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+}

Cofactors are **electrophiles** because

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

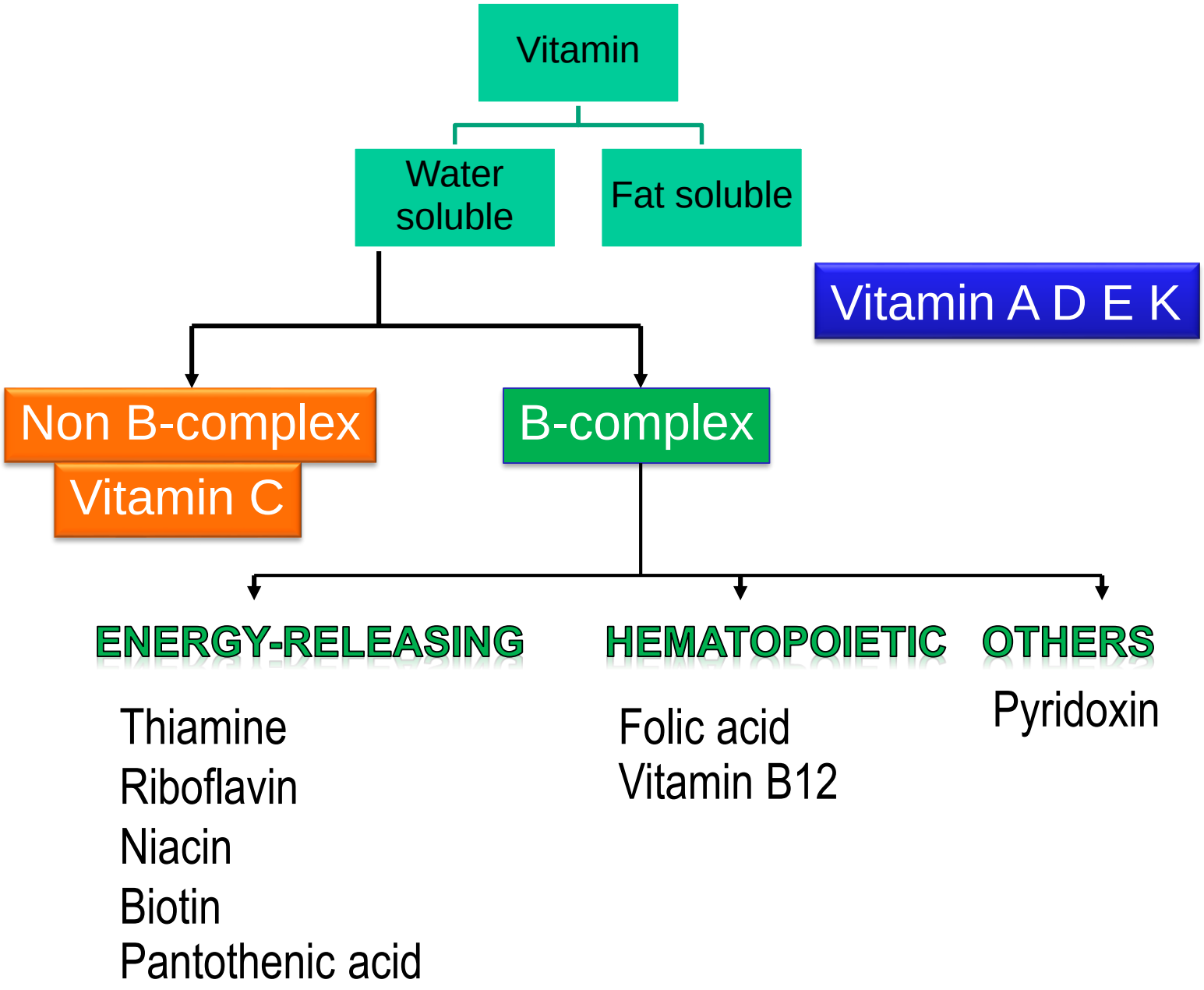
Some vitamin are precursor of coenzymes

Classification of coenzymes by binding substrates

- Cosubstrates (loosely bound)
- Prosthetic groups (tightly bound)

Flavin coenzymes
Biocytin
Lipoamide (lipoic acid)

Classification of vitamin by solubility



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

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

Classification of coenzyme by their functions in chemical reactions

1.e- carrier (ox-red rx.)

Energy metabolism e.g. ETS

Coenzyme	Vitamin precursor
FAD, FMN	Vitamin B2 (riboflavin)
NAD+, NADP+	Vitamin B3 (niacin or nicotinic acid)
Co Q (ubiquinone)	No

2.group transfer

General rx. in the body

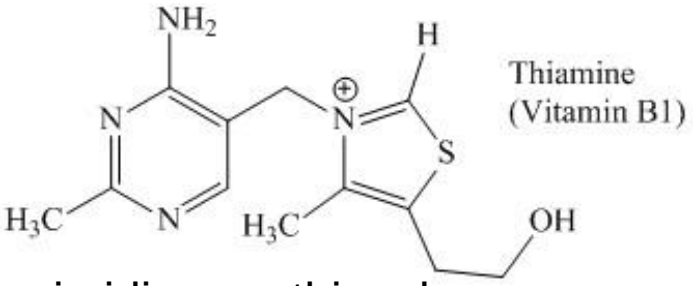
B1, B5, B6, B12, H, folic acid

Lipoic acid, SAM

Vitamin B1 (Thiamine)

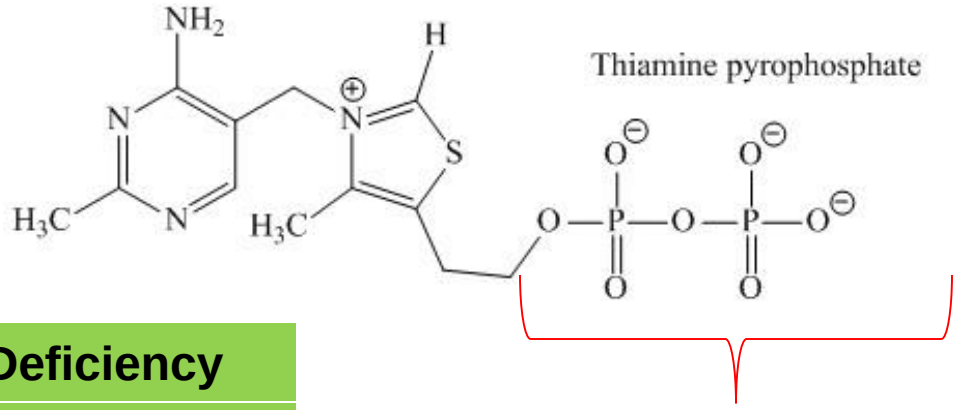
Coenzyme - Thiamine pyrophosphate (TPP)

Thiamine



pyrimidine thiazole

TPP



Deficiency

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

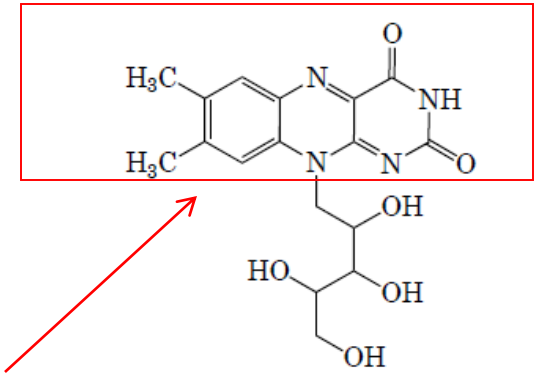
- Function
- energy metabolism
- group transfer (aldehyde)
- Maintain nerve system
- Improve brain by acting as neurotransmitter

Destroyed by

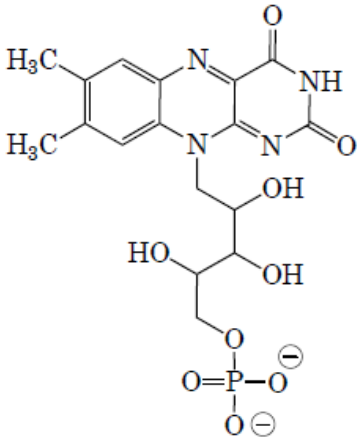
- thiaminase (fermented fish)
- caffeic acid, tannic acid
- heat

Vitamin B2 (Riboflavin)

Flavin coenz.(FAD, FMN)

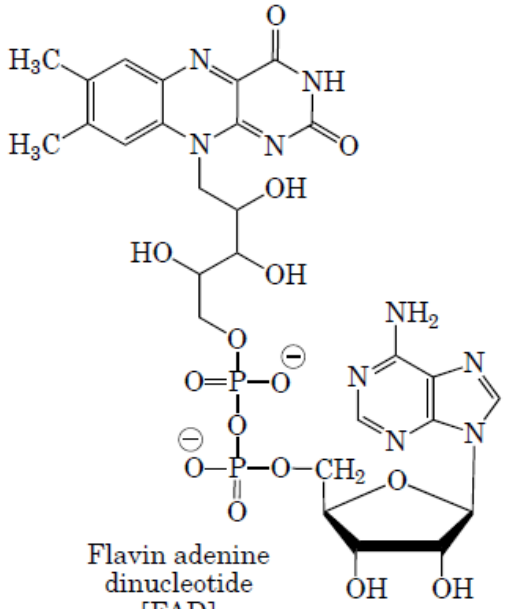


Isoalloxazine ring



Riboflavin
(Vitamin B_2)

Flavin
mononucleotide
[FMN]



Flavin adenine
dinucleotide
[FAD]

angular
stomatitis

พบครั้งแรกในนม และเรืองแสงสีเหลือง “flavin” และในโครงสร้างมีน้ำตาล ribose เกาะติดอยู่

