

Definition: vitamin, coenzyme, cofactor

Vitamin - organic compound required in trace amount (micronutrient) in mg or g per day e.g. A, D, E, K, B, C

Coenzyme - complex organic or metallo-organic molecule e.g. TPP, Coenzyme A, bound to the active site of an enzyme (covalent or non-covalent) and participate in catalysis

Cofactor - metal ion for proper function of enzyme e.g. K^+ , Mg^{2+} , Ca^{2+} , Fe^{2+} , Zn^{2+}

Some vitamin are precursor of coenzymes

Classification of coenzymes by binding substrates

Cosubstrates
(loosely bound)

Prosthetic groups
(tightly bound)

Flavin coenzymes
Biocytin
Lipoamide (lipoic acid)

Cofactors are **electrophiles** because

1. Positive charge
2. Act as Lewis acids
3. Can bind ligand at least 2 positions in the same time

Some vitamins are precursor of coenzymes

Vitamin	coenzyme
Thiamin (B1)	Thiamin pyrophosphate
Riboflavin (B2)	Flavin coenz.
Pantothenate (B5)	Coenzyme A
Pyridoxine (B6)	Pyridoxal phosphate
Cobalamin (B12)	Cobalamin B12 coenz
Nicotinamide	Nicotinamide coenz.
Folic acid	Tetrahydrofolate
Biotin	Biocytin

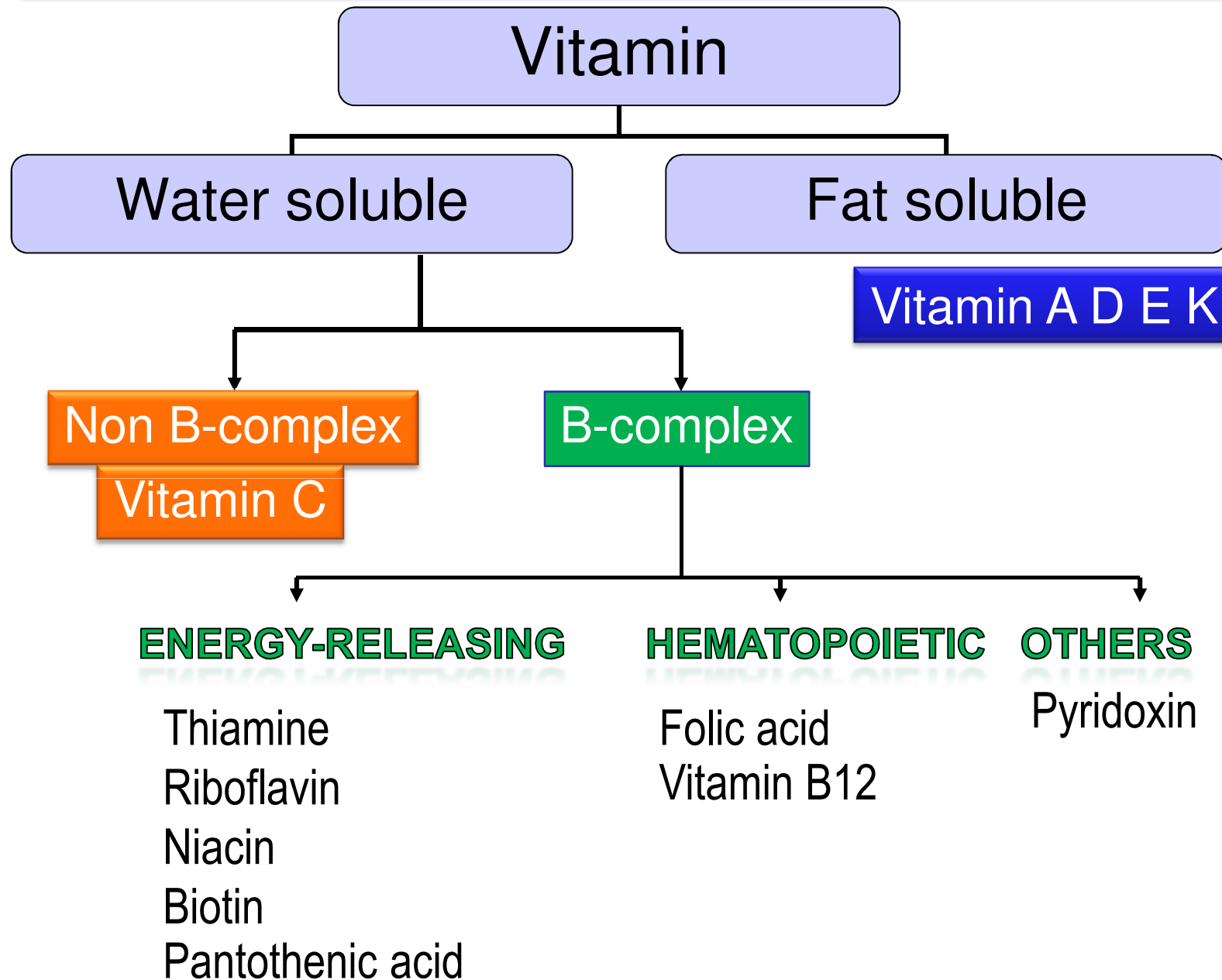
Cofactor	Enzyme
Coenzyme	
Thiamine pyrophosphate	Pyruvate dehydrogenase
Flavin adenine nucleotide	Monoamine oxidase
Nicotinamide adenine dinucleotide	Lactate dehydrogenase
Pyridoxal phosphate	Glycogen phosphorylase
Coenzyme A (CoA)	Acetyl CoA carboxylase
Biotin	Pyruvate carboxylase
5'-Deoxyadenosyl cobalamin	Methylmalonyl mutase
Tetrahydrofolate	Thymidylate synthase
Metal	
Zn ²⁺	Carbonic anhydrase
Zn ²⁺	Carboxypeptidase
Mg ²⁺	<i>EcoRV</i>
Mg ²⁺	Hexokinase
Ni ²⁺	Urease
Mo	Nitrate reductase
Se	Glutathione peroxidase
Mn ²⁺	Superoxide dismutase
K ⁺	Propionyl CoA carboxylase

Mechanism of action (coenzyme & cofactor)

- Help enzyme to bind with substrate
- Charge or interaction between molecules
- Change active site of enzyme to fit with substrate
- Stabilize enzyme structure
- Acts as catalytic components

oregonstate.edu/.../enzymesoutline.html

Classification of vitamin by solubility



Classification of coenzyme by their functions in chemical reactions

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graph TD; A[Classification of coenzyme by their functions in chemical reactions] --> B[1.e- carrier (ox-red rx.)]; A --> C[2.group transfer];
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1.e- carrier (ox-red rx.)

Energy metabolism e.g. ETS

Coenzyme

FAD, FMN

NAD⁺, NADP⁺

Co Q (ubiquinone)

Vitamin precursor

Vitamin B2 (riboflavin)

Vitamin B3 (niacin or
nicotinic acid)

No

2.group transfer

General rx. in the body

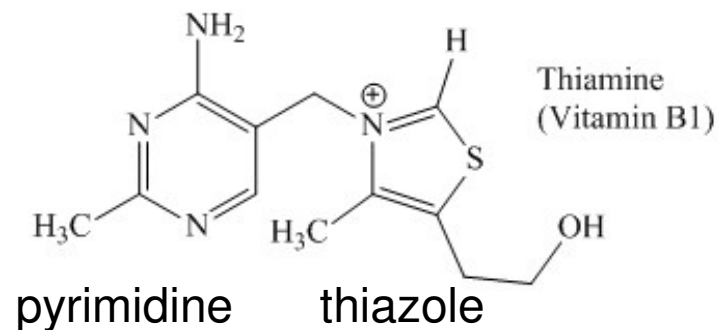
B1, B5, B6, B12, H, folic
acid

Lipoic acid, SAM

Vitamin B1 (Thiamine)

Coenzyme - Thiamine pyrophosphate (TPP)

Thiamine

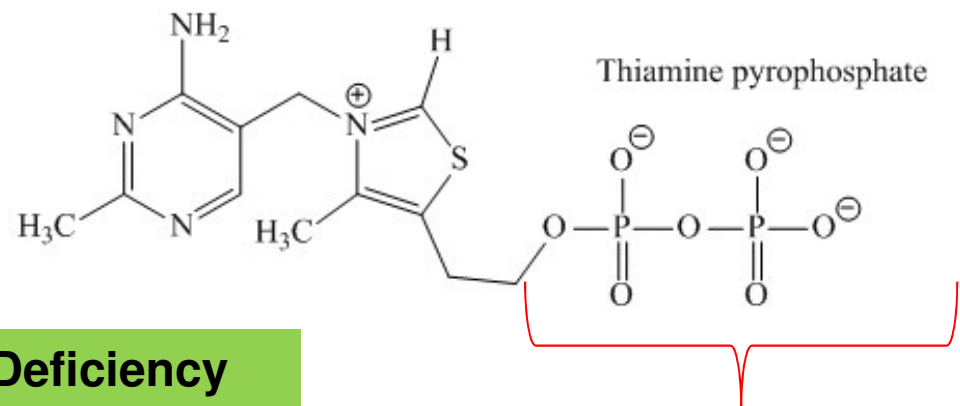


- Function
- energy metabolism
- group transfer (aldehyde)
- Maintain nerve system
- Improve brain by acting as neurotransmitter

Deficiency

- Beri-beri
- Damage nervous system, heart and muscle

TPP



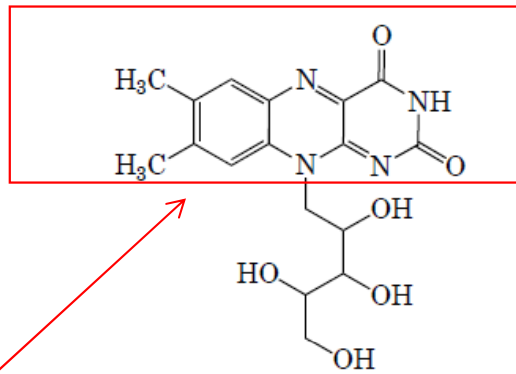
Destroyed by

- thiaminase (fermented fish)
- caffeic acid, tannic acid
- heat



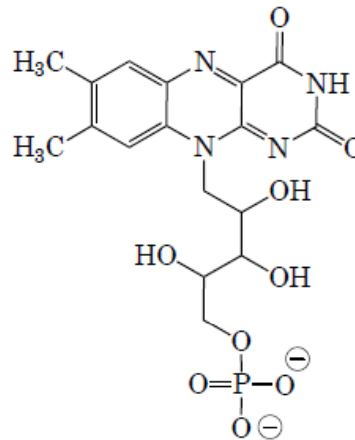
Vitamin B2 (Riboflavin)

