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Metal Toxicity: Significant Health Assessment

Babita Tiwari[1], Ghizal Fatima*[2], Najah Hadi[3], Jan Fedacko[4], Aminat Magomedova[5], Ammar Mehdi Raza[6], Nada Alharis[7], Heider Qassam[8], Hekmat B Alhmadi[9], Sidrah Parvez[10]

[1,2,10] *Department of Biotechnology, Era University, Lucknow, India.*

[3,8] *Department of Pharmacology and Therapeutics, Faculty of Medicine, University of Kufa, Iraq.*

[4] *Department of Gerontology and Geriatric, Medipark, University Research Park, PJ Safarik University, 040-11 Kosice, Slovakia.*

[5] *Department of Population, Moscow State University by Lomonosov, Moscow, Russia.*

[6] *Department of Pediatric Dentistry, Career Dental College and Hospital, Lucknow, India.*

[7] *Radiological Department, Kufa Medical College, University of Kufa, Najaf, Iraq.*

[9] *College of Medicine, AL-Muthanna University, Samawah, Iraq.*

E-mail: ghizalfatima8@gmail.com,drnajahhadi@yahoo.com ,janfedacko@hotmail.com , heiders.qassam@uokufa.edu.iq

ABSTRACT

Background: *The deleterious effects of these heavy metals are contingent on the quantity ingested, the issue of exposure mode, exposure duration, and whether it is acute or chronic. Additionally, heavy metals interfere with numerous cellular functions, encompassing growth, proliferation, differentiation, DNA damage repair, and programmed cell death. This disturbance can lead to various diseases and inflict significant damage. Heavy metal toxicity alters the operation of the central nervous system, resulting in cognitive dysfunction, alterations in blood parameters, and impairment of liver, kidney, and lung functions, among other crucial physiological activities, culminating in the exacerbation of diverse human illnesses. Prolonged presence and consumption of heavy metals in the organism's body worsen the progression of somatic, neuromuscular, and neurodegenerative processes that mimic specific situations such as Alzheimer's and Parkinson's diseases. Heavy metals mimic hormonal functions, causing changes in the functioning of the endocrine system. Consequently, efforts should be focused on reducing human exposure and the build-up of heavy metals in the body due to anthropogenic and industrial activities to prevent detrimental health issues. This article delivers a thorough analysis of seven individual metals, and their toxicity including lead, cadmium, chromium, iron, arsenic, aluminium, mercury, etc., elucidating their toxic mechanisms, environmental presence, the potential for human exposure, and toxicity-induced health consequences such as nephrotoxicity, genotoxicity, and carcinogenicity. a potential future research avenue could involve investigating the efficacy of chelation therapy on a large scale for the management of metal poisoning.*

Keywords: Metal toxicity, Oxidative stress, Free radicals, Health concern.

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INTRODUCTION

Human consumption of toxic heavy metals is inevitable due to the perpetual presence of these hazardous metals in the atmosphere, water sources, and food supply. The escalation of human contact with heavy metals has been rapidly propelled by human-induced and industrial undertakings (1). The concern for heavy metal toxicity is of substantial significance for both environmental preservation and human well-being, particularly in emerging countries. These metallic components possess qualities of being non-biodegradable, toxic, xenobiotic, and capable of bioaccumulation. **(Table-1).** The toxicity associated with heavy metals is contingent upon several factors, including the specific characteristics of the metal in question, the dosage administered, the route of exposure, the duration of the exposure (whether acute or chronic), and the degree of bioaccumulation that occurs. The adverse effects of heavy metals on human health are predominantly associated with their ability to disrupt antioxidant defense mechanisms, primarily via their interactions with intracellular glutathione (GSH) or the sulfhydryl groups (R-SH) present in antioxidant enzymes such as superoxide dismutase (SOD), catalase, glutathione peroxidase (GPx), glutathione reductase (GR), along with various other enzymatic systems (2). The excessive abundance of any metal has the potential to induce illnesses and impose a significant health burden on the population. It is imperative to acknowledge that toxic metals are not exclusively a by-product of human activities they also emanate from a variety of natural processes, including volcanic eruptions, wildfires, erosion of rocks, and soil formation (3). These substances occur naturally in the environment and are distributed across various sectors such as industrial, residential, agricultural, medical, and technological domains. The industrial origins responsible for the accumulation of heavy metals encompass a wide array of operations. These operations entail the processing of metals in refineries, the burning of coal in power stations, the combustion of petroleum, the functioning of nuclear power facilities and high-voltage cables, the manufacturing of plastics, textiles, and microelectronic devices, preservation of wood, and processing of paper in factories (4).

