Vitamins
slides from lecture/seminar

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Vitamins

- essential substances, necessary for the physiological functions in the body
- the organism can not synthesize (except vitamin K, and some of vitamins of B complex) → intake from diet
- **vit** - from *Latin* vita - life, essential for life + **amin** from amine (so called because they were originally thought to be amines)
- r. 1912 Casimir Funk; biochemist who believed the substances to be amines
Vitamins

• most **water-soluble vitamins**, such as the vitamin B complex, act as catalysts and coenzymes in metabolic processes and energy transfer and are excreted fairly rapidly

• **fat-soluble vitamins**, such as vitamins A, D, and E are necessary for the function or structural integrity of specific body tissues and membranes and are retained in the body

• **antivitamin** - substance that inhibits or inactivates the normal functioning of vitamin

• **provitamin** - substance that may be converted within the body to vitamin
VITAMIN DEFICIENCY

- reduced supply
- malabsorption (mucosal disorders of GIT, decreased secretion of bile)
- drug interactions (suppress the activity of intestinal microorganisms, antivitamin’s character)
- liver disease (reduced capacity to store vitamin, reduced activation of vitamin)
- ↑ need for vitamins (period of growth, pregnancy, lactation/breastfeeding, infection)
VITAMIN DEFICIENCY

Hypovitaminosis
• relative deficiency of vitamin/vitamins

Avitaminosis
• absolute deficiency of vitamin/vitamins, causing pathological changes - any disease (such as scurvy, beriberi or pellagra) caused by chronic or long-term vitamin deficiency
Hypervitaminosis (vitamin poisoning, vitamin overdose)

- refers to a condition of high storage levels of vitamin/vitamins, which can lead to toxic symptoms

- hypervitaminosis usually occurs more with fat-soluble vitamins, which are stored in the liver and fatty tissues of the body. These vitamins build up and remain for a longer time in the body than water soluble vitamins.
VITAMINS

Fat-soluble vitamins
- vitamin A
- vitamin D
- vitamin E
- vitamin K

Water-soluble vitamins
- vitamins B
- vitamin C
Fat-soluble vitamins

- in the intestine are absorbed depending on the fat absorption (malabsorption of lipids - hypovitaminosis)
- are stored in the body
- may be toxic in the higher doses (hypervitaminosis)
Vitamin A

Forms:
- retinol (cis, trans form)
- retinal (cis, trans form)
- retinoic acid

Sources:
- retinol (retinol-esters present in the liver, kidney, butter, egg yolk)
- carotenoids (pigments - β-carotene (provitamin A), present in carrot)

Daily dose: 800 μg
↑ intake → lactation (breastfeeding) 1 300 μg
!!! pregnancy → teratogenic effect
Vitamin A

**Function:**

- participates in the process of vision
- affects the growth of the organism
- affects reproductive processes
- maintains the functional state of mucous membranes
- has antioxidant effect
Vitamin A - PROCESS OF VISION

- *retinal cells uptake trans*-retinol from the blood

- oxidation

- *trans*-retinal

- isomerisation

- *cis*-retinal

- *cis*-retinalopsin
  - rhodopsin

- *trans*-retinalopsin

- opsins

- action potential

- brain

- eyes
Deficiency:

• storage in the liver → deficiency in the case of long-term insufficient intake

mild/slight deficiency

• thickening keratinizing (rough) skin, dry eyes, night blindness, increased susceptibility to infections (eye, corneal inflammation, respiratory and urinary infections), risk of cancer

severe deficiency

• keratinization in the corneal epithelium, loss of vision

• growth retardation in children
Vitamin A

Toxicity
• 15 - 50 mg/day during months and years → toxic for children and adults

Hypervitaminosis A
• bone pain, skin damage, liver and spleen enlargement, nausea, diarrhea, teratogenic effect
• natural or synthetic substances whose biological activity is similar to vitamin A (a class of chemical compounds that are related chemically to vitamin A)

• affect epidermal growth and differentiation of cells → support proliferation of epidermal cells, but in the case of pathological hyperproliferation lead to its normalization

• have an effect on the activity of sebaceous glands → ↓doses promote growth and differentiation of sebaceous glands;
  ↑doses cause atrophy of sebaceous glands and reduce sebum secretion
Indications:

- dermacological conditions
- acne
- psoriasis
Contraindications:

- tanning and UV radiation - photosensitisation
- pregnancy - teratogenic effect
- children < 12 years
RETINOIDS

