MUNI
PHARM

Toxicologically important inorganic substances

PharmDr. Zuzana Široká, Ph.D.

NaCl

- The poisoning is typical for veterinary practice, rare in people (bad concentration of saline during gastric lavage!)
- Salt (sodium chloride) is toxic only in high doses (quantitative toxicity)
- 2 types of poisoning – ingestion of high amounts of NaCl (direct poisoning, develops within 24h, acute) or lack of water (indirect poisoning, develops within 3-5 days)
- The intake of salt as mash or liquid is much worse (immediate absorption)
- Poisoning worse in babies - taste not developed yet + lower content of blood proteins = lower oncotic pressure and bigger oedemas

NaCl

Mechanism of action:

- Na+ (sodium) and Cl- (chloride) are extracellular ions important for osmotic balance in an organism
- NaCl is absorbed completely from guts (based on concentration gradient)
- In excess irritates GIT and causes liquefaction of its content
- In vessels causes shrinking of endothelial cells and increase the size of pores
- High content of these ions in interstitium induces passage of water from cells to interstitium = inner dehydration of cells
- These mechanisms lead to accumulation of water around cells and cause oedemas, which oppress organs, brain is the most sensitive one

NaCl

Clinical signs:

Direct poisoning:

- Increased salivation, thirst, vomiting, diarrhoea, colic pains
- Oedemas
- Coordination disturbances, head pressing, tremors and seizure attacks

Indirect poisoning:

- Thirst, dry mucosa, dehydration
- Constipations, colic pain
- Paresis and paralysis

Treatment:

- Administration of water, but NEVER ad libitum !!! This could deteriorate oedemas and cause immediate death
- Gradual slow infusion based on natraemia, if not possible, then recommended dosage is 0,5 % of body weight every hour (for 2-3 days)

KCl

- Medical use (supplementation of potassium), present in food (melon, bananas)
- Also used for judicial executions, assisted death, and, rarely, suicides
- Reasons of poisoning - overdose of KCl medication, kidney failure (also due to uncontrolled diabetes), Addison´s disease, potassium-conserving diuretics
- **Mechanism of action:** Hyperkalaemia disrupts the depolarization and repolarization of myocardial cells, resulting in diverse types of arrhythmias and cardiac arrest. Similar effect on neurotransmission = paralysis.
- Slow overdose - muscle weakness, numbness, tingling, nausea, or other unusual feelings
- If hyperkalaemia comes on suddenly - heart palpitations, shortness of breath, chest pain, nausea, or vomiting, fibrillations, asystole, death
- **Treatment:** diuretics, IV fluids, dialysis, potassium binders (patiromer)

NO_3^- - nitrates

- Nitrates are industrial fertilizers and laboratory chemicals, used to produce pyrotechnics (fireworks)
- Fertilizing can cause increased levels of nitrates in feed, especially in vegetables (mainly lettuce and spinach)
- These agents can also contaminate drinking water
- Dangerous especially to sucklings:

a) Higher pH in stomach – microflora lives there and converts NO_3^- to more toxic NO_2^-

b) Foetal haemoglobin more sensitive to oxidation (See NO_2^- slide)

c) Lower activity of methaemoglobin reductase

NO_2^- - nitrites

- Industrial and laboratory chemicals, chemicals used in food industry for preservation of meat (also cause the rich pink colour of meat products), parts of fertilisers
- Quickly absorbed from GIT

Nitrite form of poisoning (minutes)

- in massive intake of pure nitrites – direct effect on vessels (similar to nitroprusside or nitroglycerin which release NO) = paralysis of vascular muscles, vasodilatation, decrease of blood pressure, circulatory collapse
- treatment: elimination of non-resorbed substance from GIT (charcoal is not working on NO_2^- and NO_3^-), administration of analeptics (reinforce circulatory system), adrenalin in collapse

NO_2^- - nitrites

Methaemoglobin form of poisoning (more common, hours)

- nitrites convert = oxidize haemoglobin (Fe^{2+}) into methaemoglobin (Fe^{3+}) = insufficient oxygen transport to tissues = hypoxia to asphyxia
- Significant cyanosis, dyspnoea, tachycardia, apathy, fatigue, decreased mobility, convulsions, abortions in pregnant, coma, death