The build-up of heavy metals primarily stems from human activities and the prevailing level of industrial advancement. Humans taking these metals occur through the intake of food, air, and water. Individuals come into contact with heavy metals through various pathways, including breathing, swallowing, and skin contact. Nevertheless, excessive consumption of any metal may result in acute or chronic toxicity. Apart from potential allergic reactions, prolonged and recurrent encounters with specific metals or their compounds could potentially culminate in the development of cancer. Heavy metals exhibit their toxic properties when the body fails to completely metabolize them, leading to their accumulation in soft tissues (5). At present, pose a threat to human health and are categorized as heavy metals. This categorization primarily stems from economic progress, notably in the energy sector, chemical industry, mining, and metallurgy sector, along with the surge in the establishment of new waste disposal sites and the application of composts. Each of these reasons contributes to the contamination of the environment. According to the World Health Organization and the International Agency for Research on Cancer, arsenic and cadmium are classified as Group I human carcinogens, with arsenic identified as the second leading cause of water-borne mortality globally. Metalloids, including arsenic, are frequently categorized within the heavy metals classification due to their analogous properties. Prolonged exposure to elevated concentrations of arsenic, cadmium, and other hazardous metals has been correlated

with an increased incidence of malignancies affecting the bladder, kidney, liver, lung, and skin. Recent studies indicate that these toxic metals may exert deleterious effects on health outcomes even at diminished concentrations, which could be widespread in numerous regions across the globe. Once absorbed into the body, heavy metals accumulate in tissues, disrupting physiological processes and leading to severe health consequences, including neurological, renal, and cardiovascular disorders, and in some cases, carcinogenesis.

This manuscript aims to provide a comprehensive assessment of the health impacts associated with heavy metal exposure, grounded in recent epidemiological and mechanistic studies. It seeks to bridge gaps in understanding by exploring the multifaceted pathways of toxicity and the biomarkers critical for early detection. Furthermore, the manuscript highlights existing regulatory frameworks and evaluates their effectiveness in mitigating exposure across diverse geographical regions. By synthesizing current research and policy insights, the work intends to contribute actionable recommendations for improving public health strategies and regulatory policies. Ultimately, this study endeavours to underscore the urgency of addressing heavy metal toxicity as a global health priority, fostering interdisciplinary dialogue and catalysing advancements in prevention, monitoring, and remediation efforts.

Mercury, derived from mining operations and medical waste, contributes to elemental fever and chronic nephropathic syndrome. Lead, prevalent in batteries and fuel, is linked to emesis and chronic osteoporosis. Exposure to chromium from the steel manufacturing sector is correlated with renal failure and lung carcinogenesis. Iron, sourced from mining activities, is responsible for gastrointestinal disturbances and organ impairment(3). Arsenic, originating from ore extraction, is associated with acute manifestations and prolonged carcinogenic risks. Aluminium exposure is implicated in neurological dysfunction and skeletal disorders. Acceptable thresholds for these heavy metals range from 0.01 to 0.3 mg/L.

Table 1: Analysis of acute and chronic heavy metal exposure in humans (6).

