Vitamins

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Learning Objectives

At the end of these lectures, student will be able to

- ✓Define & Classify vitamins
- ✓Describe main functions of vitamins
- ✓Demonstrate the role of Vitamins in disease process.

References

Biochemistry (Lippincott's Illustrated Review)

Authors: Richard A. Harvey - Denise R. Ferrier 2017

Definition and Overview

- *Vitamins defined as ……*

"are group of unrelated ***organic compound*** that **cannot** be synthesized in *adequate* quantities by human and therefore must be supplied in micro amount in the diet"

Kazimierz Funk
Polish American Biochemist

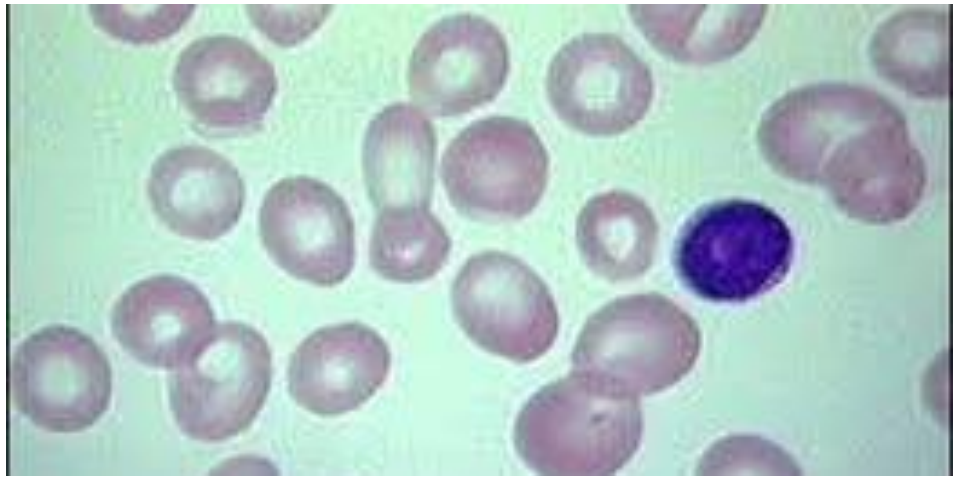
Vitamin *named by Funk*

Vital (Latin vita means Life)

amines (although thiamine have amine)

So,

The absence of a vitamin from the diet or an inadequate intake results in characteristic deficiency signs and ultimately death.



- Vitamins are required to perform specific cellular functions,

(**coenzymes** for the enzymes of intermediary metabolism) so their deficiency will affect cell functions.

- Some vitamins also act as **hormones**
- The amount of each vitamin required in the diet is **small** (µg, mg range)
- consumption of vitamins A and D in excess of the Dietary Reference Intakes (DRIs) can lead to accumulation of toxic quantities of these compounds and the risk of adverse effects increases.

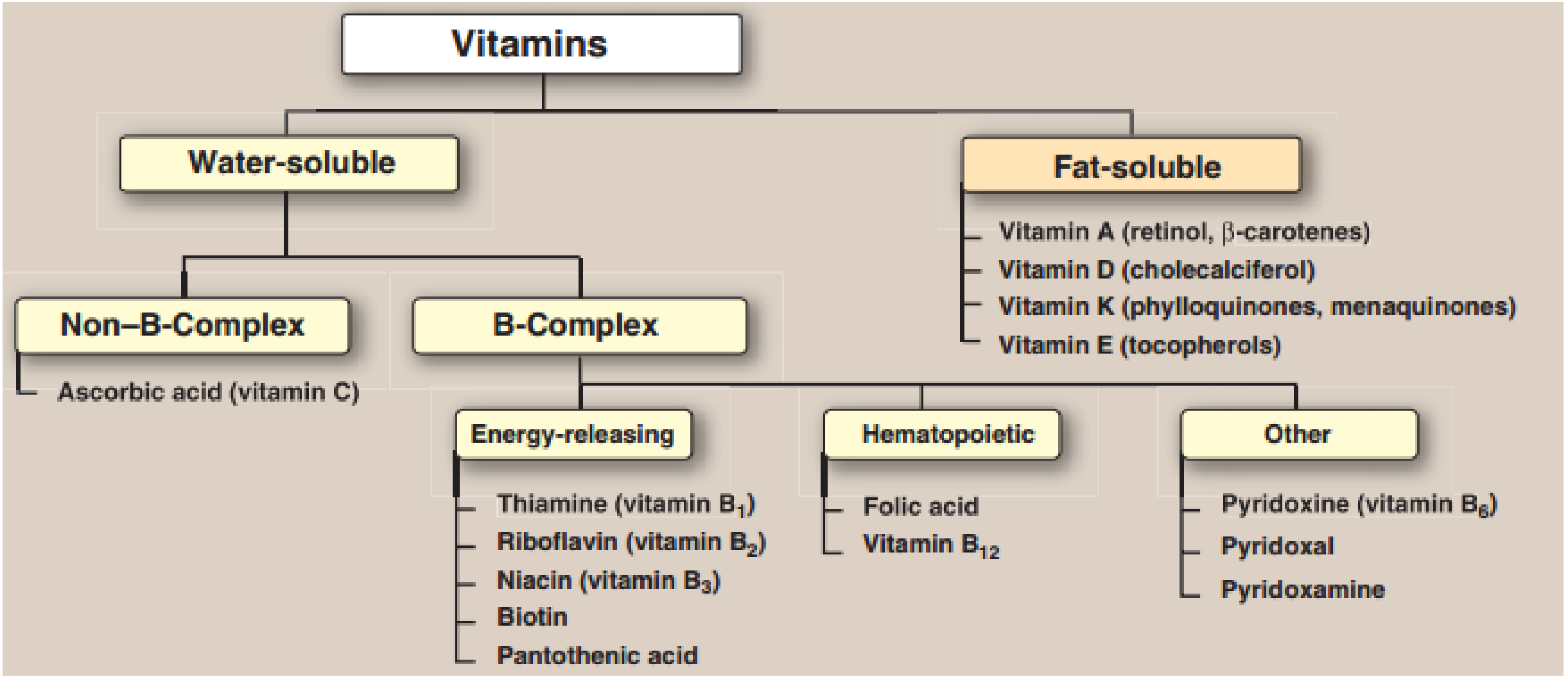
Classification

- They are classified into 2 group

  - Water Soluble Vitamins (**9 vitamins**)
  - Lipid Soluble Vitamins (**4 vitamins**)

This classification has little relationship to their **function** but is related to the **absorption** , **transport** and **storge** of vitamins.

Classification



Water Soluble Vitamins	
Vitamin:	Name:
B1	Thiamine
B2	Riboflavin
B3	Niacin
B5	Pantothenic Acid
B6	Pyridoxine
B7	Biotin
B9	Folate
B12	Cobalamin
C	Ascorbic Acid

Water Soluble Vitamins

B Complex Vitamins

THIAMINE (VITAMIN B1)

Sources and causes of deficiency

Humans cannot synthesize thiamine.

- It is found in many dietary components; wheat germ, oatmeal and yeast (rich sources)
- Adequate amounts are present in a normal diet
- Deficiency is most common in **alcoholics** and in patients with **anorexia nervosa**

Function:

Thiamin is utilized for the intracellular synthesis of thiamin pyrophosphate (TPP) by the action of enzyme called (Thiamin diphosphotransferase)

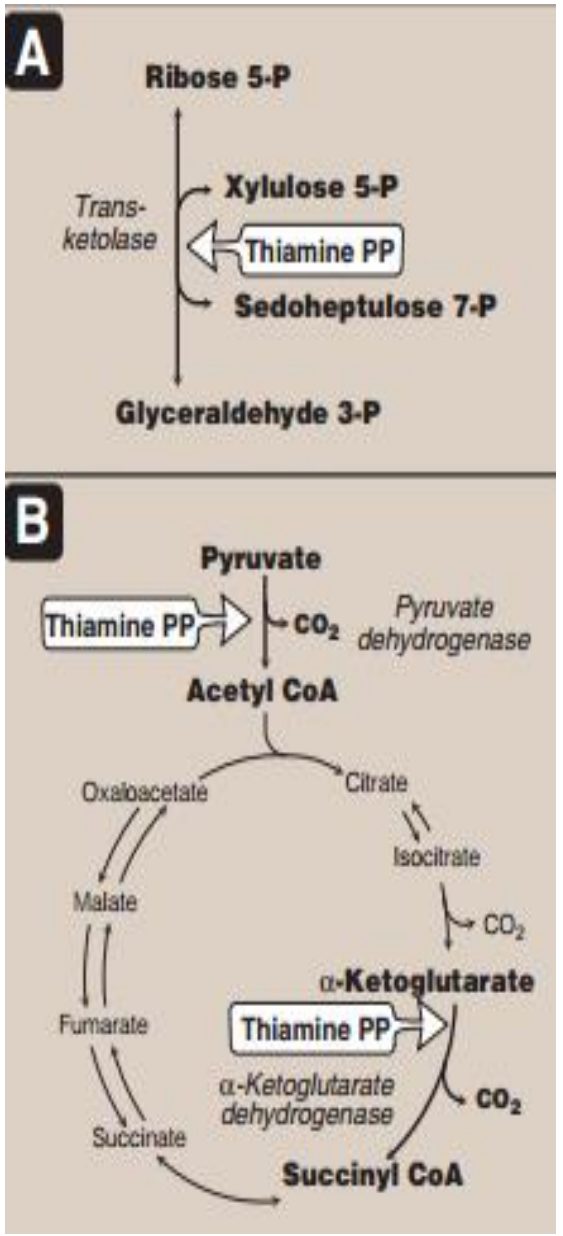
Thiamin + ATP→→→ TPP + AMP

- Thiamine pyrophosphate (TPP) is the biologically active form.

