

Heavy metals intoxication: The facts

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World Journal of Advanced Research and Reviews, 2024, 24(03), 2916-2923

Publication history: Received on 16 November 2024; revised on 28 December 2024; accepted on 30 December 2024

Article DOI: <https://doi.org/10.30574/wjarr.2024.24.3.4018>

Abstract

Heavy metal toxicity has proven to be a major threat and there are several health risk associated with it. The toxic effects of these metals, even though they do not have any biological role, remain present in some form harmful for the human body and its proper functioning. They sometimes act as a pseudo element of the body while at certain times, they may even interfere with metabolic processes. Few metals such as aluminium can be removed through elimination activities, while some metals get accumulated in the body and food chain exhibiting a chronic nature. Various public health measures have been undertaken to control, prevent and treat metal toxicity occurring at various levels, such as occupational exposure, accidents and environmental factors. Metal toxicity depends upon the absorbed dose, the route of exposure and duration of exposure. i.e acute or chronic. This can lead to various disorders and can also lead in excessive damage due to oxidative stress induced by free radical formation. This review gives details about some heavy metals and their toxicity mechanisms along with their health effects.

Keywords: Toxicity; Heavy Metals; Environment; Nature

1. Introduction

Metals are substances with high electrical conductivity, malleability and lustre, which voluntarily lose their electrons to form cations. Metals are found naturally in the earth's crust and their compositions vary among different localities, resulting in spatial variations of surrounding concentrations. The main objective of this review is to provide insight into the sources of heavy metals and their harmful effects on the environment and living organisms. Heavy metals are generally referred to as those metals which possess a specific density of more than 5g/cm^3 and adversely affect the environment and living organisms (1).

Toxic metals sometimes imitate the action of an essential element in the body, interfering with the metabolic process resulting in illness. Many metals, particularly heavy metals are toxic but some are essential and some such as bismuth, have a low toxicity. Most of the definitions of toxic metals include at least Cadmium, manganese, lead, mercury and radioactive metals.

Toxicity is a function of solubility. Insoluble compounds as well as the metallic forms often exhibit negligible toxicity. The toxicity of any metal depends on its ligands. In some cases, organometallic forms, such as methylmercury and tetraethyl lead can be extremely toxic. In other cases, organometallic derivatives are less toxic such as the cobaltocenium cation (2).

Although there is no specific definition of a heavy metal, literature has defined it as a naturally occurring element having a high atomic weight and high density which is five times greater than that of water (2). Among all the pollutants heavy metals have received a paramount attention to environmental chemists due to their toxic nature. Heavy metals are usually present in trace amounts in natural waters but many of them are toxic even at very low concentrations. Metals

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such as arsenic, lead, cadmium, nickel, mercury, chromium, cobalt, zinc and selenium are highly toxic even in minor quantity.

Heavy metals become toxic when they are not metabolized by the body and accumulate in the soft tissues. They may enter the human body through food, water, air or absorption through the skin when they come in contact with humans in agriculture, manufacturing, pharmaceutical, industrial or residential settings. Industrial exposure accounts for a common rate of exposure for adults. Ingestion is the most common route of exposure in children. Natural and human activities contaminate the environment and its resources, they are discharging more than what the environment can handle (1).

Heavy metal contamination is increasingly been recognized as dramatic in large parts of the developing world particularly in India and China. Contamination of dietary substances by chemicals and non-essential elements such as heavy metals is known to have a series of adverse effects on the body of humans and animals. Because they are ubiquitous and recalcitrant, their entry into the body poses a potential health risk to human populations.

Metals can escape control mechanisms such as; Homeostasis, transport, compartmentalization, and binding to specific cell constituents, thus they can have toxic and even lethal effects. Heavy metals can cause malfunctioning of the cellular processes in displacement of essential metals from their respective sites. Symptoms are often the first indicators of contamination, and as such help to identify the contaminant (3).

