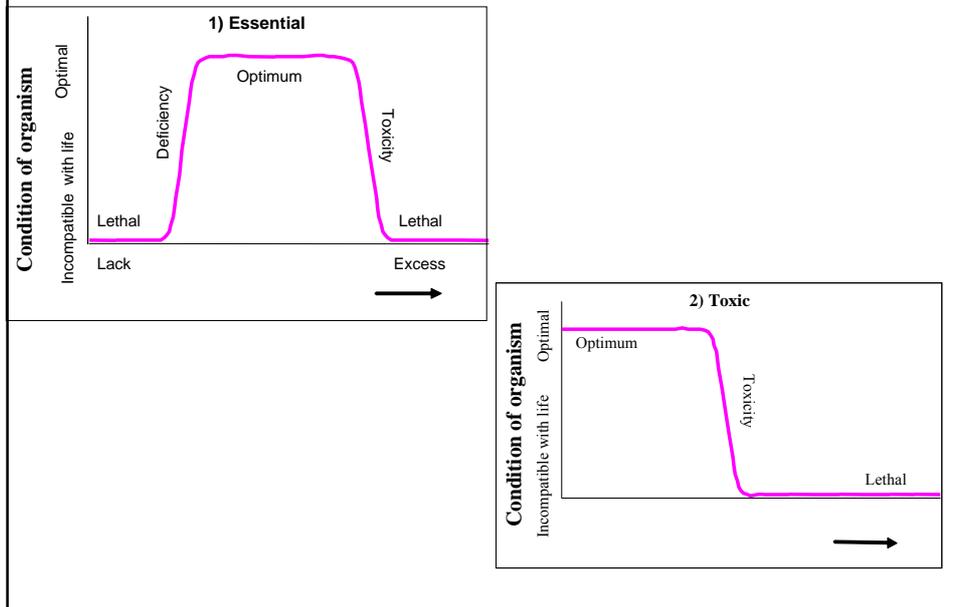


Essentiality and toxicity of elements and compounds in general



Elements of group I.A and their compounds

- **Hydrogen** (macrobiogenic, 1st order)
- **Lithium** (microbiogenic, 4th order)
- **Sodium** (macrobiogenic, 2nd order)
- **Potassium** (macrobiogenic, 2nd order)
- **Rubidium**
- **Cesium**

H – Hydrogen

Gaseous H₂ has no effect on organism (unless explodes).
Above 20 % in the air is choking due to displacement of O₂.

Some compounds very toxic (arsane AsH₃, phosphane PH₃, sulfane H₂S).

Flammable, forms explosive mixtures.

D (²H) - deuterium, T (³H)-tritium – half-life of decay 12.5 years, soft β-radiation

Rapid excretion, unless bound to cell nucleus

Li – Lithium

In 1978 it was found that Li is an essential trace element, whose deficiency affects endocrine glands. Lack of Li lowers fertility in animals. People with insufficient Li intake reportedly display higher occurrence of psychiatric disorders. Higher doses of Li can cause damage to the kidney (proximal tubuli) and convulsions. Doses close to toxic levels (500 mg/d) are used in psychiatry for treatment of manic-depressive psychosis, but the mechanism of action is still unknown.

Na – Sodium

The major extracellular cation, continuously removed from interior of living cells by means of 'sodium pump'. Together with chloride ion is important in acid-base balance, and maintenance of osmotic pressure and volume of the extracellular fluid. Low intake of Na in food and high loss (sweating) lead to decrease in blood pressure and faintness. On the other hand, chronically high intake of NaCl leads to hypertension. Daily Na intake in diet should not exceed 4-5 g.

Compounds: NaCl – 0.154 M – physiologic solution ('saline') – isotonic. Administration as intravenous infusion rather 'acidifies' the body. In contrast, NaHCO₃ causes 'alkalisation'. In cases of small deficits Na salts can be given orally.

Na₂SO₄ – 'Glauber's salt' - is an effective laxative.

NaOH – strongly corrosive, damages skin, mucosae and in particular eyes.

K – Potassium

The major intracellular cation. Both deficit and excess affect in particular heart and nervous system. Hypokalemia as well as hyperkalemia can lead to heart arrest!

!ATTENTION! Accidental exchange of CaCl₂ or NaCl for KCl can, if given intravenously, result in immediate death of the patient!!! Deficit of K causes muscle weakness and apathy. High losses of K occur in diarrheic diseases, which may also result in weakness of intestinal smooth muscles and obstipation. In such a case laxatives (that would further deepen deficit of K) must not be given; rather, the lacking K must be supplemented as soon as possible.

Daily intake of K should be at least 2-3 g.

Compounds: KOH - likewise NaOH is strongly corrosive. Other compounds of K can also have caustic effects, e.g. KCl that in oral administration can at higher concentrations damage the mucosae of digestive tract.

Rb – Rubidium

Higher doses are toxic due to displacement of potassium and can induce seizures

Cs – Cesium

Higher doses toxic. Accumulates in muscles. Radioactive.

There are no known symptoms or Rb or Cs deficiency.

Elements of group II.A and their compounds

- **Beryllium** (TOXIC)
- **Magnesium** (macrobiogenic, 2nd order)
- **Calcium** (macrobiogenic, 1st order)
- **Strontium** (TOXIC)
- **Barium** (TOXIC)
- **Radium**

Be – Beryllium

Also called ‚glucinium‘ for sweetish taste of its salts. One of the lightest metals; becomes very technically important nowadays. Be is very toxic, less after oral intake, more in injuries, when it gets into blood stream, and when powder or aerosols containing Be are inhaled. Be and its compounds are strongly irritating. Be-contaminated injuries do not heal well (ulcers, fistulas). In the lungs Be causes inflammations that manifest as severe breathlessness and cough with only moderate fever. Berylliosis.

Inflammations heal badly, tend to become chronic and often end lethally. Be is cancerogenic in animals. Contact of skin with powdered Be causes damage similar to I or II degree burns. Effect of Be is explicable as displacement of biologically significant Mg that is bound to many enzymes, and also to ATP. Long latency.

Mg – Magnesium

Biogenic element, bound mainly in bones, constitutes part of many enzymes and ATP. As for other cations, its level in blood is quite strictly regulated, so that tissue deficit of Mg may not manifest as decrease in plasma Mg. Symptoms of Mg deficiency are: increased muscle excitability, convulsions, and increased muscular tension. High tension of smooth muscles manifests as elevated blood pressure and abdominal pain. In patients with hypotension supplementation with Mg must be rather cautious. If kidney function is impaired, Mg is readily overdosed, which leads to flaccidity, slow heart rate, and faintness. Recommended daily intake is 350 - 400 mg for adults (major natural source: whole-grain bakery products, cereals)

Mg – Magnesium -cont.

