

Water Soluble Vitamins



Definition and Classification

- 📖 Non-caloric organic nutrients
- 📖 Needed in very small amounts
- 📖 Facilitators – help body processes proceed; digestion, absorption, metabolism, growth etc.
- 📖 Some appear in food as precursors or provitamins



Definition and Classification

📖 2 classes, Table 7.1

- Fat soluble:
- Water soluble:



Water Soluble Vitamins: Characteristics

- 📁 Essential
- 📁 Organic Structure
- 📁 Non-energy Producing
- 📁 Micronutrients
- 📁 Stability
- 📁 Bioavailability
- 📁 Toxicity



Fat vs. Water Soluble Vitamins

Characteristics	Water Soluble	Fat Soluble
Absorption	Directly to blood	Lymph via CM
Transport	free	Require carrier
Storage	Circulate freely	In cells with fat
Excretion	In urine	Stored with fat
Toxicity	Possible w supplements	Likely w supplements
Requirements	Every 2-3 days	Every week



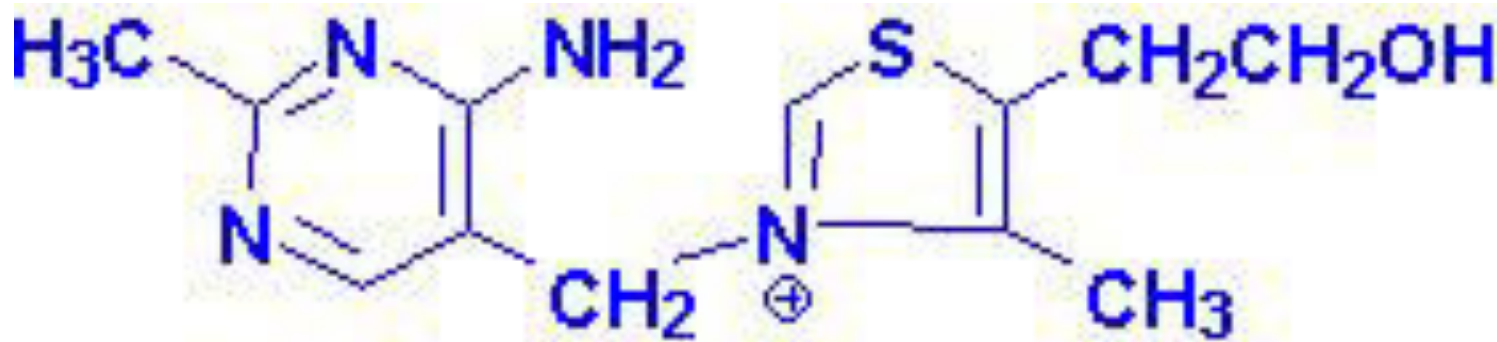
Thiamin

Structure

- pyrimidine ring
- thiazole ring
- methyl bridge

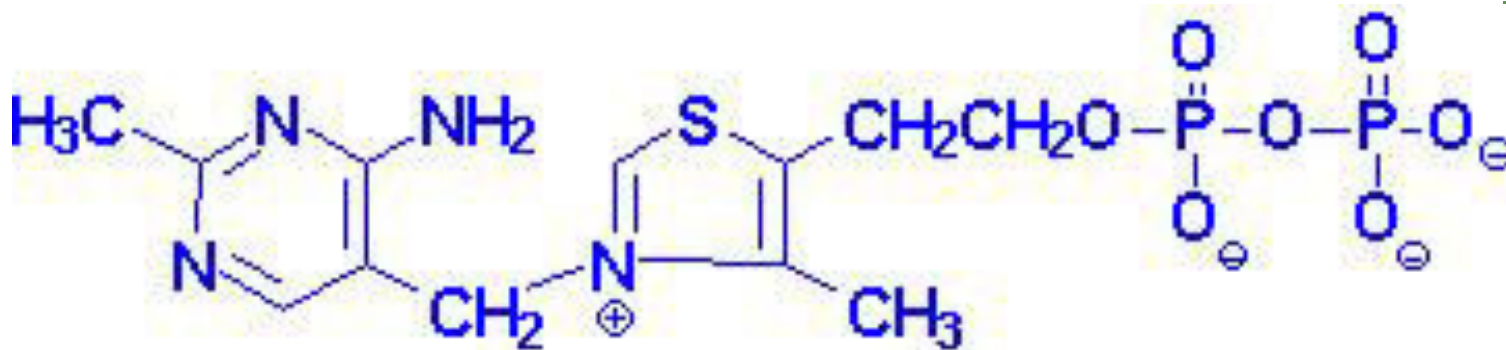


Thiamin : vitamin form



Pyrimidine ring

Thiazole ring



Thiamin pyrophosphate: coenzyme form

Chemical Characteristics

📁 Very labile nutrient

📁 Heat

- stable in crystalline form
- less stable in solution

📁 Alkali - very unstable with heat

- baking soda



Chemical Characteristics

📁 Sulfites - decomposes B-1

📁 High cooking/processing
losses

- heat
- leaching



Absorption of B-1

📁 in duodenum

📁 active transport (low thiamin levels)

– requires sodium and folic acid

📁 passive transport (hi B-1 levels)



Absorption of B-1

- 📁 phosphorylation to active form inside cells (TPP)
- 📁 transported via portal blood
- 📁 no significant storage, excess to urine