- In erythrocytes and liver, there is an enzyme called methaemoglobin-reductase (MetHb reductase, NADH dependent), which reduces iron in haem back to Fe2+. This enzyme is only of limited capacity – signs after depletion
- babies, pregnant(+ cats and ferrets) have very low activity or amount of this enzyme
- antidote is **methylene (or toluidine) blue -** reduces Fe^{3+} back to Fe^{2+} by adding electron to iron and also to MetHb reductase. Administered slowly IV
- vitamin C and other antioxidants may be added

Ammonia

- Colourless, highly irritating gas with a pungent, suffocating odour
- Lighter than air, flammable at high concentrations and temperatures
- Dissolves in water = an alkaline corrosive solution
- Exposure to ammonia may be fatal if it is inhaled - ammonia's odour threshold is fortunately sufficiently low to provide adequate warning of its presence
- NH_3 present in non-ionized (NH_3 – toxic) and ionized form NH_4^+

Ammonia

Clinical signs:

- Even low concentrations of ammonia produce rapid eye and nose irritation
- Throat irritation, cough, bronchospasm.
- Higher concentrations cause immediate laryngospasm and laryngeal oedema resulting in upper airway obstruction, pulmonary oedema can occur
- Skin contact with concentrated ammonia can cause serious corrosive injury
- Swallowing causes immediate burning in the mouth and throat, chest, and abdomen with swallowing difficulty, drooling, and vomiting. Perforation of the oesophagus or stomach may occur

Treatment:

- Wash skin and visible mucosas with cold water, IV fluids
- Fresh air, supplemental oxygen if available, inhalation of aerosol containing 2% of citric acid and 1% procaine
- In p.o. intake water (neutralise stomach content – solution of 1-2 % acetic acid if absorption and systemic effects are expected)

Cyanides (KCN, NaCN, HCN)

- Industrial and laboratory chemicals (salts of hydrocyanic acid), cyanide poisoning is often a component of smoke inhalation poisoning
- Present in plants (cyanogenic glucosides)
- LD50 is approximately 2 mg/kg
- Poisonings caused by CN^- ions

Acute poisoning:

- CN^- binds to, and inhibits, the ferric (Fe^{3+}) haem moiety form of mitochondrial cytochrome c oxidase = inhibition of the mitochondrial electron transport chain = arrest of aerobic metabolism = systemic hypoxia, and death from histotoxic anoxia
- Tissues that heavily depend on aerobic metabolism such as the heart and brain are particularly susceptible to these effects
- Cyanide also binds to other haem-containing enzymes, such as members of the cytochrome P450 family, and to myoglobin

Cyanides (KCN, NaCN, HCN)

Chronic poisoning:

– cyanide-related hypothyroidism due to disruption of iodide uptake by the follicular thyroid cell sodium-iodide symporter by thiocyanate, a metabolite in the detoxification of cyanide

Clinical signs:

- Excitement initially, accompanied by rapid respiration rate. Then dyspnoea and tachycardia. „Bitter almond" breath smell may be present; however, the ability to detect this smell is genetically determined in people, and anosmic people (a significant proportion of the population) cannot detect it. Salivation, lacrimation, vomiting, inability to hold urine and faeces, muscle fasciculations, convulsions, arrhythmias, coma, death

Treatment:

– Hydroxycobalamin (vitamin B_{12a}) to yield cyanocobalamin (vitamin B_{12})

– Nitrites + sodium thiosulfate (binding to Fe^{3+} in blood, not in cells)

Carbon monoxide - CO

- A colourless and odourless gas, slightly lighter than air (Mr = 28 (12+16), air mainly N_2 and O_2 (28 a 32 = cca 29)
- It is the product of the incomplete combustion (lack of oxygen) of carbon-containing compounds (e.g. fossil fuels) – use detectors!
- Dangerous in spaces with bad ventilation – gas flow-heaters, gas heating, gas oven, stoves and fire places with blocked chimney, car and other engine exhaust fumes in a closed garage, cigarette smoke etc. – LC in the air only 0,4 %

- **Mechanism of action:** Bond to iron in porphyrin rings = in blood mainly binds to haemoglobin and produces very stable product called carbonylhaemoglobin (or synonym carboxyhaemoglobin) = COHb

CO

- The affinity of CO to haemoglobin is approx. 240x higher than the affinity of oxygen, in foetal haemoglobin even higher. The bond is reversible, but very firm
- Moreover, CO binds also to myoglobin (rhabdomyolysis and renal failure)
- CO blocks oxidative phosphorylation (cytochrome oxidase, breathing enzyme in mitochondria) in muscle – decrease of myocardial contractility
- CO blocks the function of liver enzymes including Cytochrome P450 – inhibition of detoxification

