# Metal poisoning – copper, zinc, thallium, tin, selenium, arsenic

Lecture No. 10

# Copper - Cu

- Intoxications quite rare
- Mainly from copper fungicides, coins etc.
- $CuSO_4$ – for seeds, plants, antiparasitic for fish, $Cu(OH)_2$, $CuCl_2.3Cu(OH)_2$, $Cu_2O$
- $Cu^{1+}$ salts are water insoluble, $Cu^{2+}$ salts are water soluble
- Nutritional essential element
- A part of superoxiddismutase, cytochrome-c-oxidase, monoamine oxidases etc.

- In blood transported bound to albumin, ceruloplasmin
- Stored in liver and bone marrow
- Excretion in bile
- Most sensitive species are sheep (unable to increase elimination process into bile – Cu/adenosine ATPase), other ruminants less, monogasters are quite insenstitive
- In dogs – Bedlington + West higland white + Skye terriers,  Dalmatians, Labrador retrievers and Doberman pinschers can have genetic predisposition for Wilson disease

- **Mechanism of action**:

- Haematotrophic poison – directly toxic to erythrocytes
- Hepatotoxic – directly toxic to hepatocytes
- Probably due to oxidation potential - catalyzes the production of very reactive radical ions – oxidative stress

- **Clinical signs**:

- Corrosive effect on GIT mucosa (haemorrhagic gastritis and enteritis), vomiting (green colour), colic, black excrements
- Hypoxia – acute hemolytic crisis, damage to liver and kidneys
- In chronic intake: apathy, anorexia, icterus, hepatic encephalopathy – neurological signs

- **Pathological examination**:

- Inflammatory changes on GIT mucosa, green-blue colour of mucosa, hypertrophy of kidneys and liver, icterus and dark kidneys in chronic poisoning

- **Treatment**:

- Activated charcoal, laxatives, GIT protection – sucralfat, treatment of anaemia, hypoxia, etc.
- Addition of molybdenum and zinc in diet in sheep – decrease in copper absorption
- Chelating agents – penicilamin (in Wilson disease)

# Zinc - Zn

- Poisonings quite rare
- Zinc from medicines – common in dogs; zinc from containers made of galvanized metal plates – cattle
- An essential element of the body
- Present in about 200 metalloenzymes – e.g. carbonic anhydrase, alkaline phosphatase, lactate and alcohol dehydrogenases
- Necessary for nervous system development, for immune system, required for vitamin A metabolism and calcification of bones, etc.
- Chelates with cysteine and histidine, forms so called zinc fingers – bind to DNA, regulation of genetic activity

- Intestinal absorption of zinc influenced by iron and copper
- Transported bound to albumin and macroglobulin
- Excreted in faeces, less in urine, milk, saliva
- Detectable in every organ system, especially the prostate and liver, and is at its highest concentration in the tapetum lucidum

- **Mechanism of action**:

- Probably competes with copper and iron in the organism – decreased serum copper (in breathing enzymes, hematopoesis) – decreased utilisation of oxygen, oxidative stress
- Decreased ceruloplasmin – antioxidant
- Decreases glutathione levels

- **Clinical signs**:

- gastrointestinal upset from direct irritation, anorexia, lethargy, hyperventilation, liver damage, pancreatitis, arthritis, multiorgan (mainly kidney) failure
- intravascular haemolytic anaemia, morphological changes of erythrocytes including nucleated erythrocytes, Heinz bodies and spherocytes

- **Pathological examination**:

- Degeneration of liver, kidneys, pancreas, petechias, haemorrhage in lymphatic nodes, spleen and brain, gastroenteritis, arthritis, in ZnO inhalation intoxication lung emphysema and oedemas in chest area

- **Treatment**:

- Eradication of metal particles from stomach, administration of $Na_2CO_3$ – formation of insoluble $ZnCO_3$
- Blood transfusion in severely anaemic patients
- EDTA

# Thallium - Tl

- Used for making low-melting point
  special glass for highly reflective lenses
- In developing countries still permitted as a pesticide (rodenticide, insecticide)
- Body absorbs thallium very effectively, especially through the skin, lungs, GIT
- Two-phase elimination – most within 24 hours in urine, but the rest stays for weeks and is excreted via faeces
- Undergoes enterohepatic circulation
- Cummulated in brain, kidneys, bones

- **Mechanism of action:**
- Inhibition of respiration enzymes and oxidative phosphorylation
- Interference with porphyrin and collagen metabolism
- Exchange with $K^+$ in muscles, neurons (Na/K ATPase), stabilisation of ribosomes etc.
- Inhibition of mitosis, sweating and sebaceous glands
- **Clinical signs:**
- Acute - Stomach ache, colic, diarrhoea, bradycardia or tachycardia (exchange with K+, damage to nervus vagus), nervous system damaged – tremors, paralysis, reversible hair loss
- Chronic – anorexia, stomach ache, nerve pains and joint pains, peripheral neuropathies, alopecia, red skin, kidney damage