Metal	Source of exposure	Effect		Permissible Limits (mg/L)
		Acute	Chronic	
Cadmium	Plastic stabilizers, Electroplating, Phosphate fertilizers, Paints and pigments	Pneumonitis	Proteinuria, osteomalacia, lung cancer	0.06
Mercury	Au-Ag mining, medical waste, Coal combustion	Elemental fever, vomiting, diarrhoea, acute lung injury. Inorganic salts: caustic gastroenteritis	Nausea, metallic taste, neurasthenia, gingivostomatitis, tremor, nephritic syndrome, hypersensitivity	0.01
Lead	Herbicides, Batteries waste, Leaded fuel, Insecticides	vomiting, diarrhoea, abdominal pain	Osteoporosis, neurologic degeneration, copper deficiency: anaemia	0.1

Metal	Source of exposure	Effect		Permissible Limits (mg/L)
		Acute	Chronic	
Chromium	Steel industries, Tanneries, Fly ash	acute renal failure, gastrointestinal haemorrhage, haemolysis	Lung cancer, pulmonary fibrosis	0.05
Iron	Mining and Smelting, Steel Manufacturing	Gastrointestinal distress, liver toxicity	Organ damage (liver, heart, pancreas)	0.3
Arsenic	Ore mining, Smelting, biosolids, Wood preservatives, Pesticides, Fungicides	nausea, diarrhoea, vomiting, painful neuropathy, encephalopathy	Diabetes, hypopigmentation/ hyperkeratosis, cancer: skin, bladder, lung, encephalopathy	0.01
Aluminium	Bauxite mining, vehicles, electronics	Confusion, headaches, and memory loss	Neurological and bone disorders	0.05

Table 1 delineates various heavy metals cadmium, commonly utilized in plastic stabilizers and fertilizers, is associated with acute and the onset of chronic effects.

METHODOLOGY

A systematic literature review was undertaken to evaluate the implications of metal toxicity on human health, with a particular emphasis on heavy metals including lead, cadmium, chromium, iron, arsenic, aluminium, and mercury. The literature search was executed across databases such as PubMed, Scopus, and Web of Science, Science Direct spanning from January 2000 to December 2023, utilizing the search terms "metal toxicity," "heavy metals," "human health," and "toxicology." This review was employed to refine the search outcomes, and only publications that were peer-reviewed and presented in the English language were considered for inclusion. The inclusion criteria encompassed studies focused on human populations, investigations into the ramifications of chronic or acute exposure to heavy metals, environmental effects, and research about specific health consequences (e.g., neurotoxicity, renal impairment, malignancies).

Literature reviews, or investigations lacking significant data on human exposure levels or toxicity. The preliminary search resulted in the identification of 150 articles. Following the elimination of duplicate entries and the screening of titles and abstracts, a total of 200 studies were subjected to full-text eligibility assessment. Data extraction was concentrated on various parameters including study design, exposure levels, health outcomes, and toxicity effect on human mechanisms. A qualitative synthesis was conducted, organizing the results into thematic categories such as toxicity mechanisms, biomarkers, and clinical consequences. The quality of the studies was evaluated employing a risk of bias assessment tool, with studies identified as having a high risk of bias being excluded from the final synthesis.

Toxic heavy metal concern of environment and human health:

Environmental pollution:

Particularly heavy metals, in our environment - water, soil, and air, have attracted significant global attention due to their negative impacts. This emergence is directly linked to the rapid growth of agriculture and metal industries, inappropriate waste disposal practices, and the use of fertilizers and pesticides (7). The significant environmental risk posed by this pollution affects many individuals worldwide, endangering the well-being of humans, plants, and animals alike.

Soil contamination:

Soil contamination has the potential to arise from deliberate or inadvertent actions. Deliberate contamination includes practices like the application of pesticides and fertilizers, irrigation with wastewater, utilization of animal manures, disposal of lead-based paint, mine ore waste, sewage sludge, as well as seepage of petroleum products, coal combustion residues, and waste disposal (8).

The presence of heavy metals in agricultural soils due to untreated sewage and wastewater has led to their absorption by crops, consequently posing risks to human health. Unintentional pollution may result from the flooding of rivers and seas carrying sewage and polluted water to land, as well as mishaps during the transportation of hazardous chemicals (9). Owing to the non-biodegradable nature of heavy metals, they endure in the soil for prolonged periods without undergoing degradation by microbes or chemicals.