Thiamine pyrophosphate (TPP) :is a coenzyme in the following enzymatic :

- pyruvate dehydrogenase enzyme
- α- ketoglutarate dehydrogenase enzyme
- transketolase reaction in pentose phosphate pathway.

The oxidative decarboxylation of pyruvate and α-ketoglutarate,which plays a key role in energy metabolism of most cells, is particularly important in tissues of the nervous system



Deficiency of Thiamine (Vitamine B1)

- The activity of these **two dehydrogenase-catalyzed** reactions is decreased, resulting in a decreased production of **ATP** and, thus, impaired cellular function in nervous tissue .

Clinical Effect of Thiamine Deficiency

- **Beriberi:** This is a severe thiamine-deficiency syndrome found in areas where **polished rice** is the major component of the diet.

Symptoms are classified into:

- Dry beriberi symptoms: dry skin, Muscle atrophy, irritability, disordered thinking, and progressive paralysis.
- Wet beriberi symptoms: Tachycardia, Edema of extremities and abdomen, Dyspnea, convulsions, and if not treated death.

Clinical Effects of Thiamine Deficiency

- **Wernicke-Korsakoff syndrome**

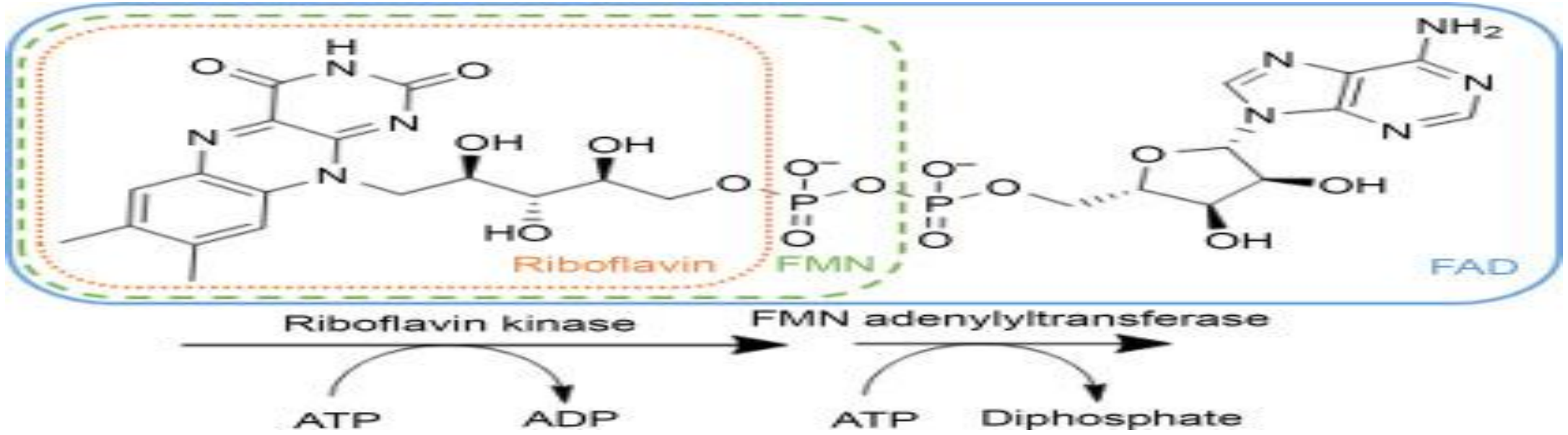
- Dietary insufficiency
- Impaired intestinal absorption. **(Alcoholics)**

A thiamine deficiency state characterized by **apathy**, **loss of memory**, **ataxia**, and **nystagmus**

RIBOFLAVIN (VITAMIN B2)

The two biologically active forms

- Flavin MonoNucleotide (FMN)
- Flavin Adenine Dinucleotide (FAD)



RIBOFLAVIN (VITAMIN B2)

Function:

- FMN and FAD are each capable of reversibly accepting two hydrogen atoms , forming FMNH2 or FADH2 .
- FMN and FAD are bound tightly to Flavoenzymes that catalyze the oxidation or reduction of a substrate
- Both FMN and FAD are reversible **electron carriers** in biological oxidation

Clinical Effects Of Riboflavin Deficiency

Causes of Deficiency

- Poor intake
- Malabsorption
- Alcoholism
- Increased metabolic rate in severe illness.

Deficiency symptoms

Angular, stomatitis, cheilosis, glossitis and dermatitis

cheilosis

(fissuring at the corners of the mouth)

Glossitis

(the tongue appearing smooth and purplish)

cheilitis and glossitis

seborrheic dermatitis

NIACIN (VITAMIN B3)

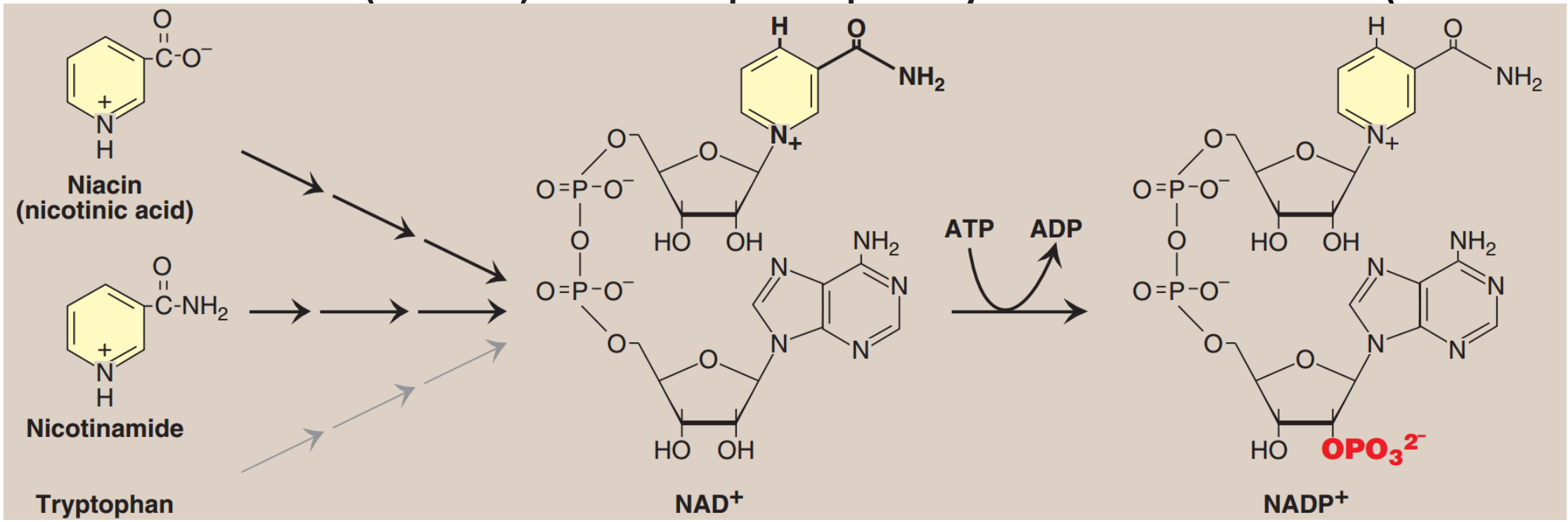
Sources

- Niacin is found in unrefined and enriched grains and cereal, milk, and lean meats, especially liver

- Some nicotinic acid can also be synthesized in humans from tryptophan

NIACIN (VITAMIN B3)

- Niacin, or nicotinic acid, is a substituted pyridine derivative. The biologically active coenzyme forms are nicotinamide adenine dinucleotide (NAD+) and its phosphorylated derivative (NADP+)

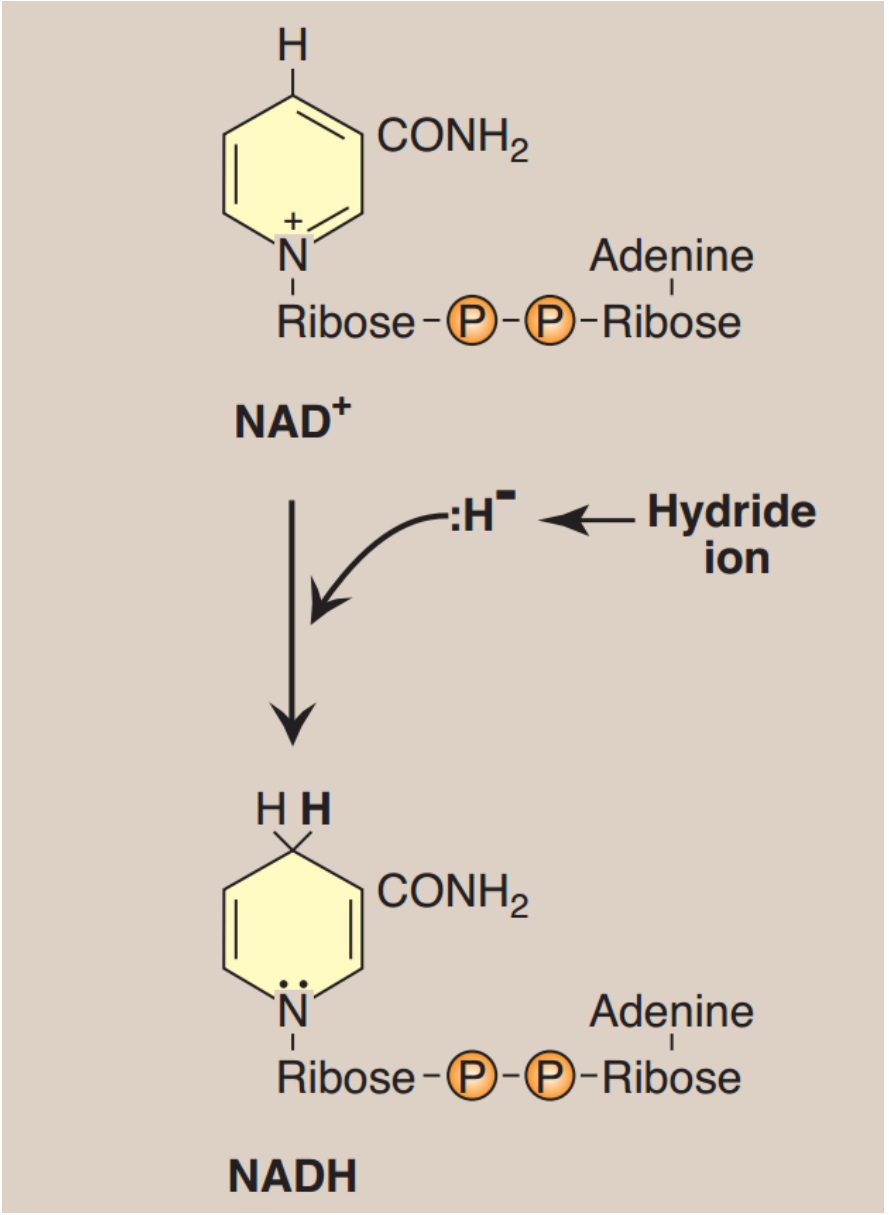


NIACIN (VITAMIN B3)

