CLINICAL PHARMACOLOGY OF VITAMINS, MACRO- AND MICROELEMENTS

Vitamins – low molecular weight organic compounds that have different chemical structure and are not synthesized or are synthesized in small amount in the human organism, are not used as building material, but have marked biological effect and are necessary components of diet

Hypovitaminosis – decrease of vitamin amount in the organism
Hypervitaminosis – increase of vitamin amount in the organism
Avitaminosis – lack of vitamin in the organism

Two types of hypo- and avitaminosis: exo- and endogenic

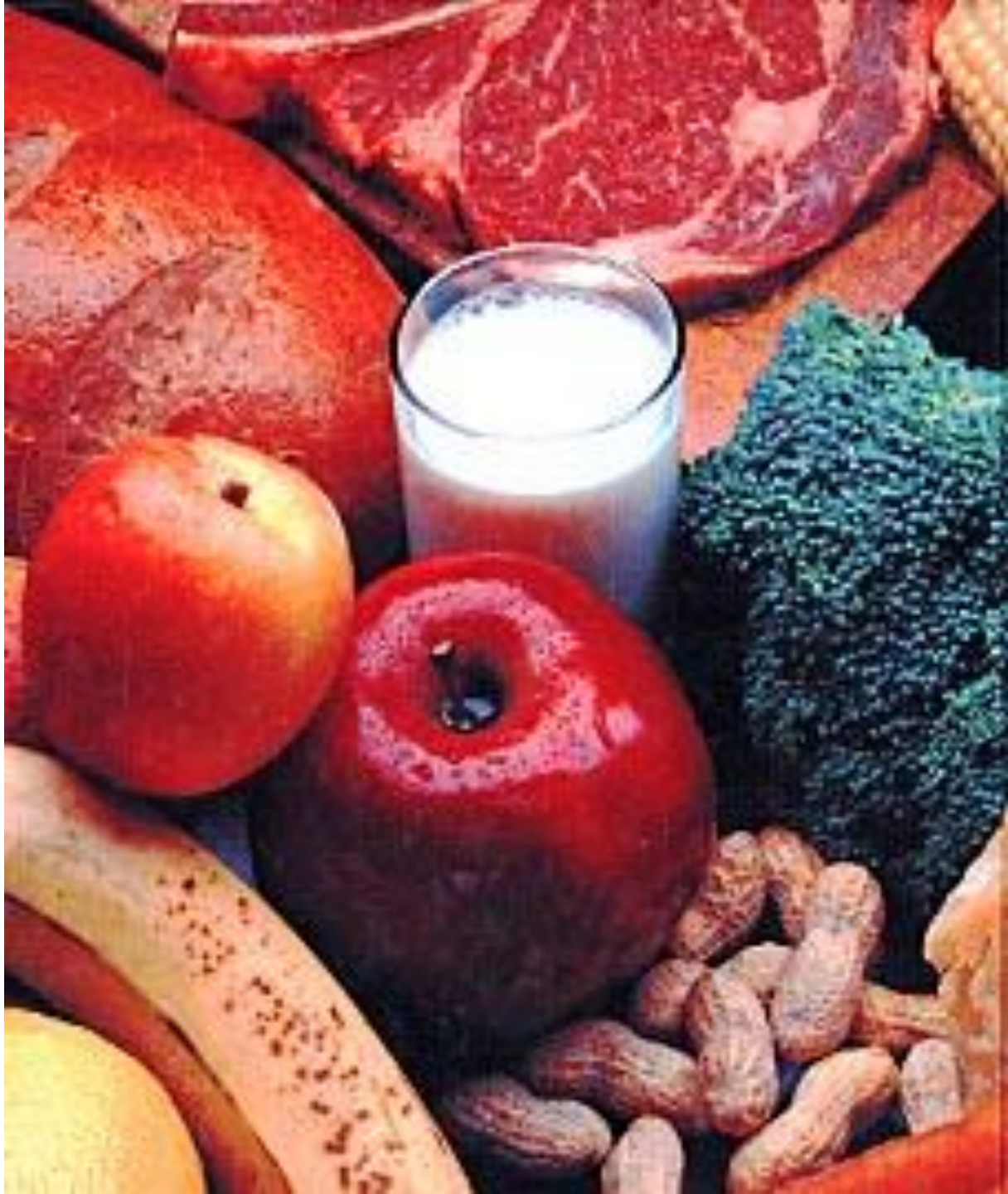
Classification of vitamins

Water soluble:

- group B
- C
- H
- P

Fat soluble:

-A
-D
-E
-K
-F



Water soluble vitamins	Fat soluble vitamins
Form coenzymes	Do not form coenzymes
Do not affect membranes	Modulators of membranes
Do not have antioxidant properties (except vit. C)	Most are antioxidants
Do not affect genetic apparatus	Cause the expression of genes
Do not cause hypervitaminosis	Cause hypervitaminosis
Do not have provitamins	Have provitamins

Water-soluble and fat-soluble vitamins

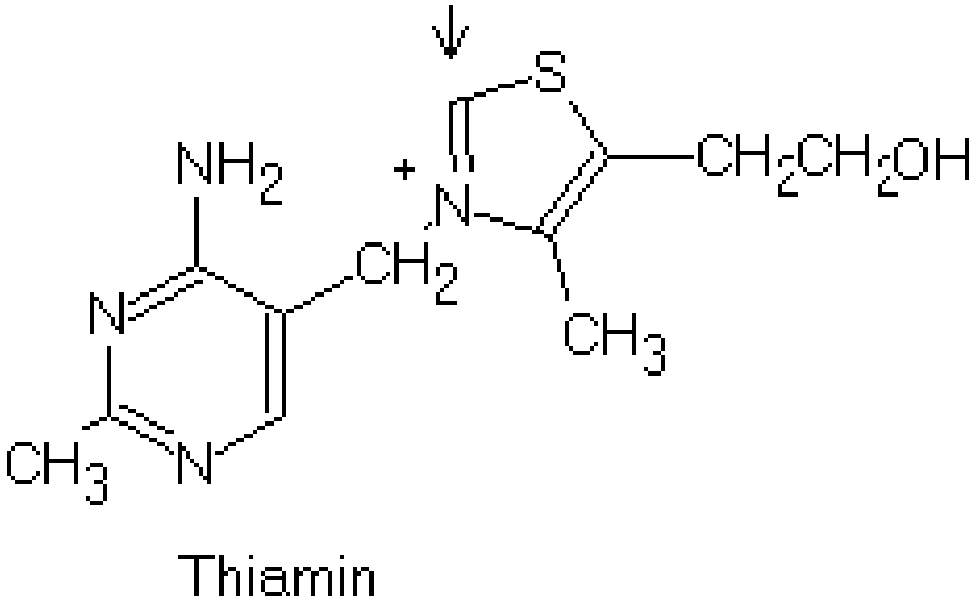
	Water-Soluble Vitamins: B Vitamins and Vitamin C	Fat-Soluble Vitamins: Vitamins A, D, E, and K
Absorption	Directly into the blood.	First into the lymph, then the blood.
Transport	Travel freely.	Many require protein carriers.
Storage	Circulate freely in water-filled parts of the body.	Stored in the cells associated with fat.
Excretion	Kidneys detect and remove excess in urine.	Less readily excreted; tend to remain in fat-storage sites.
Toxicity	Possible to reach toxic levels when consumed from supplements.	Likely to reach toxic levels when consumed from supplements.
Requirements	Needed in frequent doses (perhaps 1 to 3 days).	Needed in periodic doses (perhaps weeks or even months).

NOTE: Exceptions occur, but these differences between the water-soluble and fat-soluble vitamins are valid generalizations.

-Soluble Vitamins

Vitamin	Coenzyme	Typical reaction type	Consequences of deficiency
Thiamine (B_1)	Thiamine pyrophosphate	Aldehyde transfer	Beriberi (weight loss, heart problems, neurological dysfunction)
Riboflavin (B_2)	Flavin adenine dinucleotide (FAD)	Oxidation–reduction	Cheliosis and angular stomatitus (lesions of the mouth), dermatitis
Pyridoxine (B_6)	Pyridoxal phosphate	Group transfer to or from amino acids	Depression, confusion, convulsions
Nicotinic acid (niacin)	Nicotinamide adenine dinucleotide (NAD^+)	Oxidation–reduction	Pellagra (dermatitis, depression, diarrhea)
Pantothenic acid	Coenzyme A	Acyl–group transfer	Hypertension
Biotin	Biotin–lysine complexes (biocytin)	ATP-dependent carboxylation and carboxyl-group transfer	Rash about the eyebrows, muscle pain, fatigue (rare)
Folic acid	Tetrahydrofolate	Transfer of one-carbon components; thymine synthesis	Anemia, neural-tube defects in development
B_{12}	5′-Deoxyadenosyl cobalamin	Transfer of methyl groups; intramolecular rearrangements	Anemia, pernicious anemia, methylmalonic acidosis
C (ascorbic acid)		Antioxidant	Scurvy (swollen and bleeding gums, subdermal hemorrhages)

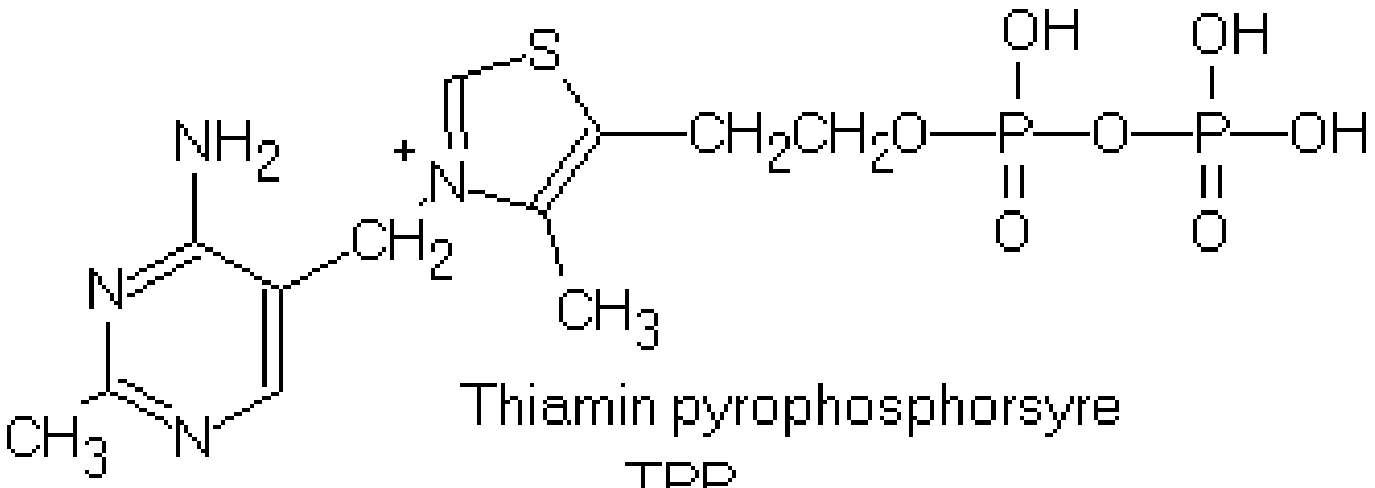
Vitamin B_1 (thyamin, antineuritic)



Thiamin

Consists of two rings – pyrimidine and thiazole

Is phosphorylated in liver to TMP, TPP and TTP



Thiamin pyrophosphorsyre

TPP

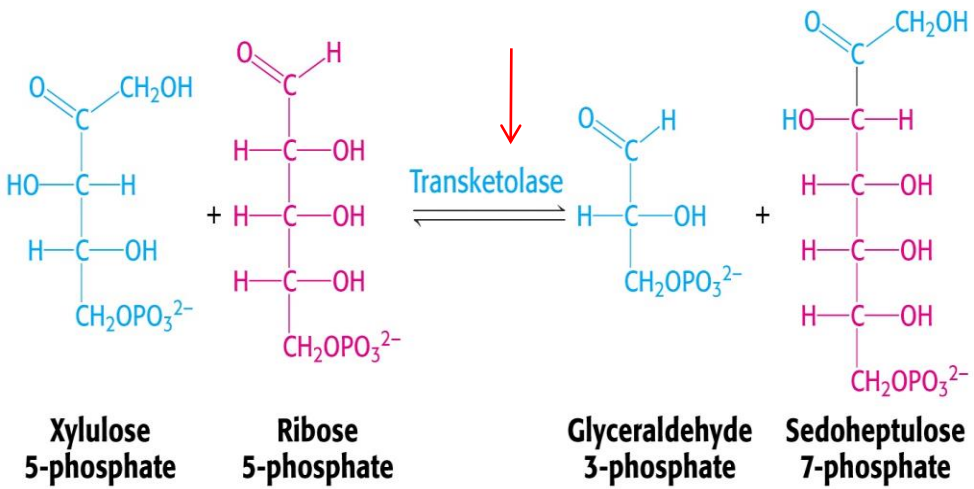
TMP, TPP and TTP are coenzymes of:

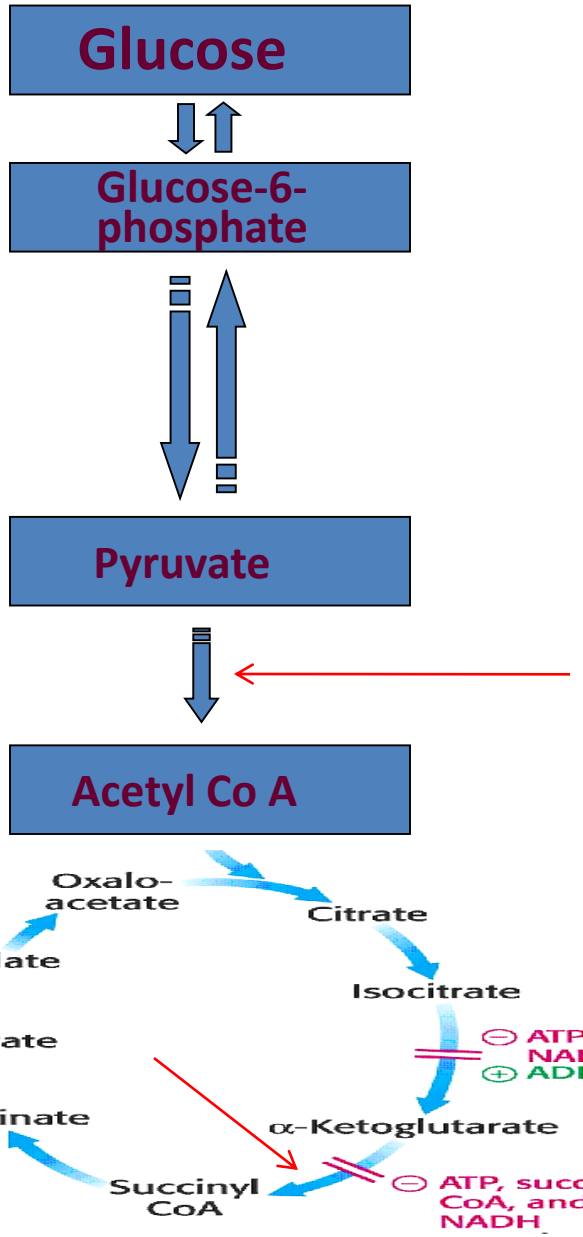
-pyruvate- and alpha-ketoglutarate dehydrogenase

-transketolase

In the thiamin deficiency ketoacids that are toxic for nervous system are accumulated.
Acidosis.
Carbs are not used, energy deficit.
Organism uses lipids and proteins, loss of weight, dystrophy, growth retardation.
Catabolism prevails.

Inhibition of transketolase, inhibition of PPC, deficit of NADPH and riboses, disorders of fatty acids synthesis, steroid hormones, cholesterol, nucleic acids.





Chronic deficiency of thiamine

Berry-berry disease

Often found in
-Asian countries
-alcoholics

Two types: **dry** and **wet**

Dry: disseminated polyneuritis, partial paralysis, weakness and pain in the limbs, atrophy, loss of weight, impaired sensory perception

Wet: heart failure, edema, dystrophy of myocardium

Wernicke-Korsakoff syndrome : hemorrhage in CNS. Mental disorders, amnesia, encephalopathy, psychosis

Berry-Berry

Vitamin B1

Vitamin B1 (Thiamine)
is found in fortified breads
and cereals, fish, lean meats and milk

Daily requirement:
1-3 mg

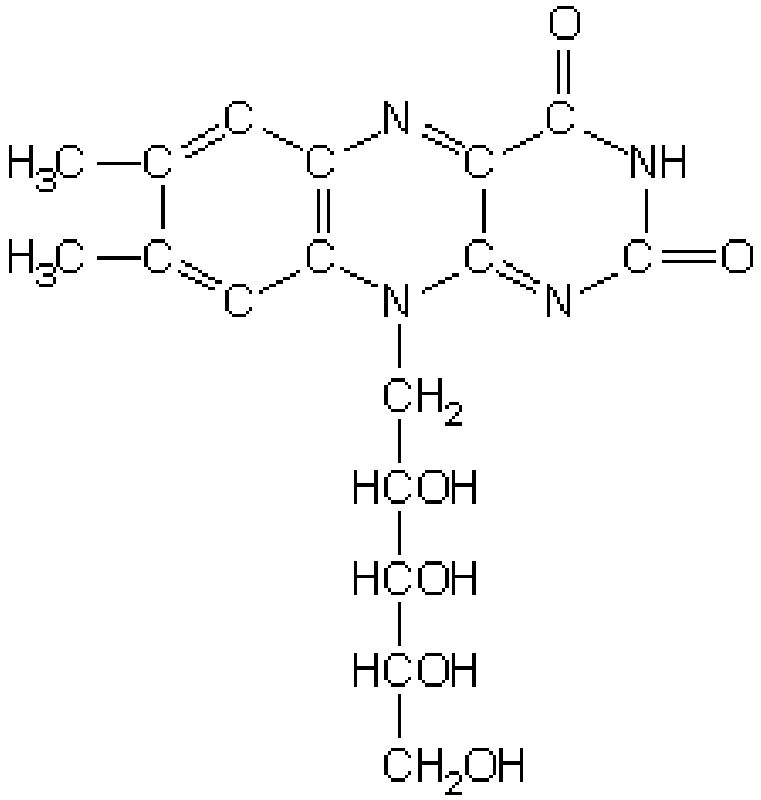
Preparations:
-thiamine,
-cocarboxylase

Are used in cardiac, nervous diseases, diabetes mellitus, muscle dystrophy

Vitamin B_2 (riboflavin, growth vitamin)

Is composed from isoallaxasine and alcohol ribitol

Flavus - yellow



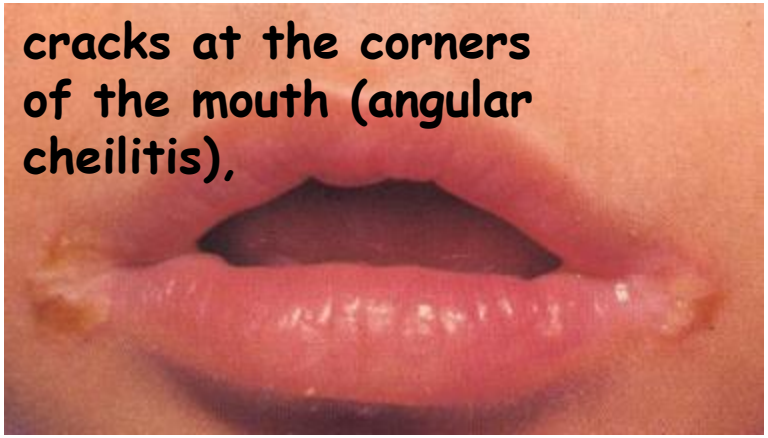
Forms the coenzymes FMN and FAD

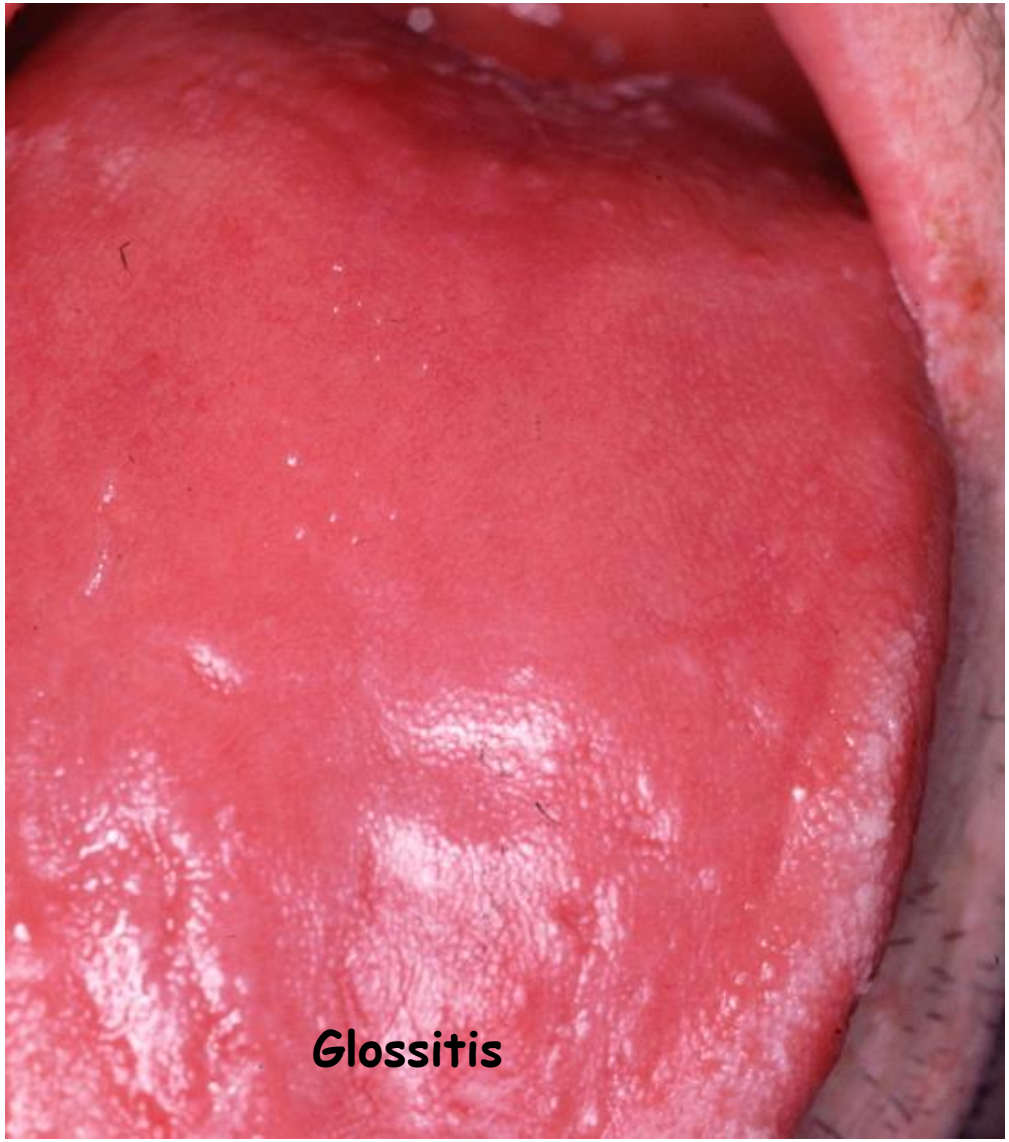
Are necessary for the action of more than 30 enzymes – oxido-reductases (oxidation-reduction reactions)

