# Heavy Metal Toxicity and Human Health - A Review

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*Abstract:* **Heavy metal poisoning occurs when microscopic molecules of metals accumulate within our body after exposure. Heavy metals attach to our cells and prevent them from performing their functions, which causes symptoms that could be life threatening without treatment.**

**Heavy metals are naturally occurring elements that have a high atomic weight and a density at least five times greater than that of water. Their multiple industrial, domestic, agricultural, medical, and technological applications have led to their wide distribution in the environment, raising concerns over their potential effects on human health and the environment. Their toxicity depends on several factors including the dose, route of exposure, and chemical species, as well as the age, gender, genetics, and nutritional status of exposed individuals. Because of their high degree of toxicity, arsenic, cadmium, chromium, lead, and mercury rank among the priority metals that are of public health significance. These metallic elements are considered systemic toxicants that are known to induce multiple organ damage, even at lower levels of exposure. They are also classified as human carcinogens (known or probable) according to the US Environmental Protection Agency and the International Agency for Research on Cancer.**

*Key words:* **Heavy metal, Sources, Toxic effects, Accumulation, Human health.**

## INTRODUCTION

Heavy metals are naturally occurring elements that have a high atomic weight and a density at least five times greater than that of water. Although some heavy metals are essential trace elements, most of them can be toxic to all forms of life at high concentrations due to formation of complex compounds within the cell. Unlike organic pollutants, heavy metals once introduced into the environment cannot be biodegraded. They persist indefinitely and cause pollution of air, water, and soils. Their multiple industrial, domestic, agricultural, medical, and technological applications have led to their wide distribution in the environment, raising concerns over their potential effects on human health and the environment. Their toxicity depends on several factors including the dose, route of exposure, and chemical species, as well as the age, gender, genetics, and nutritional status of exposed individuals. Because of their high degree of toxicity, arsenic, cadmium, chromium, lead, and mercury rank among the priority metals that are of public health significance. These metallic elements are considered systemic toxicants that are known to induce multiple organ damage, even at lower levels of exposure. They are also classified as human carcinogens (known or probable) according to the US Environmental Protection Agency and the International Agency for Research on Cancer.

Water may become contaminated by the accumulation of heavy metals and metalloids through emissions from the rapidly expanding industrial areas, mine tailings, disposal of high metal wastes, leaded gasoline and paints, land application of fertilizers, animal manures, sewage sludge, pesticides, wastewater irrigation, coal, electronic waste. Heavy metal toxicity has proven to be a major threat and there are several health risks associated with it. The toxic effects of these metals, even though they do not have any biological role, remain present in some or the other form harmful for the human body.

Heavy metals have damaged soil and water eco-systems worldwide. Heavy metal have been discharging into the environment through a variety of practices, including irrigation with polluted water , the use of chemical based fertilizers, the dumping of industrial effluents into the bodies of water , volcanic eruption, forest fire and so on. Metal toxicity causes the formation of free radicals which causes DNA damage. Free radical formation has mostly been investigated for iron, copper, nickel, chromium and cadmium. The last three metals are recognised for the carcinogenic properties[1].

Sources of heavy metal pollution: Heavy metals are inorganic pollutant that can enter the environment through two main routes.

1. Natural processes. Heavy metals are found naturally on the Earth's crust since the Earth's formation. Due to the astounding increase of the use of heavy metals, it has resulted in an imminent surge of metallic substances in both the terrestrial environment and the aquatic environment[2]. Natural causes can also increase heavy metal pollution such as volcanic activity, metal corrosion, metal evaporation from soil and water and sediment re-suspension, soil erosion, geological weathering [3,4,5,6]. Metals have been present on the planet since the origin through regular biogeochemical cycles [7]