Biochemical Functions of B-1

Oxidative Decarboxylation Reactions

Pyruvate Dehydrogenase

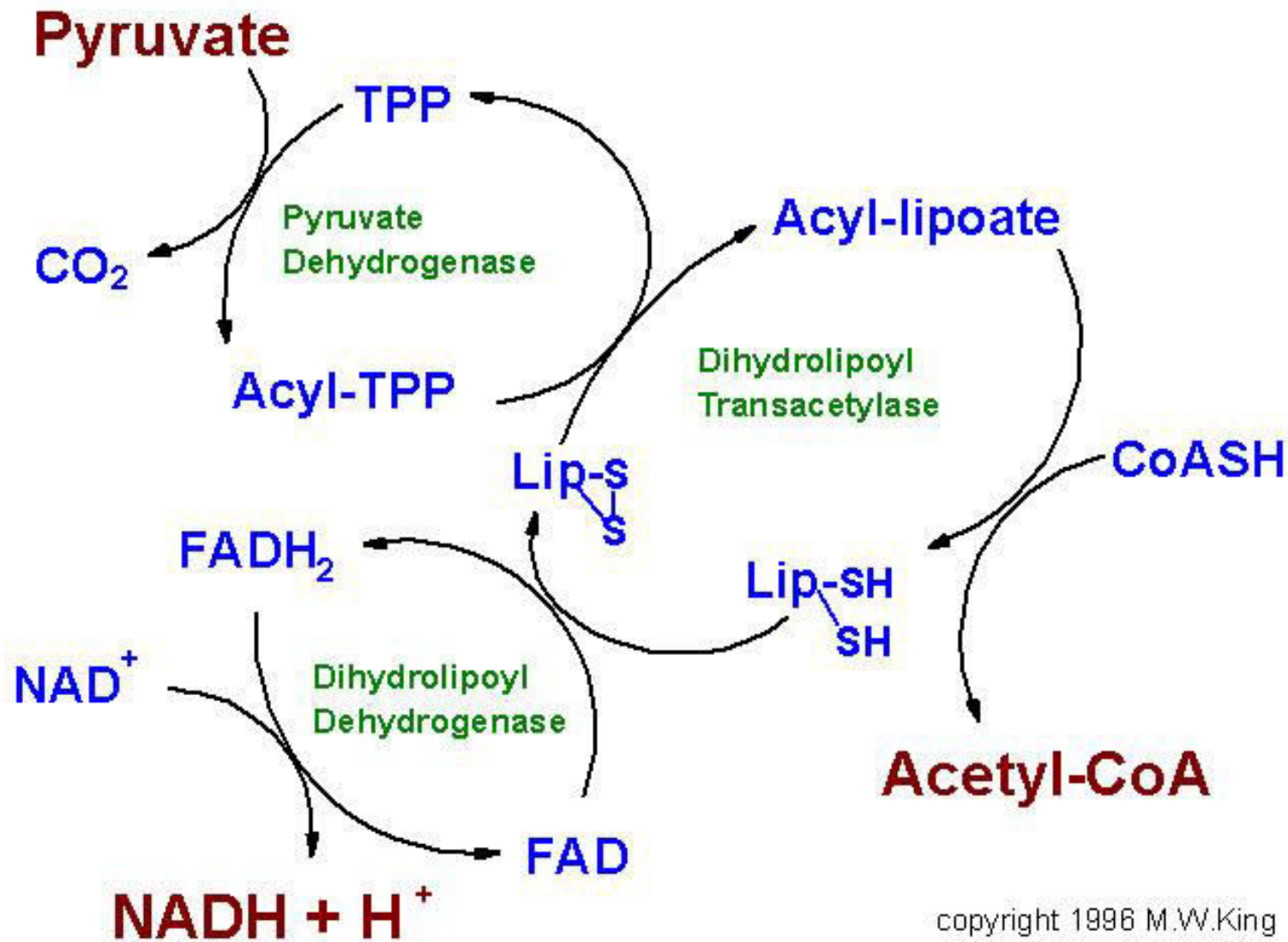
– $\text{Pyr} + \text{CoA} + \text{NAD} \rightarrow \text{AcCoA} + \text{CO}_2 + \text{NADH}$

α -keto-glutarate dehydrogenase

– $\alpha\text{KG} + \text{CoA} + \text{NAD} \rightarrow \text{SuccCoA} + \text{CO}_2 + \text{NADH}$