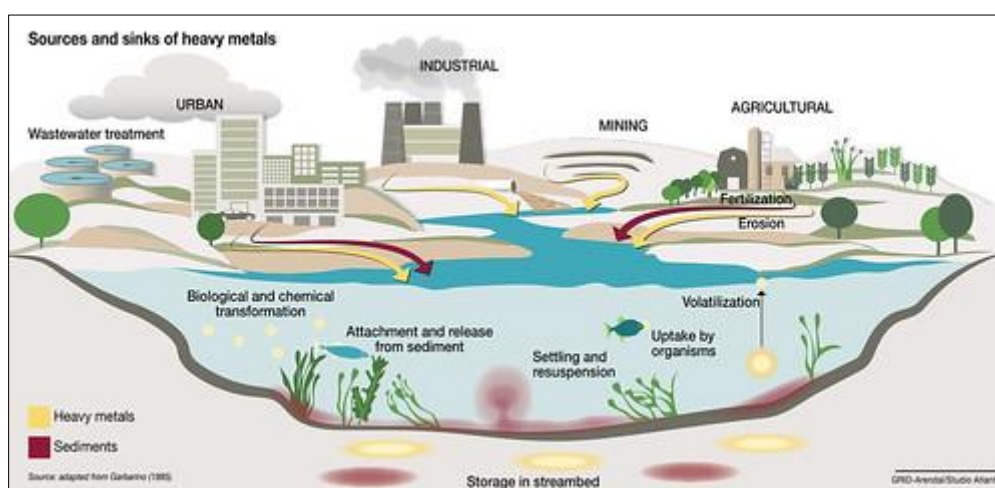


Figure 1 Sources and sinks of heavy metals (3)

Although toxicity that arises from sudden exposure to substantial quantities of metals (such as from occupational exposure) typically affects multiple organ systems, severity of the health outcome of toxic metals depends on the type and form of the element, route and duration of the exposure, and to a greater extent on a person's individual susceptibility. In times of health perspective, pathophysiology of metals depends primarily on the generation of oxidative stress, which is characterized by (a) Increased Reactive Oxygen Species (ROS) and Reactive Nitrogen Species (RNS) production, (b) Depletion of intracellular antioxidant stores and free-radical scavengers and (c) Detoxification of reactive oxygen species (4).

Radioactive metals have both radiological toxicity and chemical toxicity. Metals in an oxidative state abnormal to the body may also become toxic; Chromium (III) is an essential trace element, but Chromium (VI) is a carcinogen (5).

Decontamination for toxic metals is different from organic toxins because toxic metals are elements that cannot be destroyed. Toxic metals may be made insoluble or collected possibly by the aid of chelating agents or through bioremediation. Alternatively, they can be diluted into a sufficiently large reservoir, such as the sea because immediate toxicity is a function of concentration rather than amount (4,5).

Toxic can bioaccumulate in the body and in the food chain. Therefore, a common characteristic of toxic metals is the chronic nature of their toxicity. This is particularly notable with radioactive heavy metals such as radium, which imitates calcium to the point of being incorporated into human bone, although similar health implications are found in lead or

mercury poisoning. The exceptions to this are barium and aluminium which can be removed efficiently by the kidneys (5,6).

1.1. Sources of heavy metals

Heavy metals can emanate from both Natural and Anthropogenic processes and end up in different environmental compositions (soil, water, air, and their interface).

1.2. Natural processes

Studies have documented different natural sources of heavy metals. Under different and certain environmental conditions, natural emissions of heavy metals occur. Such emissions include volcanic eruptions, sea-salt sprays, forest fires, rock weathering, biogenic sources and wind-borne soil particles. Natural weathering processes can lead to the release of metals from their endemic spheres to different environment compartments. Heavy metals can be found in the form of hydroxides, oxides, sulphides, sulphates, phosphates, silicates and organic compounds. The most common heavy metals are; Lead(Pb), nickel(Ni), chromium(Cr), cadmium(Cd), arsenic(As), mercury(Hg), zinc(Zn) and copper(Cu) (7).