Water pollution:

Water pollution can be linked back to the processes of urbanization and industrialization. Metals present in water bodies are conveyed through runoff from rural regions, towns, cities, and industrial areas, eventually settling in sediments (10). Even minimal concentrations of these metals can present substantial hazards to humans and diverse ecosystems. The degree of danger is influenced by factors like the specific metal, its characteristics, biological functions, the affected organism, and the life stage of the organism during exposure. Disruption of one organism can have cascading effects throughout the entire food chain. Humans, typically situated at the highest trophic level, tend to amass elevated levels of heavy metals. Both industrial and household waste are frequently discharged into sewage systems. **(Fig.1)** delineates the ramifications of environmental pollution on human health as a consequence of heavy metal contamination. Various sources, including atmospheric, aquatic, and terrestrial pollutants, release hazardous metals such as cadmium (Cd), mercury (Hg), lead (Pb), chromium (Cr), iron (Fe), arsenic (As), and aluminium (Al) into the ecosystem.

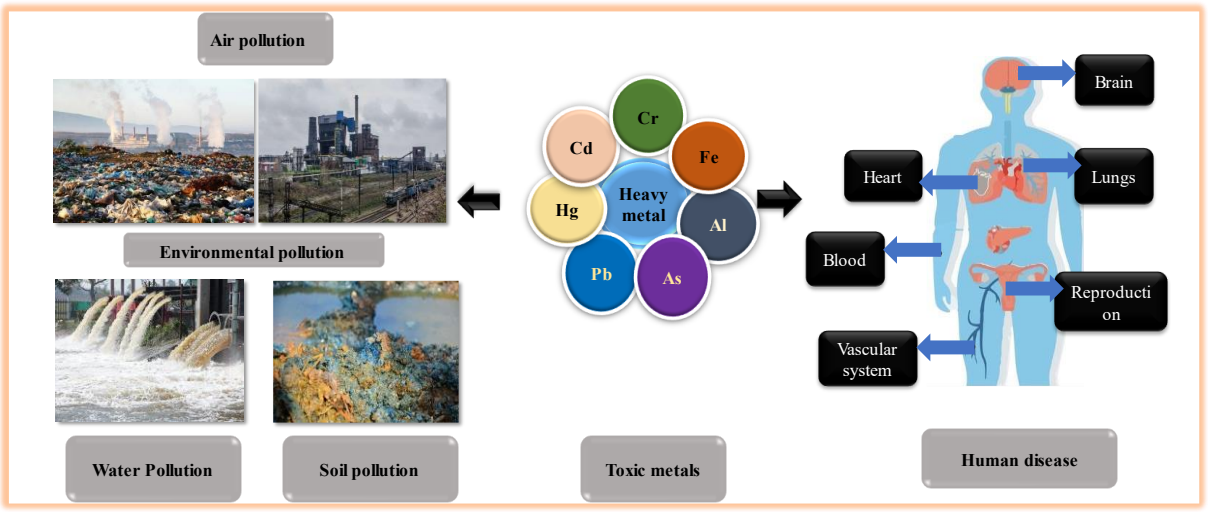

Figure 1: Impact of Environmental Pollution and Heavy Metal Exposure on Human Health.

Air pollution:

Air pollution, analogous to water pollution, has been worsened by the processes of urbanization and industrialization. Contaminants infiltrate the atmosphere in the guise of particles, droplets, and gases. The emission of particulate matter, notably fine particles, and dust, is linked to both natural events and human endeavour (11). Natural occurrences such as sandstorms, volcanic eruptions, soil erosion, and rock weathering release particulate matter, while human activities like industrial operations, combustion of fossil fuels, vehicle discharges, and smelting contribute to emissions of particulate matter. These particles present substantial health hazards, accelerate infrastructure deterioration, foster the formation of acid rain, induce corrosion, and lead to eutrophication when they settle in water bodies during precipitation (12). They also contribute to mist formation. Certain occupations are associated with an inherent risk of exposure and toxicity to specific heavy metals. Chimneys serve as primary sources of atmospheric pollution, releasing a multitude of gases. Internal combustion and jet engines, as well as diesel engines, older cars, and excessive vehicular traffic, also contribute to atmospheric pollution. The use of pesticides, refrigerators, aerosols, and radioactive substances also contributes to pollution.

