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Metal Poisoning: A Brief Overview



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ABSTRACT

Metals and its compounds are constituents of our natural environment. Their distribution depends on the existence of natural sources and their use in human activity. Metals required for the normal physiological function in the human beings are called as essential metals and metals having no implication in physiological functions are termed as non essential metals. Presence of even a minute quantity of non essential metals in the body can be termed as metal toxicity, as they do not have any biological role. Excessive presence of essential metals in the body may also lead to toxicity. The source of metals may be natural or anthropogenic. These metals enter the human by various exposures such as inhalation, ingestion or transdermal. The present article reviews the exposure and toxicity produced by various metals in the human beings.



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INTRODUCTION

Metals occur naturally in the earth's crust and their contents in the environment can vary between different regions¹. Environmental pollution from metals can arise from natural as well as anthropogenic sources. Natural sources are seepage from rocks into water, volcanic activity, forest fires etc. Anthropogenic sources of environmental pollution are mainly by industrialization which may occur at the production level or at the level of use of the products². Metals may be further classified as essential metals which are required for the normal physiological function of the body. The example of essential metals are cobalt which is a cofactor for the vitamin B12 required for production of red blood cells, copper is essential for absorption of iron, which in turn is essential for synthesis of hemoglobin. Zinc, Magnesium, Manganese are cofactor of many enzymes. Arsenic and chromium are regarded as essential metal at low doses. Nonessential metals are those that have no known beneficial role to play in biological function. These metals include beryllium, cadmium, lead, mercury, thallium, titanium, and uranium³. Any toxic metal may be called heavy metal, irrespective of their atomic mass or density. The other definition is "heavy metals are metallic elements with high atomic weight and density at least five times greater than that of water"⁴. Human beings may get exposed to these metals in many ways. Inhalation exposure is most common for cadmium and mercury metals. Whereas ingestion through food or water is most common in case of lead and arsenic. Absorption through skin is most common in case of nickel⁶. In India exposure to heavy metals are common through herbal medicinal practices which includes Ayurveda and siddha⁵. Most commonly toxicity causing metals to human are lead (Pb), cadmium (Cd), mercury (Hg), arsenic (As), chromium (Cr), copper (Cu), selenium (Se), nickel (Ni), silver (Ag), and zinc (Zn). Other less common metallic contaminants include aluminium (Al), cesium (Cs), cobalt (Co), manganese (Mn), molybdenum (Mo), strontium (Sr), and uranium (U)⁶.

Lead (Pb)

Lead is the most important heavy metals causing serious health hazards to humans all over the world⁷. In developing countries like India lead poisoning remains a serious problem. In India lead poisoning is common in places such as Ratlam (Madhya Pradesh), Bandalamottu Mines

(Andhra Pradesh), Vadodara (Gujarat), Korba (Chattisgarh)⁸. Lead is used in storage batteries, cable coverings, plumbing, ammunition, manufacture of tetraethyl lead, sound absorbers, radiation shields around X-ray equipment and nuclear reactors, paints. Oxideform is used in producing fine "crystal glass" and "flint glass" with a high refractive index for achromatic lenses, solder and insecticides⁹. Lead gains entry into the human body by many ways. Oral ingestion through contaminated food and water is most important. Plant food may be contaminated by lead following its uptake from the soil and animals may ingest these contaminated vegetation. Human acquire lead in the body after consuming these contaminated vegetation or the animal. Lead may also gain entry by oral ingestion through water which would have been contaminated while being supplied through leaded pipes. Inhalation is the other route by which the lead from the automobile exhausts gaining entry into the body¹⁰. Organic tetra ethyl lead may undergo transdermal absorption. In humans 20 to 50% of inhaled and 5 to 15% of ingested inorganic lead is absorbed. In contrast 80% of inhaled organic lead is absorbed, and ingested organic lead is absorbed readily. Children absorb lead around 40% when compared to adults who absorb only 20%¹². Lead absorption is increased in individuals with fasting or whose diet is deficient in calcium, iron, phosphorus and zinc. The permissible level of lead in blood is 0.1 mg/l¹¹.

Initially absorbed lead distributes to the soft tissues particularly tubular epithelium of the kidney and liver. Later it gets redistributed and gets deposited in the bones, teeth and hair. Growing bones will acquire higher level of lead which is visible on radiography as transverse lines. Small amount gets deposited in the brain and also crosses placenta. Half-life of lead in serum is 1-2 months whereas of that in the bone is average of 6 months. Lead is excreted mainly through kidney and in little quantities it is also secreted in sweat and milk¹².