First generation
- tretinoin
- isotretinoin
- alitretinoin

Second generation
- etretinate
- acitretin

Third generation
- tazarotene
- bexarotene
- adapalene
Vitamin D

Forms:
• cholecalciferol - vitamin D3
  - is formed in the skin by UV radiation from 7-dehydrocholesterol
• ergocalciferol - vitamin D2
  - is formed by irradiation of ergosterol in plants

Sources:
• cholecalciferol (D3) (UV radiation; food - seafood, liver, egg yolk)
• ergocalciferol (D2) (yeast, plants)

Daily dose: 5 μg of cholecalciferol (200 IU of vitamin D)
Vitamin D - metabolism

Skin

ProD₃ → PreD₃ → Vitamin D₃

Liver

Diet
Vitamin D₃, Vitamin D₂

25(OH)D

Kidney

1,25(OH)₂D

Intestine

Increase calcium and phosphorus absorption

PTH (+)
(+ Low PO₄)

Bone

Mobilize calcium stores

Maintain serum calcium and phosphorus

Metabolic functions

Bone health

Neuromuscular functions
Vitamin D

**Function:**
- with PTH and calcitonin → regulation of calcium homeostasis
- maintaining physiological levels of calcium in plasma
- increases calcium absorption from GIT
- mobilizes calcium stores in bones
- reduces calcium renal excretion
- steroid → effect of vitamin D is mediated by receptors that control gene transcription
Vitamin D

Deficiency:

• reduced intake
• insufficient activation of provitamin by UV radiation in the skin
• liver and kidney damage
• GIT and bile secretion disorders

• rickets in children - bone deformities, abnormal bone growth, increased bone fragility
• increased bone fractures in adults
Vitamin D

Toxicity

- > 25 μg/day in children, > 50 μg/day in adults during months and years → toxic for children and adults

Hypervitaminosis D

- hypercalcaemia - deposition of calcium in soft tissues, bone pain, headache, fatigue, anorexia, vomiting, diarrhea, dehydration, muscle cramps, abdominal pain and cramps, thirst, fatigue, dizziness, heart and renal failure
Vitamin D

Interactions

• drugs which reduce the absorption of fat and cholesterol (cholestyramine) - reduce the absorption of vitamin D from GIT
• alcohol - slows the conversion of vitamin D to its active form
• antacids, thiazide diuretics - disorders of mineral homeostasis
• digitalis cardiac glycosides (digoxin) - increase toxicity
• corticosteroids - reduce the effect of the active form of vitamin D
Vitamin E

**Forms:**
- 8 naturally occurring forms → tocopherols
- \( \alpha \)-tocopherol - the most effective form → measurement of vitamin E effect (1mg of \( \alpha \)-tocopherol = 1IU of vitamin E)

**Sources:**
- **food** - vegetable oils, cereals, animal fats, milk, eggs, meat

**Daily dose:** 10 mg
**Function:**
- natural antioxidant → recaptures free radicals that by oxidation can damage vital organs
Vitamin E

Deficiency:

- reduced intake
- malabsorption of lipids

- newborns - edema, hemolytic anemia
  (increased erythrocyte membrane fragility, shortening the life of erythrocytes)

- adults - damage of erythrocytes, muscles, creatininuria, neurological symptoms
  (lipoperoxidation of membranes)
Vitamin K

Forms:
• *phylloquinone* - vitamin K1 in plants
• *menaquinone* - vitamin K2 in bacteria

Sources:
• plant foods, egg yolk, liver
• production by bacteria of GIT

Daily dose: 70 μg
Vitamin K

**Function:**

- important in the blood clotting process

- in the liver stimulates production and secretion of prothrombin (activates conversion of prothrombine to thrombin) **and some blood clotting factors** (VII, IX, X)

- regulatory function in the processes of bone mineralisation (modification of calcium binding proteins)
Deficiency:
• prolonged malnutrition
• reduced bacterial intestinal flora (ATB)
• overdose of anticoagulant therapy (dicoumarol)

• newborns - sterile guts, ↓ intake in breast milk → i.m. vitamin K (prevention of bleeding)
• adults - disorders of blood clotting with bleeding in the skin, mucous membranes, muscles, internal organs
Water-soluble vitamins

- are usually of plant origin
- are not stored in the body → regular intake is needed (except B12 - in the liver)
- in reduced intake, concentration of vitamins rapidly decreases → hypovitaminosis → avitaminosis

- ↑↑ intake → rare adverse effects, either they are rapidly eliminated or are degradated to inactive metabolites
Water-soluble vitamins

- act mainly as a coenzymes (cofactors) of enzymatic reactions
- without their presence serious metabolic disorders are occurred