Recently, owing to wide availability of commercial Mg preparations, overdosing with Mg occurs fairly often. An uninformed person, initially in moderate Mg deficit, feels better after Mg supplementation, and keeps increasing the doses. Exceeding the optimal tissue saturation with Mg, however, causes weakness again, and further attempts to overcome it with even higher Mg doses may lead to really dangerous overdosing.

Compounds: MgCl_2 and MgSO_4 for parenteral administration. For oral supplementation organic compounds are more suitable (citrate, lactate or aspartate). Orally given MgSO_4 acts as a powerful laxative, and is used for clearing the digestive tract before surgical or endoscopic procedures. $\text{Mg}(\text{OH})_2$ (or MgO) is an antacid and laxative. Lethal dose of a soluble Mg salt is about 30 g.

Ca – Calcium

Very important biogenic element, constituting 1-2 % of human body weight. Much of this amount is deposited in bones (decay: osteoporosis), as phosphates (hydroxyapatite). The small fraction of Ca circulating in blood is very significant in many biological processes, including blood clotting (hemocoagulation). Inside the cells calcium acts as a second messenger in transduction of signal information from outside (hormones), and also in propagation of nervous stimulus from one neuronal cell to another. Calcium is necessary for initiation of muscular contraction.

Compounds: CaO (lime) and $\text{Ca}(\text{OH})_2$ (slaked lime) often cause working injuries at construction sites, in particular if they get into the eye. Contact with skin is dangerous especially for small childrens (falls into lime) – can be even fatal.

Ca – Calcium -cont.

Daily intake of Ca should be about 1 gram. The major source is milk and dairy products that some people avoid in their diet because of digestive problems. Quite high amount of Ca is found in nuts. Nowadays, sufficient Ca intake should be supervised, especially in children, pregnant women and the elderly. Deficit Ca affects bones in the first place, which bend in children and break in adults. Calcium contents in bones is best examined with X-ray or ultrasonic bone densitometry. In Ca deficiency either inorganic (CaCl_2) or (nowadays preferred) organic (gluconate, citrate) compounds of Ca are given orally. Another possibility is ground limestone, especially dolomite that contains an ideal ratio of Ca and Mg. Soluble Ca compounds used as parenteral drugs have mainly anti-inflammatory and anti-allergic effects. Metabolism of calcium in the body is further discussed in biochemistry.

Sr – Strontium

Toxic, accumulates in bones. Especially dangerous is its radioactive isotope ^{90}Sr , present in fall-out following nuclear explosions and accidents. In trace (ultramicro) quantities perhaps biogenic.

Intoxication: digestive ailment, seizures, breath arrest

^{90}Sr originating from U or Pu, soft β -irradiation, half-life of decay about 20 years, deposits in growing bones (threat to bone marrow hematopoiesis), poor excretion.

Ba – Barium

Also strongly toxic, in particular its soluble compounds (BaCl_2 , $\text{Ba}(\text{NO}_3)_2$), from insoluble ones those able to react with HCl in the stomach (BaS a BaCO_3). Completely insoluble BaSO_4 is widely used as a contrast substance in X-ray examinations of digestive tract. It must not contain even traces of above-mentioned soluble salts, because absorbed Ba excites and damages muscles, in particular heart muscle, and also the central nervous system. Small contents of Ba, however, is found even in healthy persons, hence essentiality of extremely low doses is not excluded.

BaO and $\text{Ba}(\text{OH})_2$ – caustic

Ra – Radium: Radioactive effects of ^{88}Ra

Elements of group III.A and their compounds

- **Boron**
- **Aluminium**
- **Galium**
- **Indium**
- **Thalium (TOXIC)**

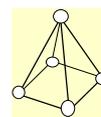
B – Boron

Boron is an essential trace element for plants and some animals. Growth disorders in chicken resulting from boron deficiency were reported. It is found mostly in food of plant origin, vegetables and fruits (soya, tomato, pears, apples). Its contents in animal food (meat, fish, milk) is very low. Some studies suggest boron deficiency aggravates course of osteoporosis. Daily intake in food should be about 3 mg.

Toxicity: Oral poisoning damages digestive tract, kidney and liver; and manifests as vomiting, abdominal pain and diarrhoea. Nervous system is strongly affected as well (headache, seizures, irritability or even aggressivity, tremor, sometimes mental derangement and inhibition). Intoxication from inhalation or absorption through skin (from compresses) is also possible.

B – Boron -cont.

Usage in medicine: boric acid (H_3BO_3) – 3% solution, antiseptic eye wash. In compresses or liniments even higher concentrations are used. Sodium tetraborate $Na_2B_4O_7$ (borax) has also a mild antiseptic effect, and is used as aqueous wash or in liniments. Higher amounts cause skin rash or digestive disorders. The lethal dose for adult is 15-30 g, for small children especially newborn even 100times lower dose can be fatal. Boron hydrides (boranes) are also very toxic. Diborane (B_2H_6 , very interesting chemical structure) is a gas that smells similarly as sulfane. Other examples are pentaborane (B_5H_9 – atoms of boron form pyramid and some H atoms are bound through hydrogen bridges), which is a liquid of sweetish odour, and decaborane ($B_{10}H_{14}$), solid substance. Borane poisoning also affects mainly the nervous system, causing its hyperexcitability. Decaborane, owing to its solid state, is less dangerous.



Al – Aluminium

Abundant element in mineral world, but very rare in living organisms. Soluble salts at higher amounts – tens of grams – are toxic, lethal dose is about 4g/kg body weight. Al displays a dangerous tendency to accumulate in the body (liver, kidney, bones, brain). There is no evidence for essentiality of aluminium. In contrast, longer administration of Al impairs bone formation and its mineralisation. Higher doses suppress intestinal absorption of phosphates and fluorides that are needed for bone structure. This condition is associated with strong bone pain (‘growth pain’ in children?). Higher amount of Al is found in the brain in certain types of dementia (Alzheimer disease); and Al has been, together with genetic factors, implicated in disease pathogenesis. Excess of aluminium can bind to ferritin and decrease body iron stores.

Al – Aluminium -cont.

For these reasons there is a general tendency to avoid drugs containing Al (sulfapyridin, some antacids), or replace them with similar preparations containing Mg. Likewise, aluminium utensils are not recommended for cooking. Especially sour dishes and chlorinated water cause a fairly intensive release of aluminium and enable its subsequent intake in food. In the brain Al probably interferes with activation of enzymes by Ca^{2+} ions; it can also bind to chromatin and impair the essential function of Zn in genetic expression.

Compounds: aluminium acetate $(\text{CH}_3\text{COO})_3\text{Al}$ is used in compresses on swellings resulting from injuries without skin perforation (e.g. ankle sprain). $(\text{CH}_3\text{COO})_3\text{Al}$ and $\text{Al}_2(\text{SO}_4)_3$ have caustic and irritating effects. Inhalation of powdery Al or Al_2O_3 causes lung disease.