 important in CHO/energy metabolism





Biochemical Functions of B-1

Transketolation

– HMP pathway

Peripheral Nerve Function

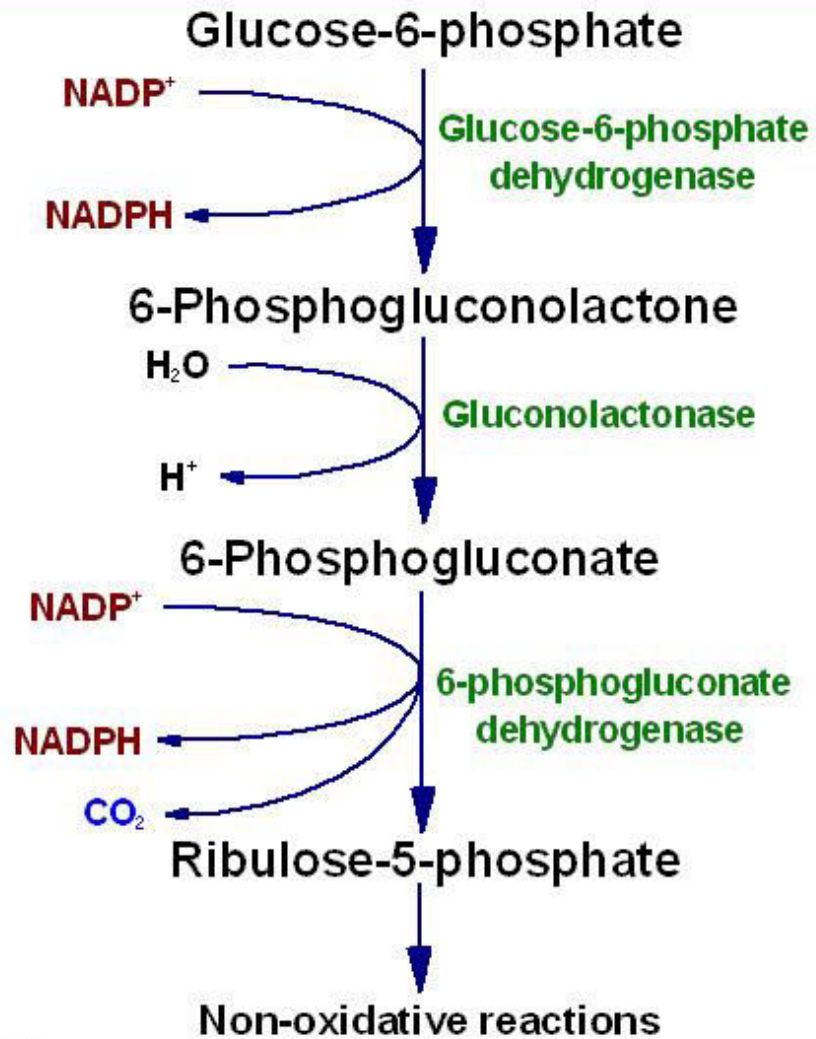
 TPP or TPPP

 non-cofactor function

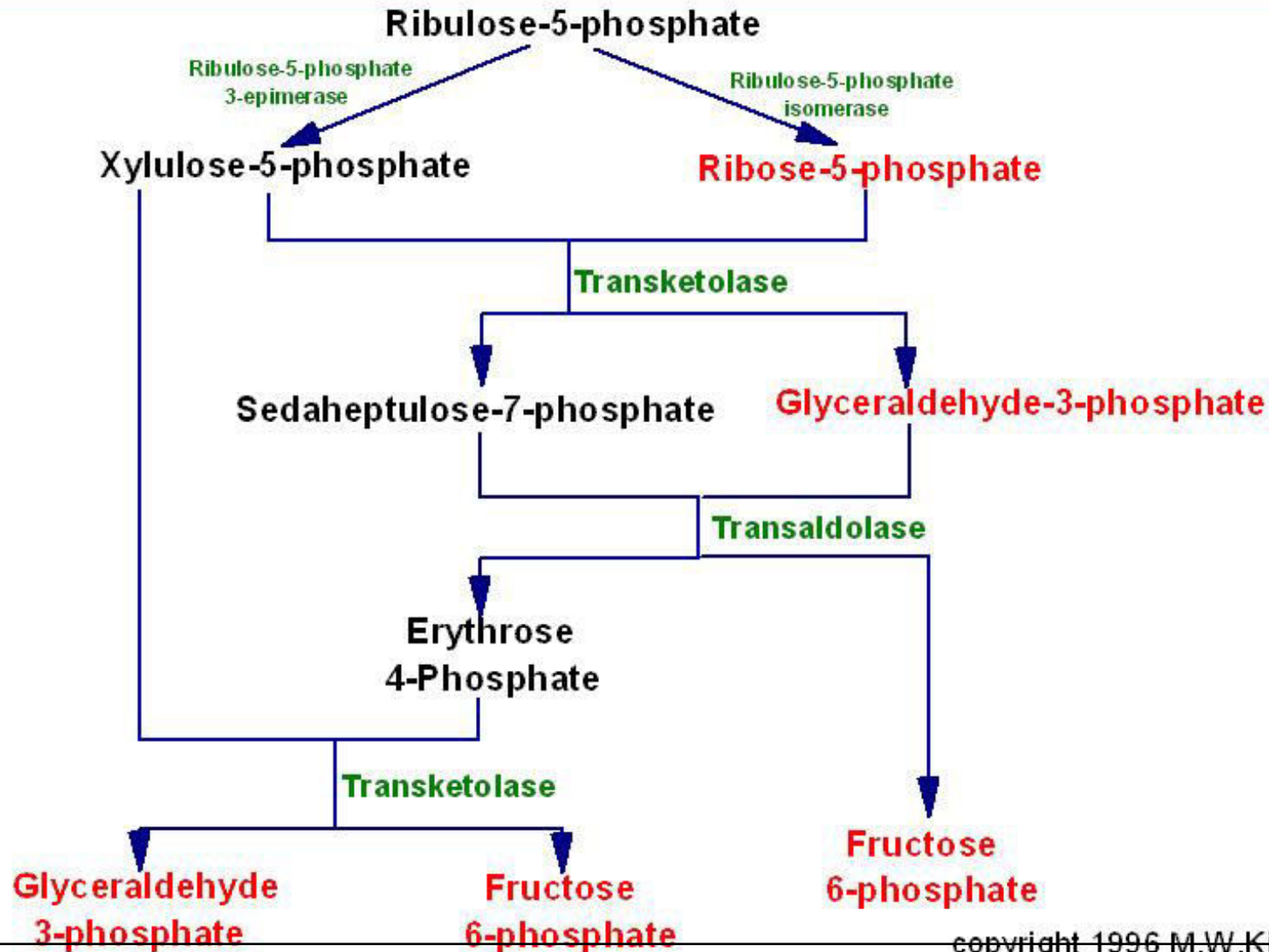
 mechanism?



Oxidative Stage of Pentose Phosphate Pathway



Non-Oxidative Stage of Pentose Phosphate Pathway



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Thiamin Deficiency

Beri-Beri

 anorexia, fatigue, depression

 effects on

- cardiovascular system
- nervous system



Infantile Beri-Beri

- 📁 first 6 months
- 📁 breast milk deficient in B-1
- 📁 mother w/o symptoms
- 📁 rapid onset
- 📁 cyanosis, tachycardia, labored breathing
- 📁 heart failure and death