Stable- acid, oxidation

Unstable- base, UV

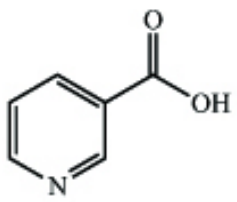
Deficiency

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

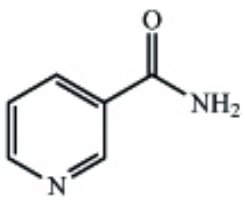
glossitis

Vitamin B3 (Niacin or Nicotinic acid)

Coenzyme- Nicotinamide

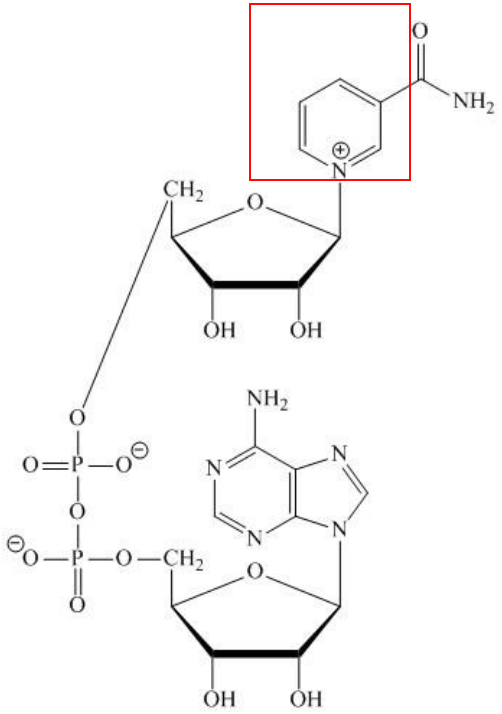


Niacin
(nicotinic acid)

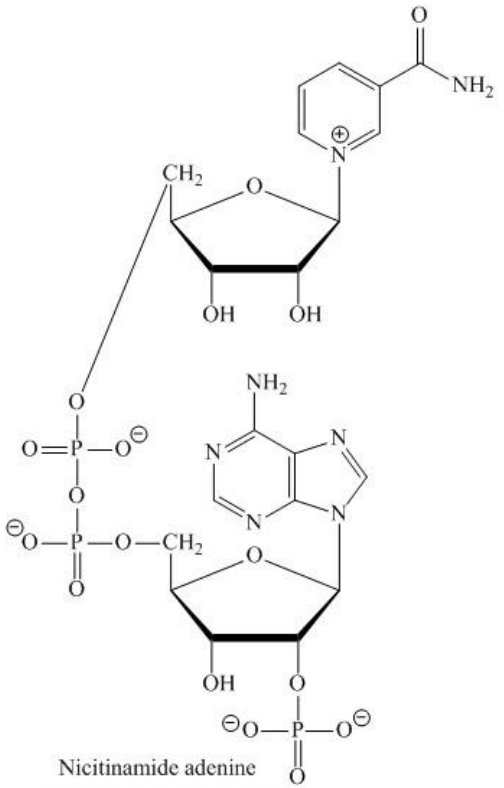


Niacin
(nicotinamide)

aniline ring



Nicitinamide adenine
dinucleotide
(NAD^+)



Nicitinamide adenine
dinucleotide 2'-phosphate
($NADP^+$)

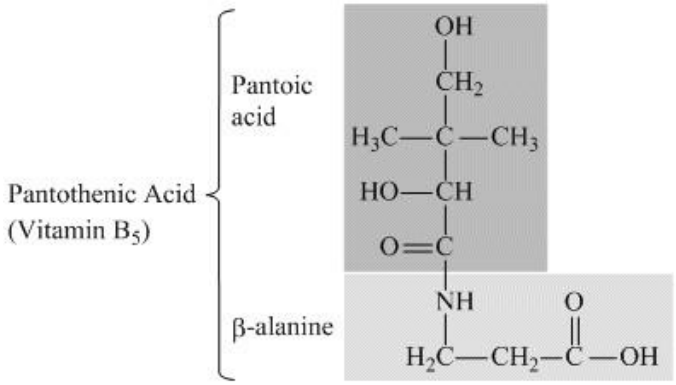
Stable- acid, base, heat, light

Deficiency

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

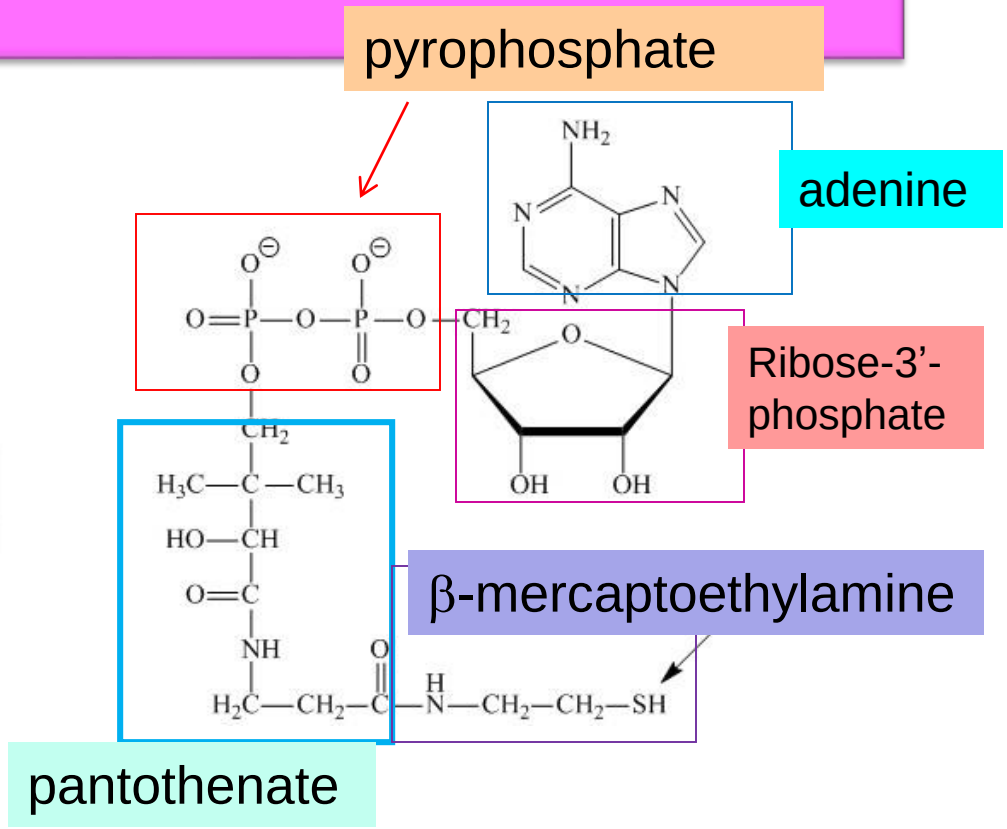
Vitamin B5 (Pantothenic acid)

Part of Coenzyme A



Pantothenic acid

Unstable- acid, base, heat



Coenzyme A

Deficiency- rare

Fatique, nausia, insomnia, irritability

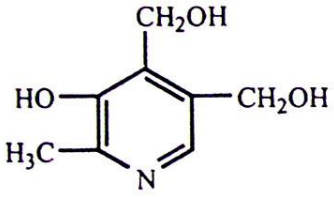
Vitamin B6 (Pyridoxine)

Coenzyme - Pyridoxal phosphate (PLP)

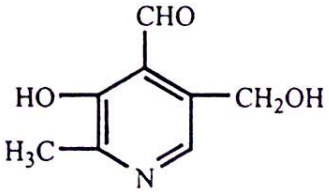
vitamin

ในธรรมชาติมี 3 รูปแบบ

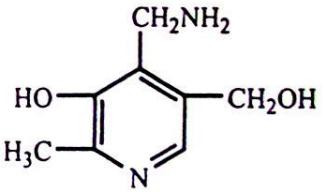
ถูกแสงทำลายได้



Pyridoxine

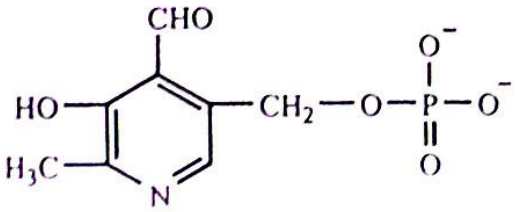


Pyridoxal

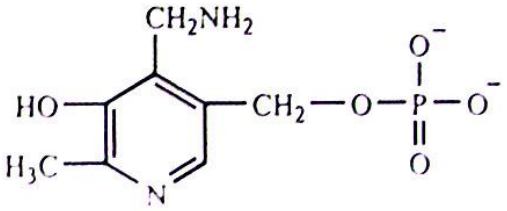


Pyridoxamine

coenzyme



Pyridoxal phosphate (PLP)



Pyridoxamine phosphate

α–keto acid$_1$ + α–amino acid$_2$ → α–amino acid$_1$ + α–keto acid$_2$

Deficiency

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

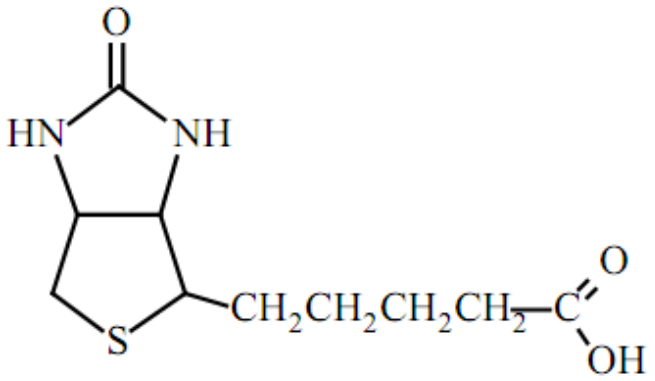
Vitamin H (Biotin)