Flavin coenz.(FAD, FMN)

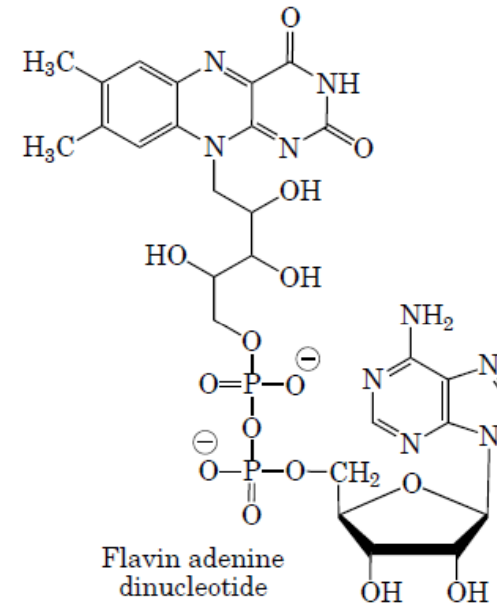


Isoalloxazine ring

Riboflavin
(Vitamin B₂)



Flavin
mononucleotide
[FMN]



Flavin adenine
dinucleotide
[FAD]



angular
stomatitis

พบครั้งแรกในนม และเรืองแสงสีเหลือง “flavin”
และในโครงสร้างมีน้ำตาล ribose เกาะติดอยู่

Stable- acid, oxidation

Unstable- base, UV

Deficiency

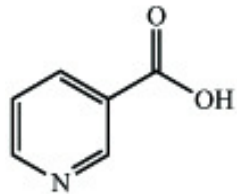
- Ariboflavinosis (inflammation of membrane linings of eyes, mouth, GI tract, cracks at corner of mouth)
- Symptoms – dermatitis, tongue darkening, anemia



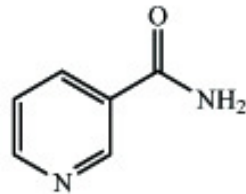
glossitis

Vitamin B3 (Niacin or Nicotinic acid)

Coenzyme- Nicotinamide



Niacin
(nicotinic acid)

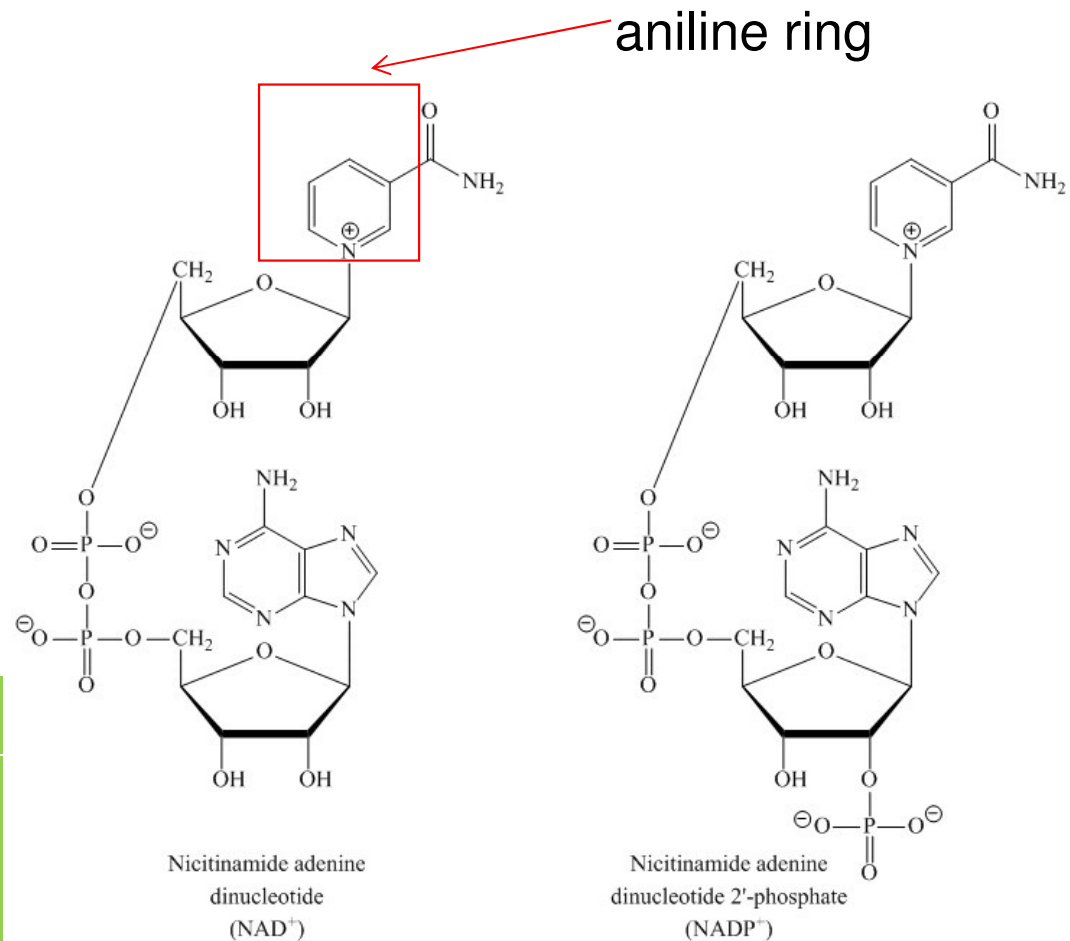


Niacin
(nicotinamide)

Stable- acid, base, heat, light

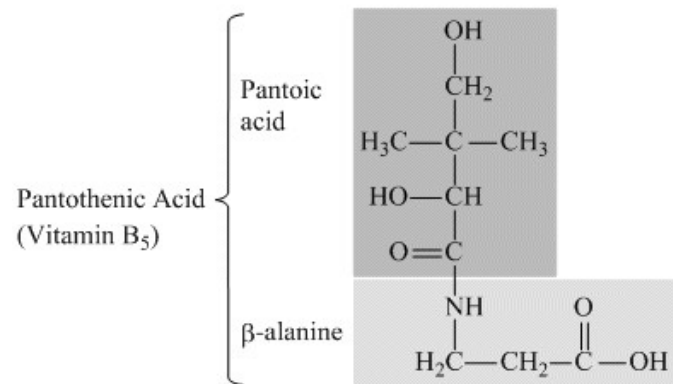
Deficiency

- Pellagra, **d**iarrhea, **d**ermatitis, **d**ementia, death
- Symptoms – dermatitis, tongue darkening, anemia



Vitamin B5 (Pantothenic acid)

Part of Coenzyme A

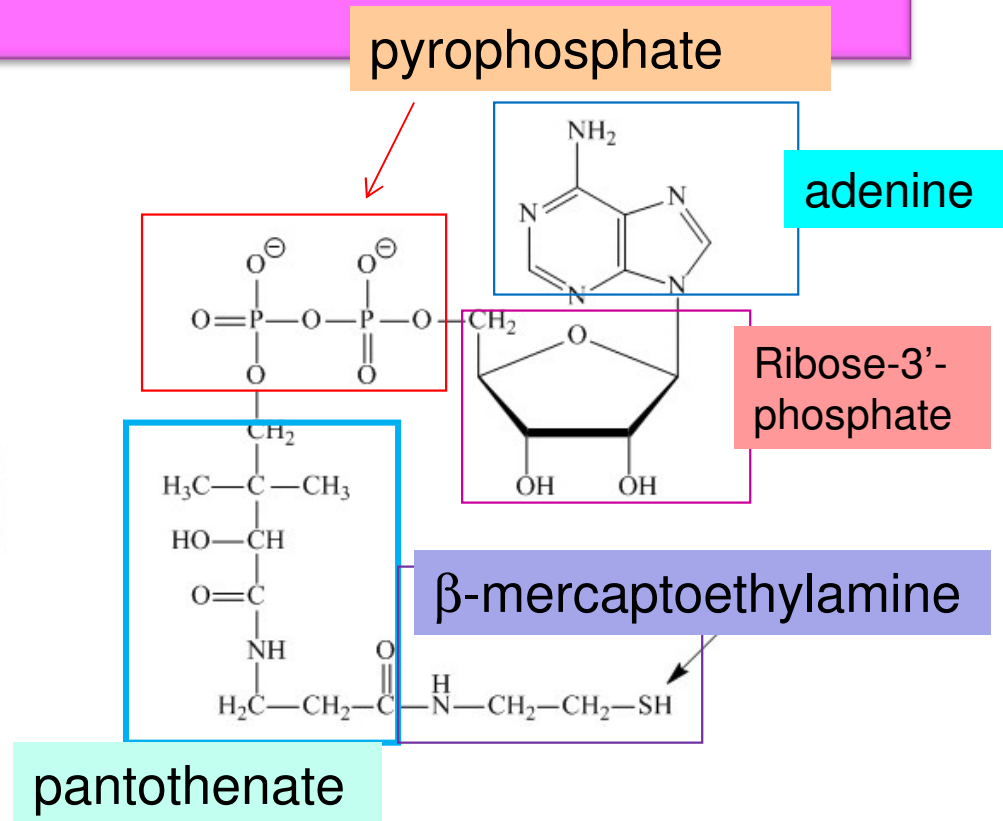


Pantothenic acid

Unstable- acid, base, heat

Deficiency- rare

Fatigue, nausea,
insomnia, irritability



Coenzyme A

Vitamin B6 (Pyridoxine)