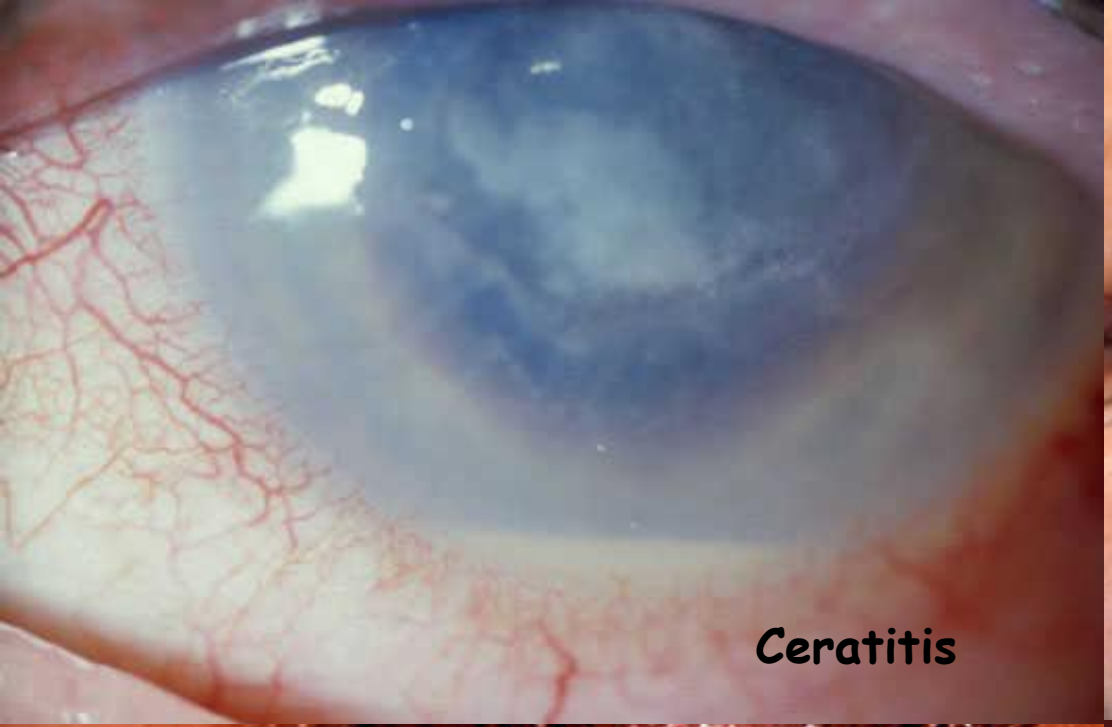
-AA deamination (oxidases of AA)
-pyruvate dehydrogenase and alpha-ketoglutarate complexes
-succinate dehydrogenase (Krebs cycle)
-fatty acids oxidation (acyl CoA dehydrogenase)
-uric acid formation (xanthine oxidase)
-electron transport in respiration chain

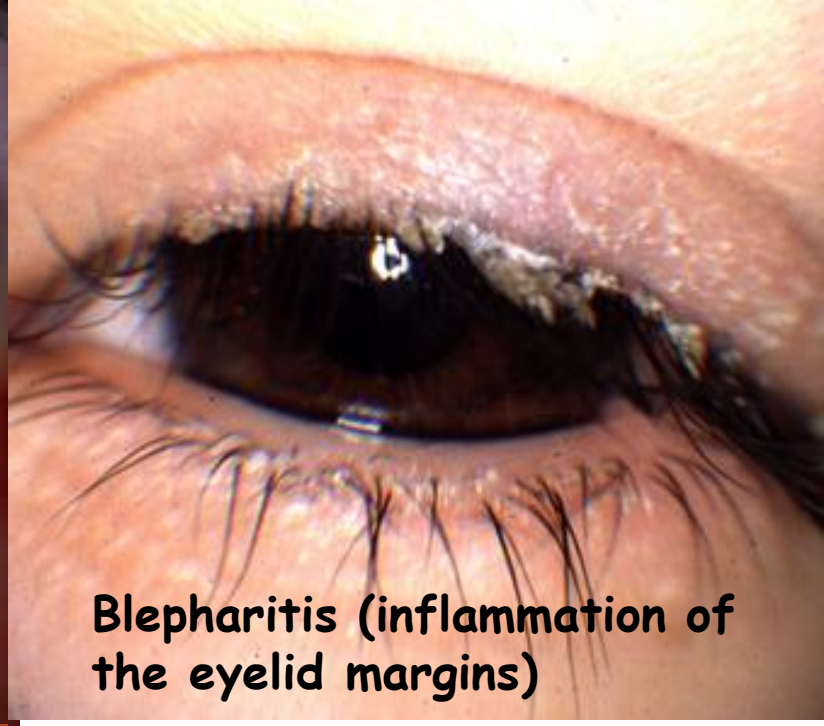
Hypovitaminosis – disorders of the processes of biological oxidation

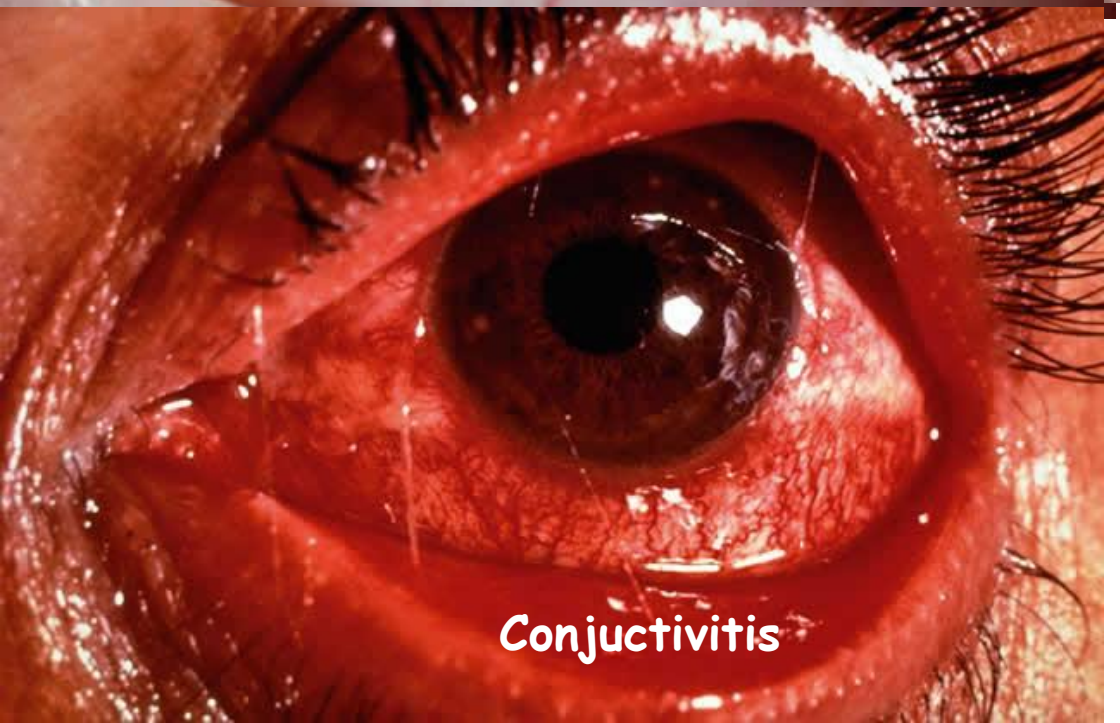
Symptoms:











Ceratitis
Blepharitis
Conjuctivitis
Anemia
Leucopenia

Vitamin B2

Food sources of Riboflavin (vitamin B2):

Cereal, nuts, milk, eggs, green leafy vegetables and lean meat

Daily requirement:
1-3 mg

Partially is synthesized by the intestine microorganisms

Preparation:
riboflavin

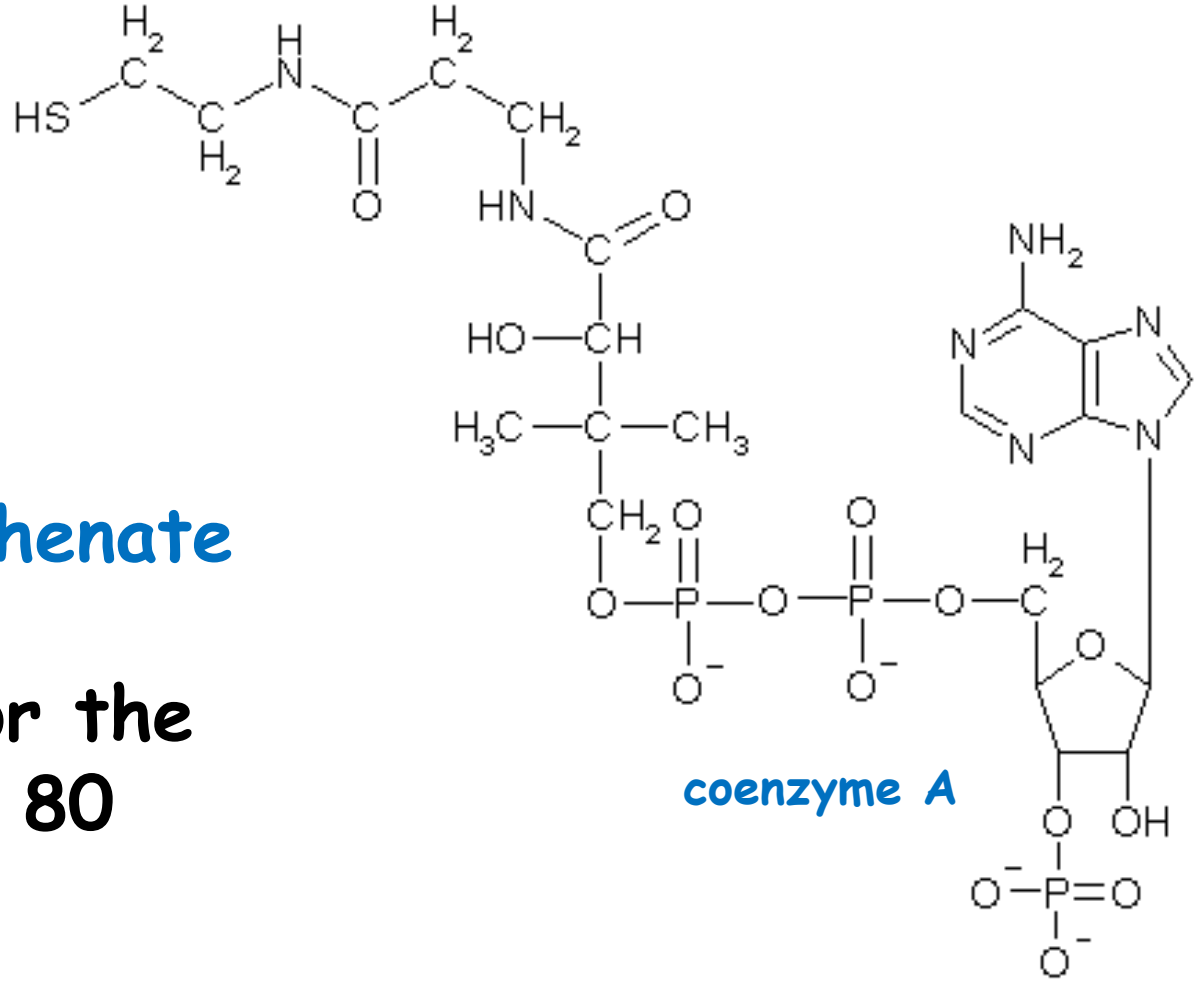
Vitamin B_3 (pantothenic acid, antidermatitic)

Coenzymes:

-coenzyme *A*

-phosphopantothenate

Is necessary for the action of about 80 enzymes

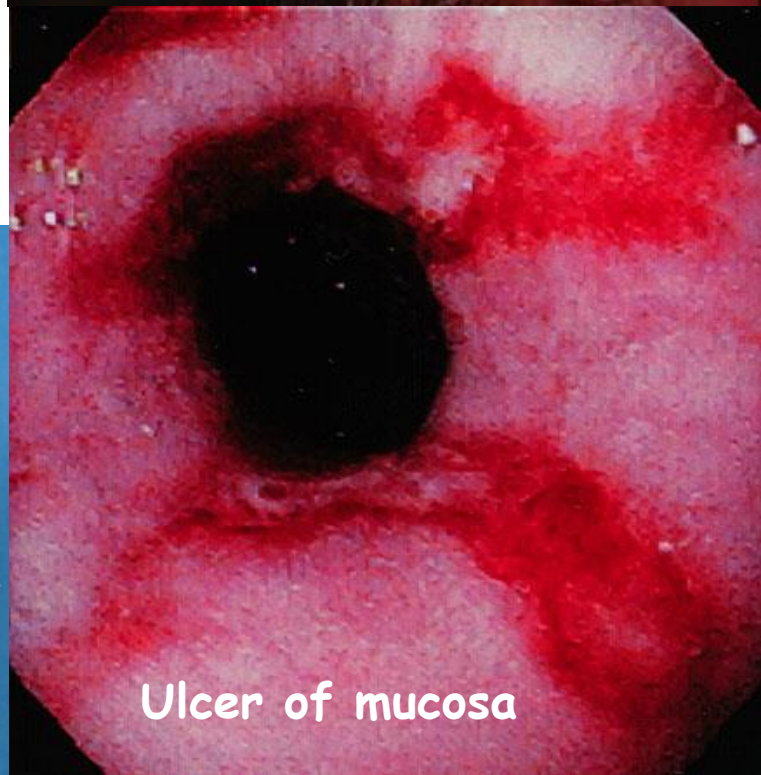


coenzyme *A*

Processes which are inhibited in vitamin B_3 deficiency

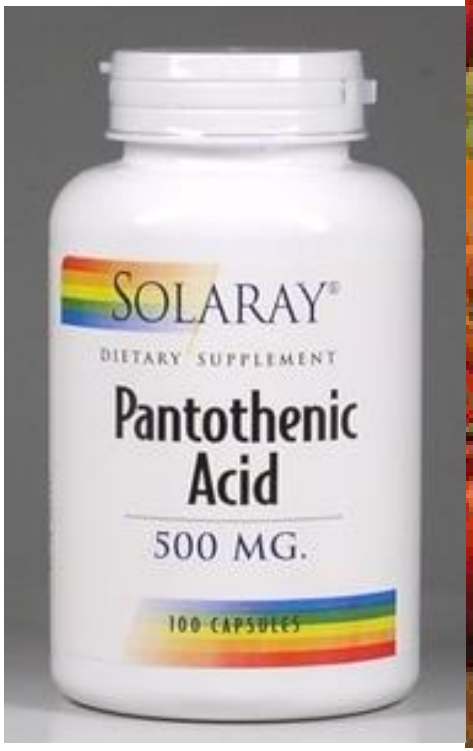
-oxidative decarboxilation of pyruvate and alpha-ketoglutarate
-transport of the fatty acids residues
-synthesis of purine nucleotides
-activation of fatty acids
-phosphopantothenate is a constituent of multienzyme complex – fatty acids synthase
-cholesterol synthesis
-ketogenesis

Hypovitaminosis:
- dermatitis
- ulcers of mucosa
- spasms, paresis
- hypolipidemia,
- liver steatosis



Daily requirement:
10-15 mg

Food:
liver, eggs, fish, bread

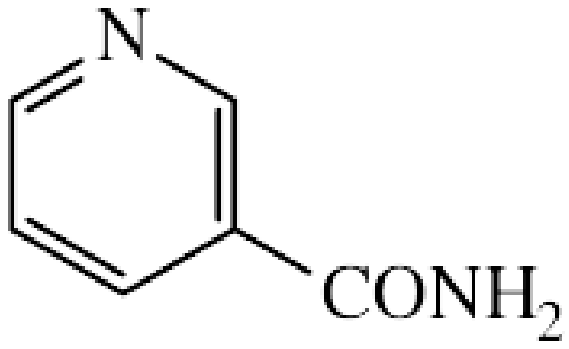


Preparation:
pantothenic acid

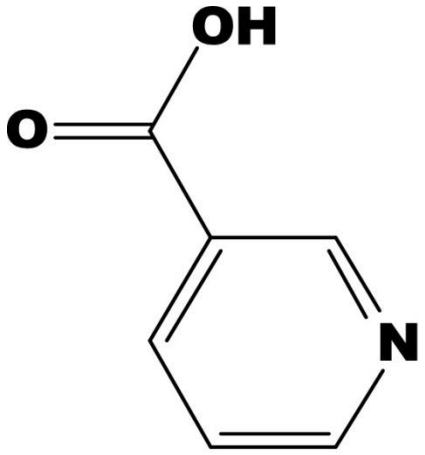
Vitamin B_5 (PP, nicotinic acid, nicotinamide (niacin), antipellagric)

Nature – derivative of pyridine

Form the coenzymes NAD and NADP



NIACIN



Niacin

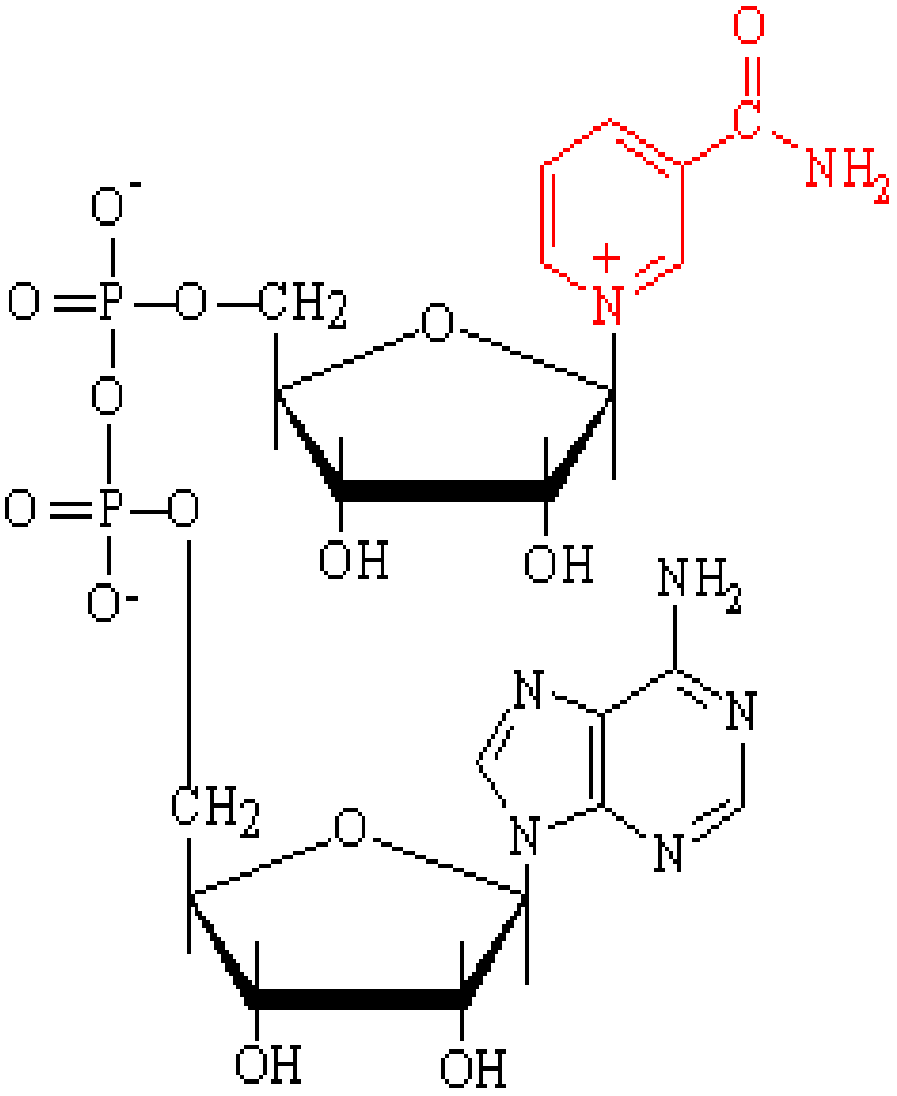
NAD and NADP – coenzymes of many oxido-reductases (about 100)

Take part in:

-glycolisis
-gluconeogenesis
-PPC
-FA synthesis and oxidation
-AA deamination
-Krebs cycle (3 enzymes)
-ETC
-nucleic acids formation

NADP takes part in:

-FA synthesis
-cholesterol synthesis



Hypovitaminosis – disease pellagra

Causes:

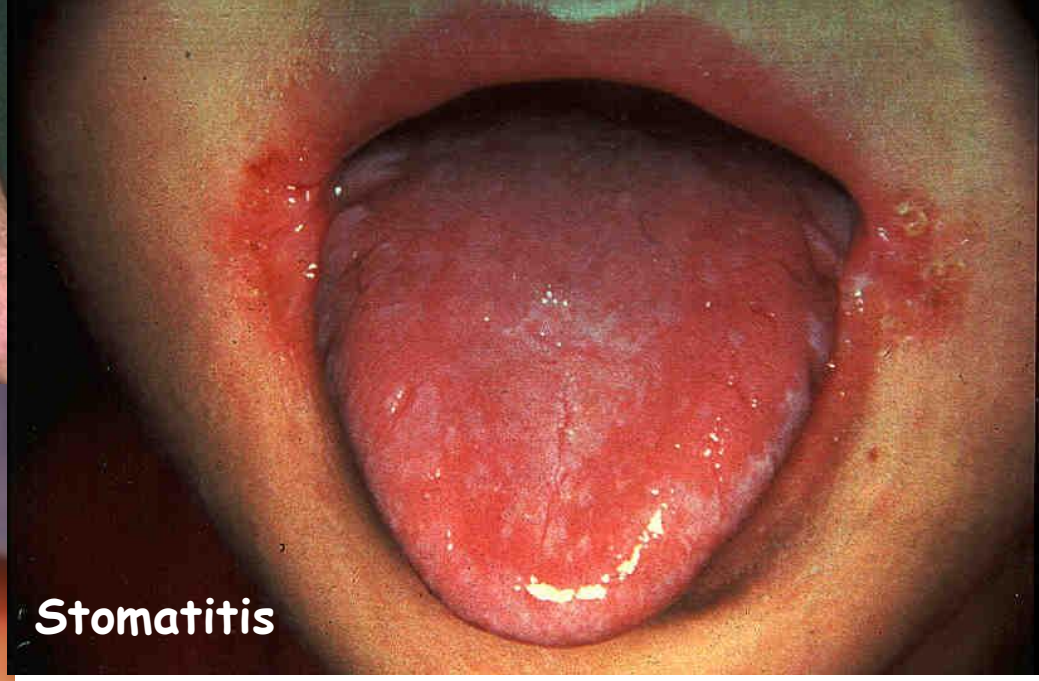
-malabsorption
-alcoholism
-taking of cytostatics and isoniazide for a long time
-protein starvation
-in persons who eat a lot of corn (lack of tryptophan from which B_5 can be synthesized by bacteria)

Pellagra – disease of 3 D

-dermatitis,
-diarrhea,
-dementia

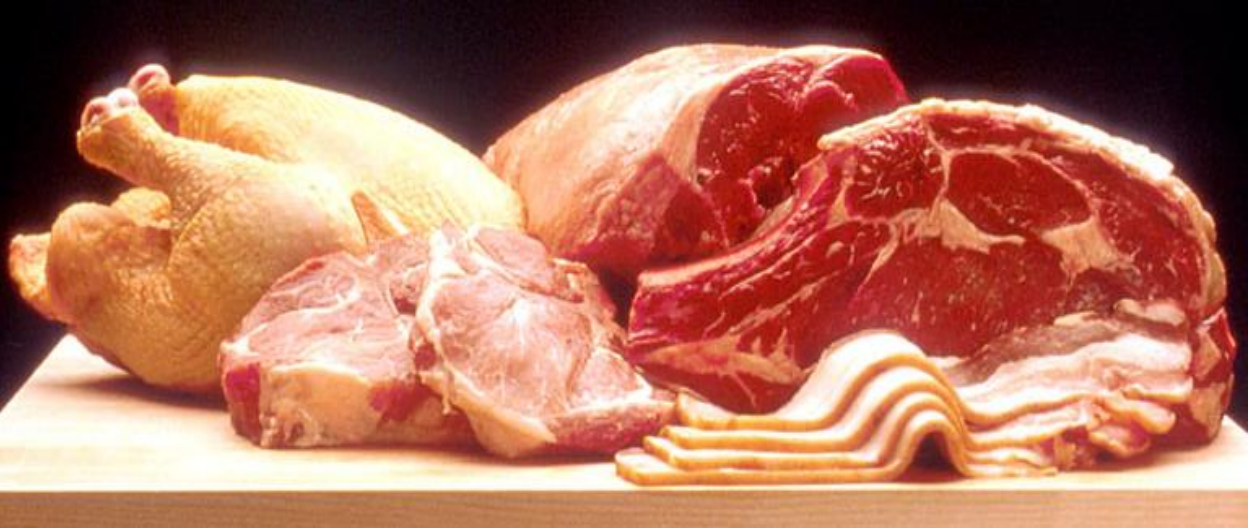
Dermatitis:

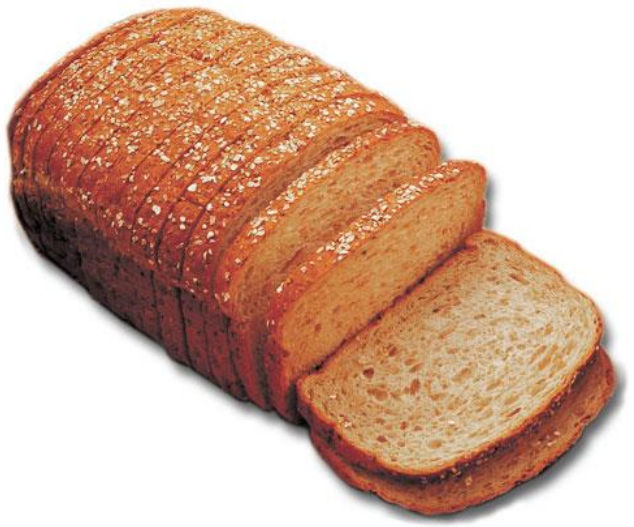
- symmet-rical,
-on the open areas of body,
-hyper-keratosis



Diarrhea as result of the atrophy of stomach and intestine endothelium
Glossitis, stomatitis.

