Vitamins, Minerals and trace elements
Vitamins

- Organic compounds in animal and human diet
- Important for basic functions **(essential exogenous factors)**.

- Biochemical function – catalyzers – part of enzyme cofactors

  • RDA is smaller than normal dietary compounds (AA, saccharides, proteins, lipids etc.

  • **Provitamins**: dietary form of vitamin – inactive – changed to the active vitamins

  • **Antivitamins**: compounds inhibiting vitamins and their function (competition, non specific binding of the vitamine)
Vitamins

A. Water-soluble vitamins II

- Vitamin: Active form, coenzyme, Function in metabolism

- B6
  - Pyridoxal
  - Pyridoxal phosphate
  - Activation of amino acids
  - Metabolism
  - D-5-deoxyadenosyl cobalamin
    - Isomerization
    - Methionine synthase
    - S-adenosylmethionine

- Folic acid
  - Folate
  - Tetrahydrofolate
  - Tryptophan metabolism
  - Meat, yeast products, fruits, and vegetables

- Nicotinic acid
  - Niacinamide
  - NAD+/NADH
  - Hydrolysis
  - Preservation of enzyme systems, coenzyme, antioxidant

- Ascorbic acid
  - Ascorbate
  - Fruit, vegetables

- Biotin
  - Biotin
  - Transfer of carboxyl groups

- Pantothenate
  - 7 mg
  - Widely distributed
  - Activation of carboxylic acids

- Thiamine
  - 1.5 mg
  - B1
  - Transfers of hydroxyalkyl residues

- Riboflavin
  - 1.8 mg
  - B2
  - Hydrogen transfer
  - Meat, yeast products

- Pantothenate
  - 7 mg
  - B7
  - Widely distributed
  - Activation of carboxylic acids

- Pantothenate
  - 7 mg
  - B7
  - Widely distributed
  - Activation of carboxylic acids
**Vitamins**

**B. Lipid-soluble vitamins**

* Adult daily requirement

<table>
<thead>
<tr>
<th>Provitamin</th>
<th>Functional form</th>
<th>Important for</th>
</tr>
</thead>
<tbody>
<tr>
<td>β-Carotene</td>
<td>Retinal</td>
<td>Sight</td>
</tr>
<tr>
<td>Vegetables</td>
<td>Visual pigments</td>
<td></td>
</tr>
<tr>
<td>Fruit</td>
<td>Retinol</td>
<td>Sugar transport</td>
</tr>
<tr>
<td>1 Milk</td>
<td>Coenzyme</td>
<td></td>
</tr>
<tr>
<td>Egg yolk</td>
<td>Retinoic acid</td>
<td>Development differentiation</td>
</tr>
<tr>
<td></td>
<td>Signal molecule</td>
<td></td>
</tr>
<tr>
<td>Cholesterol</td>
<td>Calcitriol</td>
<td>Calcium metabolism</td>
</tr>
<tr>
<td></td>
<td>Hormone</td>
<td></td>
</tr>
<tr>
<td>UV</td>
<td>Calciferol</td>
<td></td>
</tr>
<tr>
<td>0.01 Cod liver oil</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Milk</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Egg yolk</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tocopherols</td>
<td>Tocopherols</td>
<td>Antioxidant</td>
</tr>
<tr>
<td></td>
<td>Reducing agent</td>
<td></td>
</tr>
<tr>
<td>10 Cereals</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Liver</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Eggs</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Seed oil</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Phyloquinones</td>
<td>Phytohydroquinones</td>
<td>Blood clotting (carboxylation of plasma proteins)</td>
</tr>
<tr>
<td>0.08 Intestinal bacteria</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vegetables</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Liver</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Vitamins

1. Fat soluble vitamins (A, E, D, K)

2. Water soluble vitamins (B, C, H)

<table>
<thead>
<tr>
<th>Vitamins</th>
<th>Deficiency state</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Water soluble</strong></td>
<td></td>
</tr>
<tr>
<td>C (Ascorbate)</td>
<td>Scurvy</td>
</tr>
<tr>
<td>B$_1$ (Thiamin)</td>
<td>Beri-beri</td>
</tr>
<tr>
<td>B$_2$ (Riboflavin)</td>
<td>Rarely single deficiency</td>
</tr>
<tr>
<td>B$_6$ (Pyridoxine)</td>
<td>Dermatitis/Anaemia</td>
</tr>
<tr>
<td>B$_{12}$ (Cobalamin)</td>
<td>Pernicious anaemia</td>
</tr>
<tr>
<td>Folate</td>
<td>Megaloblastic anaemia</td>
</tr>
<tr>
<td>Niacin</td>
<td>Pellagra</td>
</tr>
<tr>
<td><strong>Fat soluble</strong></td>
<td></td>
</tr>
<tr>
<td>A (Retinol)</td>
<td>Blindness</td>
</tr>
<tr>
<td>D (Cholecalciferol)</td>
<td>Osteomalacia/rickets</td>
</tr>
<tr>
<td>E (Tocopherol)</td>
<td>Anaemia/neuropathy</td>
</tr>
<tr>
<td>K (Phytomenadione)</td>
<td>Defective clotting</td>
</tr>
</tbody>
</table>
Fat soluble vitamins

- Vitamin A

**Sources** - liver, milk products and fat fishes, yolk, yellow and orange vegetable, dried apricots, leafy vegetable

**Provitamin A**

![Chemical structures of vitamin A precursors](image)
Vitamin A

Conversion of pro vitamin A (carotene) to active forms
Vitamin A

Metabolism, absorption

Conjugation
Esterification

Intestinal lumen
Intestine cell

Liver
Storage

RE → R → Chy

RE = Retinol ester
R = Retinol
RA = Retinoic acid
Chy = Chylomicrons
RBP = Retinol binding protein

Target cell

RA

Retina, Skin
Gonads

Retinolpalmitate
**Vitamin A**

**Biochemical importance**

**Visual Cycle (Wald)**

- Retinal epithelium
- All-trans-retinol
- 11-cis-retinaldehyde
- Lysine residue in opsin
- Photorhodopsin
- Bathorhodopsin
- Lumirhodopsin
- Metarhodopsin I
- All-trans-retinaldehyde
- Hydrolysis

**Brain stimulation**

**VISION**
Vitamin A

Adaptation to darkness

11-cis-retinal + opsin → Rodopsin

Rodopsin – regeneration of visual cycle
Conopsin – colour vision
Cyanopsin – blue colour
Iodopsin – green colour
Porphyrropsin – red colour
Vitamin A

