Vitamins

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Vitamins classification

•**Vitamins** are essential organic compounds that the animal organism is not capable of forming itself, although it requires them in small amounts for metabolism.

•Most vitamins are precursors of coenzymes; in some cases, they are also precursors of hormones or act as antioxidant.

•The body requirements from these elements are variant depending on the age, sex, physiological condition (pregnancy, breast feeding, exercise).

•Nine vitamins (folic acid, ascorbic acid, pyridoxine, thiamine, niacin, riboflavin, biotin, and pantothenic acid) are classified as water-soluble vitamins many of them are coenzyme.

•Four vitamins (vitamins A, D, K, and E) are termed fat-soluble where only vit K has a coenzyme function.

Vitamins classification

- **Vitamins**
  - **Water-soluble**
    - **Non–B-Complex**
      - Ascorbic acid (vitamin C)
    - **B-Complex**
      - **Energy-releasing**
        - Thiamine (vitamin B_1)
        - Riboflavin (vitamin B_2)
        - Niacin (vitamin B_3)
        - Biotin
        - Pantothenic acid
      - **Hematopoietic**
        - Folic acid
        - Vitamin B_{12}
      - **Other**
        - Pyridoxine (vitamin B_6)
        - Pyridoxal
        - Pyridoxamine
  - **Fat-soluble**
    - Vitamin A (retinol, β-carotenes)
    - Vitamin D (cholecalciferol)
    - Vitamin K (phylloquinones, menaquinones)
    - Vitamin E (tocopherols)

Vitamin supply

•Healthy diet cover the average body need from vitamins. Otherwise could develop hypovitaminosis .

•**Hypovitaminosis** caused by malnutrition insufficient uptake of vitamin from daily uptake, because of resorption disturbances in extreme cases (chronic –long term) **avitaminosis** can occur. For example, antibiotics that kill bacterial flora could lead to vitamin deficiency (K, B12, H) which are synthesized by bacteria.

•Not all vitamins can be stored in the body (A, D, E, B12). For this reason, the body needs continuous supply of vitamins to avoid their lack which affect skin, blood, and nervous system.

• Overdose of vitamins A and D leads to toxic **hypervitaminoses**.

Water soluble vitamin – B complex vitamins

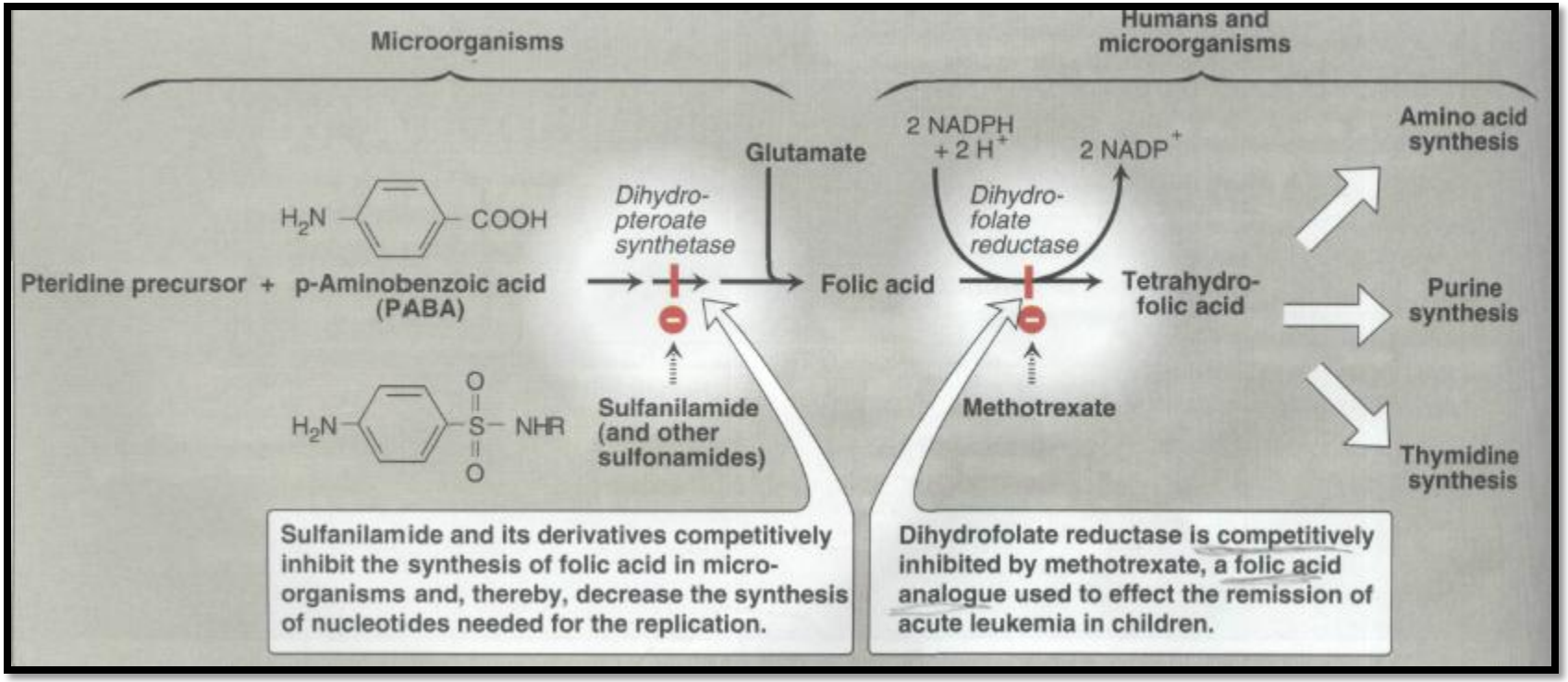
- **Folic acid or folate :**

○Play a key role in C1 metabolism receive one carbon from one-carbon fragments from donors such as serine, glycine, and histidine and transfers them to intermediates in the synthesis of amino acids, purines, and thymine a pyrimidine found in DNA. After reduction to THF, folate serves as coenzyme in C1 metabolism.

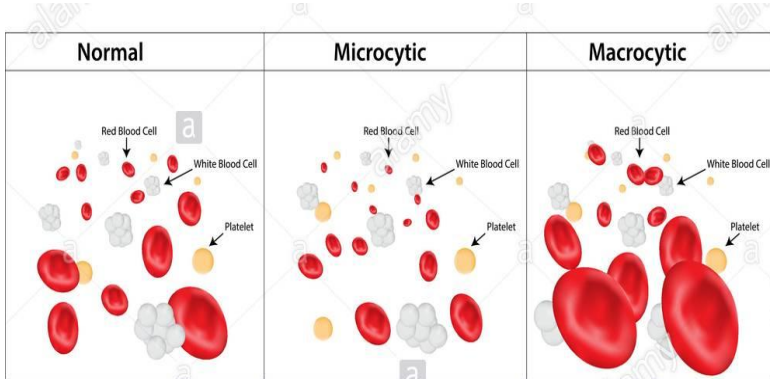
○Folate deficiency leads to disturbances in nucleotide biosynthesis and thus cell proliferation.

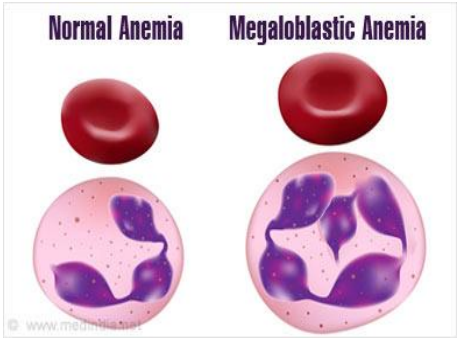
○As precursors for blood cells which divide rapidly, the deficiency leads to megaloblastic anemia accumulation of abnormal giant red blood cells megaloblast, later disturbances on the phospholipids and aminoacids synthesis can occur.

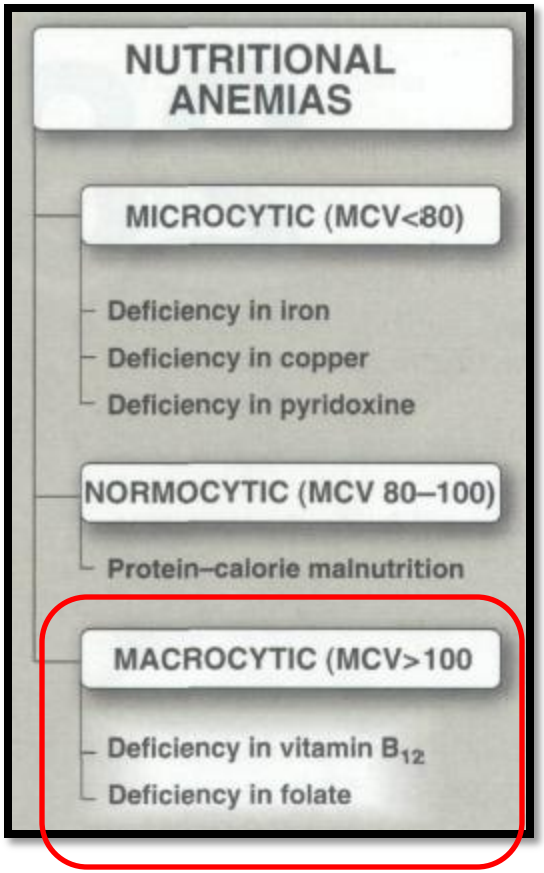
THF synthesis

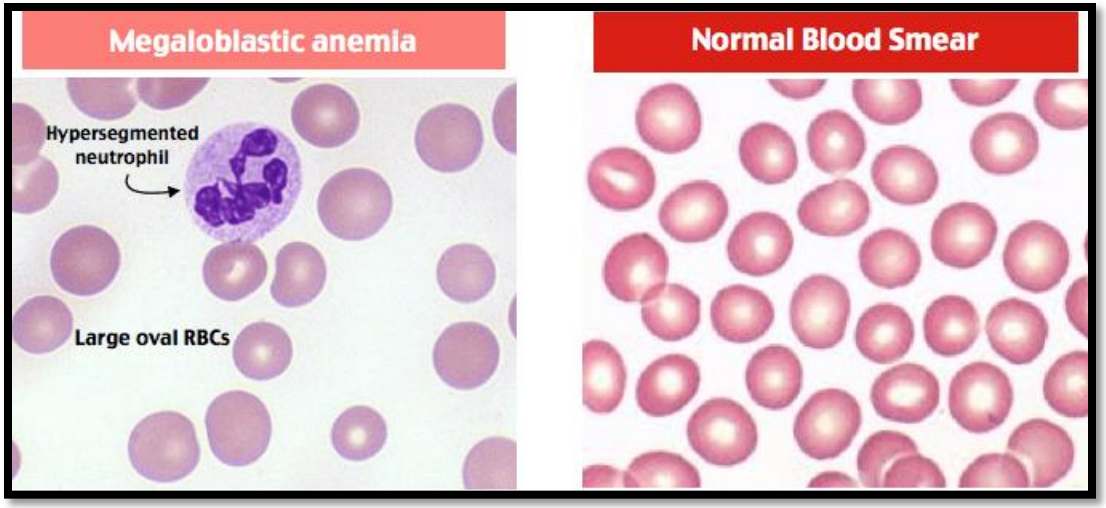


Nutritional anemia









Folate and anemia

•Folate deficiency could be occur when the body consume a large quantity like pregnancy and lactation, problem of intestine, drug interaction like methotrexate.

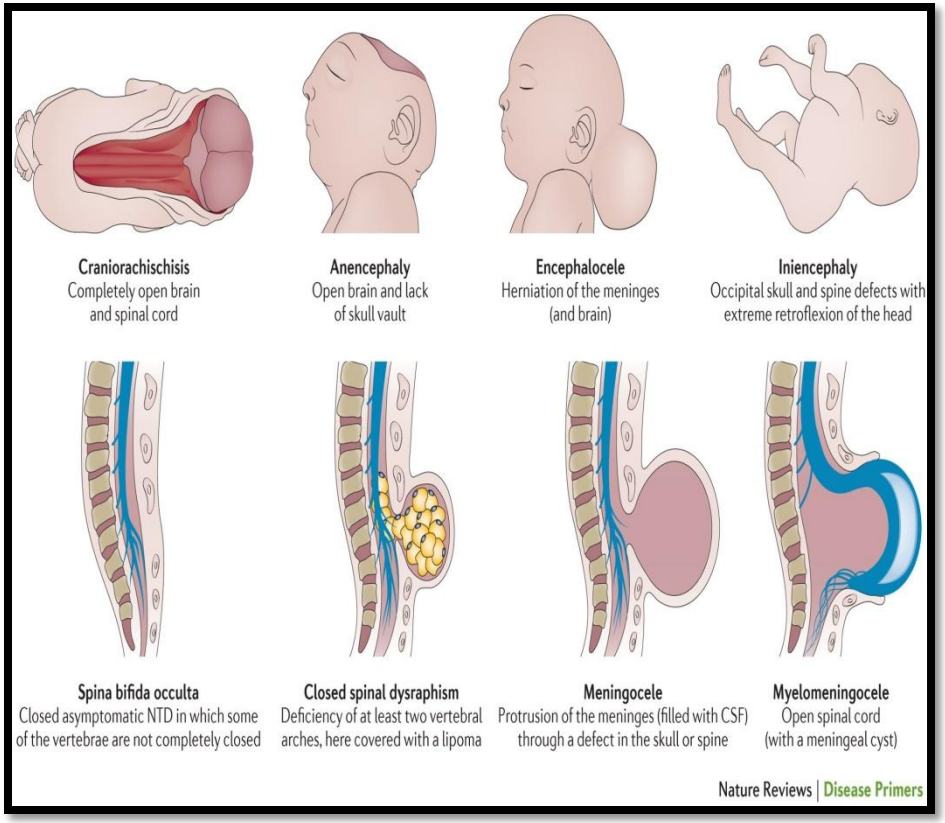
•The deficiency leads to megaloblastic anemia caused by decrease in the synthesis of thymidine and purine which impair the ability of the cells to make DNA and therefore divide.

•Vit B12 deficiency also cause megaloblastic anemia .

