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Review Article

Environmental Heavy Metals: Adverse Effects on the Human Skeletal System

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Abstract

Heavy metals (HM) are naturally occurring elements throughout the Earth's crust, spreading through natural/geogenic/lithogenic and anthropogenic sources. These metals can enter the human body through various means, including food and water consumption, inhalation of polluted air, skin contact, and, most significantly, occupational exposure in the workplace. Some HM, such as copper (Cu), colbalt (Co), iron (Fe), nickel (Ni), molybdenum (Mo), chromium (Cr), selenium (Se), manganese (Mn), and zinc (Zn), play essential functional roles in diverse physiological and biochemical activities in the body. However, when present in high doses, particular HM can be harmful, while others, like cadmium (Cd), mercury (Hg), lead (Pb), silver (Ag), and arsenic (As), even in minute quantities, can have harmful effects, causing acute and chronic toxicities. Cancer, neurodegeneration, cardiovascular disorders, and kidney damage in humans can occur. The industrial activities of the last century have significantly increased human exposure to HM. The toxicity of these elements depends on several factors, including their chemical forms, concentrations, interactions, and bioavailability. Therefore, monitoring and controlling the levels of HM in the environment and human health is crucial. Various methods and techniques have been developed to detect, measure, and remove HM from different environmental matrices and biological samples.

Moreover, several strategies have been proposed to prevent or treat HM-induced diseases, including remediation techniques, chelation therapy, activated sludge processes, antioxidant supplementation, and detoxification. This review aims to provide a brief overview of HM sources, pathways, effects, and environmental and human health management. It also highlights the current challenges and future perspectives in this field of research.

Keywords: *Cardiovascular Disorders; Kidney Damage; Neurodegeneration; Oxidative Stress and Damage to DNA*

Introduction

Heavy metals (HM), including semimetals and metalloids, are naturally occurring substances that can accumulate in the environment, causing harm to living beings, including humans [1]. These elements are believed to have originated from asteroid impacts and are found in the Earth's crust in concentrations ranging from low parts per billion (noble metals) to as high as 5% (Fe). They exist in various chemical forms, bound in rocks like carbonate, sulfate, oxide, and silicate or as metallic elements. Over billions of years, weathering and erosion processes have leached this HM into soil, rivers, and groundwater. Earth's core predominantly consists of Fe and nickel (Ni), which sank to the center during the planet's early liquid mantle phase [2].

Throughout history, ancient civilizations knew and used certain HMs like Fe, Cu, Tin (Tn), Ag, Au, and Platinum (Pt) for metallurgy, art, medicine, agriculture, and warfare. As societies evolved and industrialization progressed, the extraction, production, and utilization of HM increased, leading to the discovery of other HM over time. Table 1 lists the timelines of various HM [3].

Heavy Metal	***First recorded use (approximate)***
Gold (Au)	6000 BCE
Copper (Cu)	4200 BCEE
Silver (Ag)	4000 BCE
Lead (Pb)	3500 BCE
Tin (Sn)	1750 BCE
Iron (Fe)	1500 BCE
Arsenic (As)	1250 BCE
Mercury (Hg)	750 BCE
HM identified in the 18th and early 19th centuries	
Platinum (Pt)	1735
Cobalt (Co)	1737
Antimony (Sb)	1750
Nickel (Ni)	1751
Bismuth (Bi)	1753
Barium (Ba)	1772
Manganese (Mn)	1774
Molybdenum (Mo)	1781
Uranium (Ur)	1789
Chromium (Ch)	1797
Cadmium (Cd)	1817
Selenium (Se)	1817

Table 1: *Origin years of various HM.*

The effects of HM on health have been observed since ancient times by different civilizations. The Greek philosopher Hippocrates (400 BCE) noted that environmental factors influenced disease distribution and that water contaminated with metals such as Fe, Cu, Ag, gold (Au), alum, bitumen, or nitrite was harmful to health. A Roman architect (c.100 BCE) warned that mining could cause health problems because of the water and air pollution near mines. The Greek doctor Galen (c. 150 CE) confirmed that mining could produce acid mists that could harm the lungs. Chinese medical texts dating back to the third century BCE also linked HM with health issues. Lung problems and symptoms of Pb poisoning from occupational exposure were recognized during the Song Dynasty (1000 BCE) and the Ming Dynasty

(fourteenth–seventeenth centuries). The Thang Dynasty alchemist Chen Shao-Wei identified several toxic metals, including Pb, Ag, Cu, Fe antimony (Sb), and Au) [4].