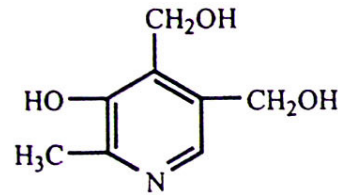
Coenzyme - Pyridoxal phosphate (PLP)

vitamin

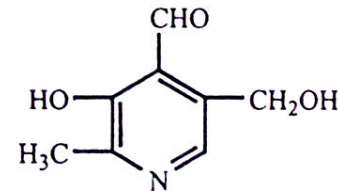
ในธรรมชาติมี 3 รูปแบบ

ถูกแสงทำลายได้

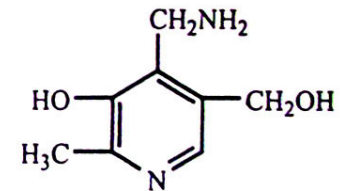
coenzyme



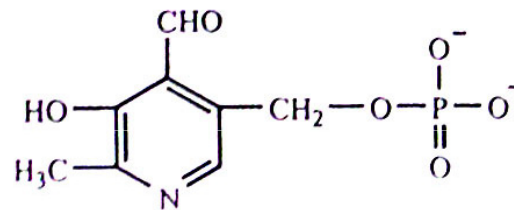
Pyridoxine



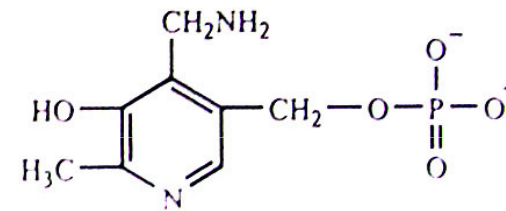
Pyridoxal



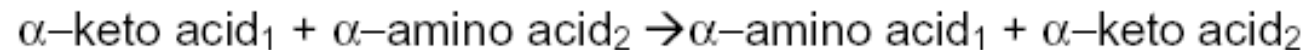
Pyridoxamine



Pyridoxal phosphate (PLP)



Pyridoxamine phosphate



Deficiency

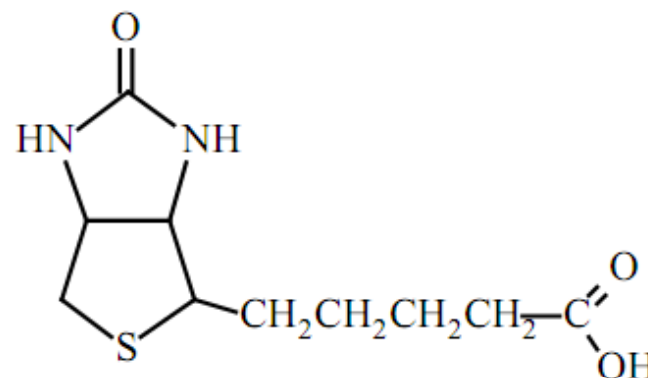
- Symptoms – depression, confusion, weakness, nausea, microcytic anemia
- Rare – can be caused by some drugs
- Requirement related to protein intake

Vitamin H (Biotin)

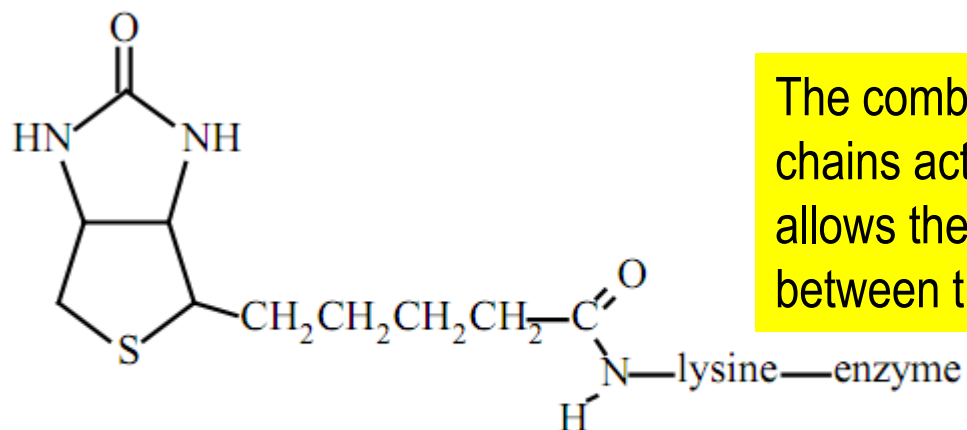
Biocytin

ทนร้อน ถูกทำลายโดยออกซิเดชัน

Biotin link with enz by amide bond
(COOH of biotin and NH₂ of Lys)



Biotin



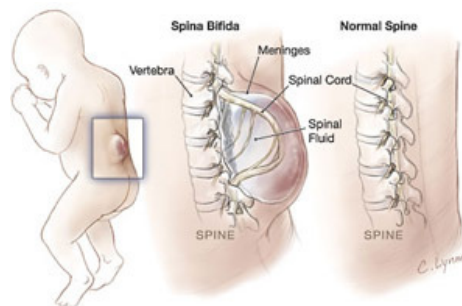
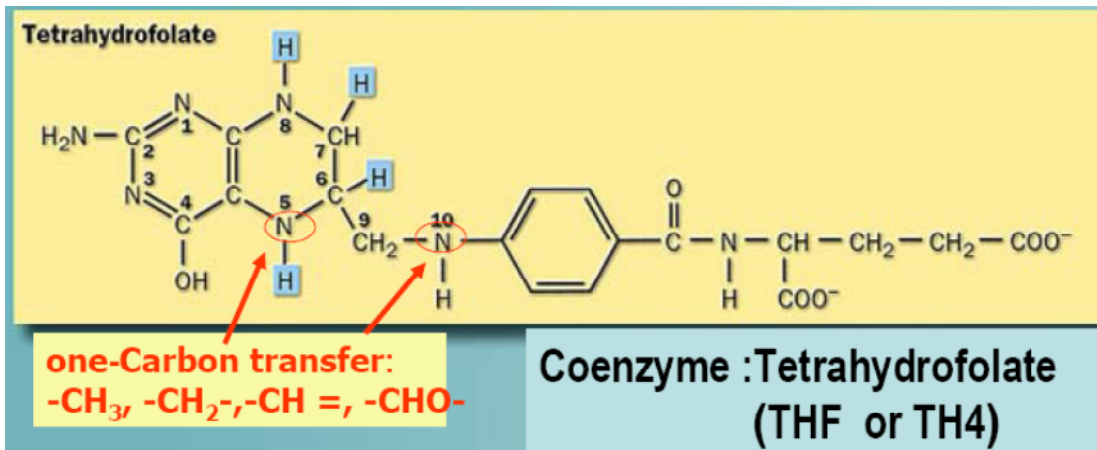
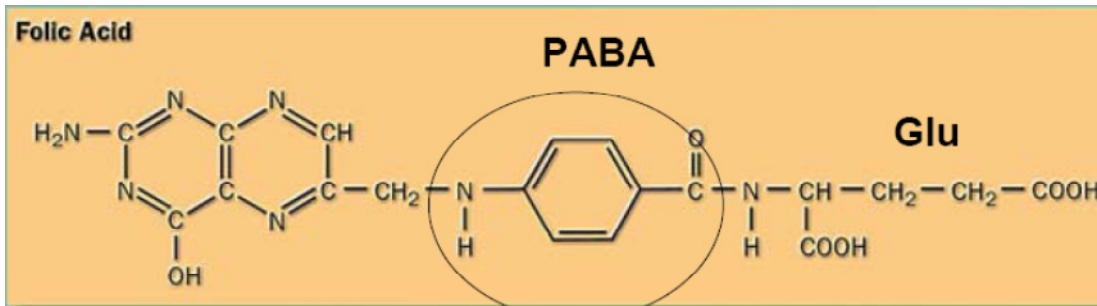
BIOCYTIN

The combined biotin and lysine side chains act as a **long flexible arm** that allows the biotin ring to translocate between the 2 active sites

Inhibitor – avidin in white egg bind with biotin, inhibit absorption

Folic acid

Tetrahydrofolate (THF)



spinal bifida improper development of spinal chord in fetus (neural tube defect)

Destroyed by heat and oxygen

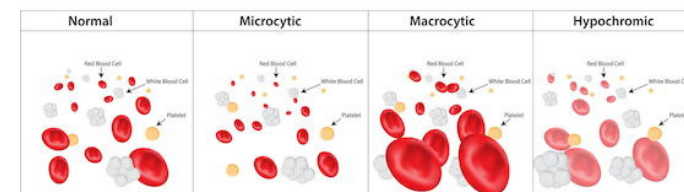
carry and transfer various forms of 1-C units (e.g. methyl, methylene, methenyl, formyl or formimino groups) during biosynthetic rxs.

Deficiency

poor growth, mental confusion, irritability, fatigue, GI tract deterioration

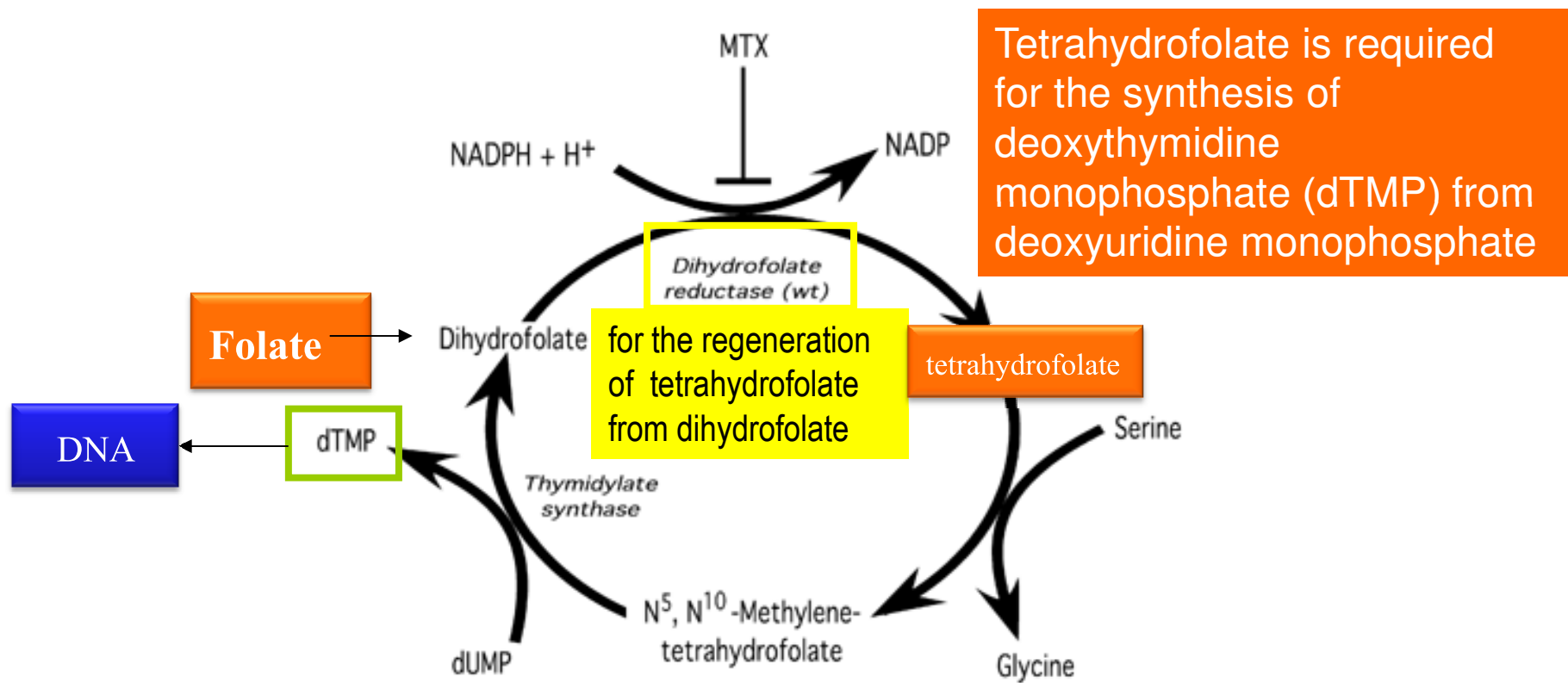
macrocytic anemia due to inability to synthesize DNA during erythrocyte maturation → leads to **macrocytic anemia** (abnormally large erythrocytes).