Although the aforementioned heavy metals can be found in traces, they still cause serious health problems to humans and other mammals (5,8).

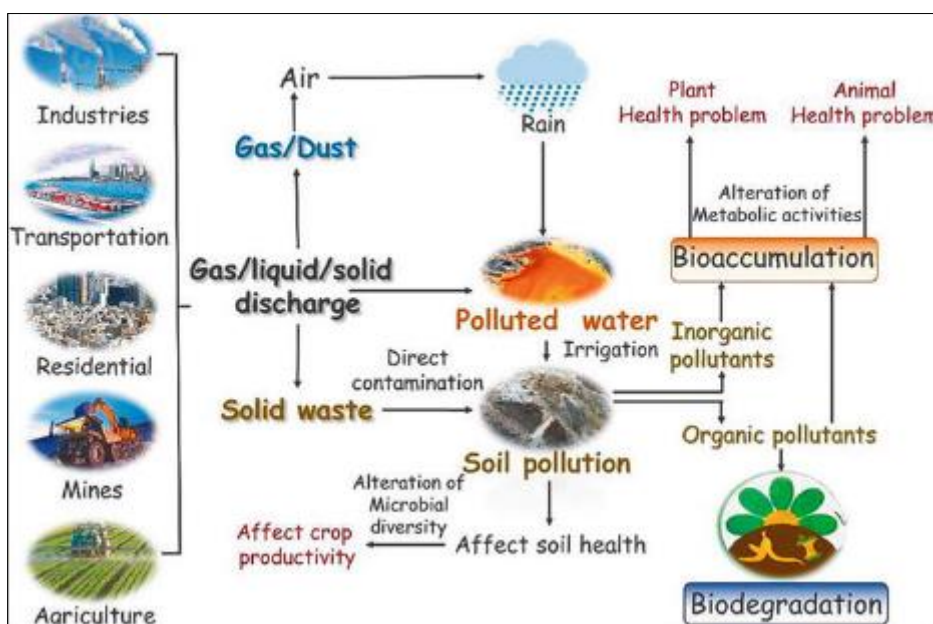


Figure 2 Environmental cycle of Heavy Metal Pollution (9)

1.3. Anthropogenic processes

Industrial agriculture, wastewater, mining and metallurgical processes and runoffs also lead to the release of pollutants to different environmental compartments. Anthropogenic processes of heavy metals have been noted to go beyond the natural fluxes for some metals. Metals naturally emitted in wind-blown dusts are mostly from industrial areas. Some important anthropogenic sources which significantly contribute to the heavy metal contamination in the environment include; Automobile exhaust which releases lead, smelting which release arsenic, copper and zinc, insecticides which release nickel, vanadium, mercury, selenium and tin. Human activities have been found to contribute more to environmental pollution due to the everyday manufacturing of goods to meet the demand of the large population (9).

1.4. Biochemistry behind metal toxicities

The presence of heavy metals in aqueous streams, air, soil and food have become a problem due to the harmful effects on human health even at low concentration in the environment. Heavy metal pollutants in waste water is one of the problems facing human beings. Heavy metals can be very toxic to life.

For example in Malaysia a particularly vexing problem is the presence of toxic and hazardous heavy metals in industrial effluents. When such metal bearing waste streams are insufficiently treated before discharge, they find their way into the environment and subsequently into the food chain.

Low toxicity			Very toxic, relatively accessible			Toxic, low solubility		
Na	C	F	Be	As	Au	Ti	Ga	Hf
K	P	Li	Co	Se	Hg	La	Zr	Os
Mg	Fe	Rb	Ni	Te	Cu	W	Rh	Nb
Ca	S	Sr	Pd	Pb	Zn	Ir	Ta	Ru
H	Cl	Al	Ag	Sb	Sn	Re	Ba	
O	Br	Si	Cd	Bi	Pt			

Figure 3 Classification of elements according to toxicity (10)

According to the World Health Organization, the metals of most immediate concern internationally are aluminium, chromium, manganese, iron, cobalt, copper, zinc, mercury and lead (11). Economic development has become synonymous with industrial progress in Malaysia. This is also in line with the federal government's policy, the industrial master plan to promote growth in the nation's industrial sector (9).

