MERCURY POISONING

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Abstract: *Certain heavy metals such as mercury, lead, arsenic and cadmium are toxic even in reduced concentrations in blood. Their accumulation in the body causes serious illnesses. The most important heavy metals in human pathology are: mercury (Hg), cadmium (Cd), arsenic (As) and lead (Pb). The author mentions the heavy metal sources of poisoning, their toxicokinetics and toxicodynamics, clinical features and treatment of heavy metal poisoning.*

Keywords: *child, heavy metals, poisoning.*

Rezumat: *Câteva metale grele neesenţiale pentru sănătatea umană, sunt toxice chiar şi la concentraţii sangvine reduse, acumulându-se în ţesuturi în urma expunerilor îndelungate. Cele mai importante metale grele cu importanţă în patologia umană sunt Arsenul (As), Plumbul (Pb), Mercurul (Hg) şi Cadmiul (Cd). Sunt abordate sursele de intoxicaţii pentru metalele grele, toxicocinetica şi toxicodinamica acestora, fiziopatologia intoxicaţiilor cu metale grele abordate individual, tabloul clinic, precum şi terapia intoxicaţiilor.*

Cuvinte cheie: *copil, metale grele, intoxicaţie.*

Heavy metals:

Definition: The term of *heavy metals* has different meanings. One of the definitions considers that heavy metals are those metals included between copper and lead in the periodic table and which have a larger specific gravity than 4,0. A more restrictive theory defines heavy metals as those chemical elements that are heavier than the rare telluric metals. Classically speaking, metallic elements are divided in 2 categories:

a. "heavy" metals, respectively those metals with a density of more than 5 g/cm^3 (for example: iron, lead and copper);

b. "easy" metals with a more reduced density (for example, sodium, magnesium and potassium).

People come into contact with these metals as a result of water and food consumption, or by breathing polluted air. Certain metals, such as sodium, potassium, magnesium, calcium and iron are widely spread in the organism and are considered essential for the cellular life. According to certain studies made starting with 1979, other metals (molybdenum, manganese, cobalt, copper and zinc) intervene in the processes of growth, development and reproduction of the human organism. Even these metals may become toxic when their concentrations are too high. (2,3). Some of the heavy metals (cadmium, lead and mercury), unessential for the human health are toxic even in reduced concentrations in blood, being accumulated in tissues as a result of long term exposure. Out of the heavy metals which are important for the human pathology, mercury poisoning will be hereby presented.

Mercury (Hg) is a metal widely used in industry. Mercury exists under three forms: **elemental** mercury (the only metal in liquid state at room temperature), **inorganic** mercury (has 3 oxidation states) and **organic** mercury (includes the short and long chain compounds) (5,6,7). Further, we will analyse elemental and organic mercury poisoning, taking into account their importance. Out of the products associated to the possible mercury exposure, we mention: dental amalgam, batteries, barometers, standardisation devices, caustic soda production, manometers, paints, fluorescent lamps with neon or mercury, thermometers, disinfecting agents, explosive materials, fireworks, vinyl chloride production, acetaldehyde production, fungicide production, bactericide and insecticide production, paper production etc. General population is exposed to mercury secondarily to fish consumption and inhalation. Mercury contaminates the air as a result of the mining activities, of iron ores exploitation and carbon burning. Hg level in the air varies between 3,9 – 50 ng/m^3, and the water of the oceans contains mercury in a concentration of 3,0-6,0 ng/ml. Surface waters contain mercury below the level of 50 ng/l. There are micro-organisms of the Methanobacterium class that transform mercury into mercury methylate, thus favouring mercury accumulation in fish and human body. The use of mercury in mining has been substantially reduced and retired from the fungicide fabrication process and of other pharmaceutical products.

Elemental mercury. It is used almost frequently in medical equipment fabrication. Mercury vapours occur as a result of ores processing or of accidental leakage.

Toxic dose. Due to its reduced absorption, elemental mercury is not toxic in case of ingestion. Chronic inhalation of mercury vapours in a concentration more than 1 μg/m^3 causes toxicity. (6)

Mercury vapours exposure that brought about serous levels of 0,4-0,9 mg/l led to death. (6)

Toxicokinetics and toxicodynamics. Gastro-intestinal absorption is less than 0,01%, except for the gastro-intestinal diseases with secondary alteration of the intestinal mucous permeability. In exchange, more than 75% of the inhaled mercury is absorbed. The release is made by urine and faeces under the form of mercuric ion and is made after a biphasic pattern: initially, it is rapidly released, than slower with a halving time up to 60 days.