Ga – Galium

Biological and toxicological significance of galium is rather small. Both the pure metal and its compounds are poorly absorbed from digestive tract. In cases of inhalation of higher doses alterations of liver, kidney and lungs are found, also skin eruptions and hematopoietic disorders appear. Because of Ga high affinity to neoplastic (tumour) tissue, a radioisotope of Ga is employed in „in vivo“ detection of tumours (gamagraphy).

In – Indium

Industrial intoxications have not been reported so far. Its high toxicity to experimental animals, however, suggests it should be considered with caution from the point of view of industrial toxicology. Industrial utilization of indium, especially in electrical engineering, is increasing; and possibility of intoxication during work with indium or its compounds (alteration of liver, kidney, heart, blood count) cannot be ruled out.

Tl – Thallium

High toxicological significance. Poisoning can result from oral intake, inhalation, or even skin contact with elemental thallium as well as its compounds. High doses promptly affect CNS and lead to death. Lower doses damage digestive tract, skin, mucosae, heart and blood vessels; also inflammations of nerves and psychic disorders were reported. Particularly characteristic feature of thallium intoxication is loss of hair and pubescence (3-10 days following exposition). This sign in previously healthy person must always lead to suspicion of Tl intoxication. In the past Tl was used for extirpation of rodents and ants. Nowadays is no longer employed for this purpose because of high risk of human poisoning (esp. children). In the industry Tl is currently used in infra-red technology (IR detectors and photosensitive diodes); and here possibility of intoxication remains.

Elements of group IV.A and their compounds

- **Carbon** (macrobiogenic 1st order)
- **Silicon** (microbiogenic 3rd order)
- **Germanium**
- **Tin** (microbiogenic 4th order)
- **Lead** (TOXIC)

C – Carbon

Macrobiogenic element. Forms an enormous number of compounds that are subject of organic chemistry.

Toxicology: elemental carbon (graphite, coal dust) causes pneumoconiosis. Among compounds, oxides, esp. carbon monoxide (CO) is toxicologically important. CO is actually the most widespread toxin produced by human activity (carbon dioxide is not considered as toxin). Origin in burning with relative lack of oxygen: $C+O_2 \rightarrow CO_2$; $CO_2+C \rightarrow 2CO$. Not $2C+O_2 \rightarrow CO$. Carbon monoxide acts chiefly on hemoglobin, producing carbonyl-hemoglobin, but probably also directly on the nervous tissue, CNS in particular. Poisoning with CO manifests as loss of free will – the intoxicated person realizes his/her condition, but cannot compel himself/herself to move to fresh air or seek help. The damage to CNS is long-term, sometimes permanent. Severe intoxications often lead to unconsciousness and death. Very significant are also chronic expositions to small doses of CO (smokers), very harmful to children (passive smoking). Symptoms: headache, bleeding, throbbing heart (palpitation), sleepiness or even tonic muscular spasms.

C – Carbon -cont.

Carbon dioxide, CO₂, can also at higher concentration cause poisoning - headache, narcotic effect on CNS, even death due to breath arrest. It is heavier than air and hence tends to accumulate at the ground (danger to small children!!!). Poisoning with CO₂, unlike CO, does not leave permanent damage (unless the intoxicated person dies). Solid and liquid CO₂ (‘dry ice’) is used therapeutically (cryotherapy).

Accumulation of CO₂ in the atmosphere due to human activity is nowadays held responsible for the global warming effect, representing a global threat to human civilisation and life on the Earth.

Carbonic acid and its salts: Hydrogen salts are used in medicine (NaHCO₃ for correction of pH and acid-base balance). Alkaline salts (K₂CO₃, potash, and Na₂CO₃·10H₂O, soda) rather in industry (cleaners, and so on). They act through their alkalinity and caustic properties. Lethal dose about 3 g/kg (less in children). Long-term exposition is harmful to skin and mucosae.

¹⁴C – half-life of radioactive decay 5720 years. Intake through inhalation, food. Accumulates in respiratory vessels and bones.

C – Carbon -cont.

Hydrogen cyanide (HCN), hydrocyanic acid (aqueous HCN), as well as its salts potassium cyanide (KCN) and sodium cyanide (NaCN) are very dangerous poisons. The hydrocyanic acid/hydrogen cyanide smells characteristically after bitter almonds and penetrates even through intact skin. Effect of oral intake of salts - cyanides - depends on gastric acidity that releases hydrogen cyanide. Cyanide anion (CN⁻) blocks tissue respiration through inhibition of mitochondrial cytochrome oxidase. Particularly dangerous are acute intoxications! Death comes swiftly even after doses 0.5-0.6 g. There are various antidotes, e.g. vitamin B₁₂.

Cyanogen bromide (CNBr), fluoride (CNF), chloride (CNCl) and iodide (CNI) are toxic, strongly irritating substances, in the past employed as warfare chemical agents. CNBr is nowadays used in biochemistry in synthetic reactions (immune affinity sorbents).

Cyanic acid (HOCN) and thiocyanic acid (H-S-C≡N) (do not confuse with isothiocyanic acid H-N=C=S) are strongly irritating, but (including their compounds) do not reach toxicity of HCN.

C – Carbon -cont.

Carbon disulfide, CS_2 , is of high toxicological significance because of wide usage in industry. In acute intoxication narcotic effect prevails, death comes from inhibition of CNS, seizures, or paralysis of respiratory centre. Chronic poisoning occurred more often, associated with manufacture of viscose fiber; damage to CNS dominated. The mental and neurological disorders resulting from CS_2 poisoning tend to last long; digestive disorders are also common. Carbon disulfide is readily flammable (ignition point merely $43\text{ }^\circ\text{C}$).

Phosgene (carbonyl dichloride, $COCl_2$) is another poisonous compound of carbon widely used in industry. It has its characteristic odour after rotten leaves. Phosgene was employed extensively as warfare agent (responsible for 80 % of all victims of chemical attacks during the First World War). It kills mainly through induction of oedema (swelling) of lungs. Phosgene is still used in many organic syntheses, therefore intoxications happen fairly often. !ATTENTION! Symptoms of intoxication (lung oedema) can come with latency as long as 12 hours. Phosgene-poisoned patient must be monitored!!!

Si – Silicon

Silicon is in small amounts an essential trace element. Its deficit leads to growth disorders in chicken. Formation of connective tissue (synthesis of glycosaminoglycans) is impaired. Some studies demonstrate that Si deficiency accelerates atherosclerosis. The highest contents is found in whole grains of oat and barley (also in flakes), and in whole soya beans. Amount in industrially processed food (sugar, flour) is negligible. Low amount is also in carrot, potatoes, meat (including fish), milk or dairy products.

