

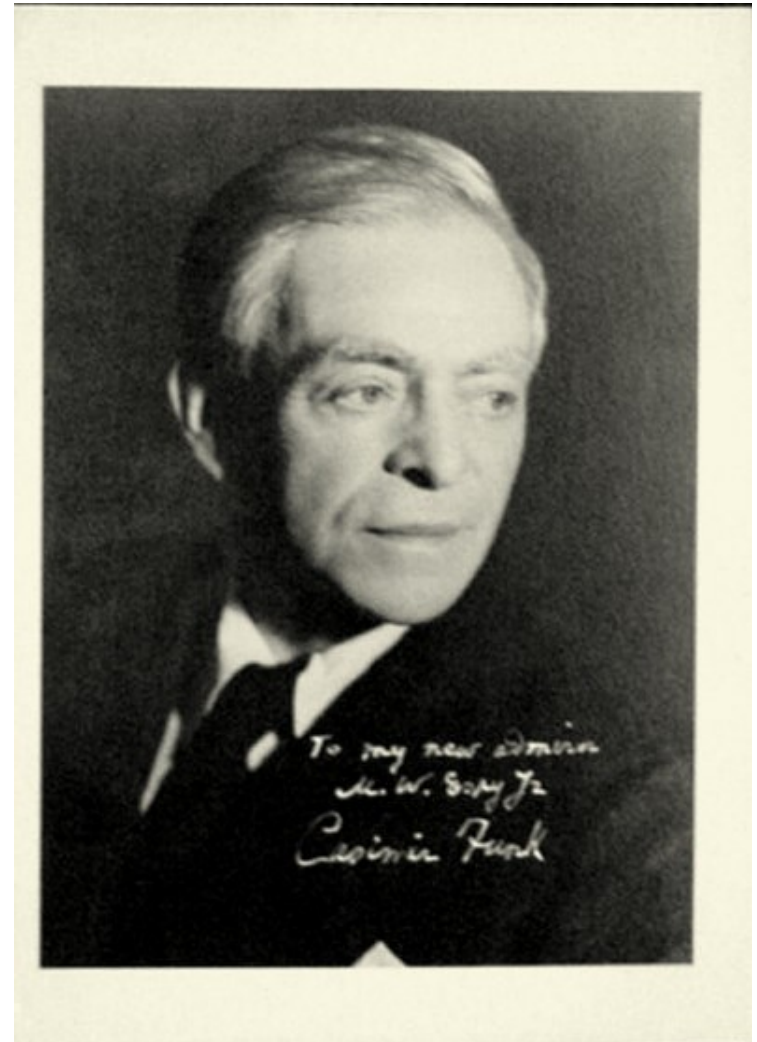
Vitamins



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History

- **Casimir Funk** – in 1912 first introduced the word "**vitamine**" derived from words vital and amine
- later the final "e" was dropped



Definition

Vitamins are low molecular weight organic compounds with different chemical properties, that human body cannot synthesize and in low quantities are necessary for many biochemical and physiological functions.

They belong to essential nutrients together with nutrients of energetic metabolism (for example linoleic acid), essential amino acids, minerals and trace elements.

Characteristics

- solubility – basic dividing characteristic
- stable when in crystal powder
- less stable in water solutions (risk of oxidation)
- pH (acidic pH OK, alkaline not - acidification)
- temperature
- oxygen (reducing agents)
- UV radiation (vit. A, B2), light (flavonoids)
- metal ions (chelating agents)

Determination

- **microbiological tests** – obsolete, incubation of sample extract with microbe dependent on vitamin
- **chemical methods without separation** – mostly analyses of food and pharmaceutical samples, not biological ones (too many interferences), these methods use physical and chemical characteristic of vitamins

Determination II.

- **separative methods** – most often used, mostly HPLC with different types of detection, or in combination with mass spectrometry; they enable also detection of isomers
- **enzymatic methods** – activity of vitamin-dependent enzyme is determined

Determination III.