Domestic exposures to metal:

The systemic exposure levels to metals from the usage of these household items, and the presence of metallic components in household detergents, soaps, and cleaning agents raise environmental and health concerns for several main reasons. These reasons include:

- Direct exposure of individuals to these metal impurities in soaps during washing.
- Ingestion of these impurities from poorly rinsed household items like cups and plates, among others.
- Discharge of effluents from washing processes directly into the environment without treatment, potentially increasing environmental contamination.

Metals present in soaps and detergents have the potential to be transferred onto clothing and may not be fully removed during the rinsing process (13). The clinical presentations of heavy metal poisoning can vary based on the specific substance involved, stemming from either acute exposure to significant amounts or chronic exposure to repeated small doses, leading to cumulative toxicity. The impacts of heavy metals on various physiological systems are a

consequential result. The level of toxicity exhibited by these metals is influenced by factors like the amount ingested, exposure route, and specific chemical composition, and Factors such as age, gender, genetic composition, and dietary status of the affected individuals play a role in the consequences of exposure. Arsenic, cadmium, chromium, lead, and mercury are categorized as priority metals owing to their notably high levels of toxicity, prompting significant concerns for public health. These metallic components are acknowledged as systemic toxic substances capable of causing damage to multiple organs, even at minimal levels of exposure.

Metal toxicity and Oxidative stress:

The concept of oxidative stress involves an imbalance between the production of reactive oxygen species (free radicals) and the protective functions of antioxidants within cells and tissues, along with the biological system's ability to eliminate these reactive by-products (14). Our research focused on the potential role of oxidative stress in initiating cellular and tissue damage, as well as the effectiveness of the biological system in combating these reactive substances, such as free radicals. Specifically, Oxygen-based free radicals, like the hydroxyl radical, superoxide anion radical, hydrogen peroxide, singlet oxygen, hypochlorite, nitric oxide radical, and peroxyl nitrite radical, play crucial roles in various pathological conditions. Free radicals, known for their high reactivity, jeopardize essential biological components like DNA, proteins, carbohydrates, and lipids in the cell nucleus and cellular membranes. The origins of these radicals and the main defence mechanisms of antioxidants were discussed, along with examples illustrating the potential harm caused by free radicals, with a particular emphasis on lipid peroxidation (15).

Toxic metals generate free radicals:

The toxic and carcinogenic properties induced by metals, focusing on the production of reactive oxygen species (ROS), carry significant importance in the scientific field. Metallic toxins can produce radicals that are crucial in damaging genetic material. ROS and reactive nitrogen species (RNS) are identified as the main culprits in triggering oxidative stress. For example, arsenic has been shown to generate various radical entities like superoxide, oxygen, nitric oxide, hydrogen peroxide, and peroxyl radicals (16). Exposure to Pb results in a notable reduction in important antioxidant components such as glutathione peroxidase, catalase, superoxide dismutase, glutathione-S-transferase, and reduced glutathione.

Conversely, the presence of lead is associated with an increase in oxidative markers such as malondialdehyde and hydrogen peroxide (17). Cr (VI) initiates the production of ROS and the onset of oxidative stress, which negatively impacts the cellular antioxidant defence, leading to damage to DNA, lipids, and proteins. Furthermore, chromium and cadmium are acknowledged as carcinogens. **(Fig.2)** The diagram elucidates the pathways of metal toxicity, commencing from exposure and culminating in biological ramifications. Metals infiltrate the human body, undergoing processes of absorption, distribution, biotransformation, and excretion, thereby disrupting cellular mechanisms. Notable consequences encompass oxidative stress (which inflicts damage on lipids, proteins, and nucleic acids), enzyme inhibition (resulting in metabolic dysfunctions), DNA damage (exhibiting mutagenic properties), and modified gene expression, culminating in aberrant protein synthesis and cellular impairment. The production of reactive oxygen species and the onset of oxidative stress play crucial roles in the development of toxicity and carcinogenicity linked to metals, such as arsenic. High levels of

heavy metals can result in decreased energy levels and dysfunction of vital organ systems like the brain, lungs, kidneys, liver, and blood composition, among other outcomes (18). These metals can interfere with different cellular components including the cell membrane, mitochondria, lysosomes, endoplasmic reticulum, nuclei, and specific enzymes participating in vital metabolic pathways, detoxification mechanisms, and repair processes. Moreover, they can impede essential cellular functions like growth, replication, differentiation, repair, and programmed cell death. Chromium, cadmium, and arsenic, recognized as hazardous metals, have been found to cause genetic instability. The deficiencies in DNA repair induced by oxidative stress and DNA damage initiated by these three metals are presumed to be the probable causes of their carcinogenic properties.