Lead has high affinity for SH groups of enzymes and hence impairs the activity of zinc dependent enzymes like *δ-aminolevulinic acid dehydratase* involved in haem synthesis. Cytochrome synthesis, steroid metabolism, membrane integrity, synthesis of active metabolite of vitamin D in renal tubular cells are also affected¹³. General symptoms of lead toxicity include fatigue, irritability, lethargy, paresthesia, myalgia, abdominal pain, tremor, headache, vomiting, weight loss, constipation, loss of libido, motor neuropathy. Blood levels of 10 µ g/dl may cause hypertension in adults were as in children causes impairment of IQ, growth and may partially inhibit haem synthesis. 20 µ g/dl causes inhibition of haem synthesis in adults were as in children

causes impairment of nerve conduction. 30 µg/dl causes impairment of hearing in adults. In children it causes impairment of Vitamin D metabolism. 40 µg/dl causes infertility in males, renal effects, neuropathy, fatigue, headache, abdominal pain. 50 µg/dL in adults causes anemia, gastro-intestinal disorder, headache, tremor. In children causes colicky abdominal pain and neuropathy. Blood level >70µg/dl in children causes encephalopathy were as in adult it is caused when blood levels >100µg/dl¹⁴.

Mercury (Hg)

Mercury is the only metal which exists in liquid state in room temperature. It is been used from ancient period due to its capacity to amalgamate with other metals¹⁵. Mercury exists in three forms basically the elemental form which is liquid in state. Inorganic form poorly absorbed from GIT and organic form which is lipid soluble and easily absorbed. Mercury is used in chloralkali plants, thermal plants, production of fluorescent lamps, electrical appliances and hospital equipments such as thermometer, sphygmomanometer. The exposure is through inhalation or oral ingestion¹⁶.

Mercury vapors are released naturally into environment through volcanic activity and of gassing from soils. Mercury also enters atmosphere through the human activities such as combustion of fossil fuels. Metallic mercury in air may get converted to inorganic form and get deposited in the aquatic environment through rain. The other important way of exposure is by oral ingestion. The inorganic form of mercury in the aquatic environment is converted to the organic form mainly methyl mercury by microorganism. Methyl mercury being lipid soluble get accumulated in the aquatic organisms and later get entry into the food chain. Mercury may also get exposure through the dental amalgam, broken thermometers or other devices containing mercury. Thiomer-sal is an antimicrobial agent releases ethyl mercury which is similar to methyl mercury¹⁷. The permissible level of mercury in the body is 0.01 mg/l¹⁸. In India exposure to mercury is common in places such as Kodaikanal (Tamil Nadu), Ganjam (Orissa), Singrauli (Madhya Pradesh)⁸.

Clinical symptoms following the metallic mercury inhalation at high concentration over a short period of time may have respiratory symptoms such as cough, tightness in chest and pain which may progress to interstitial pneumonitis. On chronic inhalation it causes toxicity to nervous system with symptoms like tremors, emotional liability, insomnia, memory loss, muscular

atrophy, weakness, paraesthesia and cognitive defects²⁸. Ingestion of the inorganic mercury salts (Hg^{2+}) leads to renal tubular necrosis, resulting in decreased urine output and acute renal failure. Chronic ingestion also has similar effect on kidney. Consumption of organic form (methyl mercury) causes toxicity to the nervous system. The symptoms include cognitive deficits, muscle tremor, movement disorder, paralysis and death following severe exposure¹⁹.

Arsenic (As)

Arsenic is a metalloid common in soil and rock. It exists in elemental form, trivalent form (arsenites/arsenious acid) and pentavalent form (Arsenates). Arsine is gaseous form of trivalent mercury. The toxicity of the arsenic is based on the rate of its clearance from the body and its concentration in tissues. The toxicity of arsenic form is organic arsenic As^{5+} , As^{3+} , < Arsine gas²⁰.