Other biochemical importance

Glycoprotein biosynthesis
Steroid biosynthesis
Vitamin A

Causes of deficiency

- Low dietary intake
- Obstructive icterus with absorption deficiency
- Liver cirrhosis - RBP deficiency
- Severe malnutrition – Lack of AA for RBP formation
- Chronic nephrosis – Increased excretion of RBP in urine
Vitamin A

Manifestation of deficiency

- Night blindness (nyctalopia)
- Xerophtalmy and keratomalatia
- Muscle membrane lesions and epitelial atrophy
- Increased occurence of generalized infections
- Growth retardation
- Decreased synthesis of acute phase proteins
Vitamin A

**Hypervitaminosis**
- Anorexia
- Head Aches
- Dry Skin
- Vomiting
- Bone Pain
- Hepatomegaly
- Teratogenic risk
- Hyperlipidemia
- Defect of Ca Homeostasis

**Therapeutic importance**
(20 – 50x nad RDA)
- adjuvant leukemia treatment
- syntetic analoga
- treatment of dermatitid
Vitamin D (Cholecalciferol)

Sources

-Fishes (mackerel, tuna, herring), yolk, liver, milk, butter

prohormone Vitamin D$_3$
Vitamin D

Metabolism

Liver
- Calcidiol (cholecalciferol)
- Calcidiol 25-hydroxylase
- Calcidiol 24-hydroxylase
- 24-Hydroxycalcidiol

Kidney
- Calcidiol (25-hydroxycholecalciferol)
- Calcitriol (1,25-dihydroxycholecalciferol)
- Calcidiol 24-hydroxylase
- Calcitriol 1-hydroxylase
- Calcitriol (1,25-dihydroxycholecalciferol)
- Calcitroic acid

Active form (increase S-Ca)
Vitamin D (Cholecalciferol)

Biochemical importance

1. Ca P homeostasis
2. Insulin and thyreoidal hormones secretion
3. Inhibition of T-lymphocyte produces interleukin
4. Cell proliferation and modulation
Vitamin D (Cholecalciferol)

Vitamin D regulation

25 - OH - D

- Vitamin D deficiency
- 25-OHD deficiency
- Calcium deficiency
- Hypocalcemia
- PTH secretion
- Hypophosphatemia
- Phosphate deficiency

Vitamin D sufficiency

24,25-(OH)₂D

- 1,25-(OH)₂D

Active vitamin D₃

Normocalcemia
Normophosphatemia

Hypercalcemia
Hyperphosphatemia

Inactive Vitamin D₂
Vitamin D

Causes of deficiency

- Nutritional – low Vit D in diet
- Malabsorption – obstructive icterus, steatorrhea
- Impaired Vitamin D activation - hydroxylation
- Deficiency in renal phosphate absorption
Vitamin D

Manifestation of deficiency

- Rickets
- Osteomalacia
- Obezity
- Bone deformations
- Impaired immunity
- Metabolic syndrome
Vitamin D

Hypervitaminosis

- Weakness
- Polyuria
- Intense thirst
- Hypertension
- Weight loss
- Calcification of weak tissues
Vitamin E (tocopherol)

Sources
Sprouting corn (wheat), cotton oil, poppy, nuts, yolk
Vitamin E

Metabolism, absorption

Bioavailability of vitamin E in humans: an update, Patrick Borel, Damien Preveraud, Charles Desmarchelier, DOI: http://dx.doi.org/10.1111/nure.12026 319-331 First published online: 1 June 2013
**Vitamin E**

**Biochemical importance**

1. Most powerful natural antioxidant
2. Protect erythrocytes from hemolysis
3. Deterioration of aging
4. Immune response stimulation
5. Reduces risk of atherosclerosis
6. Membrane fluidity
7. Cellular signalization (?)
Vitamin E

Manifestation of deficiency

- Hemolytic anemia, decreased life of RBC
- Increased thrombocyte aggregability
- Morphological and functional changes of peripheral nerves
- Decreased serum creatinine concentration and increased renal excretion

Hypervitaminosis

- Hemorrhage, anticoagulation effect
**Vitamin K**

**Sources**

- green leaves vegetables, vegetable oils
- Menaquinones are in fermented diets (cheese, yoghurts) and ruminant livers

**K1**

Phylloquinone

In diet

**K2**

Menaquinone

Intestinal bacteria

**K3**

Menadiol

Synthetic analogs

---

To obtain 45mcg of Vitamin K2 one should consume:

- 4kg Beef
- 5L Milk
- 5L Whole Yoghurt

- 80g Soft Cheese
- 59g Hard Cheese
- 8 Egg Yolks

---

Natto
Vitamin K

Vitamin K regulation – Competitive inhibition during anti-coagulation therapy
Vitamin K1 function
Vitamin K

Biochemical importance

1. Activation of coagulation factors FII, FVII a FXII a FIX

2. Posttranslational modification (gamma carboxylation of glutamic acid residues)

3. Bone formation stimulation

4. Anti cancerous effect

Binding of coagulation factors in membrane
Vitamin K

**Metabolism and absorption**

- Absorption is related to the dietary fat
- Transport in lipoprotein particles
- Different biological half lives

**Vitamin K Storage**
- liver
- Bones, muscle, brain
Vitamin K

Causes of deficiency

- Lipid malabsorption due to obstructive icterus or pancreatitis
- Prolonged ATB therapy
- GIT infection
- Diarrhoea
Vitamin K

**Manifestation of deficiency**

- Hemorragic disease in newborns
- Post-traumatic bleeding
- Prolongation PT time
- Competitive inhibition warfarin and dicoumarole
- Bone abnormalities in newborns due to inadequate therapy

**Hypervitaminosis**

- Hemolysis
- Hyperbilirubinemia
- Brain defects
- Kernicterus

*Bleeding Due To Vitamin K Deficiency*
Water soluble vitamins

- **Vitamin B₁**

  **Sources** - yolk, liver, chocolate, cauliflower, yeast, sea fishes,

\[
\text{Thiamin} \quad \text{Thiamin diphosphate}
\]

Pyrimidine    Thiazol
Vitamin B<sub>1</sub>

**Biochemical importance**

**Cofactor**
- Pyruvate dehydrogenase
- Alpha-ketoglutarate dehydrogenase
- BCKA dehydrogenase
- Transketolase

**Causes of deficiency**
- Beri-beri: anorexia, dyspepsia, body weakness, palpitation, oedema, CNS disorders, heart ailment
- Wernicke encephalopathy and Korsakoff psychosis
- Polyneuritis in chronic alcoholism
Vitamin B₂ (Riboflavin)

**Sources** - Cheese, egg, liver, meat, broccoli, parsley, yeast, milk products

izoalloxazine + ribitol

Riboflavin

Riboflavin monophosphate (flavin mononucleotide, FMN)

Flavin adenine dinucleotide (FAD)
Vitamin B<sub>2</sub>

Biochemical importance

Part of flavoproteinases (FMN) and FAD)

- Succinate dehydrogenase
- Xantine oxidase
- Pyruvate dehydrogenase
- Alpha-ketoglutarate dehydrogenase

Symptoms of deficiency

- Magenta colored tongue
- Vascularisation
- Angular stomatitis
- Dermatitis
- Bulbar capillary proliferation
Vitamin B₃ (Niacine)

Sources

Meat (liver, tuna, turkey) sunflower seeds, black bread, legume, yeast.