Pb poisoning was also documented in clay tablets from Assyria (1550 to 600 BCE), Egyptian papyri, and Sanskrit texts (over 3000 years ago), reflecting the widespread use of lead for over six millennia in various products and industries [4-6]. During Roman times, Pb (550 grams per person per year) was extensively used for plumbing, construction, and shipbuilding. Additionally, Pb was added to food and wine for preservation and flavor enhancement. However, this augmentation led to widespread health issues, including gout, infertility, stillbirths, and mental disorders. Even several Roman emperors suffered from Pb poisoning. Furthermore, Hg was used for teething babies and syphilis, copper for military and civilian purposes, and arsenic for cosmetic or poisonous applications [4,7-9].

The Greeks, Arabs, and Peruvians used arsenic for skin care or medicine, but it killed them. Arsenic can cause skin lesions, lung cancer, or heart disease [10]. Se is a mineral that, depending on its concentration, can be beneficial or harmful to health. In China, some places have too much or too little Se. During his travels to China in 1275, Marco Polo observed a mysterious and debilitating disease afflicting horses in certain regions. This disease pattern is now understood to be linked to the high Se content in those specific areas [4]. Box 1 shows some famous people who studied HM and its effects.

Box 1: Notable Researchers in the Field of HM

- Paracelsus (1493–1541): A Swiss physician and alchemist who studied Hg and other metals' toxicity, coining the term "poison" to describe their harmful effects [11].
- Bernardino Ramazzini (1633–1714) was an Italian doctor who started occupational medicine. He described how Pb poisoning affected workers in different jobs, such as painting, pottery, mining, and smelting [12,13].
- Mathieu Orfila (1787-1853), a Spanish-born French toxicologist, conducted studies on poisoning and is considered one of the founders of modern toxicology. He studied the effects of HM like Pb and Hg on the human body [14].
- Alfred Stock (1876–1946), a German chemist who suffered from Hg poisoning and campaigned for the elimination of Hg from scientific and medical instruments [15].
- Rachel Carson (1907–1964), an American biologist and writer who exposed the environmental damage caused by pesticides and other chemicals in her influential book Silent Spring. She also warned about the accumulation of HM in the food chain and their effects on wildlife and human health [16].
- Clair Cameron Patterson (1922–1995), an American geochemist who determined the age of the Earth using Pb isotopes and discovered the widespread contamination of Pb in the environment due to human activities. He also advocated for the removal of Pb from gasoline, paints, and other products [17].

Since the nineteenth century, environmental HM like Pb, Hg, As, and Cd have been recognized as significant health risks due to reported poisoning and mortality among exposed workers. However, scientists, regulators, and the public only realized this issue's full extent and severity in the second half of the twentieth century. Some of the events that raised awareness about this issue were:

- Minamata Disease in Japan was a significant incident related to Hg poisoning. It was caused by industrial wastewater containing methylHg (MeHg) being discharged into Minamata Bay, leading to severe health effects on the local population [18].

- The Itai-itai disease outbreak in Japan in the 1950s and 1960s was caused by Cd poisoning from mining activities that contaminated rice fields and irrigation water. The disease mainly affected older women suffering from severe bone pain, fractures, kidney damage, and death [19].
- The lead poisoning epidemic in Nigeria in 2010–2012 was caused by artisanal gold mining that released large amounts of Pb dust into the environment. The epidemic affected over 400 children who died from acute Pb encephalopathy and thousands more who suffered from neurological impairment, anemia, and liver damage [20].

Discussion

Essential and nonessential HM

Living organisms have varying requirements for HM. Some HM is essential for living organisms, while others are nonessential. Essential HM are needed for growth, stress resistance, biosynthesis, and function of different biomolecules, such as carbohydrates, chlorophyll, nucleic acids, growth chemicals, and secondary metabolites. Examples of essential HM are Co, Cu, Cr, Fe, Mg, Mo, Ni, Se, and Zn (Figure 1) [21-30]. Both deficiency and excess essential HM can lead to diseases or abnormal conditions in living organisms [26,30].