- **immunochemical methods** – they use specific antibodies; simple; main problem are cross reactions
- preparation of sample – protection before and during transport (see p. 4), concentration and purification of a sample

RDA*

Recommended dietary allowance of vitamins		
Vitamin	Unit	Quantity
B ₁	mg	1,1
B ₂	mg	1,4
B ₃	mg	16
B ₅	mg	6
B ₆	mg	1,4
B ₉	µg	200
B ₁₂	µg	2,5
Vitamin C	mg	80
Biotin	µg	50
A	µg	800
D	µg	10 (=400 IU)
E	mg	12
K	µg	75

*valid for healthy people between 23-50 years, non-pregnant women, also sex-related charts exist

Classes of vitamins

water-soluble vitamins		fat-soluble vitamins	
B ₁	thiamine	A	retinoids
B ₂	riboflavin	D _{1, 2, 3}	
B ₃	niacin (vitamin PP)	E	tocopherols
B ₅	pantothenic acid	K _{1, 2, 3,}	
B ₆	pyridoxine		
B ₇	biotin (vitamin H)		
B ₉	folic acid/folate		
B ₁₂	cobalamin		
C	ascorbic acid		

„B – complex“

Comparison of vitamin classes

	water-soluble vitamins	fat-soluble vitamins
Absorption	easy*	with lipids (+ bile salts)
Transport proteins	no*	yes
Storage	no*	yes
Excretion	yes	no
Deficit	arise quickly*	after depletion of reserves
Toxicity	rare	possible hypervitaminosis
Therapy of deficit	regular intake	single high dose possible

*except vitamin B₁₂

Disorders

- hypervitaminosis – especially vitamins A and D
- hypovitaminosis – inappropriate intake
 - deficit in food
 - malabsorption
 - increased need
- avitaminosis – severe stage of deficit

Water-soluble vitamins

Vitamin B1 - thiamine

- active form is thiamine pyrophosphate (cofactor of enzymes)
- **functions:**
 - oxidative decarboxylation of 2-oxoacids in citrate cycle (pyruvate, α -ketoglutarate)
 - cofactor of transketolase in pentose phosphate pathway (PNS, CNS, cardiomyocytes, erythrocytes)
 - stimulation of neutrophils a leukocytes
- **sources** – yeast, bran, liver, oatmeal, natural rice, nuts, buckwheat, sprouted grains
- alcohol inhibits active transport into enterocytes!!! (passive is functioning, but is able from dose 5mg/day, (RDA 1.1mg))

saccharide metabolism

Deficit of thiamine

- beriberi (means fatigue or weakness)
 - first signs: anorexia, dyspepsia, weakness, fatigue
 - "*dry*" form: affection of peripheral nerves, especially on lower limbs, paresthesia or anesthesia, paralysis
 - "*wet*" form: edema, dyspnea, hepatomegaly, tachycardia, heart failure, lactic acidosis (pyruvate is converted to lactate)
- Wernicke-Korsakoff syndrome
 - symptoms of beri beri + psychosis, ataxia, nystagmus, ophthalmoplegia
- beware of parenteral nutrition!! (acidosis non-reacting on alkalization)

Vitamin B₂ - riboflavin

- part of cofactors FAD and FMN
- functions:
 - transport of electrons in respiratory chain
 - redox reactions of AA, saccharides, purines
 - integrity of cell membrane
 - cofactor of glutathione reductase (antioxidative effect)
 - detoxification of drugs and xenobiotics
- sources – cheese, eggs, meat, broccoli, parsley, yeast, milk, whole wheat products

Deficit of riboflavin

- syndrome resulting from isolated deficit is not known, symptoms result mostly from malnutrition and deficit of all vitamin B complex
- inflammation of conjunctiva and cornea, neural disorders, angular cheilitis, glossitis
- possible influence on decreased immune function
- avitaminosis – deprivation of growth



<http://healthh.com/cheilosis/>

Vitamin B₃ - niacin

- part of cofactors NAD⁺ and NADP⁺, in humans partially synthesized from tryptophan (provitamin)
- functions:
 - cofactor of at least 200 of enzymes involved in redox reactions, citric acid cycle, synthesis and β -oxidation of FA
 - vasodilatation
 - reduction of total cholesterol and LDL (inhibits flow of free FA from adipose tissue)
 - replication and reparation of DNA, apoptosis
- sources – meat, liver, tuna fish, sunflower seeds, peanuts, beans, yeast, lower amount in cereals

Deficit of niacin

- deficit occurs when the diet is deficient in niacin AND ALSO tryptophan
- deficit of vitamins B₁, B₂, B₆, copper, iron and magnesium worsen the conversion of tryptophan to niacin
- pellagra – „three D disease“
 - **dermatitis** (rash occurs predominantly on areas exposed to sun, typical is so called Casal's collar)
 - **diarrhoe**
 - **dementia**, irritability, later disorientation and hallucinations
 - others – smooth beefy red glossitis, neuritis, ataxia, convulsions



FIGURE 6-6 Pellagra from niacin deficiency causing the typical rash around the neck known as Casal necklace. (Reproduced with permission from Rick Hodes, MD.)