A  = Nicotinic acid, B  = Nicotine amide
C  = NAD (P)
Vitamin $B_3$
Vitamin B₃ (Niacin)

Biochemical importance

Coenzymes (NAD and NADP)

**NAD**
- Lactate dehydrogenase
- Glyceraldehyde-3-phosphate dehydrogenase
- Pyruvate dehydrogenase
- Alphea-keto glutarate dehydrogenase
- Glutamate dehydrogenase
- Beta –hydroxyacyl CoA dehydrogenase

**NADPH utilising reactions**
- Ketoacyl-ACP dehydrogenase
- HMG CoA reductase
- Methemoglobin reductase
- Folate reductase
- Phenylalanine hydroxylase

**NADPH**
- Glukose-6-phosphate dehydrogenase
- 6-phosphoglukonate dehydrogenase
- Isocitrate dehydrogenase
- Malate dehydrogenase
Vitamin B₃ (Niacine)

Deficiency of symptoms
- Pelagra – dermatitis, diarrhea, dementia, spasticity

Causes of deficiency
- Lack of tryptophane in diet
- Deficiency in synthesis (kynureinase)
- Isoniazide treatment
- Hartnup disease
- Carcinoid (liver tumor metastases)

Therapeutic importance
- Decrease S - cholesterol and Lp (a)

But
- Dilatation of veins, dermatitis
- Liver dysfunction
Vitamin B₆ (Pyridoxine)

Sources

Yeast, wheat sprouts, black bread, melasa, bananas, potatoes, nuts, sunflower seeds, buckwheat, bran, meat (chicken, fish, liver), legumes.
Vitamin B₆ (Pyridoxine)

Biochemical importance

1. Coenzyme in reactions:
   - Transamination
   - Dekarboxylation
   - Transport a metabolism of sulphur aminoacids
   - Heme synthesis
   - Niacin production
   - Glycogenolysis

2. Regulation of steroid hormones

Symptoms of deficiency

- Neurologic – decreased GABA, serotonin and catecholamine synthesis
- Dermatologic – pelagra
- Hematologic - anemia

Decreased concentration

- Isoniazides
- Cycloserine
- Oral contraceptives
- Etanol

Toxicity

- Senzoric neuropathy
Pantothenic acid

Sources

Grains, vegetables, meat
Pantothenic acid

Biochemical importance

1. Acetyl CoA synthesis

Symptoms of deficiency

- Rare - paresthesia, Burning foot syndrome
Biotin (Vitamin H, vitamin B$_7$)

**Biochemical importance**

1. **Carboxylation**
   - Acetyl CoA carboxylase
   - Propionyl CoA carboxylase
   - Pyruvate carboxylase

2. **Cell cycle regulation**

**Causes of deficiency**
- antibacterial drugs

**Symptoms of deficiency**
- dermatitis, anorexia, halucination
- muscle weakness

**Sources**
Yolk, liver, soya, chocolate, cauliflower, legumes, yeast, sea fishes
Folic acid

Sources

Yeast, leafy vegetable, nuts, liver, kidney, orange juice
Folic acid

Biochemical importance

1. Transfer of monocarbonic substituents

- Formyl (-CHO)
- Formimino (-CH = NH)
- Methenyl (-CH=)
- Methylen (-CH₂ -)
- Hydroxymethyl (-CH₂OH)
- Methyl (-CH₃)
Folic acid

2. Transmetylation reactions

One carbon pool

Methyl-THFA

1

THFA

Vitamin B₁₂

Homocysteine

Methylcobalamin

Methionine

2

Adenosine

ATP

PPi + Pi

Methyltransferase

S-adenosyl methionine

3

S-adenosyl homocysteine

CH₃

Methyl acceptor

Methylated product

Homocysteine methyltransferase
Folic acid

3. Nucleotide biosynthesis
Folic acid

Causes of deficiency

- Pregnancy
- Impaired folate absorption – coeliac disease, jejunum resection, gastroileostomy
- Anticonvulsant (hydantoin, dilantin, fenytoin, fenobarbiton)
- Hemolytic anemia
- „Folate trap“ – combined deficiency of folate and vitamin B\textsubscript{12} – impaired methylation

Symptomes of deficiency

- Alteration of DNA synthesis and methylation
- Makrocytic anemia, retikulocytosis, leukopenia
- Neural tube defects (spina bifida) in newborns
- Bronchial carcinoma and endocervical carcinoma
Folic acid

Decreased folate concentration

- antagonists – antibacterial drugs (sulfonamides)
- antimalarics – Pyrimethamin
- Folate reductase inhibitors (aminopterine, amethopterine) – anticancer leukemia treatment (methotrexate)

Terapeutic use

- Reduction of neurologic signs in anemias
- Reduction of incidence neural tube defects in newborns
- Reduction of cardiovascular risk and cancerogenesis
Vitamin B$_{12}$ (Cobalamine)

**Sources**

Meat, calf liver, milk products, yeast

<table>
<thead>
<tr>
<th>R</th>
<th>Name</th>
</tr>
</thead>
<tbody>
<tr>
<td>Me- B$_{12}$</td>
<td>CH$_3$</td>
</tr>
<tr>
<td>Ado- B$_{12}$</td>
<td>5$'$-deoxyadenosine</td>
</tr>
<tr>
<td>OH- B$_{12}$</td>
<td>OH</td>
</tr>
<tr>
<td>CN- B$_{12}$</td>
<td>CN</td>
</tr>
</tbody>
</table>
Vitamin $B_{12}$

Absorption, transport and storage

Cbl = cobalamin, R = cobalophilin, IF = intrinsic factor, TC = transcobalamin
Vitamin $\text{B}_\text{12}$

Biochemical importance

1. Cofactor of methyl malonyl CoA isomerase
2. Cofactor of homocysteine methyl transferase
3. Regulation of folate metabolism (regeneration THF in folate cycle)