Biocytin

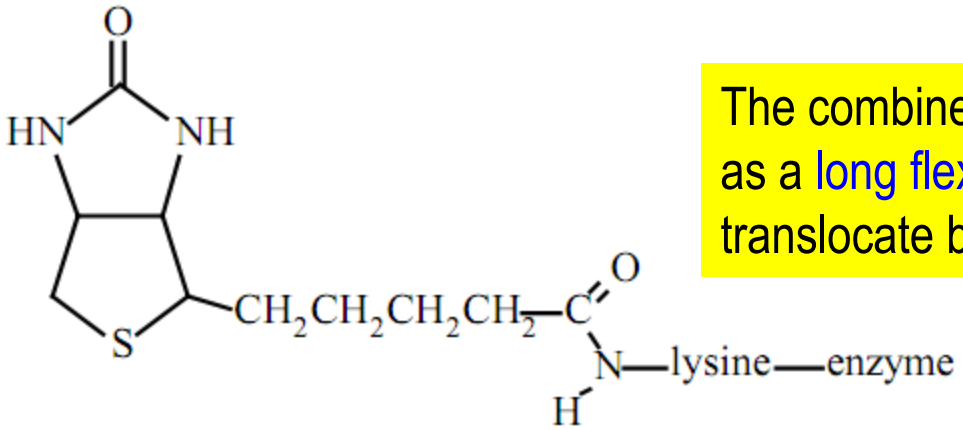
ทนร้อน ถูกทำลายโดยออกซิเดชัน

Biotin link with enz by amide bond

(COOH of biotin and NH_2 of Lys)



Biotin



BIOCYTIN

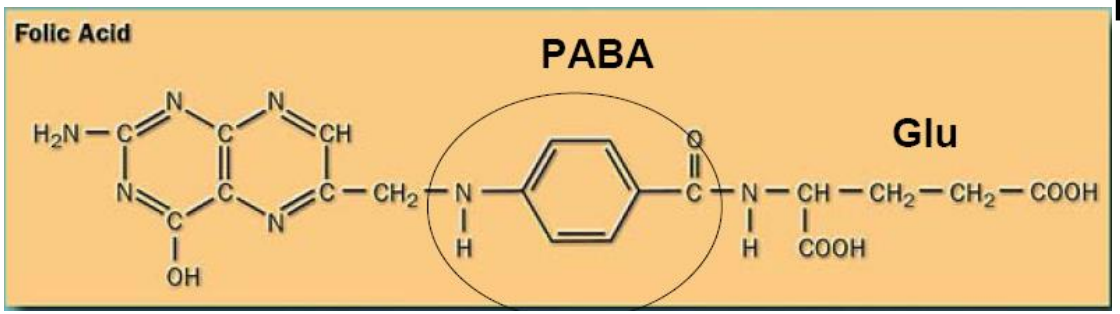
The combined biotin and lysine side chains act as a long flexible arm that allows the biotin ring to translocate between the 2 active sites

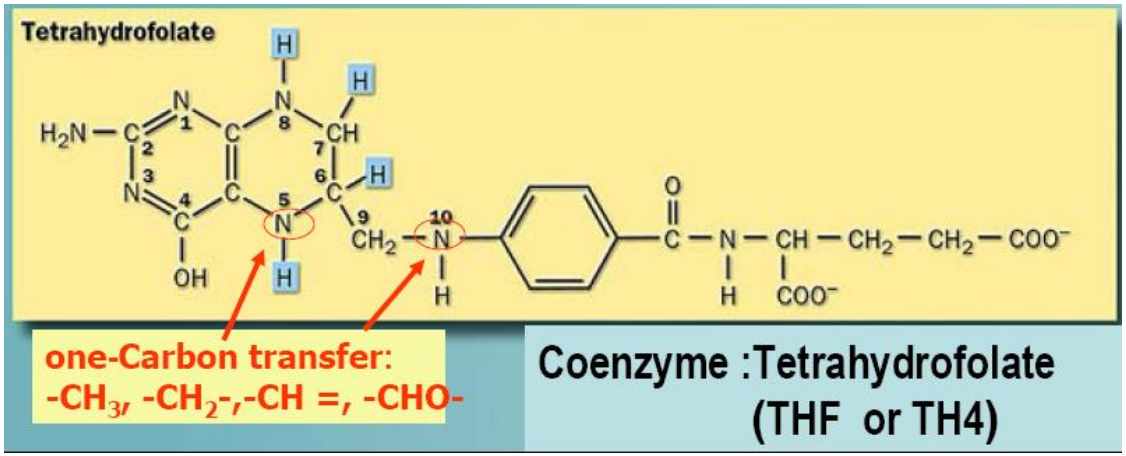
Inhibitor – avidin in white egg bind with biotin, inhibit absorption

Folic acid

Tetrahydrofolate (THF)

Destroyed by heat and oxygen



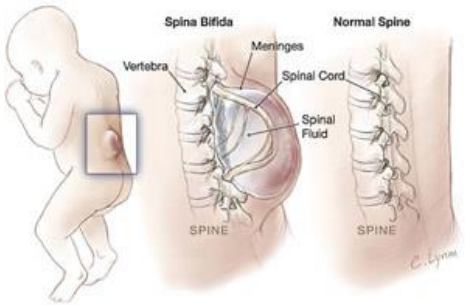


carry and transfer various forms of 1-C units (e.g.methyl, methylene, methenyl, formyl or formimino groups) during biosynthetic rxs.

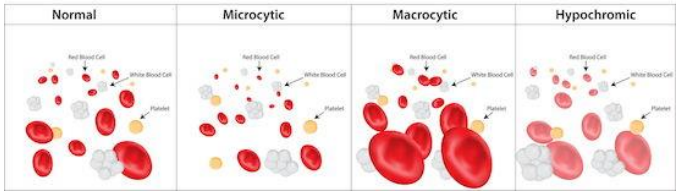
Deficiency

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).

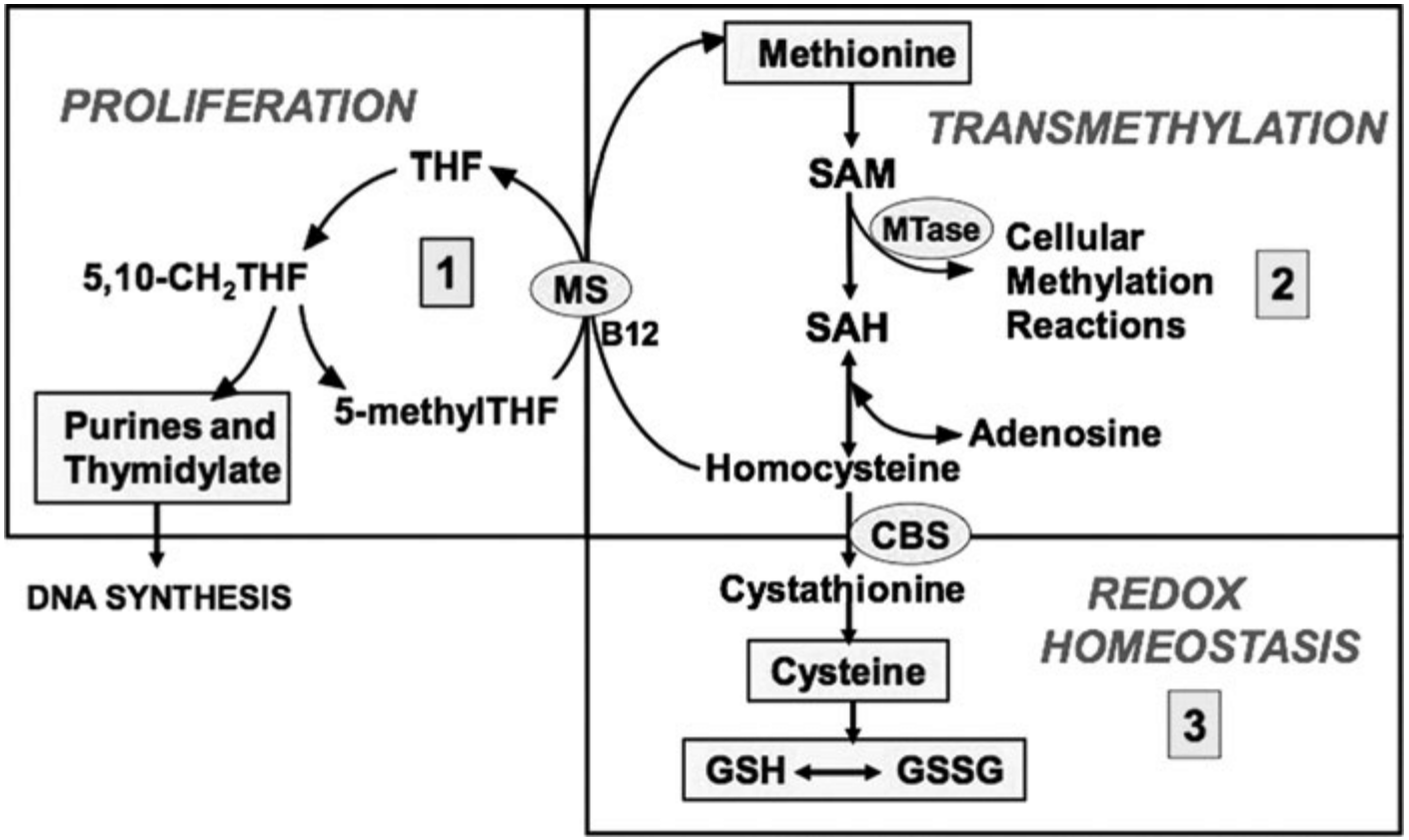


spinal bifida improper development of spinal chord in fetus (neural tube defect)