Hypervitaminosis of niacin?

- it is possible after prolonged intake of higher doses than RDA (e.g. in diabetic patients is niacin used for increase in glucose tolerance and improving of metabolism of saccharides and lipids)
- vasodilatation (headache, nausea, vomiting)
- hepatitis, even fulminant liver failure
- thrombocytopenia
- myopathy

Vitamin B₅ – pantothenic acid

- part of coenzyme A
- functions:
 - essential for reactions in metabolism of lipids and saccharides, release of energy in lipids and saccharides
 - synthesis of hem, sterols and lipids
 - acetylation reactions, gluconeogenesis
- sources – small quantities of pantothenic acid are found in nearly every food (pantos = everywhere), with high amounts in fortified whole-grain cereals, egg yolks, liver, partially synthesized by human microflora

Deficit of pantothenic acid

- very rare (famine, chronic alcoholics)
- possible symptoms:
 - Burning Feet Syndrome (Grierson-Gopalan Syndrome)
 - impaired hearing, fatigue, depression, insomnia
 - impaired wound healing and transplant recovery
 - impaired immune system, disposition to infections
- despite the fact, that normal varied diet is rich in pantothenic acid, it's still favourite dietary supplement

Vitamin B₆ – pyridoxine

- active form is cofactor pyridoxal phosphate
- function:
 - cofactor of at least 100 of enzymes
 - decarboxylation, transamination, deamination of AA
 - metabolism of lipids, methionine and cysteine
 - gluconeogenesis, glycogenolysis
 - synthesis of DNA, hem, niacin, neurotransmitters, myelin, taurine
- sources – yeast, sprouted grains, whole wheat bread, bananas, nuts and seeds, buckwheat, bran, meat

Deficit of pyridoxine

- neurological symptoms (lack of serotonin, adrenaline, noradrenaline, GABA), neuritis (disorders of myelin)
- hypochromic sideroblastic anemia
- hyperhomocysteinemia
- inflammations of eye and mouth corners, follicular hyperkeratosis
- developmental anomalies of apoenzymes coupled with pyridoxine leads in infants to mental retardation, bone deformations, osteoporosis, thrombosis and vision disorders



<http://www.medyouth.com/2015/04/the-treatment-methods-to-remove.html>

Vitamin B₇/H – biotin

- cofactor of carboxylases
- function:
 - reactions of acetyl-CoA, propionyl-CoA, pyruvate
 - FA synthesis
 - metabolism of PUFA, leucin, cholesterol
 - gluconeogenesis, catabolism of branched chain AAs
 - cell growth
- sources – synthesized by microflora, egg yolk, liver, soya beans, chocolate, cereals, yeast, sea fish

Deficit of biotin

- very rare
- possible symptoms: nausea, anorexia, vomiting, pale skin, muscle pain, dry skin, hair loss, increased concentration of cholesterol, bile pigments, depression

Vitamin B₉ – folic acid/folate

- active form is tetrahydrofolate
- functions:
 - synthesis of methionine (together with vitamin B₁₂)
 - normal function of erythrocytes and leukocytes
 - synthesis of purines, DNA
 - conversion of homocysteine to methionine, serine to glycine
 - key role in growth, division and differentiation of cells
 - antitumor effect (colon)
 - prevention of neural-tube defects in embryos
- sources – yeast, green leafy vegetables, nuts, organ meats, orange juice

Deficit of folate

- neural-tube defects in embryos,
- hyperhomocysteinemia, increased risk of cardiovascular disorders
- macrocytic anemia, thrombocytopenia
- gastrointestinal disorders (inflammation and ulceration of mucosa, diarrhea, nausea)
- depression and psychical instability

Vitamin B₁₂ – cobalamins

- active forms are methyl cobalamin and adenosyl cobalamin
- functions:
 - maturation of erythrocytes
 - cofactor of DNA/RNA synthesis
 - cell proliferation, hematopoiesis
 - synthesis of myelin and nucleoproteins
 - recycling of folate coenzymes
- sources – meat, eggs, milk

Deficit of cobalamin

- has several stages (decreased plasmatic concentrations, decreased intracellular concentration, metabolic aberration and clinical manifestation)
- megaloblastic and pernicious anemia, disorders in methionine, purine and pyrimidine metabolism, homocystinuria
- impaired myelin synthesis cause combined degeneration of sensory and motoric neurons → paresthesia, proprioception disorders, impaired body balance, confusion, impaired memory, depression
- high doses of folate can cover the signs of deficit in cardiovascular system, but not in nervous system