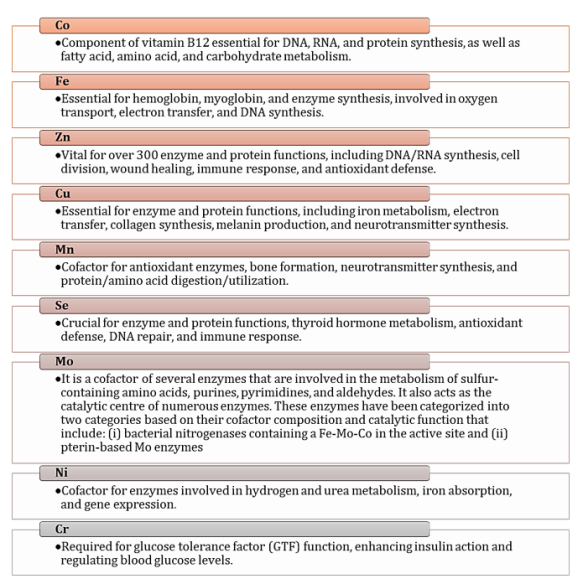

Figure 1: *Importance of essential HM [21-30]*

Nonessential HM (e.g., As, Cd, Pb, Ag, and Hg) have no biological role in living organisms [26]. They enter the human body through the environment and various ways. They can cause toxicity, affecting metabolism in vital organs and glands like the liver, kidney, bone marrow, brain, heart, and spleen. They also replace essential minerals, blocking their function. [31,32]. Table 2 shows the types of HM, their effects on human health, and their significant sources [32-37].

HM chemical structure, physicochemical properties, and characterization

HM are generally called metals with relatively high atomic weights of 63.5-200.6 g mol^{-1} and densities of more than 5 gr cm^{-3} [38]. They have such characteristics as luster, ductility, malleability, and high electric and thermal conductivity. Table 3 shows different HM and their physicochemical properties and characterization [39-52].

HM	Effect on human health	Major sources
Cd	Renal dysfunction, lung disease, lung cancer, bone defects, increased blood pressure, kidney damage, bronchitis, gastrointestinal disorder, bone marrow and cancer.	Welding, electroplating, pesticide, fertilizer, Cd and Ni batteries, nuclear fission plant
Se	Selenosis, nausea, vomiting, diarrhea, hair loss, nail brittleness, gastrointestinal disorders, skin lesions, and neurological disorders. High-level exposure in air can cause respiratory tract irritation, bronchitis, difficulty breathing, and stomach pains.	Mining , smelting , coal combustion, fertilizers , shampoos , electronics
As	Bronchitis, dermatitis, poisoning. Lower-level exposure can cause nausea, vomiting, decreased production of blood cells, abnormal heart rhythm, damage to blood vessels, and tingling sensation in hands and feet. Very high-level ingestion can possibly lead to death. Long-term low-level exposure can cause skin darkening and small "corns" or "warts" on palms or torso.	Pesticides, fungicides, metal smelters
Ag	Argyria (skin discoloration), breathing problems, eye lung and throat irritation, stomach pains, and mild allergic reactions.	Mining, smelting, photography, jewellery, silverware, electronics, disinfectants
Mg	Deficiency can cause impaired growth, bone loss, skin rash, and impaired glucose tolerance. Toxicity can cause manganism, a neurological disorder characterized by tremors, rigidity, and dystonia.	Natural weathering of rocks and soils, mining, smelting, steel production, battery manufacturing, fertilizers, pesticides, and industrial effluents