Function…

NAD+ and NADP+ serve as coenzymes in oxidation-reduction reactions

coenzyme undergoes reduction to NADH and NADPH, respectively.



NIACIN (VITAMIN B3)

Causes of Niacine deficiency :

- The diet should be poor in both Niacin and tryptophan for the disease to occur.
- Other condition leading to pellagra like disease include:

- Drugs such as isoniazid.
- Carcinoid tumor: tryptophan metabolism is diverted to serotonin.
- Hartnup disease: tryptophan absorption is impaired.

Clinical Effects Of Nicotinamide Deficiency

- A deficiency of niacin causes **pellagra**,
- A disease involving the skin, gastrointestinal tract, and CNS.
- The symptoms of pellagra progress through the three Ds:
- Dermatitis, Diarrhea, Dementia—and, if untreated, Death

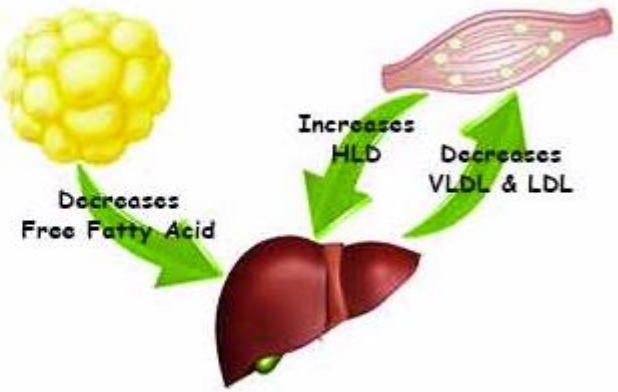
eFig. 51.1 Pellagra. The photodistribution of erythema (**A**), erythema plus shiny desquamation (**B**), and erythema plus bullae (**C**) is apparent. Note the sparing under the watchband and shoes. *Courtesy, Luis Requena, MD.*

Treatment of Hyperlipidemia

- Niacin inhibits lipolysis in adipose tissue
- Niacin causes A decrease in liver triacylglycerol synthesis
- It lower both plasma triacylglycerol (in VLDL) and cholesterol

Niacin is particularly useful in the treatment of

type IIb hyperlipoproteinemia



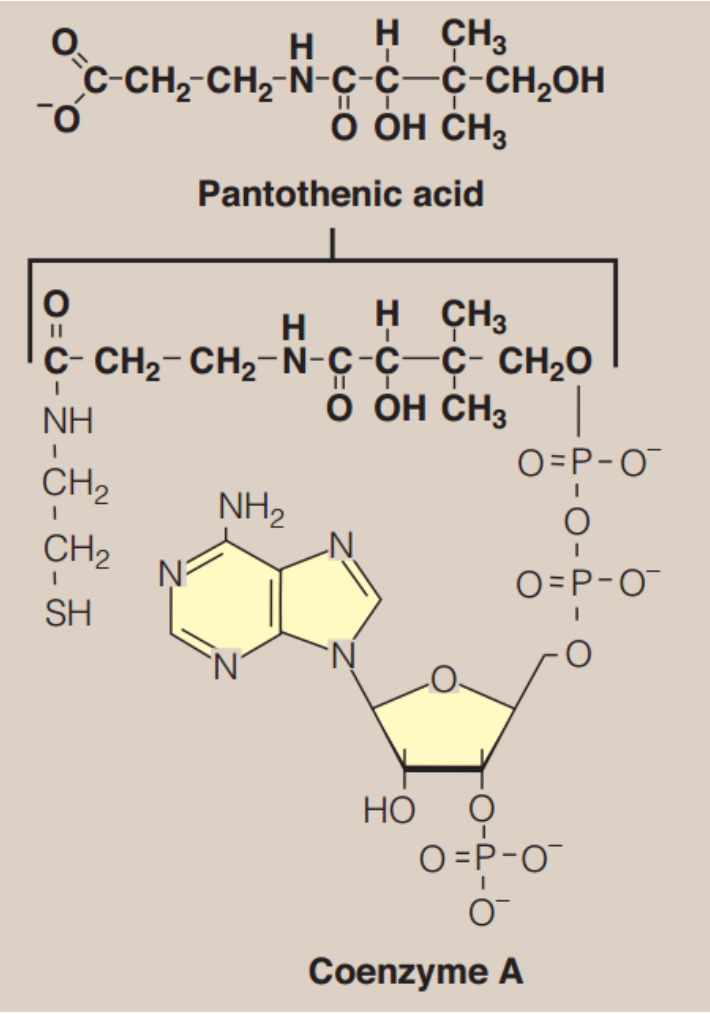
PANTOTHENIC ACID (VITAMIN B5)

Pantothenic acid is required for the structure of the following:

1- Coenzyme A (CoA – SH)

2- Acyl carrier protein (ACP – SH)

The thiol group act as carrier of acyl radicals in both CoA and ACP ex. In fatty acid oxidation and synthesis.



Sources:

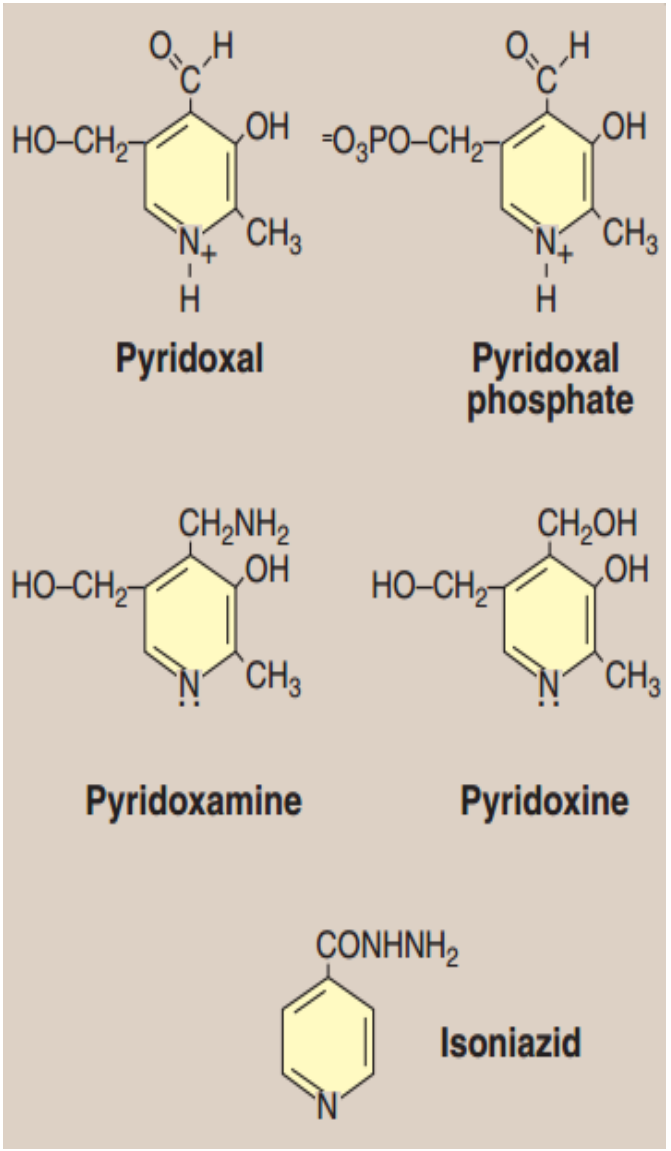
Eggs, liver, and yeast .

Deficiency:

It is rare because this vitamin is widely distributed in food.

PYRIDOXINE (VITAMIN B6)

- Vitamin B6 is a collective term for **pyridoxine**, **pyridoxal**, and **pyridoxamine**, all derivatives of pyridine
- They differ only in the nature of the **functional group** attached to the ring
- **Pyridoxine** occurs primarily in **plants**, whereas **pyridoxal** and **pyridoxamine** are found in foods obtained from **animals**
- All three compounds can serve as precursors of the biologically active coenzyme, pyridoxal phosphate



PYRIDOXINE (VITAMIN B6)

- Pyridoxal phosphate functions as a coenzyme for a large number of enzymes, particularly those that catalyze reactions involving amino acids

Reaction type	**Example**
Transamination	Oxaloacetate + glutamate $\leftrightarrow$ aspartate + α-ketoglutarate
Deamination	Serine $\rightarrow$ pyruvate + NH3
Decarboxylation	Histidine $\rightarrow$ histamine + CO2
Condensation	Glycine + succinyl CoA $\rightarrow$ δ-aminolevulinic acid

Clinical Effects Of PYRIDOXINE Deficiency

Deficiency of B6 alone is rare (usually occur as part of generalize nutritional deficiency), however deficiency of B6 alone could occur in the following conditions:

- **Isoniazid** (iso nicotinic acid hydrazide), a drug frequently used to treat tuberculosis, can induce a vitamin B6 deficiency by forming an inactive derivative with pyridoxal phosphate

"Dietary supplementation with B6 is, thus, an adjunct to isoniazid treatment"

Clinical Effects Of PYRIDOXINE Deficiency

- Infants fed formulas low in B6.
- In women taking oral contraceptives .
- In alcoholics .