Neural tube defects NTD

•**Anencephaly** is the partial or complete absence of the baby's brain. Most of these babies die soon after birth.

•**Spina bifida** occurs when there is an opening of the spine. These babies need to have surgery soon after their birth to close the spine and prevent further damage.



Neural tube defects NTD

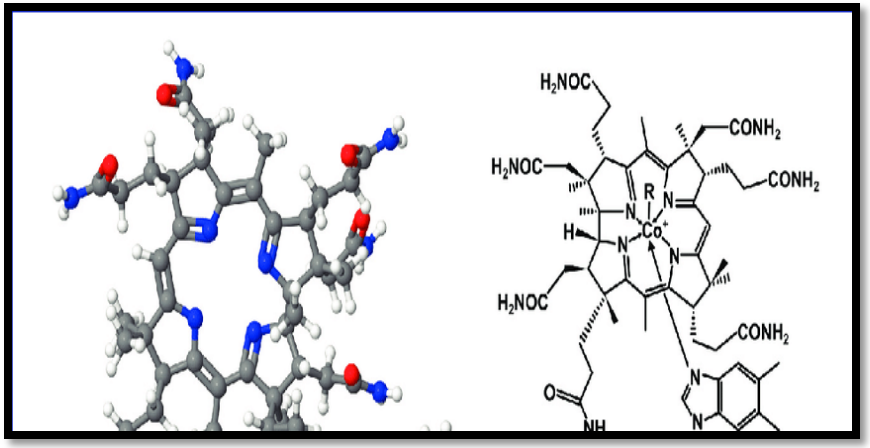
Babies with spina bifida suffering from
•lack feeling in their legs.
•problems with walking.
•problems with bowel and bladder control.
•learning problems.
•mental retardation.
In the United States about 2.500 babies are born each year with

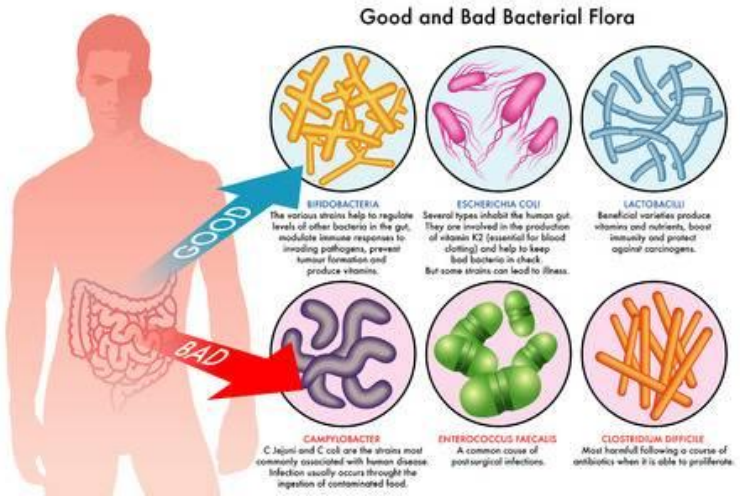
Risk factor
Inadequate uptake before and during pregnancy .

Recommendation
•all women with childbearing age should take 0.4 mg/day as supplement.
•Folate supplement should be at the time of conception and during the firs trimester of pregnancy.
•The supplement should not exceed 1mg/day.

Cobalamin Vit B12

- Is one of the most complex low-molecular-weight substances occurring in nature.
- The core of the molecule consists of a tetrapyrrol system (corrin), with cobalt as the central atom.
- It is abundant in liver, meat, eggs, and milk, but not in plant products.
- The vitamin is exclusively synthesized by microorganisms (Pseudomonas denitrificans, Bacillus megaterium, and Propionibacterium freudenreichii). Is not present in plant. Animals synthesis it by their bacterial flora and uptake it also by eating food derived from other animals.

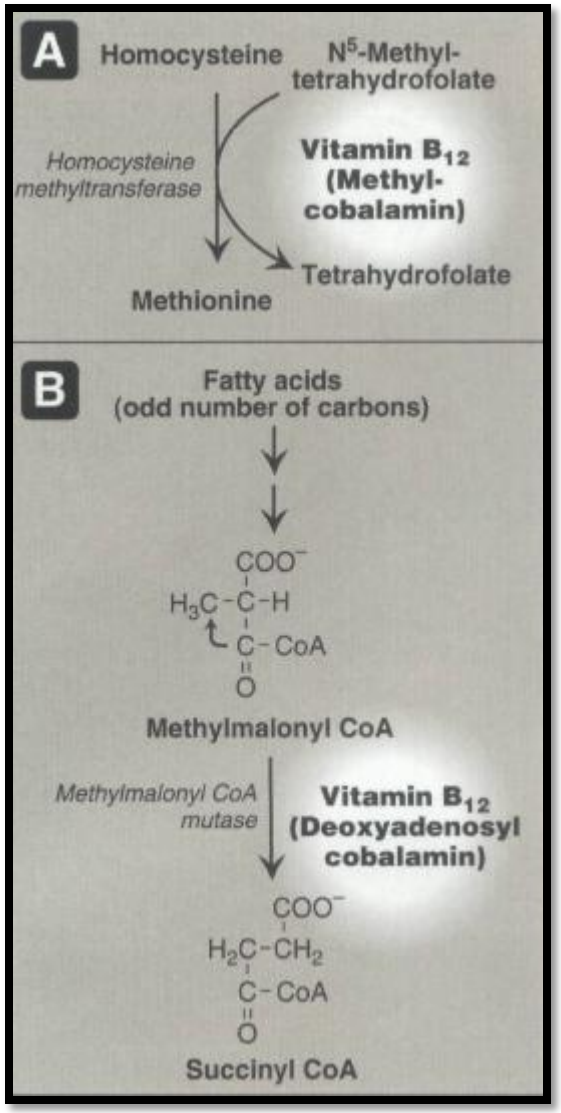




Vit B12 function

•Required for two essential enzymatic reaction.
- Synthesis of mythionine
- Isomerization of methylmalonyl CoA produced by degradation of some amino acids and fatty acids.

•In deficiency leads to abnormal fatty acids accumulation in the cell membrane like nervous system.

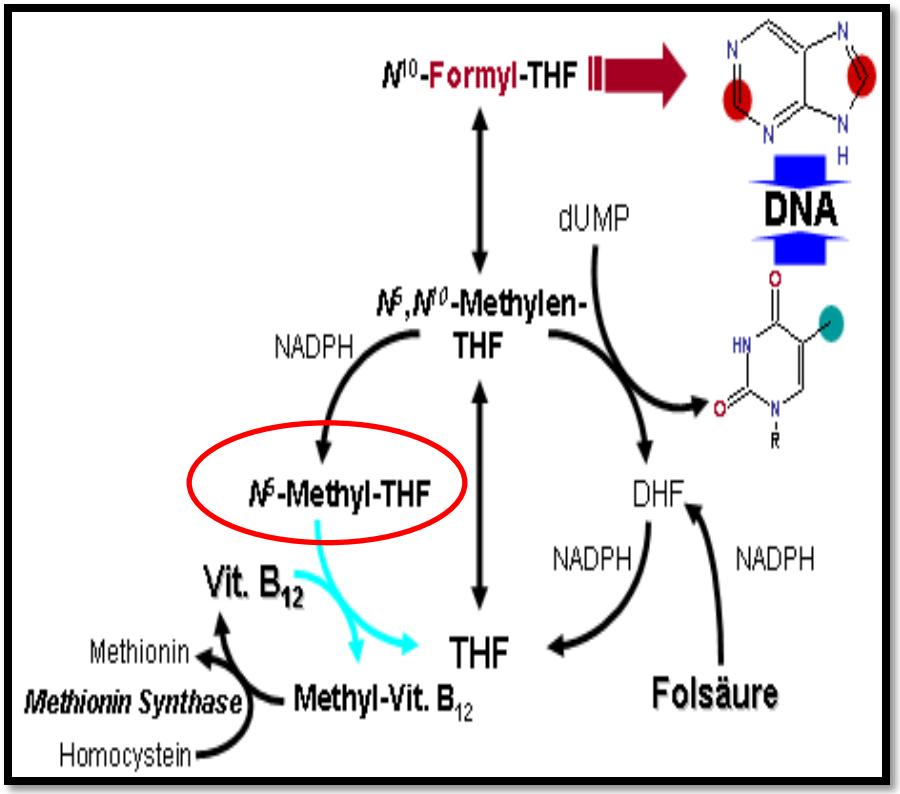


Vit B12 deficiency

•The N5-N10 methylen and N10 formyl two forms of THF are necessary for DNA replication .

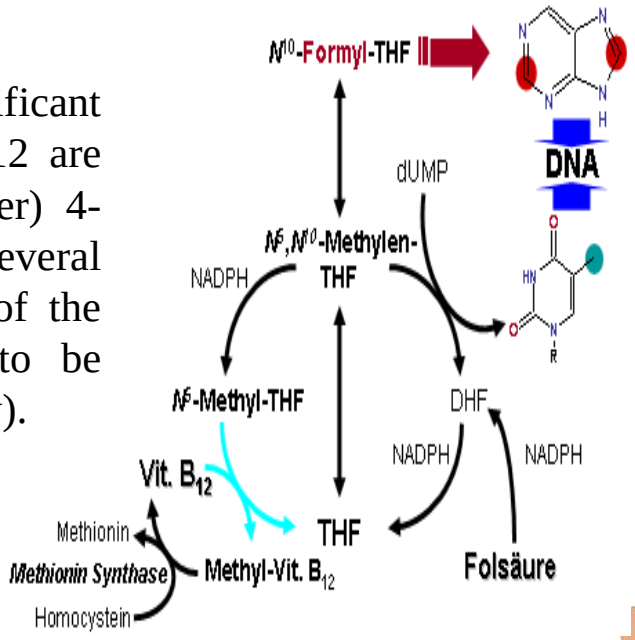
•In the vit B12 deficiency the N-methyl form accumulate.

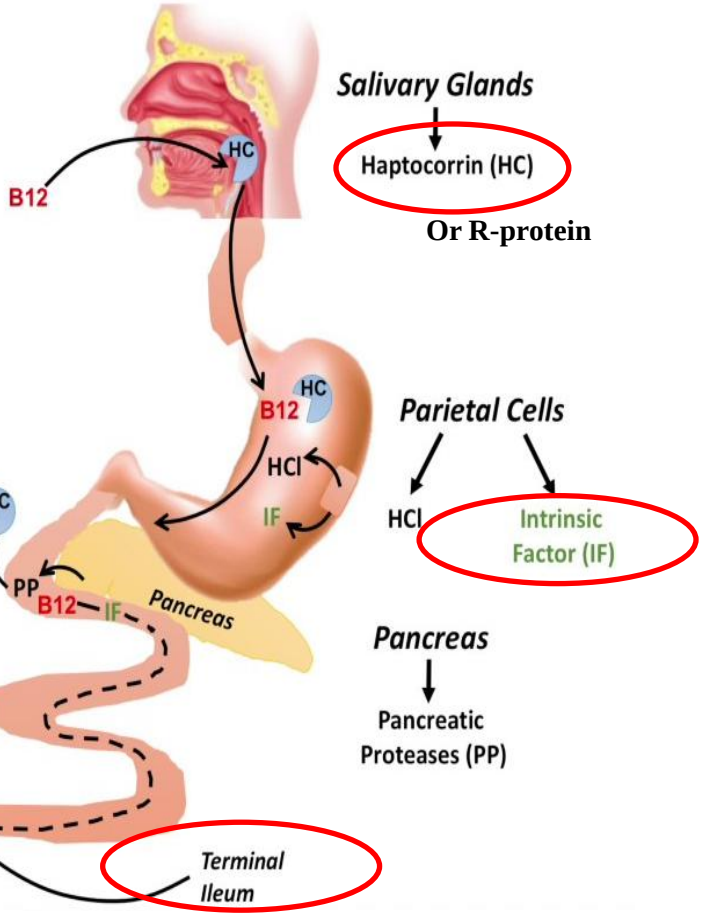
•The effect of deficiency appear in erythropoietic tissue of the bone morrow. Leads to megaloblasic anemia.



Vit B12 absorption

•There is a significant amount of the vit B12 are stored in the body (liver) 4-5 mg it could take a several years for symptoms of the vit B12 deficiency to be appeared.(gastrectomy).





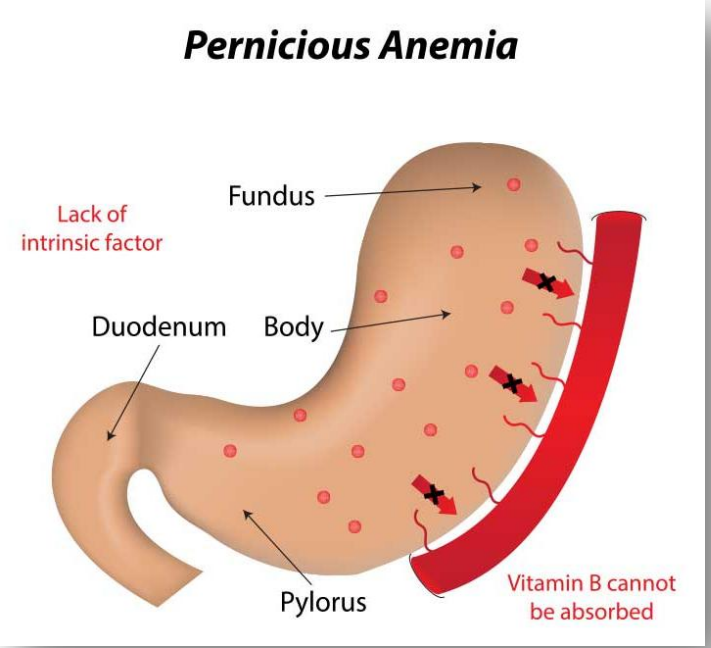
The absorbed vitamin B12 then binds to transcobalamin II where approximately 50% of the vitamin B12 will be delivered to the liver and the remainder will be delivered to other tissues

Pernicious anemia

•The disease is most commonly a result of an autoimmune destruction of the gastric parietal cells that are responsible for the synthesis of a glycoprotein called **intrinsic factor.**

•**The deficiency cause pernicious anemia and then**
later in the development of the disease they show neuropsychiatric symptoms.
•CNS symptoms may occur in the absence of anemia.