Anemia



Function

Involved in DNA synthesis, amino acid metabolism, cell division, formation of neural tube in developing fetus

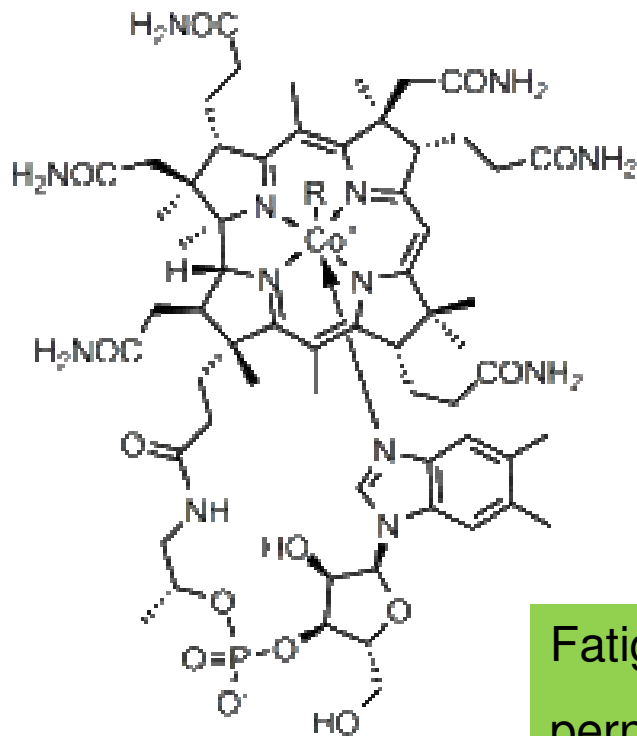


Vitamin B12

Cobalamine B12 coenzyme

Methylcobalamine (methyl B12) – main in plasma

Deoxyadenosylcobalamine – main in tissue

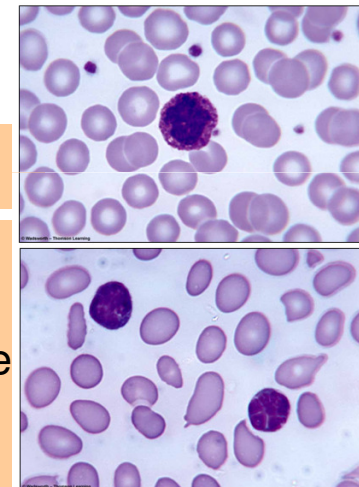


Absorption – ileum

Storage - in liver 2-4 years

Function

Development of rbc,
nerve function, cell
division, homocysteine
conversion to
methionine



Normal blood cells. The size, shape, and color of the red blood cells show that they are normal.

Blood cells in pernicious anemia (megaloblastic). Megaloblastic blood cells are slightly larger than normal red blood cells, and their shapes are irregular.

Figure 10-1:
Page 342
Slide 39

Deficiency

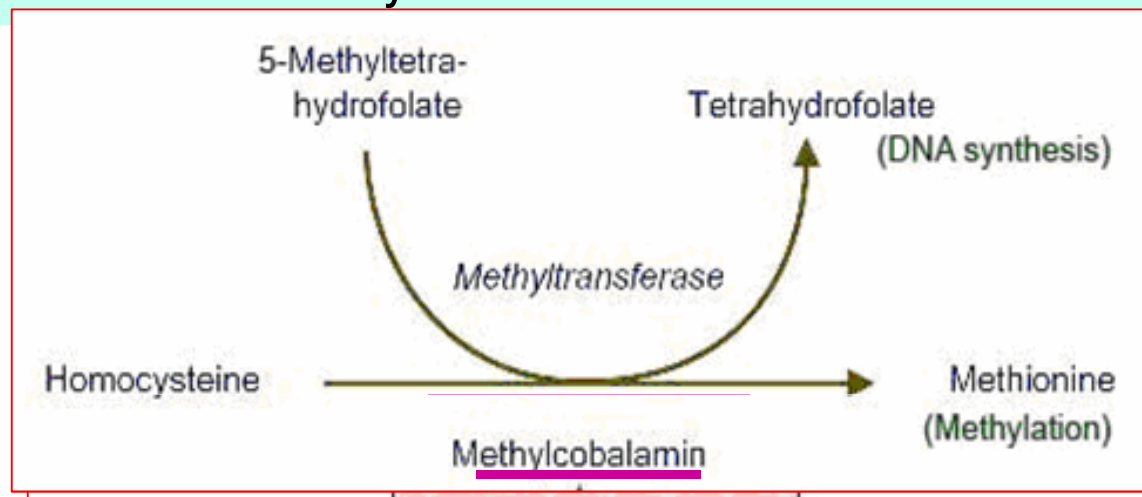
Fatigue, low energy, shortness of breath and

pernicious anemia (**megaloblastic anemia**) (lack of intrinsic factor in the stomach leading to malabsorption of the vitamin)

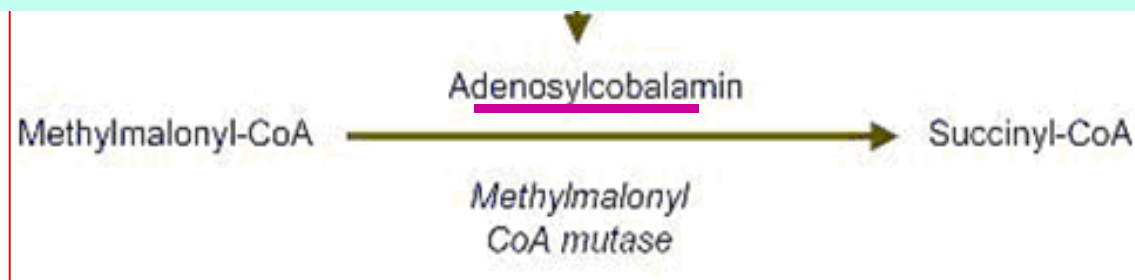
Deficiency found in vegetarians, older people

only two reactions in the body that require vitamin B12 as a cofactor

1. conversion of homocysteine to methionine



2. oxidation of odd chain fatty acids

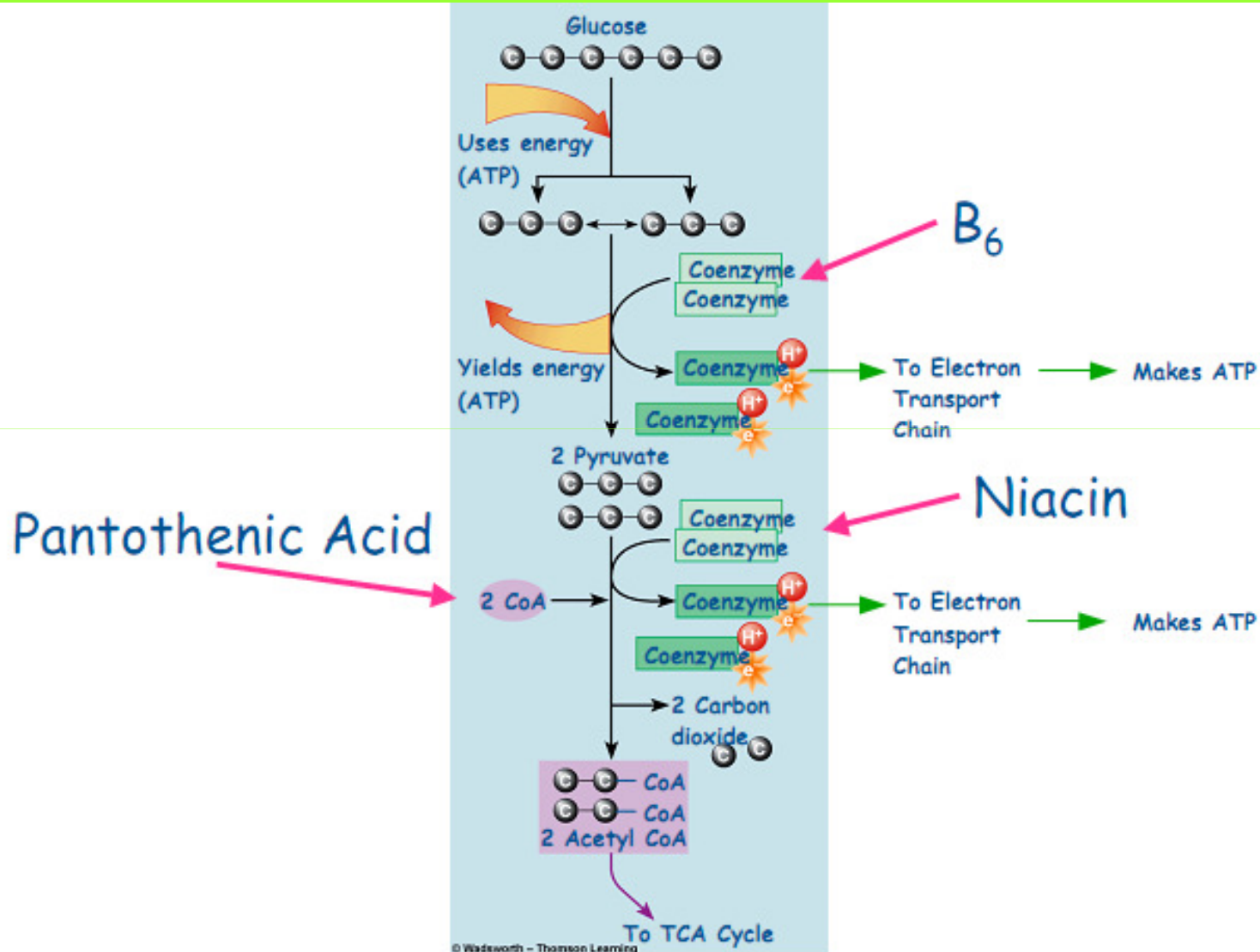


ขาด B12 ทำให้สังเคราะห์ DNA ลดลง และ มีการกั่งของ methylmalonyl CoA ซึ่งจะยับยั้งการสังเคราะห์ myelin sheath ของ nerve cell