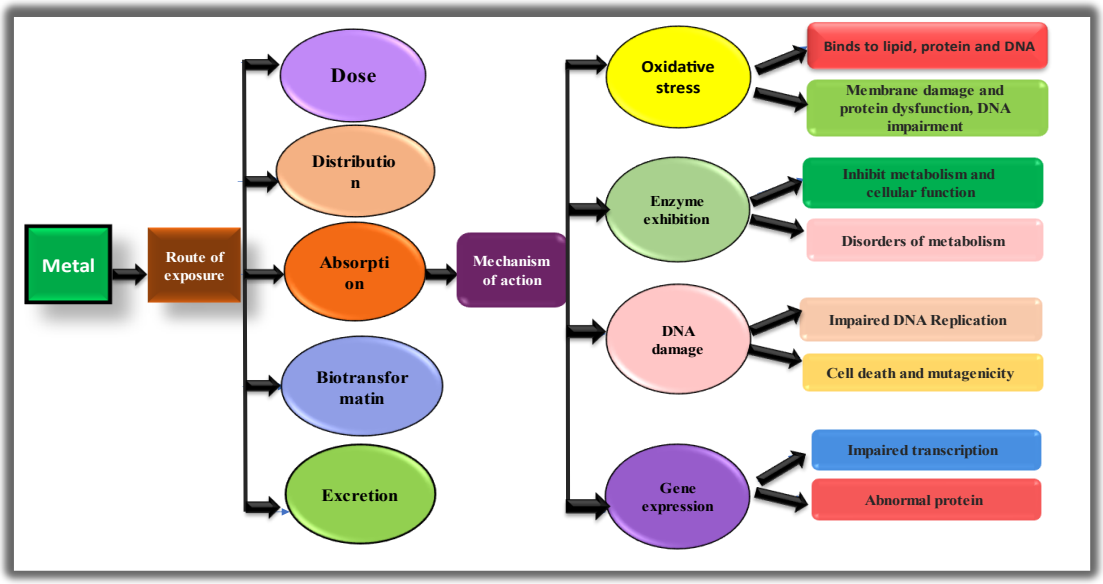

Figure 2: Route of Exposure and Toxicological Mechanisms of Heavy Metals in Humans.

Route of exposure:

When examining heavy metals, the primary sources of concern are mainly present in the environment, particularly in contaminated water, air, and soil. Inhaling contaminated air and ingesting polluted water are the primary pathways through which heavy metals infiltrate the human body. Furthermore, heavy metals can enter the human body through soil predominantly via the soil-plant-human or soil-plant-animal-human pathways (19). The transmission of heavy metals from soil to humans and animals mainly occurs through plants. It is crucial to acknowledge that human activities are not the exclusive contributors. Heavy metal contamination. These substances are also naturally produced through phenomena such as volcanic eruptions, wildfires, rock erosion, and soil development. **(Fig.3)** The origins of heavy metals can be traced back to both natural phenomena, such as volcanic eruptions, mineral weathering, soil erosion, and forest fires, as well as anthropogenic activities, including mining operations, industrial activities, agricultural practices, fossil fuel combustion, and improper waste management. These undertakings facilitate the release of toxic metals into the air, water, and soil, thereby significantly contributing to environmental pollution and associated public health hazards.

Heavy metals are ubiquitous in various aspects of everyday human life and professions. The pivotal element in safeguarding human well-being and security lies in evaluating the quantity of heavy metals that enter the human system. The respective levels for the four most prevalent hazardous metals are mercury - 0.005 mg/kg BW, cadmium - 0.007 mg/kg BW, lead - 0.025 mg/kg BW, and arsenic - 0.025 mg/kg BW. Consequently, mercury emerges as the most harmful metal to human health. Even a minute of mercury can adversely impact an individual's health status.

