

# Poisoning with metals, metalloids and their derivatives.

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# Metal poisoning

- Metals are inhaled primarily as dusts and fumes. Metals poisoning can also result from exposure to vapors (e.g. mercury in the manufacture of fluorescent lamps).
- When metals are ingested in contaminated food or drink or through hand-to-mouth activity, their gastrointestinal absorption varies greatly with the specific chemical form of the metal and the nutritional status of the host.

# Metal poisoning

- Once a metal is absorbed blood is the main medium for its transport, with the precise kinetics dependent on diffusibility, binding forms, rates of biotransformation, availability of intracellular ligands, and other factors.
- Some organs (such as bone, liver, and kidney) sequester metals in relatively high concentration for years.
- Most metals are excreted through renal clearance and gastrointestinal excretion;
- Some proportion is also excreted through salivation, perspiration, exhalation, lactation, skin exfoliation, and loss of hair and nails.

# Exposure

- ***Occupational***
- ***Domestic***
- ***Environmental***
- ***Acute***
- ***Chronic***
- ***Accidental***
- ***Intentional***

# Principles of treatment

- The most important component of treatment for metal toxicity is the termination of exposure.
- **Chelating agents**, which are used to bind metal into stable cyclic compounds with relatively low toxicity and to enhance their excretion.
- **The principal agents are**
- DIMERCAPTOL,
- EDETATE (EDTA),
- SUCCIMER (DMSA, dimercaptosuccinic acid ),
- PENICILLAMINE
- ***Activated charcoal does not bind metals and thus is of limited usefulness in cases of acute metal ingestion***

# Aluminum

- the most abundant metal on earth, occurring in natural rocks as mica, feldspar, and bauxite.
- a light metal which resists corrosion and is a good conductor of both heat and electricity.
- used in packaging materials, kitchen utensils, car and airplane construction, paints, insulating materials, cosmetics and foods.
- Aluminum hydroxide is used as an antacid and as a phosphate binder in the management of chronic renal failure.
- Aluminum sulfate is employed for water purification and in paper manufacture.

# Mechanism of action

- **Aluminum may be absorbed orally and by inhalation.**
- More than 90% of absorbed aluminum is bound to transferrin which does not cross the blood-brain barrier readily.
- The remaining 10% is associated with low molecular weight complexes, such as citrate which can accumulate in brain tissue.
- Most body aluminum is stored in bone and the liver.
- ***Aluminum is excreted mainly via the kidney.***
- High levels of aluminum are found in the neurofibrillary tangles in the cerebral cortex and hippocampus of patients with Alzheimer's disease as well as in the drinking water and soil of areas with an unusually high incidence of Alzheimer's disease.

# Acute poisoning

**Ingestion** of soluble aluminum salts may produce:

- Burning in the mouth and throat
  - Nausea
  - Vomiting
  - diarrhea,
  - abdominal pain,
  - hypotension,
  - seizures,
  - haemolysis,
  - haematuria and
  - rarely hepatorenal failure.
- 
- Topical aluminum sulphate may produce: irritation of the skin and eyes.



# Chronic poisoning

**Inhalation** can cause:

lung fibrosis,

pneumothorax

Occupational asthma

Also may be a increased risk of developing lung cancer .

# Chronic poisoning

- There is substantial evidence that aluminum is a neurotoxin. Dialysis dementia involves the accumulation of aluminum mainly in the brain, in patients on haemodialysis where the dialysis water contain significant amounts of aluminum, usually as aluminum sulfate. Aluminum poisoning in these circumstances may be enhanced by the administration of oral aluminum hydroxide as a phosphate binder.
- **Typical features include** – speech and memory disturbances, altered personality, dementia, apraxia, myoclonic seizures. The disease is progressive and usually fatal. Renal failure without dialysis may also lead to the accumulation of aluminum due to decreased clearance.

# ***Medical surveillance and treatment***

- -24-h urine aluminum excretion (normal range <15 $\mu$ g /24h) and the blood aluminum concentration (normal range <10 $\mu$ g/l)
- ***Desferrioxamine*** increases aluminum excretion in humans and experimental animals and there are reports of neurocognitive improvement following desferrioxamine therapy in aluminum –toxic dialysis patients and in patients with Alzheimer’s disease. However, there is concern about the long-term use of Desferrioxamine because of reports of hypotension, gastrointestinal upset, porphyria cutanea tarda-like lesions and transient visual disturbances.

# LEAD

- Absorbed lead is stored in the skeleton and may reenter the circulation at time of heightened bone turnover (e.g. pregnancy, lactation, osteoporosis, hyperthyroidism). Subclinical toxic effects can be prevented if chronic low-level exposure is detected early and curtailed.
- In the case of lead such exposure is detected by tests of blood level, which should be performed regularly in young children living in old neighborhoods and a precautionary measure in adults with a history of lead exposure.