Example of coenzyme/enzyme in metabolism

Coenzyme	Enzymes	Metabolic pathway
TPP	pyruvate decarboxylase	Alcoholic fermentation
	transketolase	Pentose phosphate pathway (PPP)
FMN	NADH dehydrogenase (complex I)	Electron transport system (ETS)
FAD	Succinate dehydrogenase	Krebs cycle
NAD ⁺	Lactate dehydrogenase	Anaerobic glycolysis
	Malate dehydrogenase	Krebs cycle
NADP ⁺	Glucose -6- P dehydrogenase	Pentose phosphate pathway (PPP)
Co A	Acyl CoA synthetase	β -oxidation of fatty acids
	Acyl carrier protein (ACP)	Fatty acid synthesis
PLP	Alanine aminotransferase(ALT)	Amino acid metabolism
	Aspartate aminotransferase(AST)	Amino acid metabolism
	ALA synthetase	Heme synthesis
Biocytin	Pyruvate carboxylase	Gluconeogenesis
	Acyl CoA carboxylases	Fatty acid synthesis
TPP, FAD	pyruvate dehydrogenase complex	Aerobic glycolysis
CoA, NAD ⁺	α -ketoglutarate DH complex	Krebs cycle
Lioamide		

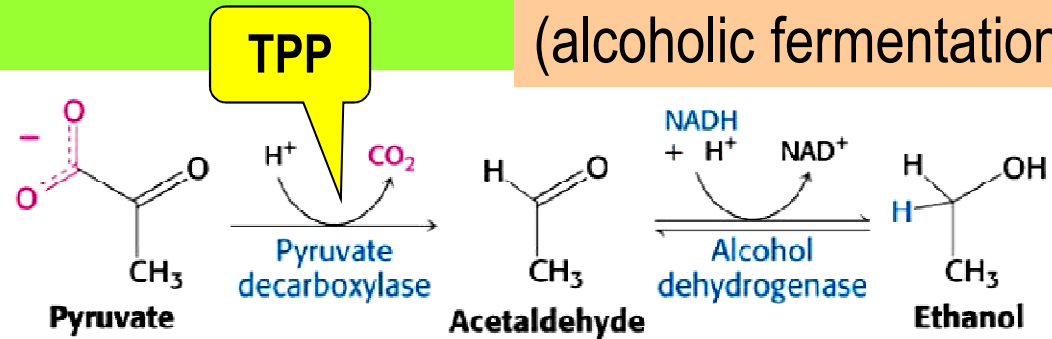
Vitamins/coenzymes in glucose metabolism



Vitamins/coenzymes in Krebs' cycle

Energy metabolism

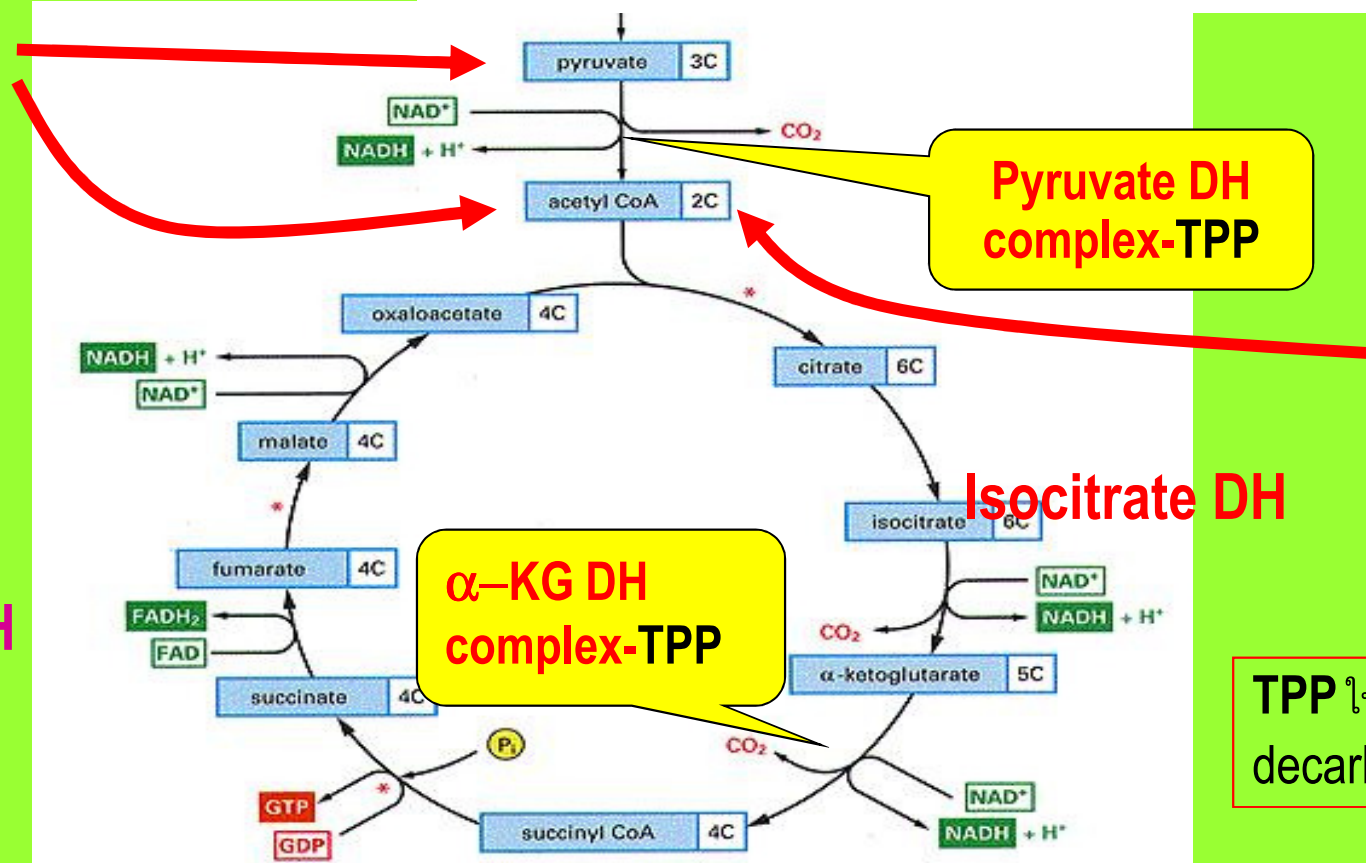
(alcoholic fermentation)