- Often consequences such as trembling, paralyses and behavioural changes remain

- Pathological examination: haemorrhagic gastritis, ulceration, damage of spleen, kidneys, hyperaemia of brain

- Treatment: Prussian blue - $Fe_7(CN)_{18}(H_2O)_x$ – p.o., formation of non-soluble complexes that are excreted in bile – inhibition of enterohepatic circulation
- + fluid therapy to maintain kidney function

# Tin - Sn

- Mainly applied as various organic substances – phenyl- and methyl-tin compounds used as fungicides
- The number of applications of organic tin substances is still increasing - the paint industry, the plastic industry, agriculture
- Triethyltin is the most dangerous organic tin substance
- Absorption through food, breathing and skin
- Accumulation in an organism
- **Mechanism of action**:

  Increases permeability of mitochondria membranes for anions – mineral imbalance ($Ca^{2+}$). Also inhibition of Ala-D, but weaker then in lead. Disturbance in steroid hormone synthesis.

- **Acute intoxication**:
  - Local irritation on mucosas, eye and skin irritations, headaches, stomach ache, severe sweating, urination problems, severe tremor and convulsions

- **Chronic intoxication**:
  - Depressions, liver damage, shortage of red blood cells, brain damage (anger, sleeping disorders, forgetfulness, headaches)
  - Malfunction of immune system – inhibition of NK cells function – thus increased risk of carcinogenesis

- **Pathological examination**: necrosis on liver and kidneys, brain oedema, corrosive lesions on mucosa

- **Treatment**: Carbo adsorbens, symptomatic

# Selenium - Se

- In soil, cumulation in plants –
  can transform it into more toxic compounds
- In middle Europe lack of selenium in soil and food !
- Poisonings in north America and south Africa, here due to overdose during treatment (in pigs and cattle)
- Very good absorption through guts, deposition in liver, spleen, kidneys, hair and horn of hoof
- Substitutes sulphur in amino-acids, inhibition of oxidation-reduction enzymes

- **Acute form**:

- depression, ataxia, dyspnoe, salivation, cyanosis, anaemia, decreased fibrinogen and prothrombin, death due to respiration collapse

- **Chronic form**:

- weight decrease, anorexia, loss of hair, disturbances in hoof formation, leg paresis, damage of joints and long bones

- **Pathological examination**: generalised haemorrhages, ascites, lung oedema, degenerative changes on liver, kidneys – acute form; atrophy of myocardium and liver cirrhosis in chronic form

- **Treatment**: symptomatic

# Arsenic - As

- Metallic arsenic not toxic – insoluble in water and acids
- Its compounds toxic
- Nowadays poisonings quite rare, but its effect known since ancient times
- Used as a pesticide, in industry
- Absorption via guts or skin – systemic toxicity
- Excretion via urine
- Deposition in skin, in nails and hair for many years
- If administered in low doses – addiction - mithridatism

- **Mechanism of action**:

- Trivalent compounds most toxic (pentavalent less)
- Binds to –SH groups – block of many enzymes (oxidative phosphorylation, glycolysis)
- Damage of mucosa, endothelium,
- Increased permeability of vessels, decrease in blood pressure

- **Clinical signs**:

- Peracute poisoning (within a few seconds to a few minutes):

  - collapse of blood circulation, dilatation of vessels, sometimes vomiting and diarrhoea

- Acute poisoning:
  - violent stomach pains, tenderness and pressure, retching, vomiting, sense of dryness and tightness in the throat, thirst, hoarseness and difficulty of speech
  - the matter vomited, greenish or yellowish, sometimes streaked with blood
  - convulsions, delirium, death due to circulatory collapse

- Chronic poisoning:
  - strong profuse diarrhoea, inappetence, dehydration
  - changes in skin colour, formation of hard patches on the skin
  - skin cancer, lung cancer, cancer of the kidney and bladder

- **Pathological examination**:

- haemorrhage on mucosa of GIT, pseudomembranes, necrotisation, fatty degeneration of parenchymatic organs

- **Treatment**:

- dimercaprol, sodium thiosulphate, symptomatic

More info:

http://www.inchem.org/documents/ehc/ehc/ehc200.htm

http://www.vet.uga.edu/VPP/clerk/Hardy/

http://www.lenntech.com/Periodic-chart-elements/Tl-en.htm

http://en.wikipedia.org/wiki/Arsenic_poisoning

http://www.emedicine.com/emerg/topic42.htm