Toxicology: most important is inhalation of silica (silicon(IV) oxide) particles and fibrous silicates (asbestos).

Si – Silicon

Asbestos (crocidolite) (from Greek ,asbestos‘ =undestroyable): Inhalation causes respiratory distress, decrease in vital capacity and impairment of gas exchange in lungs. Particularly harmful is its cancerogenic effect (induction of malignant tumours) in lungs and surrounding tissues (mesothelioma, cancer originating from pleural or peritoneal lining epithelium).

Silica: is not truly toxic. Similarly as asbestos causes ,dusty lung‘ (pneumoconiosis-silicosis), which in comparison to asbestosis is less severe and without induction of tumours, but much more common (miners, tunnelling – metro). Small silica particles are phagocyted by the RES cells, which subsequently break down and induce local formation of connective tissue, leading finally to impairment of gas exchange. In advanced stage lung emphysema results and patient suffocates. An associated infection usually brings about the fatal end. In the past the silicosis often combined with tuberculosis. Course of silicosis is slower than asbestosis.

Ge – Germanium

Essentiality has not been excluded. Ge probably plays a role in immune reaction, but the rigorous proof is still lacking. Toxicity of Ge is relatively low. Only hydrides germane, GeH_4 , and Ge_2H_6 are more toxic (blood destruction).

Sn – Tin

Tin is demonstrably an essential element. Deficit manifests as growth disorders. Intake is regulated at the level of absorption in digestive tract, therefore toxicity after oral administration is very low. Western style diet usually contains surplus of tin (canned fruit and vegetables), but symptoms of overdosing or poisoning are not seen. Toxicity is higher in case of parenteral administration of soluble Sn compounds and manifests as excitation of central nervous system followed by depression. Halogenides of Sn are irritating (hydrolysis). The hydride SnH_4 is a nervous poison. Organic compounds of tin can be highly toxic.

Pb – Lead

Lead is the commonest cause of industrial intoxications and poisoning with this element has been occurring since ancient times. Symptoms of intoxication have been known for more than 2000 years (lead waterpipes in ancient Roma, in 20th century the lead pipes were coated with tin). Poisoning was reported in lead miners and workers that processed the metal. Up to 70's of 20th century it also occurred in pressmen; even now it can be seen in people working with lead accumulators, and glassblowers working with lead glass. Poisoning with lead impairs synthesis of blood pigment (hemoglobin), function of neuronal cells, and causes psychic alterations. Acute intoxication is rare (suicides or miraculous „healing“ pills), so most significant are chronic intoxications. Lead accumulates in the body, mostly in bones, and is suspect of carcinogenesis in lungs and kidneys. At temperatures above 600 °C there is also a danger of lead vapour inhalation. In gravid women lead is teratogenic and embryotoxic. Particularly dangerous is inhalation of lead dust or accidental oral intake of lead compounds (in children!). Interestingly, experiments with „ultrapure“ diets showed essentiality of lead in some animals.

Pb – Lead -cont.

Compounds:

Many of paints contain compounds of lead: Lead chromate PbCrO_4 . Minium Pb_3O_4 , lead oxide PbO , lead carbonate-hydroxide (lead white paint) $\text{PbCO}_3 \cdot \text{Pb}(\text{OH})_2$. All are toxic.

Organometals: $\text{Pb}(\text{C}_2\text{H}_5)_4$ – tetraethyl lead in gasoline: penetrates through skin, neurotoxic. PbO and Pb_3O_4 are partially soluble in acidic pH (... CO_2 from the air contributes to contamination of water with lead from the pipe).

$\text{Pb}(\text{CH}_3\text{COO})_2$ and $\text{Pb}(\text{NO}_3)_2$ are soluble and toxic. Do not confuse lead acetate with aluminium acetate.

$\text{PbCl}_2 + \text{PbBr}_2 + \text{halogenated hydrocarbons} + \text{Pb}(\text{C}_n\text{H}_{2n+1})_4$ arise as pollution from combustive engines burning lead-treated gasoline.

Elements of group V.A and their compounds

- **Nitrogen** (macrobiogenic 1st order)
- **Phosphorus** (macrobiogenic 1st order)
- **Arsenic** (TOXIC)
- **Antimony**
- **Bismuth**

N – Nitrogen

Nitrogen is undoubtedly a macrobiogenic element, nevertheless many of its compounds are toxic. Gaseous nitrogen constitutes almost 79 % of the atmosphere. If ambient pressure decreases abruptly (scuba divers returning too fast to the surface), i.e. decompression, bubbles of nitrogen emerge in blood and tissue and can obliterate brain microvessels (caisson disease). Similar condition threatens pilots of stratospheric planes if their hyperbaric cockpit is damaged.

Compounds:

Nitrogen oxides, in particular nitric oxide (NO), act as an important 'tissue hormones'. For instance in blood vessels NO causes their dilatation and decrease in blood pressure.

Dinitrogen oxide, N₂O – 'loughing gas' – used for light anesthesia.

N – Nitrogen -cont.

Nitrates are part of chemical fertilisers. From fields they get to drinking water.

Orally taken nitrates can be reduced to nitrites by HCl in the stomach.

Nitrates/nitrites threaten small children, esp. newborn, with methemoglobinemia; which means oxidation of ferrous ion in hemoglobin to the ferric state that is unable to transfer oxygen and the child can die of anoxia (‘blue child’). Adults are less in danger because of maturity of the enzymatic system (methemoglobin reductase) that reduces iron in hemoglobin back to its ferrous form.

However, even in adults nitrites are not harmless. In the digestive tract the nitrites can react with amino groups on protein yielding nitrosamines, very potent cancerogens (cancer inducing substances). Nitrosamines originate also from imperfect burning of tobacco, hence they are abundant in tobacco smoke.



Origin of nitrosamines (in fact, secondary amino group is the most reactive)

N – Nitrogen -cont.

Photolysis of nitrogen dioxide: $\text{NO}_2 \rightarrow \text{NO} + \text{O}$ (atomic oxygen), which then combines with O_2 from the air to give ozone (O_3), ... primary ozone, very harmful. Nitrogen oxides as pollutants come mostly from combustive engines (most from so called ‘ecological’ engines burning hydrogen or very low amount of gasoline, which must have catalyser).

Ammonia gas, NH_3 : because of pungent malodour intoxications are rather uncommon. High concentrations can cause reflex breath arrest and death. Dangerous for gravid women. Ammonia is caustic in the eye – damages cornea with possibility of a delayed injury and blindness. It can cause lung oedema. Industrial intoxications (cold stores, winter stadiums). Ammonia hydroxide (NH_4OH , aqueous ammonia) has similar properties; it is even more dangerous to the eyes than KOH and NaOH. Concentrated solutions are harmful even when taken orally.

N – Nitrogen -cont.