Dementia as result of the chronic injury of CNS. Psychosis. Mental confusion.



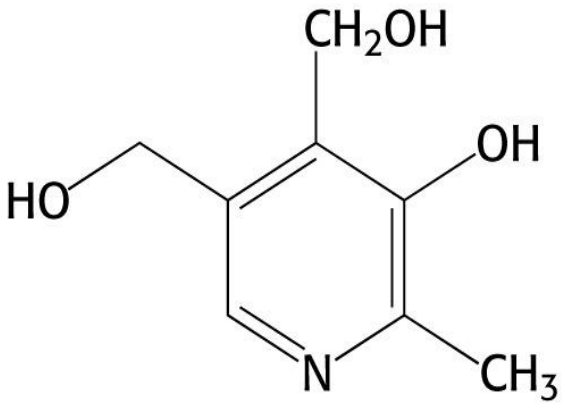


Daily requirement: 14-25 mg

Is formed in the intestine (by microorganisms) and cells from **tryptophan**

Food: liver, meat, fish, black bread, yeast, eggs

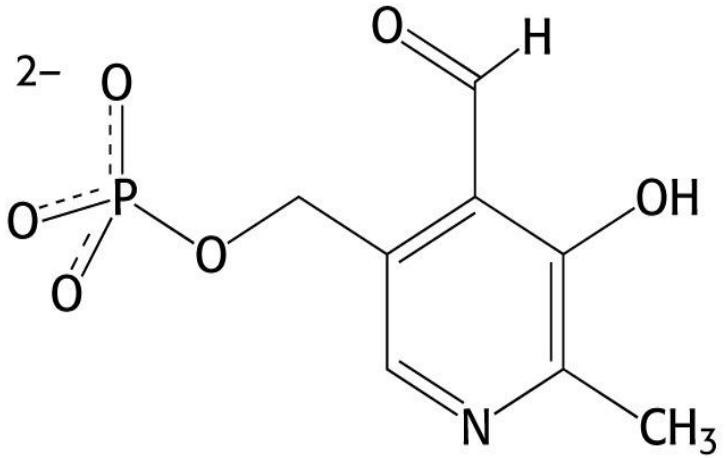
Vitamin B_6 (pyridoxine, antidermatitic)



Pyridoxine (Vitamin B_6)

In the base of structure – pyridine core

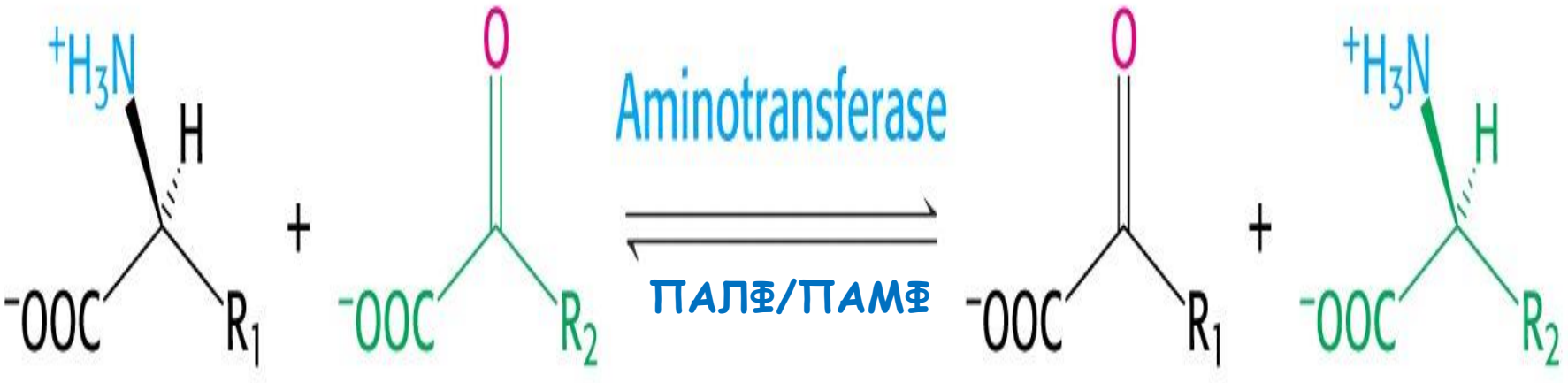
Form coenzymes pyridoxal phosphate (PLP) and pyridoxamine monophosphate (PMP)



Pyridoxal phosphate (PLP)

PLP and ПМФ – coenzymes of enzymes of AA metabolism:

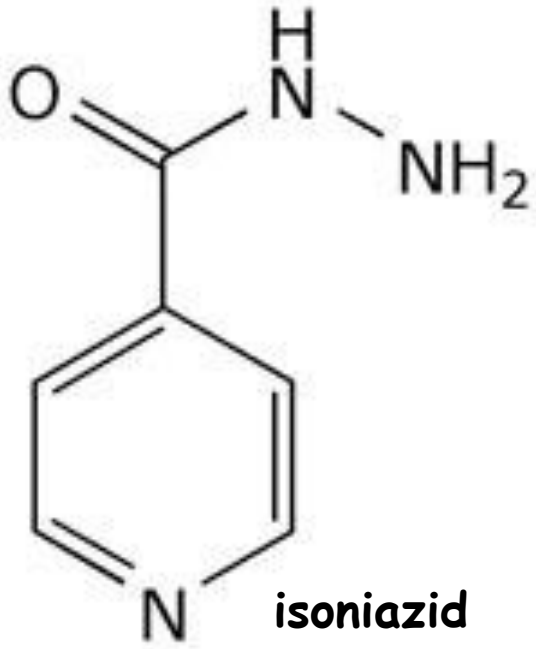
- -amino transferases
- -decarboxylases
- -participate in oxidation of amines
- -synthesis of GABA



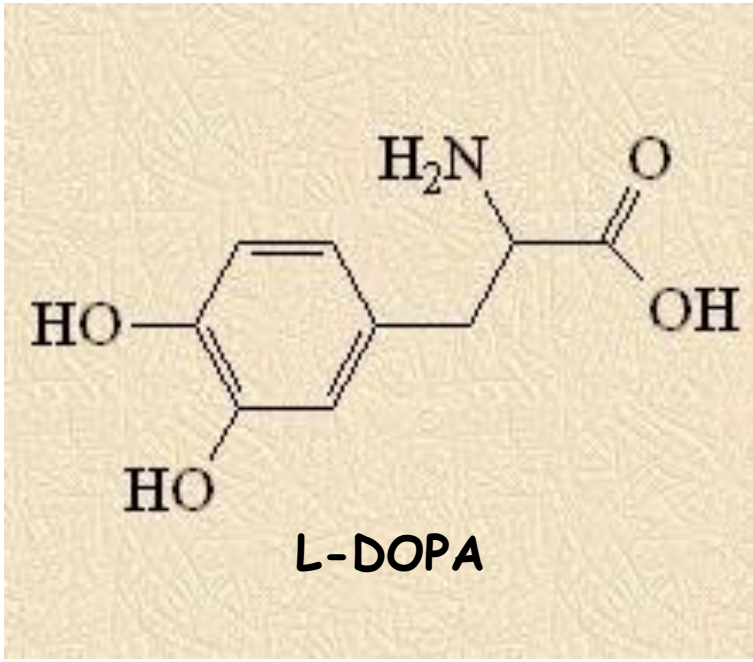
α-amino acid *α-keto acid* *α-keto acid* *α-amino acid*

Hypovitaminosis

-in the using of antagonists (isoniazid, penicyllamine, L-DOPA, estrogens)
-in malabsorption, alcoholism
-increased requirement in pregnancy



isoniazid



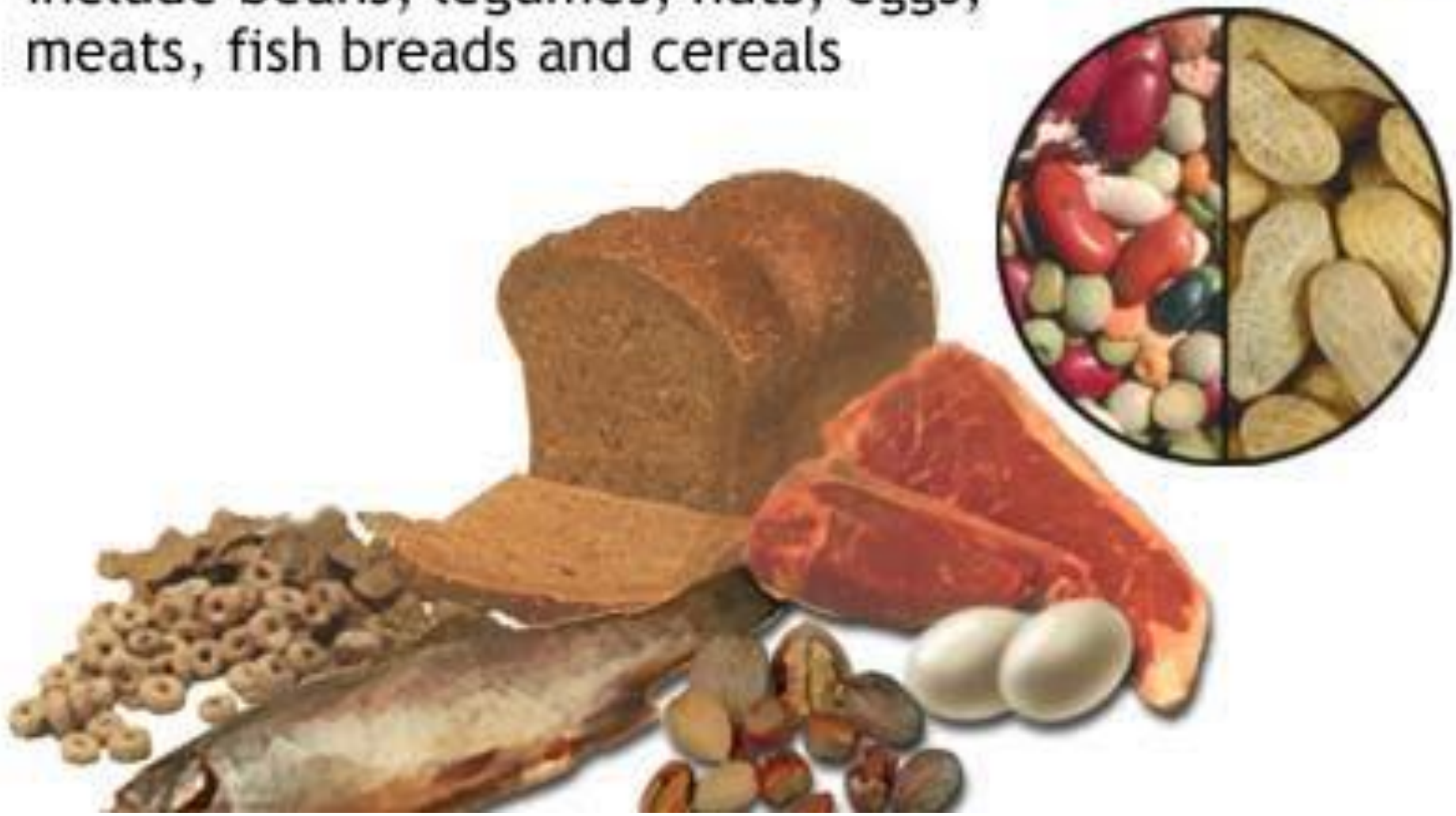
L-DOPA

Disorders of protein metabolism

-hyperaminoaciduria
-negative nitrogen balance
-dermatitis (erythema, pigmentation, edema)
-anemia (disorders of iron utilization)
-leucopenia (disorders of protein synthesis)
-growth inhibition
-convulsions, muscle spasms (GABA inhibition)

Vitamin B6

Food sources of vitamin B6 (pyridoxine) include beans, legumes, nuts, eggs, meats, fish breads and cereals



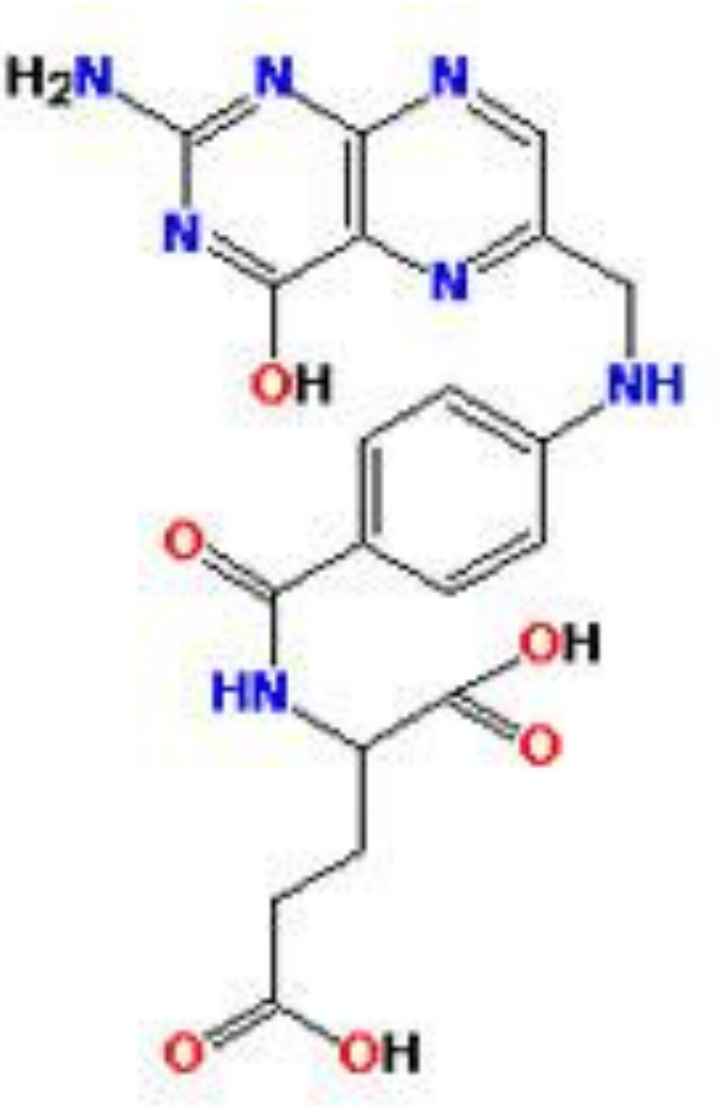
Daily requirement:
2-3 mg

Is formed by
intestinal bacteria

Photosensitive

Thermostable

Vitamin B_{10} (folic acid, antianemic)



In the base of structure -
residue of pterine, paraaminobenzoic acid, glutamic acid

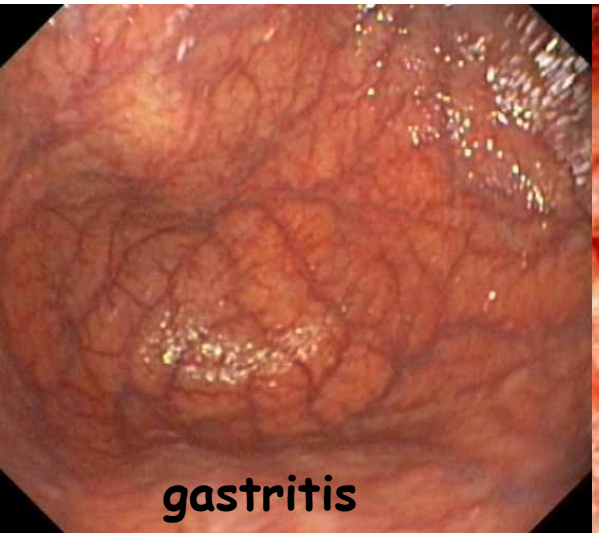
Coenzyme -
tetrahydrofolic acid (THFA)

Biological role of THFA:

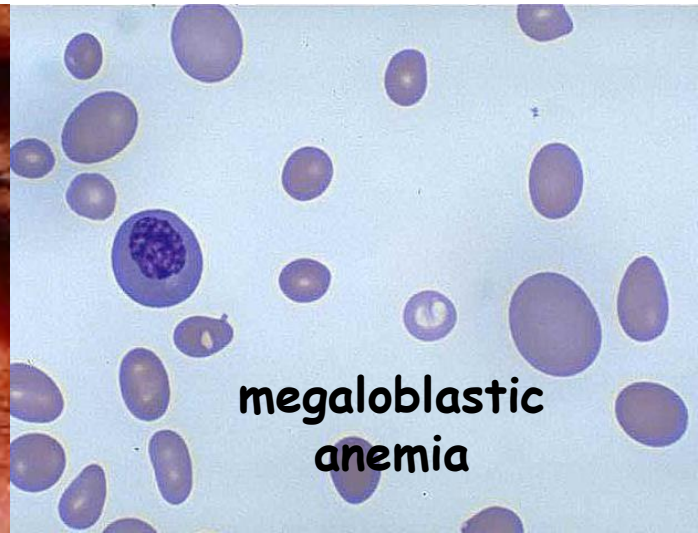
-transfers methyl groups in the synthesis of AA, pyrimidine nucleotides, creatin, methionin. In deficiency – disorders of the NA and protein synthesis, inhibition of growth and cell division

Symptoms:

-hyperchromic megaloblastic anemia
-leucopenia
-thrombocytopenia
-glossitis, conjuctivitis, gastritis (disorders of epithelium proliferation)
-growth inhibition
-impairment of the wound healing
-immunodeficiency


gastritis


conjunctivitis


megaloblastic anemia

Daily requirement:
200-500 mg

Is formed by
intestinal bacteria

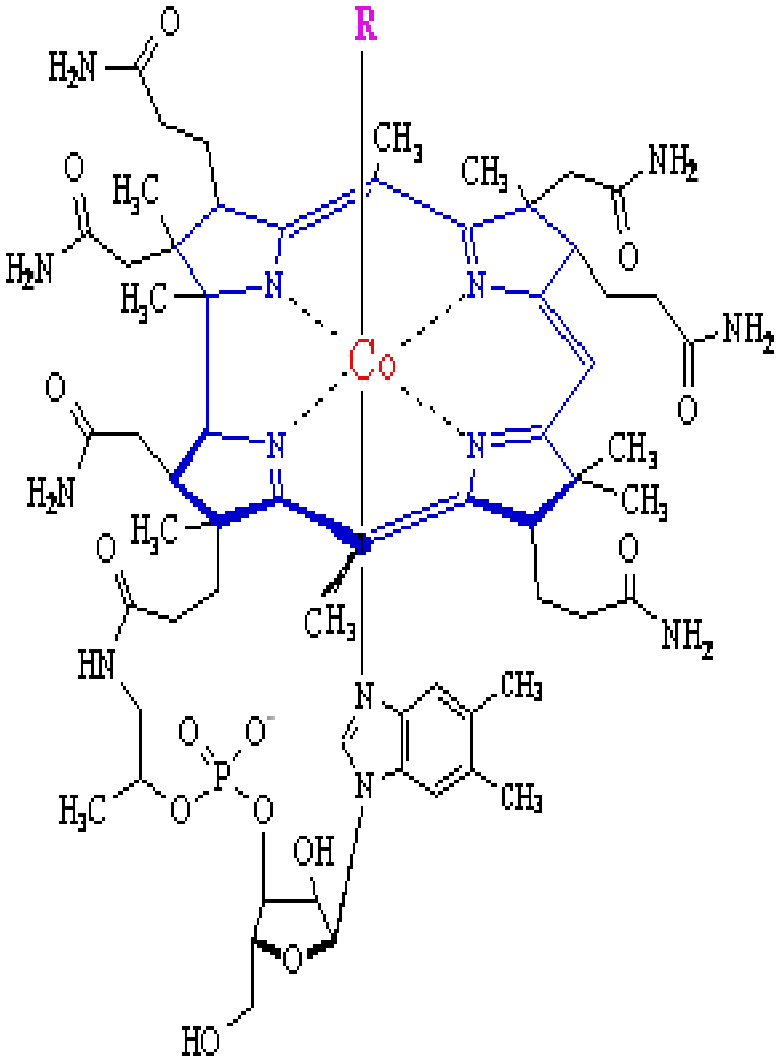
Food: bean, green leafy vegetables, lemons, mushrooms, meat, liver

There are many antivitamins of folic acid: -cytostatics (methotrexat is used for treatment of leucemia)
-sulfanilamide (structural analogs of p-aminobenzoic acid, inhibit the synthesis of folic acid (purine bases, DNA, RNA in bacteria)

Vitamin B_{12} (cyanocobalamin, antianemic)

Structure – tetrapyrrol compound, Co ion, nucleotide part

Coenzymes –
-5-deoxyadenosyl-cobalamin
-methylcobalamin

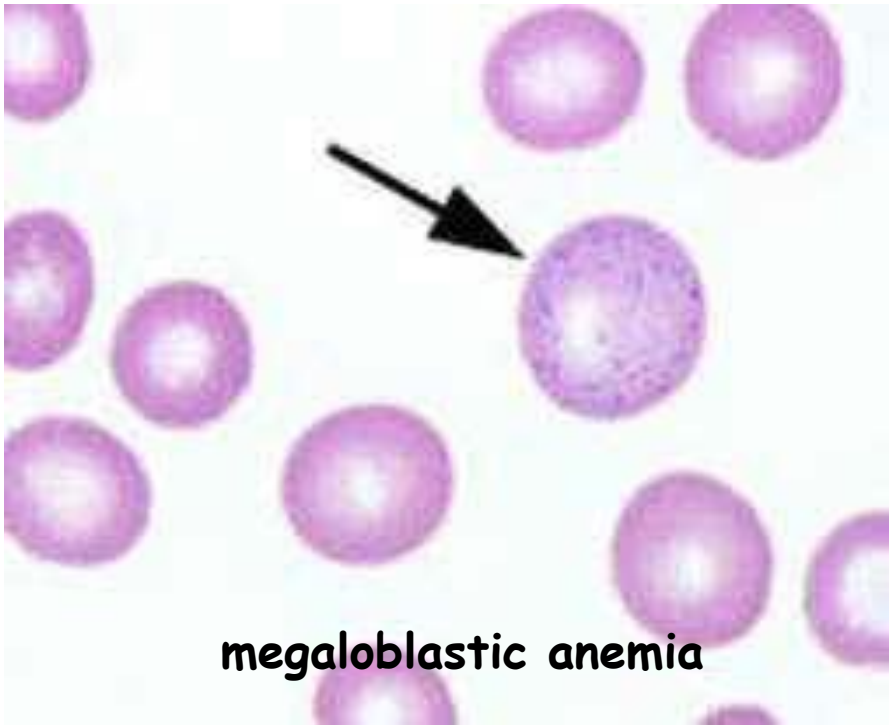


Biological role:

-tightly connected to folic acid
-synthesis of methionine from homocysteine
-synthesis of creatin, cholin
-synthesis of phospholipids
-synthesis of purine and pyrimidine bases, nucleic acids

Symptoms:

-hyperchromic megaloblastic anemia (malignant, pernicious, Addison-Birmer disease)
-fatty dystrophy of nervous cells, neurological disorders
-cardiovascular disorders (accumulation of homocystein)



megaloblastic anemia

Vitamin B12

Food sources of vitamin B12:

Eggs, meat, poultry, shellfish, milk and milk products

Daily requirement: 2-5 micrograms

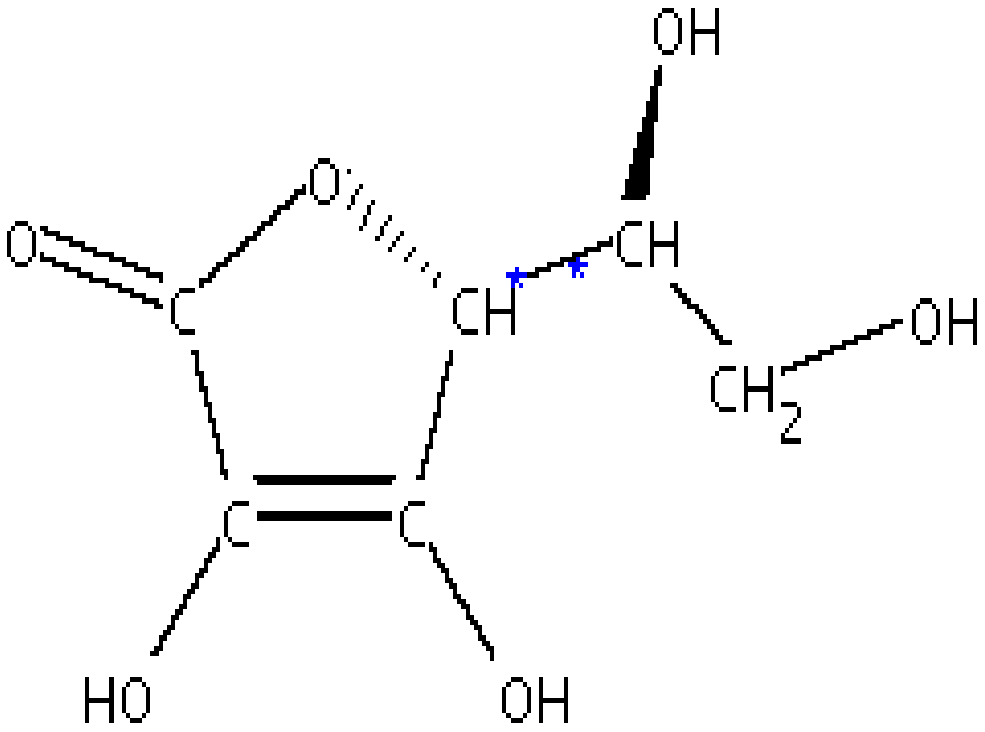
Is not synthesized neither in plants nor in animals.
Is formed only by intestinal bacteria

Is absorbed in small intestine

Vitamin C (ascorbic acid, antiscorbutic)

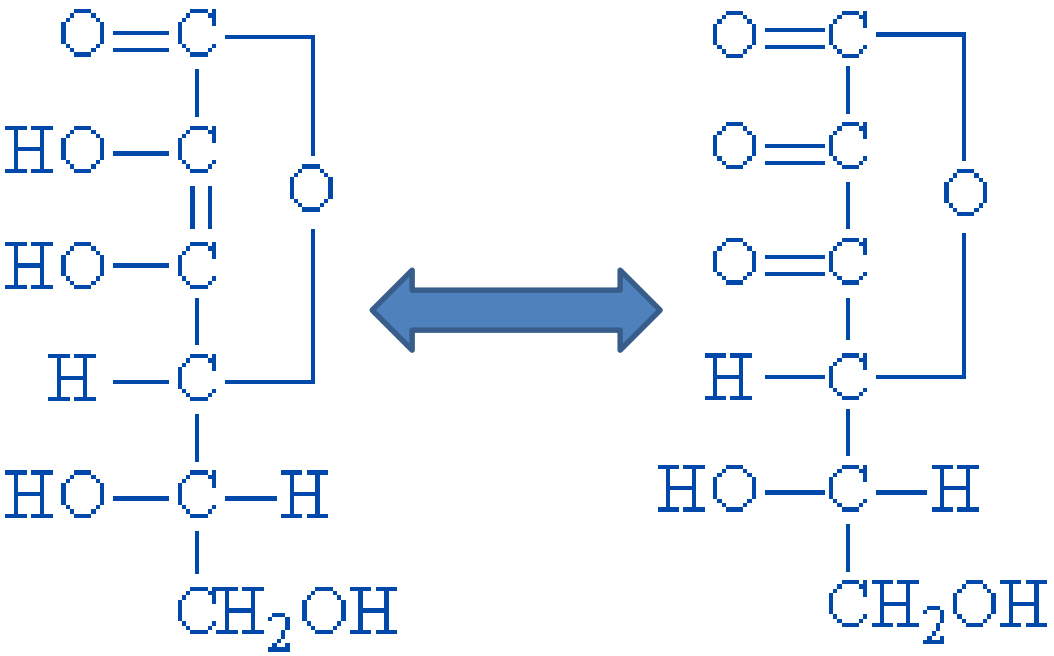
Structure – lacton of dienolgulonic acid

Coenzyme function has not been established



L-ascorbic acid

Has oxidation-reduction properties



Can donate hydrogen, as result is converted to dehydroascorbic acid

Biological role:

-reduces sulhydryl groups of proteins, enzymes
-formation of serotonin
-synthesis of norepinephrine
-synthesis of steroid hormones
-formation of carnitin
-synthesis of collagen (hydroxyprolin)
-formation of THFA
-decomposition of hemoglobin
-$Fe^{3+} \rightarrow Fe^{2+}$ - absorption in the intestine
-promote immunity defense

Hypovitaminosis - scurvy:

-hemorrhages

- loose of teeth, gums swell and bleed easily (collagen deficit)

-anemia (lack of THFA)

-pain in heart, swelling of legs, weakness, fatigue

-loss of weight

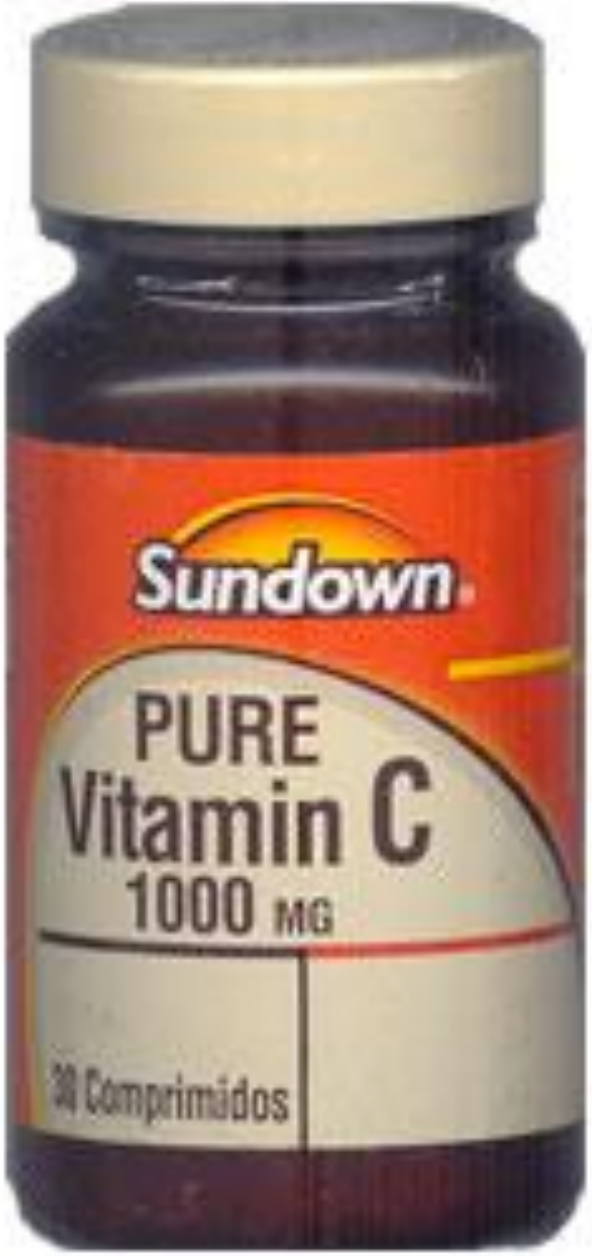
Daily requirement:
75-100 mg

Requirement is increased in infections, flue, in pregnancy

Food: rose, black currant, citrus, vegetables, fruits, needles

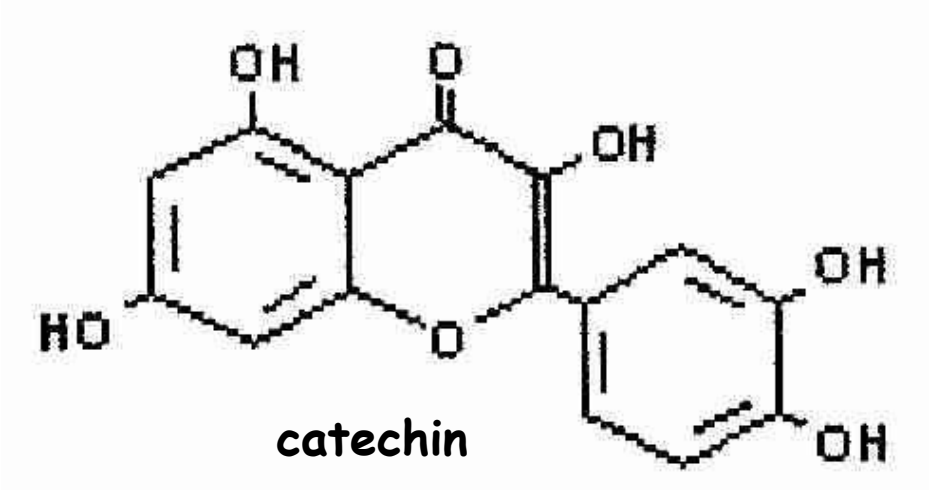
Using:

-anemia
-pregnancy
-for the stimulation of regeneration
-for the increase of immunity



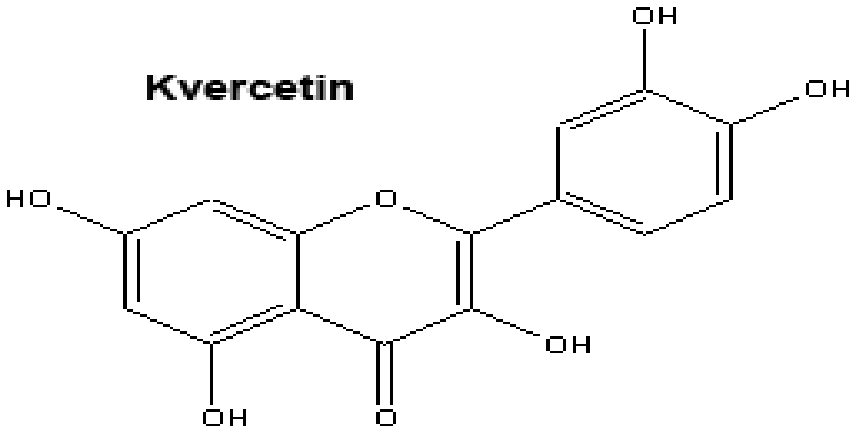
Vitamin P (biophlavonoids, factor of permeability)

Structure –
compounds having phenolic structure



catechin

Representatives:
-catechin
-rutin
-kvercetin
-hesperidin



Kvercetin

Biological role:

-synergist of vitamin C
-protects vitamin C against oxidation
-hydroxylation of proline and lysine
-inhibit hyaluronidase
-prevent oxidation of epinephrine
-antioxidants

Hypovitami-nosis:

-petechiae
-symptoms of scurvy

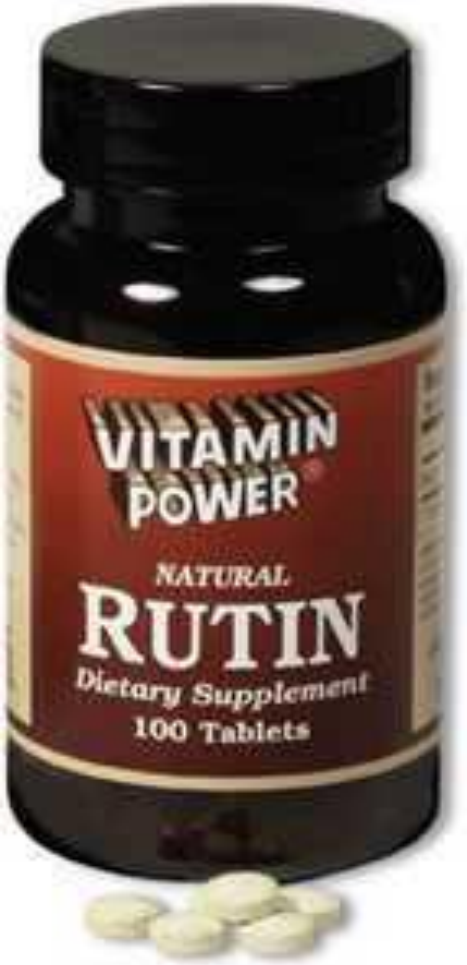
Daily requirement: 50-75 mg

Food: pepper, citrus, black currant, rowan, buckwheat, fruits



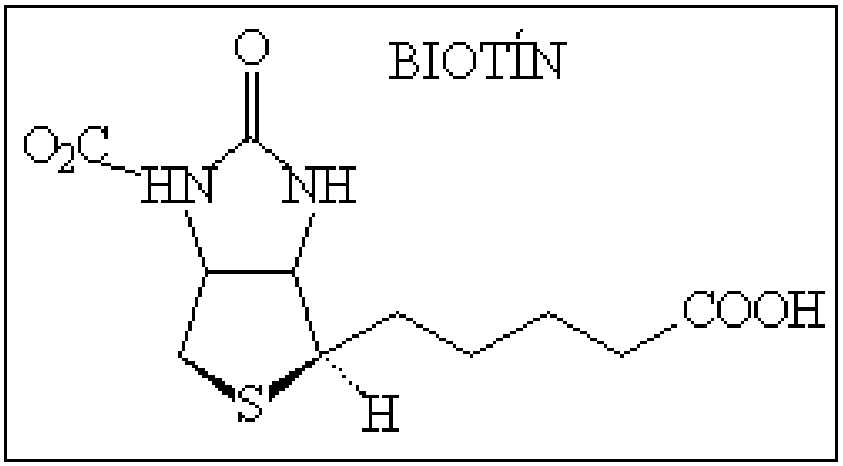



Is used to make capillaries stronger



Vitamin H (biotin, antiseborheic)

Structure –
consists of tiophen, imidazol and valeric acid



Coenzyme of carboxylase, serves as transporter of carboxylic group
-Pyruvate carboxylase – gluconeogenesis
-Acetyl-CoA carboxylase, propionyl-CoA carboxylase – lipid metabolism

Hypovitaminosis almost does not occur
Can be in malabsorption, disbacteriosis, using of large amount of eggs white (contains **avidin**)

Avidin – glycoprotein that irreversibly binds biotin - **antivitamin**

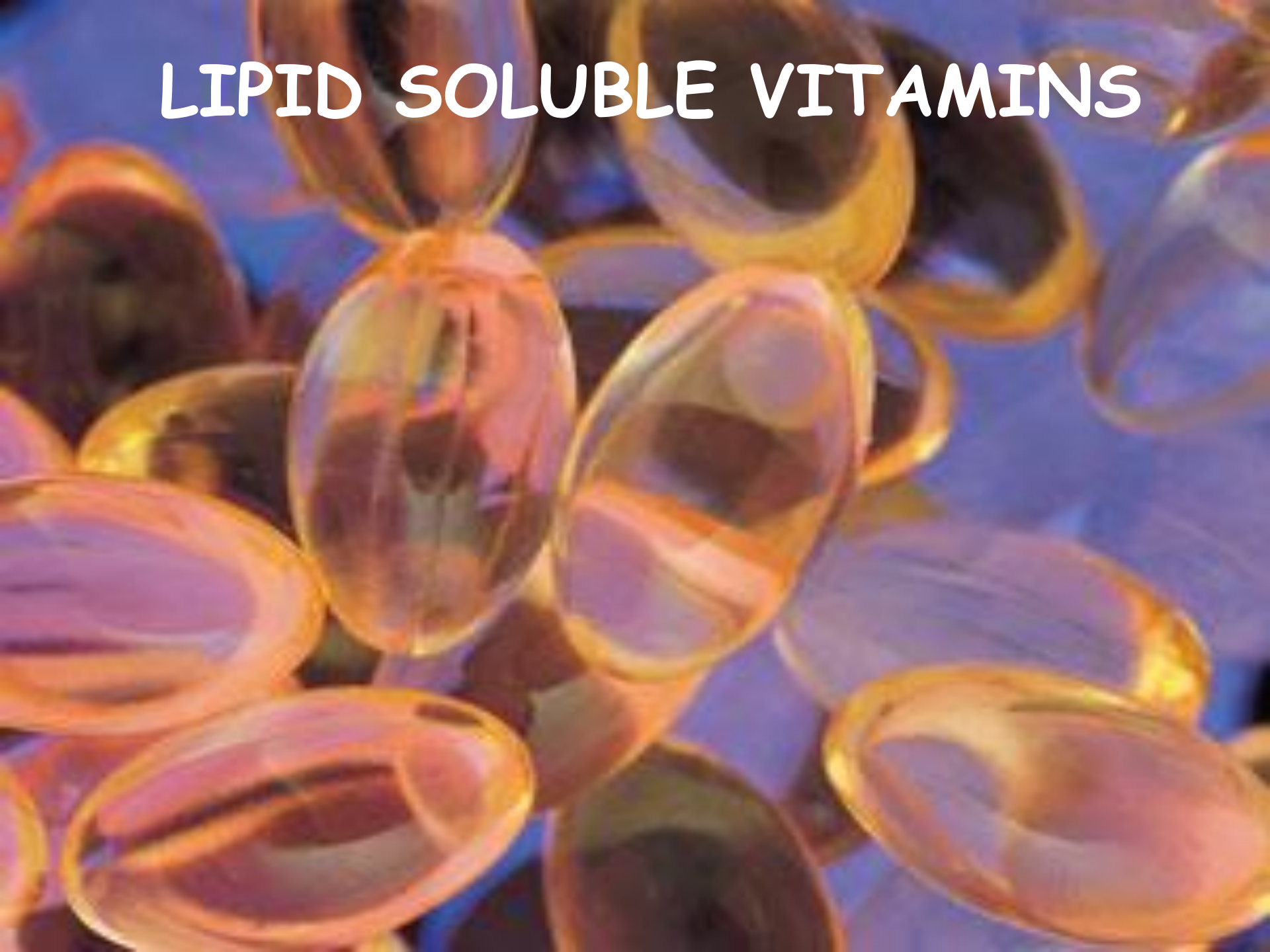
Symptoms:

-seborrheic dermatitis of the hair part of head
-conjunctivitis
-anemia
-depression

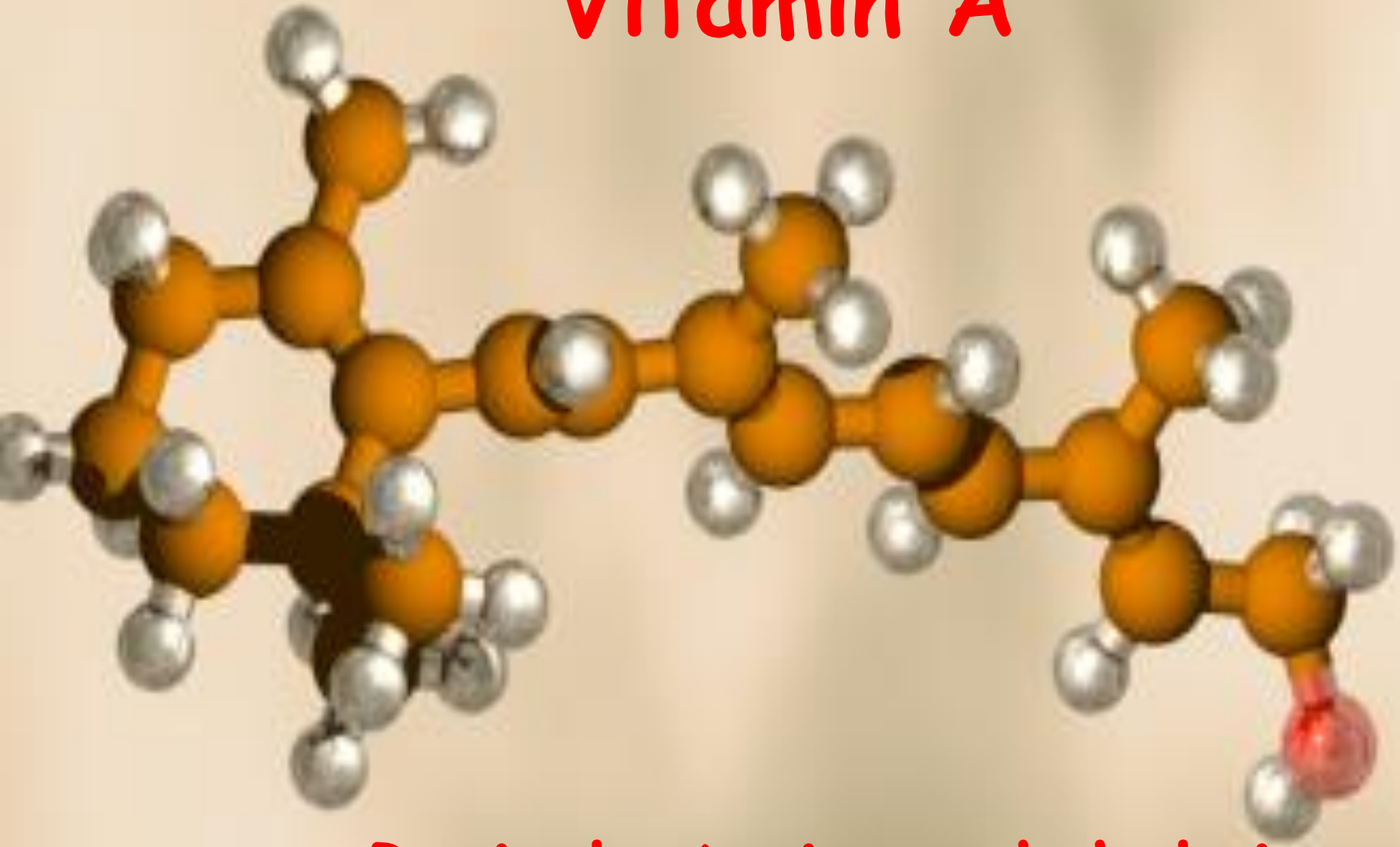
Seborrheic dermatitis

Daily requirement: 150-200 mg
Food: liver, soybeans, egg yolks, mushrooms, beans, onion, spinach

LIPID SOLUBLE VITAMINS



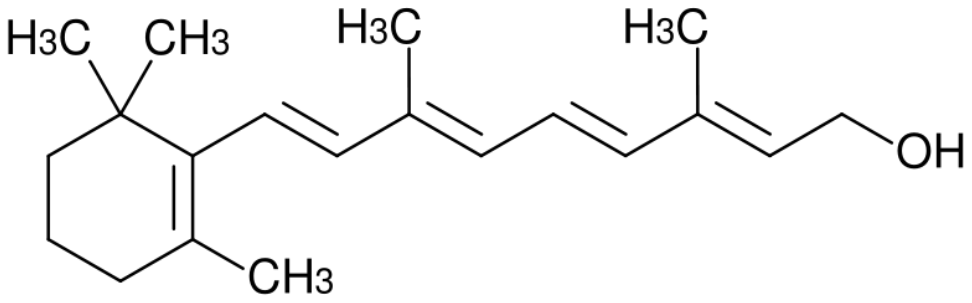
Vitamin A

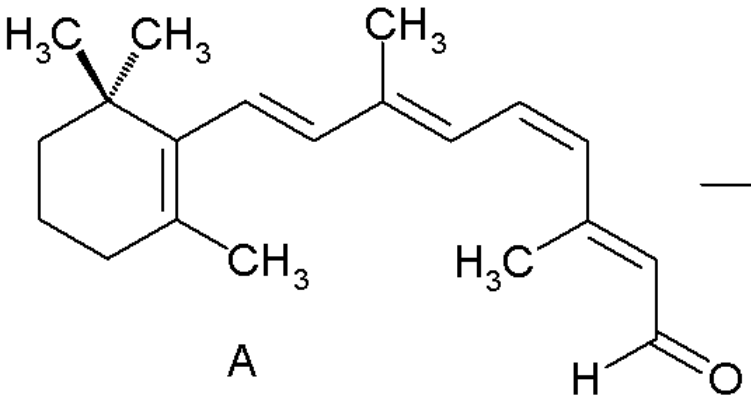


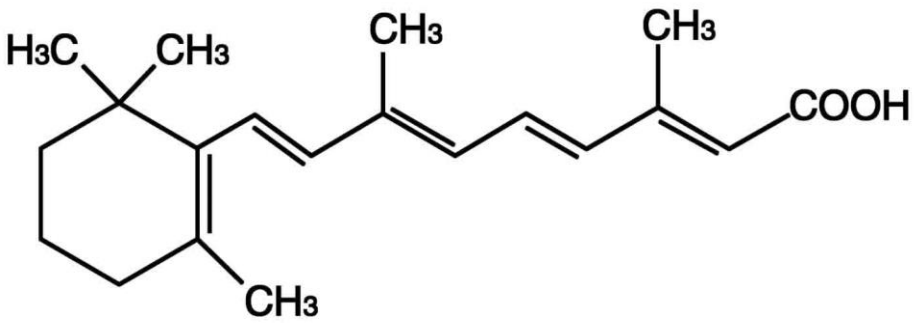
Retinol. Antixerophthalmic

Active forms

- Retinol
- Retinal
- Retinoic acid

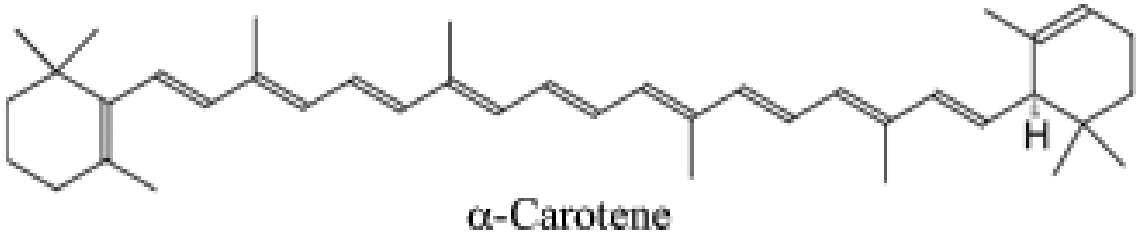




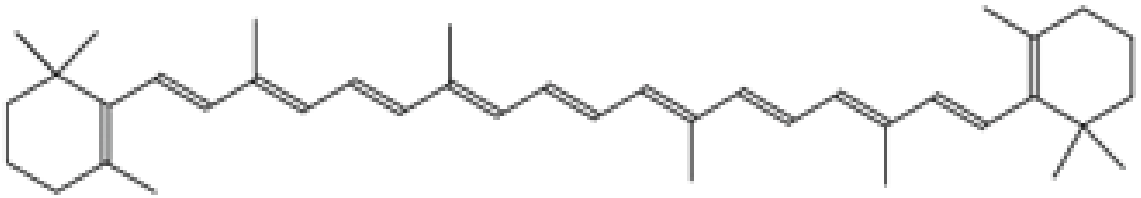


Precursors - carotenoids

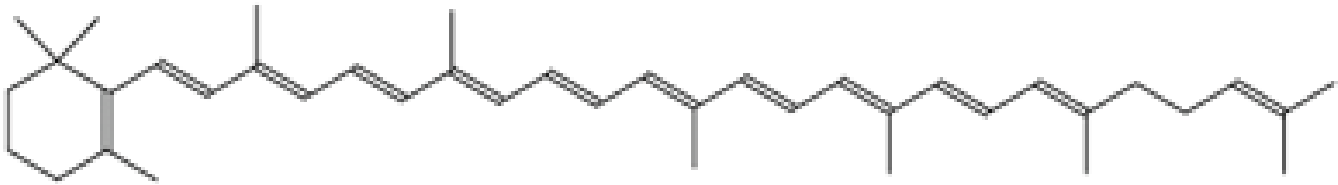
- Most important - beta-carotene
- Are cleaved to retinol in liver