- **Clinical signs:**
- according to stage of poisoning: weakness, vertigo, fast breathing, headache, cyanosis, tachycardia, convulsions of skeletal muscles, slow pupillary reaction to light, deep coma, death

CO

- also chronic poisonings described – tiredness, vertigo, problems with vision, stomach aches, parestezia
- in almost one third of affected late complications develop

Treatment:

- transfer the affected animal to fresh air, give the inhalation of 100% oxygen (at the beginning in overpressure)
- if there is a problem with heart action, administer analeptics

Diagnostics:

- the assessment of COHb content in blood (%). Lethal concentration of COHb in blood is above 60%

CO_2 – carbon dioxide

- CO_2 normal concentration in air is 0,03%
- CO_2 is heavier than air, thus is occurs downstairs
- Colourless, odourless
- It is generated during complete combustion of organic substances, during fermentative processes
- It occurs in caves, mines, during excavation of wells, sillage holes
- Haemoglobin is occupied – formation of carbaminohaemoglobin, but CO_2 is also transported freely in blood. Most commonly the reason of poisoning is just lack of oxygen
- Death due to suffocation

CO_2

Clinical signs:

- about 5% - narcotic effect, tachypnoea, tachycardia, increased blood pressure, decreased body temperature
- over 20% - induces rapid apnoe and death (used for euthanasia of fish and some other small animals)

Therapy:

- fresh air, inhalation of oxygen, analeptics to increase the frequency of breathing (in rapid intoxication)

Sulphane – H_2S

- Heavier than air, smell of rotten eggs
- In high concentration paralysis of olfactory nerve – impossible detection
- High concentration in waste containers in pig farms, from industry, laboratory chemical
- Reacts with metaloenzymes, most important is bond to Fe^{3+} in cytochrome-oxidase – similarly to cyanides – inhibition of cell respiration
- Irritation of eyes, cough, dyspnoea, lung oedema, cyanosis, tremors, death. Long-term exposure: exhaustion, inappetence, confusion
- Treatment in severe poisoning the same as in cyanides – methaemoglobin formation, then it reacts with sulphur – thiosulphates. Otherwise wash the mucosas with cold water, fresh air/oxygen

Other substances

- Poisoning possible also by **SO_2** (industry, used in wine production, dried fruits, seed treatment - fungicide, as a bleach) – irritation, corrosion, lung oedema, allergic reaction

- **Nitrosamines** – from nitrates and nitrites, nitrous acid is formed in guts – in acidic pH nitroso cations are released. They react with secondary amines (amino acids, glucosamines etc.) and form carcinogenic nitrosamines. They can be produced also during meat smoking or released from other chemicals (triazine herbicides, tensides etc.)

Acids

- Coagulation of proteins = corrosive (caustic) effect, create scab/crust
- Local irritation, corrosion of the affected place (skin, eye, GIT), necrosis, perforation
- If healed, strictures and scars often appear
- If ingested, drooling, dysphagia, and pain in the mouth, chest, or stomach appear
- After absorption from GIT, acidosis is expected (first tachycardia, tachypnoea, later deep and slowed breathing, hypotension, coma)
- **Treatment: No vomiting or lavage, no charcoal**! Wash locally with water (dilution), IV bicarbonates

Alkalis (hydroxides)

- Coagulation of proteins = corrosive (caustic) effect
- Liquefaction necrosis = do not corrode only superficially, but also deep into the tissues – worse than acids
- Local irritation, corrosion of the affected place (skin, eye, GIT), necrosis, perforation, peritonitis, shock
- If ingested, drooling, dysphagia, and pain in the mouth, chest, or stomach appear
- If healed, strictures and scars often appear
- **Treatment: No vomiting or lavage, no charcoal**! Wash locally with water (dilution), IV fluids (prevention/therapy of shock)

Both acids and alkalis

- Gastric emptying by emesis or lavage is contraindicated because it can reexpose the upper gastrointestinal tract to the caustic
- Attempts to neutralize a caustic acid by correcting pH with an alkaline substance [and vice versa] are contraindicated because severe exothermic reactions may result
- Activated charcoal is contraindicated because it may infiltrate burned tissue and interfere with endoscopic evaluation
- Insertion of a nasogastric tube is contraindicated because it can damage already compromised mucosal surfaces
- CT of chest and abdomen should be performed (endoscopy with great caution only if necessary)