**vitamin B:**
- thiamin (*vitamin B1*)
- riboflavin (*vitamin B2*)
- niacin (*vitamin B3*)
- pantothenic acid (*vitamin B5*)
- pyridoxine (*vitamin B6*)
- biotin (*vitamin B7*, *vitamin H*)
- folic acid (*vitamin B9*)
- cobalamin (*vitamin B12*)

**vitamin C**
Vitamin B1, thiamin

Forms:
• thiamin diphosphate (TDP)
• thiamin triphosphate (TTP)

Sources:
• in plant and animal tissues - in the free form, in complexes with proteins, in the form of phosphate esters
• cereal grains, legumes, liver, heart, kidney, lean meat

Daily dose: 1.5 mg
Vitamin B1, thiamin

Function:

TDP

- coenzyme of oxidative decarboxylation of 2-oxoacids (Krebs cycle)
- coenzyme of transketolase (pentose cycle)

TTP

- transmission of nerve impulses
Deficiency:
- reduced intake in the food
- presence of antithiamine factors - thiaminases (enzymes that break down vitamin B1 in GIT - tea, coffee)
- chronic alcoholism (reduced intake + reduced absorption)

- **symptoms of nervous system** (nerve inflammation, abnormal reflexes) and **cardiovascular system** (tachycardia), degenerative changes of central and peripheral nerves with paralysis, muscle pain, gastrointestinal disorders, cardiac dilation
- **beriberi** (dry skin, increased irritability, impaired nerve functions, thought disorders, paralysis)
- babies - vomiting, convulsions, death
- chronic alcoholism - apathy, memory disorders, eye muscles disorders
- degenerative diseases of CNS
Vitamin B2, riboflavin

Forms:
- flavin mononucleotide (FMN)
- flavin adenindinucleotide (FAD)

Sources:
- milk, eggs, liver, green leafy vegetables
- production by bacteria of GIT

Daily dose: 1.5 mg
Function:

- FMN/FAD or FMNH2/FADH2 - prosthetic groups, part of enzymes that catalyze oxidation/reduction of substrates
Deficiency:

- isolated deficiency - rare
- deficiency of vitamin B2 is often associated with deficiency of the other vitamins

- skin and mucous membrane damage - inflammation of the skin, mouth corners, anogenital area
- corneal damage, thrombosis, ATS changes
Vitamin B3, PP, niacin, nicotinic acid

Forms:
- nicotinamide adenine dinucleotide (NAD+)
- nicotinamide adenine dinucleotide phosphate (NADP+)

Sources:
- animal and vegetable food ingredients - grains, legumes, yeast, milk, liver

Daily dose: 10 - 15 mg
Vitamin B3, PP, niacin, nicotinic acid

**Function:**

- essential part of redox reactions (oxidation-reduction) → transmitter systems \( \text{NAD}^+ / \text{NADH} + \text{H}^+ \) a \( \text{NADP}^+ / \text{NADPH} + \text{H}^+ \)
Vitamin B3, PP, niacin, nicotinic acid

Deficiency:
• isolated deficiency - rare
• deficiency of vitamin B3 is often associated with deficiency of the other vitamins

• *pellagra* „3D“ dermatitis, diarrhea, dementia
• skin damage (skin inflammation and pigmentation), mucosal damage (stomatitis, gastritis, bloody diarrhea) and CNS damage (sleepiness, impaired vision, memory loss, hallucinations), death
Vitamin B5, pantothenic acid

Sources:
• plant and animal food ingredients - egg yolks, viscera, yeast, cereals, legumes
• production by bacteria of GIT

Daily dose: 5 mg
Vitamin B5, pantothenic acid

Function

- part of coenzyme A
Deficiency:

- rare

- vomiting, nausea, abdominal pain and convulsions, fatigue, insomnia, impaired coordination, reduced antibody production
Vitamin B6, pyridoxine

Forms:
• pyridoxine
• pyridoxal
• pyridoxamine

Sources:
• plant and animal foods - yeast, wheat, corn, nuts, liver, milk, eggs, meat, vegetables, legumes
• production by bacteria of GIT

Daily dose: 2 mg
Function

• coenzyme of enzymes metabolism of amino acids such as transaminase, decarboxylase, aldolase, enzymes of amino acid synthesis, in the process of ammonia release and fixation, dehydratase, desulfhydrase, cystationinsynthase in the metabolism of methionine, in the formation of ammonia from tryptophan, in the metabolism of porphyrins