The exposure to arsenic is most common when compared to other metals. Through ingestion Arsenic may enter environment through the use of arsenic containing pesticides, mining and burning of coal. The sea food is often contaminated with arsenic. The metal may gain entry into human beings most commonly by ingestion either through the drinking water or through contaminated food²¹. The ground water in West Bengal, India is most commonly contaminated by arsenic and people suffer from chronic arsenic toxicity. The other place where exposure is common is Tuticorn (Tamil Nadu) and Balia (Uttar Pradesh)⁸. The permissible level of arsenic in body is 0.02 mg/l^{18} . Pyruvate dehydrogenase system is sensitive to inhibition by arsenic. It also inhibits the electron transport chain. The toxicity of arsenic is mainly on the cardiovascular system was acute and chronic. Exposure to the arsenic causes myocardial depolarization, cardiac arrhythmia and ischemic heart disease. Chronic arsenic exposure may also cause peripheral vascular disease called as "Blackfoot disease". Chronic exposure of skin causes hyperkeratosis on the soles and palms. It also causes hyperpigmentation interspersed with hypopigmentation. Acute and chronic ingestion of arsenic cause gastrointestinal symptoms ranging from mild irritation to severe gastrointestinal hemorrhage and death. Chronic exposure of arsenic causes peripheral neuropathy involving sensory nerves first, later followed by motor nerves. Arsenic is also a carcinogen which can cause skin, bladder and lung cancer²².

Cadmium (Cd)

Cadmium is a byproduct of mining and smelting of lead and zinc. It is used most commonly in electroplating, galvanizing, plastics, paint pigments, Nickel and cadmium batteries. Cadmium exists as Cd^{++} and does not undergo oxidation reduction reactions. Human exposure to cadmium occurs mainly through in the inhalation in individuals working in metal processing industries and smoking cigarettes. One cigarette contains 1-2 μg of cadmium²³. Ingestion of cadmium occurs by consuming contaminated food. Cadmium is not well absorbed through GIT but is better absorbed through inhalation route. Cadmium distributes to kidney and liver which accounts for more than 50 % absorbed dose. Cadmium is primarily excreted through kidney and the biological half-life is 10-30 years⁴¹. Cadmium replaces zinc in zinc finger domain proteins and disrupts them. Cadmium induces formation of reactive oxygen species resulting in lipid peroxidation, glutathione depletion and up regulation of inflammatory mediators²⁴.

The most common toxicity is due to local irritation following inhalation. In early days it was leading to pneumonitis and chest pain. Chronic exposure ends up in chronic obstructive pulmonary disease. Oral ingestion causes nausea, abdominal cramps, bloody vomiting and diarrhea. Cadmium bound to metalloproteins is transported to kidney where it gets released. Initially it causes increased excretion of small molecular weight proteins which on chronic exposure ends up in renal failure and death. Chronic occupational exposure to cadmium may lead to lung cancer but cadmium is not genotoxic²⁵.

Chromium (Cr)

Chromium occurs in different oxidation states ranging from Cr^{3+} to Cr^{6+} but only trivalent and hexavalent forms are of biological significance. Chromium is an industrially important metal used in number alloys particularly stainless steel⁴⁶. Cr^{3+} is an essential metal involved in regulation of glucose metabolism. Cr^{6+} is responsible for the toxic effects of chromium²⁶. Exposure to chromium in general population occurs through the ingestion of chromium contaminated food. Workers in stainless steel, chromium plating, welding, chrome pigment and tanning industries are exposed for both ingestion and inhalation of chromium. Permissible level of chromium in body is 0.05 mg/l¹⁸. In India chromium exposure is common in Ranipet (Tamilnadu), Kanpur (Uttar Pradesh), Vadodara (Gujarat), Talcher (Orissa)⁸. Absorption into

blood is more in case of Cr^{6+} which is lipid soluble when compared to Cr^{3+} . 50-80 % of inhaled chromium is absorbed. Absorption of the ingested Cr is less than 10 %. The highest level of chromium in the body is attained in liver, kidney and bone. Chromium is also retained in erythrocytes. Excretion of chromium is mainly through urine while small amount is excreted through bile and breast milk. Biological half-life of Cr^{6+} is 40 hrs and Cr^{3+} is 10hrs.

Acute exposure of high doses causes death through multiple organ damage. Chronic low dose exposure causes toxicity at the site of exposure. Individuals exposed to inhalation will develop respiratory tract irritation, decreased pulmonary function and pneumonias. Chronic exposure through ingestion causes gastric irritation. Cr^{6+} is a dermal irritant that may cause ulcerations and burns. Chromium is carcinogenic which may cause lung and nasal cancer²⁷.