Clinical Effects Of PYRIDOXINE Deficiency

- In childhood can result in poor growth, anaemia, decrease immunity, and convulsion in infant.

- In adult there is no characteristic syndrome, may lead dermatitis and polyneuritis.

Toxicity of pyridoxine

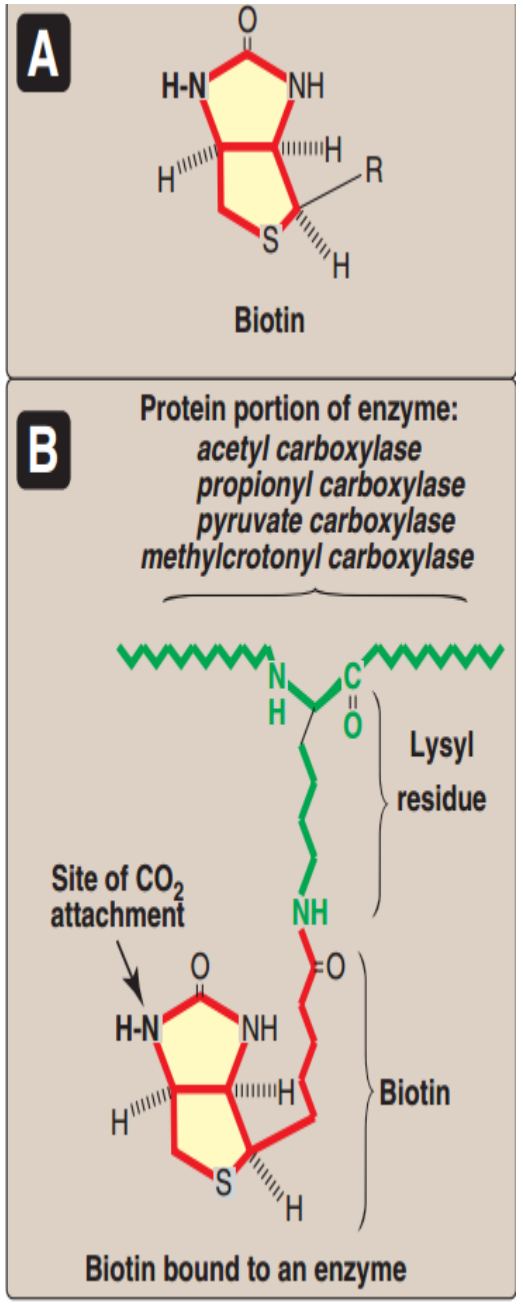
- Pyridoxine is the only water-soluble vitamin with significant toxicity.
- Neurologic symptoms (sensory neuropathy) occur at intakes above 200 mg/day, an amount more than 100 times the RDA
- Substantial improvement, but not complete recovery, occurs when the vitamin is discontinued.

BIOTIN (VITAMIN B7)

- Biotin is a coenzyme in carboxylation reactions
- Biotin is covalently bound to the ε-amino groups of lysine residues in biotin dependent enzymes .

Sources:

Widely distributed in natural foods. In addition, biotin is produced by intestinal flora which may provide most or all the required amounts.



BIOTIN (VITAMIN B7) deficiency:

- Rare except among people maintained for many months on parenteral nutrition and a very small number who eat abnormally large amount of uncooked eggs white, which contains avidin, which tightly binds biotin and prevents its absorption from the intestine .
- Biotin deficiency present with Alopecia, dermatitis, glossitis, loss of appetite, and nausea .

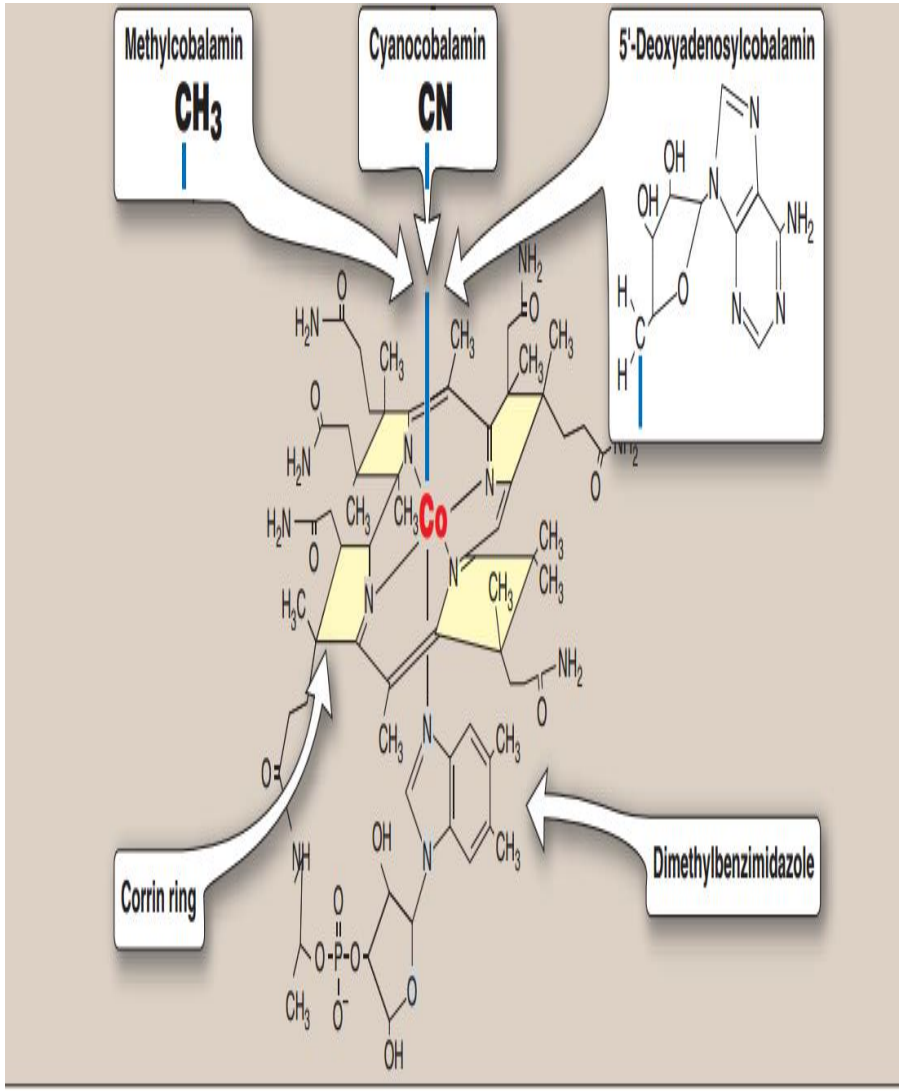
COBALAMIN (VITAMIN B12)

Structure

Corrin ring system

Cobalt is held in the center of the corrin ring

Cyanide in commercial preparations of the vitamin in the form of cyanocobalamin



COBALAMIN (VITAMIN B12)

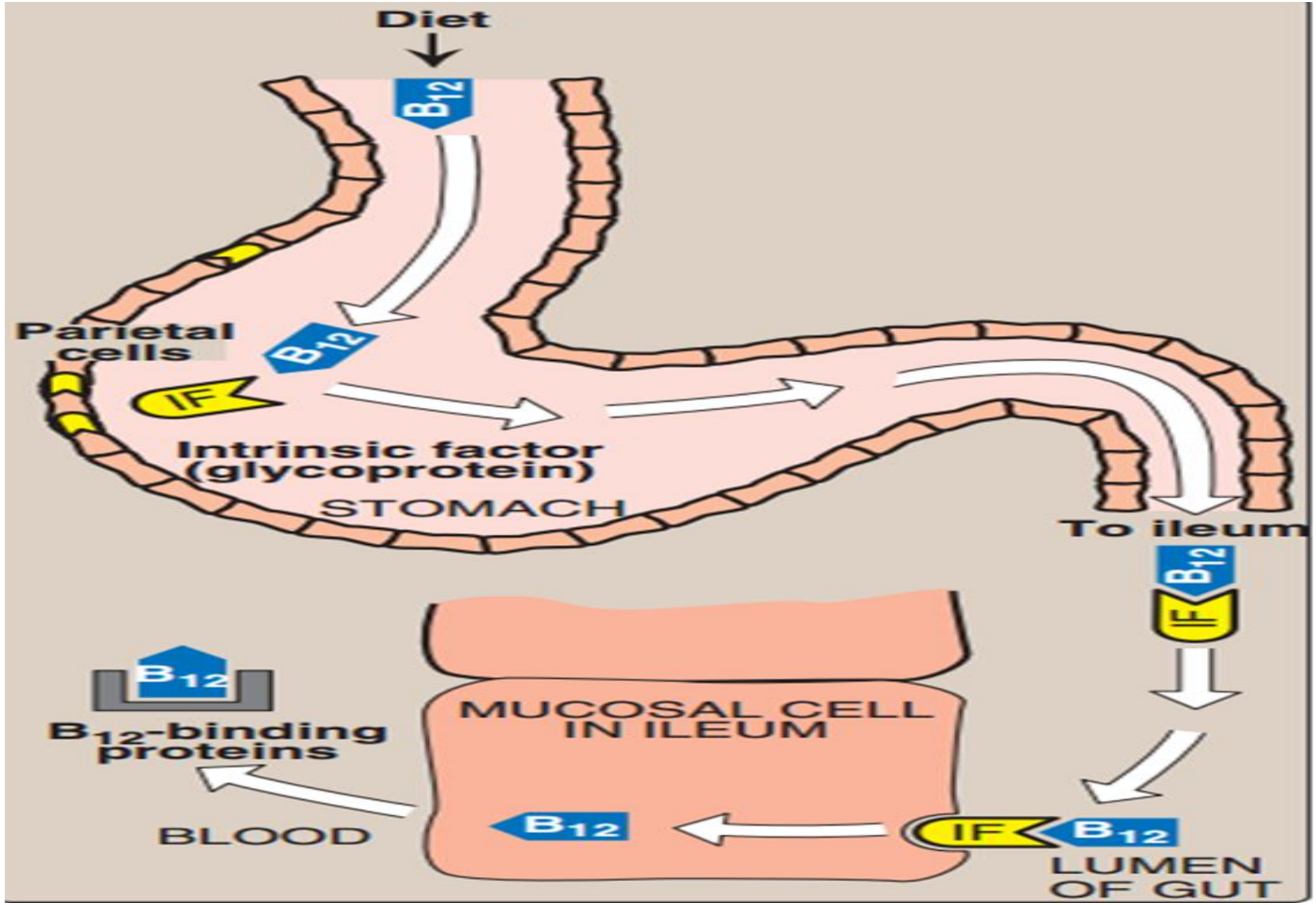
Sources:

- Is synthesized only by microorganisms (*Bacterial Flora*)
- **Not** present in **plants**

Cobalamin is present in appreciable amounts in liver as (methylcobalamin, adenosylcobalamin, and hydroxycobalamin), whole milk, eggs, oysters, fresh shrimp, pork, and chicken .

Absorption of Vitamin B12

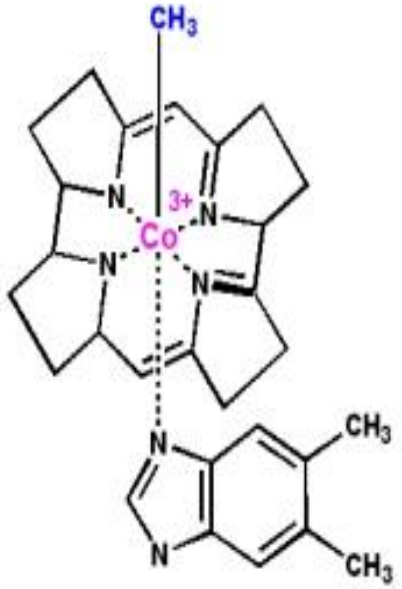
- Vitamin B12 obtained from the diet binds to **intrinsic factor (IF)** which is secreted by gastric parietal cells.
- In the intestine the **cobalamin–intrinsic factor** complex travels through the gut
- Complex binds to **specific receptors** on the surface of mucosal cells of the terminal ileum.
- The bound cobalamin is transported through the mucosal cell to the circulation where it's transported in by **B12-binding proteins.**


Diet
B12
Parietal cells
B12
IF
Intrinsic factor (glycoprotein)
STOMACH
To ileum
B12
IF
B12
B12-binding proteins
MUCOSAL CELL IN ILEUM
BLOOD
B12
IF
B12
LUMEN OF GUT

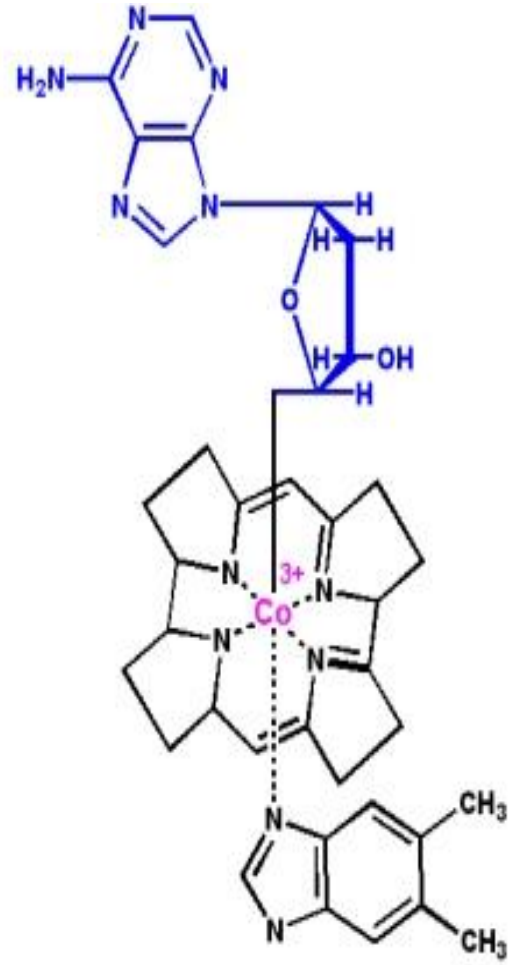
COBALAMIN (VITAMIN B12)

The active vitamin B12 are :

- **5'-deoxyadenosylcobalamin** cyanide is replaced with 5'-deoxyadenosine
- **methylcobalamin** cyanide is replaced by a **methyl** group



Methylcobalamin



5'-Deoxyadenosylcobalamin

COBALAMIN (VITAMIN B12)

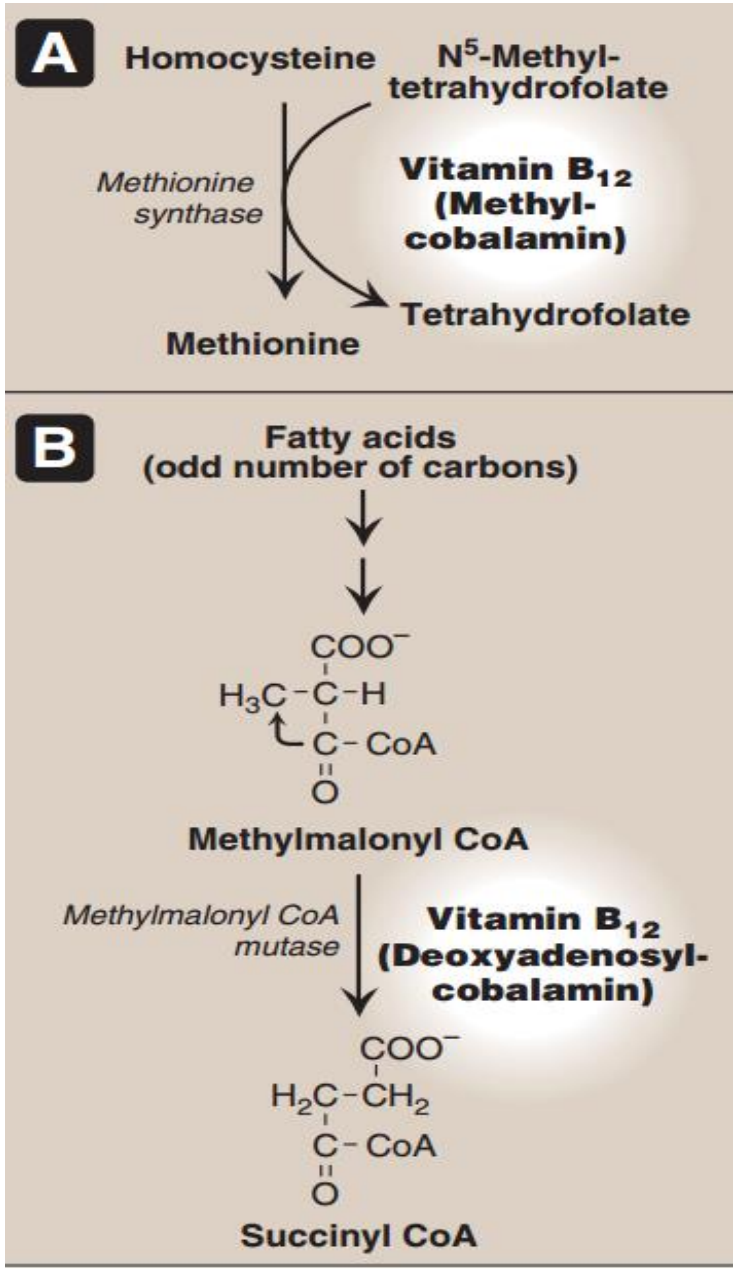
Function:

Vitamin B12 is required in humans for two essential enzymatic reaction:

A. Re-methylation:

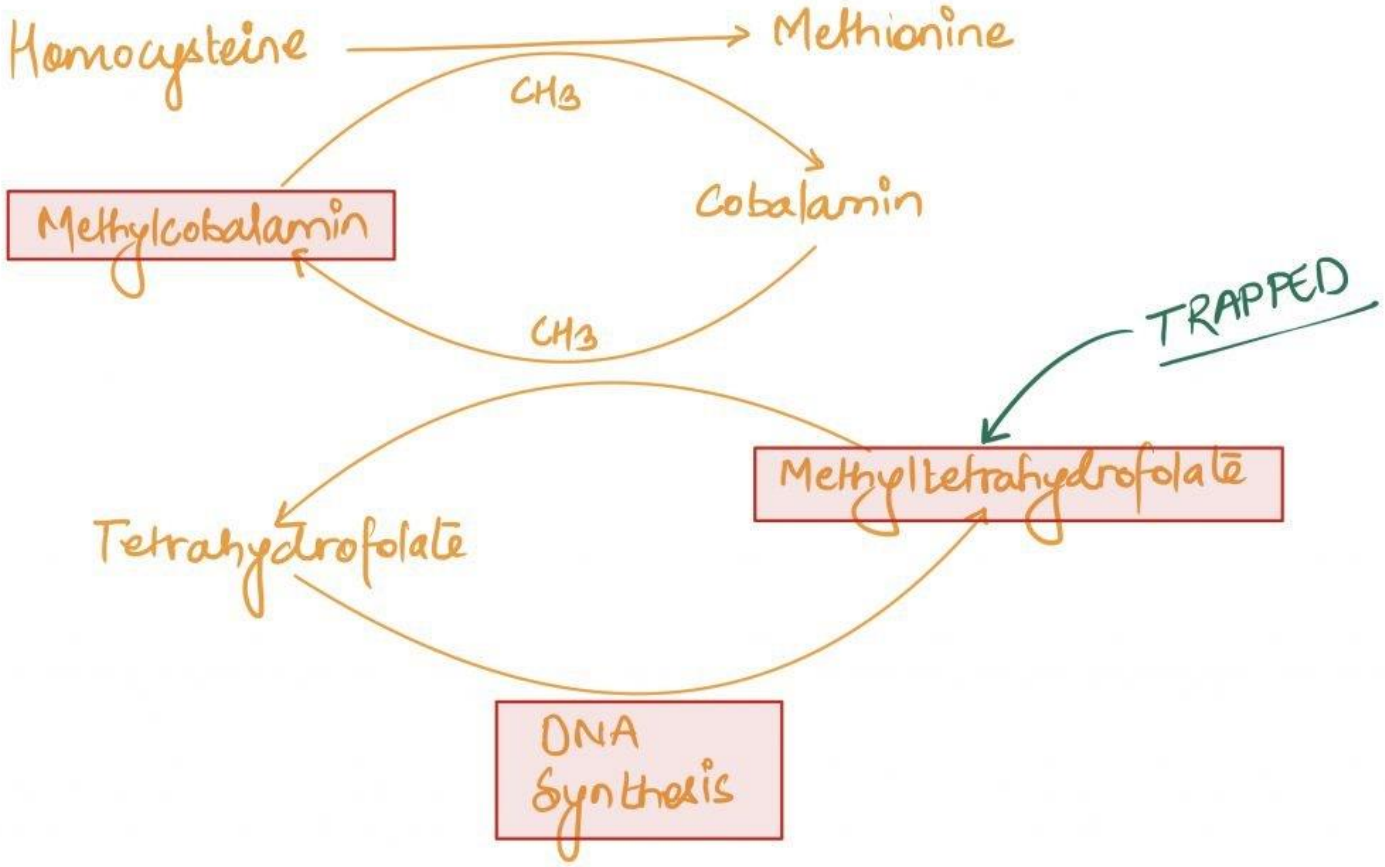
1-Synthesis of methionine from homocysteine .

2-THFA is made available for nucleotide synthesis. Because the N5 – methyl THFA is the predominant form of folic acid in human serum and liver.



Folate trap hypothesis

- Happen in rapidly dividing cell (erythropoietic, intestine)
- Deficiency of cobalamin lead to entrapment of folate in its **methyl** form



B. Isomerization of methyl malonyl coenzyme A (CoA) that is produced during the degradation of some amino acids and fatty acids with odd numbers of carbon atoms .

- **Note**: unusual fatty acids accumulate and become incorporated into cell membranes, including those of the nervous system leading to neurological manifestation of vitamin B12 deficiency .

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Clinical Effects Of Cobalamin Deficiency

In contrast to other water-soluble vitamins, significant amounts (4–5 mg) of vitamin B12 are stored in the body. As a result, it may take several years for the clinical symptoms of B12 deficiency to develop .

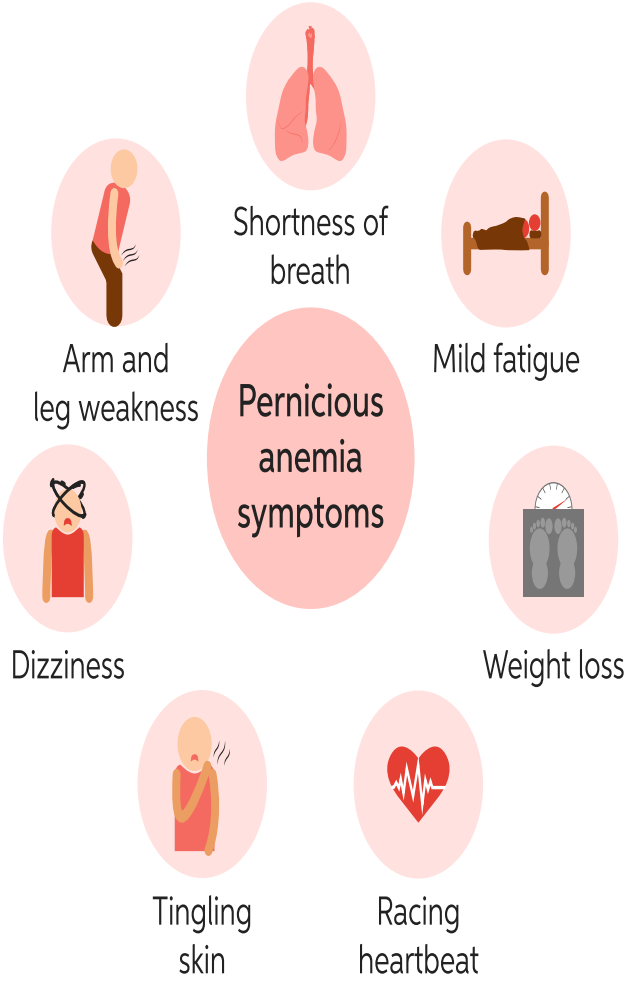
Clinical Effects Of Cobalamin Deficiency

B12 deficiency develop in individuals who have had :

- Impaired secretion of intrinsic factor (pernicious anaemia)
- a partial or total gastrectomy
- Terminal ileal resection
- Poor dietary intake is rare
- Vegans are at special risk

Pernicious anemia

- Autoimmune destruction of the gastric parietal cells
- Lack of intrinsic factor prevents the absorption of vitamin B12
- Patients with cobalamin deficiency are usually anemic (megaloblastic anemia)
- Later in the development of the disease they show neuropsychiatric symptoms
- Measured by the level of methylmalonic acid in blood,
- Treated by giving high-dose B12



Does giving folate will correct pernicious anemia ???

FOLIC ACID (VITAMIN B9)

Folic acid consist of the base pteridin, PABA, and glutamate.

Sources:

- Animals are not capable of synthesizing folic acid therefore, require folate must supply in their diet.
- Liver and green leafy vegetable are major sources.
- Higher amount should be ingested during growth, pregnancy, and lactation.

FOLIC ACID (VITAMIN B9)

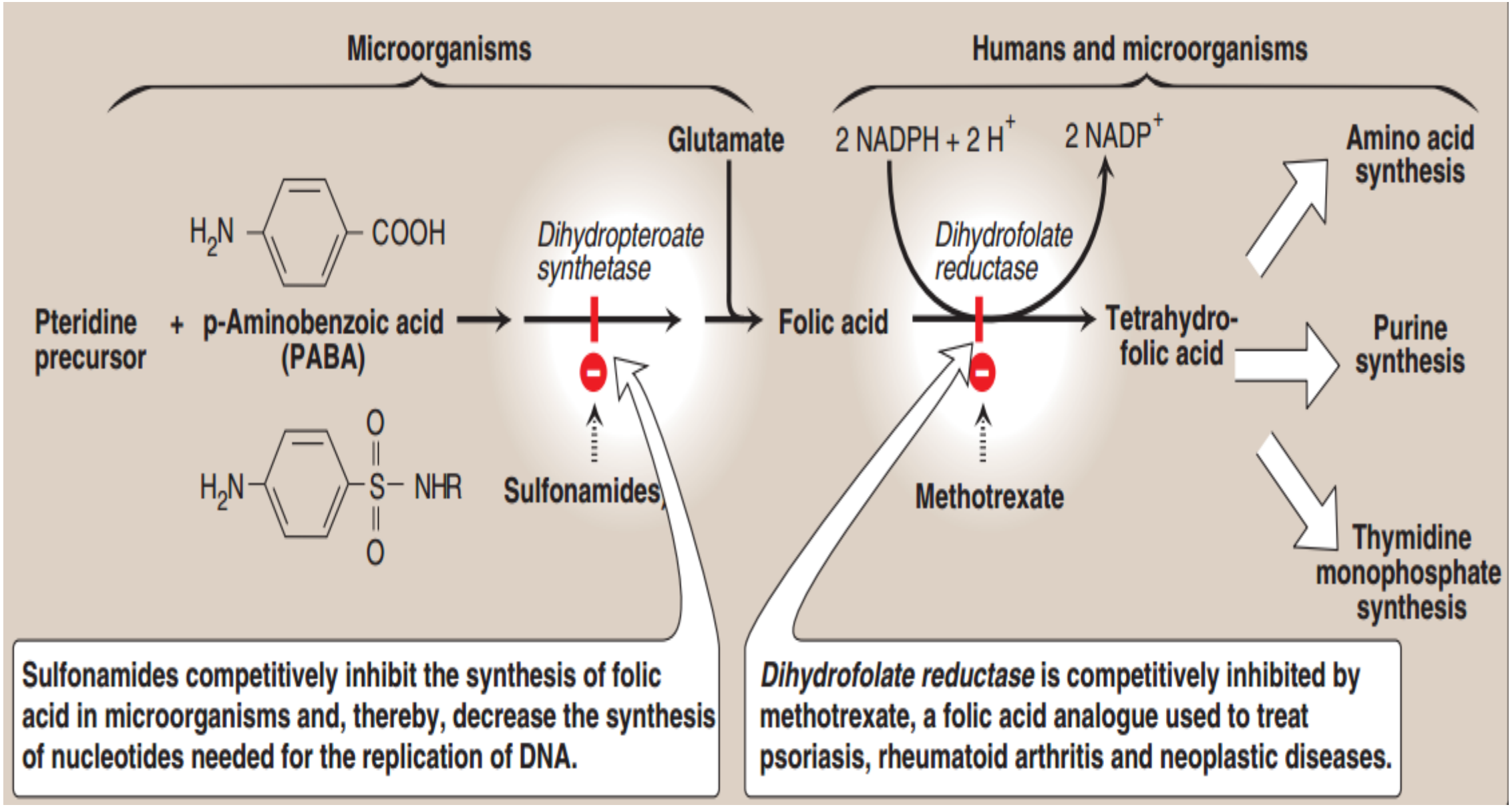
Function :

Active folate is Tetrahydrofolate (reduced folate) THFA

- plays a key role in one-carbon metabolism
- (THFA) receives one-carbon fragments from donors such as serine, glycine, and histidine and transfers them to intermediates in the:

➢ Synthesis of amino acids

➢ Synthesis of purines, and pyrimidine found in DNA.