Vitamin C – ascorbic acid

- function:
 - synthesis of collagen, formation of osteoid, synthesis of connective tissue's proteins
 - electron transporter in redox reactions
 - hydroxylation reactions (steroid hormones, adrenaline, 5-hydroxytryptophan)
 - antioxidant
 - metabolism of histamine, carnitine, cholesterol, bile acids
 - increase the resorption of iron (also part of iron dietary supplements)
 - phagocytosis of leukocytes, immunity
- sources – citrus fruits, pepper, potatoes, rose hips, black currant, horseradish, strawberries,

Deficit of ascorbic acid

- fatigue, weakness, muscle pain
- anorexia, increased disposition to infections, depression
- impaired wound healing, anemia, hemorrhage, petechiae, hemarthrosis
- fragile and swollen gums, teeth loss

scurvy (scurbute)

- beware of high doses!! (urolithiasis, interference with several biochemical urine tests, e.g. determination of glucose or blood in urine)

Fat-soluble vitamins

Vitamin A

- terminology and conversions
 - active form of vitamin A is only in animal tissues, in plant tissue is as a provitamin A - β -carotene
 - vitamin A has several trans/cis isomers (A_1, A_2, \dots)
 - all molecules with vitamin A activity have common name retinoids:
 - retinol, retinal, retinoic acid
 - conversion between retinol and retinal is reversible, conversion of retinal to retinoic acid is irreversible

Vitamin A

- functions:
 - process of vision (retinal)
 - important factor in gene expression, reproduction and embryogenesis, proliferation, differentiation and apoptosis (RAR and RXR receptor, retinoic acid)
 - lipoprotein and immunologic integrity, stability of lysosomes
 - potential antioxidant function (carotenoids are probably more potent)
 - necessary for correct function of skin and epithelium
- sources – liver, dairy products, oily fish, egg yolk (absorbed as a retinol)
- sources of carotenoids – yellow and orange vegetables and fruit, green leafy vegetables
- storage suffices under physiological conditions for 2 years

Deficit of retinol

- night blindness, xerophthalmia (inflammations of eyelid and conjunctiva, keratomalacia – softening of cornea with overgrowing of vessels – risk of loss of the vision)
- xeroderma, follicular hyperkeratosis and keratinization of epithelium in respiratory, gastrointestinal and urinary system, increased risk of infections
- disturbed immunity (potential antitumor effect)

Hypervitaminosis

- potential toxicity after administration of 20 times higher doses in kids or 100 times higher doses in adults
- teratogenic effect (abortions, developmental anomalies)
- high intake of carotenoids is not toxic
- manifestation: alopecia, anemia, dermatitis, hepatomegaly, insomnia, hyperlipidemia, vomiting

Vitamin D

- D₂ – ergocalciferol (plant origin)
- D₃ – cholecalciferol (formed in skin from precursor)
- functions:
 - regulation of calcium and phosphate metabolism (more in following lecture)
 - not fully understood function in immune system
- sources – sunlight (15 min./day), oily fish, egg yolk, liver, milk, butter

Deficit of vitamin D

- tooth decay, bone deformities, rachitis, osteomalacia
- substitution therapy
 - prophylaxis: 400 IU
 - deficit: 1000 IU
 - rachitis and osteomalacia: 5000 IU
 - involutional osteoporosis: thousands of IU

Hypervitaminosis

- cause is usually excessive substitution, not sunbathing (formation of D_3 in skin is regulated)
- manifestation: permanent thirst, skin itching, diarrhea and vomiting, calcification of vessels and kidneys

Vitamin E – tocopherols

- 8 natural tocopherols, α -tocopherol has the highest biological activity
- functions:
 - intracellular antioxidant, mostly of PUFA in membranes (nerves, erythrocytes, LDL)
 - synergic effect with selenium against lipoperoxidation
 - inhibits mutagens in digestive system
 - recently confirmed function in signaling pathways
- sources – sprouted grains, poppy seeds, nuts, egg yolk, vegetable oils