Pb	Anemia, mental retardation in children, developmental delay, fatal infant encephalopathy, congenital paralysis, sensorineural deafness, acute or chronic damage to the nervous system, epilepticus, liver, kidney, and gastrointestinal damage.	Paint, pesticide, smoking, automobile emission, mining, burning of coal
Zn	Zinc fumes have a corrosive effect on the skin and can damage nervous membranes.	Refineries, brass manufacture, plumbing
Ba	Hypertension, muscle weakness, cardiac arrhythmia. Short-term exposure can cause vomiting, abdominal cramps, diarrhea, breathing difficulties, numbness around the face, and muscle weakness. Large intake can cause high blood pressure, changes in heart rhythm, paralysis, and possibly death.	Drilling waste, ceramics, paints, fireworks
Hg	Tremors, gingivitis, minor psychological changes, acrodynia (pink hands and feet), spontaneous abortion, damage to the nervous system, protoplasm poisoning, brain, kidney, and fetal damage, increased blood pressure or heart rate, skin rashes, and eye irritation.	Pesticides, batteries, paper industry
Cu	Anemia, liver and kidney damage, stomach and intestinal irritation.	Mining, pesticide production, chemical industry, metal piping
Cr	Damage to the nervous system, fatigue. Breathing high levels can cause irritation to the nose lining, nose ulcers, runny nose, and breathing problems like asthma, cough, shortness of breath, or wheezing. Skin contact can cause skin ulcers and severe redness.	Mines, mineral sources
Co	Cobalt deficiency can cause pernicious anemia, neurological disorders, and elevated homocysteine levels. Cobalt toxicity can cause goitre, polycythaemia, cardiomyopathy, and allergic reactions.	Mining, smelting, electroplating, fertilizers, sewage sludge, and industrial effluents.
Mo	Molybdenum deficiency can cause tachycardia, headache, nausea, vomiting, and coma. Molybdenum toxicity can cause gout-like symptoms such as joint pain, inflammation, and uric acid accumulation.	Natural weathering of rocks and soils, mining, smelting, metal processing, fertilizers, animal feed supplements, and industrial effluents.
Fe	Iron deficiency can cause anemia, weakness, fatigue, pale skin, and increased susceptibility to infections. Iron overload can cause hemochromatosis, liver damage, diabetes, heart failure, and arthritis.	Natural weathering of rocks and soils, corrosion of pipes and fittings, mining, smelting, steel production, fertilizers, and industrial effluent
Ni	Lung cancer, chronic bronchitis, and reduced lung function.	Electroplating, porcelain enamelling, paint formulation, and nonferrous metal