protein

Malate DH

Succinate DH

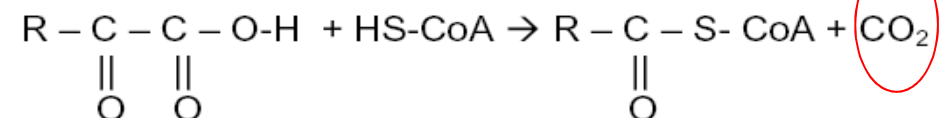


Lipid

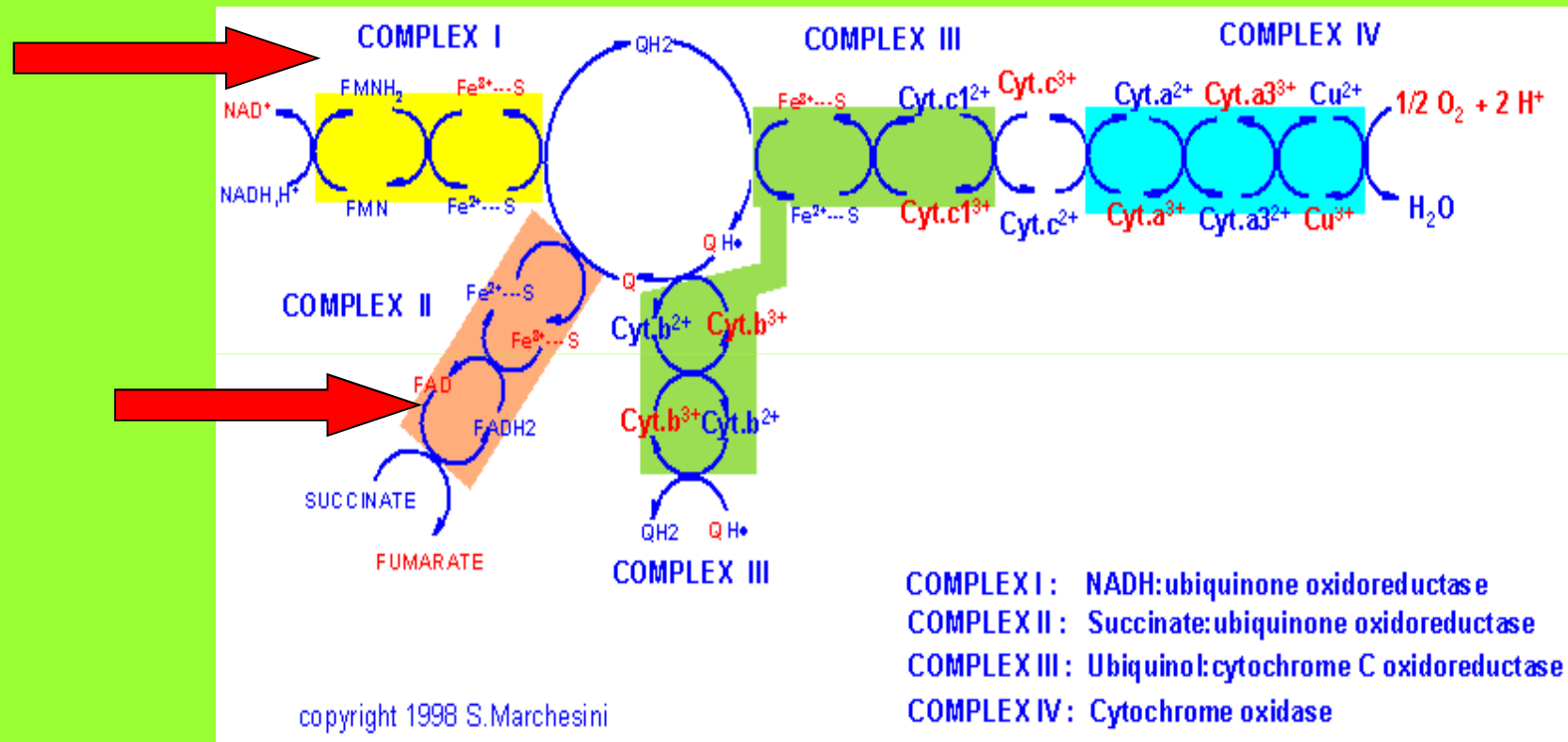
Isocitrate DH

TPP ในปฏิกิริยา decarboxylation

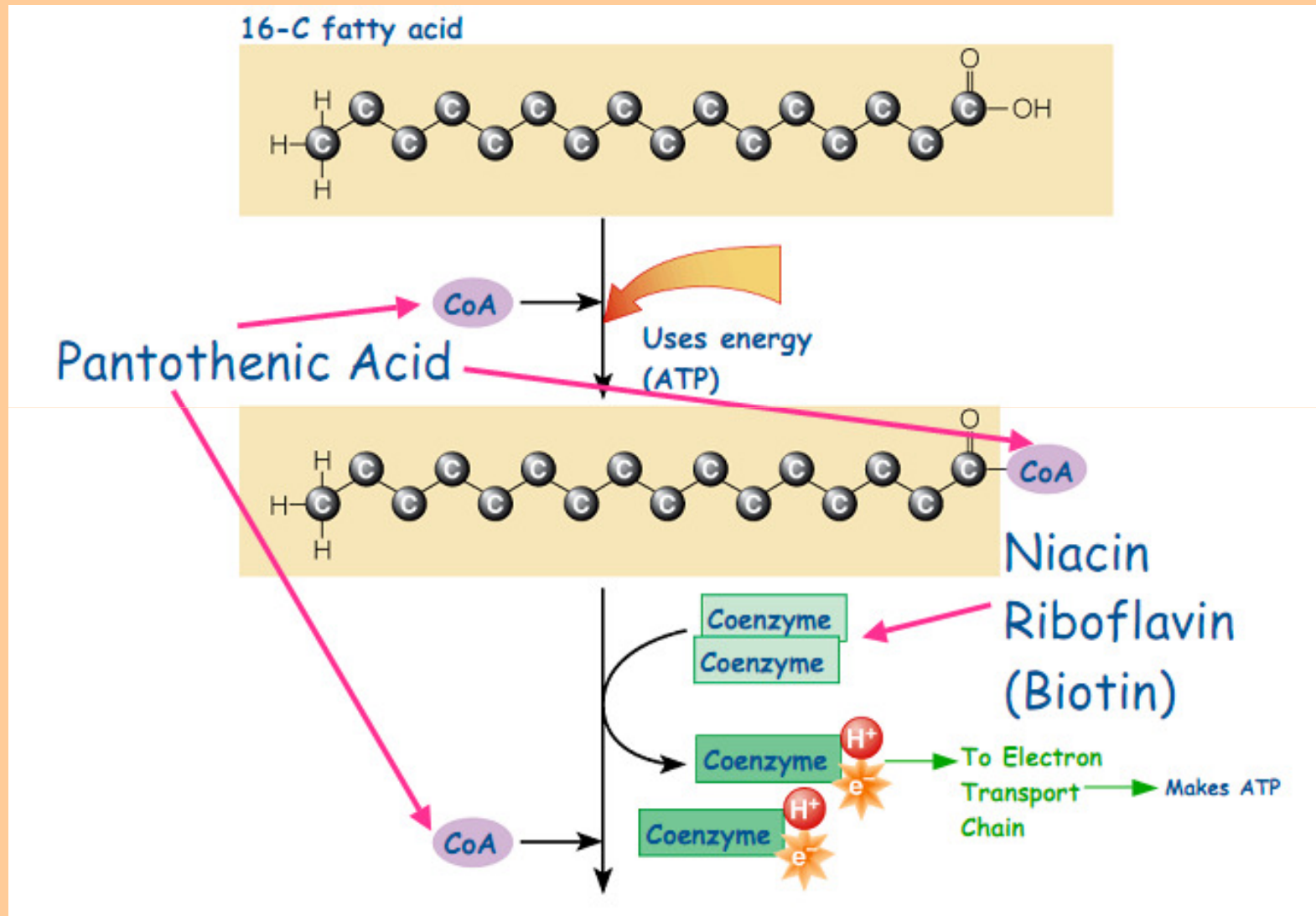
From www2.carthage.edu/~pfaffle/170/second.html



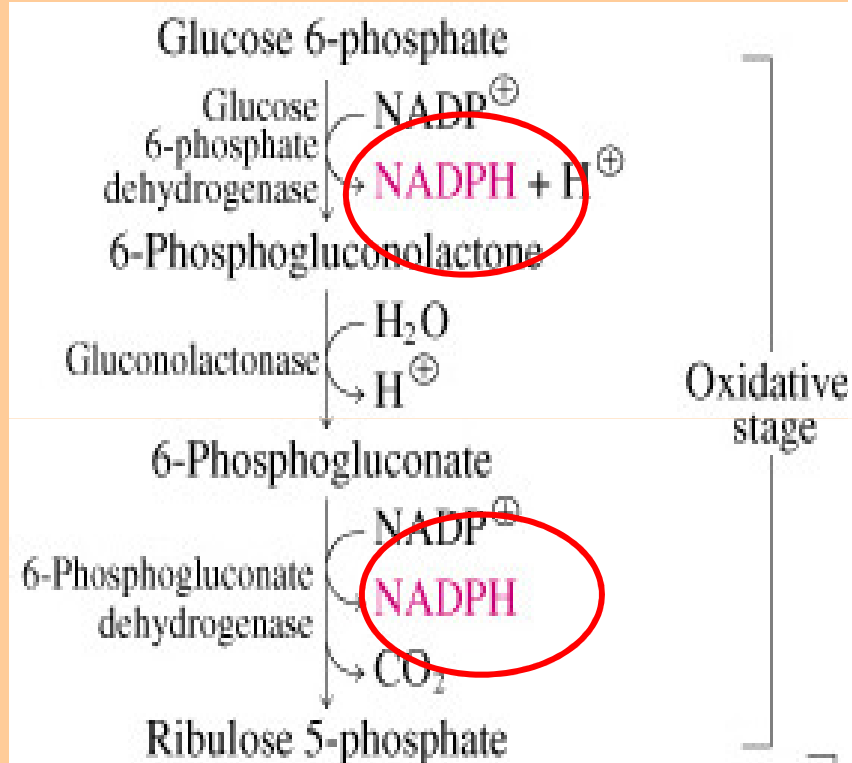
Vitamins/coenzymes in electron transport chain (ETS)