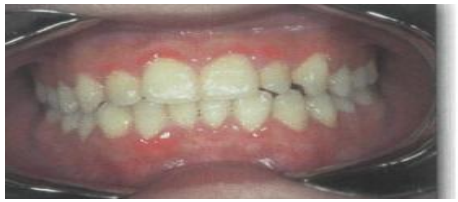
•megaloblastic anemia should not be treated with folic acid alone, but rather with a combination of folate and vitamin B12

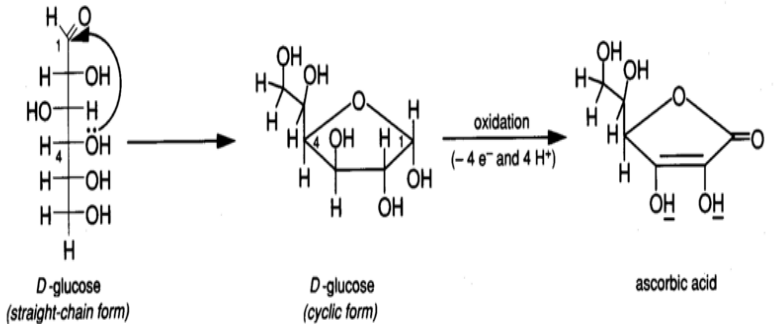


Ascorbic acid

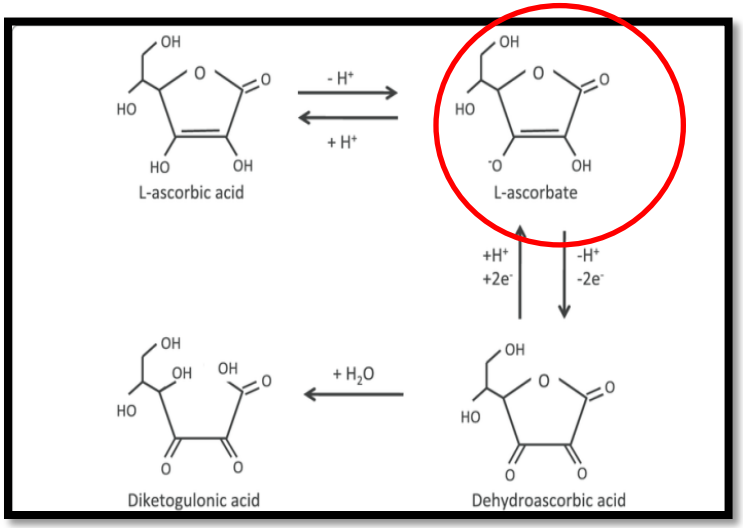
- **Vitamin C is L-ascorbic acid (chemically: 2-oxogulonolactone).** The two hydroxyl groups have acidic properties. By releasing a proton, ascorbic acid therefore turns into its anion, **ascorbate.**
- Lacking of L-gulonolactone oxidase in human and guinea pig prevent synthesis of this vitamin to convert the glucose into ascorbic acid.
- Food boiling destruct vit C.
- it is an reducing agent in the body involved in hydroxylation like collagen synthesis, tyrosine degradation, catecholamine synthesis, and bile acid biosynthesis.
- 60 mg per day is required .
- Symptoms of deficiency appear after a few months (scurvy, connective-tissue damage, bleeding, and tooth loss)

scurvy





Active form



Pyridoxine Vit B6

•Many forms of the Vit B6 exist

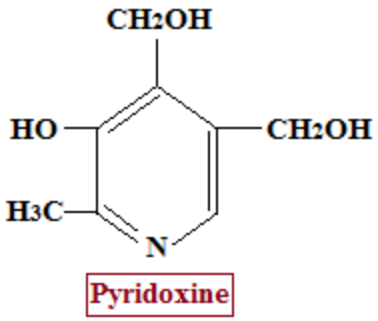
•pyridoxal phosphate is the active form all derivative of pyridine.

•Is the most important co enzyme in aminoacid metabolism (transaminations, decarboxylations, dehydrogenations)

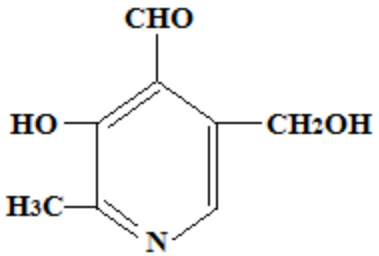
•**The deficiency is rare but** could occur:

- During tuberculosis treatment with isoniazid (isonicotinic acid hydrazide). By forming inactive derivatives.

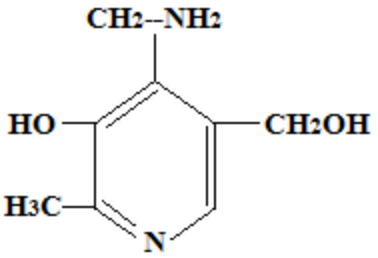
- New born fed formula low in vit B6.
- Women taking oral contraceptive and alcoholics.



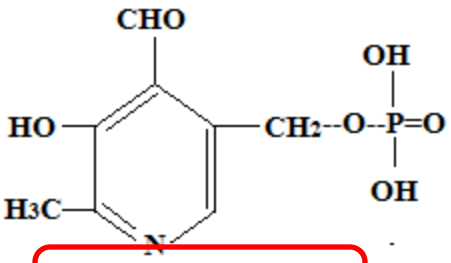
Pyridoxine



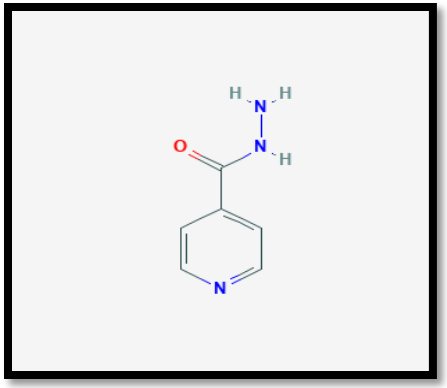
Pyridoxol



Pyridoxamin



Pyridoxal Phosphate



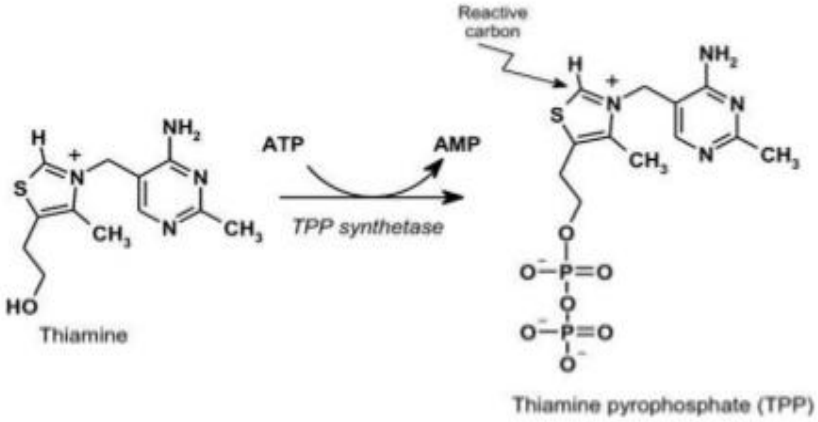
isoniazid

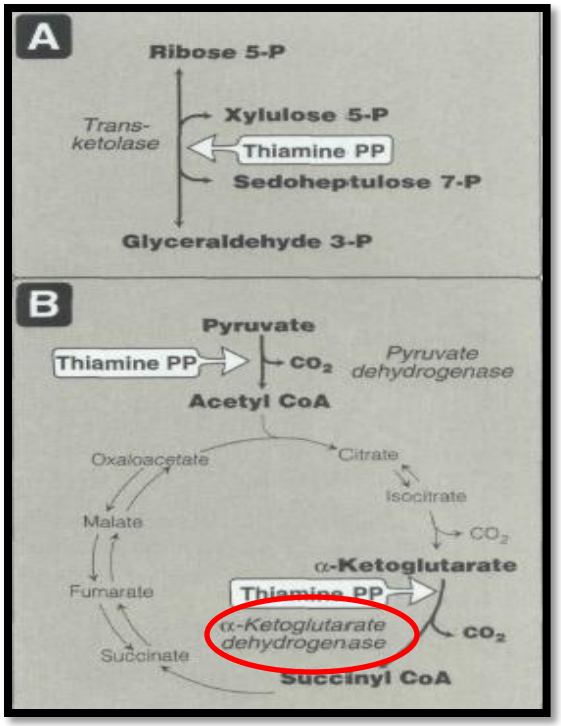
Thiamine Vit B1

•The first vitamin discovered.
•Thiamine perophosphate TPP is the biological active form. Form from thiamine by TPP synthetase .

•It is an coenzyme in the formation or degradation of of α-ketols by transketolase and in the oxidative decarboxylation of α-keto acids (α ketoglutrate). Which play an important role of the energy metabolism .

•The deficiency of this enzyme decrease ATP production and impaired cellular function.





Thiamine deficiency

•**Beriberi**

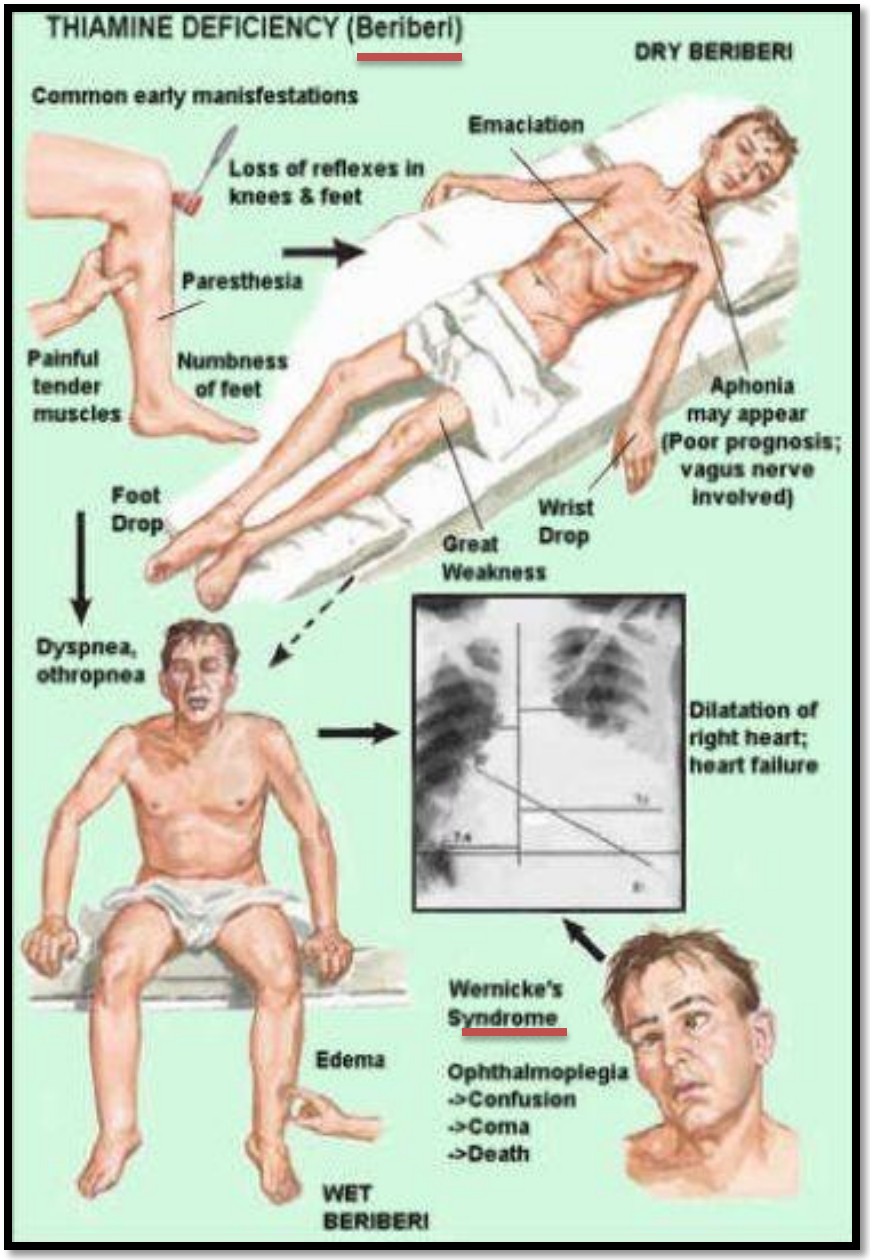
Occurs in sever cases of the deficiency, there is two types:

○ Dry Beriberi affects nervous system, resulting in numbness of the hands and feet, trouble moving the leg and pain.

○Wet Beriberi affects the cardiovascular system, leads to rapid heart rate, wake up short of breath, and swollen lower legs.

