Vitamins

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What are vitamins?

• They are chemically unrelated organic compounds that are required by an organism in tiny amounts as a vital nutrient.
• They cannot be synthesized in adequate quantities by humans and, therefore, must be supplied by the diet.
• They are compounds that are convertible to the active form of the vitamin in the body.
Classification

• Released, absorbed, and transported with the fat of the diet
• Not readily excreted in the urine
• Stored in the liver and adipose tissue

**Vitamins**

- **Water-soluble**
  - Non-B-Complex
    - Ascorbic acid (vitamin C)
  - B-Complex
    - Energy-releasing
      - Thiamine (vitamin B₁)
      - Riboflavin (vitamin B₂)
      - Niacin (vitamin B₃)
      - Biotin
      - Pantothenic acid
    - Hematopoetic
      - Folic acid
      - Vitamin B₁₂
  - Other
    - Pyridoxine (vitamin B₆)
    - Pyridoxal
    - Pyridoxamine

- **Fat-soluble**
  - Vitamin A (retinol, β-carotenes)
  - Vitamin D (cholecalciferol)
  - Vitamin K (phyloquinones, menaquinones)
  - Vitamin E (tocopherols)

**Note:** many are precursors of coenzymes
# Water-soluble vitamins

<table>
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<tr>
<th>Vitamin</th>
<th>Coenzyme</th>
<th>Consequences of deficiency</th>
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<tr>
<td>Thiamine (B1)</td>
<td>TPP</td>
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<tr>
<td>Riboflavin (B2)</td>
<td>FAD</td>
<td>Angular stomatitis (mouth lesions)</td>
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<tr>
<td>Nicotinic acid (niacin) (B3)</td>
<td>NAD⁺</td>
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<tr>
<td>Pantothenic acid (B5)</td>
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<td>Pyridoxine (B6)</td>
<td>PLP</td>
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<td>Folic acid (B9)</td>
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<tr>
<td>Cobalamin (B₁₂)</td>
<td>Deoxyadenosyl cobalamin</td>
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<td>Ascorbic acid (C)</td>
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<td>Scurvy</td>
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# Fat-soluble vitamins

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<th>Vitamin</th>
<th>Main function</th>
<th>Deficiency</th>
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<tr>
<td>A</td>
<td>Roles in vision, growth, reproduction</td>
<td>Night blindness, cornea damage</td>
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<tr>
<td>D</td>
<td>Regulation of Ca²⁺ &amp; phosphate metabolism</td>
<td>Rickets (children), Osteomalacia (adults)</td>
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<td>E</td>
<td>Antioxidant</td>
<td>RBCs fragility</td>
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<td>K</td>
<td>Blood coagulation</td>
<td>Subdermal hemorrhaging</td>
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</table>
Vitamin A

• Vitamin A: a collective term for several related biologically active molecules.
• The retinoids, a family of molecules which are essential for vision, reproduction, growth, and maintenance of epithelial tissues.
• Retinoic acid, derived from oxidation of dietary retinol, mediates most of the actions of the retinoids, except for vision, which depends on retinal, the aldehyde derivative of retinol.
Forms of vitamin A

**Retinol:** A primary alcohol containing a ring with an unsaturated side chain; found in animal tissues as a retinyl ester with long-chain FAs.

- **Retinal:** An aldehyde; derived from the oxidation of retinol; Retinal and retinol can be interconverted.
- **Retinoic acid:** An acid derived from the oxidation of retinal; cannot be reduced into retinal or retinol.
- **β-Carotene:** Cleaved in the intestine to yield two molecules of retinal.
Cellular RBP → nuclear receptors (steroids), RNA, proteins (keratin expression)
Mechanism of action of vitamin A

- Retinol is oxidized to retinoic acid, which binds to a specific nuclear receptor.
- The complex regulates gene expression (RNA synthesis)
  - Retinoids control the expression of keratin in most epithelial tissues of the body.
Functions of vitamin A

- Visual cycle: 11-cis retinal specifically binds the protein opsin (rhodopsin)
- Growth (retinoic acid): Vitamin A deficiency results in a decreased (growth rate & bone development) in children
- Reproduction: Retinol and retinal (not retinoic acid) are essential for spermatogenesis in the male and preventing fetal resorption in the female
- Maintenance of epithelial cells (retinoic acid): Vitamin A is essential for normal differentiation of epithelial tissues & mucus secretion
- Animals given vitamin A only as retinoic acid from birth are blind and sterile
Sources of vitamin A

• Liver, kidney, cream, butter, and egg yolk are good sources of preformed vitamin A.
• Yellow and dark green vegetables and fruits are good dietary sources of the carotenes.
Clinical indications