Table 2: *Types of HM, their effects on human health, and significant sources [32-37]*

Reservoirs of HM environmental exposure

HM are found throughout the earth's crust, but their accumulation in the food chain has become a global concern (raised ecological and public health alarms) in recent years [25,53]. The rapid industrialization, urbanization, agricultural runoff, and transportation, primarily since the 1940s, are attributed to HM accelerated mobilization and transport in the environment [26]. Sources of HM contamination in the environment include natural/geogenic/lithogenic and anthropogenic factors (Figure 2) [25,26,54].

HM	Physicochemical Properties and Characterization
Cd	• Soft, bluish-white metal with atomic number 48 and atomic mass 112.41. It has a hexagonal close-packed crystal structure and a density of 8.65 g/cm³. It has a relatively low melting point of 321.07°C and a boiling point of 767°C. • Detected by atomic absorption spectroscopy (AAS) or Inductively Coupled Plasma Mass Spectrometry (ICP-MS) [39].
Se	• Nonmetal with atomic number 34 and atomic mass 78.96. It has several allotropes, including gray, red, and black forms, with different crystal structures and physical properties. Gray selenium has a hexagonal crystal structure and a density of 4.81 g/cm³. It has a melting point of 220°C and a boiling point of 685°C [40]. • Detected by atomic fluorescence spectroscopy, hydride generation AAS, or gas chromatography-mass spectrometry.
As	• Metalloid with atomic number 33 and atomic mass 74.92. It has several allotropes, including yellow, black, and gray forms, with different crystal structures and physical properties. Gray arsenic has a rhombohedral crystal structure and a density of 5.73 g/cm³. Its melting and boiling point is 1135°F (616°C). • Detected by AAS, ICP-MS, or X-ray Diffraction (XRD) [41].
Ag	• Shiny, white metal with atomic number 47 and atomic mass 107.87. It has a face-centered cubic crystal structure and a density of 10.49 g/cm³. It melting point is 961.78°C and boiling point is 961.78°C. • Detected by flame AAS, Inductively ICP-MS, or voltammetry [42].
MG	• Hard, gray-white metal with atomic number 25 and atomic mass 54.94. It has a body-centered cubic crystal structure and a density of 7.3 g/cm³. Its melting point is 1246°C and boiling point is 2061°C. • Detected by flame AAS or ICP-MS [43].
Pb	• Soft, bluish-gray metal with atomic number 82 and atomic mass 207.2. It has a face-centered cubic crystal structure and a density of 11.34 g/cm³. It has a relatively low melting point of 327.5°C and a boiling point of 1749°C • Detected by flame AAS or ICP-MS [44].
Zn	• Lustrous, blue-white metal with atomic number 30 and atomic mass 65.39. It has a hexagonal close-packed crystal structure and a density of 7.13 g/cm³. It has a relatively low melting point of 419.53°C and a boiling point of 907°C. • Detected by flame AAS or Inductively Coupled Plasma-Optical Emission Spectroscopy (ICP-OES) [45].
Hg	• Shiny, silver-white liquid metal with atomic number 80 and atomic mass 200.59. It has a rhombohedral crystal structure and a density of 13.53 g/cm³. Its melting point is -39 °C and boiling point is 357 °C. • Detected by cold vapor AAS, or ICP-MS, or atomic fluorescence spectroscopy [46].
Cu	• Reddish-brown metal with atomic number 29 and atomic mass 63.55. It has a face-centered cubic crystal structure and a density of 8.96 g/cm³. Its melting point is 1083 °C and boiling point is 2595 °C. • Detected by flame AAS, ICP-OES, or anodic stripping voltammetry [47].
Cr	• Hard, gray-white metal with atomic number 24 and atomic mass 51.996. It has a body-centered cubic crystal structure and a density of 7.19 g/cm³. Its melting point is 1907 °C and boiling point is 2642 °C. • Detected by flame AAS, ICP-MS, or XRD [48].
Co	• Hard, lustrous, silver-gray metal with atomic number 27 and atomic mass 58.933. It has a hexagonal close-packed crystal structure and a density of 8.9 g/cm³. It has a relatively low melting point of 1,495 °C and a boiling point of 1,495 °C. • It can be detected by flame AAS, ICP-OES, or nitroso-R salt spectrophotometry [49].
Mo	• Hard, silvery-white metal with atomic number 42 and atomic mass 95.96. It has a body-centered cubic crystal structure and a density of 10.28 g/cm³. It has a melting point of 2622 °C and a boiling point of 4612 °C. • Detected by flame AAS, ICP-OES, or thiocyanate spectrophotometry [50].
Fe	• Strong, magnetic, gray-white metal with atomic number 26 and atomic mass 55.845. It has a body-centered cubic crystal structure and a density of 7.874 g/cm³. It has a melting point of 1,538 °C and a boiling point of 2,861 °C. • Detected by flame AAS, ICP-MS, or ferrozine colorimetry [51].
Ni	• Hard, ductile, silvery-white metal with atomic number 28 and atomic mass 58.693. It has a face-centered cubic crystal structure and a density of 8.908 g/cm³. It has a melting point of 1455 °C and a boiling point of 2730 °C. • Detected by flame AAS or ICP-OES [52].

Table 3: *HM and their physicochemical properties and characterization [39-52]*

HM spread through land, air, and water due to industrial activities, agriculture, waste disposal, and natural events like volcanic eruptions. They enter soil through industrial and agricultural processes, persisting and being taken up by plants, leading to bioaccumulation