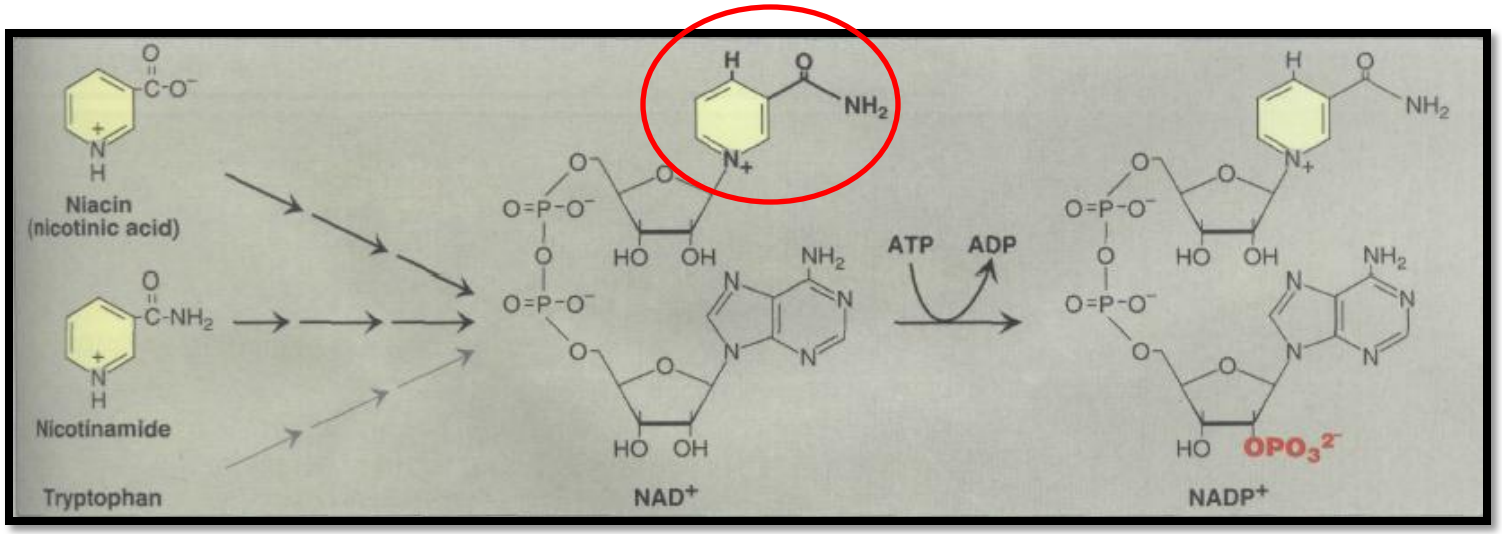
•**Wernicke-Korsakoff syndrome**

In extreme cases, characterized by confusion , loss of memory, loss of muscle coordination and involuntary eye movement.



Niacin or nicotinic acid

•It is a pyridine derivatives.
•NAD+ nicotinamide adenine dinucleotide and NADP are the biological coenzyme active forms.
• These both serve in energy and nutrient metabolism as carriers of hydride ions.
•The animal organism is able to convert tryptophan into nicotinate, but only with a poor yield.
•Vitamin deficiency therefore, only occurs when nicotinate, nicotinamide,
and tryptophan are all simultaneously are lacking in the diet.
•The deficiency manifests in the form of skin damage (pellagra), digestive disturbances, and depression.



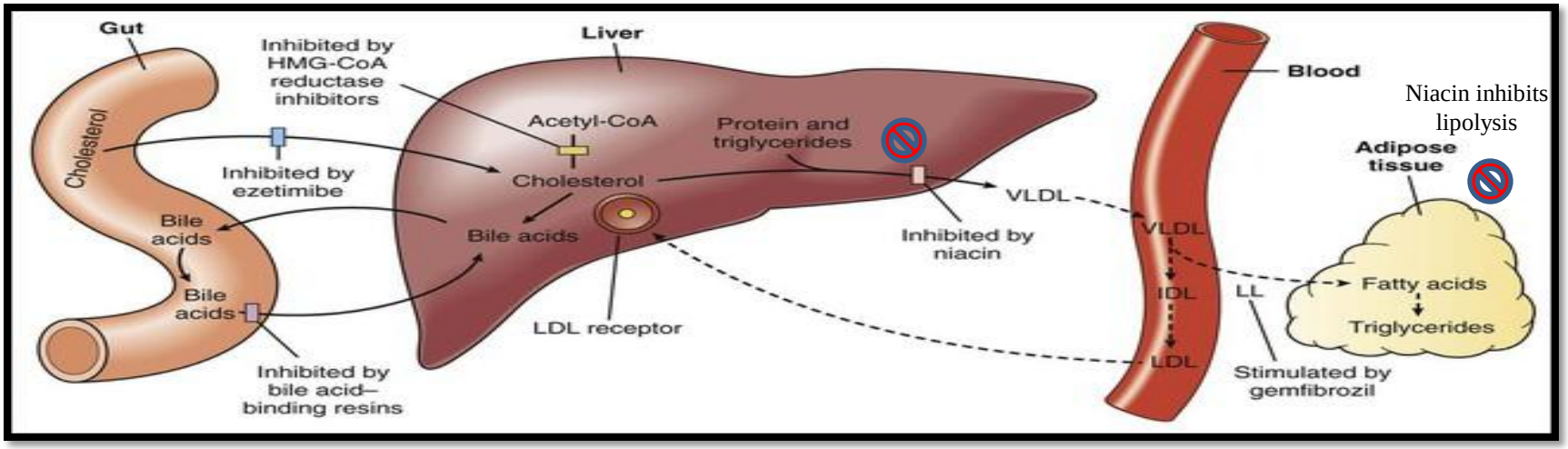
Uses of Niacin in hyperlipidemia

•Niacin is found in unrefined and enriched grains and cereal, milk, and lean meats, especially liver Niacin used at concentration1.5 mg per day for treatment of hyperlipidemia.

•By inhibiting lipolysis in adipose tissue which leads to decrease in the free circulating fatty acids being used by liver for triacylglycerol synthesis which required for VLDL synthesis.

•LDL is derived from VLDL.

•Plasma triacylglycerol in VLDL and cholesterol in VLDL and LDL are lowered which are elevated in hyperlipidemia IIb.



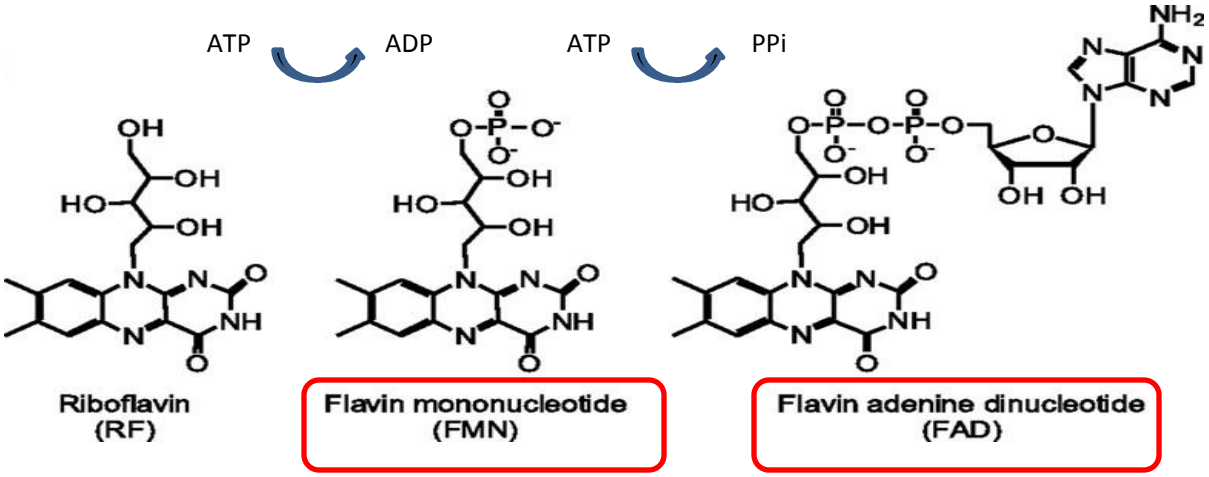
Riboflavin Vit B2

•The two biologically active forms are **flavin mononucleotide (FMN)** and **flavin adenine dinucleotide (FAD).**

• serves in the metabolism as a component of the redox coenzymes.

•As prosthetic groups, **FMN and FAD** are cofactors for various oxido reductases.

•No disease with deficiency



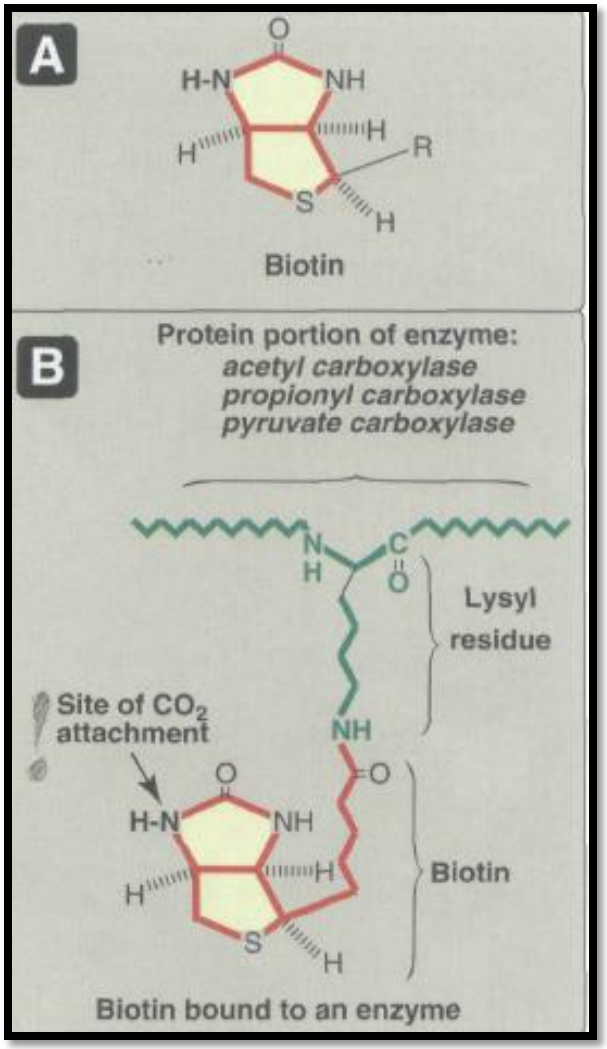
Biotin Vit H

•Biotin is a coenzyme in carboxylation reactions.

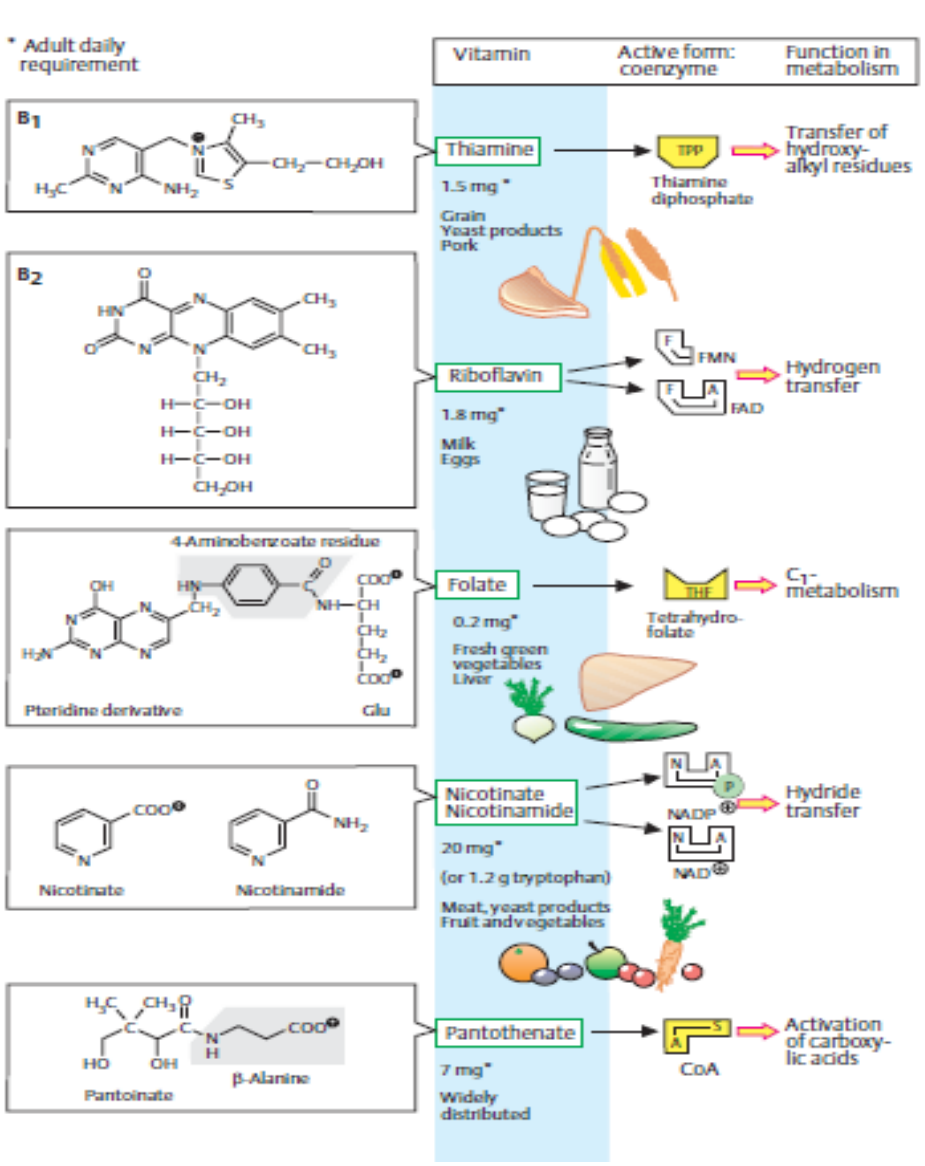
• Is present in liver, egg yolk, and other foods; it is also synthesized by the intestinal flora. In the body, biotin is covalently attached via a lysine side chain to enzymes that catalyze carboxylation reactions.**Which is biotin dependent enzyme like** pyruvate carboxylase and acetyl CoA carboxylase.