• Dietary deficiency: mild (night blindness); prolonged (irreversible loss for some visual cells); severe (xerophthalmia)
  – Xerophthalmia: ulceration & dryness of conjunctiva & cornea, followed by scar & blindness

• Acne and psoriasis: effectively treated with retinoic acid
Toxicity of retinoids

• Excessive intake → hypervitaminosis A (toxic)

• Early signs of chronic hypervitaminosis A
  – Skin: becomes dry (due to a decrease in keratin synthesis)
  – Liver: becomes enlarged and can become cirrhotic
  – Nervous system: a rise in intracranial pressure

• Pregnant women should not ingest excessive quantities of vitamin A (teratogenic).
Vitamin D

• The D vitamins are a group of sterols that have a hormone-like function.

• The active molecule, 1,25-dihydroxycholecalciferol (1,25-diOH-D3), binds to intracellular nuclear receptors.

• The most prominent actions of 1,25-diOH-D3 are to regulate the plasma levels of calcium and phosphorus.
Sources of vitamin D

Dermis /epidermis

not biologically active
Metabolism of vitamin D

7,8-dehydrocholesterol → skin → pre-vitamin D₃ → skin → vitamin D₃

vitamin D₃ → liver 25-hydroxylase → calcitriol (active form)

calcitriol → target tissues 24-hydroxylase → 1,25-dihydroxyvitamin D₃

1,25-dihydroxyvitamin D₃ → kidney 1α-hydroxylase → 25-hydroxyvitamin D₃ (The predominant form of VD in plasma)

25-hydroxyvitamin D₃ → The major storage form
Regulation of 1-hydroxylase

- Increased directly by low plasma phosphate
- Increased indirectly by low plasma calcium (PTH)
- Decreased by excess 1,25-diOH-D3, the product of the reaction
Functions of vitamin D

• The overall function of 1,25-diOH-D3 is to maintain adequate plasma levels of calcium by:
  – increasing uptake of calcium by the intestine
  – minimizing loss of calcium by the kidney
  – stimulating resorption of bone when necessary
Increased gene expression (synthesis) of a specific calcium-binding protein.
Sources of vitamin D

- Eggs
- Cheese
- Salmon
- Shiitake mushroom
- Sunlight
- Fortified foods
Clinical indications

- Nutritional rickets: rickets in children & osteomalacia in adults (a result of net demineralization of bone)

- Renal rickets (renal osteodystrophy): chronic renal failure

- Hypoparathyroidism
Toxicity of vitamin D

• High doses (100,000 IU for weeks or months) can cause loss of appetite, nausea, thirst, and stupor (lethargy).

• Enhanced calcium absorption and bone resorption results in hypercalcemia, which can lead to deposition of calcium in many organs, particularly the arteries and kidneys.
Vitamin K

- Phylloquinone or vitamin K1 (plants)
- Menaquinone or vitamin K2 (intestinal bacterial flora)
- Menadione (synthetic)
Functions of vitamin K

- The principal role of vitamin K is in the **posttranslational modification** of blood clotting factors (prothrombin and blood clotting factors II, VII, IX, and X).

- How? It serves as a coenzyme in the carboxylation of certain glutamic acid residues present in these proteins.
So what?!!

• The carboxylated glutamate can **chelate** $\text{Ca}^{2+}$
• The prothrombin–calcium complex can **then bind to phospholipids essential for blood clotting** on the surface of platelets.
• Attachment to the platelet increases the rate of proteolytic conversion of prothrombin to thrombin.
Dietary sources of vitamin K
Deficiency of vitamin K

• Rare due to intestinal bacterial (antibiotics!!)
• **Newborns** have sterile intestines and human milk can provides only about one fifth (20%) of the daily requirement for vitamin K.
• It is recommended that newborns receive a single intramuscular dose of vitamin K as prophylaxis against hemorrhagic disease.
Toxicity of vitamin K

- Prolonged administration of large doses of synthetic vitamin K (menadione) can produce hemolytic anemia and jaundice in the infant, due to toxic effects on the membrane of red blood cells.
Vitamin E

• The E vitamins consist of eight naturally occurring tocopherols, of which α-tocopherol is the most active.

• The primary function of vitamin E is as an antioxidant in prevention of the nonenzymic oxidation of cell components.
  
  – Oxidation of polyunsaturated fatty acids by molecular oxygen and free radicals.
Deficiency of vitamin E

- Almost entirely restricted to premature infants.
- In adults, it is usually associated with defective lipid absorption or transport.
- Signs: sensitivity of erythrocytes to peroxide, and the appearance of abnormal cellular membranes.