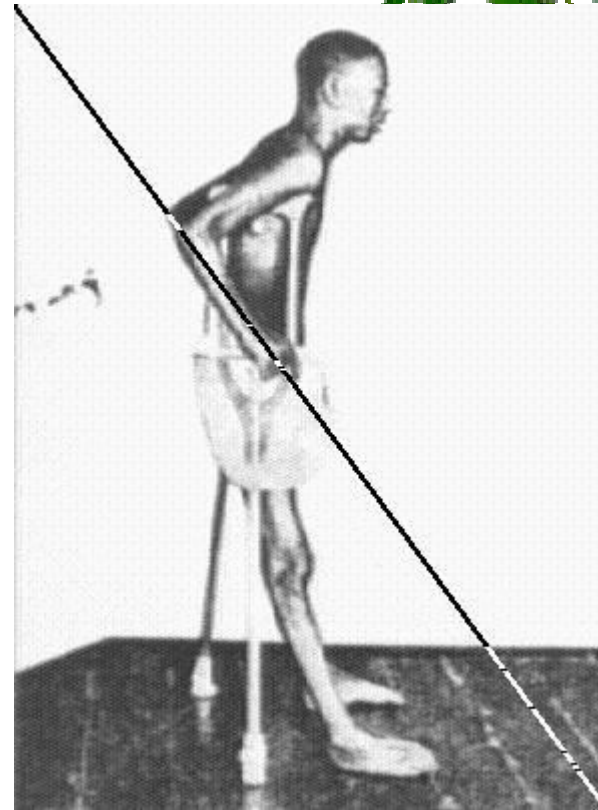
Wet Beri Beri

- 📖 symptoms similar to congestive heart failure
- 📖 Pitting edema - trunk, limbs, face
- 📖 labored breathing, tachycardia
- 📖 rapid deterioration
- 📖 fatal circulatory collapse
- 📖 responds rapidly to B-1 supplements



Dry Beri-Beri

- no edema
- progressive wasting
- numbing and weakening of extremities
- chronic infections



Assessment of Thiamin Status

- 📁 Urinary thiamin excretion
- 📁 Blood or serum thiamin concentration
- 📁 [pyr + lac] in blood
- 📁 erythrocyte transketolase activity

– stimulation with B-1



2000 RDA for Thiamin

	Males 19-30yrs	Females 19-30yrs
RDA mg/d	1.2	1.1
EAR	1.0	0.9
NHANES III Mean intake	1.78	1.45



Friday's Quiz

Read:

- Riboflavin
- Vitamin B-6
- Biotin
- Pantothenate

Know

- Functions
- Cofactor and vitamin forms
- Deficiency and toxicity symptoms and causes



Niacin

 Structure

 Nicotinic Acid = Niacin

 Nicotinamide =
Niacinamide



Cofactor Forms of Niacin

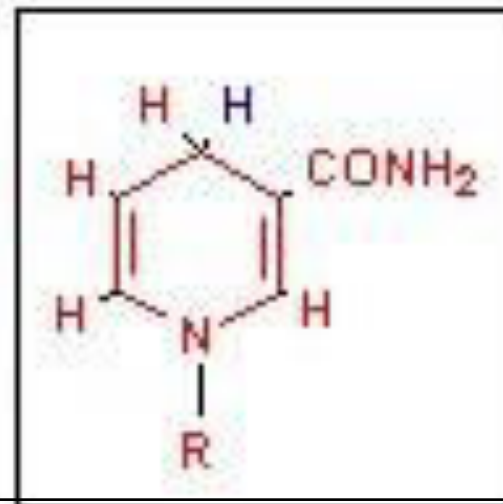
- 📁 Nicotinamide Adenine Dinucleotide
 - NAD
 - nicotinamide-ribose-PP-ribose-adenine
- 📁 Nicotinamide Adenine Dinucleotide Phosphate
 - NADP
 - nicotinamide-ribose-PP-(ribose-P)-adenine