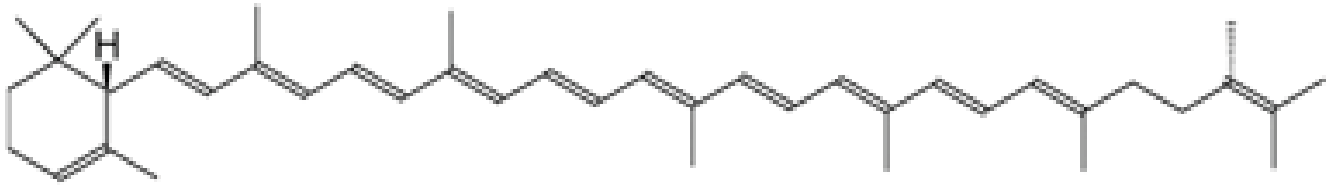
α-Carotene



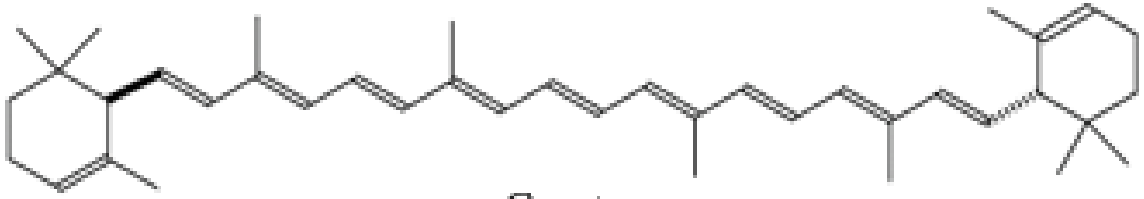
β-Carotene



γ-Carotene



δ-Carotene



ε-Carotene

Dark green and yellow vegetables are good sources for carotenoids: tomatoes, carrots, apricots, parsley, corn, radish

Organism gets $\frac{1}{4}$ of vit. A from carotenoids

Biological functions of carotenes

- Antioxidants
- Anticancer properties

Biological functions of vitamin A

- **Modulator of biomembranes**

-changes the permeability

-synthesis of membranes components

- **Growth vitamin**

-stimulates the synthesis of proteins (especially in cartilages)

-stimulates the synthesis of purine and pyrimidine nucleotides

- **Participates in oxidation-reduction reactions**

Biological functions of vitamin *A*

- Regulates the synthesis of *keratin* (prevents the conversion of cylindrical epithelium into horny
- Promotes the spermatogenesis and placenta development
- Stimulates the synthesis of antibodies and phagocytosis (antiinfectious)

Biological functions of vitamin A

Regulates the hormonal status

-prevents the oxidation of vitamin C

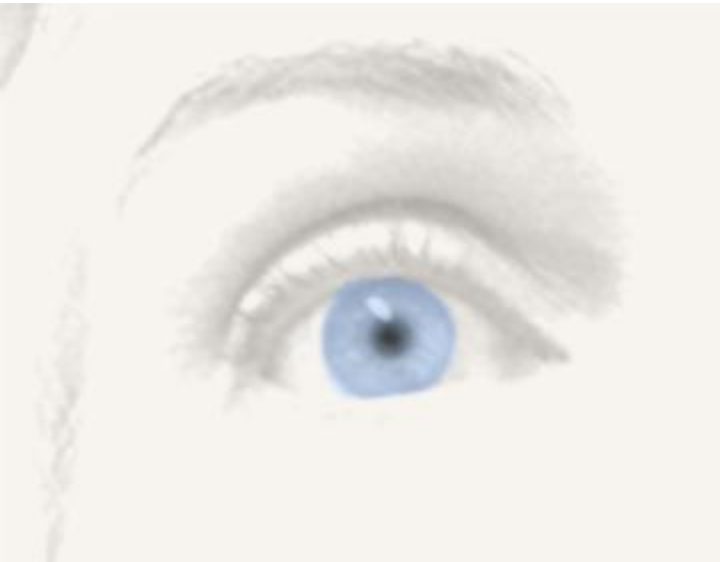
-inhibits the synthesis of thyroxin

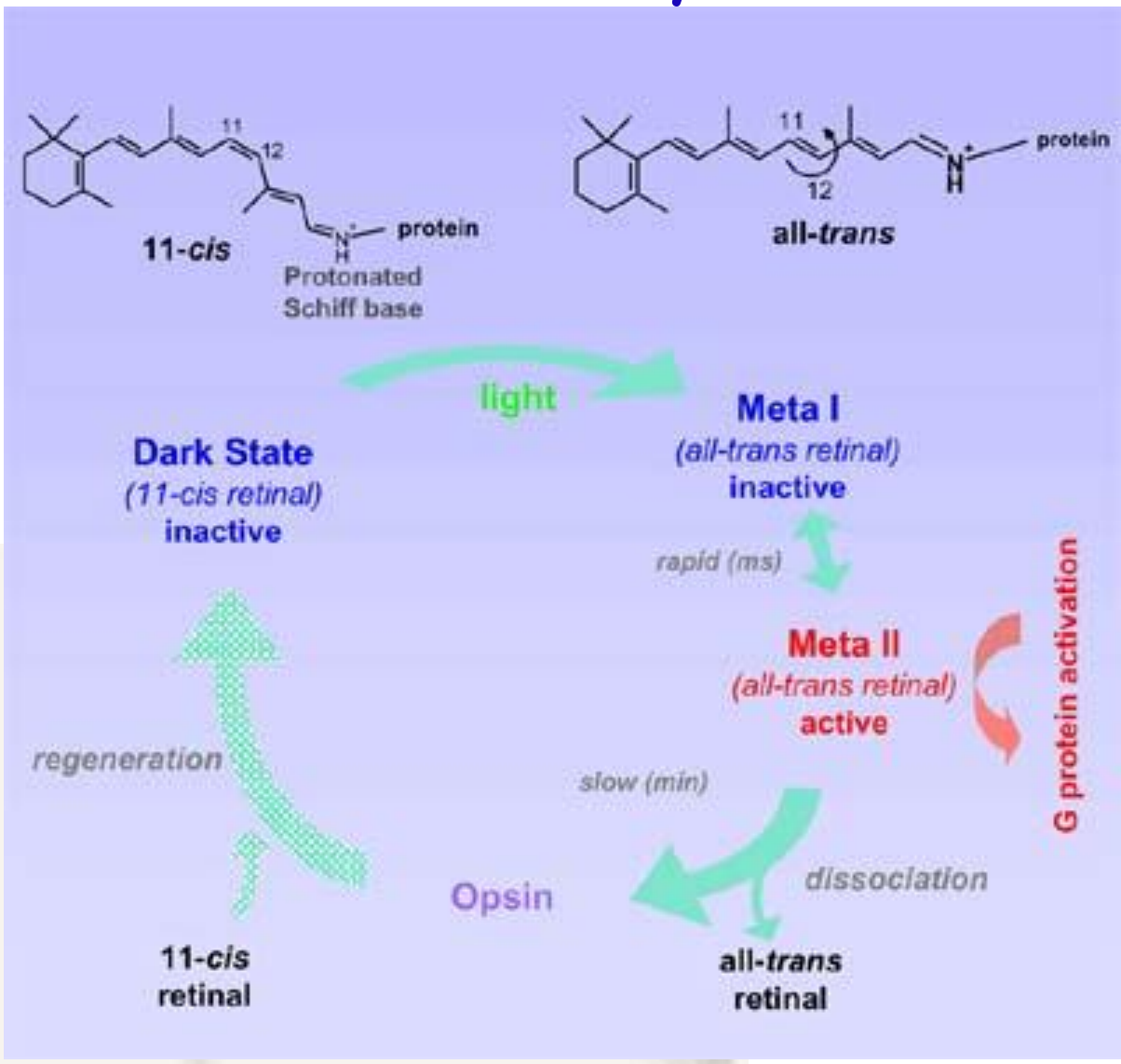
- **Maintains the antioxidant potential of different tissues**

Biological functions of vitamin A

Is responsible for the vision cycle

Night blindness
– early symptom of vitamin A deficiency



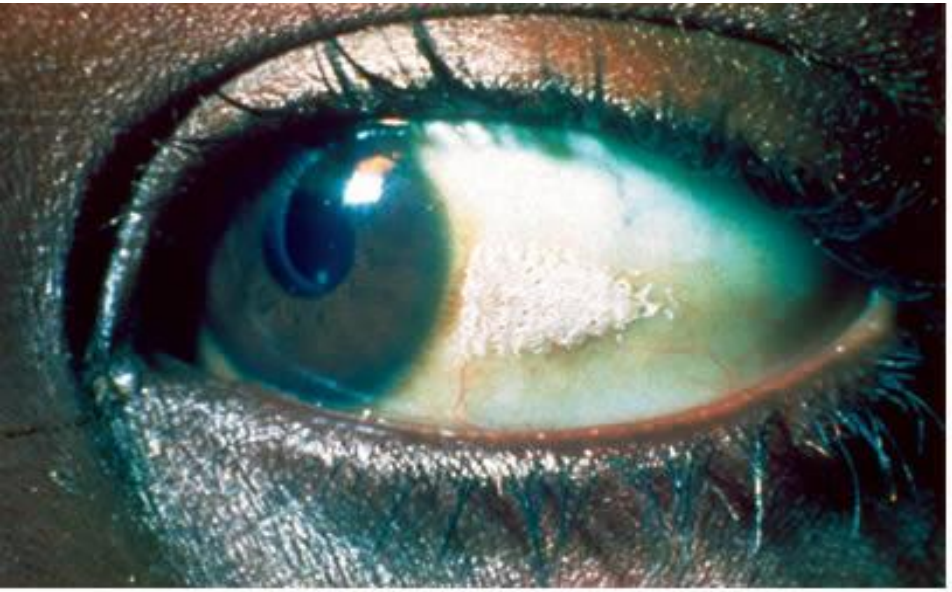


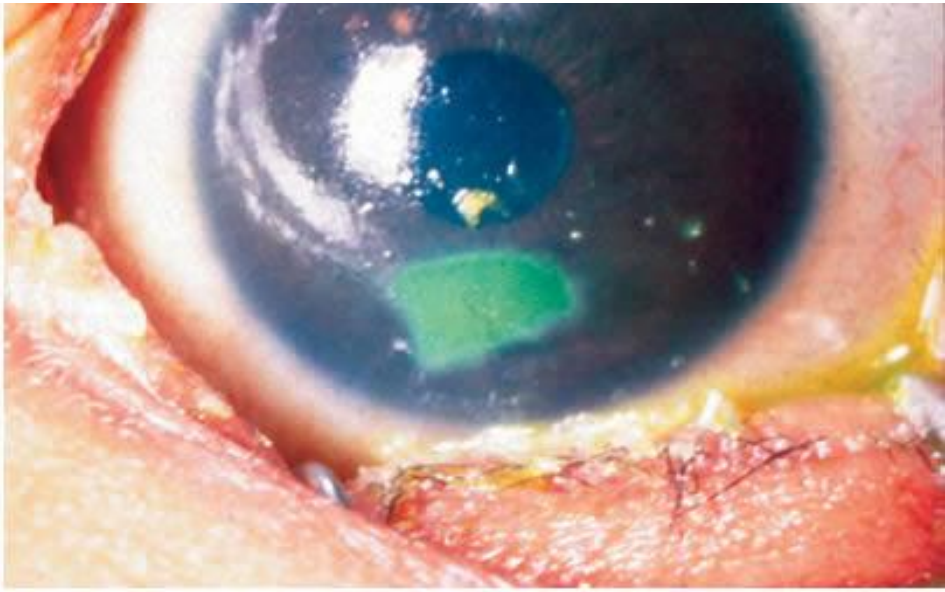
Later symptoms of vitamin A deficiency

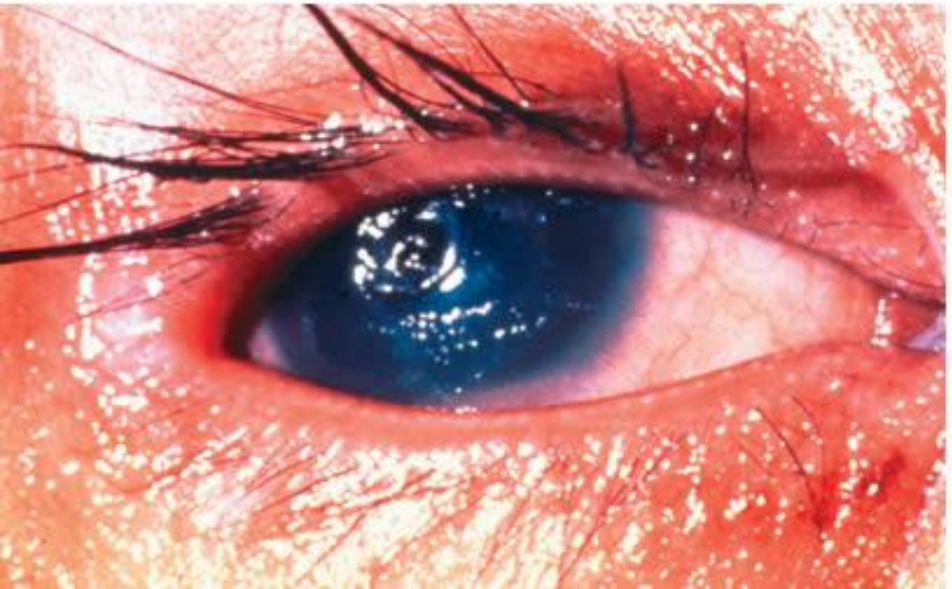
Anemia (vit. A is required for the synthesis of transferrin)
Increased susceptibility to infection and cancer
Follicular hyperkeratosis ("goosebumps" skin)

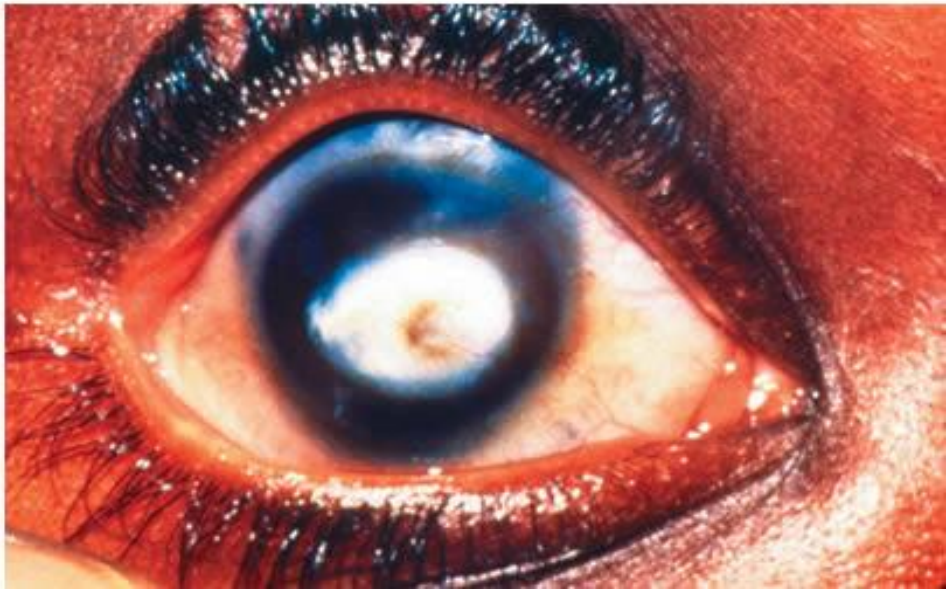
The most cosmetic creams contain retinol

Xerophthalmia (progressive keratinization of cornea)



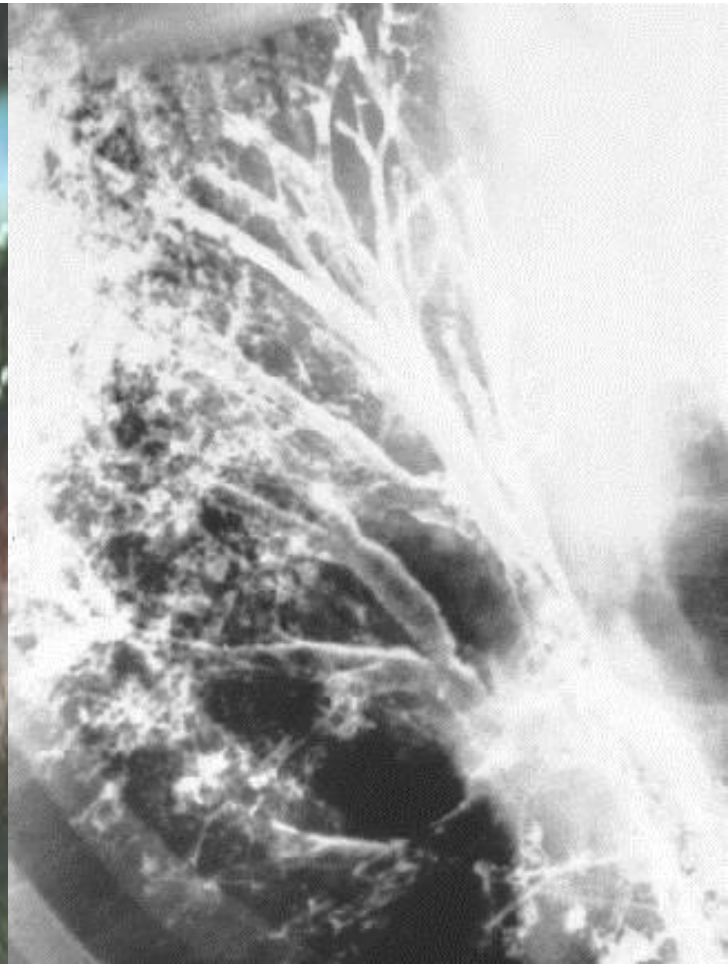




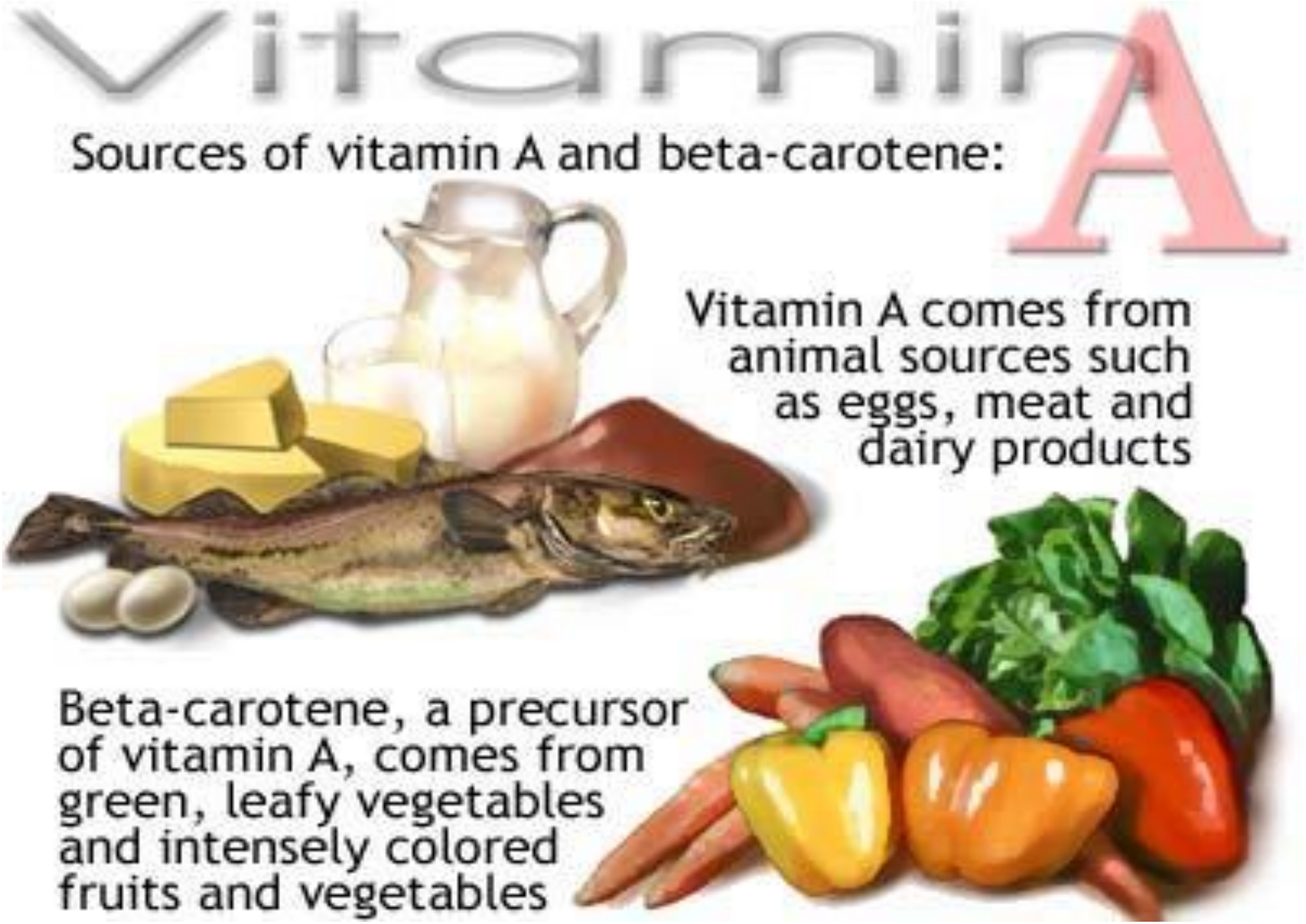


Keratomalacia (corneal ulcerations)

Bronchitis, pneumonia (metaplasia of endothelium)
Cysts in salivary glands
Cystitis, pyelonephritis (change of endothelium in nephrones)