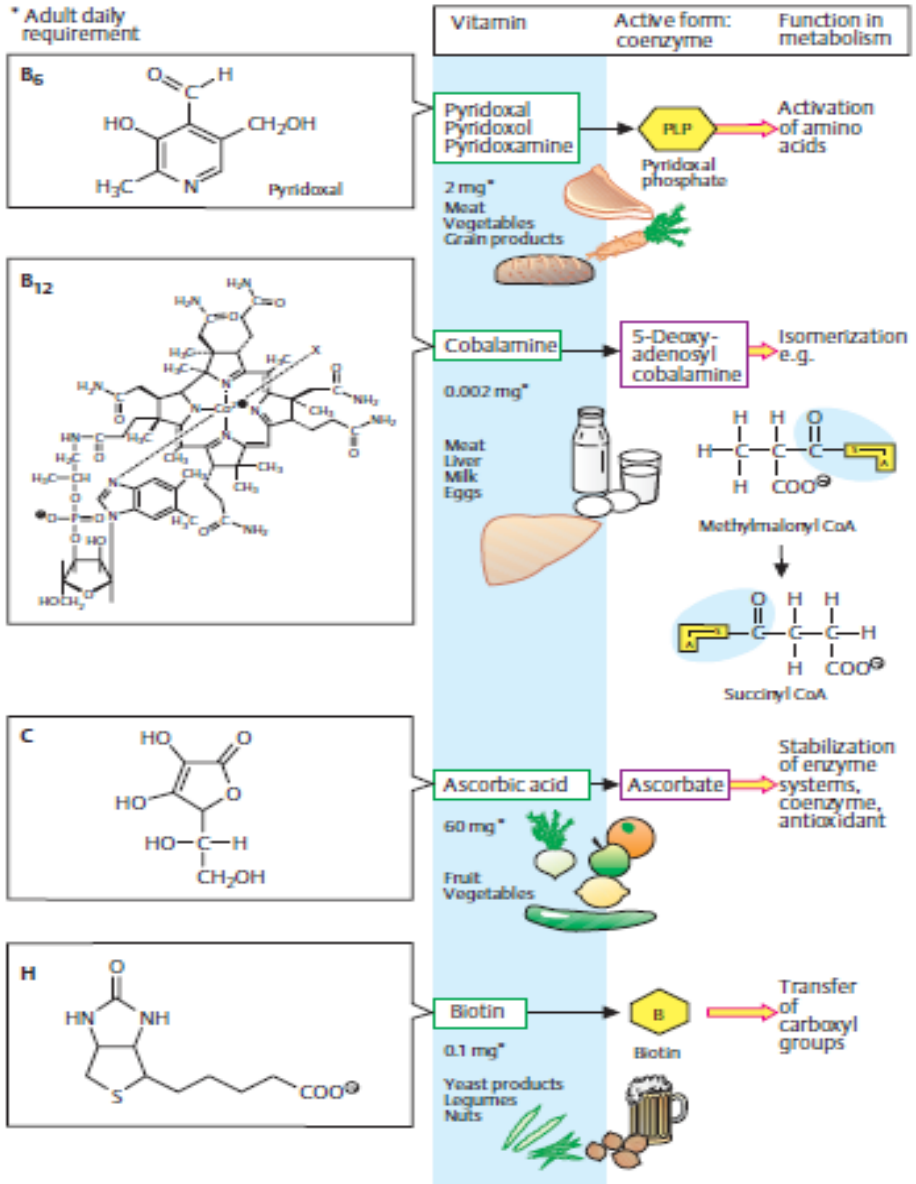
•Biotin binds with high affinity and specificity to avidin, a protein found in egg white. Since boiling denatures avidin, biotin deficiency only occurs when egg whites are eaten raw.

•CO2 binds, using up ATP, to one of the two N atoms of biotin, from which it is transferred to the acceptor.



Water soluble Vitamins





Lipid soluble vitamins

- **Vitamin A**
- **Vitamin D**
- **Vitamin k**
- **Vitamin E**

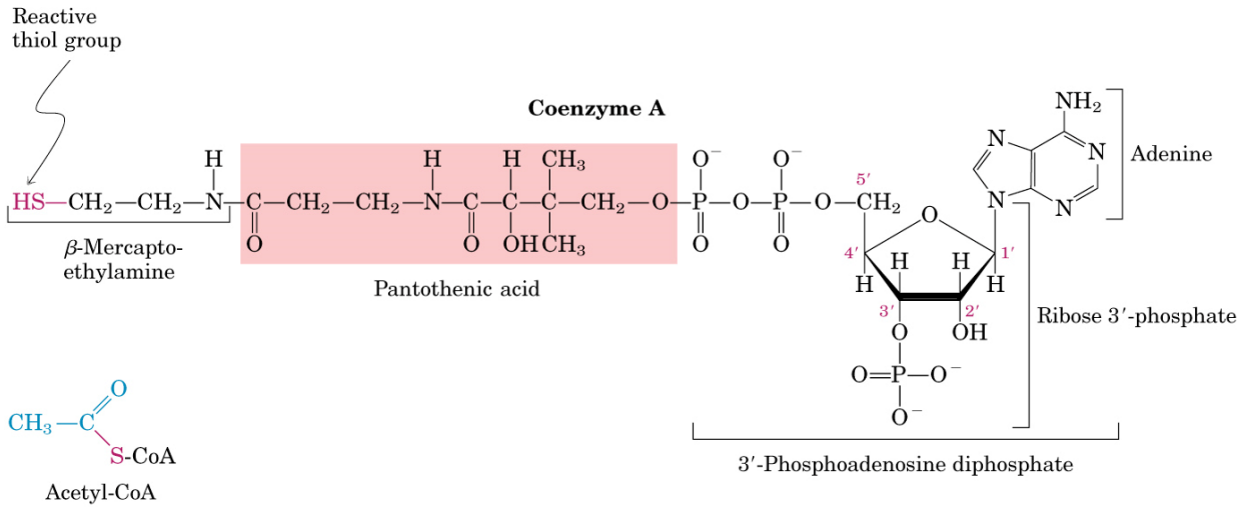
Pantothenic acid

•Is a precursor of Coenzyme A which transfer acyl group.

•The thiol group in this enzyme carry acyl compounds as activated acyl esters.

•Pantothenic acid is also component of succinyl CoA, fatty acyl CoA, and acetyl CoA.

•Enzyme deficiency is rare because its wide spread availability in the food.



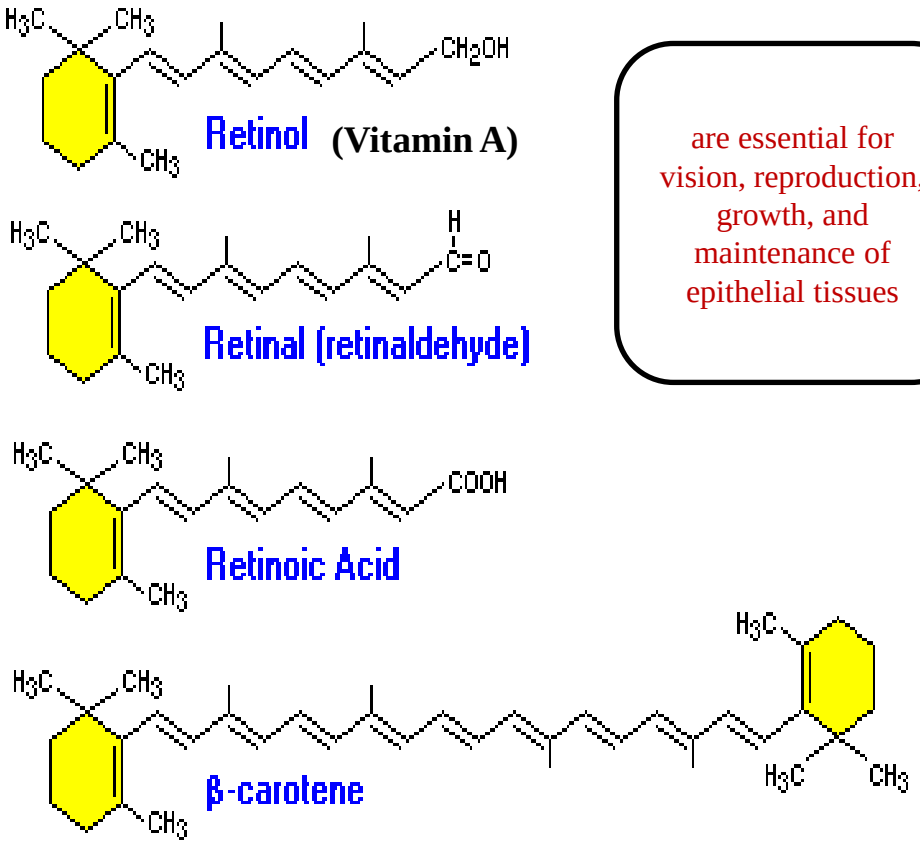
Vitamin A

•**Retinol** is a precursor of the retinoid which is include retinal and retinoic acid which present in the meat. Could be synthesized by cleavage from pro vitamin ß carotene which present in vegetables like carrots.

•**Retinal** involved in visual process, a pigment of chromoprotein rhodopsin.

•**Retinoic** like a steriod hormone involved in gene transcription in the cell nucelus.

•The vitamin deficiency cause visual impairment, night blindness and growth disturbances

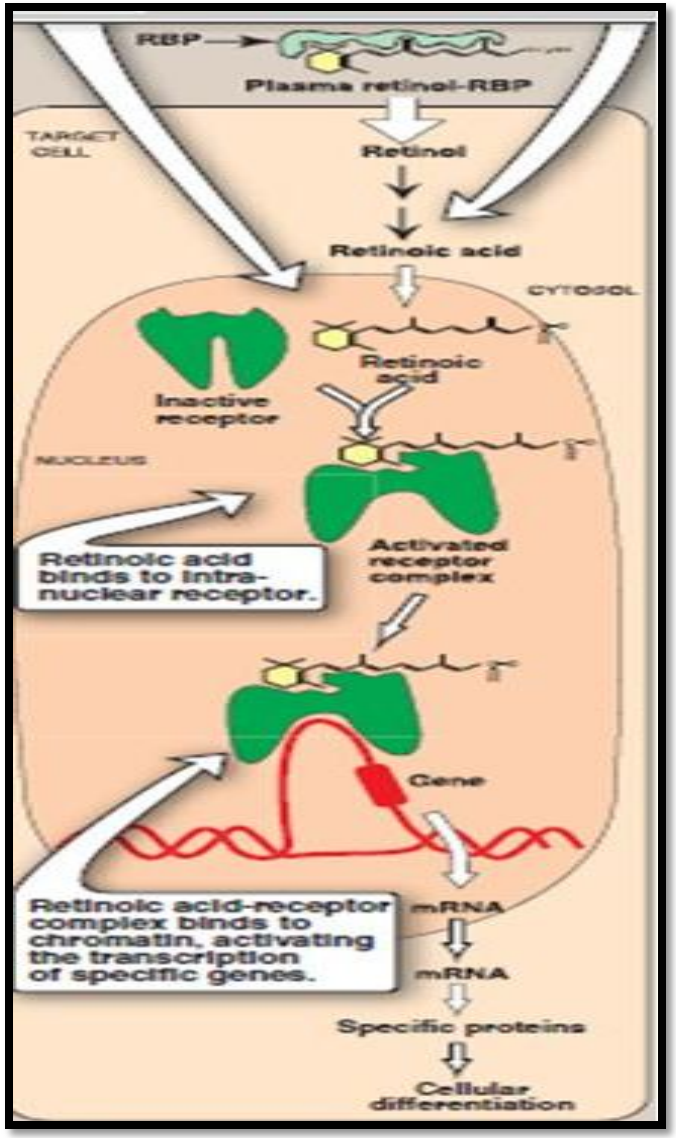


are essential for vision, reproduction, growth, and maintenance of epithelial tissues

Vitamin A mechanism of action

•**Retinol** is oxidized to retinoic acid. The movement from cytosol to nucleus is guided by cellular retinol binding protein and cellular retinoic acid binding protein.

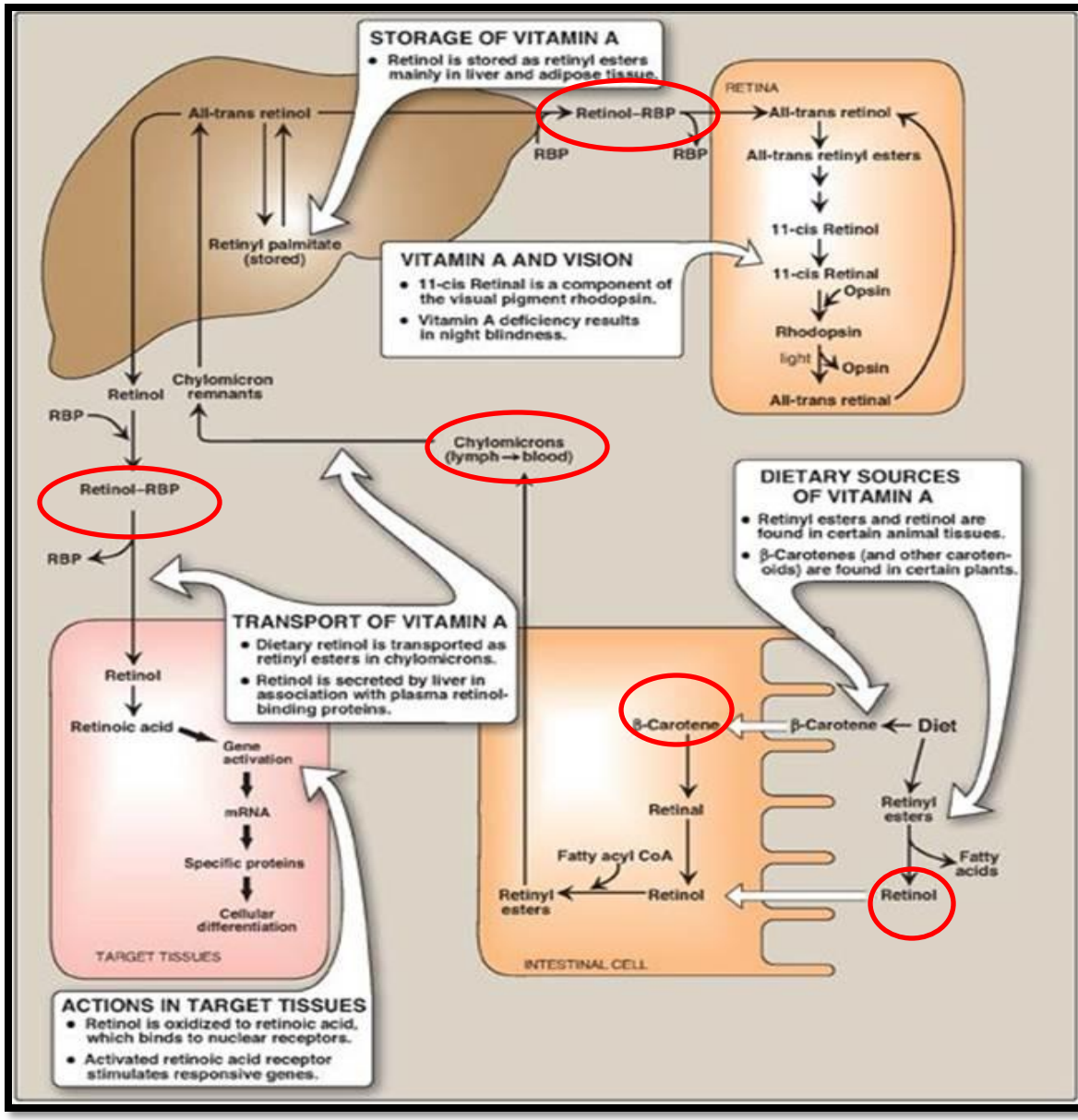
•Can control the expression of the keratin gene in most epithelial tissues of the body.