Function

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

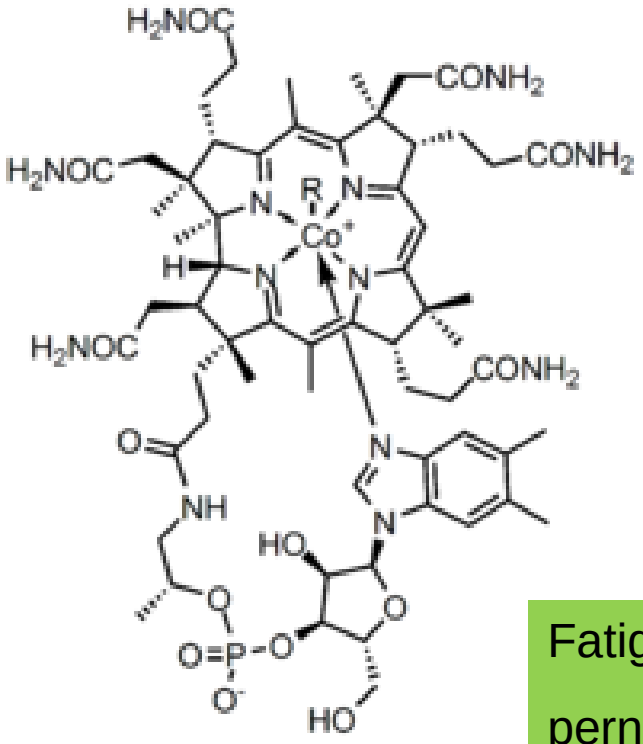


Vitamin B12

Cobalamine B12 coenzyme

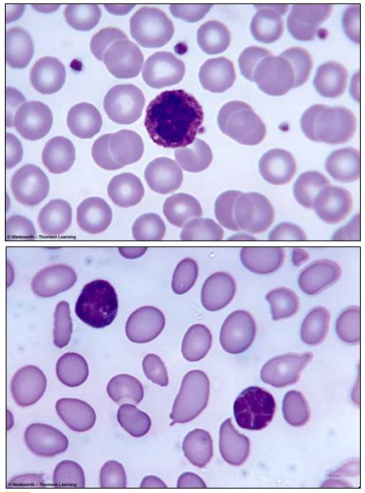
Methylcobalamine (methyl B12) – main in plasma

Deoxyadenosylcobalamine – main in tissue



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 10-12
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)

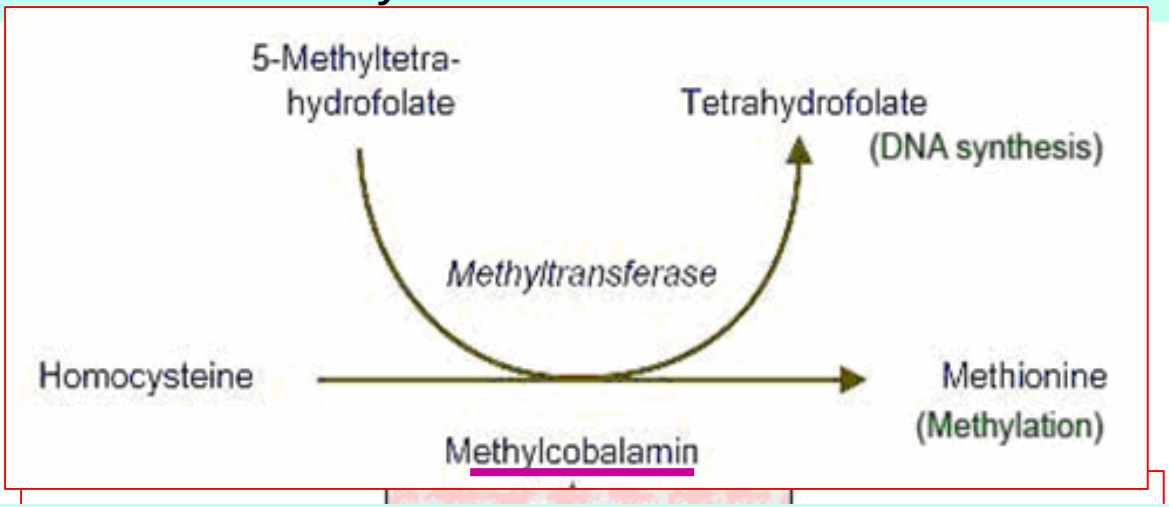
Deficiency found in vegetarians, older people

Absorption – illeum

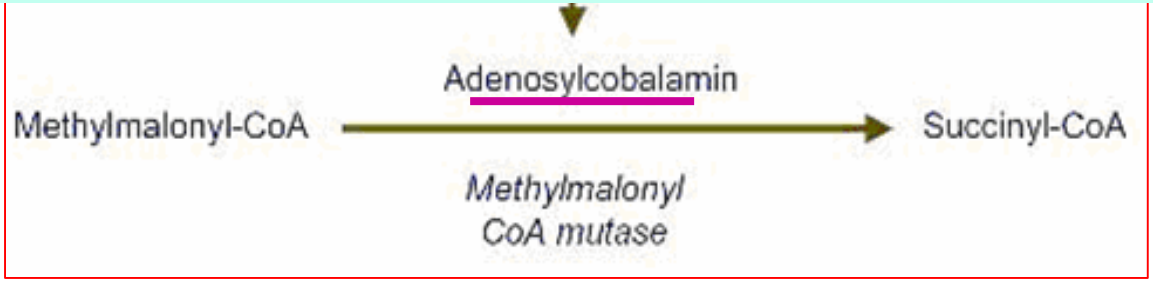
Storage - in liver 2-4 years

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

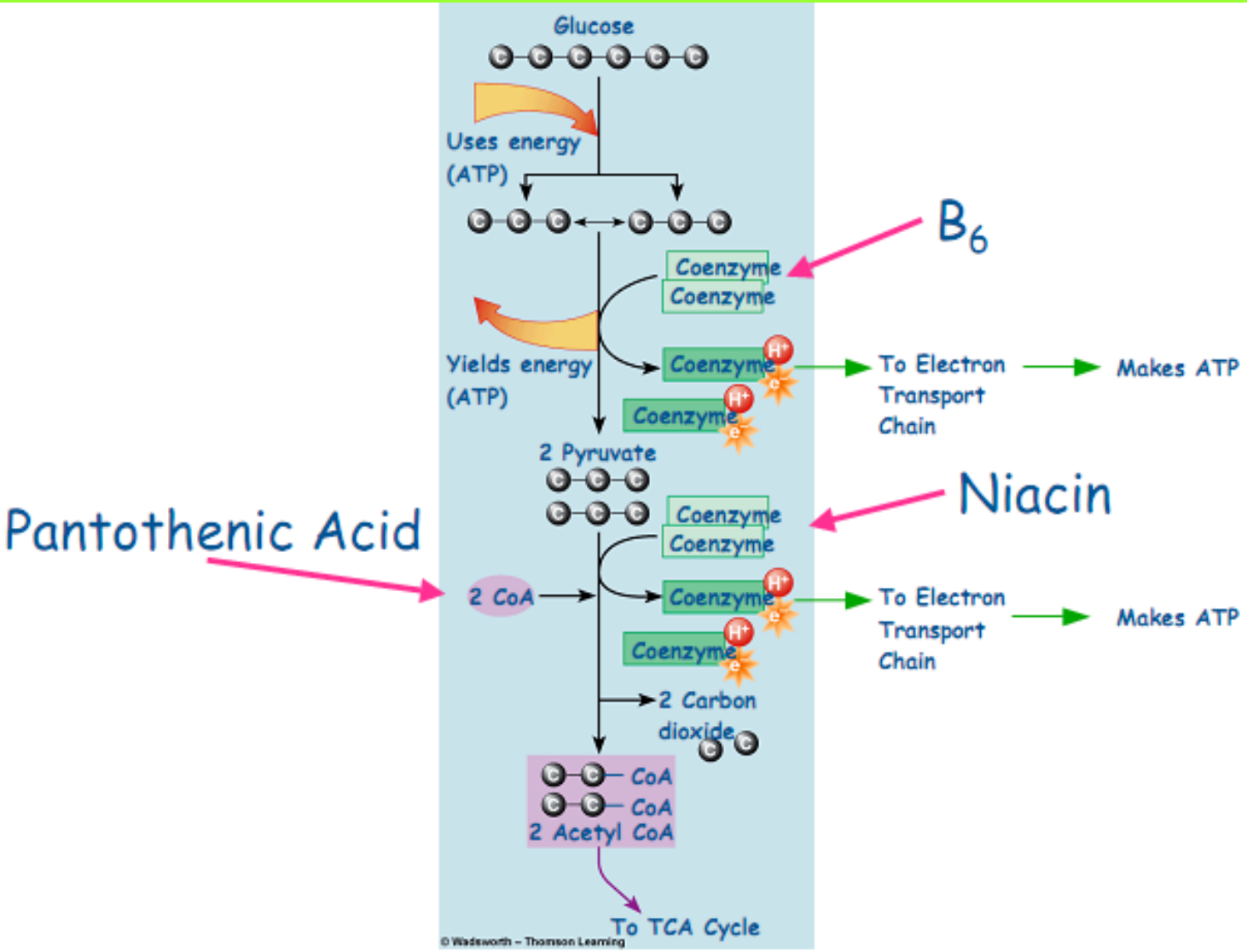


ขาด B12 ทำให้สังเคราะห์ DNA ลดลง และ มีการคั่งของ methylmalonyl CoA ซึ่งจะยับยั้งการสังเคราะห์ myelin sheath ของ nerve cell