Deficit of vitamin E

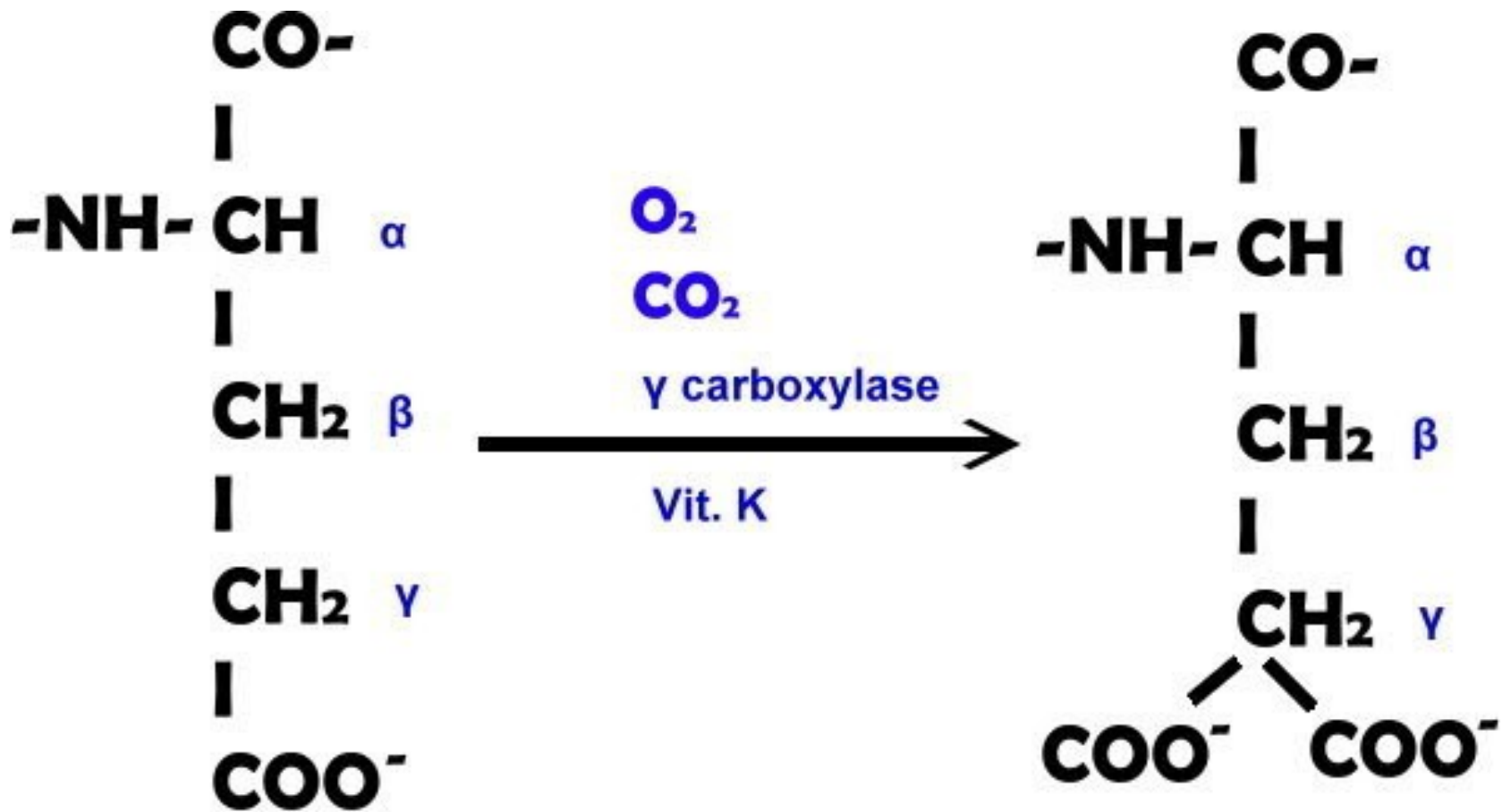
- decrease life span of erythrocytes, even hemolytic anemia
- functional defects of peripheral nerves
- increased cell death because of membrane damage (lipoperoxidation)
- long term deficit – myopathies or muscle necrosis, retinopathies, liver necrosis

Hypervitaminosis

- dyspepsia, fatigue, headache, muscle fatigue
- can cause developmental anomalies

Vitamin K

- functions:
 - vitamin K is essential factor of posttranslational carboxylation of glutamate to γ -carboxyglutamate (coagulation factors II, VII, IX, X, protein C, osteocalcin)
 - antidote for warfarin overdose (administered with heparin)
- sources – vegetables (especially green leafy vegetables), vegetable oils, cheese, yoghurts



γ CARBOXYLATION

Deficit of vitamin K

- rare, risk group are infants (vitamin K cannot pass through placenta and breast milk also contains low levels of it) and patients with lipid malabsorption
- petechiae, disposition towards bleedings and hematomas

Hypervitaminosis

- risk group are premature babies (substitution needed, but dosing must be watched)
- hemolysis, hyperbilirubinemia, kernicterus, brain damage

Thank for your attention.