Irritating: NH_3 , NH_4OH , HNO_3 , NO_3 , N_3^- , NCl_3 , NOCl

Forming methemoglobin: HNO_2 , NO_2^- , NH_2OH , NO

Synergy: sunshine+ NO_x = smog of 'Los Angeles type'

Harmful: NH_4^+ , NO_3^-

HNO_3 : Xanthoprotein reaction, irritates the airways, damages teeth

NO_2 : provokes cough, latency 5-24 hrs, then lung inflammation, oedema, shock, gangrene, dizziness, sleepiness. Chronically bronchitis, blood count alteration.

Nitration mixtures: oxidants. Harmful to respiratory tract

N_3^- , azides: explosive, excite CNS, toxicity similar to cyanide.

NCl_3 : CNS, explosive. NOCl : irritates eyes, skin and mucosae, lung oedema

NH_2OH , hydroxylamine: strong burning and irritation following contact with skin, seizures, in the body decomposes to $\text{NH}_3 + \text{NO}_2^-$...methemoglobinemia, cyanosis, hemolysis, effects on CNS, liver enlargement, alteration of thyroid function. Hydrazine $\text{NH}_2\text{-NH}_2$: also strongly irritating, in addition other toxic effects – CNS, damage to liver, kidney, heart, destroys red blood cells, demonstrated cancerogenity. Pronounced embryotoxicity. Penetrates intact skin !!!

P – Phosphorus

Phosphorus is a macrobiogenic element. It exists in several isoforms – white, red, black, and violet. Toxicologically, the most significant is white phosphorus, pyrophoric, soft, wax-like substance, in the air self-ignites even at room temperature. Ignition is catalysed by oxidants (H_2SO_4 , halogens, HNO_3) $\text{P} + \text{O}_2 \rightarrow \text{P}_2\text{O}_5$. It can be extinguished with water. White phosphorus causes severe intoxications; dose 1 mg/kg of body weight is already lethal. In the 19th century, suicidal poisoning with matches was common, that is why before the First World War manufacture of white phosphorus-based matches was forbidden. Ingestion of white phosphorus damages tissues directly. For lower doses a latency between intake and symptoms of poisoning is typical. Metabolism of minerals in the body, calcium in particular, is subverted, which results in disruption of neuronal and muscle functions, blood clotting, severe damage to liver and bones. Red phosphorus is much less toxic; if poisoning occurs, it is usually caused by admixture of white phosphorus. For the other isoforms toxicological data are lacking.

P – Phosphorus -cont.

Phosphane, PH_3 , is also highly toxic. It is a gas smelling after fish. Poisoning has many signs, chronically anemia, bronchitis, nervous disorders. Even very low doses, 10 ppm, kill after exposition lasting several hours. Higher doses (1000 ppm) are fatal within minutes.

Phosphoric acid, H_3PO_4 : one of the most important compounds in biochemistry. In the body occurs mostly as salts (phosphates), organic esters and anhydrides. These phosphate derivatives are involved in metabolism of saccharides, lipids and proteins, take part in the structures of membranes and nucleic acids, etc. (*more in biochemistry*).

P_2O_5 , P_2O_3 : irritating substances.

Salts of H_3PO_4 , hydrogen phosphates (HPO_4^{2-}) and dihydrogen phosphates (H_2PO_4^-) are important components of buffers in the body.

Apatites, mainly hydroxyapatite, fluoroapatite, and carbonate apatite, are important components of bones and teeth.

As – Arsenic

In many animal species considered essential (goat, chicken, pig, rat). In humans essentiality has not been proven and seems irrelevant because most food contains by far more As than would be its supposed daily need. In this country power plants burning inferior brown coal are a rich source of As, which is released a highly toxic As_2O_3 (arsenic(III) oxide, the 'arsenical'). Inhalation: chest pain, cough, cyanosis, lung oedema (similarly As_2O_5 , AsO_2^- , AsO_3^-). Dose 0.2 g kills within several hours; 0.10-0.15 g within several days. Abdominal pain, vomiting, diarrhoea. Low doses, when taken repeatedly, lead to chronic intoxication. Damages liver and kidney. Long-term exposition to As can result in tumour induction (skin, respiratory system etc.). Further danger comes from an easy passage of As to milk, both maternal and cow. Arsenic is abundant in fish meat due to flushing down to creeks and rivers. It also accumulates in human hair.

Arsane, AsH_3 – deadly toxic, even 25-50 ppm can be lethal. Hemolysis, kidney and liver damage (icterus), abdominal pain, chest pain, dark urine, CNS symptoms. Poisoning develops with certain latency.

Usage in medicine: As_2O_3 was in the past used in dentistry for devitalisation of teeth (causes necrosis of dental pulp).

Sb – Antimony

Sb corresponds in toxicity to arsenic, but without tendency to accumulate in the body. Particularly dangerous is inhalation of elemental Sb that enters the red blood cells, is excreted in urine and causes kidney inflammation. Oral administration is less harmful as it causes only diarrhoea (Paracelsus used antimony as 'recyclable' laxative). Poisoning is possible with soluble compounds (rather uncommon). Sb^{3+} is more toxic than Sb^{5+} . Antimony potassium oxide tartarate = 'emetic stone' – vomiting, heart damage.

Bi – Bismuth

Compounds of bismuth used to be widely used in medicine for their astringent and antiseptic effects. Until now they are present in pharmacopoeia for treatment of mild intestinal disorders. They disappeared from commercial drugs, but extemporaneous prescription is possible. Alkaline bismuth nitrate, BiONO_3 is usually used. It is unsuitable in small children because of induction of methemoglobinemia. Bismuth trifluoride, BiF_3 – poisonous, irritating. Toxicity comparable to Pb or Hg.

Elements of group VI.A and their compounds

- **Oxygen** (macrobiogenic 1st order)
- **Sulfur** (macrobiogenic 2nd order)
- **Selenium** (microbiogenic 4th order/TOXIC)
- **Tellurium**
- **Polonium**

O – Oxygen

Macrobiogenic element. Pure oxygen (100% O₂), when given therapeutically, can be toxic, damages lungs and eyes, especially in immature newborn. Ozone (O₃) is highly toxic. In ozonosphere it protects life on the Earth from UV radiation. In the bottom layer of atmosphere the ozone can originate from the reaction of nitrogen oxides with oxygen (cars!!!). Concentration as low as 0.01 ppm can cause intoxication!!! Oxygen forms many binary compounds with other elements (oxides) - discussed at each element. Hydrogen peroxide, H₂O₂ : oxidant, bleach.

¹⁸O – radioisotope of oxygen

Oxygen has in all compounds oxidation number -2 or -1. Positive oxidation number only in fluorides O₂F₂, OF₂, AgOF₃, O₂PbF₆

Reactive Oxygen Species

Originate from reduction of oxygen. Sometimes called free radicals (radical: chemical entity with unpaired electrons). Oxygen O₂ is a fairly unreactive biradical (2 unpaired electrons).