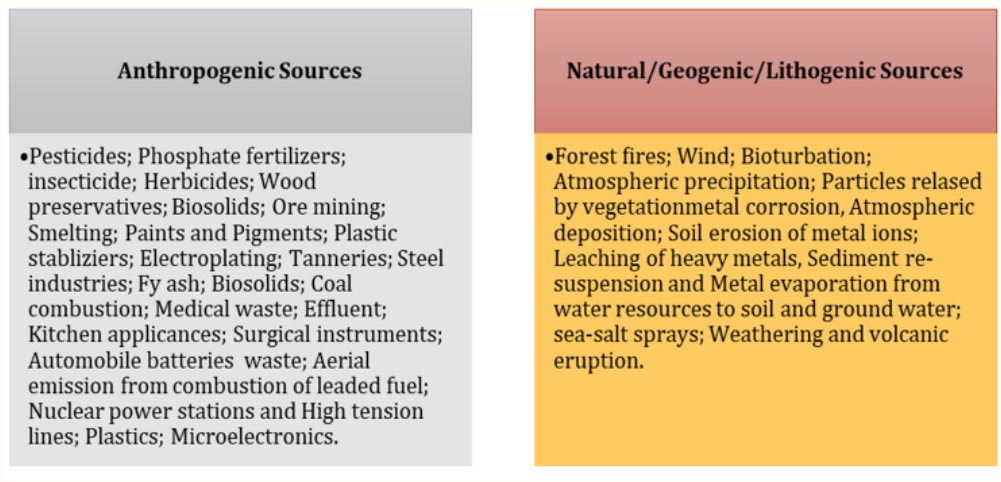

Figure 2: *Sources of HM in the environment [25,26,54]*

in the food chain. In the air, they are released by industrial emissions and vehicle exhaust, settling on land and water. In water bodies, they enter through industrial discharges and runoff. Fish absorb waterborne HM and subsequently enter the human body through the food chain, affecting human health [54,55]. HM toxicity can cause damage to the brain, lungs, kidneys, liver, blood composition, and other vital organs, leading to various degenerative processes resembling diseases like multiple sclerosis, Parkinson's disease, Alzheimer's disease, and muscular dystrophy. Prolonged exposure to certain metals and compounds may even result in cancer [56-60].

Vulnerable populations to the harmful effects of HM include infants, children, older adults, and individuals with chronic health conditions [57,61–68]. Pregnant women and their unborn babies are particularly susceptible to HMs, as these metals can cross the placental barrier and affect fetal development [58,69–74]. Certain occupational groups, such as industrial workers, miners, and agricultural workers, may face higher HM exposure due to their work environments [59,75–78]. Environmental disparities can disproportionately expose minority and low-income communities to elevated levels of HM due to proximity to industrial sites and limited access to clean resources [60,79,80]. Box 2 outlines some latent effects of HM exposure.

HM absorption pathways in the human body

The absorption pathway of HM in the human body depends on the route of exposure: ingestion, inhalation, and dermal contact. Once ingested, HM can be absorbed in the gastrointestinal tract. Some HM is more readily absorbed than others, depending on their chemical form and other substances that may enhance or inhibit absorption. After absorption, HM can enter the bloodstream and tissues of the body. The distribution depends on the affinity of the metal for specific proteins or receptors, as well as the target organ's blood flow and metabolic rate. The organs that tend to accumulate high levels of HM are the liver, kidney, bone marrow, brain, heart, and spleen. The body has mechanisms to detoxify and eliminate HM. The liver and kidneys play crucial roles in detoxification, as they help metabolize and excrete HM from the body. HM can be passed through various pathways, such as urine, feces, sweat, saliva, breast milk, hair, and nails. The

Box 2: Latent Effects of HM Exposure [81-87].

- Cognitive impairment, behavioral problems, ADHD, ASD, and learning disabilities in children.
- Reduced fertility, genital malformations, and reproductive disorders in offspring.
- Prenatal HM exposure may affect transgenerational inheritance through epigenetic changes in germ cells, impacting subsequent generations.
- HM during pregnancy can affect fetal immune development, leading to altered immune function or increased susceptibility to infections, allergies, asthma, or autoimmune diseases in offspring.
- Increased BP, endothelial dysfunction, inflammation, oxidative stress, and atherosclerosis in children and adults.
- Delayed mammary gland development can affect breastfeeding abilities, milk production, and breast health in adulthood, influencing susceptibility to breast-related conditions and diseases later in life.
- Increased cancer risk in children and adults due to genomic instability, DNA damage, epigenetic alterations, and immune suppression.

excretion rate depends on the metal's chemical form, solubility, and biotransformation. Some HM can accumulate in the body for a long time due to their low excretion or high reabsorption rate [30,33,61,62].

Adverse effects associated with HM

The adverse effects of HM depend on the type, concentration, duration, and route of exposure. HM can interfere with the normal functioning of enzymes, hormones, proteins, and cellular structures. They can also generate reactive oxygen species (ROS) that cause oxidative stress and damage to DNA, lipids, and proteins (Figure 3) [63].

HM effects on the skeletal system

HM significantly impacts the skeletal system, leading to bone loss, osteoporosis, and increased fracture risk. Clinical studies have shown that accumulated Pb in the body reduces bone density and cortical width and increases fracture risk. Additionally, Pb poisoning delays fracture healing by affecting cartilage formation and skeletal growth, reducing stature, axial skeleton growth, and chest circumference in childhood [64]. *In-vitro* research has shown that Cr (VI) reduces osteoblast survival and the number of osteoclasts, affecting bone resorption. Cd exposure increased calcium excretion, resulting in skeletal demineralization, bone fragility, and fracture risk [65].