Example of coenzyme/enzyme in metabolism

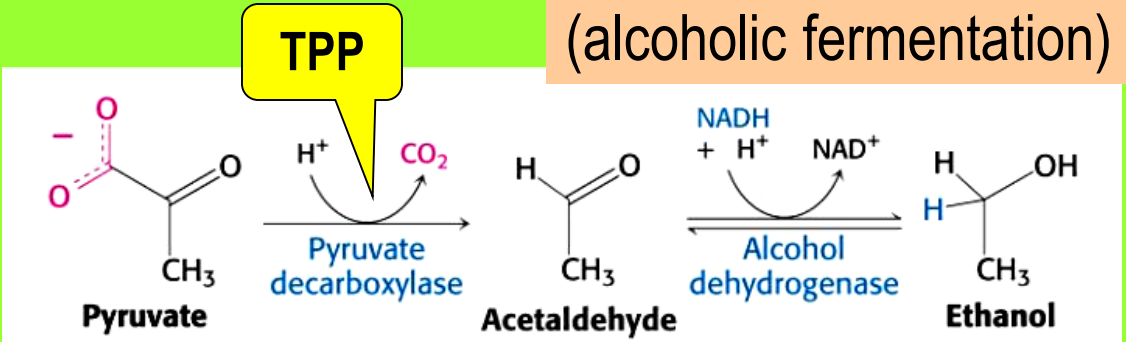
Coenzyme	Enzymes	Metabolic pathway
TPP	pyruvate decarboxylase	Alcoholic fermentation
	transketolase	Pentose phosphate pathway (PPP)
FMN	NADH dehydrogenase (complex I)	Electron transport system (ETS)
FAD	Succinate dehydrogenase	Krebs cycle
NAD^+	Lactate dehydrogenase	Anaerobic glycolysis
	Malate dehydrogenase	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

