Second practical training in occupational diseases

TOPIC:

Occupational intoxications with metals - diagnostic principles and criteria, labor expert assessment

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LEAD POISONING

- Lead is soft, malleable, gray metal with high density and corrosion resistance
- It contains between 1 and 11% in sulphide, carbonate or sulphate ores
- It is obtained by grinding ores, flotation and smelting, purification from other metal impurities (copper, arsenic, zinc, tin, bismuth) or extracted from PB scrub
- No known biological function
- There is no proven harmless lower limit for Pb
- Cheap, widely used, easy to obtain
- It is found everywhere - in the air, food, water, soil, house dust, etc.
- From Pb gasoline the air in the environment has Pb content and Pb gets into the water, soil, dust in homes, etc.

USE AND SOURCES OF LEAD

- **Paints** (**since** 1970)
- **Gasoline (tetraethyl lead)**
- **House dust (deposited by polluted air)**
- **Occupational sources**
- **Solders**
- **Ceramic glaze**
- **Pesticides (lead arsenate)**
- **Cigarettes**
- **Mines, furnaces with molten metal**
- Glazing of dishes, pots
- TV monitors, computers
- Batteries, bullets, lead weights
- Aviation

- X-ray protection
- Crystal
- Explosives
- Dyes
- Tin vessels

Endangered professions：

- production of batteries, tubes and cables, balls, lead paints, plastics, stabilizers, glass, ceramics, faience
- in metallurgy in the production of lead alloys , soldering,
- in printing, electronics,
- for glazing and decoration of ceramic products
- production and use of Pb oxides, salts and fuels containing tetraethyl lead

Risk in everyday life

- when consuming alcoholic beverages prepared in cauldrons, treated with tin-lead solder or by thermal heating of ceramic vessels
- Increased concentration of Pb in the air from automotive gases

Entry route

- The main route is respiratory , in the form of aerosols or fine dust (about 40%), the absorption depends on the size of the particles and their solubility

- Rarely Pb enters through the gastrointestinal tract - food and smoking (about 5-10%)
- Deficiency of Fe and Ca leads to increased Pb absorption
- In the blood, 99% of Pb binds to erythrocytes, and the remaining 1% is in plasma, from where it is transported to tissues
- Pb crosses the placenta and its concentration in the blood of the fetus correlates with the level in the mother

Absorption of Pb

- Pb is absorbed in the gastrointestinal tract as well as Fe and Ca
- Pb is well absorbed orally in children (~ 50%) and poorly in adults (~ 10%)
- Pb absorption is improved in diets low in Fe and Ca
- PB can be inhaled

- Tetraethyl lead can be absorbed through the skin

Pathogenesis :

- Pb inhibits enzymes involved in heme biosynthesis (DALK dehydratase) by blocking their SH groups
- Increase of DALK and coproporphyrin in urine and accumulation in Er of protoporphyrin and Fe not used in heme synthesis
- Impaired utilization of Fe is the reason for its increased level in the blood and the appearance of siderocytes (Fe containing Er)
- Hypochromic, hypersyderemic, sideroachrestic anemia develops
- Pb directly affects Er: disrupts the structure of erythroblasts and mature forms; reduces the viability of Er, shortens their life expectancy. Reticulocytosis and the appearance of basophilically punctured erythrocytes are observed.

  Pb destroys the blood-brain barrier with primary damage to astrocytes and secondary to microvascular endothelium

  The prefrontal cortex, hippocampus and cerebellum are damaged
- Pb disrupts Ca-regulated processes by replacing Ca in protein kinase C and inducing the expression of new genes

Pb affects the voltage-gaining channels in cellular function

Pb disrupts the release of neurotransmitters from presynaptic nerve endings

Pb levels are significantly associated with cognitive impairment

Cumulation and emission

- Accumulates mostly in the bones, followed by the liver, kidneys, skeletal muscles, brain
- Elimination is mainly through the kidneys, less with feces, sweat, hair, nails and epidermal cells
- The half-life is 5 to 10 years

Distribution of Pb

- 95% long bones.
- Binds to the matrix
- It is excreted during osteolysis
- 4% brain, liver, kidneys
- 1% blood
- It also passes through the placenta