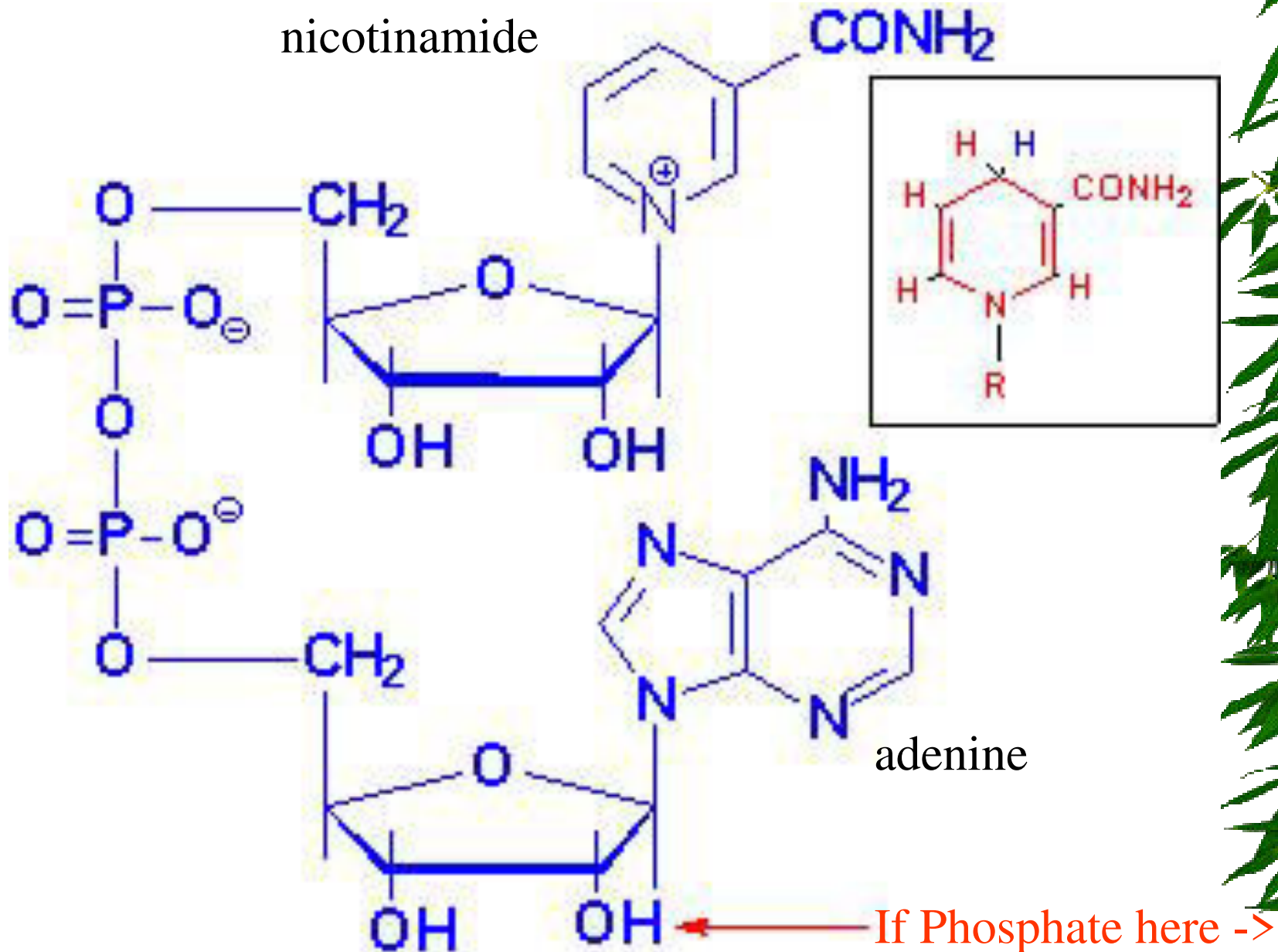




Nicotinic Acid (Plant form)

Nicotinamide (animal form)
(reduced form)





Nicotinamide Adenine Dinucleotide

NADP

Chemical Characteristics of Niacin

📁 relatively stable to

- light
- heat
- oxidation
- alkali

📁 major losses due to leaching



Digestion and Absorption of Dietary Niacin

- 📖 Coenzyme form in food
- 📖 hydrolysis in small intestine to free vitamin
- 📖 absorbed in duodenum
- 📖 nicotinic acid protein bound in corn
 - requires alkali treatment (lime) to release niacin



Metabolism of B-3

- 📁 conversion of free vitamin to coenzyme in all cells
- 📁 no storage
- 📁 excesses metabolized in liver to variety of chemicals
- 📁 metabolites excreted in urine



Synthesis of B-3

- 📁 from Tryptophan
- 📁 pathway requires B-6 (also B2)
- 📁 60 mg of TRY required to make 1 mg B-3
- 📁 corn is low in both B-3 and TRY

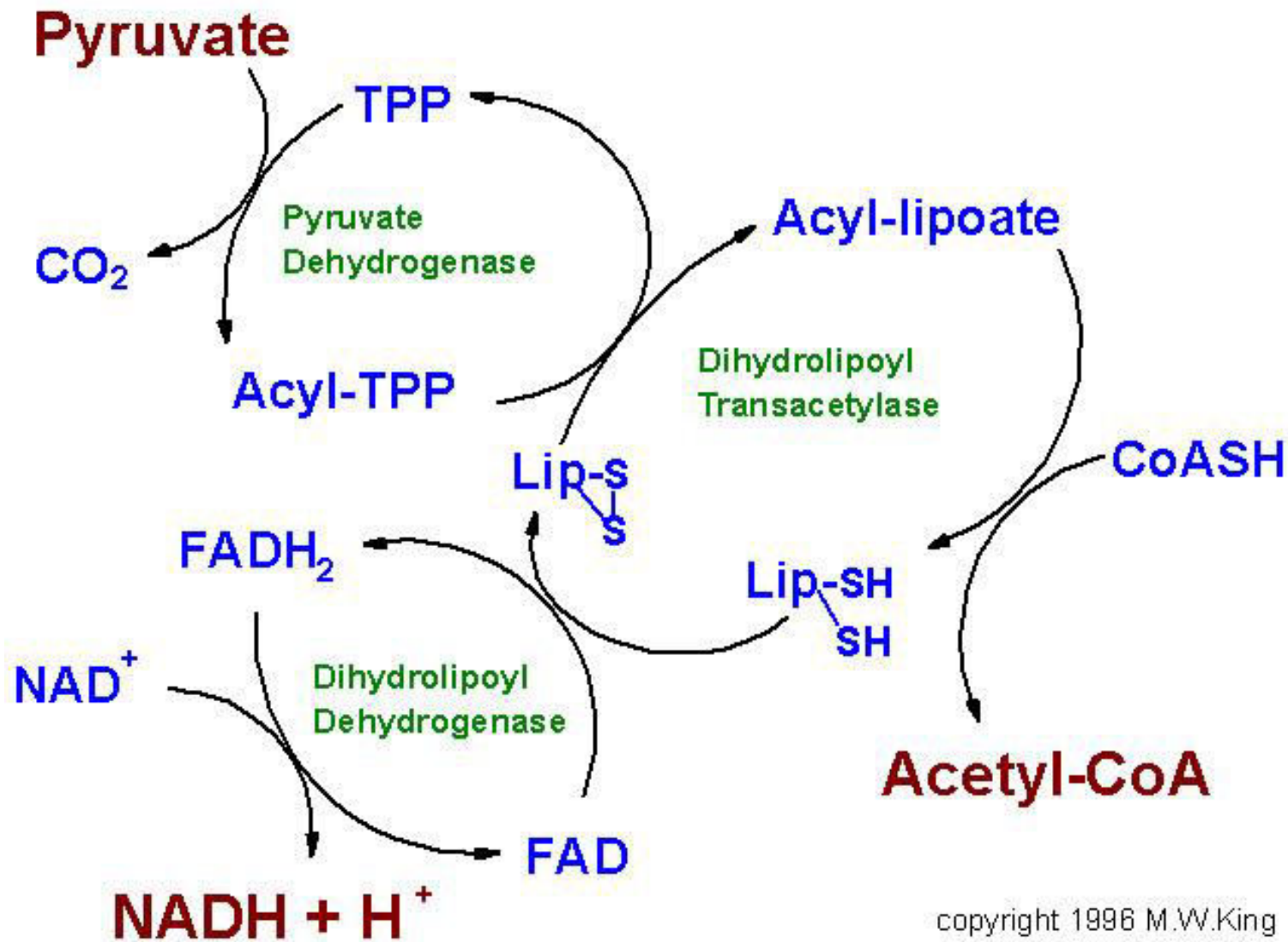


Biochemical Functions of B-3

Oxidation-Reduction Reactions (NAD/NADH)