Causes of deficiency
- Impaired absorption in gastrectomy
- Pernicious anemia
- Gastrick anemia
- Pregnancy
- Nutritional deficiency

Symptoms of deficiency
- Megaloblastic anemia
- „Folate trap“ – impaired regeneration THF
- Hyperhomocysteinemia and homocysteinuria
- Demyelinisation
- Degeneration of NS

Therapeutic importance

Treatment of megaloblastic anemia
Vitamin C (Ascorbic acid)

Sources

Citrus fluids and juices, strawberries, rose hips, parsley tops, black currant, gooseberry, vegetable, potatoes
Vitamin C

Structure and metabolism

Biochemical importance

1. Posttranslation hydroxylation Pro and Lys
2. Hydroxylation of tryptophan
3. Increasing of Fe absorption from GIT
4. Reconversion of Hb to Met-Hb
5. Cofactor of folate reductase
6. Hydroxylation of cholesterol
7. Stimulation of leukocyte phagocytosis
8. Prevention of tumorogenesis, antioxidant
9. Cataract reduction
Vitamin C

Causes of deficiency

- Scurvy
- Bleeding and epistaxis
- Gingivitis
- Osteoporosis and bone weakness
- Mikrocytic hypochromic anemia

Terapeutic use

- Adjuvans during infection
- Better recovery – ulcerous colitis, trauma, burns
## Summary of absorption – vitamins B and C

<table>
<thead>
<tr>
<th>Vitamin</th>
<th>Absorption</th>
<th>Place of absorption</th>
</tr>
</thead>
<tbody>
<tr>
<td>B₁-thiamin</td>
<td>specific active transport</td>
<td>small intestine</td>
</tr>
<tr>
<td>B₂-riboflavin</td>
<td>active transport related to Na and energy</td>
<td>jejunum</td>
</tr>
<tr>
<td>B₃-niacine</td>
<td>diffusion</td>
<td>small intestine</td>
</tr>
<tr>
<td>B₅-panthotenic acid</td>
<td>Simplified diffusion</td>
<td>small intestine</td>
</tr>
<tr>
<td>B₆-pyridoxine</td>
<td>Simplified diffusion</td>
<td>small intestine</td>
</tr>
<tr>
<td>B₇-biotin</td>
<td>Simplified diffusion</td>
<td>jejunum</td>
</tr>
<tr>
<td>B₉-folic acid</td>
<td>Specific transporter, pH-dependent</td>
<td>jejunum</td>
</tr>
<tr>
<td>B₁₂-cobalamine</td>
<td>B₁₂ coupled with CBL, and intrinsic factor</td>
<td>Distal part of ileum</td>
</tr>
<tr>
<td>C-ascorbic acid</td>
<td>active transport related to Na and energy</td>
<td>Distal part of ileum</td>
</tr>
</tbody>
</table>
### Summary of Vitamin

<table>
<thead>
<tr>
<th></th>
<th>Fat soluble vitamins</th>
<th>Water soluble vitamins</th>
</tr>
</thead>
<tbody>
<tr>
<td>Solubility in fat</td>
<td>Soluble</td>
<td>Not soluble</td>
</tr>
<tr>
<td>Water solubility</td>
<td>Not soluble</td>
<td>Soluble</td>
</tr>
<tr>
<td>Absorption</td>
<td>Along with lipids</td>
<td>*Absorption simple</td>
</tr>
<tr>
<td></td>
<td>Requires bile salts</td>
<td></td>
</tr>
<tr>
<td>Carrier proteins</td>
<td>Present</td>
<td>*No carrier proteins</td>
</tr>
<tr>
<td>Storage</td>
<td>Stored in liver</td>
<td>*No storage</td>
</tr>
<tr>
<td>Excretion</td>
<td>Not excreted</td>
<td>Excreted</td>
</tr>
<tr>
<td>Deficiency</td>
<td>Manifests only when stores are depleted</td>
<td>*Manifests rapidly as there is no storage</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Toxicity</td>
<td>Hypervitaminosis may result</td>
<td>Unlikely, since excess is excreted</td>
</tr>
<tr>
<td>Treatment of</td>
<td>Single large doses may prevent deficiency</td>
<td>Regular dietary supply is required</td>
</tr>
<tr>
<td>deficiency</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Major vitamins</td>
<td>A, D, E and K</td>
<td>B and C</td>
</tr>
<tr>
<td></td>
<td>*Vitamin B₁₂ is an exception.</td>
<td></td>
</tr>
</tbody>
</table>
Summary of diseases according to vitamin deficiency

- Vitamin A: Bitot spot
- Vitamin B7: hair loss
- Vitamin B6: seborrhoeic dermatitis
- Vitamin B2: cheilosis
- Vitamin C: inflamed gums (scurvy)
- Vitamin D: pseudofractures (osteomalacia)
- Vitamin E: haemolytic anaemia
- Vitamin B12 and folate: megaloblastic anaemia
- Vitamin B3: photosensitive dermatitis (pellagra)
- Vitamin K: easy bruising
- Vitamin B1: loss of reflexes (Beri Beri)
- Vitamin B5: peripheral neuropathy/paraesthesia
References

1. Bender, DA: Introduction to nutrition and Metabolism, 5th ed., 2014
Minerals

1. **Macronutrients**
   building of the systems (water, proteins, fats, sacharides, lipids)
   C, H, O, N, S

2. **Dietary important minerals** (More than 100 mg /day)
   Ca, P, Mg, Na, K, Cl

3. **Trace elements**
   Cr, Co, Cu, Fe, Mn, Mo, Zn, Se, I, F

4. **Added elements (not essential for human)**
   Ni, Si, Sn, V, B, Li

5. **Toxic elements**
   Pb, Hg, Cd
TRACE ELEMENTS AND MINERALS

Transport mechanisms of trace elements

- albumin - Cu, Zn
- transferin - Fe, Cr, Mn, Zn
- aminoacids - Cu, (Fe v malém množství)
- transcobalamin - Co
- globulins - Mn
TRACE ELEMENTS AND MINERALS

- Elimination of minerals and trace elements
  - Bile – Cr, Cu, Mn, Zn
  - Urine – Co, Cr, Mo, Zn
  - pancreatic juice - Zn
  - sweat - Zn
  - mucosal tissue – Fe, Zn
MINERALS AND TRACE ELEMENTS

- Manganese: 2.5 mg/d
- Copper: 1.5 mg/d
- Fluoride: 1.0 mg/d
- Molybdenum: 0.30 mg/d
- Iodine: 0.14 mg/d
- Selenium: 0.07 mg/d
- Chromium: 0.10 mg/d
- Vanadium: 0.002 mg/d
- Zinc: 12.0 mg/d
- Iron: 10.0 mg/d
DIETARY IMPORTANT MINERALS

