Vitamins

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Vitamins

- **Organic compounds** required by an organism in tiny amounts as a vital nutrient

- **Cannot be synthesized** in sufficient quantities, & mostly is obtained from the diet

- The term is **conditional both on the circumstances & on the particular organism** (ascorbic acid, humans, other animals) (vitamin D, human diet)

- **Thirteen vitamins** are universally recognized at present

- **Vitamers** are compounds that are convertible to the active form of the vitamin in the body
Vitamins

- Vitamins have diverse biochemical functions:
  - **Hormone-like functions** (regulators): regulators of mineral metabolism (e.g., vitamin D), or regulators of cell & tissue growth & differentiation (e.g., vitamin A)
  - **Anti-oxidants** (e.g., vitamins E & C)
  - **Precursors for enzyme** cofactors (vitamin B subclasses)
Classification

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
    - Hematopoietic
      - 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)
# Water soluble vitamins

<table>
<thead>
<tr>
<th>Vitamin</th>
<th>Coenzyme</th>
<th>Consequences of deficiency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thiamine (B1)</td>
<td>TPP</td>
<td></td>
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<tr>
<td>Riboflavin (B2)</td>
<td>FAD</td>
<td>Angular stomatitis (mouth lesions)</td>
</tr>
<tr>
<td>Nicotinic acid (niacin) (B3)</td>
<td>NAD⁺</td>
<td></td>
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<tr>
<td>Pantothenic acid (B5)</td>
<td>CoA</td>
<td></td>
</tr>
<tr>
<td>Pyridoxine (B6)</td>
<td>PLP</td>
<td></td>
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<tr>
<td>Biotin (B7)</td>
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<tr>
<td>Folic acid (B9)</td>
<td>TH4</td>
<td>Megaloblastic anemia</td>
</tr>
<tr>
<td>Cobalamin (B12)</td>
<td>Deoxyadenosyl cobalamin</td>
<td>Megaloblastic anemia</td>
</tr>
<tr>
<td>Ascorbic acid (C)</td>
<td></td>
<td>Scurvy</td>
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</tbody>
</table>
## Fat soluble vitamins

<table>
<thead>
<tr>
<th>Vitamin</th>
<th>Main function</th>
<th>Deficiency</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Roles in vision, growth, reproduction</td>
<td>Night blindness, cornea damage</td>
</tr>
<tr>
<td>D</td>
<td>Regulation of Ca+2 &amp; phosphate metabolism</td>
<td>Rickets (children), Osteomalacia (adults)</td>
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<tr>
<td>E</td>
<td>Antioxidant</td>
<td>RBCs fragility</td>
</tr>
<tr>
<td>K</td>
<td>Blood coagulation</td>
<td>Subdermal hemorrhaging</td>
</tr>
</tbody>
</table>
Vitamin A

The retinoids, a family of molecules related to retinol (vitamin A), are essential for vision, reproduction, growth, & maintenance of epithelial tissues

Retinoic acid, mediates most of the actions of the retinoids, except for vision and spermatogenesis
Vitamin A - structure

- Retinol: a primary alcohol, unsaturated side chain
- Retinal: an aldehyde, derived by oxidation of retinol, retinal and retinol are inter-convertible

- Retinoic acid: an acid, derived by oxidation of retinal, cannot be reduced in the body
- β-Carotene: oxidatively cleaved in the intestines to yield 2 molecules of retinal
Absorption & transport of vitamin A

- Retinol esters, intestinal mucosa, retinol
- Carotenes, retinal, retinol
- Chylomicrons, lymphatic system, liver (storage)
- Release from the liver: retinol binds the plasma retinol-binding protein (RBP)
- Cellular RBP → nuclear receptors (steroids), RNA, proteins (keratin expression)
Functions of vitamin A

- **Visual cycle**: 11-cis retinal specifically binds the protein opsin (rhodopsin)

- Reproduction: Retinol and retinal (not retinoic acid) are essential for spermatogenesis in the male and preventing fetal resorption in the female

- Growth (retinoic acid): Vitamin A deficiency results in a decreased (growth rate & bone development) in children

- 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
Mechanism of action of vitamin A

✓ Retinoic acid binds with high affinity to specific receptors (epithelial cells)

✓ The complex interacts with nuclear chromatin to stimulate retinoid-specific RNA synthesis

✓ Production of specific proteins that mediate several physiologic functions (keratin)
Sources & indications

✓ Sources: excess cause hypervitaminosis A
✓ 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 (affecting over 500,000 children worldwide every year)
✓ Acne and psoriasis: effectively treated with retinoic acid
Vitamin D

- Is a group of sterols that have a hormone-like function
- The active molecule, 1,25-dihydroxycholecalciferol (1,25-diOH-D3), binds to intracellular receptor proteins
- The most prominent actions are to regulate the plasma levels of calcium & phosphorus

Sources:
- Diet: Ergocalciferol (vitamin D₂, plants)
- Cholecalciferol (vitamin D₃, animals)
- Endogenous: 7-Dehydrocholesterol is converted to cholecalciferol in the skin
Metabolism of vitamin D

- Vitamins D₂ and D₃ are not biologically active
- Converted by two sequential hydroxylation reactions to the active 1,25-diOH-D₃
  - The first occurs in liver (25-hydroxycholecalciferol)
    - The predominant form of vitamin D in plasma
    - The major storage form
  - The second occurs in kidneys (25-hydroxycholecalciferol 1-hydroxylase)
- Regulation of 25-hydroxycholecalciferol 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 & indications

✓ The overall function is to maintain adequate plasma levels of calcium
  ✓ 1) Increasing calcium uptake by intestines (the mechanism is typical of steroid hormones)
  ✓ 2) Minimizing calcium loss by kidneys
  ✓ 3) Stimulating resorption of bone when necessary

✓ Indications:
  ✓ Nutritional rickets: rickets in children & osteomalacia in adults
  ✓ Renal rickets (renal osteodystrophy): chronic renal failure
Vitamin K

✓ Exists in several forms:
  ✓ In plants: phylloquinone (vitamin $K_1$)
  ✓ Intestinal bacterial flora: menaquinone (vitamin $K_2$)

✓ The principal role: posttranslational modification of various blood clotting factors: hepatic synthesis of clotting factors II (prothrombin), VII, IX, and X

✓ Present in low concentration in milk
Vitamin K

✓ Clinical indications:
  ✓ Deficiency of vitamin K: unusual (intestinal bacteria), antibiotics
  ✓ Deficiency of vitamin K in the newborn (sterile intestines). **Human milk (20%)** of the need, so it is recommended that all newborns receive a single intramuscular dose of vitamin K as prophylaxis against hemorrhagic disease
Vitamin E

✓ 8 naturally occurring tocopherols
✓ α-tocopherol is the most active form
✓ The primary function is as an antioxidant
✓ Vitamin E deficiency is almost entirely restricted to premature infants
✓ When observed in adults, it is usually associated with defective lipid absorption or transport