Cd and Pb exposure has been found to interactively affect bone mineral density in specific populations [66]. Additionally, titanium has been shown to stimulate osteoclastogenesis and osteoclast activity when in the presence of BMP-2 and RANKL [67,68]. These findings highlight the importance of understanding the effects of HM on the skeletal system for potential health implications.

Diagnostic tests for HM toxicity

Diagnosing HM toxicity involves several steps, including an HM panel or toxicity test, a simple blood test. Additional testing may be done if symptoms persist, including kidney and liver function tests, urine analysis, hair and fingernail analysis, electrocardiograms, and x-rays [31,69]. HM concentrations are evaluated using inductively coupled plasma with mass spectrometry (ICP/MS) or atomic absorption spectroscopy (AAS). ICP/MS is commonly used due to its low detection limit and ability to detect multiple elements simultaneously.

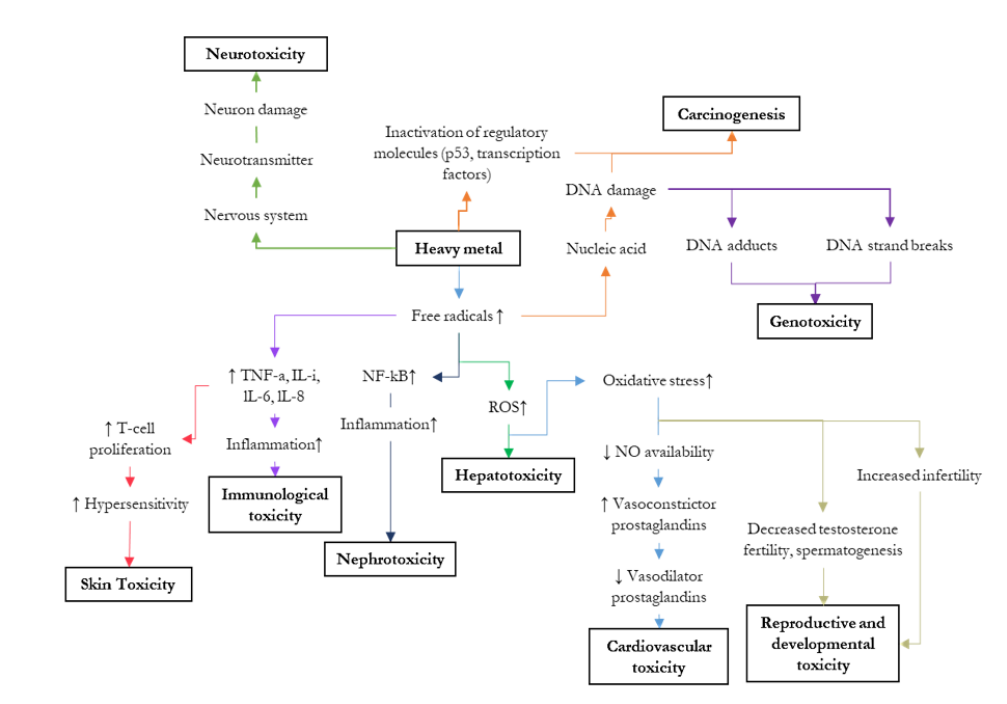

Figure 3: *Effects of HM on human health [63]*

The CDC and the ATSDR provide data on how HM is distributed and eliminated in the body. This data can help choose the best sample to test for metal exposure (Box 3) [31].

Methods to reduce or eliminate exposure to environmental HM

Box 3: Best sample to test for metal exposure

- Inorganic As can be detected in blood for 3 to 4 hours, and in urine and hair for 2 to 4 days and 6 to 12 months, respectively [56]. Seafood consumption can interfere with the test results [143].
- Pb can be detected in blood for 1 to 2 months [31].
- Cd can be detected in blood for 3 to 4 months, and in urine, hair, or nail for up to 30 years [144].
- Metallic and elemental Hg can be detected in blood for 3 days to 3 weeks, and in urine for 1 to 3 months. Methylmercury can be detected in blood and hair for 40 to 90 days [145]. Urine test is not useful for methylmercury [146].
- Thallium (Tl) can be detected in blood for 3 days, and in urine for 2 months [31].

Various methods and strategies can be employed to reduce or eliminate exposure to ecological HM. These methods primarily focus on mitigating the presence of HM in the environment and preventing their release into air, water, and soil.