Microorganisms
Humans and microorganisms
Glutamate
2 NADPH + 2 H+
2 NADP+
Amino acid synthesis
Dihydropteroate synthetase
Dihydrofolate reductase
Pteridine precursor
+ p-Aminobenzoic acid (PABA)
Folic acid
Tetrahydro-folic acid
Purine synthesis
Sulfonamides
Methotrexate
Thymidine monophosphate synthesis
Sulfonamides competitively inhibit the synthesis of folic acid in microorganisms and, thereby, decrease the synthesis of nucleotides needed for the replication of DNA.
Dihydrofolate reductase is competitively inhibited by methotrexate, a folic acid analogue used to treat psoriasis, rheumatoid arthritis and neoplastic diseases.

Folate deficiency caused by:

- **Inadequate dietary intake.**
- **Increase demand** (pregnancy, lactation)
- **Poor absorption** caused by pathology of the small intestine
- **Alcoholism**
- **Treatment** with drugs that are dihydrofolate reductase inhibitors

EX(Methotrexate).

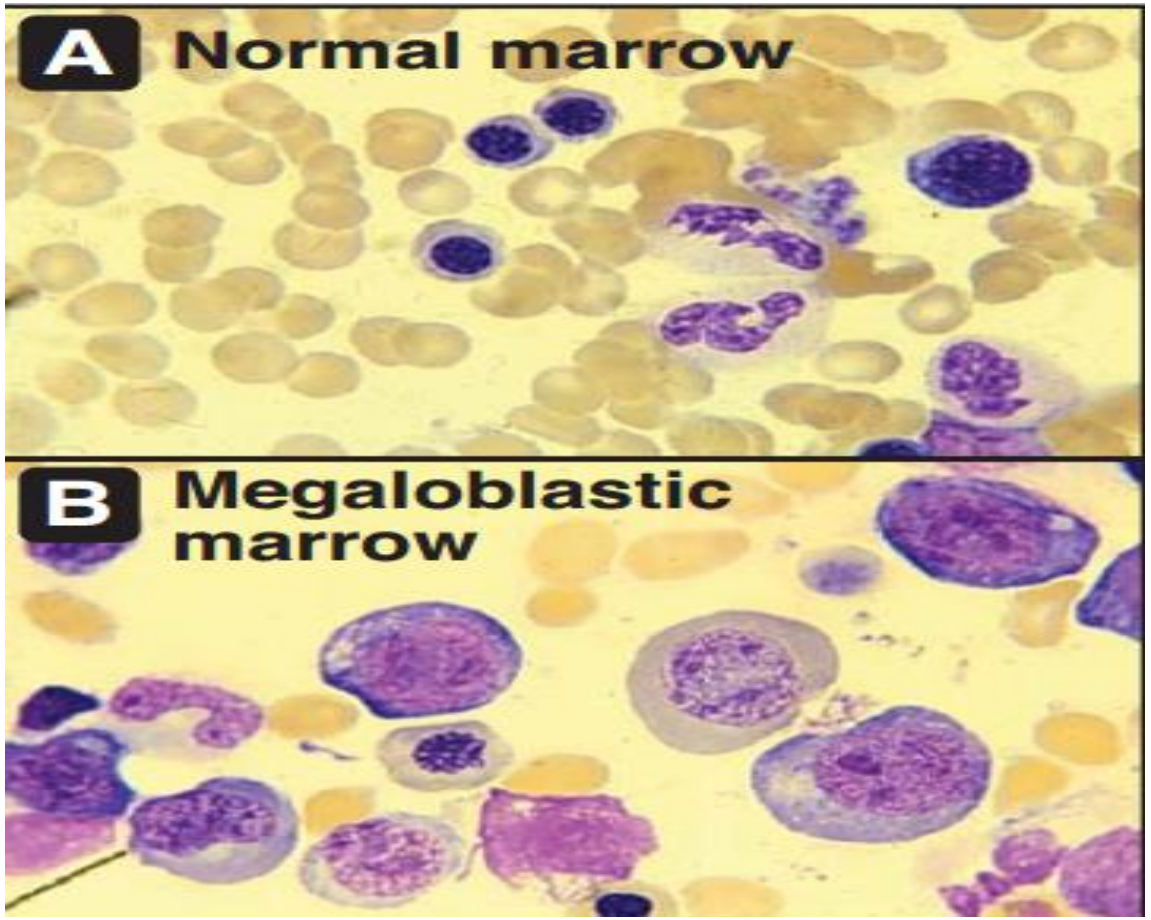
Clinical Effects Of folic acid Deficiency

The metabolic effects of folic acid deficiency are block the synthesis of purine nucleotide and in the conversion of dUMP to dTMP as consequence the synthesis of DNA can not proceed normally.

Tissues with high degree of cell multiplication are therefore first affected such as:

- Bone marrow leading to Megaloblastic anaemia.
- Epithelial cells lining the gastrointestinal tract.

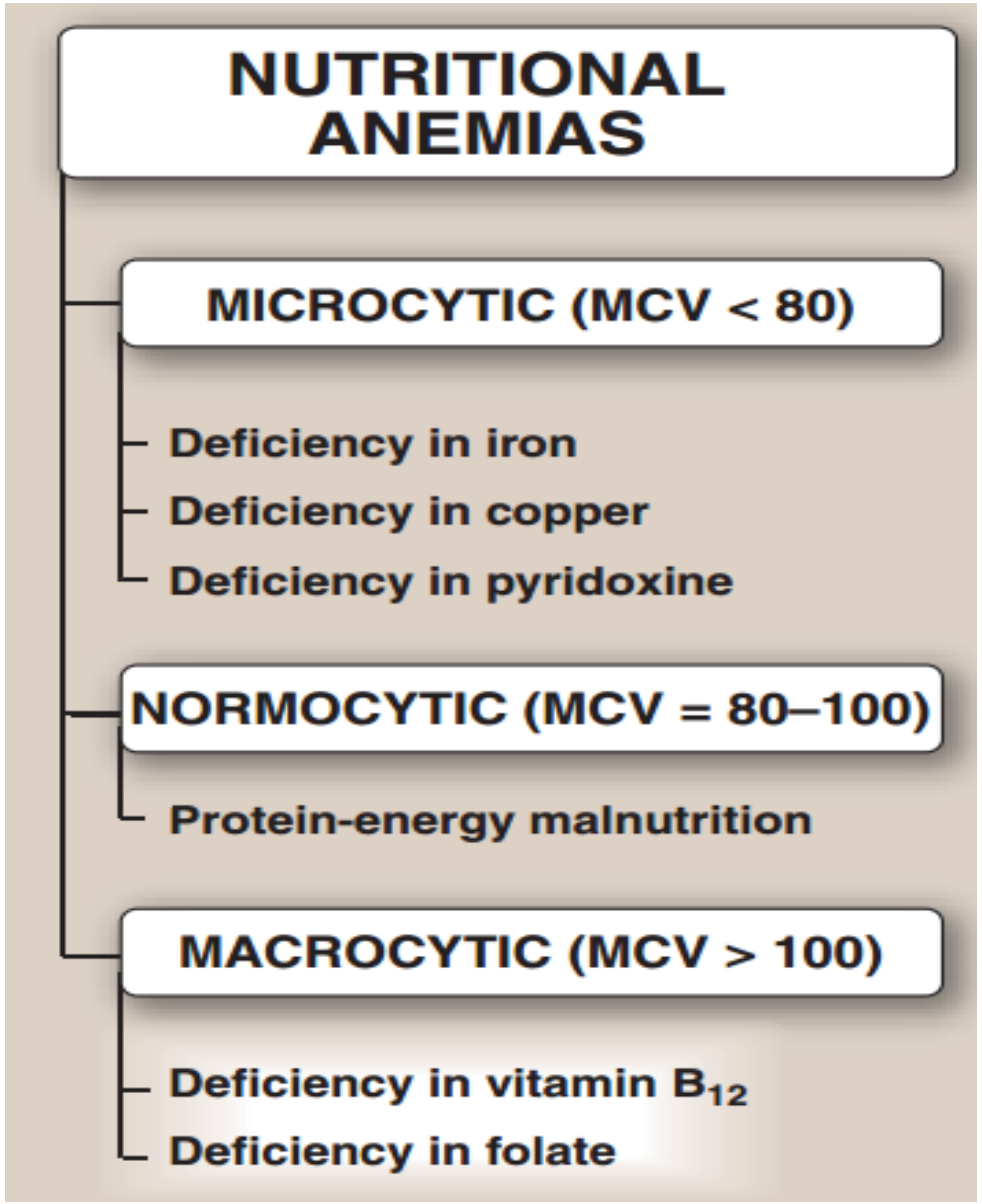
A primary result of folic acid deficiency is **megaloblastic anemia**



Nutritional Anemias

- **Anemia** is a condition in which the blood has a **lower-than-normal** concentration of **hemoglobin**

- Nutritional anemias—those caused by inadequate intake of one or more essential nutrients—can be classified according to the size of the red blood cells or **mean corpuscular volume** observed in the individual (**MCV**)



Folate and neural tube defects in the fetus

Spina bifida and **anencephaly**

(the most common **neural tube defects)**

❖Folic acid supplementation before conception and during the first trimester has been shown to significantly reduce the defects.