2. Heavy metals and their toxicity mechanisms

2.1. Arsenic

Arsenic is one of the most important heavy metals causing disquiet from both ecological and individual health standpoints (Hughes et al. 1988). It has a semi metallic property which is prominently toxic and carcinogenic and extensively in the form of oxides or sulphides or as a salt of iron, sodium, calcium, copper etc. Arsenic is the twentieth (20) most abundant element on earth and its inorganic forms such as arsenate and arsenite compounds are lethal to the environment and living creatures (12).

Humans may encounter arsenic by natural means, Industrial sources or from unintended sources. Drinking water may get contaminated by use of arsenical pesticides, natural mineral deposits or inappropriate disposal of arsenical chemicals. Arsenic is a protoplasmic poison since it affects primarily the sulphhydryl group of cells causing malfunctioning of cell respiration, cell enzymes and mitosis (7).

2.2. Mechanisms of arsenic toxicity

In arsenic biotransformation, harmful inorganic arsenic compounds get methylated by bacteria, algae, fungi and humans to give monomethylarsenic acid (MMA) and dimethylarsinic acid (DMA). In this biotransformation process, these inorganic arsenic species (iAS) are converted enzymatically to methylated arsenicals which are the end metabolites and the biomarker of chronic arsenic exposure (12).



Biomethylation is a detoxification process and end products are methylated inorganic arsenic such as MMA (V) and DMA (V) which excreted through urine are bioindication of chronic arsenic exposure. However MMA (IV) is not excreted and remains inside the cells as an intermediate product (13).

Monomethylarsonic acid (MMA III), an intermediate product is found to be highly toxic compared to other arsenicals, potentially accountable for arsenic-induced carcinogenesis.

2.3. Lead

Lead is a highly toxic metal whose widespread use has caused extensive environmental contamination and health problems in many parts of the world. Lead is a bright silvery metal, slightly bluish in a dry atmosphere. It begins to tarnish on contact with air, thereby forming a complex mixture of compounds, depending on the given conditions. Figure 4 shows various sources of lead pollution in the environment.



Figure 4 Sources of lead pollution in the environment (15)

In the U.S, more than 100 to 200,000 tons of lead per year is being released from vehicle exhausts. Some are taken up by plants, fixation to soil and flow into water bodies, hence human exposure of lead in the general population is either due to food or drinking water. Lead is an extremely toxic heavy metal that disturbs various plant physiological processes and unlike other metals, such as zinc, copper and manganese, it doesn't play any biological functions. Some research revealed that lead is capable of inhibiting the growth of the plant by reducing biomass and debases the quality by changing the quality of its component.

Even at low concentration, lead treatment was found to cause huge instability in ion uptake by plants, which in turn leads to significant metabolic changes in photosynthetic capacity and ultimately in a strong inhibitor of plant growth.

2.3.1. Mechanisms of lead toxicity

Lead metals causes toxicity in living cells by following ionic mechanisms and that of oxidative stress. Many researchers have shown that oxidative stress in living cells is caused by the imbalance between the production of free radicals and the generation of antioxidants to detoxify the reactive intermediate or to replace the resulting damage.

The ionic mechanism of lead toxicity occurs mainly due to the ability of lead metal ions to replace other bivalent cation like Ca^{2+} , Mg^{2+} , Fe^{2+} and monovalent cations like Na^{+} , which ultimately disturbs the biological metabolism of the cell. The ionic mechanism of lead toxicity causes significant changes in various biological processes such as folding, maturation and release of neurotransmitters. Lead can substitute calcium even in picomolar concentration affecting protein kinase C, which regulates natural excitation and memory storage (14,15).