Metals

Main mechanisms of action:

- Binding to –SH groups and inhibiting enzymes and structural proteins
- Trigger oxidative stress (directly by participating in Fenton reaction, or indirectly by inhibiting antioxidant enzymes and depleting glutathione)

- Often deposit in hair and skin = non-invasive detection

Treatment:

- Chelating agents (formation of inactive complexes)
- Mainly EDTA and its salts, -SH containing substances (BAL = dimercaprol, DMPS, DMSA, D-penicilamine)
- Some metals have specific chelators – Prussian blue for thallium, deferoxamine for iron and aluminium
- Sodium thiosulfate – increases elimination of metals by kidneys + induces synthesis of metalothioneins

Mercury Hg (Movie Minamata)

- The only metal which is liquid at room temperature
- Both organic and inorganic compounds, all toxic
- Abiogenic
- Sources: earth’s crust and industry, burning of fossil fuels, waste
- Cumulation in water environment - water microorganisms transform pure or inorganic mercury into methylmercury – most common source of chronic poisonings – incorporation into food chain (fish)
- Other cases of intoxication usually occupational, mistakes – Iraq (wheat seed with antifungal phenylmercury compound – exchanged for food), Minamata disease (fishermen)

Mercury Hg

Elemental mercury:

- Liquid, almost no absorption in GIT, vapours are more dangerous - perfect absorption via lungs, excreted via urine, faeces and milk
- Once in the blood circulation, the target organ are kidneys, where it can cumulate and be deposited for several months
- Also crosses blood-brain barrier (change to inorganic mercury with longer deposition times) and placental barrier
- Clinical signs: kidney failure, neurological signs (tremors, behaviour changes)

Inorganic mercury:

- $HgCl_2$, $Hg(CN)_2$, $Hg(NO_3)_2$
- Do not cross barriers as much as elemental, absorption from GIT less than 40%, only traces excreted to milk(cross placenta)
- Water soluble salts coagulate peptides and are corrosive (damage of GIT mucosa + kidney tubules)

Mercury Hg

Organic mercury:

- Methoxyethylmercury and arylmercury compounds (e.g. phenylmercury) – release mercuric ions – act like inorganic compounds

- Methyl- and ethylmercury – firm bond, whole compound toxic, absorbed from GIT (> 90 %)
- Destroy haematoencephalic (blood-brain) barrier, increase its permeability
- Don't have corrosive effect on gastric/intestinal mucosas
- They have high affinity to neural tissue (change to inorganic mercury with longer deposition times in brain), cumulate and damage also kidneys
- Cross the placenta and have fetotoxic/teratogenic effect
- Ethylmercury – preserving agent in pharmacy – elimination within 1 week, methylmercury not manufactured intentionally – eliminated within several months

Lead Pb

- Soft, grey metal
- Known since ancient times, abiogenic to organisms
- Formerly used in pipes, tetraethyl-lead as a petrol additive, red-lead (minium) primer paintings
- Still used in bullets, batteries, shields for radiation
- Poisonings in people (pipes), cattle (lead paintings, batteries in silage), predatory birds
- Both inorganic and organic compounds – different characteristics
- Inorganic lead: toxic after ingestion
- Organic lead: toxic after skin contact, ingestion, inhalation

Lead Pb

- Absorption promoted by calcium, zinc and iron deficit and by fats in food, higher in young individuals
- High deposition in tissues – first in liver, then redistributed to bones (inorg.), kidneys, muscles and hair
- Bone-lead becomes mobilized through pregnancy or fracture healing
- Excretion via bile to faeces, also to urine and milk
- Inorganic compounds accumulate more and elimination is very slow, organic compounds excreted much quicker

Acute intoxication (12 – 92 hours after absorption)

- apathy, anorexia, CNS disturbances and brain oedema – tremor, loss of coordination, salivation, gnashing of teeth, aggressiveness, convulsions, blindness, death due to respiration collapse

Lead Pb

Subacute intoxication:

- similar symptoms, but more severe GIT damage, changing of constipation and severe diarrhoea, strong colic pains (Saturnine or Poitou colic), mydriasis, opisthotonus

Chronic intoxication:

- inappetence, anorexia, paresis, greyish gum line (Burton line), CNS disturbances

Inorganic lead (mainly):

- Disturbs saccharide metabolism, metabolism of haem - inhibits Delta-aminolevulinic acid dehydratase and other enzymes involved in haem formation
- The toxicity comes also from its ability to mimic other biologically important metals - calcium, iron and zinc, and replace them

Organic lead (mainly):

- interferes with excitatory neurotransmission by glutamate - potent inhibitor of the NMDA receptor, a protein playing an important role in brain development and cognition (also in development of schizophrenia)

Cadmium Cd

- Abiotic, extremely toxic even in low concentrations, accumulates in organisms and ecosystems
- Sources: earth crust, fossil fuels, plastic materials industry, electronic industry, metallurgy and smelting, tobacco fume
- Absorption after ingestion (1-5%) or by inhalation (better bioavailability)
- The first documented case of mass cadmium poisoning in the world - in Toyama Prefecture, Japan in 1912 to 1950s – **Itai-Itai disease** (ouch ouch disease, river polluted with waste from factory containing Cd, water used on rice fields – poisoning from rice)
- Deposition in liver, kidneys and gonads. Slow excretion (up to 10 years). Does not go to milk and to foetus

Cadmium Cd

- Inhibition of many enzymes – binds to –SH groups
- Antagonist to many metals – Zn, Cu, Ca, Fe
- Formation of complexes, which are cleaved in kidney – release of Cd = damage = damage to kidneys (disturbance of cholecalciferol = vitamin D hydroxylation, disturbance in acid excretion = gout)
- Xenoestrogenic element

Acute exposure:

- Cadmium fumes may cause flu like symptoms including chills, fever, and muscle ache
- Ingestion causes damage to the liver and the kidneys. Also CNS disturbances occur and changes in blood count

Cadmium Cd

Chronic exposure:

- Osteomalacia, osteoporosis – disturbance of vitamin D and calcium metabolism = pain in the joints and the back, and also increased risk of fractures. In extreme cases of cadmium poisoning, the mere body weight causes a fracture
- Inability to remove acids from the blood. This type of kidney damage is irreversible → gout (accumulation of uric acid crystals in the joint)
- Some patients may lose their sense of smell (anosmia)
- Damage of gonads, suspected carcinogen – tumours of testes

Arsenic As

- Abiotic, if administered in low doses – addiction - mithridatism
- Metallic arsenic not toxic – insoluble in water and acids
- Its compounds toxic, As^{3+} more than As^{5+}, inorganic more than organic (arsenobetain)
- Used as a pesticide, in industry (in the past for murders)
- Absorption via guts or skin, deposited in liver, kidneys, lungs, spleen, bones, skin, nails and hair; excretion via urine + faeces ($^{5+}$ more in U, $^{3+}$ more in F)

- Inhibits many enzymes (oxidative phosphorylation, glycolysis)
- Damage of mucosa, endothelium = increased permeability of vessels, decrease in blood pressure, oedemas, circulatory shock

Arsenic As

Peracute poisoning (within a few minutes):

- collapse of blood circulation, dilatation of vessels, fluid loss, oedema, sometimes vomiting and diarrhoea, death

Acute poisoning (hours):

- 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 is greenish or yellowish, sometimes streaked with blood, bloody excrements
- convulsions, delirium, death due to circulatory collapse

Chronic poisoning (Indian subcontinent – present in soil):

- profuse diarrhoea, inappetence, dehydration, thirst, dyspnoea
- changes in skin colour, formation of hard patches on the skin
- skin cancer, lung cancer, cancer of the kidney and bladder in humans

Copper Cu

- Intoxications less common
- Mainly from copper fungicides (CuSO4 – for seeds, plants, antiparasitic for fish, $Cu(OH)_2$, $CuCl_2.3Cu(OH)_2$, Cu_2O), ingestion of coins etc.
- Cu^{1+} salts are water insoluble, Cu^{2+} salts are water soluble = more toxic
- Nutritional essential element
- A part of superoxide dismutase, cytochrome-c-oxidase, monoamine oxidases etc.
- In blood transported bound to albumin and ceruloplasmin, stored in liver and bone marrow, excretion specifically in bile
- Genetically based poisoning by copper – Wilson´s disease
- Toxic also to sheep and some dog breeds (unable to increase elimination process into bile – limited Cu/adenosine ATPase