One-electron reduction changes oxygen to more reactive superoxide radical/ion ·O₂⁻ (can be protonated to hydroperoxyl radical ·HO₂)

Addition of another electron to superoxide (+ 2 H⁺) generates hydrogen peroxide H₂O₂ (chemically no radical, i.e. no unpaired electrons)

Hydrogen peroxide can take another electron from reduced iron or copper and generates extremely reactive hydroxyl radical ·OH (the Fenton reaction) and stable water.

Hydroxyl radical finally oxidises something else and is itself reduced to water.

Safe reduction of oxygen is employed in mitochondria as source of energy. Reactive oxygen species are used for killing phagocytosed bacteria. On the other hand, their uncontrolled generation is harmful to tissues and may lead to atherosclerosis or cancer (more in pathobiochemistry).

S – Sulfur

Sulfur is an important biogenic element, found in proteins (S containing amino acids cysteine and methionine). In particular, the reactive reducing –SH groups of cysteine are critical for higher orders of protein structure, as a cellular redox buffer, and are found in active centres of many enzymes. These groups also react with heavy metals; that's why compounds rich in –SH are given as antidotes in heavy metal poisoning. Very toxic gas carbon disulfide CS₂ – already mentioned. Oxides of sulfur (SO₂, SO₃) originate from burning coal with high S content. They are toxic for plants as well as animals and give rise to ,acid rains'!

Hydrogen sulfide, H₂S, is even more toxic than HCN, but smells worse and stronger so that victim can be warned. H₂S affects enzymes and CNS. Conc. 1.4 g/m³ intoxicates immediately, 1-1.2 g/m³ within 30 min after exposition. Lower concentrations cause seizures, vomiting, oblivion, but quick recovery. Effect on liver, kidney, vision, psychic alteration.

Peroxodisulfate, persulfate, S₂O₈²⁻ – asthma.

Thiosulfate, Na₂S₂O₃, is non-toxic, aqueous solution is used diluted for treatment of skin stricken with Br₂ or I₂.

Se – Selenium

Selenium is important microbiogenic (trace) element. However, higher doses are very toxic. Vapours of Se, as well as H₂Se (hydrogen selenide, selane) smell strongly after garlic, or horseradish. Small (essential) amounts of Se (50-200 µg daily) display antioxidant and detoxication effects. Toxic effects are mostly seen in animals feeding on the ground with high Se contents, and manifest as blindness, paralysis, loss of hair, hoof deformities, and infertility.

Acute poisoning in humans: agitation, vomiting, sleepiness, seizures, respiratory arrest. Chronic poisoning is scarcer than in animals. Se has an antitumour effect. H₂SeO₃ and H₂SeO₄ are caustic and teratogenic. SeOCl₂ – blister gas similar to mustard gas.

Te – Tellurium

Less toxic than Se, smell also after garlic. Intoxications are rare. Headache, nausea, liver and kidney damage.

Elements of group VII.A and their compounds

- **Fluorine** (microbiogenic 3rd order)
- **Chlorine** (macrobiogenic 2nd order)
- **Bromine**
- **Iodine** (microbiogenic 4th order)
- **Astatine**

F – Fluorine

Microbiogenic element. Its presence in the body is necessary for correct mineralisation of bones and teeth. Human body contains 2.5-4 g of F. Daily need is about 1 mg. Gaseous elemental fluorine is extremely reactive, strongly irritating and corrosive. Contact with skin leads to ulcers (exothermic reaction – burns) that do not heal. Hydrogen fluoride, HF, H₂F₂, is strongly irritating and corrosive as well. Both cause lung oedema. Hydrofluoric acid is highly toxic and harmful as well.

Fluorides (salts of hydrofluoric acid) are also toxic. They always cause irritation; cancerogenic action is probable. Fluorides interfere with metabolism of Ca²⁺ – blood clotting disorders, calcification of connective tissue, exostosis formation, fragility of bones and teeth. Doses 0.25 g cause acute intoxication, amount above 1 g is usually lethal (for sodium fluoride per os). Inhalation is dangerous as well. Symptoms of acute intoxication: vomiting, diarrhoea, seizures, paralysis, liver and kidney damage.

Cl – Chlorine

In the form of chloride anion is Cl necessary for life. However, elementar chlorine, hydrogen chloride, HCl, and hydrochloric acid are highly irritating and corrosive. Industrial intoxications are very common. Especially irritating are compounds of chlorine with fluorine. Compounds of Cl are generally less toxic than compounds of F. Toxicology: Cl₂ and HCl severely damage respiratory tract, HCl in addition teeth and cornea (although diluted HCl is found in stomach). Longer exposition to Cl₂ leads to bronchitis and lung emphysema. Industrial accidents: chlorine destroys everything where evades.

Chlorine(IV) oxide, ClO₂, chlorate ClO₃⁻, perchlorate ClO₄⁻ are explosive. Perchlorate is strong oxidant, irritates mucosae, causes formation of methemoglobin and hemolysis, kidney disorders, damage to heart and respiration.

Br – Bromine

Br is not included among essential (biogenic) elements so far, although its content in human body is relatively high – about 200 mg. Pure element is a brown fuming liquid that is strongly irritating such as elementar chlorine.

Compounds – bromides were used in medicine for their sedative effect on CNS („tea for soldiers“). However, longer administration damages skin (inflammations, „acne bromina“). Therefore, medical usage of Br is now restricted, and Br appears in drugs rather in organic compounds (Calabron, Ambroxol, Bromhexin).

I – Iodine

Essentiality of iodine has been known over 150 years. It is necessary for thyroid gland function (more in biochemistry). Daily dose 0.10-0.25 mg. Its deficit affects physical and mental development, therefore sufficient intake must be provided (iodination of table salt). Sometimes supplementation in pills may be needed (pregnancy).

Intoxications: chronic are more common. Low doses stimulate thyroid function (weight loss, fast heart rate, insomnia). In contrast, very high doses can suppress activity of thyroid gland. Particularly dangerous are radioisotopes of iodine such as ^{131}I (half-life 8 days), which may escape due to nuclear accidents (Csernoby, nuclear fission of U and Pu). They specifically accumulate in thyroid gland, which may then suffer from radiation damage. Administration of higher dose of non-radioactive I (1g), can be used as a protective measure. On the other hand, ^{131}I is used for therapy of thyroid gland carcinomas and hormonally active thyroid tumours.

I_2 is insoluble in water or alcohol, but it dissolves in presence of iodides (NaI, KI). Resulting solution is called Lugol's solution. Bromates and iodates are more toxic than chlorates and perchlorates.