Daily requirement: 2-3 mg



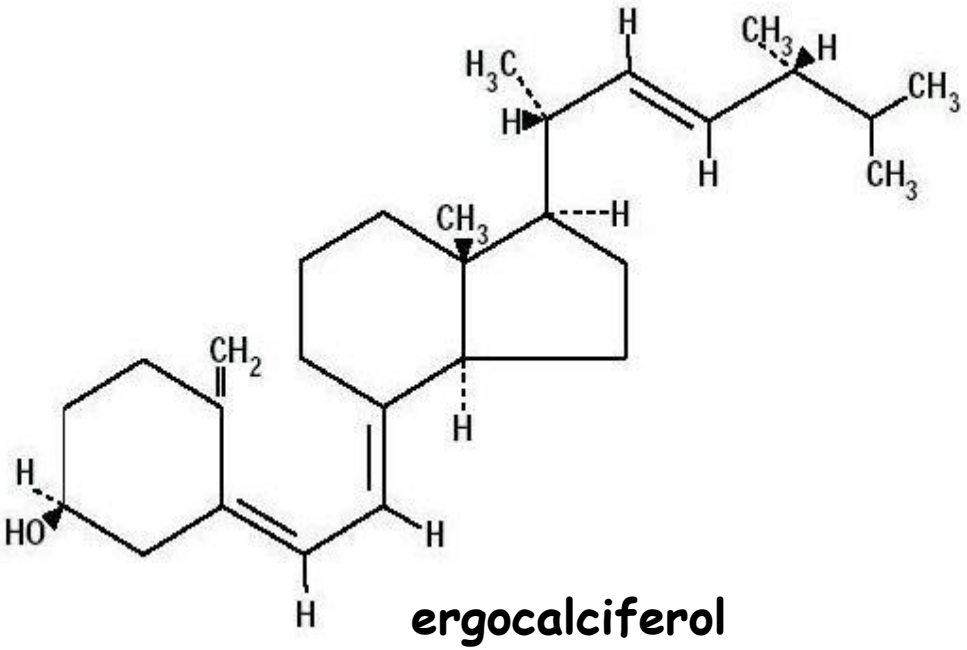
Hypervitaminosis

- Accumulates in liver
- In overdosing in treatment, consumption a large amount of fish oil, liver of polar animals
- Symptoms:
  - bone pain
  - vomiting, diarrhea
  - liver and spleen enlargement
  - dermatitis
  - loss of hair

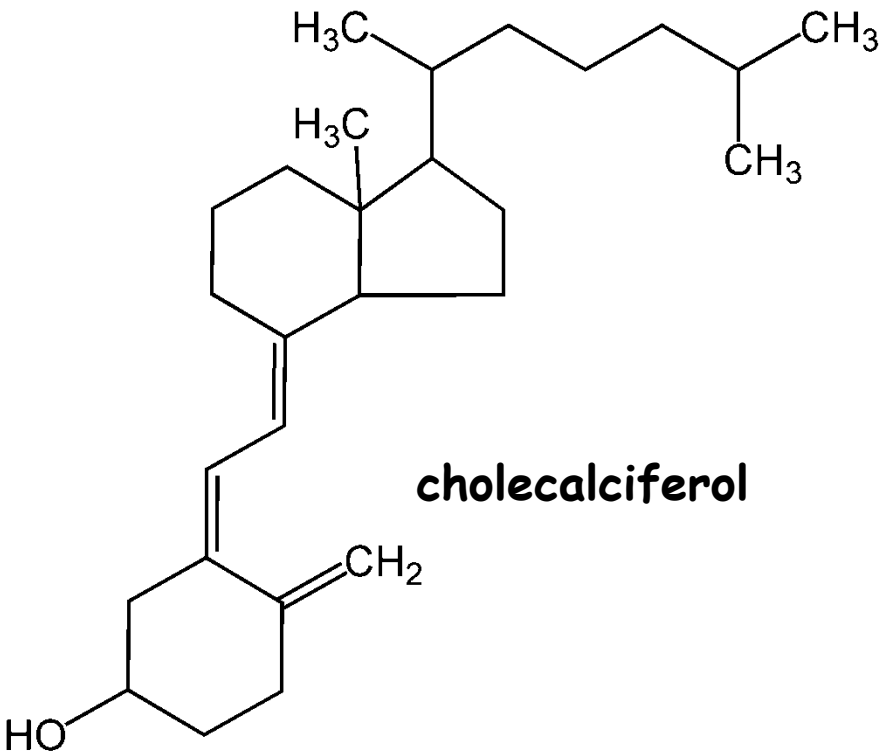
Vitamin D (cholecalciferol, antirickets)

Two forms of vitamin D

- Vitamin D2 – ergocalciferol
- Vitamin D3 - cholecalciferol

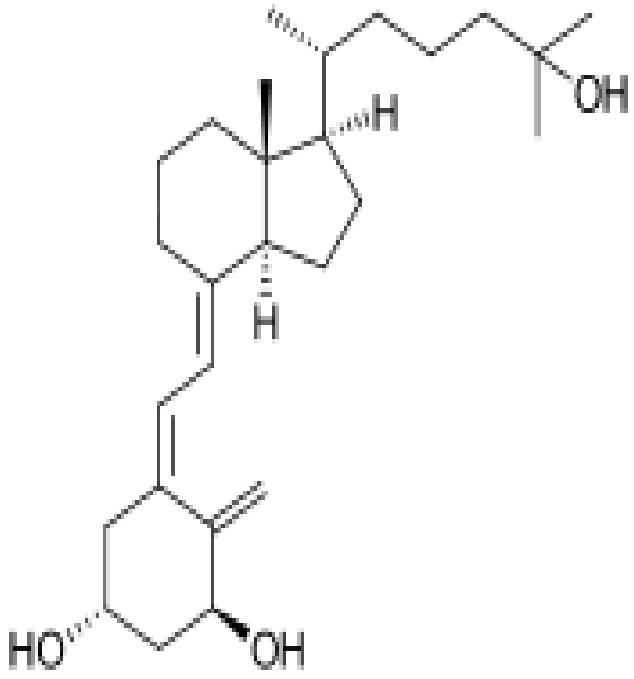


ergocalciferol

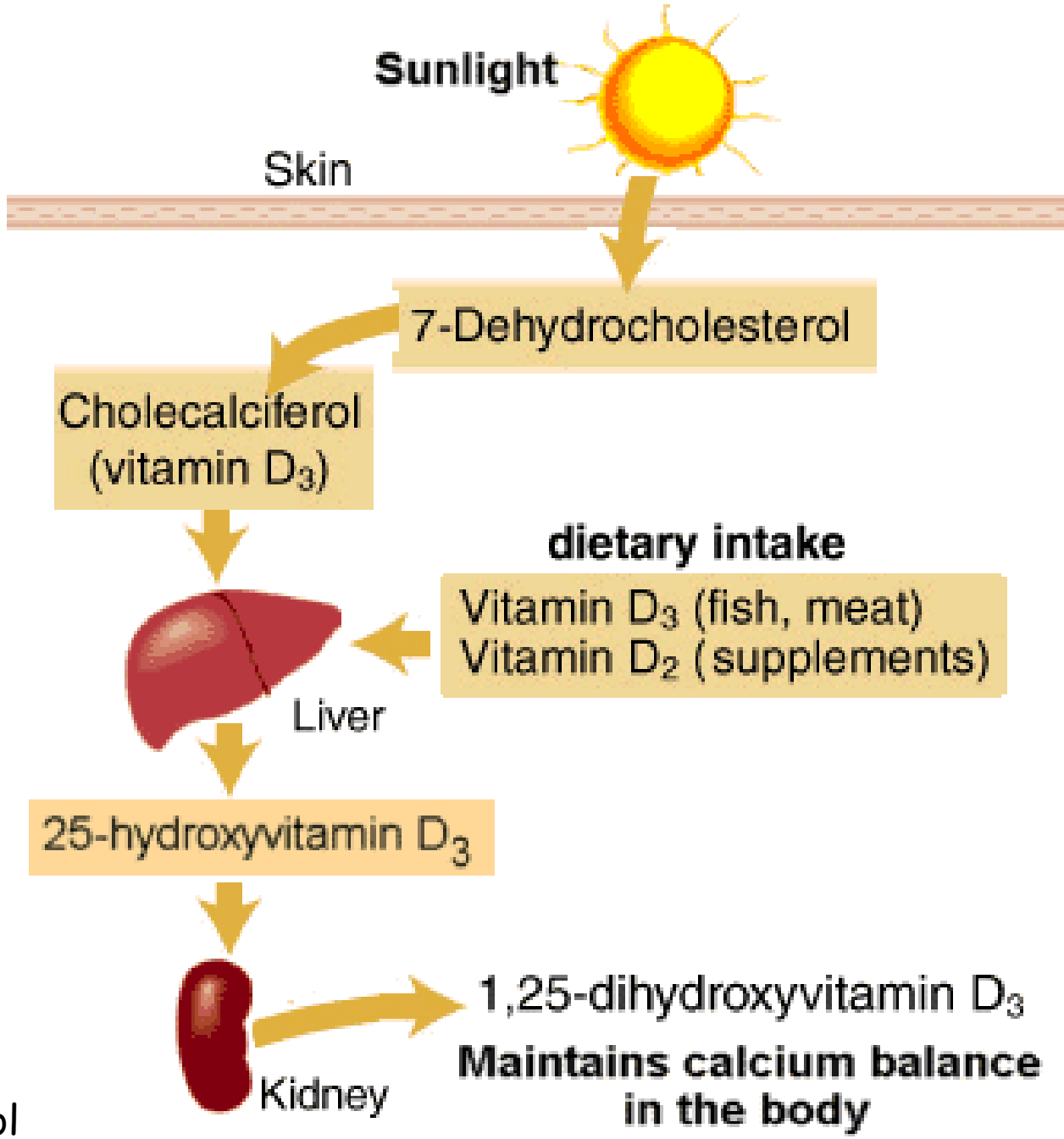


cholecalciferol

Both ergo-calciferol and cholecalciferol are metabo-lized in liver

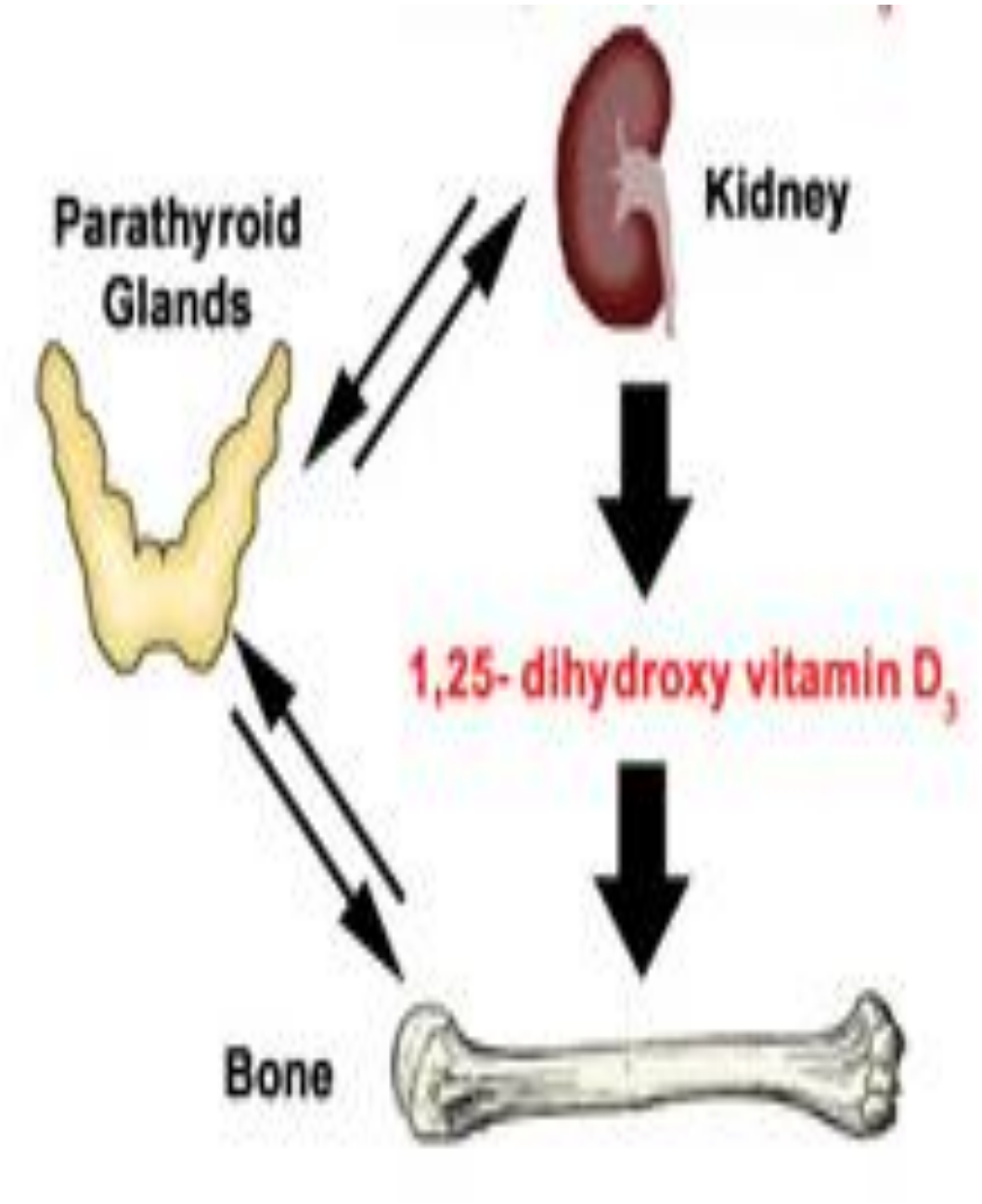


1,25-dihydroxycholecalciferol



Vit.D acts in concert with parathyroid hormone (PTH)

PTH stimulates the production of $1,25\text{-}(OH)_2D$



Functions of vitamin D

regulates the Ca and P levels in the blood

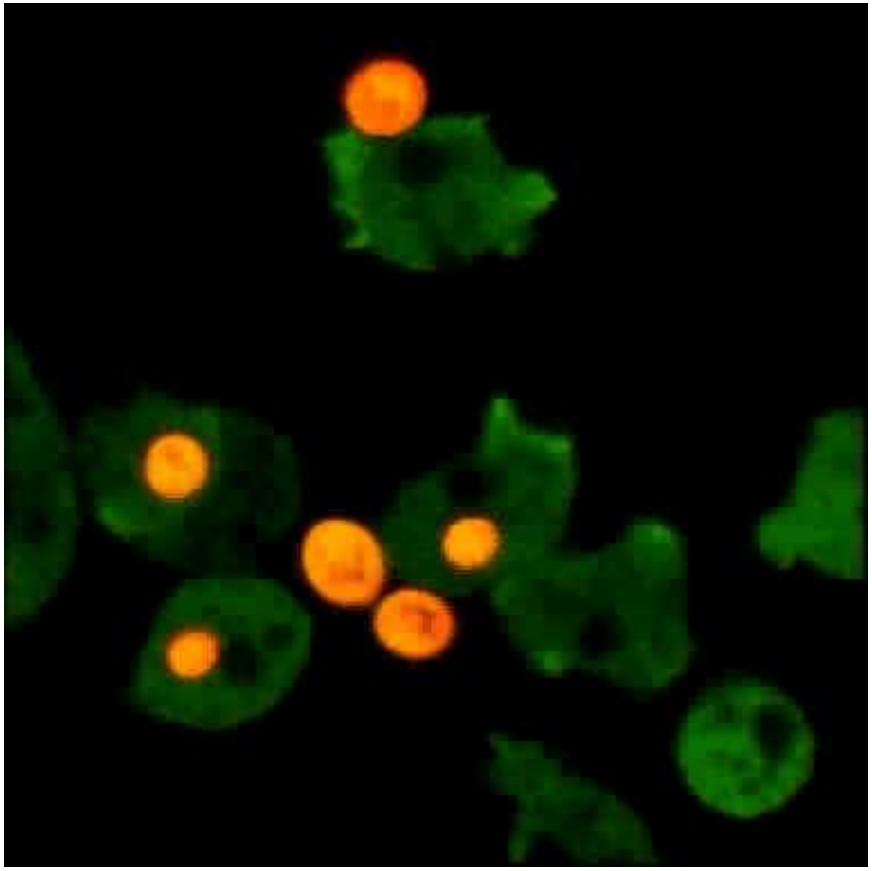
- promotes absorption of Ca and P in the intestine
- promotes reabsorption of Ca in the kidneys
- high levels of serum Ca and P increase the rate of bone mineralization
- promote bone resorption (at low Ca in blood)

Functions of vitamin D
affects immune system

- promotes phagocytosis

- immunomodu-latory activity

- induces differentiation of immune cells



Functions of vitamin D
prevents tumorgenesis

- inhibits proliferation
- inhibits angiogenesis
- induces differentiation

Functions of vitamin D

- Activates reabsorption of amino acids, especially prolin
- Activates the monosaccharides phosphorylation (glycogen synthesis)
- Promotes ATP formation

Rickets

softening of bones in children potentially leading to fractures and deformity

Causes:

- vitamin D deficiency
- lack of calcium in the diet (famine)
- severe diarrhea and vomiting
- fat malabsorption
- alcoholism
- severe liver and kidney diseases

Signs and symptoms of rickets

- Bone pain or tenderness
- Dental problems
- Muscle weakness
- Fractures (easily broken bones)
- Skeletal deformity
  - Bowed legs (genu varum)
  - Knock-knees (genu valgum) or "windswept knees"
  - Cranial, spinal, and pelvic deformities
- Hypocalcemia
- Tetany (uncontrolled muscle spasms)
- Craniotabes (soft skull)
- Widening of wrist (due to metaphysial cartilage hyperplasia)


Windswept deformity


Knock knee deformity (genu valgum)

Dietary sourses

vitamin D

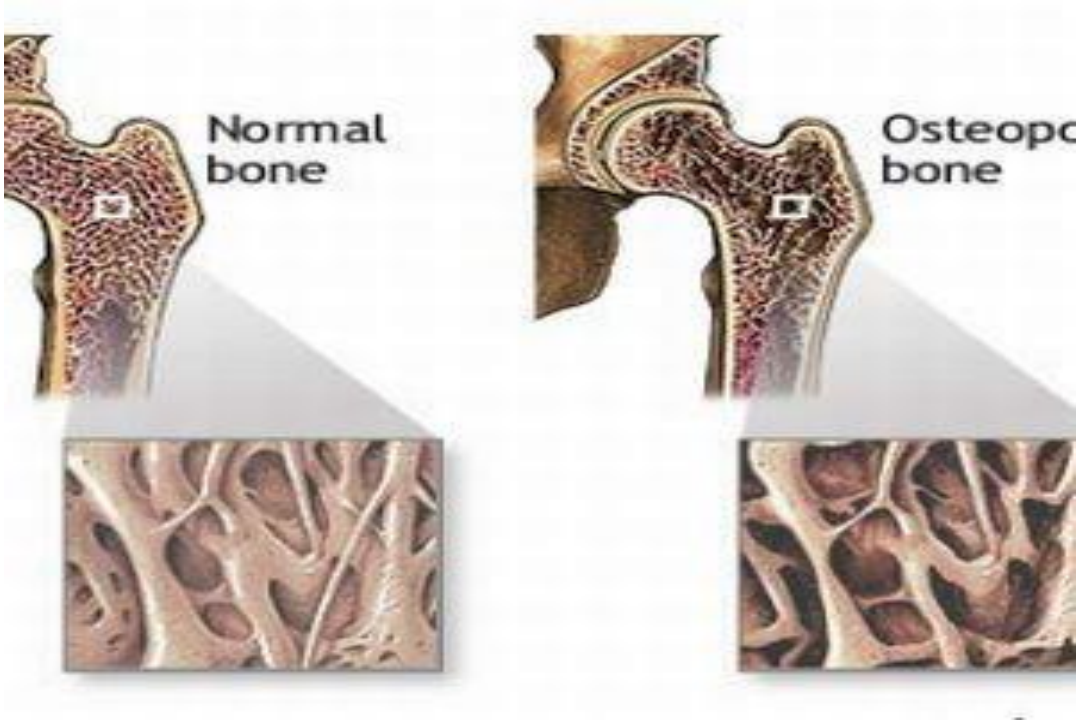
The body itself makes vitamin D when it is exposed to the sun

Cheese, butter, margarine, fortified milk, fish and fortified cereals are food sources of vitamin D

Hypervitaminosis

- Increase of Ca and P in blood
- Demineralization of bones

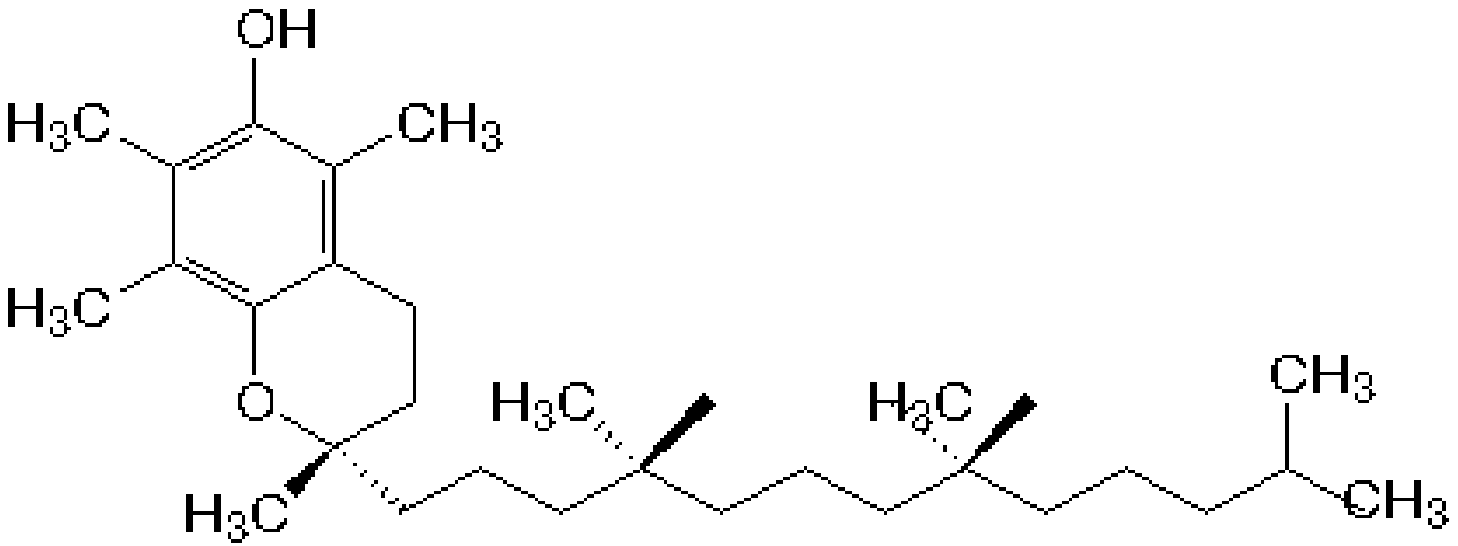
- Calcification of inner organs
- Renal stones



Vitamin E

Tocopherols and tocotrienols. Antisterile

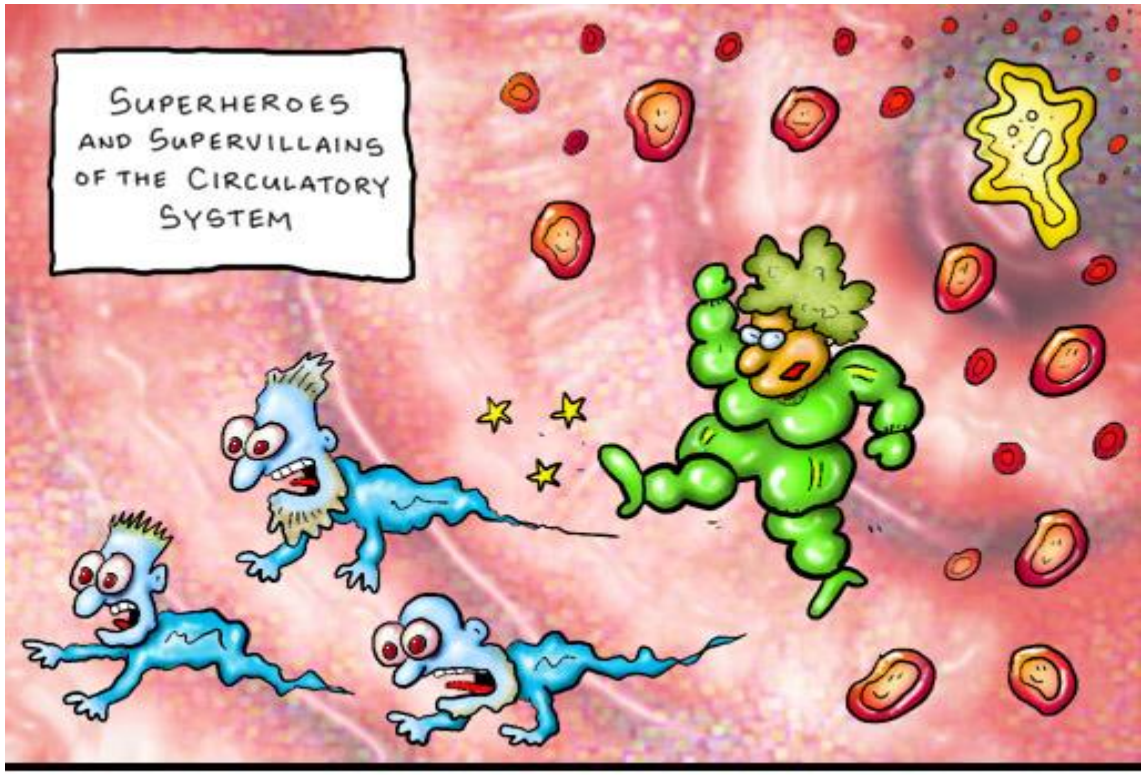
- Group of tocopherols and tocotrienols
- Most active – **alpha-tocopherol**