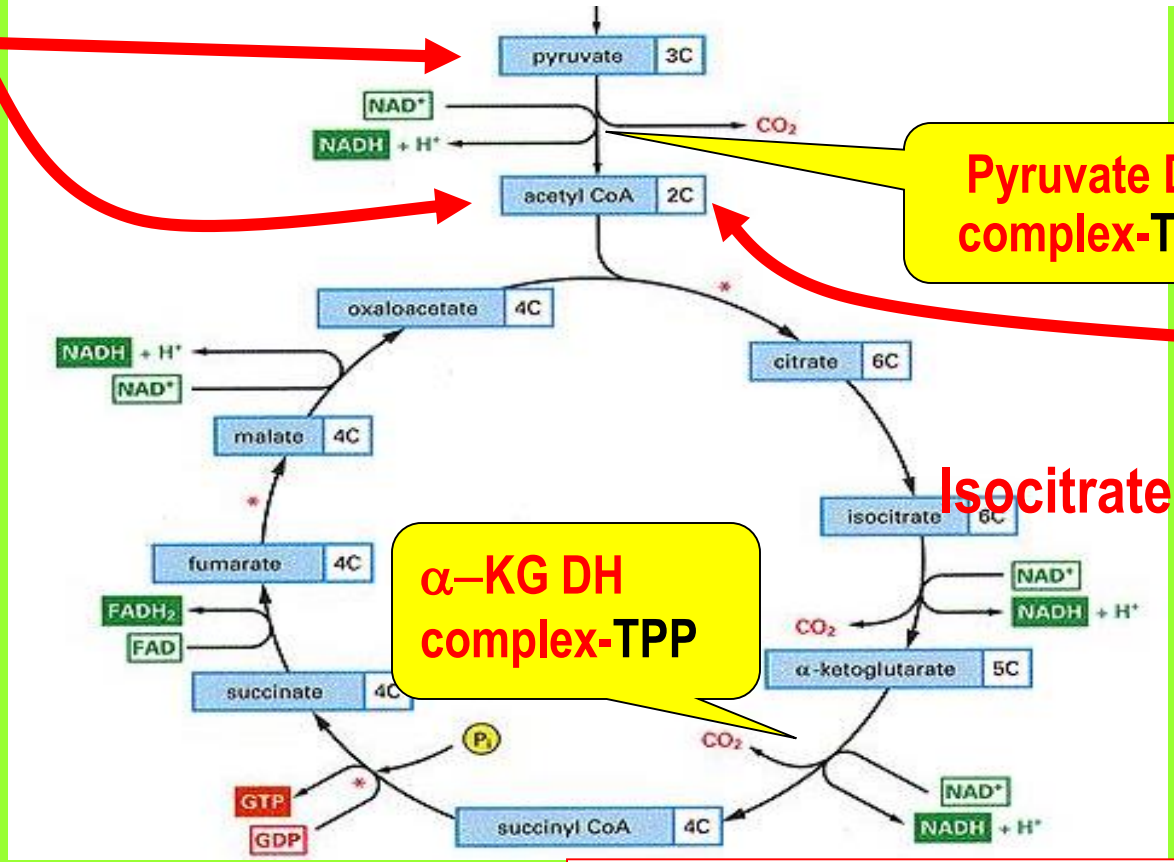


Vitamins/coenzymes in Krebs' cycle

Energy metabolism



protein



Pyruvate DH complex-TPP

Lipid

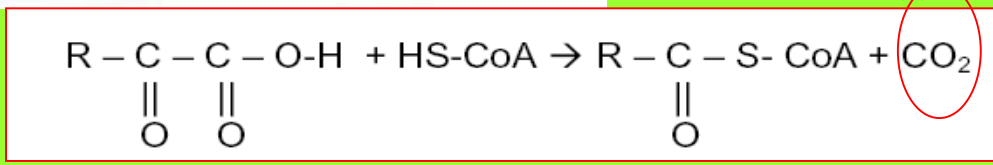
Malate DH

Isocitrate DH

Succinate DH

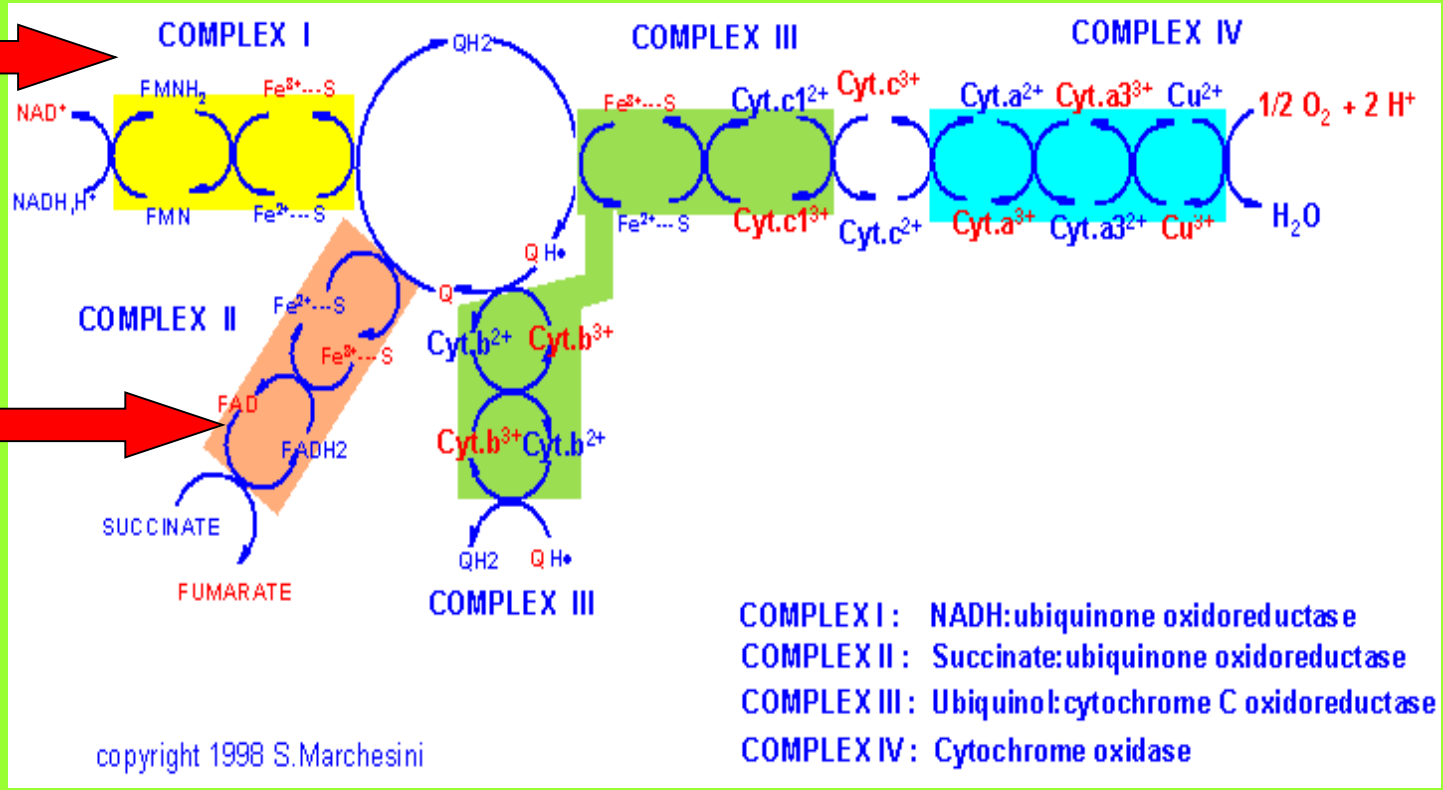
α–KG DH complex-TPP

TPP ในปฏิกิริยา decarboxylation



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

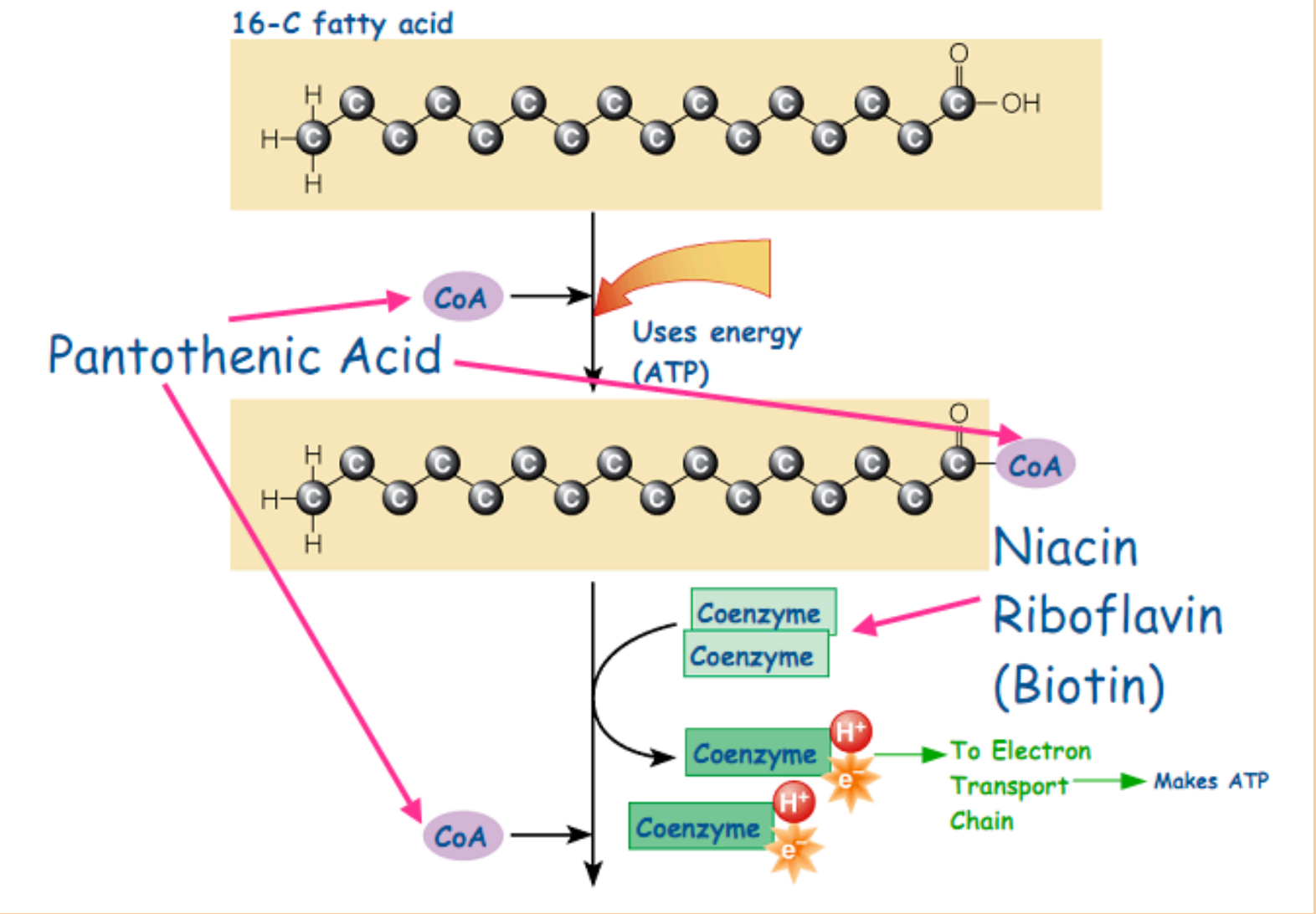
Vitamins/coenzymes in electron transport chain (ETS)



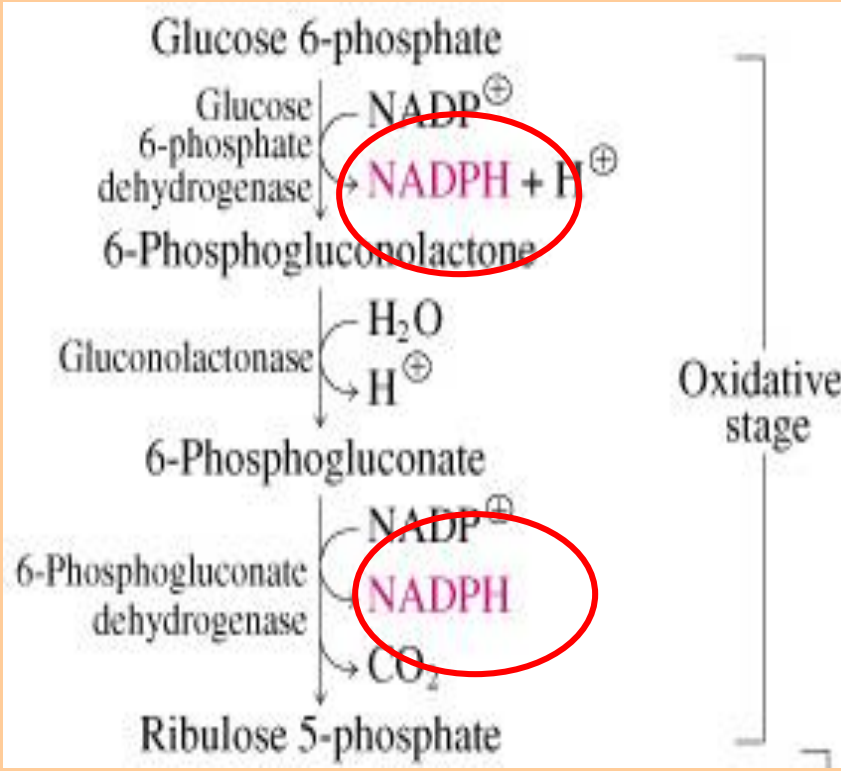
http://lhs2.lps.org/staff/sputnam/Ent801/lec1_files/beta_ox.gif