# General information

- **Lead can be absorbed**
- by inhalation, almost 100%;
- Via ingestion-10-15%, and through the skin.
- -99% is associated with erythrocyte ,
- it is mainly deposited in the bone and teeth 95%.
- **The concentration** of lead at which intervention is indicated from **250mg/l down to 100mg/l.**

# Clinical features

- Because of differences in individuals susceptibility, symptoms of lead poisoning and their onset may vary.
- **Mild intoxication** may result in no more than lethargy and occasional abdominal discomfort, whereas abdominal pain (which is usually diffuse, but may be colicky), vomiting, lethargy, constipation, and encephalopathy develop in more severe cases.
- **Lead colic** was first described by Hippocrates.
- **Encephalopathy**- seizures, mania, delirium, coma is more common in children than in adults.

# Clinical features

- **Classically** , lead poisoning results in foot drop, attributable to primary motor peripheral neuropathy , wrist drop occur only as a late sign of lead intoxication.
- **Renal effects** - include reversible tubular dysfunction causing glycosuria, aminoaciduria, and phosphaturia, and irreversible interstitial fibrosis with progressive renal insufficiency leading to hypertension.

# Clinical features

- **Lead depress the enzymes responsible for haem synthesis** and shortens erythrocyte life-span leading to a microcytic or normocytic hypochromic anaemia. In severe cases of intoxication a haemolytic anaemia may occur.
- **Lead blocks the conversion of some aminoacids.** Also blocks /inhibits ferrochelatase which results in elevated free erythrocyte protoporphyrin (FEP) levels. There is a concomitant increase in urinary coproporphyrins and FEP, commonly assayed as zinc protoporphyrin.



# Surveillance and treatment

- **Surveillance**
- Lead in urine  $>150\text{mg/l}$  is a good indicator of exposure.
- **Treatment**
- Primary prevention
- the elimination of lead hazards for children and exposed workers;
- evaluation of workplace
- **Chelation therapy**
- The BEST is sodium calcium edetate EDTA
- DMSA (succimer)-chelator of choice – increasing lead excretion but it must be given intravenously rather than orally which requires admission to hospitals.
- In severe cases EDTA –  $75\text{mg/kg}$  body weight/ day for 5 day provides rapid relief of symptoms, a second course after week.

# MERCURY

- Is the only metal which is liquid at room temperature . It exists a three forms - metallic ( $\text{Hg}^{\circ}$ ), mercurous ( $\text{Hg-2}^{+2}$ ), and mercuric( $\text{Hg}^{+2}$ ).
- Metallic mercury is used in batteries, dental amalgam, and in scientific and medical instruments such as thermometers, barometers, and sphygmomanometers. Metallic mercury is also used as the cathode in the Castner-Kellner process for the electrolysis of brine to produce chlorine gas. Methyl mercury has been used as a fungicide.

# Occupational exposure

- mercury mines,
- chloroalkali plants,
- thermometer factories
- health service maintenance workers responsible for repairing broken sphygmomanometers.
- Accidents in dental surgeries have led to mercury vapour poisoning in dentists and dental nurses.

# Kynetics

- **The absorption depends on its chemical form.**
  - Inhaled Mercury vapor is absorbed rapidly and oxidized in  $\text{Hg}^{+2}$  in erythrocytes and other tissues.
  - Absorbed mercury vapor can cross the blood – brain barrier and accumulate in the brain.
  - Mercury vapor is also absorbed via the skin;
  - Organic Mercury salts are better absorbed following ingestion.
- Excretion-** mainly in urine, in faeces, also is exhaled (inorganic mercury).

# Clinical features

**Acute inhalation** of mercury vapor causes headache, nausea, cough, chest pain, bronchitis, and pneumonia. Proteinuria or nephrotic syndrome.

- CNS- fine tremor and neurobehavioral impairment occurs and peripheral nerve involvement has also been observed.
- Kawasaki disease (acute febrile eruptive disease ) has been reported in exposed children.

# Clinical features

- Ingestion of metallic mercury is usually with severe systemic effects as metallic Mercury is poorly absorbed from the GI tract.
- May cause- irritant gastroenteritis with corrosive ulceration bloody diarrhea, and abdominal cramps and may lead to circulatory collaps and shock.
- Mercurous compounds are less soluble, less corrosive and less toxic than mercuric salts. Ingestion of mercurous chloride in teething powder has led to “pink disease” or acrodynia in infants- this condition presents as fever with a pink colored rash, irritability photophobia, painful and swollen extremities, hyperkeratosis and hypersecretion of sweat glands.

# Clinical features

- Intravascular mercury may result in pulmonary embolism or peripheral arterial embolism.
- Subcutaneous mercury initiates a soft tissue inflammation reaction with granuloma formation.

