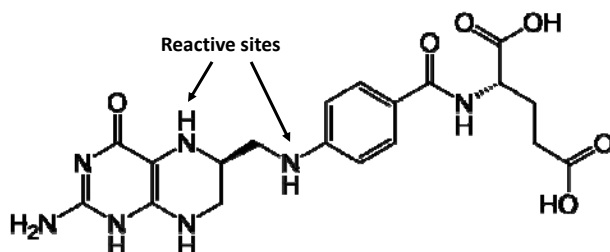
Fig. 18.1

Pyridoxal phosphate

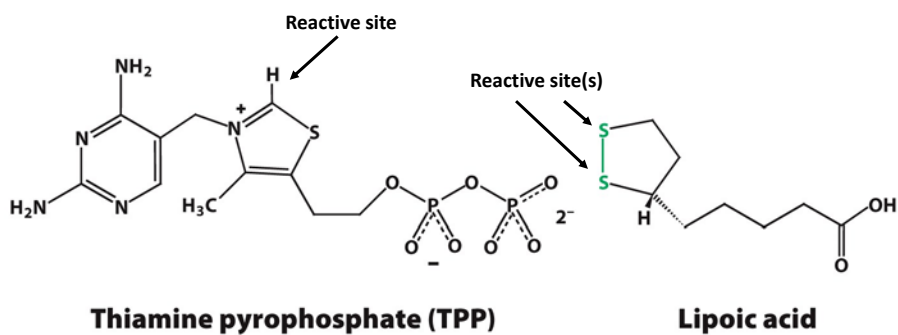


See pg. 576

Tetrahydrofolate



See pgs. 594-595

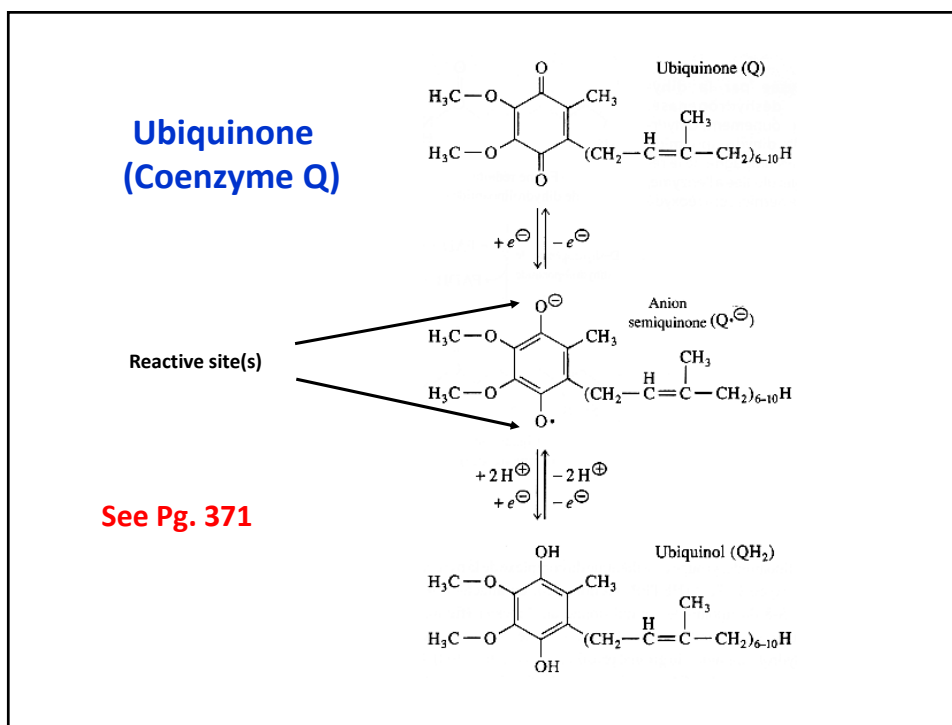
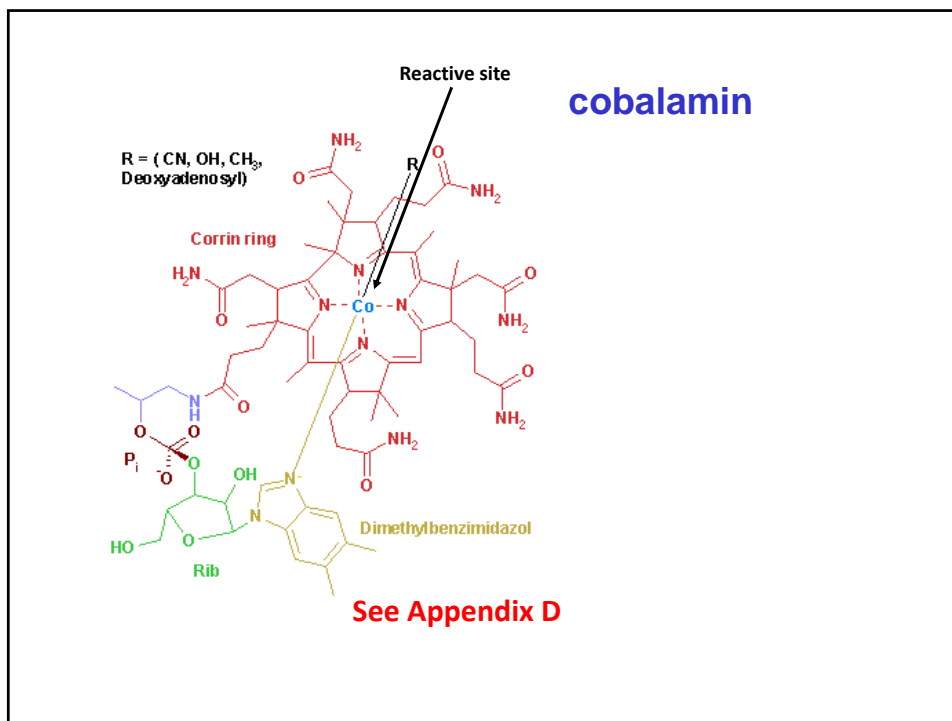


Thiamine pyrophosphate (TPP)

Lipoic acid

Unnumbered 18 p319
 Biochemistry: A Short Course, Second Edition
 © 2013 W. H. Freeman and Company

See pgs. 333-335



Group Activity on Coenzymes

Be sure to read through “Hints for learning coenzymes” as you prepare and teach your coenzymes to your group.

Be sure to work in your groups to learn the co-enzymes over the next week.