http://www.technoinhome.com/vspcite/site/wb03/jpg/008/wb03008560155aa6.jpg

Vitamins/coenzymes in fatty acid metabolism

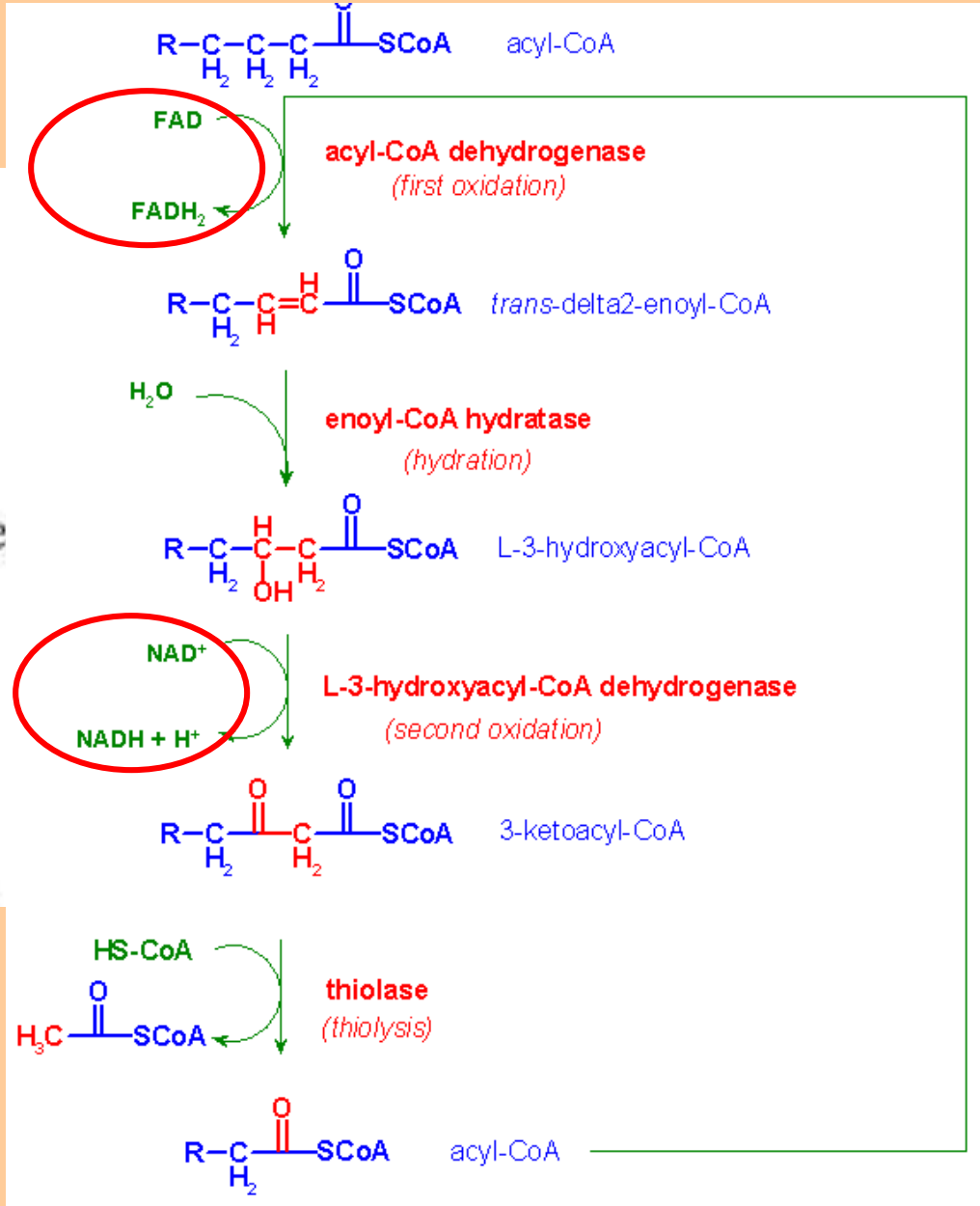


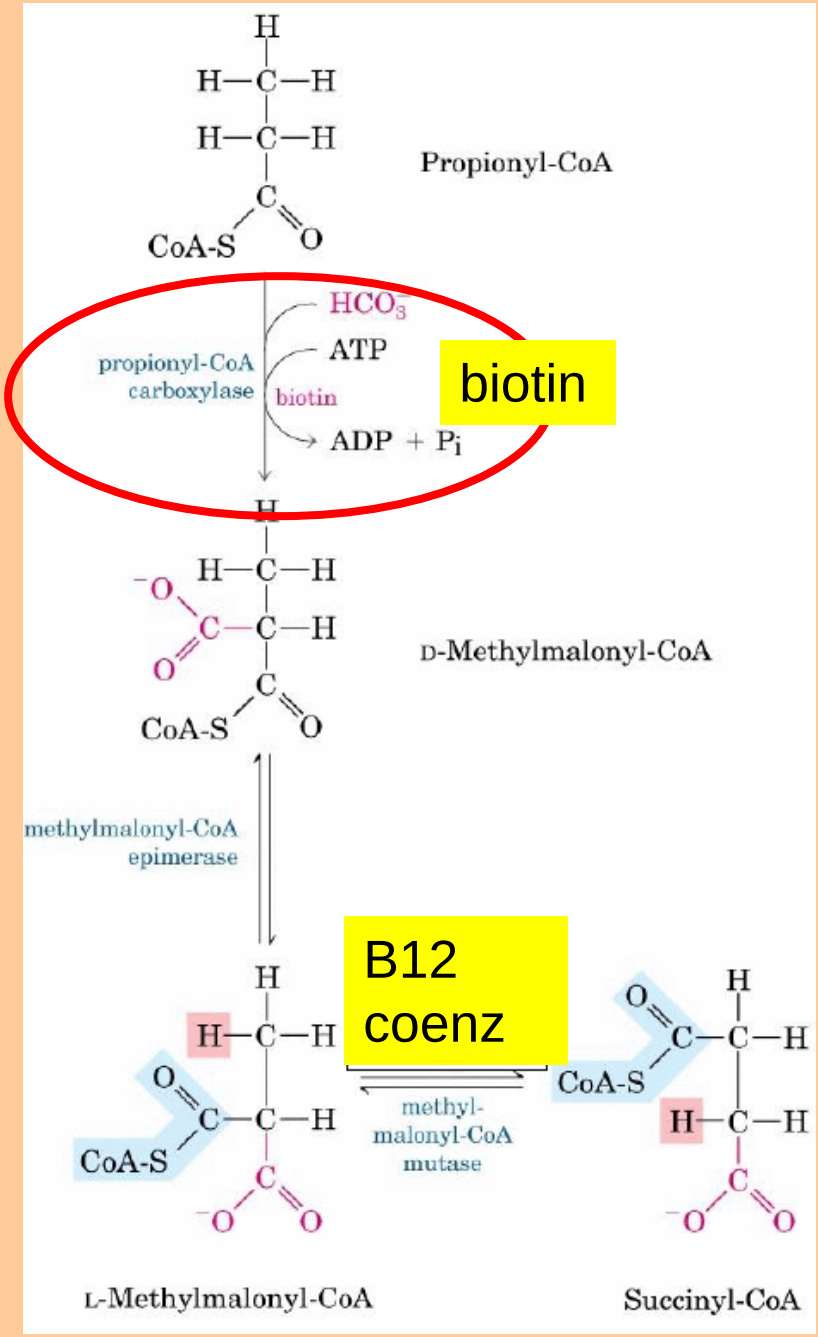
NADP+ coenzyme in pentose phosphate pathway as H+ acceptor and get NADPH