CALCIUM (Ca)

- Intake: 25 mmol
- Absorption: 10–14 mmol
- Secretion: 7 mmol
- Blood: 2.2–2.6 mmol/L
- Faecal excretion: 18–22 mmol
- Urine excretion: 3–7 mmol
- Intake: 10 mmol
- Intake: 40 mmol
- Intake: 320 mmol
Dietary important elements

**Calcium (Ca)**

**Duodenal absorption**

Increased absorption
- Vitamin D
- PTH (activation 1-alpha hydroxylase)
- Acid conditions
- Aminoacids (Lys, Arg)

Decreased absorption
- Phytic acid (cereals)
- Oxalate
- Malabsorption syndrome
- Hyperphosphatemia

C = calcitriol
CR = binding calcitriol to receptor
CB = calbindin
Calcium (Ca)

Biochemical importance

1. Signal transduction
   - Muscle excitation and contraction (calsequestrin)
   - Neuronal synapses

2. Enzyme activation

   - Adenylate cyclase
   - Ca\(^{++}/Mg^{++}\) ATPase
   - Glycerol-3-phosphate dehydrogenase
   - Glykogen synthase
   - Pyruvate carboxylase
   - Pyruvate dehydrogease
   - Phospholipase C
Calcium (Ca)

Biochemical importance – contd.

1. **Hormone secretion** (insulin, PTH, calcitonin, vasopresin)
2. **2nd messenger** (glucagon, G-protein and inositolphosphate)
3. **Decrease of the vascular permeability**
4. **Activator of coagulation (Factor IV)**
5. **Enhancer of myocardial systole**
6. **Bone and teeth formation**
7. **Cellular mobility, cell cycle progression** (Calpains)
Calcium (Ca)

Metabolic regulation of Ca

TRPV5, TRPV6 = transient receptor channels
Calcium (Ca)

Hypercalcemia

Causes
- Hyperparathyreoidism
- Thyreotoxicosis
- Multiple myeloma
- Bone tumors and metastasis
- Dehydratation
- Tuberculosis and sarcoidosis
- Drugs (thiazides, theofyline, lithium, vitamin D and A excess)

Symptoms
- Anorexia, nauzea, vomiting
- Polyuria, polydypsia
- Tumors and metastases
- Urolithiasis
- Ectopic calcifications and pancreatitis
- Hyperkalemia

Therapy
- Adequate hydratation
- Furosemid (Ca exkretion)
- Steroids (in case of Vit D3 excess)
- Beta-blockers (in thyreotoxicosis)
Calcium (Ca)

Hypocalcemia

Causes

- Vitamin D deficiency
  liver diseases and hepatopathy, nephrotic syndrome, anticonvulsives

- PTH deficiency
  hypoparathyreoidism pseudohypoparathyreoidism

- Elevation of calcitonin
  medular carcinoma thyroid

- Ca deficiency
  malabsorption
  acute pankreatitis
  alkalosis
  infusion Ca

- Mg deficiency

- P elevation
  renal failure
  renal tubular acidosis

- Hypoalbuminemia

Symptoms

- Muscle pains
- Paresthesia
- Tetany
- Neuromuscular irritability
- Spasms
Calcium (Ca)

Diseases related with hypocalcemia

- Osteoporosis
- Paget disease
- Renal osteodystrophia
- Rickets
Calcium (Ca)

Transport in blood (Serum)

- Ionized Ca (Ca$^{++}$) 50 %
- Complex with anions 10 %
- Complex with proteins 40 %

Reference values in serum

<table>
<thead>
<tr>
<th>Total Ca (TCa)</th>
<th>Ionized Ca (Ca$^{++}$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 - 6 weeks</td>
<td>0 - 6 weeks</td>
</tr>
<tr>
<td>1,75 - 2,87 mmol/l</td>
<td>1,20 - 1,48 mmol/l</td>
</tr>
<tr>
<td>6 weeks - 1 yr</td>
<td>6 wks - 15 yrs</td>
</tr>
<tr>
<td>2,15 - 2,79 mmol/l</td>
<td>1,20 - 1,38 mmol/l</td>
</tr>
<tr>
<td>1 - 60 yrs</td>
<td>15 - 60 yrs</td>
</tr>
<tr>
<td>2,05 - 2,54 mmol/l</td>
<td>1,13 - 1,32 mmol/l</td>
</tr>
<tr>
<td>60 - 150 yrs</td>
<td>60 - 90 yrs</td>
</tr>
<tr>
<td>2,05 - 2,40 mmol/l</td>
<td>1,16 - 1,29 mmol/l</td>
</tr>
</tbody>
</table>

Critical value ≤ 1,6 mmol/l.
Phosphorus (P)

Phosphate intake: 40 mmol/day

Body distribution:
- Bone: 17000 mmol
- Soft tissue: 3000 mmol
- Plasma: 1 mmol/L

Urine: 26 mmol/day

14 mmol/day
Phosphorus (P)

Absorption

Metabolic regulation

Kuro et al 2008

Hormonal regulation

Suppression
Glucocorticoids
Insulin
Calcitonin

Activation
Dopamine
GH
Thyroxine

Phosphorus (P)

Biochemical importance

1. Bone and teeth formation
2. High energy phosphates (ATP, GTP...)
3. NAD and NADPH synthesis
4. DNA and RNA synthesis
5. Phosphate esters and phosphoproteins formation
6. Phosphorylation
7. Buffer systeme \((\text{Na}_2\text{HPO}_4 : \text{NaH}_2\text{PO}_4 = 4:1 \rightarrow \text{pH} = 7.4)\)
### Phosphorus (inorganic)

#### Total phosphorus
- cca 4 mmol/l
- 0.7 - 1.5 mmol/l
- 1.6 - 3.9 mmol/l

#### Inorganic Phosphorus
- 30%

#### Organic Phosphorus (Phospholipides)
- 70%

#### Free Phosphorus
- 80%

#### Bound Phosphorus
- Bind to proteins: 15%
- Bind to Ca and Mg: 5%

### Phosphorus Levels by Age Group

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Phosphorus Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 - 6 wks</td>
<td>1.36 - 2.58 mmol/l</td>
</tr>
<tr>
<td>6 wks - 1 yr</td>
<td>1.29 - 2.26 mmol/l</td>
</tr>
<tr>
<td>1 - 15 yrs</td>
<td>1.16 - 1.90 mmol/l</td>
</tr>
<tr>
<td>15 - 60 yrs</td>
<td>0.65 - 1.61 mmol/l</td>
</tr>
<tr>
<td>60 - 90 yrs</td>
<td>0.74 - 1.29 mmol/l</td>
</tr>
<tr>
<td>90 - 150 yrs</td>
<td>0.71 - 1.36 mmol/l</td>
</tr>
</tbody>
</table>
Phosphorus