Elements of group VIII.A and their compounds (noble gases)

- Helium
- Neon
- Argon
- Krypton
- Xenon
- Radon

Among the noble gases, medically significant is radioactive radon ^{222}Rn originating from decay of radium 226. In this country it is found around deposits of U and Ra.

Elements of group I.B and their compounds

Cu – Copper

Cu is an essential trace element, necessary for metabolism of iron. Deficiency of copper may cause anemia. It acts as cofactors of important enzymes (e.g. cytochrome oxidase in mitochondrial respiratory chain). Daily need about 2 mg.

Toxicity: All soluble salts are poisonous and irritate digestive tract when given orally (enteralgia, diarrhoea). Subsequently hemolysis, icterus, liver and kidney damage develop.

Cu is a mikrobicide and spermicide – contraceptive bodies.

$\text{CuSO}_4 \cdot 5\text{H}_2\text{O}$, $\text{CuCl}_2 \cdot \text{H}_2\text{O}$, $\text{Cu}(\text{NO}_3)_2 \cdot 3\text{H}_2\text{O}$ – kill in dose about 10 g.

Elements of group I.B and their compounds -cont.

Ag – Silver

Ag is not considered as biogenic element. In medicine caustic and antiseptic effects of silver nitrate (argentum nitricum, 'lapis infernalis') are utilised locally. Alike copper, silver is a bactericide. This property is used in eye and ENT medicine (ophthalmic and nasal drops containing solution of colloidal silver stabilised with proteins). Silver forms basis of photographic chemistry (X-ray pictures !!!). Ag^+ salts are irritating and caustic. Chronic exposition leads to irreversible deposition of Ag in various organs, mucosae and skin (argyria).

Au – Gold

In the past Au was used for treatment of tuberculosis - now obsolete. Organometallic compounds of gold are nowadays employed as effective (but also quite toxic) drugs in treatment of rheumatic diseases. Damage to lungs and kidney are side effects of this therapy. $\text{AuCl}_3 \cdot 2\text{H}_2\text{O}$ is caustic.

Elements of group II.B and their compounds

Zn – Zinc

Zn is one of the most important microbiogenic elements. Among other functions, it is required for storage and expression of genetic information. More than 300 known enzymes contain Zn in their molecules. Transport of Zn in the body and its sequestration provided e.g. by proteins metalothioneins. Zn deficiency impairs reproductive functions, particularly in men; and process of wound healing (production of connective tissue – vitamin C also involved) and immune reactions (defence against infections) are also altered. The required daily intake in food is about 15 mg/day. Doses above 100 mg irritate digestive tract. Lethal dose of a soluble Zn salt (such as zinc chloride or sulfate) is 3-5 g for humans. Zn-dithiokarbamates are suspect carcinogens. Work with molten zinc metal or its alloys may cause night fevers – ‚fever of founders‘, resulting from allergic reaction to proteins denatured with ZnO.

Elements of group II.B and their compounds -cont.

Cd – Cadmium

In experiments, ultra-low amounts are essential. However, human activity increases input of cadmium into the food chain (fertilisers, coal), so that actual Cd contents in food is often close to toxic levels. Cd is strongly cancerogenic (lungs, liver). The lethal dose ranges as little as about 30 – 40 mg! Its toxic effects are explained as interference with Zn metabolism (instead of Zn, Cd may be built into Zn-dependent enzymes that become inactive), and blockage of SH-groups. Cadmium toxicity can be lowered by increased intake of zinc (competition) and selenium. Symptoms of intoxication: vomiting, diarrhoea, oblivion, internal bleeding.

Elements of group II.B and their compounds -cont.

Hg – Mercury

Mercury is toxic, especially following inhalation of its vapours and oral intake of soluble salts. Breathing of Hg vapours irritates and induces inflammation of airways and lungs. Inhaled mercury is practically completely absorbed in the lungs. Owing to high solubility in lipids mercury easily crosses the blood-brain barrier and acts as a neurotoxin, subsequently it oxidises in the brain which prevents it to cross the barrier in the opposite direction. It leads to its accumulation in cerebral and cerebellar cortex, and basal ganglia. Later similar signs like in oral intoxication appear: inflammation of mouth mucosa, severe kidney damage. Inside the red blood and other cells catalase oxidises Hg to Hg^{2+} , which is then distributed to tissues and blocks –SH groups of enzymes. Mostly the soluble Hg salts, such as HgCl_2 , sublimate, are toxic, while toxicity of similar but insoluble calomel Hg_2Cl_2 is low.

Hg – Mercury -cont.

Oral intake of metallic mercury may cause diarrhoea, but not intoxication!!!

Soluble salts in dose of about 1 g kill swiftly, 150-200 mg lead to acute intoxication that may end fatally. 0.5 – 1 mg daily for several weeks causes chronic poisoning. Hg is a protoplasmic poison, depositing in the liver, kidney, spleen, and bones. The kidney protects itself by induction of metallothioneins, organ injury develops after their saturation, and affects proximal tubuli and glomeruli the most, causing a nephrotoxic syndrom. Symptoms of acute Hg poisoning: heartburn, diarrhoea; chronic: excitation, depression, memory disorders, tremble, speech disorders, grey rim on dental gums, hallucinations.

Elements of group III.B and their compounds

Sc – Scandium

Toxicologically rather unexplored. High content in the diet affects growth and raises occurrence of tumours.

Y – Yttrium

Relatively low toxicity. Likewise Sc, high doses slow down growth and induce tumours.

La – Lanthanum

Its action mimicks the effects of aluminium. Metabolism of Ca^{2+} is affected. Toxicological significance of lanthanum is (for the present) rather low.

Lanthanides

Majority of lanthanides (lanthanoids) decreases blood coagulability, and also blood pressure and level of blood sugar. High doses damage heart and liver.

- „light“ – lanthanum, cerium, praseodymium, neodymium and promethium: toxicity rather low. Cerium has a pharmacologically useful antiemetic effect
- „heavy“ – samarium, europium, gadolinium, terbium, dysprosium, holmium, erbium, thulium, ytterbium and lutetium: more toxic, but so far (except for europium used in manufacture of coloured monitors) little used in industry.

Actinides

Thorium and protactinium display an intermediate toxicity, but they are probably also cancerogenic. ^{227}Ac is radioactive.

Uranium is harmful not only because of its radioactivity (^{238}U vs. ^{235}U), but also because of high toxicity - it damages the kidneys, blood vessels, hematopoiesis, negatively affects gravidity. Doses above 150 mg orally, or above 2.5 mg inhaled, cause intoxications. Acute intoxication manifests as kidney damage. Uranium is also cancerogenic. Transuranium elements are dangerous mainly because they are radioactive.

Elements of group IV.B and their compounds

Ti – Titanium

In traces constantly present in living organisms, but its biological function is unknown. As pure metal or oxide practically non-toxic. TiCl_4 is caustic.