- Pregnancy increases the mobilization of Pb from the maternal

skeleton

- PB is mobilized by the skeleton during the postmenopausal period more than during pregnancy
- Pb follows calcium to and from bones

Health effects of Pb

- Dependent on:
- the concentration of Pb in the blood
- The total dose in childhood

Clinical picture of lead poisoning

ACUTE POISONING

- Gastric colic - severe colic-like pain around the navel, decreasing with pressure; constipation; nausea, vomiting, black stools; high blood pressure; bradycardia
- Anemia with hemolysis
- Nephropathy, acute renal failure
- lead encephalopathy with headache, confusion, constipation, coma, seizures (more common in children)
- On funduscopy, there is edema of the papilla or neuritis of the n.opticus

CHRONIC POISONING - chronic saturnism

- Asthenia - fatigue, apathy, irritability, and in high-grade lead exposure - insomnia, confusion, impaired concentration and memory
- Arthralgias, myalgias
- Lead facies - grayish-pale, earthy complexion. rarely, more often pale skin on the face
- Yellowing of the sclera in acute hemolysis
- **Hepatic syndrome** - heaviness and pain in the right hypochondrium. Objectively - hepatomegaly, increased activity of serum transaminases, subicteric
- Changes in the oral cavity - gray-blue pigmentation of lead sulfide on the gingival margin, broken teeth, metallic taste in the mouth
- Anemic syndrome with reticulocytosis and basophilic punctured erythrocytes. Serum iron is normal or elevated
- Gastrointestinal syndrome - decreased appetite, unpleasant sweet taste in the mouth, heaviness in the epigastrium, dyspeptic disorders

- **Lead colic** - sudden, severe colic-like pain around the navel, nausea, vomiting,

persistent constipation, hypertension with bradycardia, palpation of the abdomen is not painful

- **Toxic lead nephropathy (tubulopathy)** - rare
- Gouty arthritis and gouty nephropathy, loss of libido, impaired spermatogenesis and infertility have been reported; menstrual disorders

In case of high Pb exposure - neuropathy:

- Distal motor neuropathy- drooping wrists
- Encephalopathy - seizures and coma
- Severe forms of Saturnism - lead encephalomyelo-polyradiculoneuropathy

Exposure tests:

- Pb in blood - over 2.88 μmol / l
- PB in urine above 0.53 μmol / l
- DALK over 8,000 nmol / 24h urine
- Normochromic anemia
- PE - over 15%
- occurrence of basophilically punctured erythrocytes over 0, 5 ‰
- **An increase in erythrocyte protoporphyrin that is primarily free**
- increased coproporphyrin in urine

Clinical course - chronic lead poisoning has one preclinical and four clinical stages

The preclinical stage is called lead carrying, and the four clinical stages are:

- **lead impact**
- **chronic mild lead poisoning**
- **Moderate chronic lead poisoning**
- **Severe chronic lead poisoning**

- **Lead carrying - clinically healthy individuals with increased levels of lead in blood and urine**

- Lead impact - changes in the oral cavity, inhibition of DALK dehydrase, increased free protoporphyrins in erythrocytes, reticulocytosis, DALK in the urine,lead in the blood and in the urine
- Chronic mild lead poisoning- mild anemic syndrome, functional liver disorders,

cerebrastenia; elevated blood lead, reticulocytosis, basophil punctured erythrocytes; in the urine - elevated levels of Pb, DALK and coproporphyrin

- Moderate chronic lead poisoning is considered in the presence of some of the following syndromes: severe anemia, lead colic, toxic hepatitis and motor polyneuropathy plus significantly increased lead in the blood and in the urine, DALK in the urine
- Severe lead poisoning - lead encephalopathy is diagnosed

Antidote treatment

- $CaNa_2$ EDTA 10% 10 ml in 500 ml nat. serum or glucose 1 gram daily iv in 3 consecutive days
- Succimer (Chemet) caps. x 0.350 – in cases with low Pb exposure up to 10 days x 2.1 / 24 hours (3 days). In case of high-grade lead absorption, a 20-day course with the same daily dose.
- D-penicillamine (Cuprenil) tab. x 0.250 daily dose 2.0 / 24 hours (4 times a day) - 5 days. Suitable for low lead exposure; in high grade it is recommended as a final treatment after administration of $CaNa_2$ EDTA