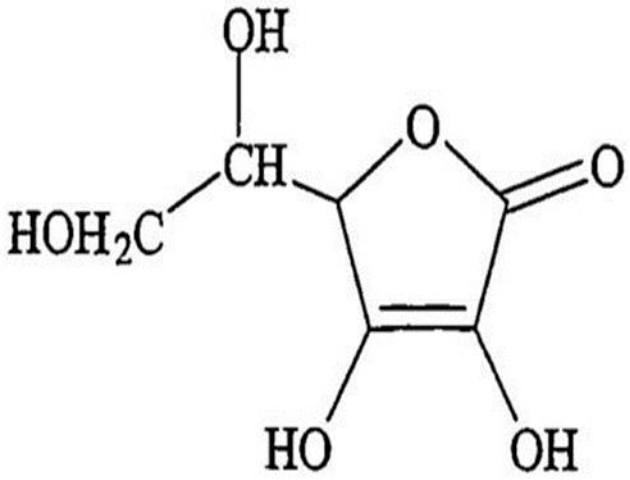
Open spina bifida

Anencephaly

Vitamin C

ASCORBIC ACID (VITAMIN C)

The active form of vitamin C is **Ascorbic acid .**



Ascorbic Acid

Sources:

- The best sources are citrus fruits, tomatoes, melons, and fresh vegetable.
- The vitamin is thermolabile.

ASCORBIC ACID (VITAMIN C)

Function of ascorbate is as a reducing agent in several different reactions:

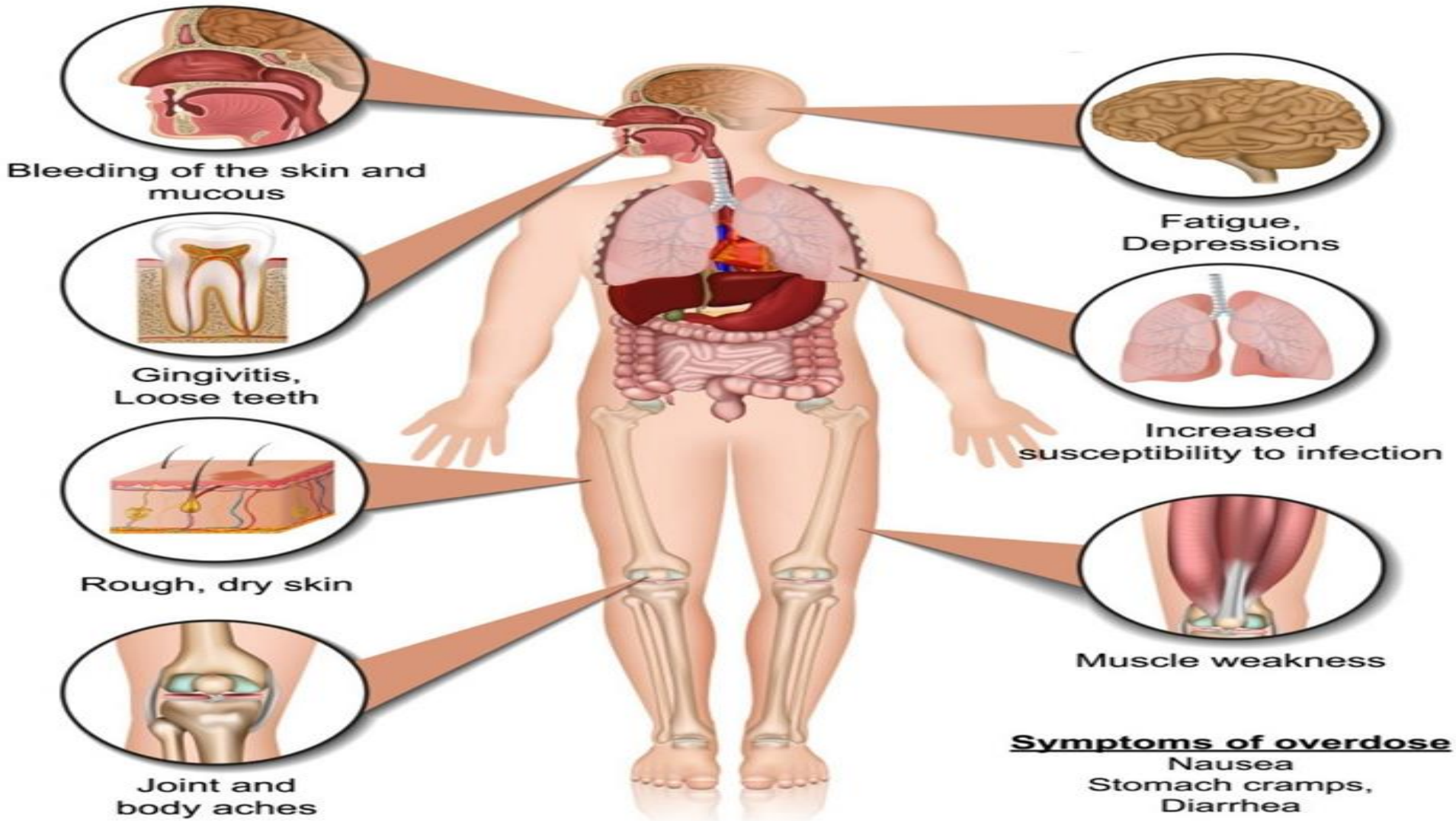
- As a coenzyme in **hydroxylation** reactions, for example, hydroxylation of prolyl and lysyl residues of collagen for maintenance of **normal connective tissue**, as well as for **wound healing.**
- Facilitates the absorption of dietary **iron** from the intestine .

Deficiency of ascorbic acid

- Deficiency of ascorbic acid results in **Scurvy** a disease characterized by sore and spongy gums, loose teeth, fragile blood vessels, swollen joints, and anemia .

- Deficiency in the hydroxylation of collagen, resulting in defective connective tissue

SCURVY
SYMPTOMS




A
B

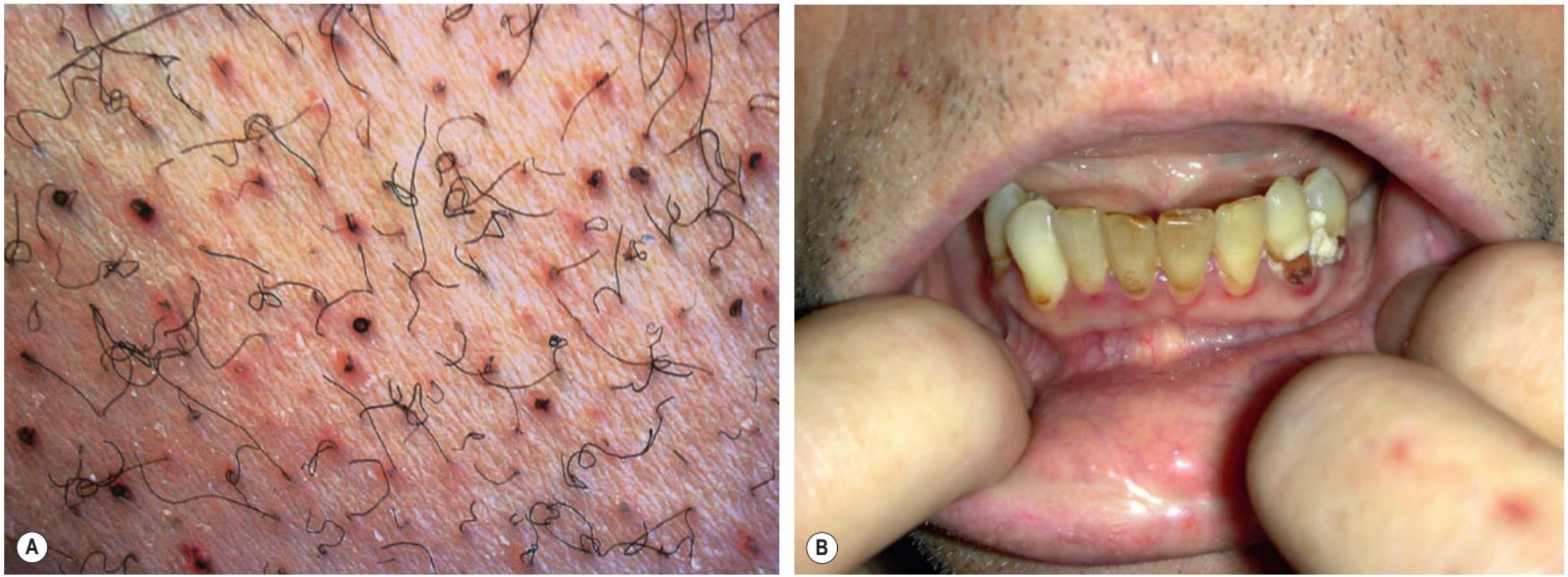


Fig. 51.8 Scurvy. A Corkscrew hairs and perifollicular hemorrhage on the lower extremities. **B** Gingivitis and gingival erosions. *B, Courtesy, Jeffrey P Callen, MD.*

Prevention of chronic disease

- Vitamin C is one of a group of nutrients which are known as antioxidants that includes (vitamin E and β-carotene and Vitamin C).
- Consumption of diets rich in these compounds is associated with a decreased incidence of some chronic diseases, such as coronary heart disease and certain cancers .

Thank you