2. Human activities. Heavy metal pollution has emerged due to anthropogenic activity which is the prime cause of pollution, primarily due to mining the metal, smelting, foundries, and other industries that are metal-based, leaching of metals from different sources such as landfills, waste dumps, excretion, livestock and chicken manure, runoffs, automobiles and road works. Heavy metal use in the agricultural field has been the secondary source of heavy metal pollution, such as the use of pesticides, insecticides, fertilisers, and more. HMs trace levels in fertilizers are important sources of heavy metal contaminants in our food. Inappropriate industrial waste management, traffic pollution, use of lead (Pb) as fuel antiknock, aerosol cans, metallurgy and smelting, discharge of sewage and construction materials are the anthropogenic practices responsible for HMs contamination (Srivastava et al., 2016, , Srivastava et al., 2017) Furthermore, metallurgical, refractory, and chemical industries release a large amount of Cr into soil, ground water, and air which causes health issues in humans, animals, and marine life [8] .

## ACCUMULATION

HMs accumulate in the soil, human and animal tissues as a result of absorption and, in certain cases, inhalation, and as well as accidents or mishandling. . Human exposure to heavy metals comes mostly through edible vegetables, which account for around 90% of the overall intake, while the remaining 10% comes from skin contact and breathing of pollutant.[9,10]. Using sewage and wastewater that are not treated have caused a lot of heavy metals in our agricultural lands and thus have been absorbed by the crops that tend to be eaten by humans themselves. Non-deliberate pollution may be brought about through flooding of seas and rivers which brings sewage and contaminated water to the land and accidents involving vehicles transporting toxic chemicals. Since heavy metals are nondegradable, since they cannot undergo microbial or chemical degradation, they stay in the soil for a very long time. The ecosystem is being ruined to the fact that the heavy metals are entering the food chain. Heavy metals also affect the biodegradability of organic pollutants, making them less degradable and thus causing double the effect of polluting the environment. These metals present in the soil cause risks to all the biosphere and are taken up through direct ingestion, absorbed by plants which can be hazardous both to the plant and also to the food chain that eats the plant, altering the properties of the soil such as the pH, colour, porosity and natural chemistry thus impacting the quality of the soil, and also contaminating the water [11, 12, 13, 14] . Heavy metals present in soils and sediments remain present for an extended period until they are eluted to other compartments. They can also react with other elements in the soil or sediment and form or degrade to become more toxic. An example of this is the formation of poisonous methyl mercury from the inorganic mercury and activity of bacteria found in water, sediment and soil [15]. Mercury (Hg) is found in air, water, and soil and exists in three forms: elemental or metallic mercury ($Hg^0$), inorganic mercury ($Hg^+$, $Hg^{2+}$), and organic mercury (commonly methyl or ethyl mercury)[16]. $Hg^0$ (vapor) is readily absorbed from lungs (80%) and distributed throughout the body. $Hg^0$ can pass the blood brain barrier (BBB) and placenta; thus, its neurotoxicity is higher than inorganic Hg which passes through membranes at a slower rate. Microorganisms in marine environments perform natural biomethylation reactions to produce Me-Hg. Me-Hg enters the food chain of aquatic animals and eventually enters the human body through the consumption of fish[17] Elements, such as arsenic, cadmium, lead, and mercury, are non-essential and play no useful role in plants, animals, or people. They also serve no nutritional purpose since they are exceedingly poisonous [18]. When the heavy metals are inhaled into our bodies, they bioaccumulate in our system. Thus they are classified as dangerous. This bioaccumulation causes biological and physiological complications.