# Chronic poisoning

- is characteristic by non-specific early symptoms such as anorexia, insomnia, abnormal sweating, headache and lassitude.
- **The classical features** of chronic mercury poisoning are increased excitability, tremor, gingivitis and hypersalivation. Other central nervous system effects are extreme shyness, personality changes, and memory and intellectual deterioration. Emotional lability (“mercurial erethism”), the fine tremor causes the characteristic changes.
- Severe cases developed frank psychosis with suicidal tendency and hallucinations.



# Chronic poisoning

- ***Mercury*** may also be deposited on the lens of the eye giving rise to a permanent discoloration of the anterior capsule of the lens which does not affect visual acuity (mercurialentis).
- Kidney - glomerular and tubular damage may follow chronic exposure to mercury and renal tubular acidosis, has been described in children.
- The main features of organic mercury poisoning are paraesthesia of the lips, hands and feet, ataxia, tremor, dysarthria, constriction of visual fields, deafness, and emotional and intellectual changes.
- There is often a latent period of several weeks between the last exposure and the development of symptoms.

# Medical surveillance

- measurement of urinary mercury concentration- is indicator of long exposure
- tubular protein excretion
- blood mercury concentration – indicator of acute exposure.

# Treatment

- prompt removal from exposure to mercury vapor may not prevent the development of serious sequelae. In those who do develop symptoms no antidote has been shown to be effective.
- Gastric lavage is best avoided oesophagos erosions.
- Dimercaptol in the treatment of inorganic mercury poisoning
- Oral DMSA (succimer) and DMSP (unitiol)- 30mg/kg body weight.
- There is no effective treatment for chronic mercury poisoning.

# Arsenic

- is a metalloid as it has properties of both metals and non-metals.
- It forms both trivalent (e.g. arsenic trioxide, arsenious acid, and arsenites) and pentavalent (e.g. arsenic pentoxide, arsenic acid, and arsenates) derivatives.
- Arsenic is used in the electronics industry, in the production of special types of crystals and optical glass, in hardening lead and copper alloys, in the manufacture of fireworks, and as a wood preservative and pesticide.
- It is a byproduct of copper smelting. Some 90% of an ingested dose of most inorganic trivalent and pentavalent arsenicals is absorbed, the exception being some insoluble compounds such as arsenic selenide.

# Kynetics

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# Kynetics

- Soluble arsenicals compounds can be absorbed by inhalation but skin absorption is generally poor.
- In exposed individuals high concentration of arsenic are present in bone, hair, and nails. The half-life is in the range of 1 to 3 days.
- Excretion is predominantly in the urine as mono- and dimethyl-derivatives.

# Acute poisoning

This can follow accidental, suicidal, or deliberate ingestion, the toxicity being largely dependent on the water solubility of the ingested compound.

- Within 2 hours of substantial ingestion of a soluble arsenical compound, severe hemorrhagic gastritis or gastroenteritis may ensue with collapse and death usually within 4 days.

# Acute poisoning

- A metallic taste , salivation, muscular cramps, facial oedema, difficulty in swallowing, hepatorenal dysfunction, convulsions, and encephalopathy are reported.
- A peripheral neuropathy (predominantly sensory), striate leukonychia (Mees'lines), hyperkeratosis, hyperpigmentated skin lesions are common in those surviving a near fatal ingestion. ESG-QT prolongation, ventricular arrhythmias.
- Also may be irritation of the eyes, nose, throat and lower respiratory tract.



# Chronic poisoning

- The ingestion of arsenic in contaminated drinking water or in “tonics” containing inorganic trivalent arsenical compounds has led to progressive weakness, anorexia, nausea, vomiting, stomatitis, colitis, increased salivation, epistaxis, bleeding gums, conjunctivitis, weight loss, and low grad fever.
- - hyperkeratosis of the palms and soles of the feet, raindrop, pigmentation of the skin and Mees’lines on the nails.
- There is an increased risk of skin cancer

# Chronic poisoning

- Symmetrical peripheral neuropathy is typical
- Sensory symptoms predominate but motor involvement is recognized and may cause confusion with the Guillain-Barre syndrome.
- CNS symptoms hearing loss, psychological impairment and ECG changes have been reported.
- Other chronic effects include disturbances of liver function and ***ulceration and perforation of the nasal septum.***

# ***Medical surveillance***

- Arsenic concentration in hair and nails have been used to indicate chronic systemic absorption.
- Urinary arsenic concentrations correlate closely with airborne arsenic concentrations in arsenic workers. (A 24 hours urine collection is the most reliable sample)
- Regular examination of the skin should be included in an occupational health screening programs.

# Treatment

- ***Dimercaptol*** has been the recommended chelator in the treatment of arsenic poisoning i/m injection 2.5-5 mg/kg four hourly for 2 day followed by 2.5 mg/kg i/m twice daily for 1 to 2 weeks.
- ***DMSA (succimer) and DMPS (unitiol)*** may be preferable- orally 30mg/kg body weight daily.

Thank you for attention!