- Dehydrogenases
- Electron Transport System
- Involved in energy production





Biochemical Functions of B-3

Synthetic Pathways (NADPH)

- FA synthesis
- Cholesterol synthesis
- NEAA synthesis
- Purine & Pyrimidine synthesis



Deficiency of B-3

 **Pellegra**

 **Dermatitis**

- scaly dermatitis, sun exposed

 **Dementia**

- confused, disoriented

 **Diarrhea**

- irritation/inflammation of mucous membranes



Assessment of B-3 Status

 Urinary excretion of niacin metabolites

- N-methyl nicotinamide
- 2-pyridone



2000 RDA for Niacin

📁 Niacin Equivalents (NE)

📁 1 NE = 1 mg B-3 = 60 mg TRY

	Males 19-30 yrs	Female 19-30 yrs
RDA (NE/d)	16	14
EAR (NE/d)	12	11

Niacin Toxicity

- 📖 1-3g/day for treatment of hypercholesterolemia
- 📖 increases histamine release
 - skin flushing
 - increase risk of peptic ulcers
- 📖 liver injury
- 📖 time release forms greater risk of liver injury



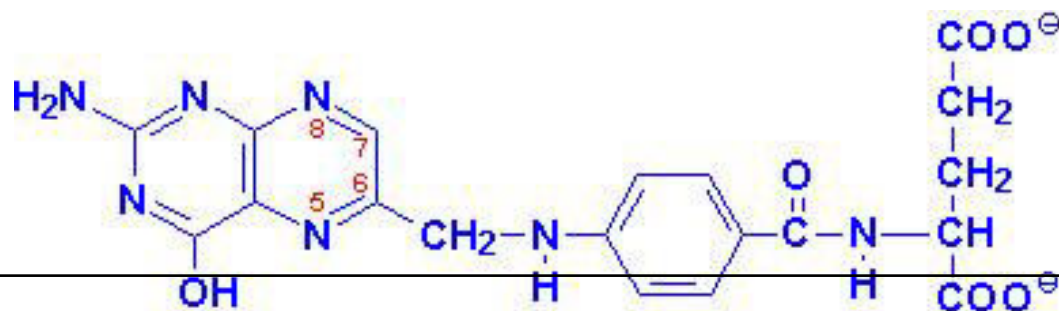
Folic Acid / Folacin

Structure

- pteridine ring - PABA - glutamate

Stability

- very sensitive to heat
- easily oxidized
- leached



Digestion & Absorption

- 📖 dietary form: polyglutamyl folate
 - glutamate gamma linked
- 📖 Folate conjugase
 - Zinc deficiency
 - alcoholism
 - drug interactions
- 📖 folate absorbed as monoglutamate (free folate)
- 📖 dietary supplement: free folate



Folate Metabolism

📖 Intestinal Cells

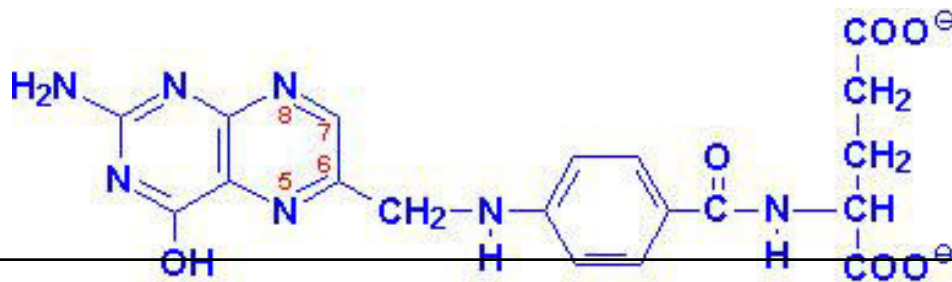
📖 folate reduced to tetrahydrofolate

– folate reductase

📖 inhibited by methotrexate (chemotherapeutic drug)

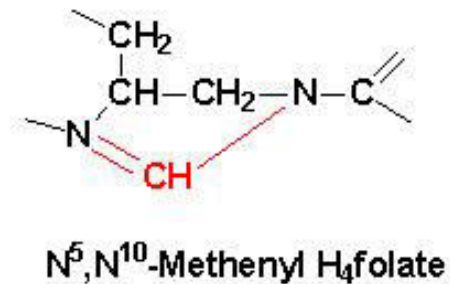
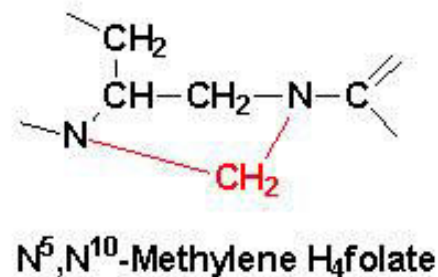
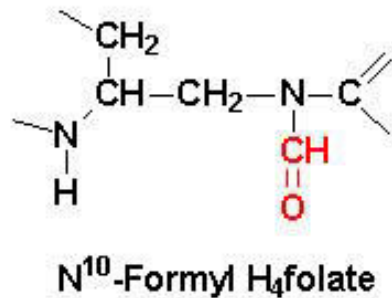
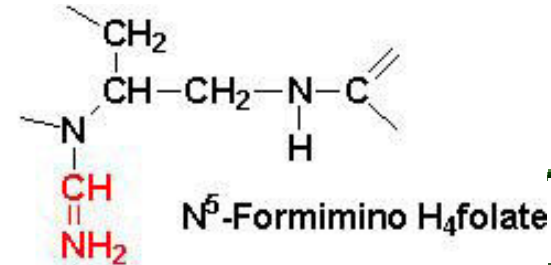
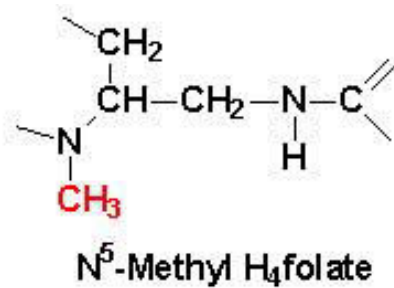
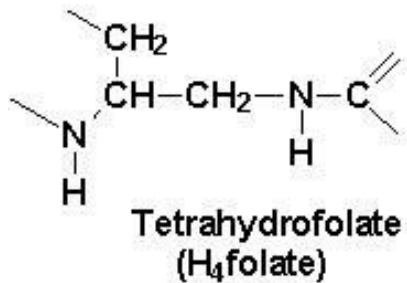
📖 methylated to N₅-methyl-THF