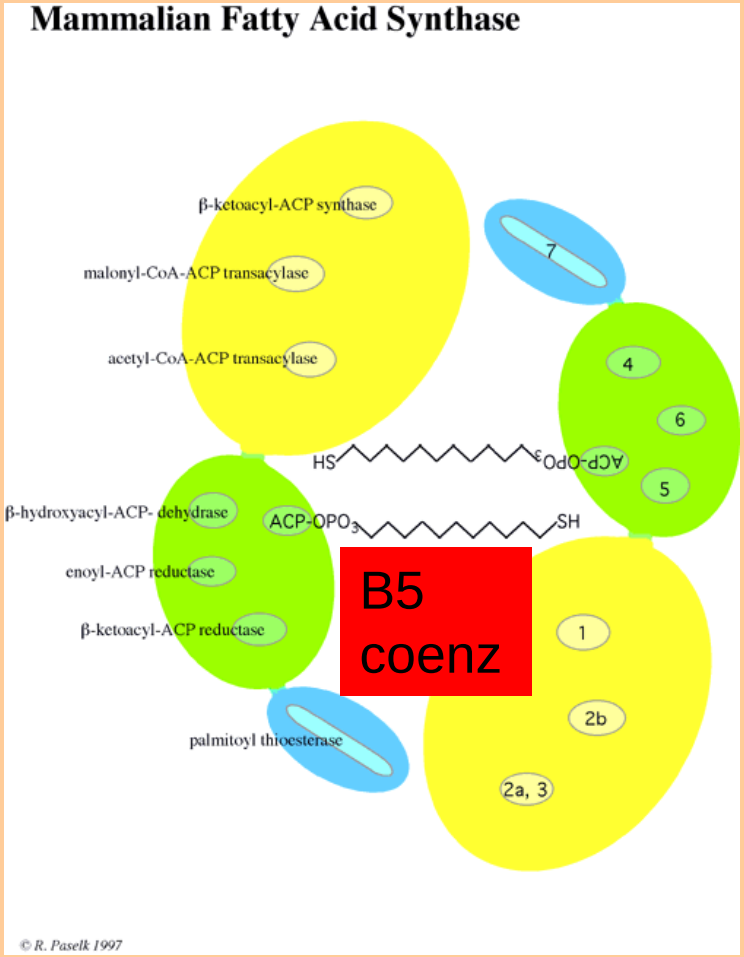


NADPH coenzyme in biosynthesis of fatty acid, cholesterol, amino acid

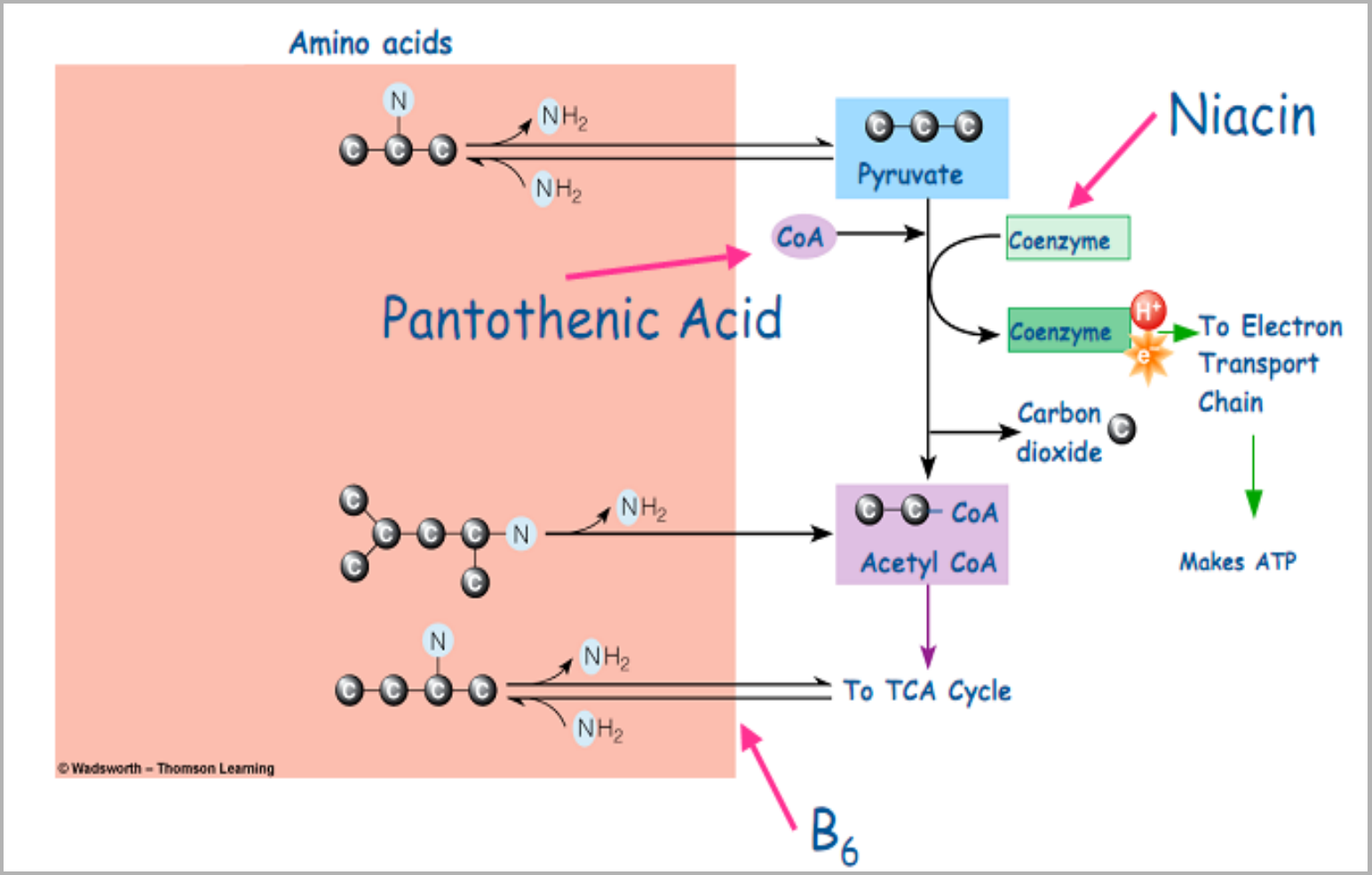
NAD and beta-oxidation of fatty acid

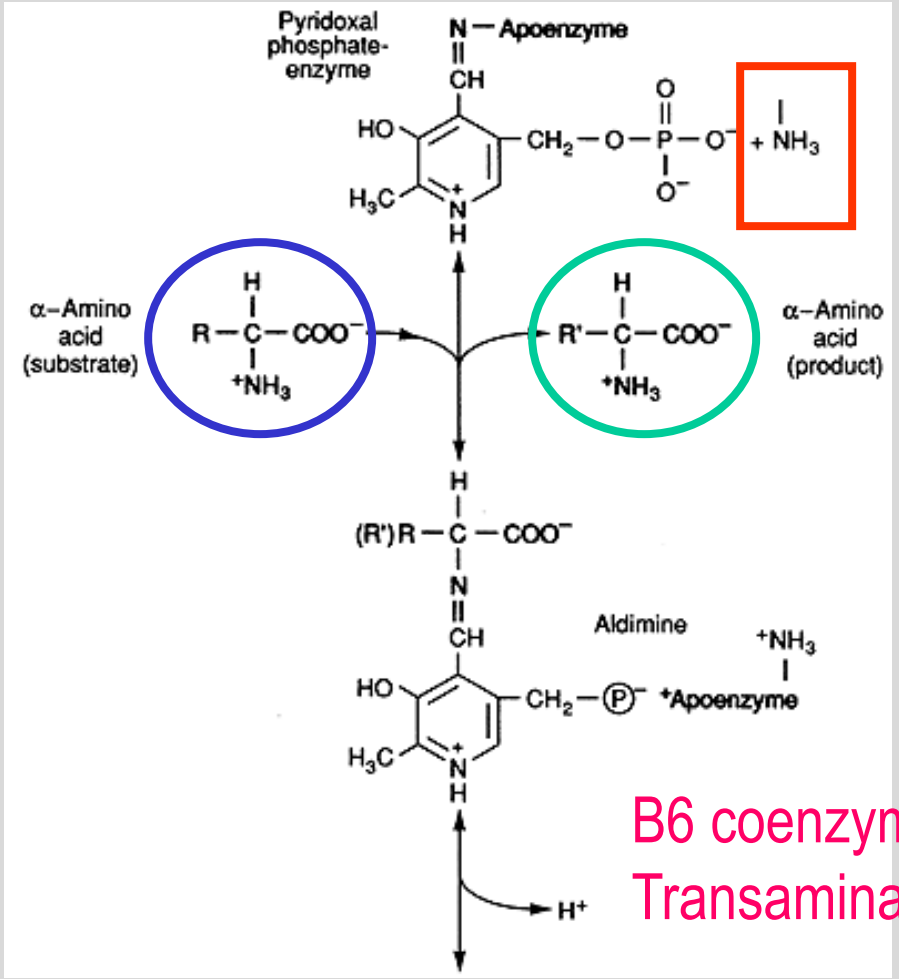


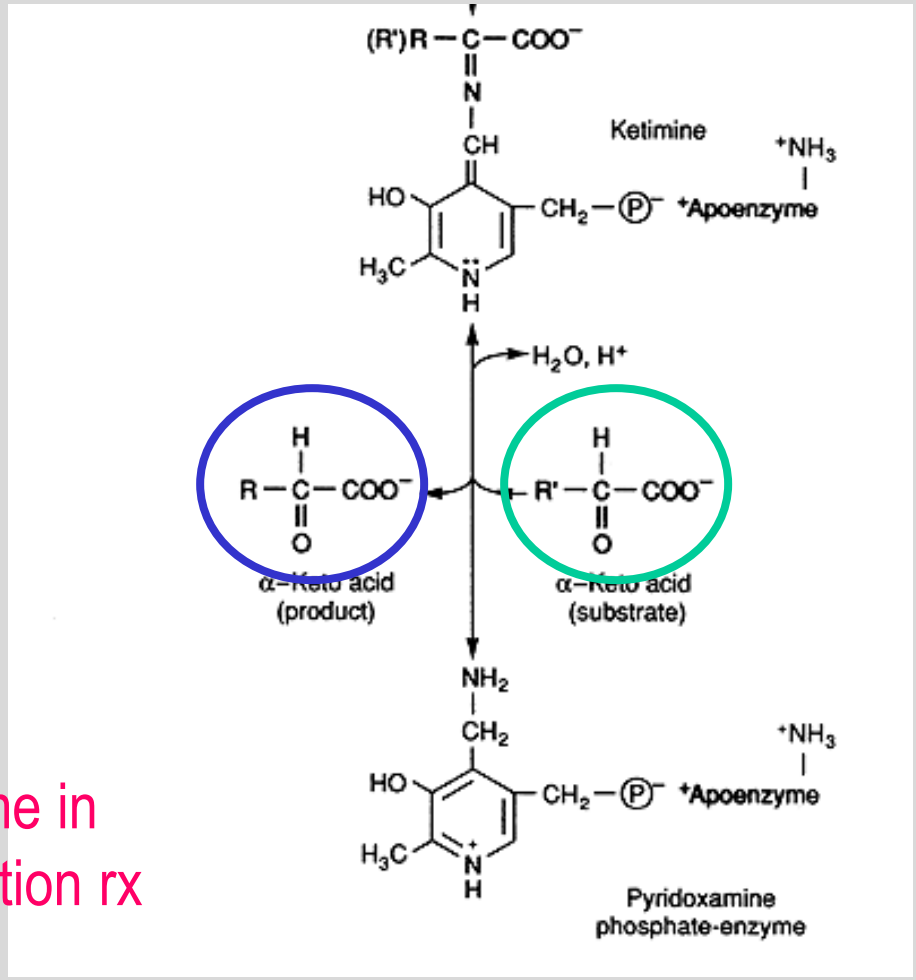

Propionyl-CoA
propionyl-CoA carboxylase
HCO3−
ATP
biotin
ADP + Pi
biotin
D-Methylmalonyl-CoA
methylmalonyl-CoA epimerase
B12 coenz
methyl-malonyl-CoA mutase
L-Methylmalonyl-CoA
Succinyl-CoA


Mammalian Fatty Acid Synthase
β-ketoacyl-ACP synthase
malonyl-CoA-ACP transacylase
acetyl-CoA-ACP transacylase
β-hydroxyacyl-ACP- dehydrase
enoyl-ACP reductase
β-ketoacyl-ACP reductase
palmitoyl thioesterase
HS
ACP-OPO3
ACP-OPO3
SH
7
4
6
5
1
2b
2a, 3
B5 coenz
© R. Paselk 1997

Vitamins/coenzymes in amino acid metabolism



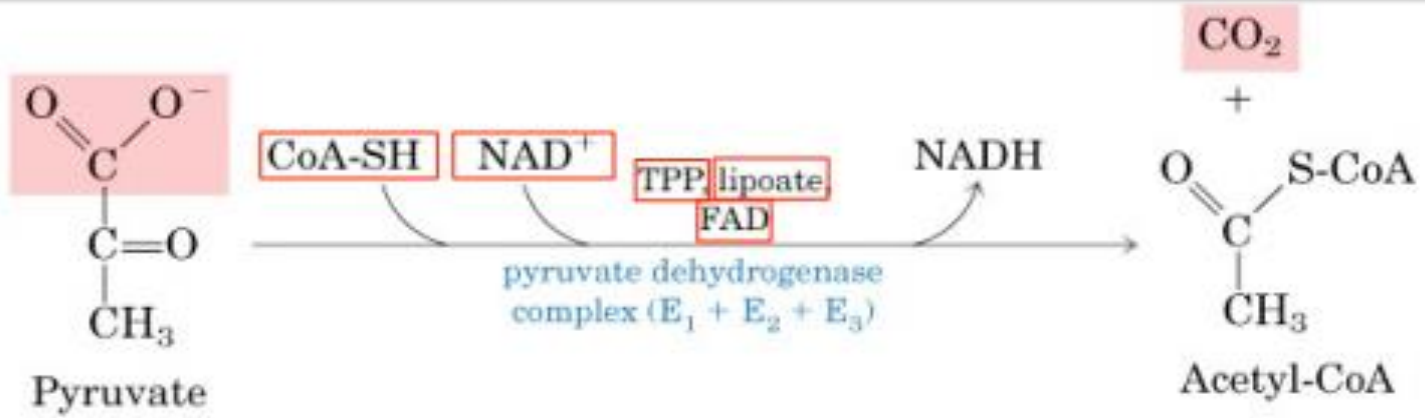




B6 coenzyme in Transamination rx

Some enzymes need many coenzymes

Pyruvate dehydrogenase complex (PDH)



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

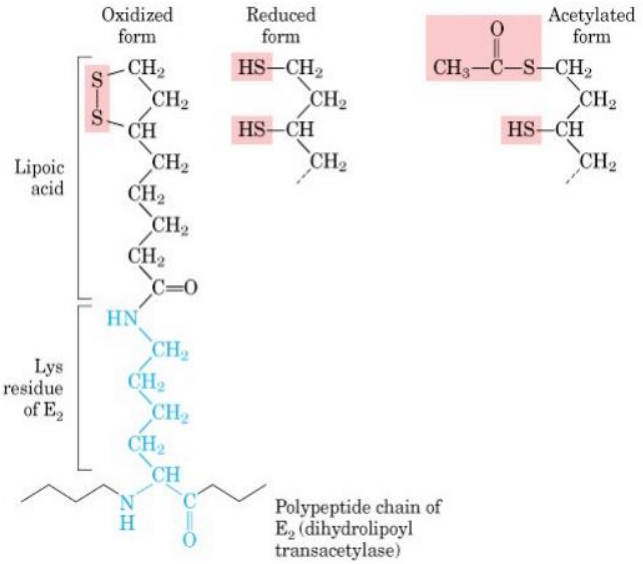
Coenzyme A (pantothenate) - reactive thiol is an acyl carrier

NAD+ (niacin) – e carrier

FAD (riboflavin) – e carrier

TPP (thiamine) – clevage bond next to carbonyl

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



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.