## SERIOUS PROBLEMS THROUGH HEAVY METAL ABSORPTION IN HUMAN HEALTH-

Arsenic has a long history of use, either as a metalloid substance or as a medicinal product. It is notoriously known as the king of poisons and poison of kings [19] . Arsenic is present as a contaminant in food, water, and environment. Arsenic exists in the forms of metalloid ($As^0$), inorganic ($As^{3+}$ and $As^{5+}$), organic, and arsine ($AsH_3$). The order of increasing toxicity of As compounds is defined as organic arsenicals < $As^0$ < inorganic species ($As^{5+}$ < $As^{3+}$) < arsine [20,21,22] .,It has been documented that in 1955 Arsenic was accidentally mixed into the Morinag's Powdered Milk "MF" (Japan) due to which 600 new born babies died and 624 were afflicted by severe mental retardation, developmental difficulties, and brain damage-related paralysis [23] . In humans arsenic toxicity occurs due to ingestion of As containing powders or solutions accidentally, suicide, homicide, or consumption of contaminated food or drinking water. Arsenic has been reported to be associated with hypertension and serious impacts on the cardiovascular system, and even hepatic damage at high doses [24, 25]. It has a suppressive effect on spermatogenesis and gonadotrophin and testosterone release in rats [26] . Besides, inorganic arsenic ingestion arsenic leads to various dermal effects like: hyperkeratosis, hyperpigmentation and hypopigmentation; periorbital swelling; the occurrence of spontaneous abortion and damage of the nervous system (if high doses are taken in). Arsenic causes epigenetic alterations, damage to DNA, changes in the p53 protein's expression, histone modifications, DNA methylation, and reduced p21 expression [27,28]. Arsenic poisoning raises the risk of cancer by attaching to DNA-binding proteins and slowing down the DNA-repair process [29] .

Cd is classified by the International Agency for Research on Cancer (IARC) as carcinogenic to humans [30] . Due to the importance of the subject, Cd level in the air is routinely monitored in some countries [31] . Tragically, the outbreak of Itai-itai disease in Japan was due to the mass Cd contamination of food and water supplies. The patients suffered from painful degenerative bone disease, kidney failure, and the GI and lungs diseases [32]. . Unlike low GI absorption, Cd is more efficiently taken from the lungs via industrial dust. Acute or chronic inhalation of Cd in industrial areas might lead to renal tubular dysfunction and lung injuries. Cd blood concentration in smokers is almost twice higher than that of nonsmokers. Batáriová et al. (2006) found Cd blood levels of 0.4 against 1.3 μg/L for nonsmokers vs. smokers in adult population [33] . This seems to be related to the nature of tobacco plants to accumulate relatively high Cd concentrations in tissues especially in the leaves [34] . Neurodegenerative defects, including amyotrophic lateral sclerosis, Parkinson's disease, Alzheimer's disease, and multiple sclerosis, result from neurotoxicity induced by cadmium [35] . The neurotoxicity of cadmium arise from neural cell death via apoptosis; providing plenty of apoptosis-induction factors, including impairment of neurogenesis, inhibition of neuron gene expression, offering epigenetic effect, endocrine disruption, etc. [36] Hepatotoxicity induced by cadmium, both acute and chronic, causes liver failure and therefore can increase the risk of cancer[37] . Nephrotoxicity induced by cadmium leads to intense clinical symptoms such as glucosuria, Fanconi-like syndrome, phosphaturia, and aminoaciduria [38,39] .

Chromium (Cr) is found in the earth's crust and seawater and is a naturally occurring heavy metal in industrial processes [40] . Cr has multiple oxidation states ranging from −2 to + 6, in which the trivalent and hexavalent forms are the most common stable forms [41] . Cr (VI) is related to a series of diseases and pathologies while Cr (III) is required in trace amounts for natural lipid and protein metabolism and also as a cofactor for insulin action [42,43,44,45] . Based on the International Agency for Research on Cancer (IARC) report (2018), hexavalent chromium has been classified as a group I occupational carcinogen [46] . The primary route of exposure for non occupational human populations occurs via ingestion of chromium containing food and water or dermal contact with products containing chromium [47] . Cr can cause a variety of diseases through bioaccumulation in human body. This ranges from dermal, renal, neurological, and GI diseases to thedevelopment of several cancers including lungs, larynx, bladder, kidneys, testicles, bone, and thyroid [8] .The results of a recent meta-analysis showed exposure to Cr (VI) may cause increased mortality and incidence of some cancers including lung, larynx, bladder, kidney, testicular, bone, and thyroid cancer in humans [48] . Another study in 2012 in India showed increased incidence of GI and dermatological complications among population exposed to Cr (VI) contaminated ground water [49] .