– primary blood form



Folate Functions

Single carbon metabolism



Folate Functions

Interconversion of serine and glycine

 ser + THF <---> gly + 5,10-Me-THF

Degradation of histidine

 his->->->formiminoglutamate(FIGLU)

 FIGLU+THF -> glu + 5-forminino-THF

 histidine load test

– Functional test for folate status



Folate Functions

Purine and Pyrimidine Synthesis

 $\text{dUMP} + 5,10\text{-Me-THF} \rightarrow \text{dTMP} + \text{THF}$

Methionine Synthesis

 $\text{homocysteine} + 5\text{-Me-THF} \rightarrow \text{MET} + \text{THF}$

 MET as a methyl donor for choline synthesis



Folate Deficiency

Megaloblastic Anemia

-  decreased DNA synthesis
-  failure of bone marrow cells to divide
-  normal protein synthesis
-  results in large immature RBC's
-  contrast with microcytic hypochromic anemia



Folate Deficiency

Homocysteine

- Coronary Heart Disease risk factor ?
-  genetic homocystinuria - premature CHD
-  hi [homocys] related to hi CHD risk
-  lo [folate, B-12, B-6] related to hi CHD risk
-  lo intake of B-vit related to hi CHD risk



Folate and Neural Tube Defects

- 📁 Defects in formation of neural tube (brain & spinal cord)
- 📁 First two months gestation
- 📁 Anencephaly
 - absence of cerebral hemispheres



Folate and Neural Tube Defects

Spina bifida

- defective closure of vertebral column
- spinal cord protrusion from spinal column results in damage to spinal cord
- lower limb and hip paralysis
- rectal and bladder problems



NTD Prevalence

 US:

- 4000 live births with NTDs/yr
- 1/1000 pregnancies

 World:

- 400,000 live births with NTDs/yr



NTDs and Folate

- NTDs associated with mothers with low blood [folate]
- Estimated that 50% of NTDs prevented with folate supplementation w/ 200 ug/d
- DRI adults = 400 ug/d
- DRI pregnancy = 600 ug/d
- typical US intake = 280-300 ug/d



Folate and Grain Enrichment

📅 Jan 1, 1998

📅 140 ug/100g enriched grain

📅 results in additional 100 ug/d

📅 may reduce about 25% of NTDs

📅 limited because of masking of B-12 deficiency



Folate: 2000 DRI

Dietary Folate Equivalents (DFE)

– 1 DFE =

 1 ug food folate

 0.6 ug fortified food folate taken with food

 0.5 ug folate supplement on empty stomach



Folate DRI (2000)

	Males 19-30 yr	Females 19-30 yr
RDA (ug/d)	400	400
EAR (ug/d)	320	320
UL (ug/d)	1000	1000
NHANES III Median intake (prior to fortification)	277	223

For women capable of becoming pregnant, it is recommended that they consume 400 ug of folate as supplements or fortified foods in addition to folate containing foods.