Vitamin E (α-tocopherol)

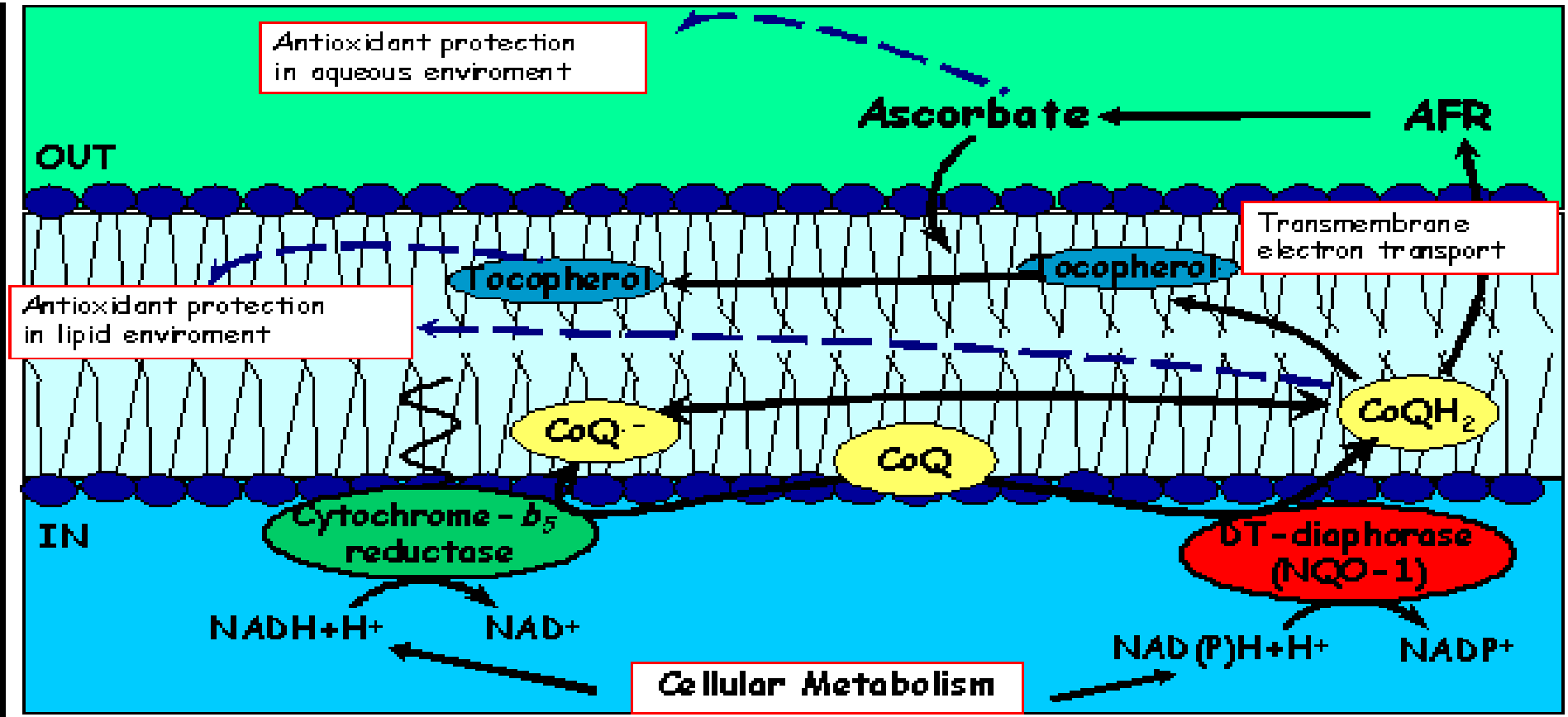
Biological role

- Most potent **antioxidant**
- Active scavenger of free oxygen and nitrogen radicals
- Protects vit. A from oxidation
- Prevents oxidation of Se

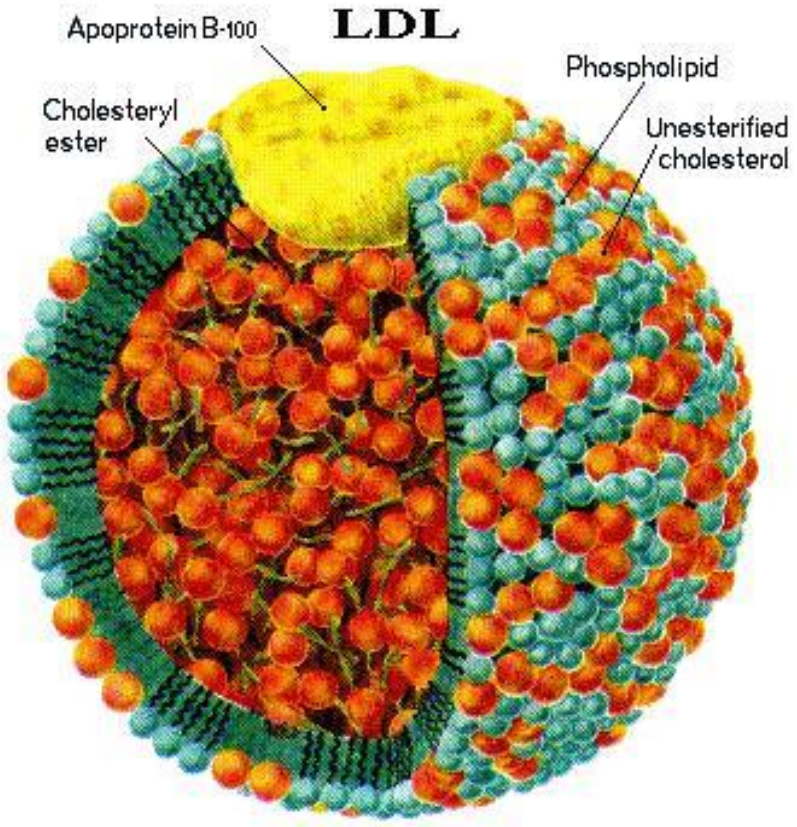


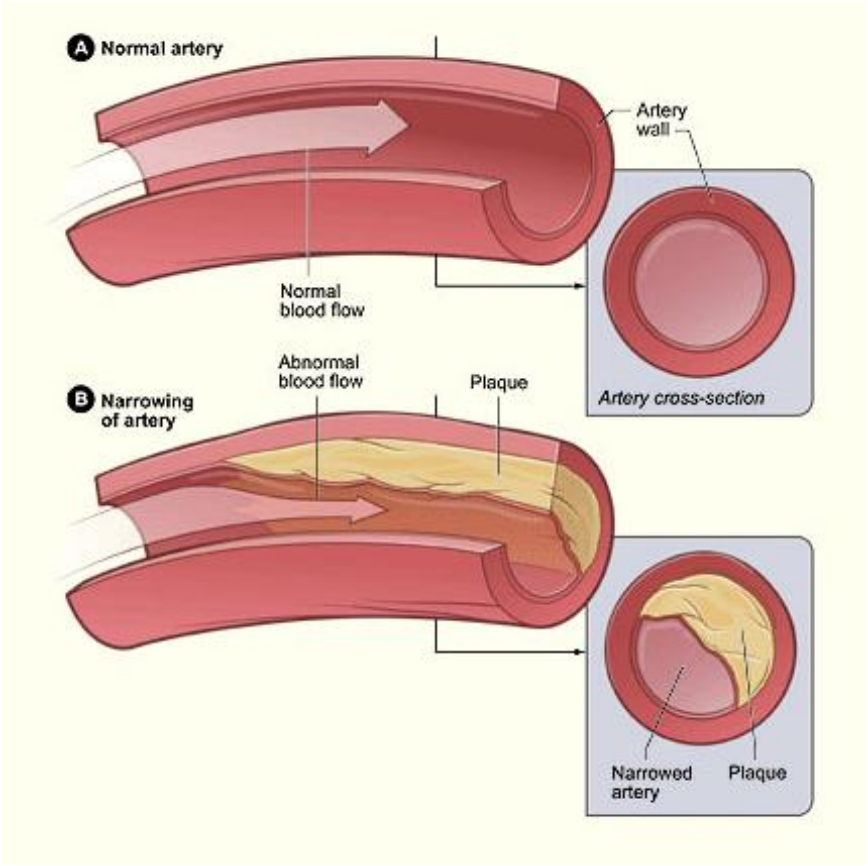
Auntie Oxidant kicks out the Free Radicals.

- Stabilizes the cell membranes
- Increases the resistance of membranes to oxidation and toxic effects
- Improves cellular respiration stabilizing ubiquinone

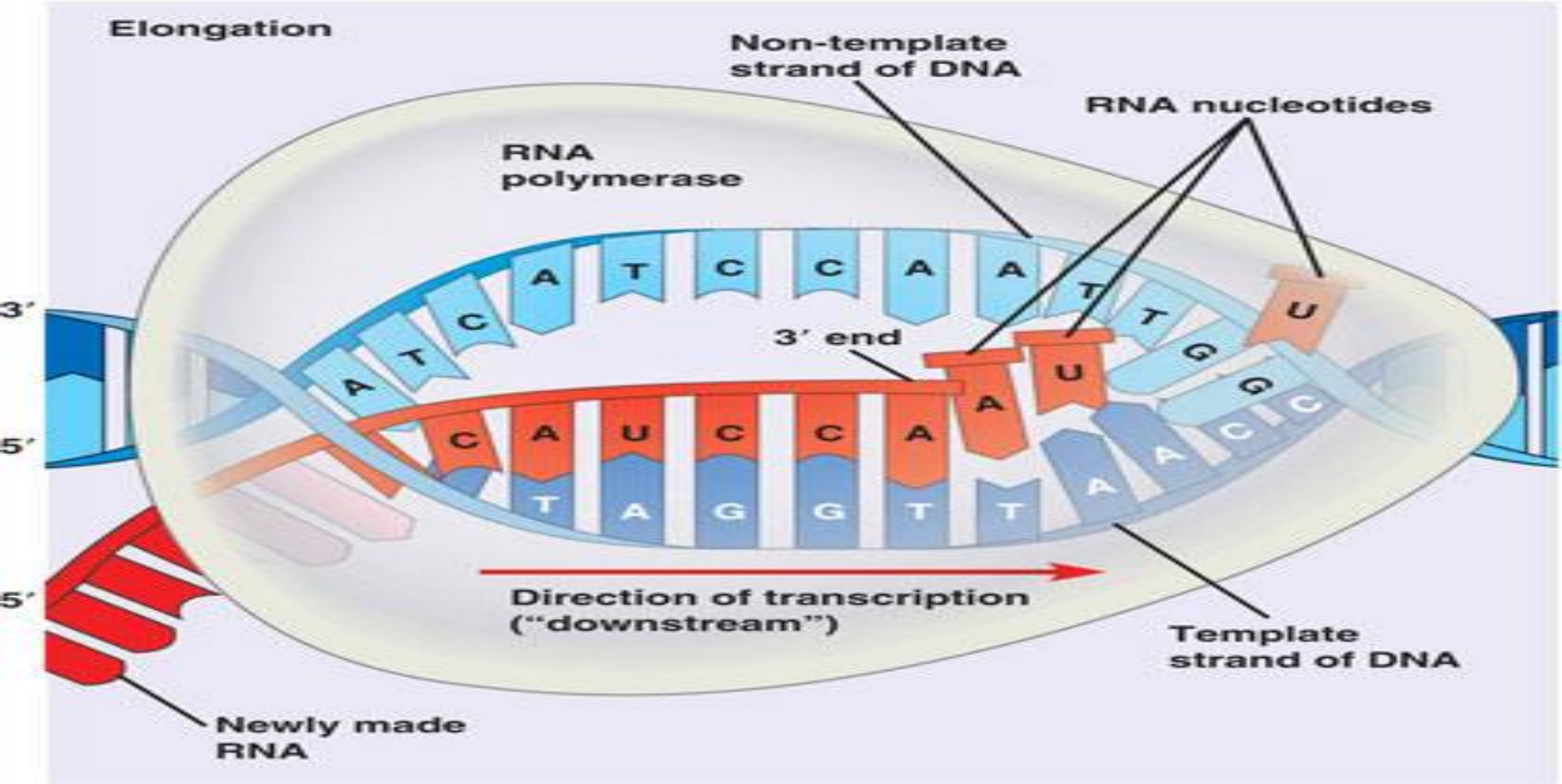


- Prevents oxidation of LDL
- Reduces risk of atherosclerosis





- Regulates transcription
- Maintains normal immune function
- Inhibits cholesterol biosynthesis



Hypovitaminosis

- Causes: malabsorption, famine
- Symptoms:
  - Activation of FRO
  - Increase of membrane permeability
  - Hemolysis of erythrocytes
  - Deficit of ATP
  - Muscle dystrophy (creatinuria)
  - Demyelization of nerves (CNS changes)
  - Disorders of reproductive function (atrophy of testis, azoospermia, inability to implantation)

Daily requirement: 20-50 mg

Vitamin E is found in corn, nuts, olives, green, leafy vegetables, vegetable oils and wheat germ, but food alone cannot provide a beneficial amount of vitamin E, and supplements may be helpful

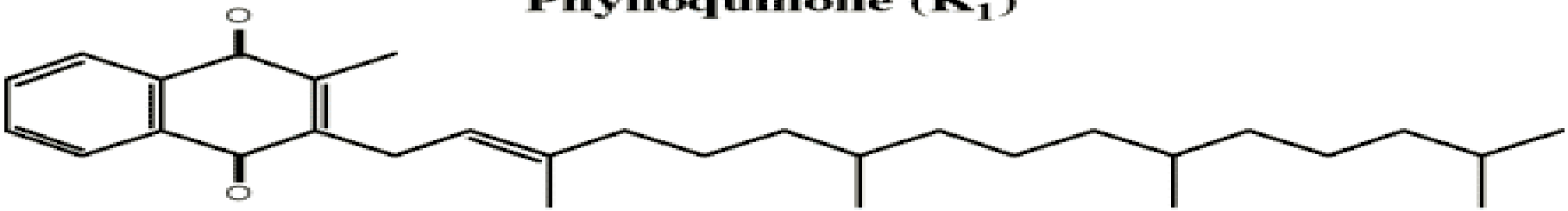
Using:

- Cardiovascular diseases
- Stimulation of immunity
- Tumors
- Miscarriages

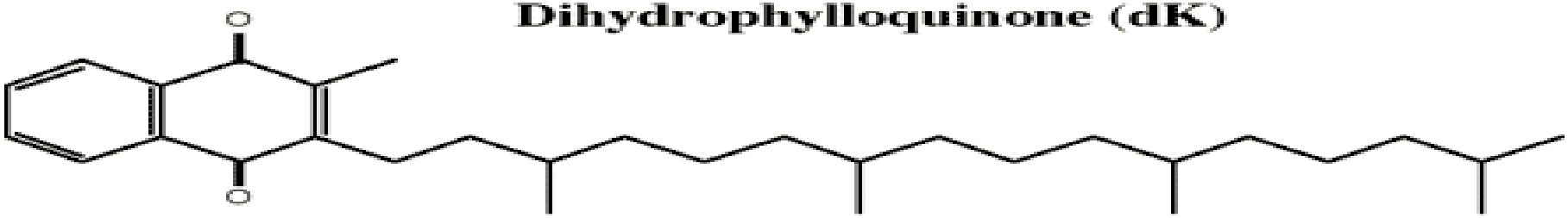

Vitamin K
Quinone derivatives
Antihemorrhagic

K1, phyloquinone (in green vegetables)
K2, menaquinone (is synthesized by intestinal bacteria)

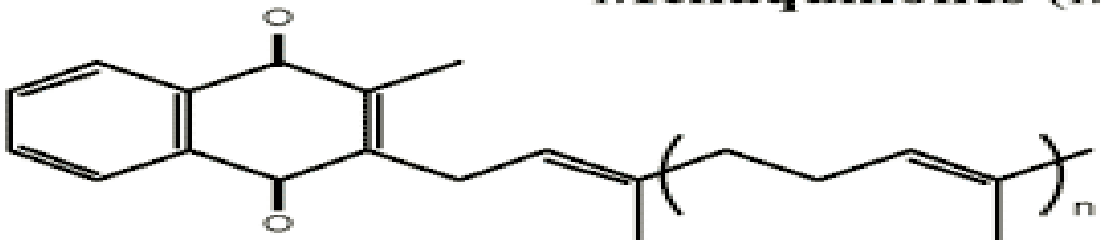
Phylloquinone (K_1)



Dihydrophylloquinone (dK)



Menaquinones (MK-n)



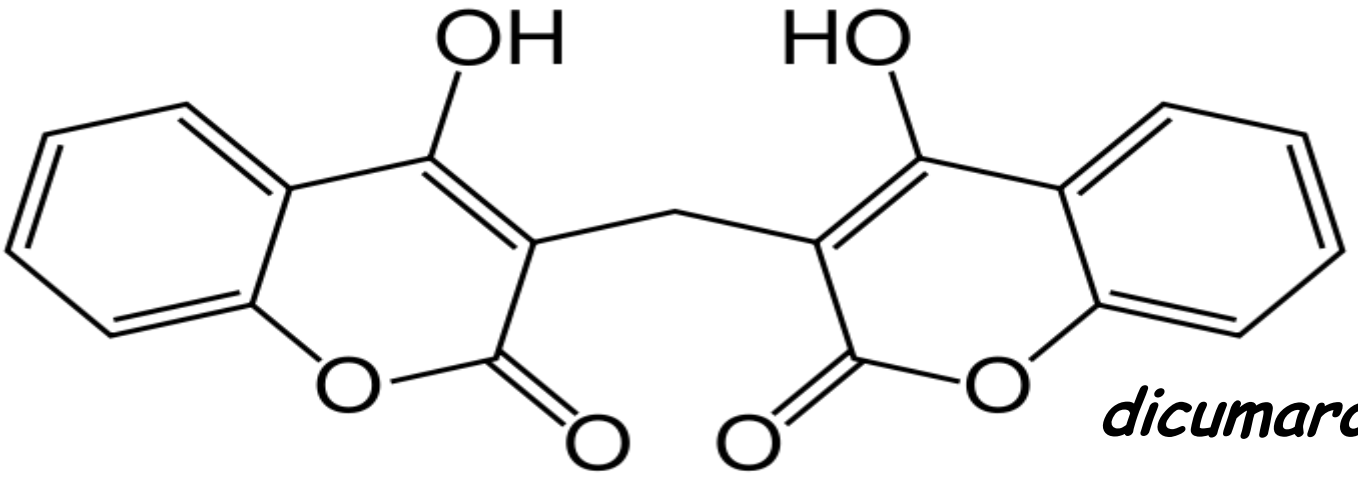
Biological functions

- Stimulates the synthesis of coagulation factors in liver
- Increases the resistance of capillaries
- Stimulates the synthesis of albumins, pepsin, trypsis, lipase, amilase
- Increases the peristalsis of intestine
- Inhibits free radical oxidation

Hypovitaminosis

Causes:

- Lipids malabsorption (lack of bile acids)
- Disbacteriosis (vit. K is synthesized by intestinal microflora)
- Taking of antivitamins (*dicumarol*)

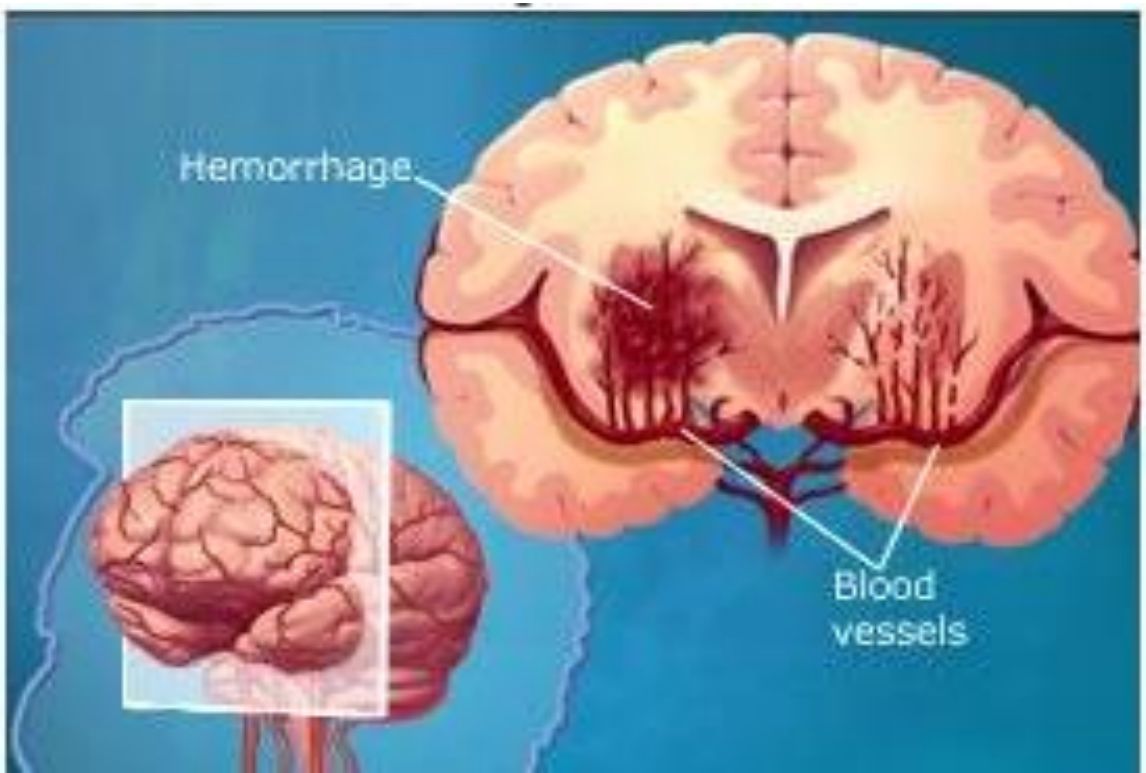


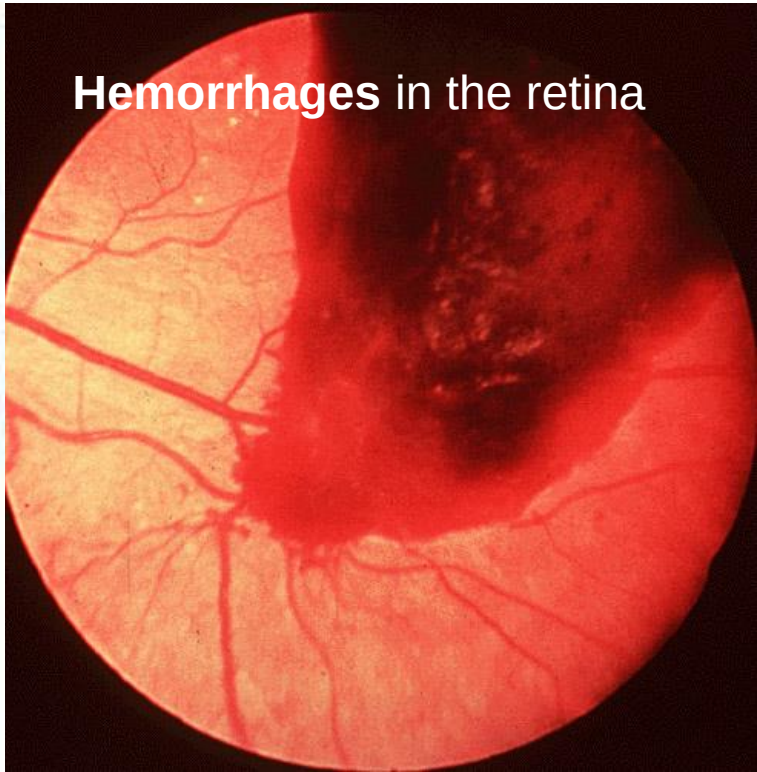
dicumarol

Hypovitaminosis

Symptoms:

- Hemorrhages (subcutaneous, intramuscular, into inner organs)
- Increased coagulation time





Daily requirement: 0.2-0.3 mg

Vitamin K

Food sources of vitamin K include cabbage, cauliflower, spinach and other green, leafy vegetables, as well as cereals

Vikasol

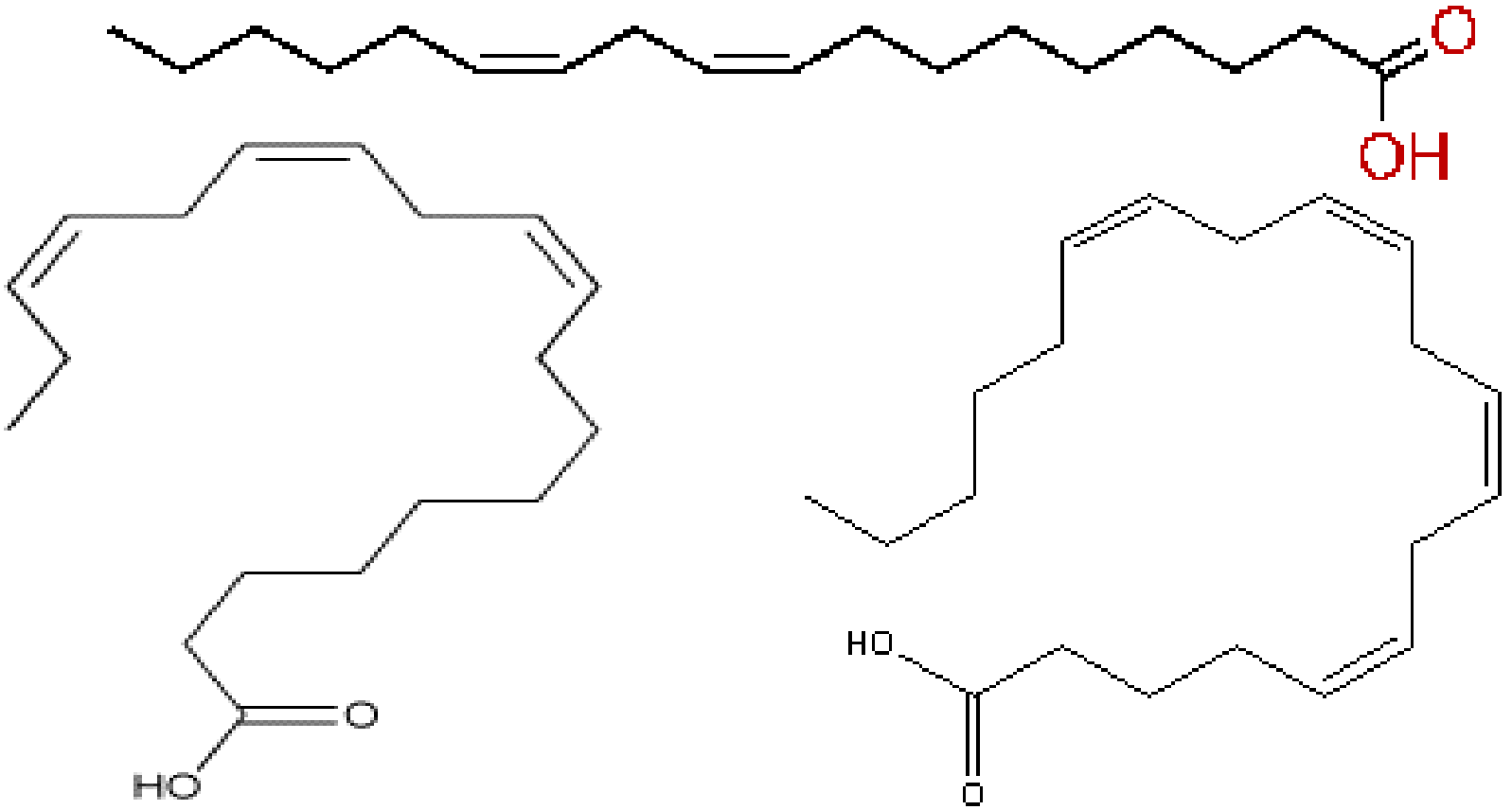
- Water soluble analog of vit. K
- Is used to stop bleeding
- Can be administered parenterally

Vitamin F

Polyunsaturated fatty acids

Antisclerotic

Linoleic acid
Linolenic acid
Arachidonic acid



Biological functions

- Participate in the organism growth and development
- Components of phospholipids (cell membranes)
- Regeneration of skin epithelium
- Synthesis of prostaglandins
- Decrease cholesterol level
- Increase the organism resistance

Hypovitaminosis

Causes:

- Growth retardation
- Dermatitis
- Dry skin
- Exema
- Atherosclerosis

Daily requirement: 10-15 g

Minerals

- minerals are elements of the periodic table
- more than 25 have been isolated
- 21 elements have been shown to be essential (excluding C,H, and O)
- minerals make up about 4 to 5% of body weight (for a 70 kg individual: 2.8 kg)
- many minerals are found in ionic form (others as ligands or covalent compounds)

Minerals

- Two categories:
  - macrominerals > 0.005%
  - microminerals < 0.005%
- macrominerals are essential at levels of 100mg or more per day for human adults
- microminerals are often referred to as trace elements

Functions of minerals

- provide a suitable medium for cellular activity
  - permeability of membranes
  - irritability of muscles and nerve cells
- play a primary role in osmotic phenomenon
- involved in acid base-balance
- confer rigidity and hardness to certain tissues (bones and teeth)
- become part of specialized compounds

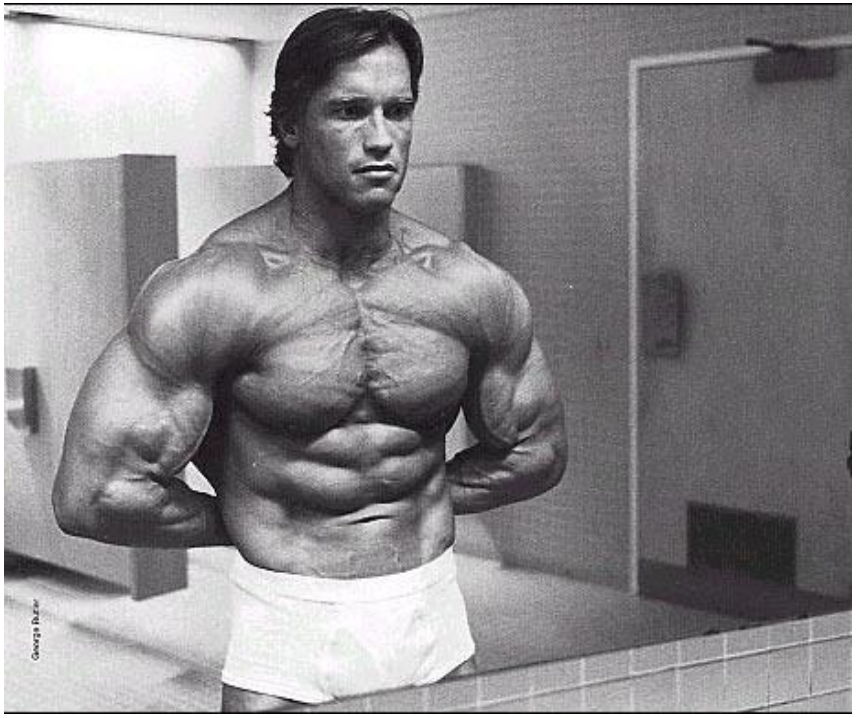
Macronutrients

Mineral	Content* (g)	Major source	Daily requirement (g)	Functions/Occurrence
Macroelements (daily requirement >100 mg)				
Na	100	Table salt	1.1-3.3	Osmoregulation, membrane potential, mineral metabolism
K	150	Vegetables, fruit, cereals	1.9-5.6	Membrane potential, mineral metabolism
Ca	1 300	Milk, milk products	0.8	Bone formation, blood clotting, signal molecule
Mg	20	Green vegetables	0.35	Bone formation, cofactor for enzymes
Cl	100	Table salt	1.7-5.1	Mineral metabolism
P	650	Meat, milk, cereals, vegetables	0.8	Bone formation, energy metabolism, nucleic acid metabolism
S	200	*S*-containing amino acids (Cys and Met)	0.2	Lipid and carbohydrate metabolism, conjugate formation

- The important microelements in human nutrition are zinc, copper, selenium, chromium, molybdenum, manganese, iodine, and iron. Although they only represent a small fraction of the human body's total mineral content, they play important roles in various metabolic routes.

- Preterm babies can present with deficiencies, even without clinical signs, due to low concentrations of the elements at birth because these minerals are only incorporated in the last trimester of pregnancy.

Micronutrients



- Iron (Fe)
- Copper (Cu)
- Zinc (Zn)
- Boron (B)
- Molybdenum (Mo)
- Manganese (Mn)

Micronutrients

Mineral	Content* (g)	Major source	Daily requirement (g)	Functions/Occurrence
Microelements (trace elements)			(mg	
Fe	4-5	Meat, liver, eggs, vegetables, potatoes, cereals	10	Hemoglobin, myoglobin, cytochromes, Fe/S clusters
Zn	2-3	Meat, liver, cereals	15	Zinc enzymes
Mn	0.02	Found in many foodstuffs	2-5	Enzymes
Cu	0.1-0.2	Meat, vegetables, fruit, fish	2-3	Oxidases
Co	<0.01	Meat	Traces	Vitamin B_{12}
Cr	<0.01		0.05-0.2	Not clear
Mo	0.02	Cereals, nuts, legumes	0.15-0.5	Redox enzymes
Se		Vegetables, meat	0.05-0.2	Selenium enzymes
I	0.03	Seafood, iodized salt, drinking water	0.15	Thyroxin
Requirement not known				Metals Non-metals
F		Drinking water (fluoridated), tea, milk	0.0015-0.004	Bones, dental enamel

Zinc supplements

Zinc

- Biological roles
  - Involved in many enzymes (over 20 metalloenzymes)
    - Carbonic anhydrase
    - Carboxypeptidase A
      - Four types of proteases
        - » Serine
        - » Cysteine
        - » Aspartic acid
        - » Zinc
    - ACE (angiotensin I convering enzyme)
    - RNA and DNA polymerases

Zinc

- zinc absorption appears to be dependent on a transport protein, metallothionein
- deficiencies include poor growth, delayed wound healing, impairment of sexual development and decreased taste acuit
- zinc is present in gustin, a salivary polypeptide that is necessary for the development of taste buds

Zinc

- severe zinc deficiency is seen primarily in alcoholics (especially if they have developed cirrhosis), patients with chronic renal disease or severe malabsorption diseases
- occasionally seen in patients on long term total parenteral nutrition (TPN) –patient develop a dermatitis
- zinc is occasionally used therapeutically to promote wound healing and may be of some use in treating gastric ulcers

Zinc Deficiency

Iron (Fe)

- 2 types of body iron
  - heme iron
    - hemoglobin, myoglobin, catalases, peroxidases, cytochromes (a, b and c – involved in electron transport), cytochrome P450 (involved in drug metabolism)
  - non-heme iron
    - ferritin, hemosiderin, hemofuscin, transferrin, ferroflavoproteins, aromatic amino acid hydroxylases
- food iron is also classified as heme and non-heme

Food iron

heme iron

- meats
- poultry
- fish

20-23% of heme-iron is absorbable

non-heme iron

- vegetables
- fruits
- legumes
- nuts
- breads and cereals

only ~ 3% on non heme iron is absorbed

Diagnosis of iron deficiency

- hematology (microcytic hypochromic cells)
- low serum iron
- low serum ferritin(indicates low body stores)
    - in some conditions (inflammation, hepatitis) ferritin may be high
- low hemosiderin
- high total iron binding capacity (TIBC)

Iron Deficiency

ANEMIA - DEFINITION

- REDUCTION OF HEMOGLOBIN CONCENTRATION BELOW REFERENCE VALUE

BLOOD PARAMETERS

- Hemoglobin concentration (Hg)
  - F: 7,2 –10; M: 7,8-11,3 mmol Fe/l (12-18 g/dl)
- Erythrocytes count (RBC)
  - F: 4-5,5; M: 4,5-6 x10^{12}/l (4-6 x10^{6} /μl)
- Hematocrit (Hct)
  - F: 37-47; M: 40-54; (37-54%)
- Platelet count (Plt)
  - 150 – 450 x 10^{3}/μl (150-450 x 10^{9}/l)
- Leukocytes count (WBC)
  - 4-10 x 10^{9}/l (4-10 x 10^{3}/ μl)

Erythrocytes parameters

- Mean corpuscular volume (MCV)
  - N: 80-100 fl
- RDW(Red cell Distrubution Width)
- Mean corpuscular hemoglobin (MCH)
  - N: 27-34 pg
- Mean corpuscular hemoglobin concentration (MCHC)
  - N: 310 – 370 g/lRBC (31-37 g/dl)

Reticulocytes

- RET: 0,5-2%
- ARC: 25-75x 10^9/l
- CRC
- RPI

IRON DEFICIENCY ANEMIA

- IRON METABOLISM
  - ABSORPTION IN DUODENUM
  - TRANSFERRIN TRANSPORTS IRON TO THE CELLS
  - FERRITIN AND HEMOSYDERIN STORE IRON
- 10% of daily iron is absorbed

- Most body iron is present in hemoglobin in circulating red cells
- The macrophages of the reticuloendotelial system store iron released from hemoglobin as ferritin and hemosiderin
- Small loss of iron each day in urine, faeces, skin and nails and in menstruating females as blood (1-2 mg daily)

IRON METABOLISM

- Iron concentration (Fe)
  - N: 50-150 μg/dl
- Total Iron Binding Capacity
  - N: 250-450 μg/dl
- Transferrin saturation
- Transferrin receptor concentration
- Ferritin concentration
  - N: 50-300 μg/l

IRON DEFICIENCY ANEMIA

- ETIOLOGY:
  - CHRONIC BLEEDING
    - » MENORRHAGIA
    - » PEPTIC ULCER
    - » STOMACH CANCER
    - » ULCERATIVE COLITIS
    - » INTESTINAL CANCER
    - » HAEMORRHOIDS
  - DECREASED IRON INTAKE
  - INCREASED IRON REQUIRMENT (JUVENILE AGE, PREGNANCY, LACTATION)

IRON DEFICENCY - STAGES

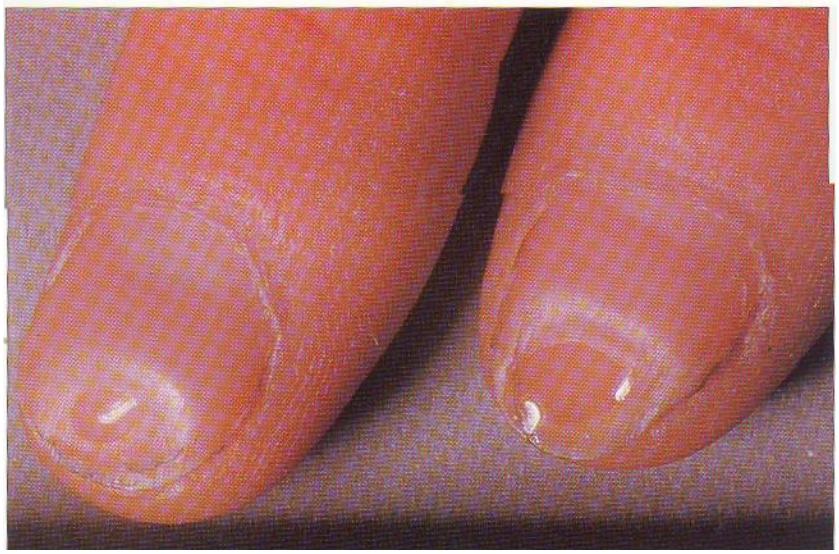
- Prelatent
  - reduction in iron stores without reduced serum iron levels
    - Hb (N), MCV (N), iron absorption (↑), transferin saturation (N), serum ferritin (↓), marrow iron (↓)
- Latent
  - iron stores are exhausted, but the blood hemoglobin level remains normal
    - Hb (N), MCV (N), TIBC (↑), serum ferritin (↓), transferrin saturation (↓), marrow iron (absent)
- Iron deficiency anemia
  - blood hemoglobin concentration falls below the lower limit of normal
    - Hb (↓), MCV (↓), TIBC (↑), serum ferritin (↓), transferrin saturation (↓), marrow iron (absent)

IRON DEFICIENCY ANEMIA

- GENERAL ANEMIA'S SYMPTOMS:
  - FATIGABILITY
  - DIZZENES
  - HEADACHE
  - SCOTOMAS
  - IRRITABILITY
  - ROARING
  - PALPITATION
  - CHD, CHF

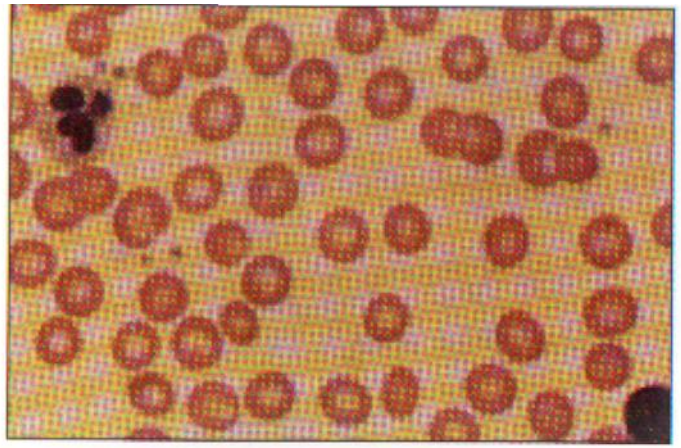
CHARACTERISTICS SYMPTOMS

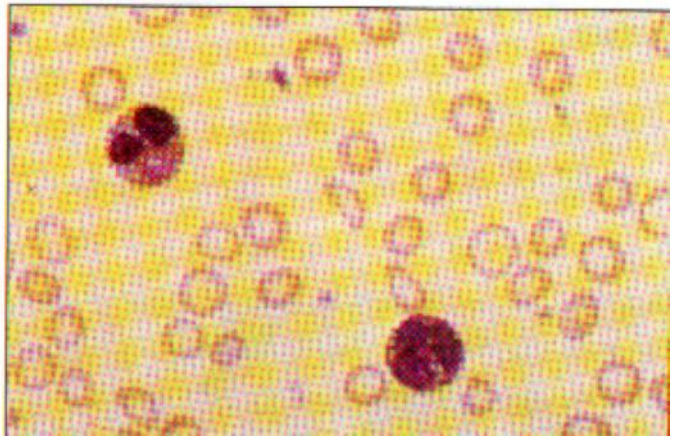
- GLOSSITIS, STOMATITIS
- DYSPHAGIA (Plummer-Vinson syndrome)
- ATROPHIC GASTRITIS
- DRY, PALE SKIN
- SPOON SHAPED NAILS, KOILONYCHIA,
- BLUE SCLERAE
- HAIR LOSS
- PICA (APETITE FOR NON FOOD SUBSTANCES SUCH AS AN ICE, CLAY)
- SPLENOMEGALY (10%)
- INCREASED PLATELET COUNT



BLOOD AND BONE MARROW SMEAR

- BLOOD:
  - microcytosis, hipochromia, anulocytes, anisocytosis poikilocytosis
- BONE MARROW
  - high cellularity
  - mild to moderate erythroid hyperplasia (25-35%; N 16 – 18%)
  - polychromatic and pyknotic cytoplasm of erythroblasts is vacuolated and irregular in outline (micronormoblastic erythropoiesis)
  - absence of stainable iron





Management

- History and physical examination is sufficient to exclude serious disease (e.g pregnant or lactating women, adolescents)

  - CURE ANEMIA

- History and/or physical examination is insufficient (e.g old men, postmenopausal women)

  - FIND ETIOLOGY OF ANEMIA AND CURE (CAUSAL TREATMENT)

    - Benzidine test
    - Gastroscopy
    - Colonoscopy
    - Gynaecological examination

ORAL IRON ABSORPTION TEST

1. baseline serum iron level
2. 200 - 400 mg of elemental iron orally
3. serum iron level 2-4 hours after ingestion

IRON DEFICIENCY ANEMIA CURE

- ORAL
  - 200 mg of iron daily 1 hour before meal (e.g. 100 mg twice daily)
  - How long?
    - 14 days + (Hg required level – Hg current level) x 4
  - half of the dose - 6 – 9 months to restore iron reserve
  - Absorption
    - is enhanced: vit C, meat, orange juice, fish
    - is inhibited: cereals, tea, milk

IRON DEFICIENCY ANEMIA CURE

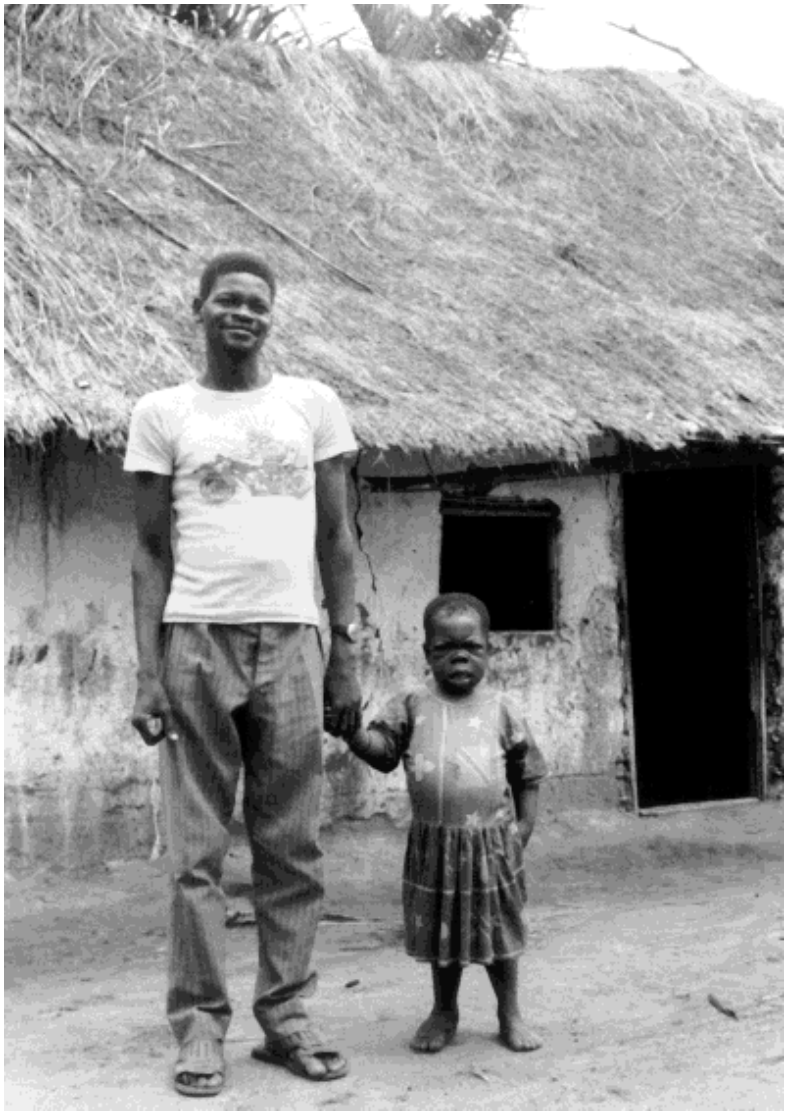
- PARENTERAL IRON SUBSTITUTION
  - Bad oral iron tolerance (nausea, diarrhoea)
  - Negative oral iron absorption test
  - Necessity of quick management (CHD, CHF)
  - 50 - 100 mg daily
  - I.v only in hospital (risk of anaphilactic shock)
  - I.m in outpatient department
  - *iron to be injected (mg) = (15 - Hb/g%/) x body weight (kg) x 3*

Calcium (Ca)

- function of calcium:
  - structural unit of bones and teeth
  - contraction and relaxation of muscles
  - stabilizes nervous tissue
    - low calcium --- irritable nerves --- tetany
    - high calcium --- depresses the nervous irritability
  - required for blood clotting
  - activates various enzymes (glycogen phosphorylase kinase, salivary and pancreatic amylase)

Ca Deficiency Rickets

Iodine Deficiency



Iodine

- iodine is necessary for the formation of thyroid hormones (T-4 and T-3)
- deficiency of iodine is manifested by a goiter (enlargement of the thyroid gland)
- salt water fish and seaweeds are a good source of iodine
- to prevent the development of endemic goiter, tablet salt has been spiked with sodium iodide