Hyperphosphatemia

Causes

1. **Increased absorption**
excess of vitamin D infusion

2. **Increased cell lysis**
chemotherapy rhabdomyolysis

3. **Decreased excretion**
renal failure hypoparathyreoidism

4. Hypocalcemia
5. Massive blood transfusion
6. Thyreotoxikosis
7. Drugs (chlorothiazid, Nifedipin, Furosemid)

Hypophosphatemia

Causes

1. **Decreased absorption**
malnutrition malabsorption diarrhoea Vitamin D deficiency

2. **Intercellular transport**
respiration alcalosis inzulin therapy

3. **Increased renal exkretion**
hyperparathyreoidism hypophosphatemia Fanconi syndrome

4. Hereditar hypophosphatemia
5. Hypercalcemia
6. Chronic alkoholism
7. Drugs (antacid, diuretics, salicylates)
Magnesium (Mg)

- Magnesium intake: 15 mmol/day
- 30% absorbed
- 70% excreted
- Body distribution:
  - Bone: 750 mmol
  - Soft tissue: 450 mmol
  - ECF: 15 mmol
- Urine: 5–10 mmol/day
Magnesium (Mg)

- 30% Mg^{2+} bind to protein (albumin)
- 13% Mg^{2+} as phosphate, citrate and complexes
- free Mg^{2+} - spontaneous diffusion through cell membrane

Reference values

Mg Total

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Reference Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 - 6 wks</td>
<td>0.75 - 1.15 mmol/l</td>
</tr>
<tr>
<td>6 wks - 1 yr</td>
<td>0.66 - 0.95 mmol/l</td>
</tr>
<tr>
<td>1 - 15 yrs</td>
<td>0.78 - 0.99 mmol/l</td>
</tr>
<tr>
<td>15 - 60 yrs</td>
<td>0.66 - 0.91 mmol/l</td>
</tr>
<tr>
<td>60 - 90 yrs</td>
<td>0.66 - 0.99 mmol/l</td>
</tr>
<tr>
<td>90 - 150 yrs</td>
<td>0.70 - 0.95 mmol/l</td>
</tr>
</tbody>
</table>

Mg ionized (Mg^{++})

<table>
<thead>
<tr>
<th>Reference Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.45 - 0.62 mmol/l</td>
</tr>
</tbody>
</table>

Critical value ≤ 0.5 mmol/l.
# Magnesium (Mg)

## Hypermagnesemia

<table>
<thead>
<tr>
<th>Causes</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Increased intake</td>
</tr>
<tr>
<td>2. Renal failure</td>
</tr>
<tr>
<td>3. Hyperparathyreoidism</td>
</tr>
<tr>
<td>4. Oxalate poisoning</td>
</tr>
<tr>
<td>5. Rickets</td>
</tr>
<tr>
<td>6. Multiple myeloma</td>
</tr>
<tr>
<td>7. Dehydratation</td>
</tr>
<tr>
<td><strong>8. Drugs</strong> (Aminoglycosides, antacids, calcitriol, tacrolimus)</td>
</tr>
</tbody>
</table>

## Hypomagnesemia

<table>
<thead>
<tr>
<th>Causes</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Tubular necrosis</td>
</tr>
<tr>
<td>2. Hyperaldosteronism</td>
</tr>
<tr>
<td>3. Familial hypomagnesemia</td>
</tr>
<tr>
<td>4. Loss by GIT: ulcerous colitis, vomiting</td>
</tr>
<tr>
<td>5. Liver cirrhosis</td>
</tr>
<tr>
<td>6. Malabsorption</td>
</tr>
<tr>
<td>7. Protein malnutrition</td>
</tr>
<tr>
<td>8. Hypoparathyreoidism</td>
</tr>
<tr>
<td>9. Toxemia in pregnancy</td>
</tr>
<tr>
<td>10. Drugs (thiazides, aminoglycosides, cisplatin, haloperidol, alcohol)</td>
</tr>
</tbody>
</table>
Copper (Cu)

Dietary copper: 25 μmol/day

50% absorbed

Body distribution: 1200 μmol

Liver: 10%

Muscle, kidney, heart, brain: 70%

Plasma: 10–22 μmol/L

Biliary excretion

24 μmol/day

Urine: < 1.0 μmol/day
Copper (Cu)

Biochemical importance

1. Absorption and incorporation of Fe to hemoglobin
2. Tyrosinase activity
   - cofactor hydroxylases
3. Increase HDL
4. Cofactor of transoxygenases
   - superoxid dismutase (Cu/Zn-SOD)
   - cytochrom c oxidase (COX)
   - monoaminooxidase
   - lysyloxidase
5. Immune response regulation (lymphocyte activation)
Copper (Cu)

**Transport systems**

**Ceruloplasmin** (CP) - glycoprotein, Cu-dependent ferroxidase

- binds 6 – 7 Cu atoms
- contents 80 – 95 % of total Cu in plasma,
- Oxidation Fe$^{2+}$ to Fe$^{3+}$ and absorption in GIT.

![Ceruloplasmin diagram]

**Metallothionein** – Intracellular protein regulating Cu metabolism (distribution and utilization of Cu in the cells).
Copper (Cu)

**Deficiency Cu**

**Wilson disease**
- Autosomal recessive disorder – Cu is not bind to apoceruloplasmin
- Decreased plasma Cu
- Mental retardation, liver failure.
- Ceruloplasmin does not acts as ferroxidase.