Physiopathology. During respiration, mercury traverses the alveolar membrane, enters the blood circulation system and is absorbed in tissues (1) and red cells, than it is oxidised and turned into mercuric ion (Hg^{2+}). It may traverse the hemato-encephalic barrier with its accumulation on CNS even before being oxidised (2,3). It may also traverse placenta and may enter many organs and tissues (1), where it interacts the sulphydryl groups along with the secondary inhibition of the enzymatic systems and the destruction of the cellular membranes. As a result of acute inhalation of elemental mercury vapours, interstitial edema may occur, as well as alveolar exsudate, erosive bronchitis and bronchiolitis with the desquamation of the bronchial epithelium. The consequences of these processes are represented by ventilatory dysfunction, pulmonary emphysema, pnuematocele formation, pneumothorax and mediastinal emphysema.

Clinical picture. Acute exposure. Mercury inhalation will primarily affect the CNS and lungs (target organs), manifesting under the form of nausea, vomiting, fever, tachypnea, headaches, dyspnea, metallic taste, cough, thoracic and abdominal pains. In few days, pneumonitis, bilateral pulmonary infiltrates, noncardiogenic pulmonary edema, haemoptysis and pulmonary fibrosis may also occur. Acute intense inhalation may lead even to death. Children under 30 months years old are more susceptible to mercury poisoning (desquamation of the bronchial epithelium brings about the alteration of ventilation-perfusion relation with severe hypoxemia). Mercury ingestion. Elemental mercury is absorbed in small quantity, although absorption may be amplified by the long term contact of mercury with the affected intestinal membrane (for example, intestinal inflammatory disease). Elemental mercury may remain at the level of appendix with secondary inflammation, perforation and systemic poisoning with mercury.

Chronic exposure. Mercury vapours chronic inhalation produces gingivostomatitis tirade, tremble and neuropsychiatric affection. Out of the somatic manifestation, we mention: fatigability, insomnia, anorexia, memory disorders.

Ophthalmic toxicity is manifested by the occurrence of cornea opacities and vascular anomalies at the level of corneoscleral junction. Acrodynia was described in the infants and children chronically exposed to mercury by the occurrence of pink painful areas at extremities level, tumefaction and desquamation at the same level, symptoms that may be accompanied by anorexia, apathy, photophobia or hypotonia. Peripheral neuropathy and nephrotoxicity are rarely encountered in chronic mercury poisoning.

Diagnosis. Diagnosis is established by integrating all clinical data with the suggestive anamnesis for mercury exposure and dosage of the serous and urinary level of this one.

Treatment is based on removing the patient out of the contaminated environment (in case of inhalation or poisoning with elemental mercury), therapy of pulmonary effects, followed by the identification and elimination of the contamination source.

Decontamination. In case of inhalation – it is necessary the tracheal intubation, mechanical ventilation and in the severe cases, PEEP ventilation is recommended. Oxygenotherapy and bronchodilatators are often required. Mercury may be aspirated from the respiratory paths, completing with the postural drainage and washing the respiratory paths (bronchoscopy may be used). In case of ingestion – enema is necessary in case of massive quantities ingestion of elemental mercury. Extra measures are not necessary due to the high poisoning risk. Abdominal radiography is used for the monitorization of mercury flux in the intestine. Surgical removal of the affected areas must be taken into consideration in patients with mercury persistent retention. In case of mercury injection – prompt excision is required, followed by abundant irrigation and aspiration of mercury drops. Granulomae that occur as a second result of mercury injection are also removed surgically.

Mercury elimination increase. Once absorbed, mercury is released by using the kelator agents. Kelators efficacy is better when they are used immediately after mercury poisoning. In such cases, Dimercaprol, Succimer, D-Penicillamine or DMPS are used.

Organic mercury. Organic mercury is a compound in which mercury atom is covalently linked to a carbon atom. Organic compounds toxicity is produced by the stability of the covalent link:

- Short chain alkyl compounds (methyl, propyl, ethyl) are relative stable;
- Long term alkyl compounds (phenyl) are instable and rapidly converted into organic mercury. These act like the inorganic mercury, toxicologically speaking. Short chain alkyl compounds, especially mercury methyl, are the most toxic compounds.