Vitamin (A) absorption

•**Transport to the liver:** after hydrolyzation of the retinol ester in the intestinal mucosa to retinol and free fatty acid. Then the retinol reesterfied and transferred by lymph and blood as chylomicrons.

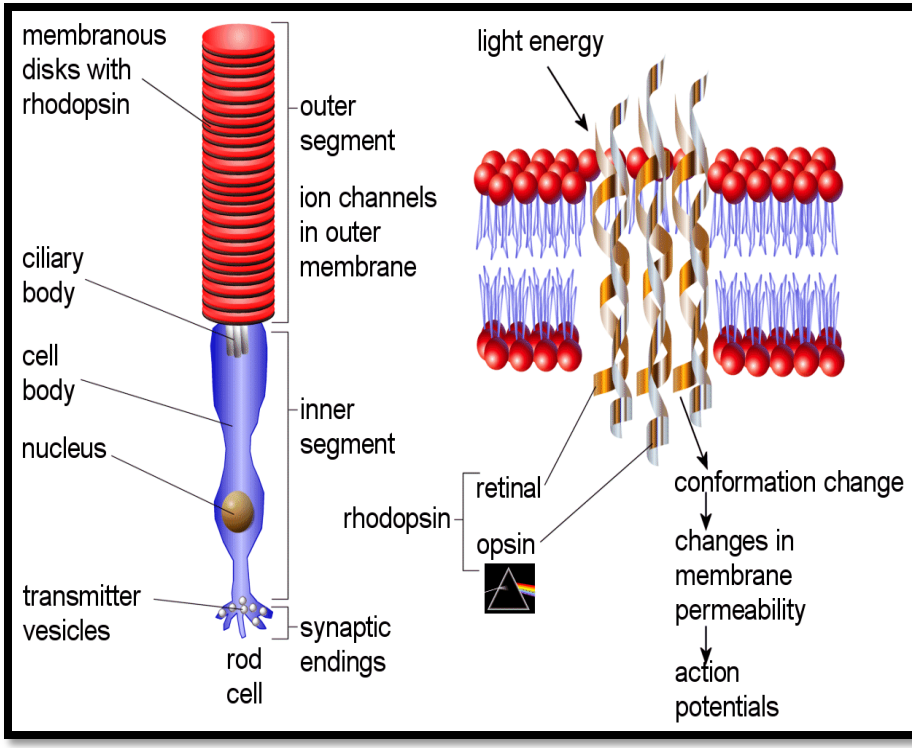
•**Release from the liver:** the ester retinol in the chylomicron stored in the liver release retinol as RBP-retinol to arrive to the active site in the tissue by binding to the retinol receptor.

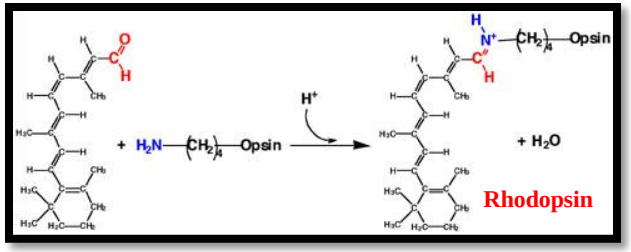


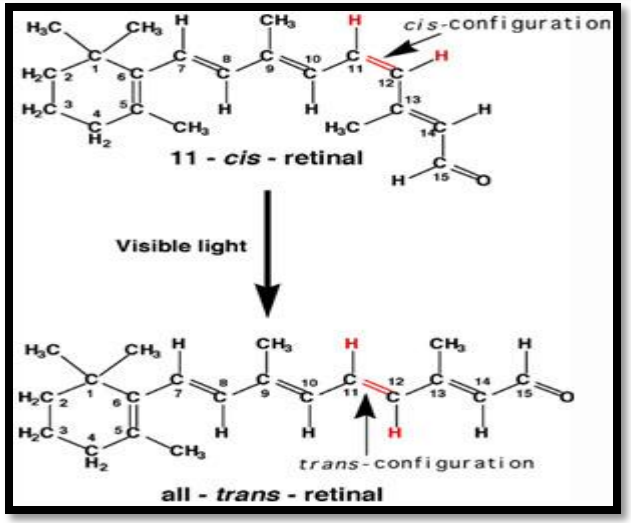
Vitamin (A) functions

•**Visual cycle:** the rhodopsin is a 11 cis retinal bind with opsin., When rhodopsin is exposed to light, a series of photochemical occurs, which results in the bleaching of the visual pigment and release of all trans retinal and opsin, This process triggers a nerve impulse that is transmitted by the optic nerve to the brain .

•**Reproduction:** retinol, retinal supporting spermatogenesis in male and prevent fetal resorption in female.



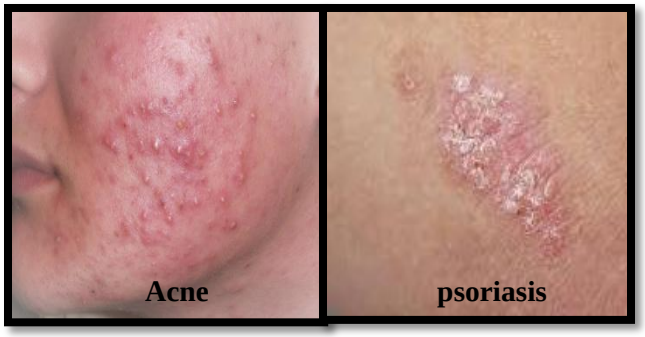




Vitamin (A) deficiency

•**Dietary deficiency:** leads to growth problem, CNS development, decrease appetite, night blindness, prolonged deficiency leads to xeropthalmia (dryness of the conjunctiva and cornea. If untreated, xerophthalmia results in corneal ulceration and, ultimately, in blindness.

•**Acne and psoriasis:** retinol derivatives like retinoic acid use to treat this dermatological problem. Like tretinoin which is a trans retinoic acid and used topical with antibiotic to treat acne mild cases, while in sever cases the isotretinoin (13 cis retinoic acid) used orally.



Vitamin (A) toxicity

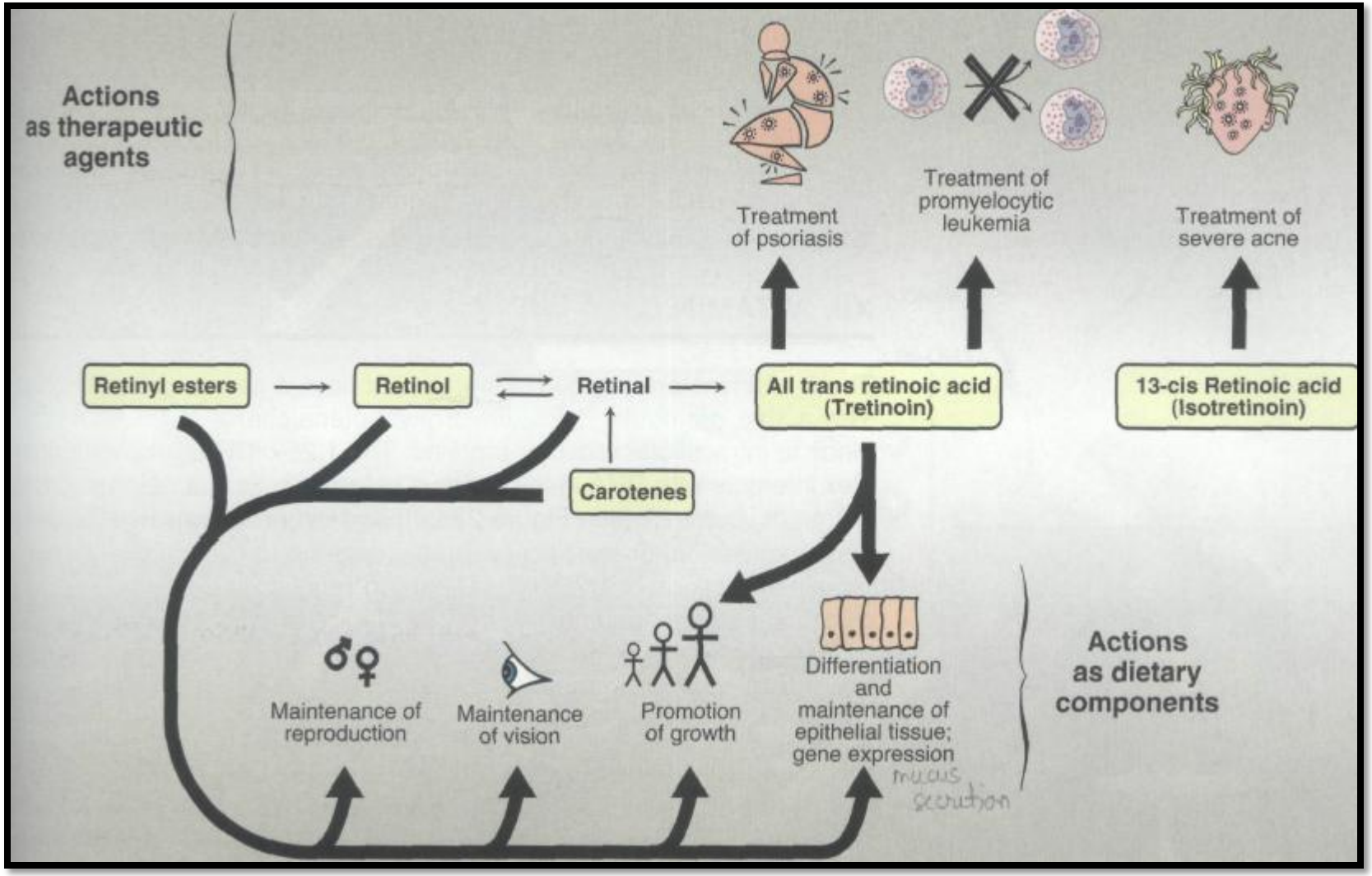
• **the daily requirement (100 ER for male and 800 ER for female).**

1 µg Retinol Equivalent	=	1 µg of all-trans retinol
	=	6 µg all-trans ß-carotene
	=	12 µg of a-carotene, ß-cryptoxanthin and other provitamin A carotenoids
1 International Unit (IU) retinol	=	0.3 µg Retinol Equivalents

•Over consumption of the retinol over 7.5 mg /day leads to pruritic dray skin, enlarged and cirrhotic liver arise the intracellular pressure of the cells in the nervous system. Congenital malformation in the fetus of the pregnant women.

•Isotretinoin is contraindicated during pregnancy, prolonged use leads to hyperlipidemia and increased the ratio LDL/HDL which increase the risk of cardiovascular disease.

Actions of retinoids



Vit D

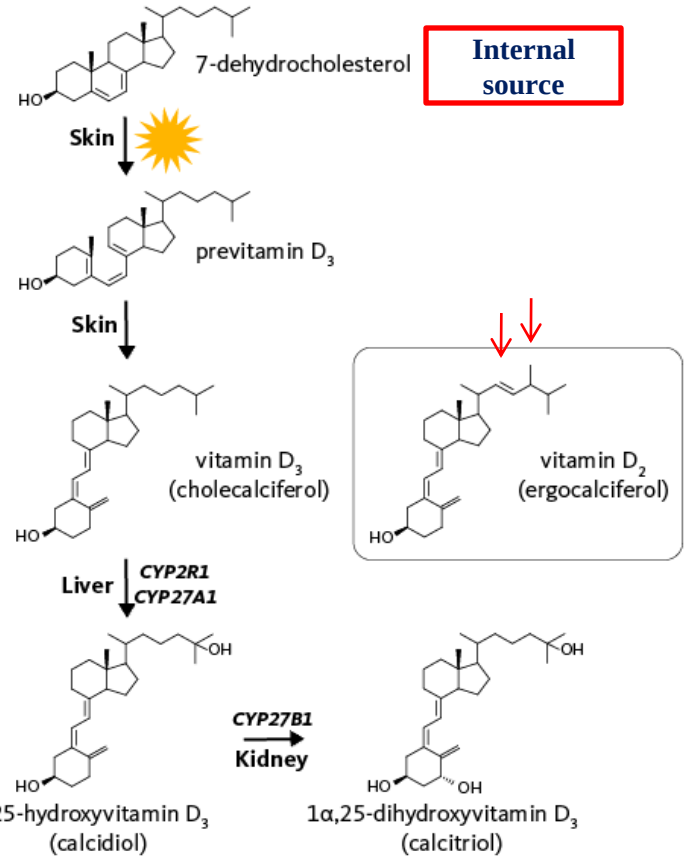
• Is a group of sterols that have a hormone like function, the active molecule is 1,25-dihydroxycholecalciferol (1.25 di OH D3).

• Have an intracellular receptor form complex interact with DNA of the target cell to stimulate or inhibit the gene transcription.

•Main function of this vitamin is to regulate the calcium and phosphorous plasma levels.

•**External source** from a diet as a Ergocalciferol (Vit D2) found in plants and cholecalceferol (vit D3) found in animal tissue.