<table>
<thead>
<tr>
<th>Investigation</th>
<th>Normal adult</th>
<th>Wilson’s disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum copper μmol/L</td>
<td>10–22</td>
<td>&lt;10</td>
</tr>
<tr>
<td>Caeruloplasmin g/L</td>
<td>0.15–0.6</td>
<td>&lt;0.15</td>
</tr>
<tr>
<td>Urinary copper μmol/24h</td>
<td>&lt;1</td>
<td>5–15</td>
</tr>
<tr>
<td>Liver copper μg/g dry weight</td>
<td>20–50</td>
<td>&gt;250</td>
</tr>
</tbody>
</table>

**Menkes syndrome**
- Inherited disorder of Cu absorption in intestine, X-linked
- Impaired Cu absorption
- Increased Cu excretion in urine
  - Hair twisting, defect of arterial wall, spasms
  - Skin and hair hyperpigmentation, delayed growth development.
  - Affected children die until 3 years of age.
Copper (Cu)

**Other metabolic aspects of copper deficiency**

- Cu deficient anemia (mikrocytic normochromic anemia)
- Arterial wall weakening (aneurysma)
- Hypopigmentation (defect of melanine synthesis)
- Brain dysfunction (ataxia)

**Toxicity**

- Increased lipid peroxidation, free radical formation
- Chronic toxicity – hemoglobinuria, proteinuria, renal failure

**Copper concentration in various clinical situations**

<table>
<thead>
<tr>
<th></th>
<th>SERUM COPPER</th>
<th>URINE COPPER</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nutritional deficiency</td>
<td>↓</td>
<td>↓</td>
</tr>
<tr>
<td>Menkes syndrome</td>
<td>↓</td>
<td>↑</td>
</tr>
<tr>
<td>Acute copper toxicity</td>
<td>↑ or ↑↑</td>
<td>↑</td>
</tr>
<tr>
<td>Chronic copper toxicity</td>
<td>↑</td>
<td>↑</td>
</tr>
<tr>
<td>Wilson’s disease</td>
<td>N or ↓</td>
<td>↑ or ↑↑</td>
</tr>
<tr>
<td>Smoking, inflammatory conditions</td>
<td>↑ or ↑↑</td>
<td>N</td>
</tr>
<tr>
<td>Estrogen, pregnancy</td>
<td>↑ or ↑↑</td>
<td>N</td>
</tr>
</tbody>
</table>

N, normal; ↓, decreased; ↑, increased; ↑↑, Significantly increased.
Zinc (Zn)

- Dietary zinc: 150 µmol/day
- 30% absorbed
- Biliary excretion: 140 µmol/day
- Body distribution: 30 mmol
- Muscle: 60%
- Bone: 30%
- Other tissues: 10%
- Plasma: 11–23 µmol/L
- Urine: <10 µmol/day
Zinc (Zn)

Biochemical importance

1. Cofactor of enzymes
   - Carboanhydrase
   - Lactate dehydrogenase
   - Glutamate dehydrogenase
   - Alkaline phosphatase
   - Superoxide dismutase
   - Thimidine kinase
   - Matrix metaloproteinase
   - Gustin – salivary protein (taste regulation)

2. Biosynthesis of proteins (part of RNA proteinase)
3. Insulin stabikisation in Langerhans islets

- Transported bind in metallothionein

Deficiency Zn

- Alzheimer disease
- Depression
- Dementia
- Dermatitis
- Alopecia
- Acrodermatitis enteropathica
Iron (Fe)

- Iron intake: ~20mg/day, ~0.35mmol/day
- ~5–10% absorbed
- ~90% excreted

Body distribution:
- Red cell mass: ~75%
- Ferritin stores: ~20%
- Myoglobin: ~5%

Iron loss:
- Desquamation
- Menstrual flow
- Urine excretion
Iron (Fe)

Metabolism

<table>
<thead>
<tr>
<th>Name</th>
<th>Molecular weight</th>
<th>No. of iron atom</th>
<th>Site</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Heme containing proteins</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hemoglobin</td>
<td>65,000</td>
<td>4</td>
<td>RBC</td>
</tr>
<tr>
<td>Myoglobin</td>
<td>17,000</td>
<td>1</td>
<td>Muscle</td>
</tr>
<tr>
<td>Cytochrome oxidase</td>
<td>180,000</td>
<td>2</td>
<td>Mito</td>
</tr>
<tr>
<td>Cytochrome b</td>
<td>30,000</td>
<td>1</td>
<td>do</td>
</tr>
<tr>
<td>Cytochrome c1</td>
<td>37,000</td>
<td>1</td>
<td>do</td>
</tr>
<tr>
<td>Cytochrome c</td>
<td>12,000</td>
<td>1</td>
<td>do</td>
</tr>
<tr>
<td>Cytochrome b5</td>
<td>15,000</td>
<td>1</td>
<td>ER</td>
</tr>
<tr>
<td>Cytochrome P450</td>
<td>55,000</td>
<td>1</td>
<td>ER, Mito</td>
</tr>
<tr>
<td>Catalase</td>
<td>240,000</td>
<td>4</td>
<td>RBC</td>
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<tr>
<td>Lactoperoxidase</td>
<td>93,000</td>
<td>1</td>
<td>Milk</td>
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<tr>
<td>Tryptophan pyrrolase</td>
<td></td>
<td>4</td>
<td>Cytosol</td>
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<tr>
<td>Nitric oxide synthase</td>
<td></td>
<td>1</td>
<td>Endothelium</td>
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<tr>
<td><strong>Iron-sulfur complexes</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Complex III Fe-S</td>
<td>30,000</td>
<td>2</td>
<td>Mito</td>
</tr>
<tr>
<td>Succinate DH</td>
<td>27,000</td>
<td>4</td>
<td>Mito</td>
</tr>
<tr>
<td>Xanthine oxidase</td>
<td>275,000</td>
<td>8</td>
<td>Liver</td>
</tr>
<tr>
<td><strong>Non-heme iron containing proteins</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aconitase</td>
<td>66,000</td>
<td>2</td>
<td>TCA cycle</td>
</tr>
<tr>
<td>Phe-hydroxylase</td>
<td>110,000</td>
<td>2</td>
<td>Liver</td>
</tr>
<tr>
<td>Transferrin</td>
<td>77,000</td>
<td>2</td>
<td>Plasma</td>
</tr>
<tr>
<td>Ferritin</td>
<td>450,000</td>
<td>4,000</td>
<td>Tissues</td>
</tr>
<tr>
<td>Hemosiderin</td>
<td></td>
<td>Many</td>
<td>Liver</td>
</tr>
</tbody>
</table>

Mito = mitochondria; ER = endoplasmic reticulum; DH = dehydrogenase; Phe = phenyl alanine
Iron (Fe)