Symptomatic treatment

- **Pb colic** - antispasmodics + antidotes
- **Toxic hepatitis** - diet, levulose systems, Carsil 3x2, Essentiale 3x1
- **Toxic anemia** - antidote therapy has a good effect on anemia and leads to normalization of porphyrin metabolism.There is no need of iron supplements
- Pb polyneuritis - vasodilators, NSAIDs, neurotrophics - vit. from B group, geritamine, neurotransmitters
- In case of high-grade Pb absorption and excretion after the antidote courses - balneotherapy with S-rich waters (Kyustendil)

OCCUPATIONAL INTOXICATION WITH MERCURY

Medical Hg

- **Hg compounds in the past have been used as diuretics, antiseptics, laxatives, for the treatment of eye and skin diseases (mercurochrome)**
- **The use of Hg salts in the 19th century to treat syphilis caused many side effects and death**
- **Workers in wool felt factories developed symptoms of**

excitability and irritability due to inhaled Hg, some of the effects were irreversible

- In the soil, mercury is relatively harmless in divalent form. It is harmful when it is converted into methylmercury (CH3Hg +).

Hg in the modern environment

- 70% of Hg in the environment comes from anthropogenic sources:

mines, metal smelting, civil and medical waste, sewerage, burnt coal, cement production

Over the last century, Hg in the environment has tripled due to industrialization

Population at risk

- workers in the production of mercury and quartz lamps, measuring instruments and apparatus, dentists

- **Pathogenesis:**

Hg has an affinity for SH groups of cellular proteins and enzymes

Nephrotoxicity

- Hg is toxic to the proximal tubular cell membrane
- At low concentrations Hg binds to SH groups of membrane proteins and acts as a diuretic by inhibiting Na + reabsorption

Neurotoxicity of MeHg

- All forms of Hg are neurotoxic
- MeHg is highly neurotoxic. MeHg levels even lower than those that cause postnatal effects impair fetal development

MeHg exposure

- Intrauterine exposure is predominant in newborns and children, but also important is the exposure from breast milk and the consumption of fish and fish products.

Incidents of industrial MeHg poisoning

- In the 1950s in Minamata and Niigata, Japan, more than 21,000 people became a victim to the so-called Minamata disease, which killed about 600 people, consumed fish industrially contaminated with MeHg (Takizawa & Kitamura, 2001), and to date the victims are already 1874. Leading were neurotoxic manifestations.

- In 1971-72, massive Hg poisoning occured in Iraq from the consumption of bread made from grain treated with a MeHg fungicide (Bakir et al., 1973)

Minamata disease

The Japanese government has announced that Minamata's disease is poisoning with MeHg , a by-product of acetaldehyde production at two factories along the Agano River. Affects the CNS.

It is characterized by:

- Sensory disturbances in the distal parts of the limbs
- Cerebellar ataxia
- Bilateral concentric narrowing of the visual fields
- Central impairment of eye movements, hearing and balance

In child population:

- Intellectual disorders
- Different degrees of neurological disorders after the ataxia

Clinic - inorganic Hg:

- gingivitis, stomatitis, pharyngitis, dental erosions, grayish-purple stripe
- Atkinson's syndrome - reddish-brown coloration of the eye lens
- tremor
- Hg heresy - increased excitability, emotional lability
- vegetative syndrome - hypersalivation, hyperhidrosis, tachycardia, polyuria
- neuralgia, neuritis, polyneuritis, early myasthenia of the extensors of the arm
- nephrosis - proteinuria,renal failure
- mental disorders - hallucinations, dementia
- enlargement of the thyroid gland
- anemia

Clinic - organic compounds of Hg:

- paresthesia
- loss of coordination
- atactic gait
- tremor
- muscle rigidity
- narrowing of the visual field - "tunnel vision" - to complete blindness
- reduction to hearing loss
- mental disorders - depression, memory disorders, obsession. psychosis, schizophrenia
- erythroderma, desquamation, skin rash
- renal dysfunction (rare)

Exposure tests:

- Hg in blood> 0.054 olmol / l

- **Hg in urine> 0.118 µmol / l**
- **Hg in saliva > 0.15 µmol / l**

Treatment:

ANTIDOTS:

- **Unithiol 5% 5 ml x 1 amp Z i . m . daily for 5 days**
- **Succimer (Chemet) capsules 0.350; daily dose 2.1g for 5 days**
- **Na thiosulfuricum - 10-20% - 10 ml, 5 days**
- **SYMPTOMATICALLY :**
- **antidepressants,**
- **hepatoprotective,**
- **vasodilators.**
- **Vitamin therapy -**
- **vit. B1, B6, C**
- **Balneo-sanatorium treatment with sulfide waters**

Chronic cadmium intoxication

Occupations at risk:

- **Cd - Ni batteries, cadmium lamps, alloys, electroplaters, metallurgists**

Pathogenesis of cadmium intoxication

- **Disrupts the metabolism of Ca and P**
- **Decreases the activity of alpha-antitrypsin in the lung mucosa**
- **Connects SH groups of cellular enzymes and proteins**
- **It has a direct irritating effect on the mucous membranes**

Clinical picture

ACUTE POISONING:

- **Metal fever**
- **Dyspnoea, pneumonia, pulmonary edema**
- **Gastrointestinal disorders**
- **Hepato-renal syndrome,acute renal failure**

CHRONIC POISONING :

- **Kidney syndrome - tubulopathy with proteinuria**
- **Fanconi syndrome - aminoaciduria, glucosuria, calcium and phosphaturia**
- **Emphysema, bronchitis, diffuse interstitial fibrosis**
- **Osteomalacia, osteoporosis, spontaneous fractures**
- **Anosmia, rhinopharyngitis, yellow discoloration of the dental necks**

Long-term consequences :

- **Carcinoma of the lungs and prostate**

Laboratory tests:

- **Cd blood> 0.03µmol / l;**
- **Cd urine> 0.01 µmol / l;**
- **B2 microglobulin, lysozyme in urine**

Treatment - Cd intoxication:

Antidote

CaNa $_2$ EDTA 10% 10 ml in 5% 500 ml physiol. serum iv - 6 days

- **Symptomatic - depending on the type and degree of organ damage**

- **Prophylactic: Vit . D -amp . - 600,000 IU i . m . once a month**
- **Calcium C - 2 x1 tablets; Calcium phospho C- 3x1 tab.**

MANGANESE POISONING

Occupations at risk:

- **extraction and processing of manganese ores**
- **production of ferroalloys, steel, electrolytic alloys for non-ferrous metals**

Pathogenesis:

- **affinity for thiol groups with the formation of complex compounds with methionine, cysteine, cystine**

- **direct damage to extrapyramidal structures (palidum, substantia nigra, corpus striatum)**

- **disturbance in the metabolism of adrenergic neurodiators.**

Clinical picture:

ACUTE POISONING

(MnO; manganese carbonyl)

- **metal fever,**
- **dyspnea**

CHRONIC POISONING:

- **fatigue, headache, apathy**
- **changes in behavior to psychosis**
- **Parkinson's syndrome - slow monotonous speech, face like mask, tremor, brady-, akinesia, micrography, increased muscle tone.**
- **Pneumofibrosis**

Laboratory researches:

- **Mn-blood> 3μmol / l;**
- **Mn- urine > 1μmol / l;**

- **Mn levels increase in exposed workers, but do not correlate with its toxic effects!**

Treatment:

I. Antidote:

- **CaNa 2 EDTA 10 % 10 ml 1x daily in 5% 500 ml glucose i . v .**
- **D-Penicillamine / Cuprenil / 0.250g; 4x2 tablets, 5 days**

II. Symptomatic

- **Vitamin therapy - B1; B6; B12; Geritamin**

Anti-Parkinsonian drugs

- **Dopaminergic:**
- **For correction of dopamine deficiency in the CNS - Levodopa , Sinemet , Madopar , Izicom - according to the protocol**
- **Dopaminergic agonists - bromocriptine**
- **Stimulating endogenous dopamine - Amantadin 0.100-1 to 4 t.**
- **MAO inhibitors - Selegiline -5-10 mg daily**
- **Cholinolytics with central action: Biperidin (Akineton 2 mg / day with increase of the dose)**
- **Triperidin (Norakin 2 mg, 3-4 days); Parkizan 1 mg starting dose; by protocol**