Vitamin B-12

Structure

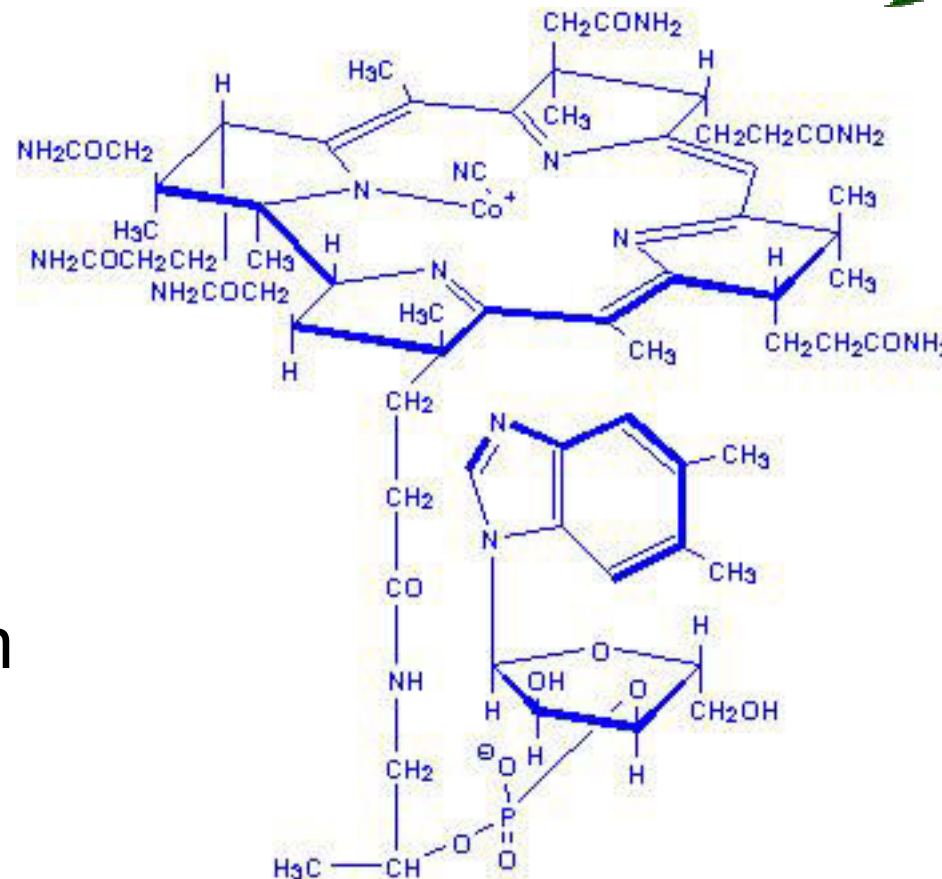
cobalamine

methyl cobalamine

- transport and
coenzyme form

adenosyl cobalamine

- storage and
coenzyme form



Dietary Sources

- 📁 Animal products
 - including milk and eggs
- 📁 GI microorganisms
- 📁 Vegan sources
 - N-fixing legumes
 - fortified grains
 - vitamin supplements



Digestion & Absorption of B-12

📁 **Protein bound in foods**

📁 released by acid and pepsin
– Elderly at risk

📁 **R-protein**

📁 gastric secretion

📁 binds with free B-12

📁 protects B-12 from bacterial use ?



Digestion & Absorption of B₁₂

Intrinsic Factor

-  gastric glycoprotein
-  binds with B₁₂ in small intestine
-  IF-B₁₂ complex binds to B₁₂ receptor in ileum for absorption
-  B₁₂ absorption requires functioning stomach, pancreas, and ileum



Causes of B-12 Deficiency

Inadequate intake - rare

 DRI adults 2.4 ug/d

 Usual intake 7-30 ug/d

Malabsorption of B-12

 IF deficiency

 other GI tract problems



Shilling Test for Malabsorption

- 📁 Saturation of B₁₂ by injection
- 📁 Oral administration of radiolabeled B₁₂
 - free B₁₂
 - IF-B₁₂
- 📁 Measure urinary excretion of labeled B₁₂



Functions of B12

Homocysteine to Methionine

- methionine synthetase
-  requires 5-methyl THF
-  deficiency of B₁₂ results in “methyl-trap” of folate
 - results in megaloblastic anemia
 - synergistic effect of B₁₂ and folate



Functions of B12

Mutases

 methyl malonyl CoA mutase

 propionyl-CoA $\rightarrow$ succinyl-CoA

 accumulation of methyl-malonate
may inhibit AcetylCoA carboxylase



B-12 Deficiency

Pernicious anemia

megaloblastic anemia

- Methyl-folate trap
- Delayed or failure of normal cell division due to impaired DNA synthesis

neuropathy

- defective myelination
- progressive peripheral weakening
- unresponsive to folate
- upper limit to folate supplementation/enrichment

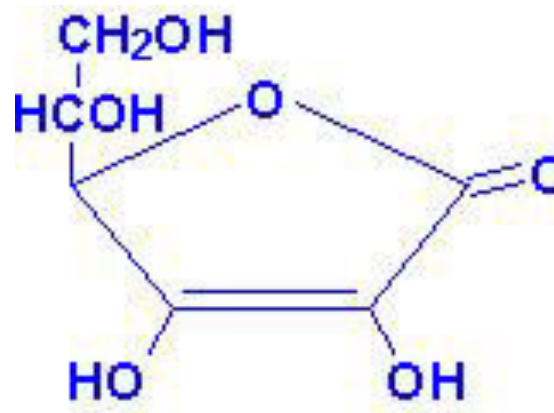


Vitamin C - Ascorbic Acid

📖 Structure

📖 Metabolism

- oxidation/reduction
- dehydroascorbic acid
- dehydroascorbate reductase
- glutathione (GSH)
 - 📖 glutamate-cysteine-glycine



Functions of Vitamin C

- 📁 **Enhances absorption of iron**
- 📁 reduces iron to more absorbable ferrous form
- 📁 chelates with ferrous ion to make it more soluble



Functions of Vitamin C

- 📁 Hydroxylation of proline and lysine
- 📁 post-translational reaction of procollagen
- 📁 hydroxylated collagen can be cross-linked to triple helix collagen
- 📁 Scurvy - weak collagen



Functions of Vitamin C

Hydroxylation Reactions

-  Involves O_2 and metal coenzyme
– (ferrous, cuprous)
-  Carnitine synthesis
-  Tyrosine synthesis & catabolism



Functions of Vitamin C

📁 Hydroxylation Reactions

📁 Synthesis of Neurotransmitters

- Dopamine
- Norepinephrine
- Serotonin

📁 Bile acid synthesis



Functions of Vitamin C

Antioxidant Activity

 Reacts and removes active oxygen species

Pro-oxidant Activity

 Reduces metals to their pro-oxidant forms



Scurvy

- 📖 Bleeding gums
- 📖 petechiae
- 📖 easy bruising
- 📖 impaired wound healing and bone repair
- 📖 joint pain
- 📖 anemia



RDA for Vitamin C

- 📁 10 mg/day prevents scurvy
- 📁 historic RDA's 45-70 mg
(60mg in 1989), 75mg in 2000
- 📁 prevention of scurvy vs
antioxidant effect with
supplements?



Toxicity of Vitamin C

- 📖 UL adults: 2000mg/d
- 📖 Osmotic diarrhea
- 📖 Oxalate kidney stones
- 📖 Decreases uric acid reabsorption resulting in increased risk of gout
- 📖 Affects diagnostic tests in feces and gout
 - fecal blood
 - urinary glucose



Variety is the Key