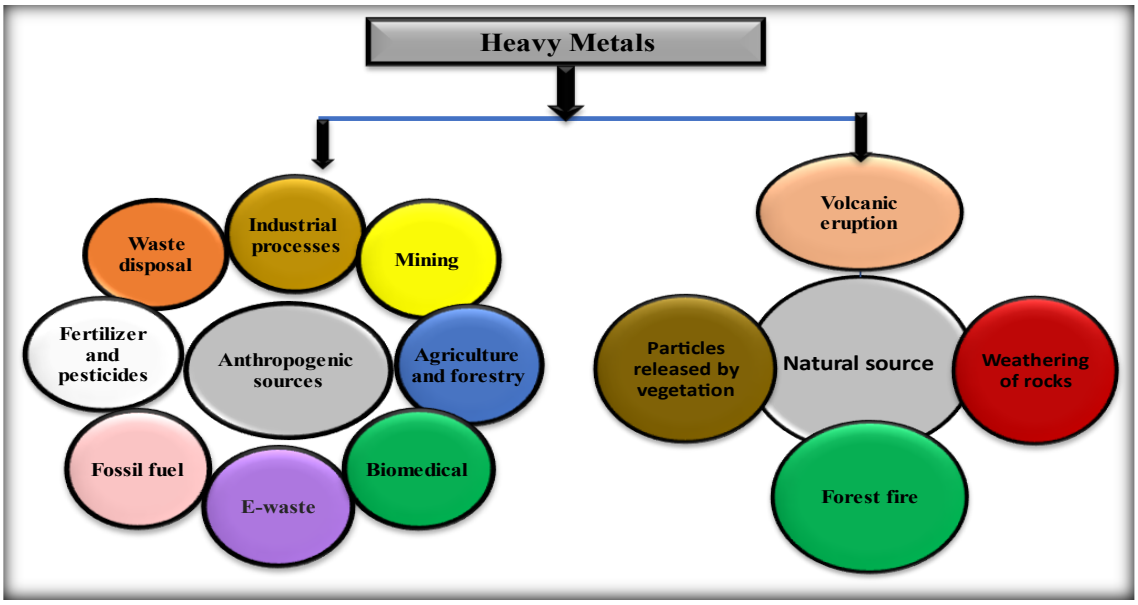

Figure 3: Sources of heavy metals-Anthropogenic and Natural origins.

Toxic metals found in the food items:

The main origin of exposure to toxic metals lies in food items, especially those obtained from plants. Due to human industrial operations, various harmful substances have entered the ground and may be taken in by plants. Currently, the quantities of heavy metals in food and drinks do not present notable dangers to human health in many different regions (20). Common dietary essentials like fruits, vegetables, dairy, meat, oils, and some alcoholic beverages such as beer and wine contain heavy metals (21).

These food types form the fundamental components of everyday diets in numerous areas. The stages of heavy metals in food fluctuate due to a variety of factors that impact their accumulation. **(Fig.4)** Heavy metal contamination within food chains is a consequence of polluted air, water, and soil, leading to the incorporation of metals such as iron, aluminium, chromium, arsenic, lead, cadmium, and mercury into agricultural produce, livestock, and seafood. Principal sources of this contamination include industrial effluents, pesticides, and fertilizers. The associated health risks encompass neurotoxicity, organ dysfunction, carcinogenesis, and developmental anomalies, thereby underscoring the imperative for stringent contamination control measures.