2.4. Mercury

The metallic mercury is a naturally occurring metal which is a shining silver-white odourless liquid and becomes colourless and odourless gas when heated. Mercury is very toxic and exceedingly bio accumulative. Its presence adversely affects the marine environment and hence many studies are directed towards the distribution of mercury in water environment.

Major sources of mercury pollution include anthropogenic activities like agriculture, municipal waste water discharge. Mercury exists mainly in three forms; Metallic elements, Inorganic salts and bioavailability. These forms of mercury are present widely in water resources such as Lakes, rivers and oceans where they are taken up by microorganisms and get transformed into methyl mercury which the microorganism eventually undergoing biomagnification causing significant disturbance to aquatic lives. Consumption of this contaminated aquatic animal is the major route of human exposure to methyl mercury. Mercury is extensively used in thermometers, barometers, pyrometers, hydrometers, mercury arc

lamps, fluorescent lamps and as a catalyst. It is also being used in pulp and paper industries, as a component of batteries and in dental preparations such as amalgams (7,9,16)

2.4.1. Mechanisms of mercury toxicity

Mercury is well known as a hazardous metal and its toxicity is a common cause of acute heavy metal poisoning with cases of 3,596 in 1997 by the American Association of Poison Control Centres. Methyl mercury is a neurotoxic compound which is responsible for microtubule destruction, mitochondrial damage, lipid peroxidation and accumulation of neurotoxic molecules such as serotonin, aspartate and glutamate (17).

The brain remains the target organ for mercury, yet it can impair any organ and lead to malfunctioning of nerves, kidneys and muscles. Mercury plays a key role in damaging the tertiary and quaternary protein structure and alters the cellular functioning attaching to the selenohydryl and sulphhydryl groups which undergo reaction with methyl mercury and hamper the cellular structure. The basis for heavy metal chelation is that even though the mercury sulphhydryl bond is stable and divided to surrounding sulphhydryl consisting ligands, it also contributes free sulphhydryl groups to promote metal mobility within the ligands (17).

2.5. Aluminium

Aluminium is the third most abundant element found in the earth's crust (Gupta et al., 2013). Aluminium occurs naturally in the air, water and soil. Mining and processing of aluminium elevates its level in the environment (ATSDR, 2010). Recent investigations on environmental toxicology revealed that aluminium may present a major threat for humans, animals and plants in causing many diseases. Many factors including pH of water and organic matter content greatly influence the toxicity of aluminium. With decreasing pH its toxicity increases. The mobilization of toxic aluminium ions, resulting from changes in the pH of soil and water caused by acid rains and increasing acidification of the surrounding atmosphere has an adverse effect on the environment. This is manifested by the drying of forests, plant poisoning, crop decline or failure, death of aquatic animals and also animal systems. Due to aluminium toxicity, the crop production was constrained to 67% of the total acid soil area in the world. Aluminium in high concentrations are very toxic for aquatic animals, especially for gill breathing organisms such as Fish, causing osmoregulatory failure by destructing the plasma and hemolymph ions (6).

2.5.1. Mechanisms of aluminium toxicity

Aluminium interferes with most physical and cellular processes. The exact mechanism of absorption of aluminium by the gastro intestinal tract is not understood completely. Based on literature surveys, it is difficult to give a proper time period for aluminium toxicity. Since some symptoms of aluminium toxicity can be detected in seconds and others in minutes after exposure to aluminium (WHO 1997).

Aluminium toxicity probably results from the interaction between aluminium and plasma membrane, apoplasmic and symplasmic targets. In humans Mg^{2+} and Fe^{3+} are replaced by Al^{3+} which causes many disturbances associated with intercellular communication, cellular growth and secretory functions. The changes that are evoked in neurons by aluminium are similar to the degeneration lesions observed in some patients. The greatest complications of aluminium toxicity are neurotoxicity effects such as neuronal atrophy & the locus ceruleus (11).