Vitamins/coenzymes in fatty acid metabolism

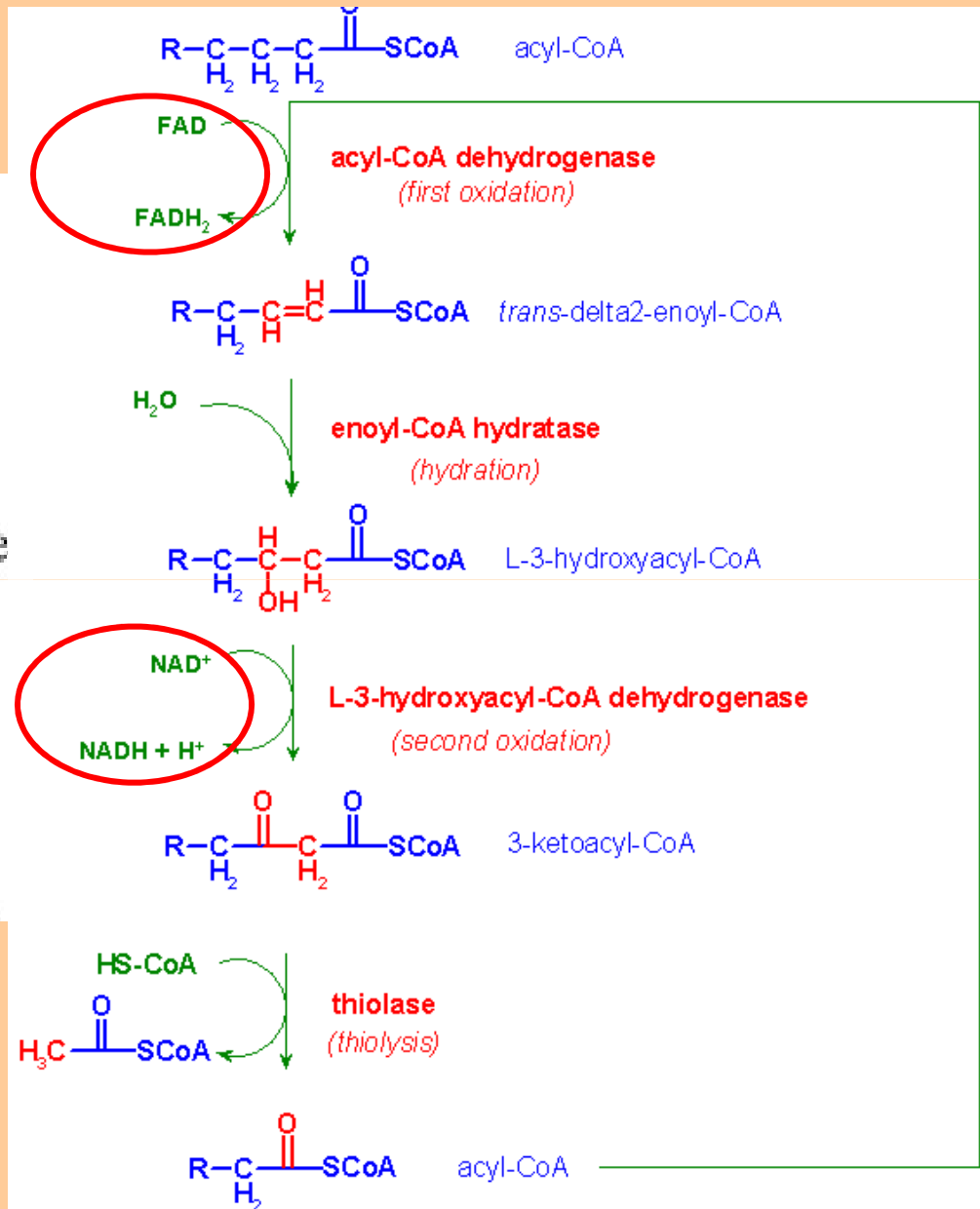


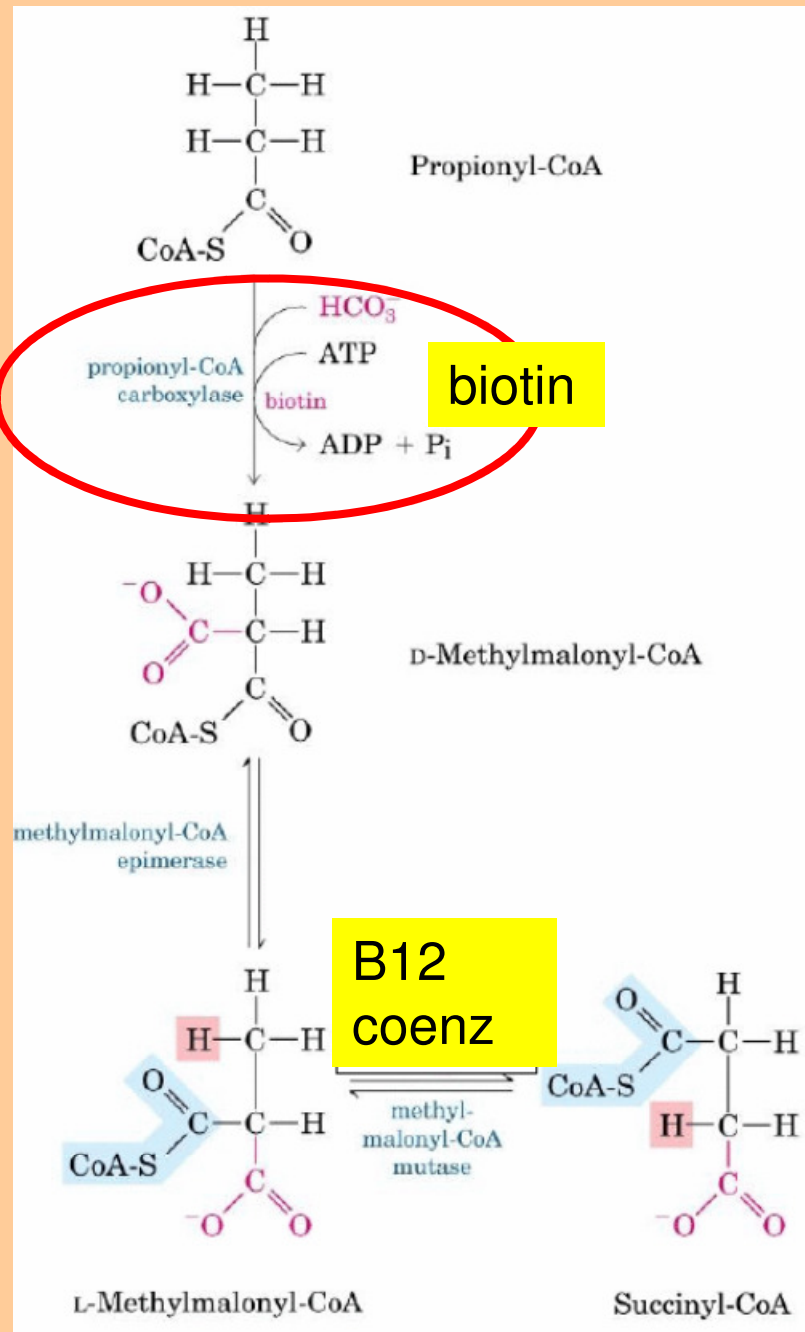
NADP⁺ coenzyme in pentose phosphate pathway as H⁺ acceptor and get NADPH



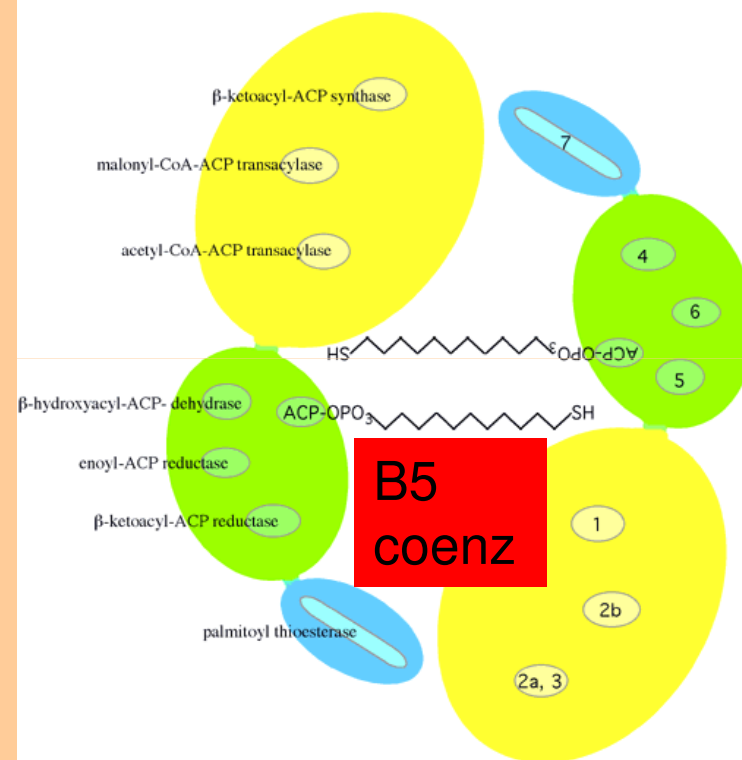
NADPH coenzyme in biosynthesis of fatty acid, cholesterol, amino acid