Lead has deleterious effects in all organs, but it has the greatest influence on the kidneys. Acute lead nephropathy causes proximal tubular dysfunction, resulting in Fanconi-like syndrome. Chronic lead nephropathy can be characterized by hyperplasia, interstitial fibrosis, atrophy of the tubules, renal failure, and glomerulonephritis . Lead is a carcinogenic substance that causes damage to the DNA repair mechanism, cellular tumor regulating genes, and chromosomal structure and sequence by releasing ROS . It disrupts transcription by shifting zinc from certain regulatory proteins. [50] . The toxicity of lead on liver cells is well established. Exposure to it increases oxidative stress resulting in liver damage. Organic solvents, combined with lead, also cause injury to the liver because of having the same characteristics as lead [51,52] . Exposure to Pb can produce alteration in physiological functions of the body and is associated with many diseases[53,54,55] . Pb is highly toxic which has adverse effects on the neurological, biological, and cognitive functions in the bodies. Adulteration of opium with Pb has been considered as a threat to human health in recent years [56].

Mercury can cause a variety of health issues, such as damage to the developing brain, depression and suicidal tendencies, paralysis, kidney failure, Alzheimer's disease, speech and vision impairment, allergies, hypospermia and impotence. Mercury converts to the highly toxic methylmercury when in contact with aquatic sediments [57] . Many skin infections are caused by mercury and mercury-containing compounds, including such acrodynia (pink disease), a common dermatological ailment in which the skin becomes pink when exposed to heavy metals, particularly mercury [58] . People tattooed with the red pigments cadmium sulfide and mercury sulfide may have inflammation restricted to specific areas typically within six months after getting tattooed. Moderate swelling, scaling, vesiculation, and irritation are symptoms of acute contact dermatitis caused by mercury-containing substances. According to several studies, mercury poisoning is the most prevalent cause of dermatological problems [59] . Mercury (Hg) is found in air, water, and soil and exists in three forms: elemental or metallic mercury ($Hg^0$), inorganic mercury ($Hg^+$, $Hg^{2+}$), and organic mercury (commonly methyl or ethyl mercury) [60] . The order of increasing toxicity related to different forms of mercury is defined as $Hg^0 < Hg^{2+}, Hg^+ < CH_3\text{-}Hg$ [61] . An incident of exposure to organic Hg via the consumption of contaminated fish occurred in Minamata Bay, Japan, in the middle of 1950's. Soon afterward, the illness came to be known as Minamata disease. Chronic Hg toxicity caused neurological damage including ataxia, muscle weakness, numb limbs, disturbance in speech, chewing, and swallowing, and brisk and increased tendon reflex among the patients exposed to massive amounts of Me-Hg. Infants with severe developmental disabilities were born from the poisoned pregnant women [62] .

In addition to arsenic,lead,chromium and cadmium, a lot of heavy metals have been established for their neurotoxic consequences. As well, copper and zinc, like iron, act as impediments to neurodevelopment when an excessive amount enters the brain [63] . Excess copper retention causes Wilson's disease, a hereditary condition which causes neurobehavioral abnormalities similar to schizophrenia. Zinc deficiency has an adverse influence on neurodevelopment, but the consequence of vast quantities is not clear [64] . As an essential element, manganese is involved in several physiological functions of the body. Its acute exposure exerts potential neuroprotective action by reducing apoptotic cellular death but exposure to a large quantity may induce harmful conditions alike neurological complications, such as alzheimer and parkinson disease which leads to apoptotic cell death and alteration of homeostasis [65] .

## FUTURE PROSPECTS AND CONCLUSION

Heavy metal toxicity is a serious problem on human health and environment. Therefore, effective removal and remediation of heavy metal pollution are crucial to protect human and ecological health. There are so many methods to remove heavy metal from air, water and soil such as ulrafiltration, chemical precipitation, reverse osmosis, ion-exchange, electro deposition and adsorption. Todays bioremediation/ phytoremediation procedure is used as a simple and appealing alternative technology due to its low energy, low cost and high efficiency. Existing control methods focus on decreasing heavy metal concentrations in soil and the food chain to decrease health hazards. To minimize the passage of metallic pollutants into the food chain and to develop appropriate remediation technique, soil and water pollution must be mapped quickly and precisely.

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