• structural role in the enzyme glycogen phosphorylase

• in the v CNS is involved in serotonin production by decarboxylation of 5-hydroxytryptophan and in conversion of excitatory neurotransmitter glutamic acid by decarboxylation to γ-aminobutyric (inhibitory neurotransmitter)
Vitamin B6, pyridoxine

Deficiency:

- inflammation of the skin and mucous membranes, hyperpigmentation
- CNS disorders - depression, ↑irritability, inflammation of the nerves with pain and cramps
Vitamin B7, vitamin H, biotin

- imidazole derivative

**Sources:**
- food - viscera, meat, dairy products, grain, fruit, vegetables
- production by bacteria of gastrointestinal tract

**Daily dose**: 100 - 200 μg
Vitamin B7, vitamin H, biotin

Function:

• coenzyme of carboxylation reactions → transporter of carbon dioxide
  • acetyl-CoA-carboxylase - reaction determining the rate of carboxylic acids synthesis
  • pyruvate carboxylase - reaction important for gluconeogenesis
  • propionyl-CoA-carboxylase - reaction in which the carboxylic acid changes through methylmalonyl-CoA to jantaryl-CoA used in the cells
Deficiency:

- rare

- depression, anorexia, muscle pain, inflammation of the skin, ECG changes
Vitamin B9, folic acid

- pterin + para-aminobenzoic acid + glutamic acid
- para-aminobenzoic acid - character of vitamin, is not synthesize in the body
- tetrahydrofolate (THF) - metabolic active form

Sources:
- food - yeast, liver and other viscera, fresh green leafy vegetables, fruit

Daily dose: 100 - 200 μg
Vitamin B9, folic acid

Function

- the role in the transport and in the use of carbon residues required for:
  - synthesis of purine and pyrimidine nucleotides
  - conversion of homocysteine to methionine (+ vitamin B12)
  - methylation of transfer RNA
Vitamin B9, folic acid

Deficiency:

- ↓ supply
- malabsorption

- megaloblastic anemia (weakness, fatigue, dyspnea, diarrhea, irritability, anorexia, headache)
- mucosal inflammation and ulceration, defects in bone growth, decrease of leucocytes and thrombocytes (failure of cell division following impaired formation of purines and pyrimidines with subsequent suppression of DNA)
Vitamin B12, cobalamin

Sources:
- food - meat and meat products, milk and milk products
- production by bacteria of gastrointestinal tract

Daily dose: 3 μg
Vitamín B12, cobalamin

Function

- coenzyme of enzymes
  - methylmalonyl-CoA-mutase - conversion of methylmalonyl-CoA to succinyl-CoA
  - THF-methyl-transferase (methioninsynthase) - regeneration of methionin from homocysteine
Vitamin B12, cobalamin

Deficiency:

• rare - sufficient supply of the liver
• malabsorption - operations, gastrointestinal diseases, intrinsic factor deficiency

• fatigue, dyspnea, anorexia, constipation, headache, palpitations
• megaloblastic (pernicious) anemia - abnormally large red blood cells, abnormal erythroblasts in the bone marrow, decreased leucocytes and platelets
• nervous system disorders - movement, reflexes and higher nervous activity disorders (demyelinating processes in the spinal cord, phospholipid metabolism disorders)
Vitamin C, ascorbic acid

Forms:
• ascorbic acid (reduced form)
• dehydroascorbic acid (oxidized form)

Sources:
• fresh fruit and vegetables

Daily dose: 60 mg
70 - 100 mg pregnancy, breast feeding

megadosis of vitamin C (1 - 4 g long-term) → formation of oxalate kidney stones
Function:

- coenzyme of redox (oxidation-reduction) reactions, including hydroxylation reactions
  - dopamin-β-monooxygenase - catalyzes the hydroxylation of dopamine to form norepinephrine
  - posttranslational hydroxylation of proline in the synthesis of collagen - reaction in the period of growth, and in healing wounds and fractures
  - hydroxylation reactions in the synthesis of some corticoids
  - hydroxylation reactions in the breakdown of cholesterol
Vitamin C, ascorbic acid

Function

• facilitates the absorption of iron from GITU
• protects against oxidation of Fe$^{2+}$ in hemoglobin in red blood cells
• is required for normal function of leukocytes, synthesis and release of histamine in stressful situations
• antioxidant
Vitamin C, ascorbic acid

Deficiency:

- slight/mild deficiency
- increased capillary fragility with petechiae

- severe deficiency
- disease scurvy - fatigue, depression, bleeding, tooth loss, dry skin, mucous membranes, slow wound healing, bone fragility
- reduced iron absorption