NICKEL INTOXICATION

Use of Ni

- **for obtaining alloys with other metals - Fe , Cr , Cu**
- **for anti-corrosion coatings**
- **for alkaline batteries**

- for chemical equipment, catalysts
- in jet technology and in nuclear reactors

Entry route:

- by inhalation of vapors and powders with nickel and its compounds
- through the skin - nickel carbonyl

Pathogenesis:

- General toxic effect mainly on the NS and metabolic disorders
- Allergic effect - on the skin and lungs
- Carcinogenic effect - CA of the lungs

Clinical picture:

ACUTE POISONING / relatively rare /

- if swallowed - profuse vomiting, colic-like abdominal pain, diarrhea, watery stools
- when inhaled - KGDP, headache, fatigue
- in contact - eczema and ulcerations on the fingers

Chronic poisoning:

- Rhinitis, sinusitis, anosmia, perforation of the nasal septum
- Metal fever
- Allergic contact dermatitis, "nickel eczema", "nickel scabies"
- Bronchial asthma, pneumosclerosis
- CA of the lungs / in the case of nickel refining workers /
- Neurocirculatory dystonia

NICKEL CARBONYL

- **Neurocirculatory dystonia**
- **Gastrointestinal disorders _**
- **Cough, shortness of breath, interstitial pneumonia, pneumosclerosis**
- **Delirium, coma**

Treatment :

- **Respiratory reanimation**
- **Corticosteroids**
- **Ca medications**
- **Intravenous infusions of water - saline and glucose solutions**
- **Dimercaprol i . m . - 3 mg / kg every 6 hours**

ARSENIC INTOXICATION

One of the most toxic metals on earth

- **Forms:**
- **Trivalent**
- **Pentavalent**
- **Routes of exposure:**
- **Digestive,**
- **Inhalation**

Endangered contingent: workers involved in the production and application of arsenic-containing pesticides, aniline, acetylene, arsenic paints, in metallurgy.

Pathogenesis: thiol poison with affinity for SH groups of a number of enzyme systems, disrupting cellular metabolism. As belongs to the first group of carcinogens for humans under the IARC

- **Health effects:**
- **Fever, anorexia, hepatomegaly, death**
- **Neurotoxicity to PNS and CNS**

- **Hepatotoxicity**
- **Gangrene of the lower extremities**
- **Skin cancer, lung cancer, kidney and gallbladder cancer**
- **Dermatitis, darkening of the skin**
- **Leukemia**

Clinic:

- **Acute poisoning:**
- **Oral - acute gastro-enterocolitis with cholera-like symptoms, tox. cardiopathy, hepato-renal system, impaired consciousness, epileptiform seizures, coma**

- **Inhalation - KGDP, pharyngitis, laryngitis**

CHRONIC POISONING:

- ***Mild*** **- rhinopharyngolaryngitis, perforation of the nasal septum**
- **hron. gastritis and gastroduodenitis, neurasthenia, polyglobulia and HB ↑**
- ***Moderate*** **- toxic polyneuropathy - ascending, vegetative-sensory with pronounced pain system**
- **toxic hepatitis and nephropathy**
- **contact dermatitis, ulceration, hyperkeratosis, melanosis, alopecia**
- ***Severe*** **- hepatorenal system, sensorimotor polyneuritis, myelopolyneuritis with manifestations of severe ataxia, "pseudotabes", toxic anemia, cardiomyopathy with rhythm and conduction disorders.**
- **CA of the lungs and skin**
- **Paraclinic: As - urine**

Treatment:

Antidote

- **BAL or Unithiol 5% 5 ml x 1 amp . i . m . daily for 5 days.**
- **Succimer capsules 0.350; daily dose 2.1g for 5 days.**
- **CaNa $_2$ EDTA 10% 10 ml in 500 ml of physical serum or glucose-1 gram daily iv for 3 consecutive days**
- **On thiosulfuricum -10-20% - 10 ml iv, 5 days.**

Symptomatic - organ protectors, antioxidants