Copper Cu

- Works due to oxidation potential - catalyses the production of high amounts of reactive radicals (ROS) – oxidative stress (free Cu joins Fenton reaction)

Clinical signs:

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

- Typical pathological findings – icterus and black kidneys

Thallium Tl

- Abiotic, used for making special glass, released during smelting of metals
- In developing countries still permitted as a pesticide (rodenticide, insecticide)
- Body absorbs thallium very effectively via all routes - skin, lungs, GIT
- Two-phase elimination – majority quite quickly via urine, but the rest stays for weeks and is excreted via faeces - undergoes enterohepatic circulation
- Cumulated in brain, kidneys, liver, heart, bones, muscles

Mechanism of action:

- Bond to –SH groups - inhibition of respiratory enzymes and oxidative phosphorylation, interference with porphyrin and collagen metabolism, inhibition of keratin disulfide bonds – hair loss
- Exchange with K+ in muscles, neurons, enzymes (inhibition of Na/K ATPase)
- Possibly also stabilisation of ribosomes, inhibition of mitosis, decreased function of sweating and sebaceous glands (mechanism unknown)

Thallium Tl

Clinical signs:

- Acute (48h) - Stomach ache, colic, diarrhoea, bradycardia or tachycardia (exchange with K+, damage to nervus vagus), neurological signs – ataxia, tremors, paralysis; reversible hair loss
- Chronic (weeks) – anorexia, stomach ache, nerve pains and joint pains, peripheral neuropathies, myopathy, alopecia, red dry skin, kidney and liver damage

- After survival, often long term to life-long consequences such as trembling, paralyses and behavioural changes remain

Chromium Cr (Movie Erin Brockovich)

- Cr III is essential (carbohydrate metabolism)
- Cr VI used in industry
- Uptake depends on the valency (III or VI) and solubility of the compound
- Insoluble inhaled chromium particles can remain in the lung for a long time
- Distributed to all tissues of the body, excreted mainly via urine
- Chromium (VI) unstable in the body - rapidly reduced to chromium (V), chromium (IV) and ultimately to stable chromium (III) – chromium VI to IV = oxidative damage to body
- Ingestion of chromium (VI) can lead to severe respiratory, cardiovascular, gastrointestinal, hepatic and renal damage and potentially death
- Inhalation of chromium (III) salts - inflammatory changes in respiratory tract
- Chromium (VI) compounds are mutagenic and carcinogenic
- Potassium dichromate toxic to reproductive system and the developing foetus

Barium Ba

- Abiotic, silvery-white to yellowish metal
- Elemental barium and barium sulphide may be flammable in moist air
- Used in industry (soluble substances), insoluble barium sulphate used as an x-ray contrast material of the gastrointestinal tract
- Mechanism of action not fully understood - may be related to the action of barium as a competitive potassium channel antagonist that blocks the passive efflux of intracellular potassium
- Ingestion of barium compounds that dissolve in water/acids = the gastrointestinal tract, may cause rapid onset of nausea, salivation, vomiting, abdominal cramps, watery diarrhoea; hypokalaemia = ventricular tachycardia, hypertension and/or hypotension, muscle weakness, and paralysis; and kidney damage

Selenium Se

- Essential nutrient, narrow safety window
- Present in glutathione peroxidase, enzymes in thyroid gland etc.
- In soil, cumulation of selenium salts in plants – can transform it into organic compounds (selenocysteine, selenomethionine)
- In middle Europe lack of selenium in soil and food !
- Poisonings e.g. in north America and south Africa, here due to overdose during treatment (common in pigs and cattle, not in humans)

- Substitutes sulphur in amino-acids (loss of disulfide bond, misfolding), inhibition of oxidation-reduction enzymes, decrease in reduced glutathione = oxidative stress
- Acute poisoning = quick respiration paralysis, chronic = disturbances in hoof formation, leg paresis, damage of joints and long bones, alopecia

Fluorine F

- Biogenic element
- Intoxications rare: endemic due to soil content – India, or near aluminium works (dust with F), overdose of food supplements (cavity prevention)
- Except humans, the most sensitive species are cattle and honey bees
- Absorption by inhalation or orally
- Deposition in bones and teeth (non-degradable fluoroapatite), thyroid gland
- Increased density of bone tissue, exostosis, hypercalcification, deformation of bones and teeth
- Excreted in faeces, cross placenta, excreted in milk

Thank you for your attention

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