Minimizing HM release into the environment requires proper waste management, reduced industrial emissions, and sustainable practices in agriculture and manufacturing. Regular air, water, and soil monitoring can pinpoint contamination sources, enabling early intervention. Adopting a multi-pronged approach involving biological, physical, and chemical methods alongside sustainable practices is essential to reduce exposure to environmental HM. For strategies to eliminate HM ingestion from food, water, and other sources, refer to box 4 [73-78].

Box 4: Preventable measures for heavy metal poisoning [166-171].

- Use protective equipment (gloves, masks, goggles) when handling HM.
- Water filters can remove HM from water by catching contaminant particles.
- Be mindful of industrial sources near the home for potential HM exposure.
- Stay informed about local fish advisories for safe consumption of fish contaminated with Hg or As.
- Test well water for inorganic substances, including metals, before drinking.
- Consider proximity to industrial sources that may impact the home or neighborhood.
- Reduce stress through relaxation techniques (meditation, yoga, breathing exercises, massage).
- Consume green leafy vegetables (cabbage, tomatoes, spinach, beets) for their antioxidant and anti-inflammatory properties.
- Include fibers from cereals and fruits to reduce enterohepatic recirculation of HM.
- Incorporate herbs and spices (parsley, basil, rosemary, ginger, turmeric, cilantro) known for their anti-inflammatory and antioxidant effects.
- Consume vitamins (C, E), minerals (Zn, Fe, Ca, etc), and antioxidant-rich foods (berries, green tea, dark chocolate, red wine, olive oil) to enhance immune system and detoxification pathways.
- Increase intake of polyphenols found in berries, green tea, dark chocolate, red wine, and olive oil for their antioxidant, anti-inflammatory, and chelating effects.

Future perspective and research regarding HM

Future research on HM toxicity shows excellent potential for addressing challenges in HM-contaminated environments. Understanding plant regulatory mechanisms can enhance crop tolerance to HM stress, and miRNA research can play a vital role in improving plant resistance. HM-induced signal transduction pathways offer insights into metal homeostasis and its impact on plants. Emerging strategies like biofortification, phytoremediation, and phytomining combat HM contamination and improve metal accumulation and soil cleanup [79]. Developing specific biomarkers for monitoring HM exposure and toxicity is essential for protective measures against HM-induced organ toxicity [30].

Future research should track toxic effects during migration and transformation processes, establish models for monitoring ecosystem changes, and explore genetic engineering for plant tolerance to HM ions [80]. Genetic engineering and optimization approaches show promise in HM bioremediation. Using multiple microbial strains simultaneously proves more effective, and genetically engineered microbes can tackle certain pollutants efficiently. Agricultural and industrial waste biomass are being explored as potential bio-remediators. However, further research is needed for commercializing diverse biosorbents after physical and chemical alterations. Collaboration among research groups, the public, government institutions, and industry is crucial for developing comprehensive and adaptable bioremediation strategies [81].

Policy formulation is essential to address HM contamination effectively and align with global regulatory policies and research efforts. Strengthening sanitary systems, conducting clinical trials to understand potential health risks, and regular monitoring through unified laboratories will ensure food safety and public health. Continued collaboration between researchers, policymakers, and environmental experts will pave the way for safer and more sustainable practices in managing HM toxicity [82].

Overall, future research on HM toxicity will continue to advance our understanding of the regulatory mechanisms in plants, the development of innovative remediation technologies, and the protection of human health and the environment from HM contamination.

Conclusion

The constant discharge of toxic substances from human activities is a global environmental issue. Due to their severe toxicity and accumulation ability, industrial effluents release HM ions into ecosystems, posing a significant danger to living organisms, humans, and the environment. Exposure to HM can result in acute or chronic toxicity, damaging organs like the brain, lungs, liver, and kidneys and causing diseases. HM causes toxicity through mechanisms such as generating free radicals, leading to oxidative stress, damaging biological molecules, and affecting DNA, potentially causing carcinogenesis and neurotoxicity. Various methods, such as bioremediation and phytoremediation, have been developed to remove HM from soil, water, and air. Simple and cost-effective approaches are crucial, especially for developing countries. Future research should focus on raising awareness and expanding knowledge about the impact of HM on human health and finding ways to reduce and eliminate these pollutants.

Conflict of Interest Statement

The authors declare that this paper was written without any commercial or financial relationship that could be construed as a potential conflict of interest.

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