Zr – Zirconium

Can irritate the skin or cause anemia. Low toxicity. Compounds: Zr-lactate, ZrOCl_2 .

Hf – Hafnium

In experiment with animals Hf is more toxic than zirconium. It causes liver damage.

Elements of group V.B and their compounds

V – Vanadium

V is an essential element. Its lack in chicken causes alterations in lipid metabolism. On the other hand, V is also fairly toxic. When inhaled, compounds of V are strongly irritating. Doses 60-120 mg are toxic. Poisoning damages liver, kidney, digestive tract, but also CNS and blood vessels. Intoxications are known mainly from experiments, in industry they are rare. Symptoms: pale complexion, green-red tongue, spastic cough, tremble of hands.

Nb – Niobium

In experiment toxic (kidney damage); industrial intoxications are not known. Enzymatic disorders.

Ta – Tantalum

Low toxicity; used in surgery (joint replacements), industrial intoxications are not known.

Elements of group VI.B and their compounds

Cr – Chromium

Cr is an essential element (even in humans). It is for instance necessary for metabolic utilization of lipids and saccharides (GTF - glucose tolerance factor). Biogenic is mainly chromium(III), Cr^{3+} ; while in contrast chromium(VI), Cr^{6+} , is highly toxic, strongly irritating, and induces ulcers, after long exposition even tumours. Cr very often causes allergic reactions.

Potassium dichromate, $\text{K}_2\text{Cr}_2\text{O}_7$ – strong oxidant, more toxic than chromate, CrO_4^{2-} .

CrO_2Cl_2 – irritating like Cl_2 .

Cr^{2+} and Cr^{3+} cause eczemas, Cr^{6+} is caustic.

Elements of group VI.B and their compounds -cont.

Mo – Molybdenum

Mo is also an essential trace element, required for excretion of sulfur, production of uric acid, and oxidation of aldehydes in the body. Cereal sprouts and beans are valuable sources of Mo. Absorption of molybdenum may be impaired by presence of sulfates and compounds of tungsten. Inhalation of Mo damages kidney and liver; Mo acts as an antagonist to Cu.

W – Tungsten

Biological significance is low; only antagonism to essential molybdenum is important. Toxicity for humans is rather low.

Elements of group VII.B and their compounds

Mn – Manganese

Likewise Zn, manganese is part of many important enzymes. Deficiency manifests as disorder in formation of connective tissue in bones and cartilage; however, it is probably rather rare, in part because in many functions Mn^{2+} can be replaced with Mg^{2+} (except for the connective tissue formation in cartilage). Cereal sprouts and leaf vegetables are rich sources of Mn (need 2 – 4 mg/day).

Toxicological significance: mainly chronic industrial intoxications (miners, metallurgists), most susceptible are persons suffering from iron deficiency. The brain is damaged the most, in particular its motoric regions. Signs: the Mn intoxication mimicks Parkinson disease, fatigue, tremble, sleepiness. Poisoning results mainly from inhalation. Acute intoxications manifest as lung injury. Among oxides, significant are beryl (MnO_2), and Mn_2O_3 . Diluted solutions of potassium permanganate, $KMnO_4$ are used in medicine as disinfectants; oral intake can cause intoxication with corrosion in GIT and kidney damage.

Elements of group VII.B and their compounds -cont.

Tc – Technetium

Biological significance is rather low, only antagonism to essential molybdenum is important. Radioactive isotope of Tc is employed for gamagraphic examination of bones. Toxicity for humans is rather low.

Re – Rhenium

Biology and toxicology of rhenium is still rather unknown.

Elements of group VIII.B and their compounds

Triad of light platinum metals (Ru, Rh, Pd)

Ruthenium, rhodium, and paladium are of rather low significance in toxicology. Damage to bone marrow, liver, kidney, impairment of enzymatic processes, respiration, teratogenic effects.

Triad of heavy platinum metals (Os, Ir, Pt)

Osmium is strongly irritating, causes ulcerations on the skin and cornea, and damages the airways in doses as low as 10 – 100 ppm. Osmium(VIII) oxide, OsO_4 , is also very dangerous. Iridium is of minor significance in toxicology. Platinum is poisonous, perhaps even cancerogenic. On the other hand, some Pt compounds are used as drugs for treatment of cancer (cis-dichlorodiamino-platinum).

Triad of iron (Fe, Co, Ni)

Fe – Iron

Essential element (microbiogenic 3rd order). Most of the body iron is found in hemoglobin and storage protein ferritin. In blood plasma iron is transported bound to transferrin (Tf). Small, but important amount of Fe serves as part of enzymes. In addition to transport of oxygen, iron is essential in cellular respiration, detoxification enzyme systems and antibacterial defence. Daily need is about 15 mg, in women somewhat more. Higher doses are toxic, especially in small children. They cause corrosion in digestive tract, shock, vomiting, hemorrhagic diarrhoea, acidosis, and loss of consciousness in which small children can die even after doses about 2 g. Parenterally administered iron compounds are more toxic. Fe as a crude metal containing As, P can with water release AsH₃ a PH₃. FeCl₃ is caustic. FeSO₄·7H₂O causes liver damage. Oxides (ores) Fe₂O₃ a Fe₃O₄ can cause „fever of founders“, bronchitis, and siderosis (lung nodules). Ferrocyanide [Fe(CN)₆]⁴⁻ and ferricyanide [Fe(CN)₆]³⁻: low toxicity, unless at higher temperature and action of acids start to release HCN. Fe(CO)₅ is toxic, causes lung oedema.

Triad of iron (Fe, Co, Ni) -cont.

Co – Cobalt

As part of one form of vitamin B₁₂ (cobalamine) is Co one of essential trace elements. Cobalamine is necessary for hematopoiesis and nervous system. Poisoning with Co is rare, toxicity similar to iron, substantially higher in small children. Signs: ECG alterations, chronically Co affects liver, kidney, causes bronchial asthma. Dicobaltooctacarbonyl, Co₂(CO)₈ – highly toxic, in the body decomposition to CO.

Triad of iron (Fe, Co, Ni) -cont.

Ni – Nickel

Nickel is also considered as essential element for mammals. It is found mostly in lymphatic nodes and testes. Contents of Ni is high in fetal liver, but very low in milk. Its deficiency impairs function of certain liver enzymes (dehydrogenases).

Toxicological and medical significance: strongly allergizes and may cause skin eruptions. Toxicity of most Ni compounds is low, except for tetracarbonylnickel $[\text{Ni}(\text{CO})_4]$, which is highly poisonous even at doses below 100 ppm; in addition it is a strong cancerogen. In particular its vapours are toxic. Poisoning affects lungs, liver, kidney and brain. Signs: nausea, dizziness, headache, respiratory distress, chest pain, death within several hours. Industrial processing of Ni: tumours of lungs and nasal cavities. Chronic exposition: skin eruptions, allergies.