In 1887, the injections with diethyl-mercury were used in syphilis treatment, but they were immediately abandoned because of its side effects on the central nervous system. In 1913, mercurial diuretics were launched on the markets and used for more than 30 years. The antifungicide and antibacterial properties of the organic mercury served for their use in antiseptic substances and ointments preparation. Other preparations of organic mercury are used for the antifungicid proprieties and for delaying the seeds germination. The ingestion of seeds treated with organic mercury may represent a cause of mercury poisoning. Mercury also

enters in the composition of antiseptic solutions, of ophthalmic use products, vaccines, nasal sprays, immunoglobulins and liophylisated powders.

Mercurochromum (Merbrominum) was the first organomercurial preparation used as an antiseptic. Its toxicity included contact dermatitis, cutaneous affection and anaphylaxis. Repeated use of merbronium at the level of decubitus lesions or surgical lesions induced mercurial toxicity and aplastic anemia.

Thiomersal (Thimerosal). It is a bacteriostatic and fungicide agent that contains 50% mercury. Serious side effects, like death, were described after its topic and prenatal use. Thiomersal is also used as an antiseptic in ophthalmic solutions and as a preserving agent in vaccines. Until 1999, pediatric routine immunisation with vaccines containing thiomersal caused the accumulation of a cumulative dose of 187,5 μg mercury up to age of 6 months. Moreover, a dose of anti-hepatitis B vaccine contained 12,5 μg mercury. In consequence, as a precaution measure, health organisations from many countries restrained the use of thimerosal in vaccines. Today, no vaccine contains thiomersal. Auricular irrigations with thiomersal induced the increase of the serous level of mercury and even signs of mercury poisoning. The lethal dose of thiomersal in children has never been established. According to certain literature data, 10 infants died as a result of the use of thiomersal tincture in omphalocele treatment (6).

Speculations have also been made on the relation between thiomersal and autism in the context in which most patients with autism were immunised with thimerosal-containing vaccines (4,10). According to certain meta-analyses, it seems that the genetic factor is playing a major part in autism etiology (4,9,10). There were numerous studies about the poisoning induced by mercury; in exchange no research was made on thimerosal. Merk Manual edition 1999 (page 2636, section "Mercury poisoning") does not even mention dental amalgam and thimerosal as possible sources of mercury that may lead to poisoning. Even FDA („Food and Drug Administration") was contradictory in its official declarations:

- In 1998 – „OTC medication that contains thimerosal and other forms of mercury are not considered, in general, safe and efficient";
- In July 2000 – „Vaccines that contain sure level of mercury".

Regarding the complications generated by mercury exposure, we may synthesise the following: Alzheimer's disease, autoimmune diseases, renal diseases, infertility, food allergies, multiple sclerosis, thyreopathy, ovarian cysts, disequilibrium at cerebral level of neurotransmitters, neurological problems, cardiac affections. Regarding the prophylactic attitudes in mercury poisoning, we mention: proper ventilation of the environment containing mercury vapours, dosage of environment mercury concentration (special devices), preventing mercury exposure, surfaces treatment with kelators, areas wrapping with polyutherane, tests repeating for decontamination conformation, supervising the exposed workers, including the medical examination and quarterly determination of mercury concentration released in urine. Concerning the therapeutic particularities, we mention DMPS (with large affinity for zinc, that is why it is necessary to add zinc in our diet), DMSA (8) (which penetrates NCS cells), Chlorella (substance extracted from algae and aquatic plants), Cilantro (substance contained in Chinese parsley whose mechanism of action remains unknown). Chemical agents are also used, which help in the dezintoxication of the organism, such as: supplementing the food with high contents of sulphur (fresh garlic), alpha-lipoid acid (useful for the reduction of toxic neurological effects), antioxidants (vitamin E with cerebral protective effect, selenium which is useful in mercury release and increases the action of glutathione with detoxifying part and vitamin C which mobilizes mercury from intracellular deposits), hyaluronic acid (in combination with DMPS) stimulates mercury elimination 2-4 times more without raising toxicity.

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