Copper (Cu)

Copper is an essential element. Sources of copper are chocolate, avocado, nuts, liver and kidneys, wheat germ and bran, copper water pipes, copper sulfate added to drinking water, compounds added to swimming pools, mineral supplements, copper cookware, birth control pills, copper intrauterine devices mining and pesticide industries. Oral ingestion is the important route of exposure²⁸. The permissible level of copper in the body is 0.1 mg/l^{18} . In India exposure is most common in Tuticorin (Tamil Nadu), Singbhum Mines (Jharkhand), Malanjkahnd (Madhya Pradesh)⁸. It is transported through serum initially bound to albumin and later more firmly to ceruloplasmin and transcuprein. The bile is the normal excretory pathway that plays a primary role in copper homeostasis. Copper toxicity occurs in the form of nausea, vomiting and diarrhea. Ingestion of large amounts of copper salts may produce hepatic necrosis and death. Excessive accumulation of copper in liver, brain, kidneys and cornea manifests into Wilson's disease. This disorder is also called ashepatolenticular degeneration. Genetic studies have identified a linkage between Wilson's disease and chromosome 13. Menke's disease or "Kinky hair syndrome", Indian childhood cirrhosis (ICC) and idiopathic copper toxicosis or non-Indian childhood cirrhosis are other disorders caused by copper²⁹.

Nickel (Ni)

Nickel is ubiquitous in nature. It occurs mainly in the form of sulfide and silicate minerals. Hydrogenated vegetable oils, contaminated alcoholic beverages, margarines and imitation whip

cream, commercial peanut butter, vegetable shortening, nickel-plated jewelry, unrefined grains and cereals, oysters, tea, nickel plating on metallic objects, cigarette smoking, manufacture of steel, batteries, machine parts, wire, electrical parts, some ceramic dental fillings. Combustion of fossil fuels and waste incineration is known to contain very low level of nickel³⁰. Human exposure may occur through inhalation, ingestion and dermal contact. Occupational exposure may be caused by elemental nickel, nickel compounds, complexes, alloy and also fumes from alloys used in welding and brazing. Food is a major route of exposure for people. Deposition, absorption and elimination of nickel particles in the respiratory tract largely depend upon the particle size and concentration of nickel. The rate of dermal absorption depends on the rate of penetration in the epidermis, which differs for different forms of nickel. Blood nickel levels provide a guideline as to the severity of exposure. Symptoms of nickel toxicity include skin rash, nausea, dizziness, diarrhea, headache, vomiting, chest pain, weakness and coughing. Contact with nickel vapor can lead to swelling of the brain and liver; degeneration of the liver; irritation to the eyes, throat and nose. Nickel compounds are carcinogenic to human. Risks were highest for lung and nasal cancers amongst workers heavily exposed to nickel sulfide, nickel oxide, and to metallic nickel. It has been hypothesized that nickel damages DNA directly through reactive oxygen species³¹.

Manganese (Mn)

Manganese is an essential element. It occurs most commonly in Mn^{2+} , Mn^{4+} , Mn^{7+} . It is cofactor for a number of enzymatic reactions those involved in phosphorylation, cholesterol and fatty acid synthesis. Manganese concentrates liver, pancreas, kidneys and intestine which are rich in mitochondria. It is eliminated through bile and is reabsorbed by the intestine but the principal route of excretion is faeces. The most common form of manganese toxicity occurs through chronic inhalation of air borne manganese in miners, steel mills, and some chemical industries. Pathologic changes include epithelial necrosis followed by mononuclear proliferation. Chronic manganese toxicity is called as “Manganism” which is a neuropsychiatric disorder characterized by irritability, difficulty in walking, speech disturbances and compulsive behavior³².

Zinc (Zn)

Zinc is a nutritionally essential metal. Seafood, meat, whole grains, dairy products, nuts and legumes are high in zinc. It induces the synthesis of metallothioneins which is a factor in regulating the metabolism of zinc including absorption and storage. Zinc is a functional component of several proteins that contribute to gene expression and regulation of genetic activity. Zinc chelates with cysteine /histidine in a tetrahedral configuration forming looped structures called “zinc fingers” which bind to specific DNA regions and are bound in various transcription factors such as steroid hormone receptors and polymerase. It has a role in immune function and the cytokines. Inhalation of freshly formed fumes of zinc has been associated with metal fume fever³³.

CONCLUSION

Heavy metals are important in many respects to man in the manufacturing of certain important products to use. The toxic effects of the same metals when unduly exposed to human beings can be life threatening. Good precaution and adequate occupational hygiene should be taken in handling them. Appropriate step should be taken while dispensing these metals from the industries. Health education should be given to the general public reading the toxic effects of the metals. The medical professional should be trained to diagnose and treat these metal poisonings effectively.

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