•**Internal source** is 7-Dehydrocholesterol which is intermediate in the cholesterol synthesis. After UV light exposure in the dermis and epidermis convert to cholecalciferol vit D3.

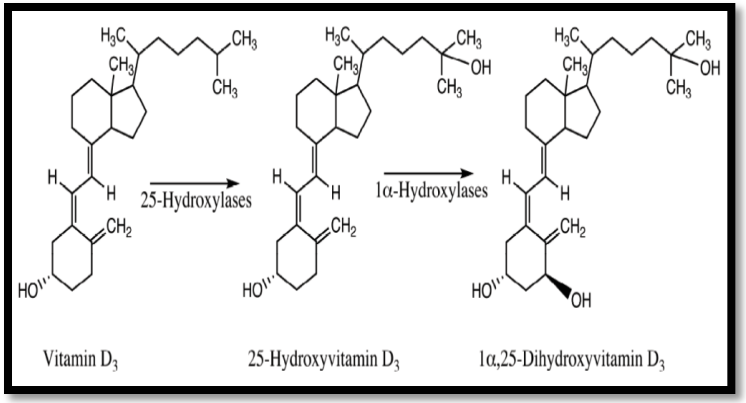


Vitamin D synthesis. Previtamin D_3 is synthesized in the upper layers of the skin from 7-dehydrocholesterol by the action of ultraviolet light (UVB). A nonenzymatic conversion of previtamin D_3 into vitamin D_3 (cholecalciferol) then occurs in lower layers of the skin. Vitamin D_3 is quickly transported to adipose tissue for storage or liver for activation. In liver cells, several cytochrome P450 (CYP) enzymes can catalyze the 25-hydroxylation of vitamin D_3 (or plant-based vitamin D_2 or ergocalciferol). The product of this step, 25-hydroxyvitamin D_3, is converted into the active form of vitamin D_3, 1α,25-dihydroxyvitamin D, in a reaction catalyzed by CYP27B1. This 1α-hydroxylation takes place primarily in the kidney.

Vit D metabolism

• **Active form formation 1.25 di OH cholecalciferol**: the vit D3, D2 are not active form converted in the body to the active one by two hydroxylation reaction first in the liver at 25 position to form 25 hydroxycholeclciferol the major storage and the major plasma form then another hydroxylation reaction in the Kidney to form 1.25 di OH cholecalciferol the active form of the vit D3

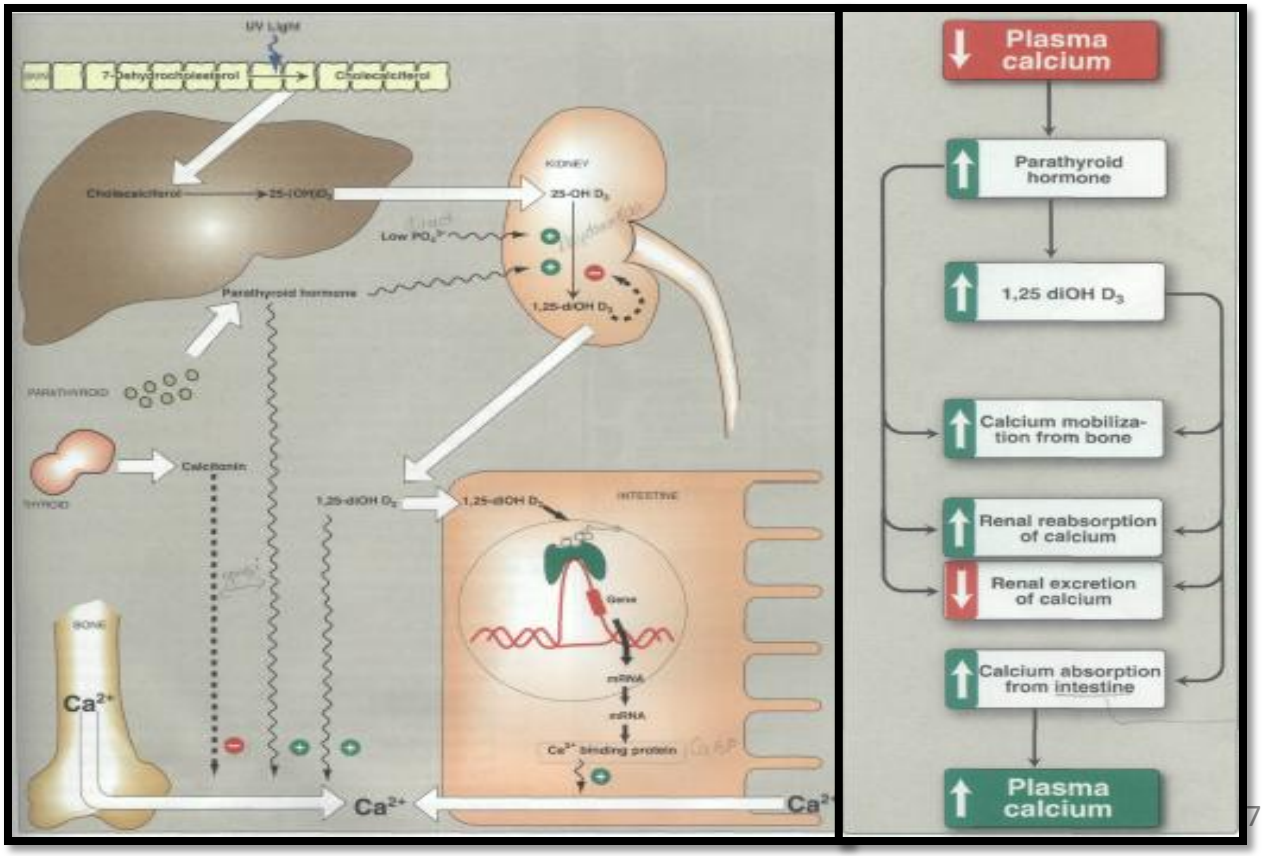
•Cytochromes mediate hydroxylation reactions in the liver and kidney.



Vit D regulation

•The 25 hydroxycholecalciferol hydroxylation is increased by low plasma phosphate or indirectly by the low plasma calcium which stimulate the release of the PTH.

•Hypocalcemia increase the 1.25 di OH cholecalciferol plasma levels



Vit D function

- **Effect on the intestine:** the active from of the Vit D3 (1.25 di OH cholecalciferol) trigger calcium absorption from the intestine by binding to the cytosolic receptor in the intestinal cells then from a complex moves the nucleus and bind to the DNA and trigger synthesis of calcium binding protein.

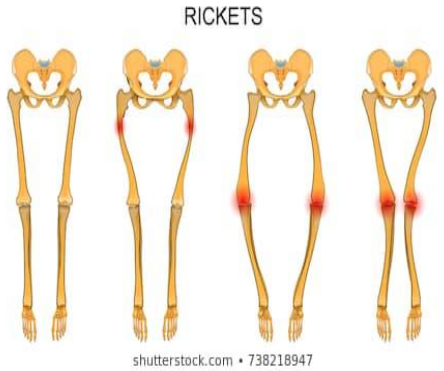
- **Effect on the bone:** the active form of the vit D3 just activate the mobilization of calcium and phosphate from bone by a process that requires protein synthesis and the presence of PTH to stabilize plasma level.

- **In addition**, calcitriol is involved in insulin secretion, synthesis and secretion of parathyroid and thyroid hormones, inhibition of production of interleukin by activated T lymphocytes and of immunoglobulin by activated B lymphocytes, differentiation of monocyte precursor cells, and modulation of cell proliferation

- Present naturally in liver, milk fatty fish the daily requirements are 5mg of cholecalciferol or 1000 IU of vit D.

Vit D clinical indication

- **Rickets as** a results of Vit D deficiency leads to demineralization of the bone causes rickets in child and osteomalacia in adults which increase is susceptibility to fractions.

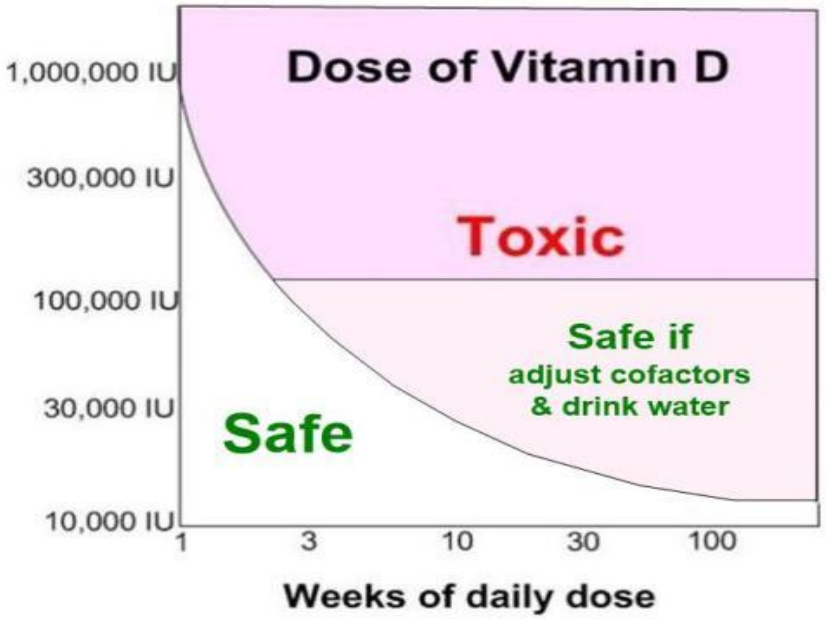


- **Renal rickets** in case of renal failure.

- **Hypoparathyriodisim** in case of lack of PTH which leads to hypocalcemia and hyperphosphatemia, treatment with any form of Vit D with PTH.

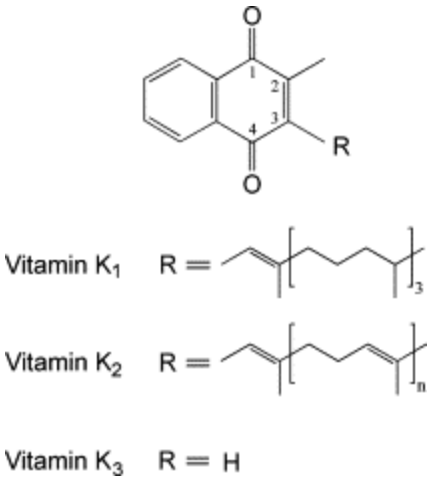
Vit D toxicity

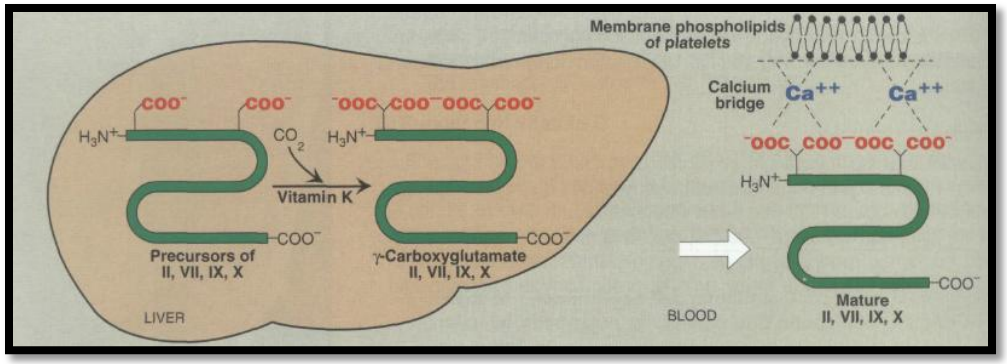
- If the amount of the vit D exceed 100.000 IU per week stored in the body and slowly being metabolized leads to toxic symptoms like nausea, lose of appetite, thirst, stupor. Increase calcium absorption and bone resorption could have a dangerous consequences like hypercalcimia and deposition of calcium in the kidney and arteries.

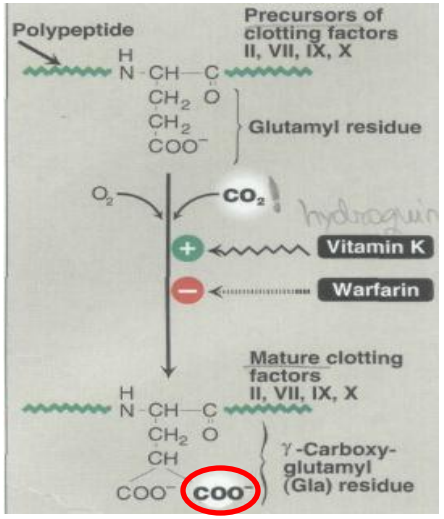


Vit K functions

- **Vit K is** a coenzyme in carboxylation reaction involved in post translation modification of the clot factors, exists in two forms vit K1 (phylloquinone) presents in plants and vit K2 (menaquinone) by intestinal bacterial flora and Vit K3 (menadione) is the synthetic form. The body store small amount of this vitamin that are rapidly depleted without regular dietary intake maybe for this the body recycles it through a process called the vitamin K-epoxide cycle.