Fe deficiency

Microcytic anemia

Fe concentrations in various clinical states

<table>
<thead>
<tr>
<th>CONDITION</th>
<th>SERUM IRON</th>
<th>TRANSFERRIN</th>
<th>FERRITIN</th>
<th>PERCENT SATURATION</th>
<th>TIBC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Iron deficiency</td>
<td>↓</td>
<td>↑</td>
<td>↓</td>
<td>↓</td>
<td></td>
</tr>
<tr>
<td>Iron overdose</td>
<td>↑</td>
<td>↓</td>
<td>↑</td>
<td>↑</td>
<td>↑</td>
</tr>
<tr>
<td>Hemochromatosis</td>
<td>↑</td>
<td>Slightly ↓</td>
<td>↑</td>
<td>↑</td>
<td>↓</td>
</tr>
<tr>
<td>Malnutrition</td>
<td>↓</td>
<td>↓</td>
<td>↓</td>
<td>Variable</td>
<td>↓</td>
</tr>
<tr>
<td>Chronic infection</td>
<td>↓</td>
<td>↓</td>
<td>↑</td>
<td>↓</td>
<td>↓</td>
</tr>
<tr>
<td>Acute liver disease</td>
<td>↑</td>
<td>Variable</td>
<td>↑</td>
<td>↑</td>
<td>Variable</td>
</tr>
<tr>
<td>Chronic anemia</td>
<td>↓</td>
<td>N or ↓</td>
<td>N or ↑</td>
<td>↓</td>
<td>N or ↓</td>
</tr>
</tbody>
</table>

N, normal; ↑, decreased; ↓, increased.
**Selenium (Se)**

**Biochemical importance**

1. Part of enzymes
   - Glutathion peroxidase
   - 5´-dejodase

2. Normal spermiogenesis
3. Activation of protein biosynthesis (selenocystein)
4. Cellular antioxidant

**Deficiency Se**

- Myocardial necrosis
- Liver necrosis
- Arrythmias
- Myopaties

**Toxicity Se**

Selenoses – hair and nail falling
- weight loss
- diarrhoea
- osteoarthrosis
Iodine (I)

Biochemical importance

Thyroid hormone synthesis

Deficiency I
- struma
- autoimunitní hypothyreoiditida
- kongenitální hypothyreóza

Excess I
- hyperthyreoidismus
# Manganese (Mn)

## Biochemical importance

1. **Cofactor**
   - Hydrolase
   - Kinase
   - Decarboxylase
   - Transferase
   - Superoxid dismutase
   - Glycosyl transferase
   - RNA polymerase

## Transport

- Coupled with protein transmanganin
- Transport is inhibited by Fe

## Deficiency Mn

- Growth and skeletal abnormalities

## Toxicity Mn

- Neuropsychical diseases
Molybdenum (Mo)

Biochemical importance

1. Cofactor
   - Xanthin oxidase
   - Aldehyde oxidase
   - Sulfite oxidase

Deficiency Mo
   - Esophageal tumors

Excess Mo
   - Molybdenosis
     growth retardation
diarrhoea
anemia

Cu and cysteine reduces Mo concentration in serum
Nickel, Cobalt, Chromium, Fluorine

**Nickel**
- Urease, methyl coenzyme reductase
  - Excess – Carcinogenesis
  - Deficit – Iron metabolism deficiency
- ACP inhibitor

**Cobalt**
- Vitamin B12
- Stimulation of erythropoietin production

**Chromium**
- Kinase signal pathway stimulation
  - Deficit – Glucose tolerance impairment
  - growth disorders
  - defects in spermiogenesis
- Inzuline binding

**Fluorine**
- Anorganic matrix in bones and teeths
  - Deficit – Osteoporosis, karies
# Trace elements - Summary

<table>
<thead>
<tr>
<th>Mineral</th>
<th>Content (g)</th>
<th>Major source</th>
<th>Daily requirement (g)</th>
<th>Functions/Occurrence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Water</td>
<td>25,000-40,000</td>
<td>Water in solid foods, From metabolism 300g</td>
<td>1200, 900</td>
<td>Solvent, cellular building block, dielectric, coolant, medium for transport, reaction partner</td>
</tr>
<tr>
<td>Na</td>
<td>100</td>
<td>Table salt</td>
<td>1.1-3.3</td>
<td>Osmoregulation, membrane potential, mineral metabolism</td>
</tr>
<tr>
<td>K</td>
<td>150</td>
<td>Vegetables, fruit, cereals</td>
<td>1.9-5.6</td>
<td>Membrane potential, mineral metabolism</td>
</tr>
<tr>
<td>Ca</td>
<td>1.300</td>
<td>Milk, milk products</td>
<td>0.8</td>
<td>Bone formation, blood clotting, signal molecule</td>
</tr>
<tr>
<td>Mg</td>
<td>20</td>
<td>Green vegetables</td>
<td>0.35</td>
<td>Bone formation, cofactor for enzymes</td>
</tr>
<tr>
<td>Cl</td>
<td>100</td>
<td>Table salt</td>
<td>1.7-5.1</td>
<td>Mineral metabolism</td>
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<tr>
<td>P</td>
<td>650</td>
<td>Meat, milk, cereals, vegetables</td>
<td>0.8</td>
<td>Bone formation, energy metabolism, nucleic acid metabolism</td>
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<tr>
<td>S</td>
<td>200</td>
<td>S-containing amino acids (Cys and Met)</td>
<td>0.2</td>
<td>Lipid and carbohydrate metabolism, conjugate formation</td>
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<tr>
<td>Fe</td>
<td>4-5</td>
<td>Meat, liver, eggs, vegetables, potatoes, cereals</td>
<td>10</td>
<td>Hemoglobin, myoglobin, cytochromes, Fe/S clusters</td>
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<tr>
<td>Zn</td>
<td>2-3</td>
<td>Meat, liver, cereals</td>
<td>15</td>
<td>Zinc enzymes</td>
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<tr>
<td>Mn</td>
<td>0.02</td>
<td>Found in many foodstuffs</td>
<td>2.5</td>
<td>Enzymes</td>
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<tr>
<td>Cu</td>
<td>0.1-0.2</td>
<td>Meat, vegetables, fruit, fish</td>
<td>2.3</td>
<td>Oxidases</td>
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<tr>
<td>Co</td>
<td>&lt;0.01</td>
<td>Meat</td>
<td>Traces</td>
<td>Vitamin B₁₂</td>
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<tr>
<td>Cr</td>
<td>&lt;0.01</td>
<td></td>
<td></td>
<td>Not clear</td>
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<tr>
<td>Mo</td>
<td>0.02</td>
<td>Cereals, nuts, legumes</td>
<td>0.15-0.5</td>
<td>Redox enzymes</td>
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<tr>
<td>Se</td>
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<td>Vegetables, meat</td>
<td>0.05-0.2</td>
<td>Selenium enzymes</td>
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<tr>
<td>I</td>
<td>0.03</td>
<td>Seafood, iodized drinking water</td>
<td>0.15</td>
<td>Thyroxin</td>
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<tr>
<td>Requirement not known</td>
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<td>Drinking water (fluoridated), tea, milk</td>
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<td>Bones, dental enamel</td>
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</table>

+ Content in the body of a 65 kg adult
References