3. Effects of heavy metals on humans

3.1. Lead

Human activities such as mining, manufacturing and fossil fuel burning has resulted in the accumulation of lead and its compounds in the environment including air, water and soil. The main sources of lead exposure are lead based paints, gasoline, cosmetics, toys, household dust and industrial emissions. Lead poisoning was considered to be a classic disease and the signs that were seen in children and adults were mainly pertaining to the central nervous system and the gastro intestinal tract. Lead poisoning can also occur from drinking water. Toxicity of lead also called lead poisoning can either be acute or chronic. Acute exposure can cause loss of appetite, headache, hypertension, renal dysfunction, fatigue and hallucinations (4).

3.2. Iron

Iron is the most abundant transition in the earth's crust. Biologically, it is the most important nutrient for most living creatures as it is the most important nutrient for most living creatures as it is the cofactor for many vital proteins and enzymes. Iron poisoning has always been a topic of interest mainly to paediatricians. Children are highly susceptible to

iron-toxicity as they are exposed to a maximum of iron-containing products. Iron salts such as iron sulphate, iron sulphate-monohydrate and iron sulphate heptahydrate are of low acute toxicity when exposure is through oral, dermal and inhalation routes and hence they have been placed in toxicity category (7).

3.2.1. Effects on soil

Emissions from activities and sources such as industrial activities, mine tallings, disposal of high metal wastes, leaded gasoline and paints, land application of fertilizers, animal manures, sewage sludge, pesticide, waste water and spillage of petrochemicals lead to soil contamination by heavy metals. There are various ways through which heavy metals present risks to humans, animals, plants and alteration of soil pH, porosity, colour and its natural chemistry which in turn impacts on the soil quality.

3.2.2. Effects on water

Heavy metals are transported by runoff from industries, municipalities and urban areas. Most of these metals end up accumulating in the soil and sediments of water bodies. Heavy metals can be found in traces in water sources and still be very toxic and impose serious health problems and other ecosystems. Therefore, the contamination of water by heavy metals actually affects all organisms.

3.2.3. Effects on air

Industrialization and urbanization, due to rapid world population growth have recently made air pollution a major environmental problem around the world. The air pollution was reported to have been accelerated by dust and particulate matters (PM₃) which are released through natural and anthropogenic processes.

3.2.4. Methods of Heavy metal removal

Physical-chemical treatment is the conventional technology employed to treat heavy metal waste. Therefore, methods for heavy metal removal are continuously being developed and developed and new techniques are being explored by researchers. Some methods used in the removal of heavy metals include;

3.2.5. Chemical precipitation

Unlike organic pollutants, heavy metals are difficult to detoxify and cannot be degraded. The most common method employed to treat heavy metal waste is chemical precipitation. This is done by adding lime or caustic soda to produce metal hydroxide precipitates. Furthermore, chemical precipitation is suitable only for wastewater containing high conc.(parts per thousand or higher) of metal pollutants (18).

3.2.6. Ion-exchange

In this method, the ion exchange resins are used to remove and concentrate the heavy metal. These resins are polymeric beads that contain functional groups that act as binding sites depending on the resin type, the appropriate heavy metal may be removed. The advantage of this method is that the heavy metals are recovered and may be reused but has limited value and is not effective if the waste contains low concentration of metal ions (19).

3.2.7. Reverse osmosis

Heavy metal removal by osmosis can be done by applying a pressure greater than the osmotic pressure of the solution and facing the water to flow through the membrane whilst retaining the metal ions. This technology is usually employed for the recovery of precious metals in the metal finishing industry (19).

4. Conclusion

Heavy metals have been seen as one of the world's problem till date. In this review, the effects of some heavy metals, i.e arsenic, lead, mercury, cadmium, chromium, aluminium and iron, on the environment and living organisms, mainly human beings are brought to light. Effective legislation, guidelines and detection of the areas where there are higher levels are necessary. Failure to control the exposure will result in severe complications in the future because of the adverse effects imposed by heavy metals. Monitoring the exposure and probable intervention for reducing additional exposure to heavy metals in the environment and in humans can become a momentous step towards prevention. National as well as International co-operation is vital for framing appropriate tactics to prevent heavy metal toxicity.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

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