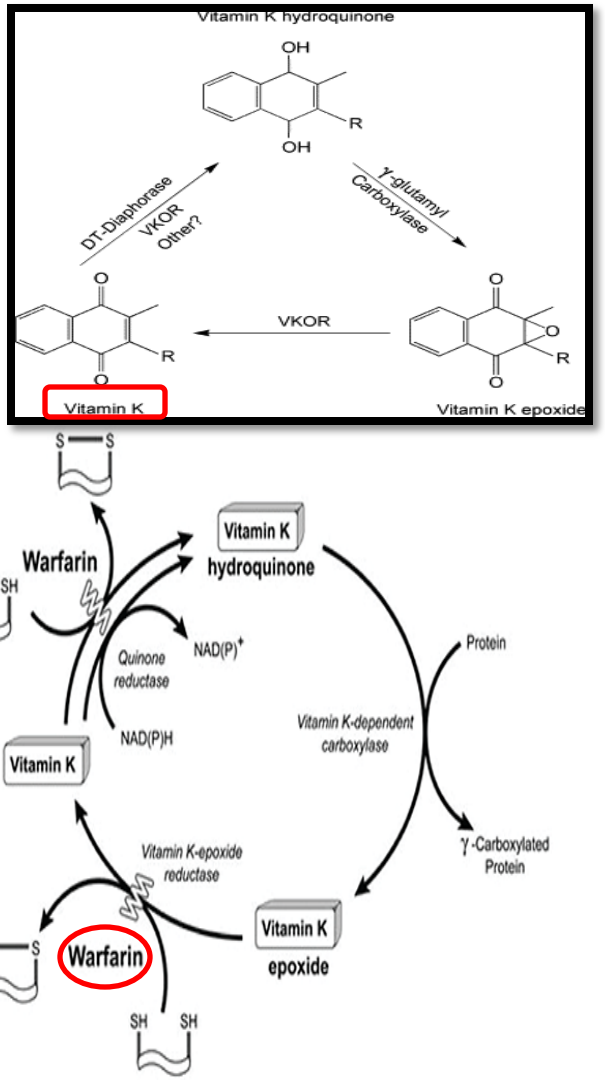
Vit K functions

- **Carboxylation of glutamic acid residue** in the prothrombine and blood clotting factors.
- II, VII, IX, and X. Which synthesized in the liver as inactive precursors. The results is active forms containing γ carboxyglutamate in presence of O2 and CO2 and the hydroquinone form of the vit K.
- This carboxylation reaction is inhibited by dicumarol natural anticoagulant present in spoiled sweet clover. And warfarine an vit K synthetic analogue.

Vit K cycle

- The vitamin K cycle allows a small amount of vitamin K to be reused many times for protein carboxylation, thus decreasing the dietary requirement. Briefly, vitamin K hydroquinone (reduced form) is oxidized to vitamin K epoxide (oxidized form). The reaction enables γ-glutamylcarboxylase to carboxylate selective glutamic acid residues on vitamin K-dependent proteins. The recycling of vitamin K epoxide (oxidized form) to hydroquinone (reduced form) is carried out by two reactions that reduce vitamin K epoxide (KO) to vitamin K quinone and then to vitamin K hydroquinone.

- the enzyme vitamin K oxidoreductase (VKOR) catalyzes the reduction of KO to vitamin K quinone and may be involved as well as another yet-to-defined reductase in the production of KH_2 from vitamin K quinone . The anticoagulant drug warfarin acts as a vitamin K antagonist by inhibiting VKOR activity, hence preventing vitamin K recyclin.



The reduced form of vitamin K (hydroquinone) donates a pair of electrons to the vitamin K-dependent carboxylase (known as γ-glutamyl carboxylase), which carboxylates glutamic acid residues in specific vitamin K-dependent proteins. The resultant oxidized form of vitamin K (epoxide) is converted back to hydroquinone in a two-step reaction. The first step, which converts vitamin K epoxide to vitamin K, is catalyzed by vitamin K-epoxide reductase; the second step is catalyzed by either vitamin K-epoxide reductase or most likely by another yet-to-defined reductase. This pathway is inhibited by the vitamin K antagonist and anticoagulant drug, warfarin. The reduction of vitamin K to hydroquinone is also possibly catalyzed by a NAD(P)H-dependent reductase that is resistant to warfarin.

Basem Battah, Pharm, Msc, PhD

Vit K clinical indications

•**Vit K deficiency** is rare because the body take sufficient amount from the vitamin synthesized by the intestinal bacteria and by the diet, but antibiotic could decrease the bacteria population and leads to hypoprothrombinemia like second generation cephalosporines (cefoperazone), could be supplemented with Vit K.

•**Newborn vit K deficiency** the intestine of the newborns is not able to produce Vit K because of lacking of some intestinal bacteria so it is recommended to give all newborns an intramuscular dose of vit K to avoid haemorrhagic disease.

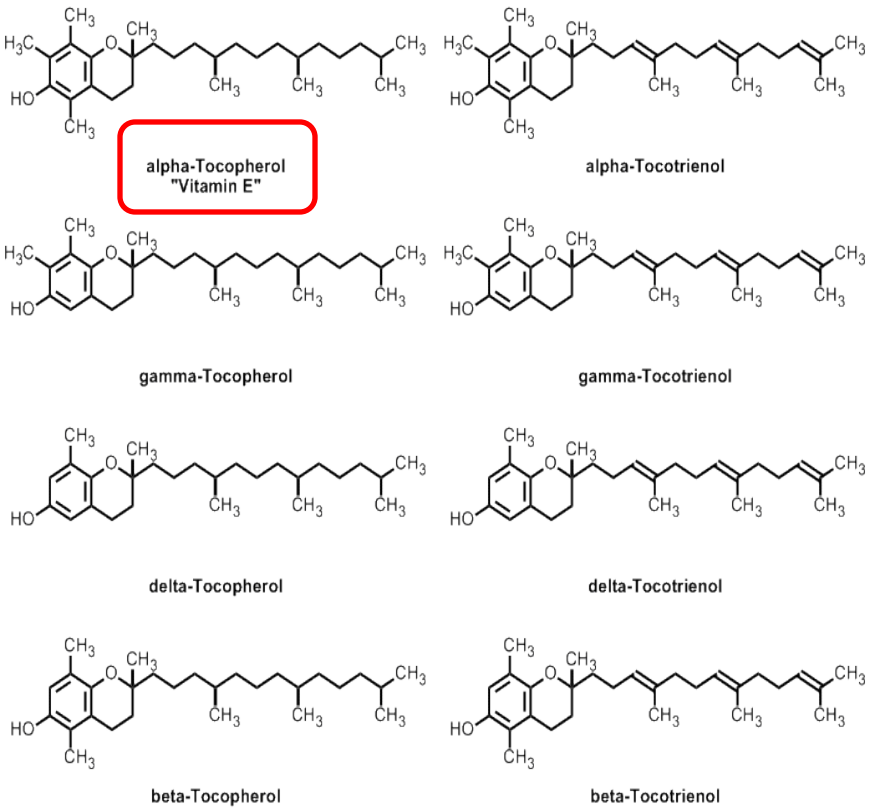
Daily requirement and toxicity

•Present in cabbage, cauliflower, spinach, egg yolk, and liver also synthesized by the bacteria gut, 70-140 mg/day could be sufficient.

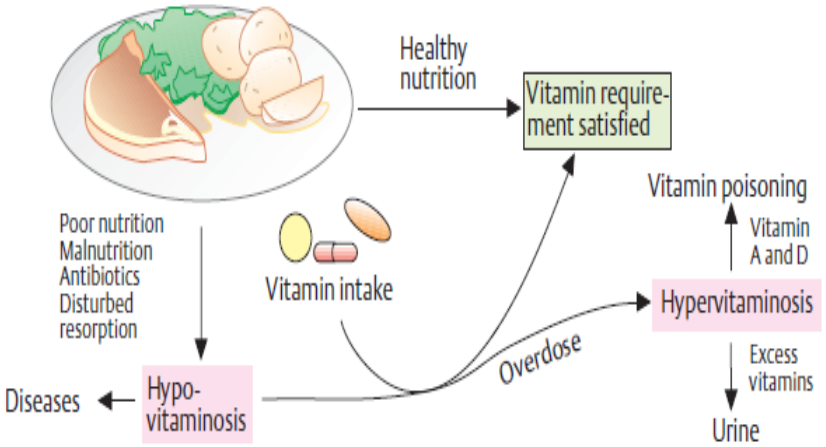
•Overdose could produce a haemolytic anaemia and jaundice in the infant, due to toxic effects on the membrane of red blood cells.

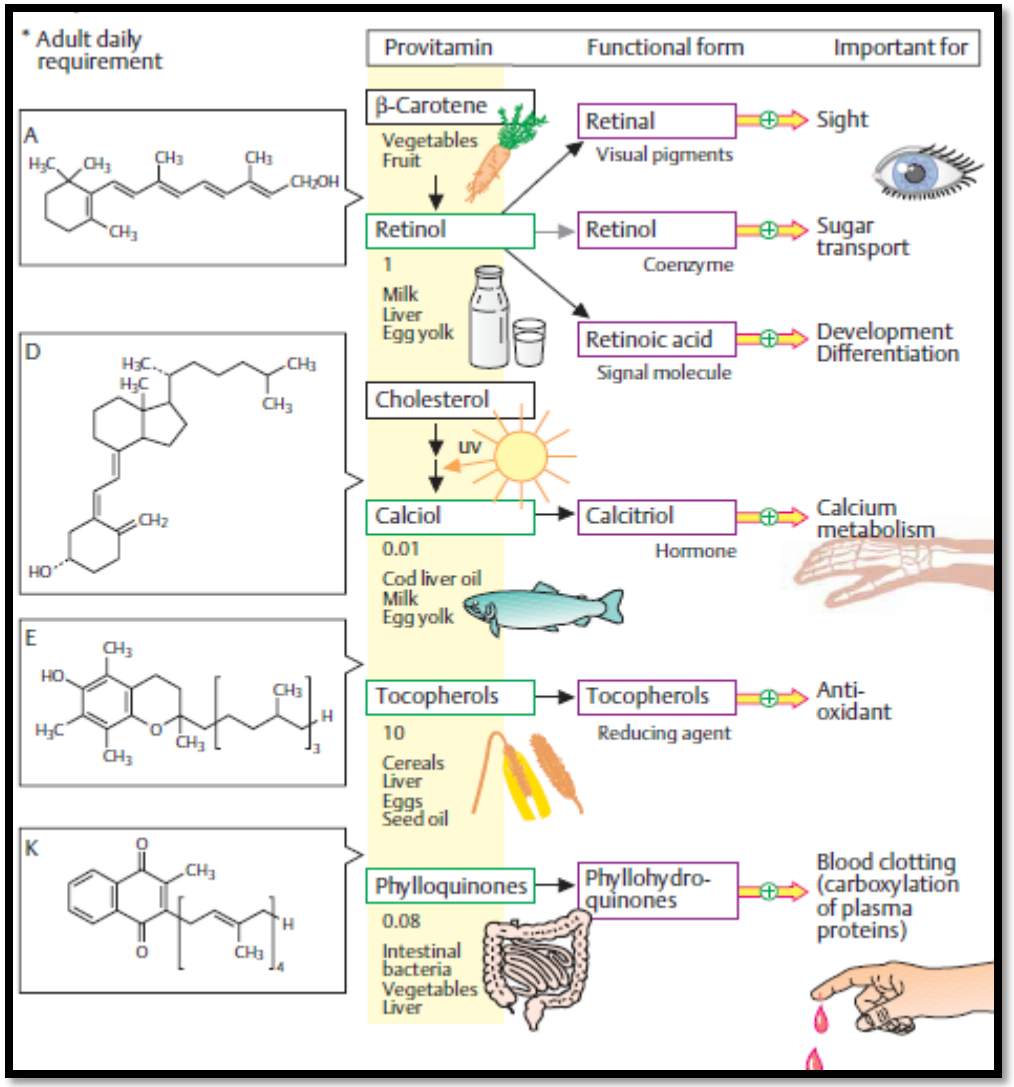
Vitamin E

- Consists of eight naturally **tocopherols** and the α one is the active one.
- Play a role as an **antioxidant** prevent the non enzymatic oxidation of the cell components.
- vitamin E is mainly located in biological membranes, where as an antioxidant it protects unsaturated lipids against reactive oxygen species ROS and other radicals.
- **Vit E deficiency** occurs almost in infants, when occurs in adults as a reason of lipid absorption impairment leads to increased the red blood cells sensitivity to peroxidase and abnormal cellular membrane.
- vegetable oils are rich in Vit E, 10 mg of alpha tocopherol for man and 8 mg for women is sufficient.



Lipid soluble vitamins





Summary table

Vitamin		Functions	Deficiency Disease
A	Retinol, β-carotene	Visual pigments in the retina; regulation of gene expression and cell differentiation; β-carotene is an antioxidant	Night blindness, xerophthalmia; keratinization of skin
D	Calciferol	Maintenance of calcium balance; enhances intestinal absorption of Ca^{2+} and mobilizes bone mineral	Rickets = poor mineralization of bone; osteomalacia = bone demineralization
E	Tocopherols, tocotrienols	Antioxidant, especially in cell membranes	Extremely rare—serious neurologic dysfunction
K	Phylloquinone, menaquinones	Coenzyme in formation of γ-carboxyglutamate in enzymes of blood clotting and bone matrix	Impaired blood clotting, hemorrhagic disease
B_1	Thiamin	Coenzyme in pyruvate and α–ketoglutarate, dehydrogenases, and transketolase; poorly defined function in nerve conduction	Peripheral nerve damage (beriberi) or central nervous system lesions (Wernicke-Korsakoff syndrome)
B_2	Riboflavin	Coenzyme in oxidation and reduction reactions; prosthetic group of flavoproteins	Lesions of corner of mouth, lips, and tongue; seborrheic dermatitis
Niacin	Nicotinic acid, nicotinamide	Coenzyme in oxidation and reduction reactions, functional part of NAD and NADP	Pellagra—photosensitive dermatitis, depressive psychosis
B_6	Pyridoxine, pyridoxal, pyridoxamine	Coenzyme in transamination and decarboxylation of amino acids and glycogen phosphorylase; role in steroid hormone action	Disorders of amino acid metabolism, convulsions
	Folic acid	Coenzyme in transfer of one-carbon fragments	Megaloblastic anemia
B_{12}	Cobalamin	Coenzyme in transfer of one-carbon fragments and metabolism of folic acid	Pernicious anemia = megaloblastic anemia with degeneration of the spinal cord
	Pantothenic acid	Functional part of CoA and acyl carrier protein: fatty acid synthesis and metabolism	
H	Biotin	Coenzyme in carboxylation reactions in gluconeogenesis and fatty acid synthesis	Impaired fat and carbohydrate metabolism, dermatitis
C	Ascorbic acid	Coenzyme in hydroxylation of proline and lysine in collagen synthesis; antioxidant; enhances absorption of iron	Scurvy—impaired wound healing, loss of dental cement, subcutaneous hemorrhage

Thank you