NAD and beta-oxidation of fatty acid

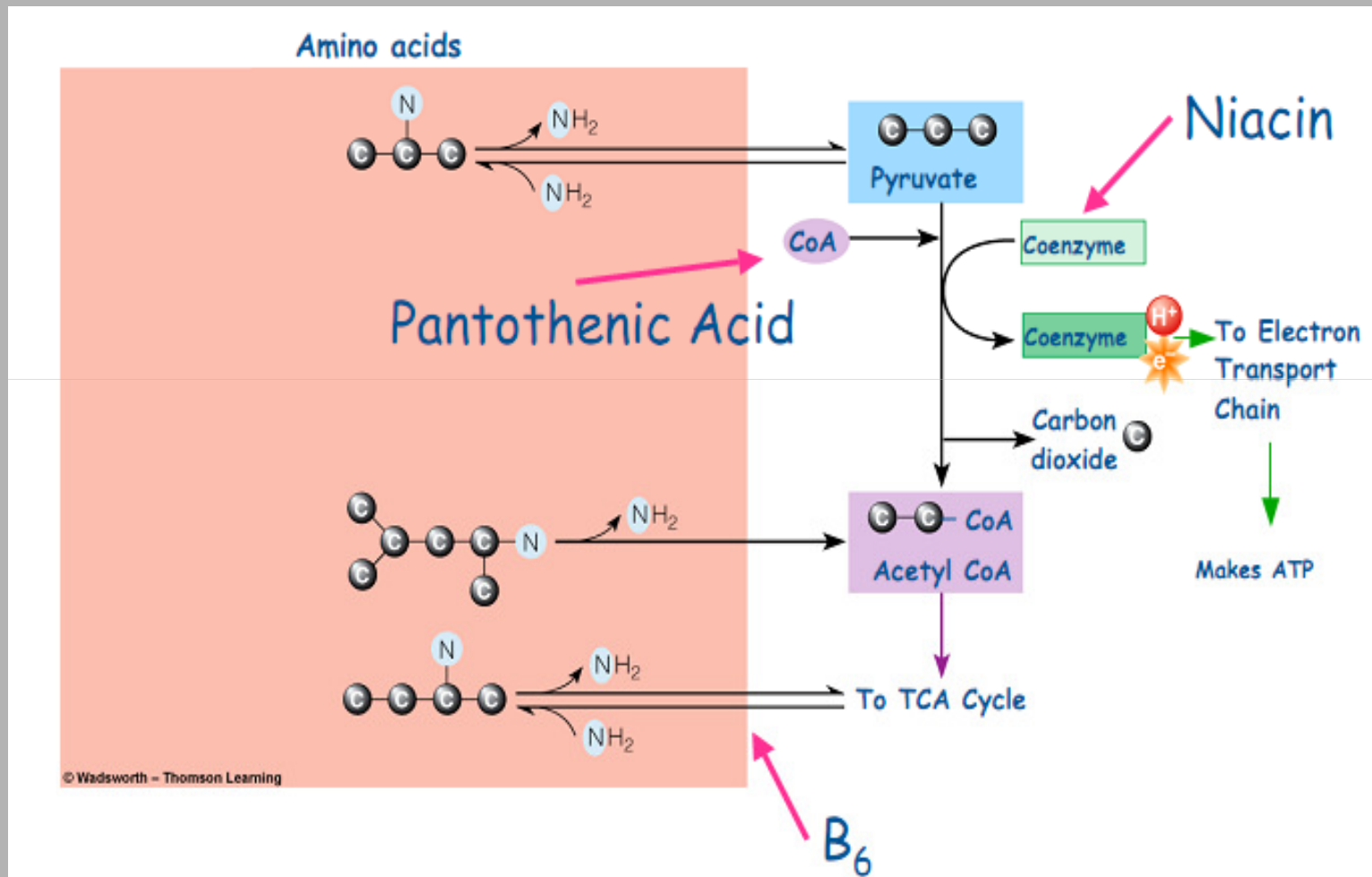


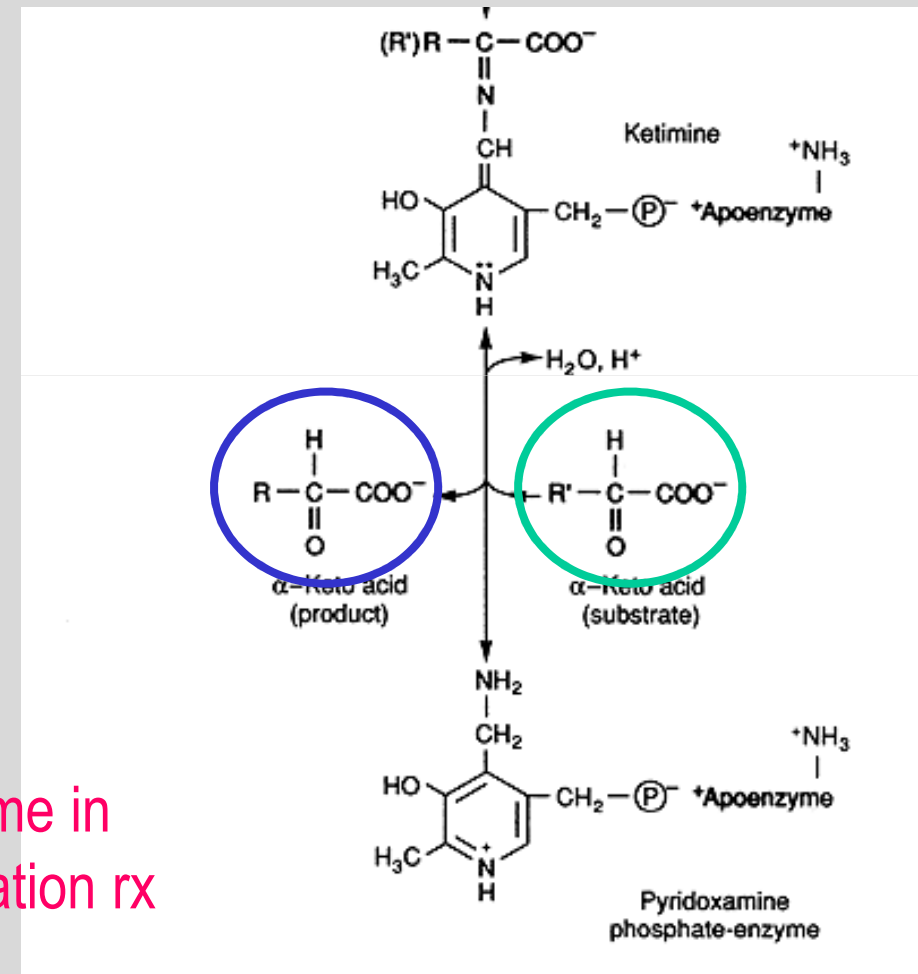
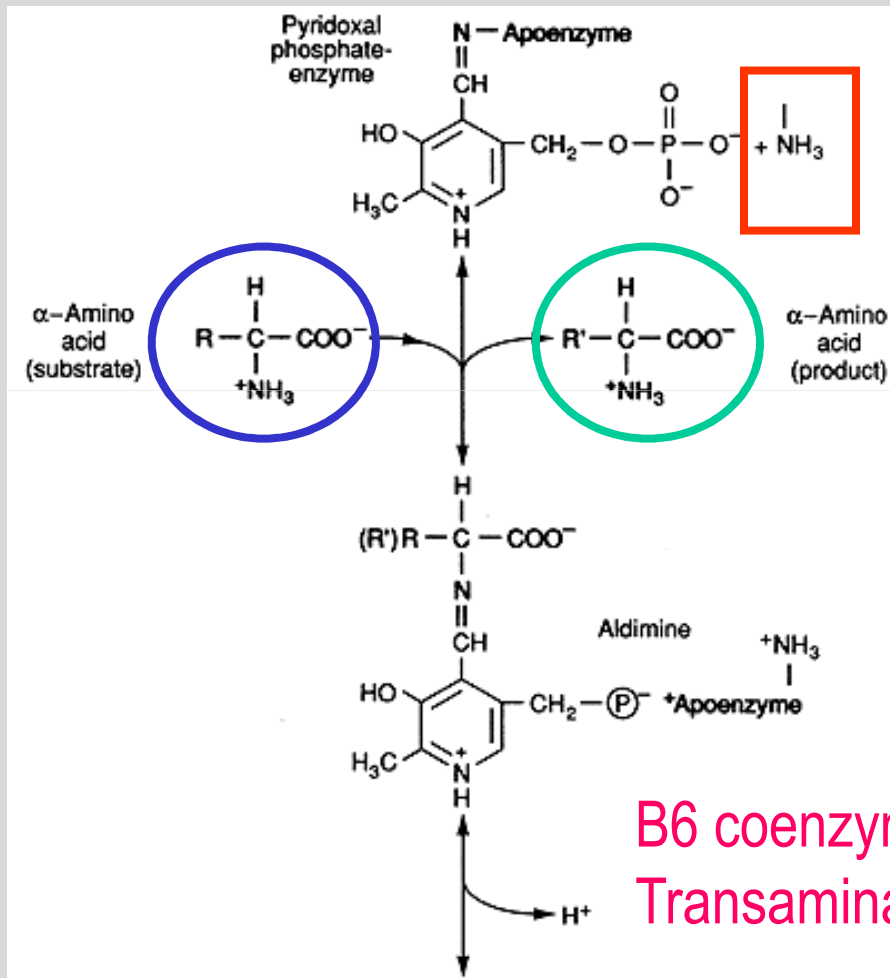


Mammalian Fatty Acid Synthase



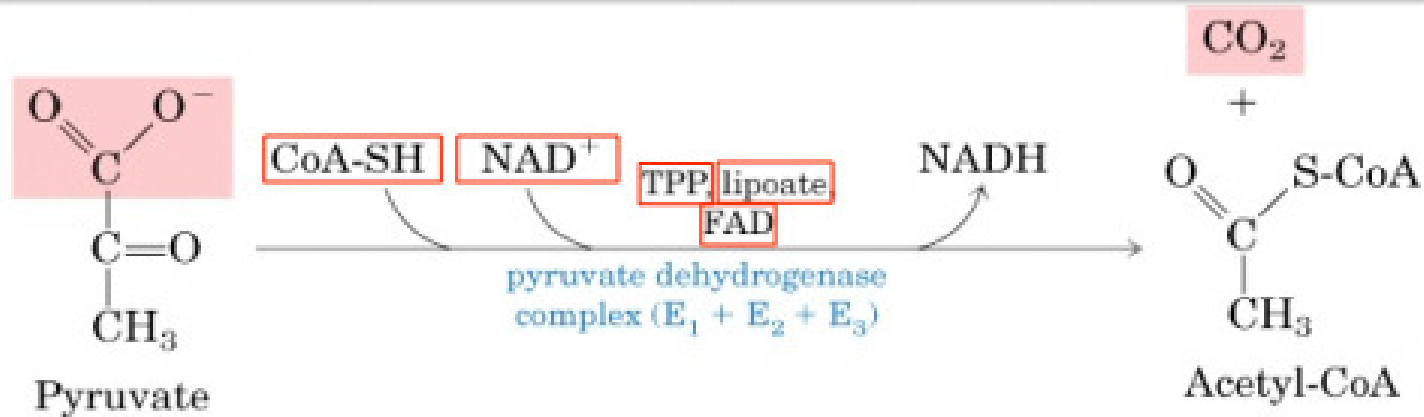
Vitamins/coenzymes in amino acid metabolism





Some enzymes need many coenzymes

Pyruvate dehydrogenase complex (PDH)



Coenzyme A (pantothenate) - reactive thiol is an acyl carrier

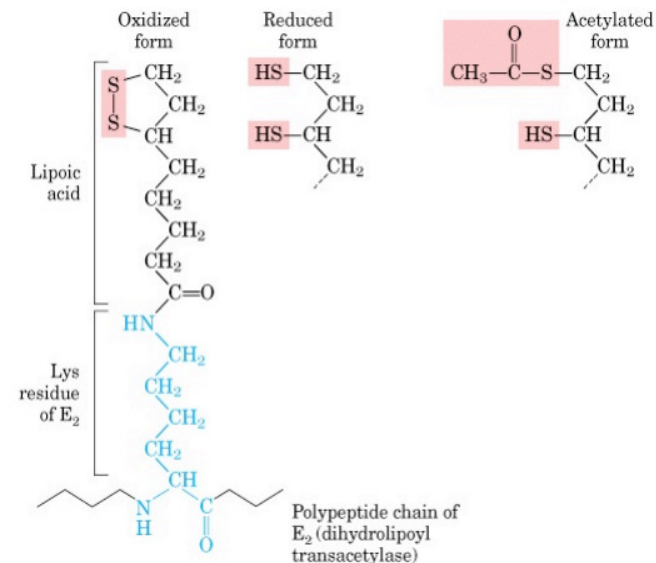
NAD⁺ (niacin) – e carrier

FAD (riboflavin) – e carrier

TPP (thiamine) – cleavage bond next to carbonyl

Lipoate – reversible oxidation at thiols, e carrier and acyl carrier

$$\Delta G'^{\circ} = -33.4 \text{ kJ/mol}$$



Summary

1. Some enzymatic rx. depend on the presence of coenzyme or cofactor.

2. Vitamins are complex organic molecules essential for life. There are water and fat-soluble vitamins.

3. Vitamins (most water-soluble) are precursor of coenzymes.

4. Coenzymes can be classified into e- carrier and group transfer.

5. Some rx. require more than 1 coenzyme.