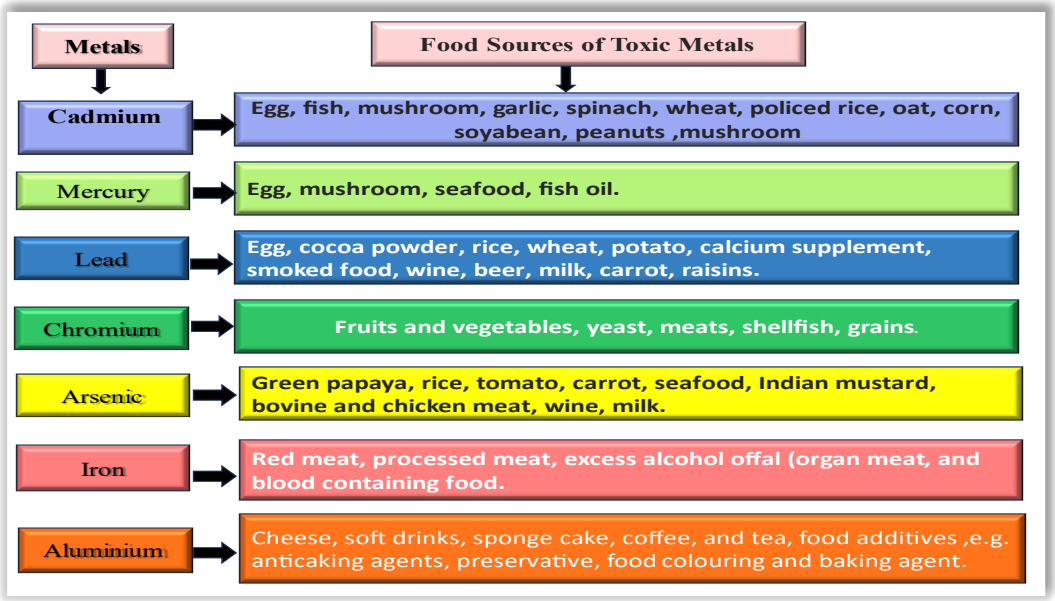

Figure 4: Heavy Metal Contamination in Food Chains, Sources and Health Risks.

Toxicity of heavy metals:

Heavy metals are categorized as trace elements because of their widespread presence. The concept of oxidative stress centers around an imbalance between the generation of (ROS) and the protective roles of antioxidants (22).It is commonly accepted that exposure to foreign metals can lead to disorders impacting the gastrointestinal, respiratory, cardiovascular, reproductive, renal, blood-forming, and nervous systems. **Table.1** defines the comparative analysis of Cd, Hg, Pb, Cr, Fe, As, and Al in terms of toxicity levels, bioaccumulation, and mitigation strategies(23).

Table 1. Shows a comparative analysis of metal toxicity, bioaccumulation, and mitigation(17).

Metal	Toxicity Level	Bioaccumulation Factor	Mitigation Strategies	Greatest Risk Conditions
Cadmium	High (kidney damage, skeletal deformities, cancer).	Accumulates in plants, aquatic systems, and kidneys.	Reduce industrial emissions, and regulate fertilizers, and chelators (e.g., EDTA).	Chronic exposure via food, contaminated water, or smoking.
Mercury	Extremely high (neurotoxicity, developmental disorders).	Bioaccumulates and biomagnifies, especially in seafood.	Minimize industrial discharge, and avoid high-mercury fish, chelators like DMSA.	High-risk for populations consuming seafood with methylmercury.
Lead	High, particularly in children (cognitive and developmental delays).	Bioaccumulates in bones and soft tissues.	Remove lead-based products, treat water systems, use chelators like EDTA.	Chronic exposure through old paint, lead pipes, and contaminated soil or water.

Metal	Toxicity Level	Bioaccumulation Factor	Mitigation Strategies	Greatest Risk Conditions
Chromium	Variable (Cr (VI) is highly toxic; Cr (III) is less harmful).	Cr(VI) bioaccumulates in aquatic life.	Regulate industrial effluents, water treatment, and chelation therapy.	Hexavalent chromium exposure in tanning, metal plating, and polluted groundwater.
Iron	Moderate; toxic in high doses (hemochromatosis).	Limited bioaccumulation; more regulated biologically.	Dietary management, phlebotomy for overload, iron chelators (deferoxamine).	High dietary or genetic susceptibility (e.g., hereditary hemochromatosis).
Arsenic	High (carcinogenic, cardiovascular diseases, neurotoxicity).	Accumulates in rice, groundwater, and aquatic systems.	Remove arsenic-contaminated water, enhance soil treatment, use chelators.	Long-term exposure via contaminated drinking water or arsenic-laden foods.
Aluminium	Low to moderate (neurotoxicity in chronic exposure).	Limited bioaccumulation but can accumulate in bones/brain.	Reduce exposure to aluminium cookware, regulate water treatment chemicals.	Chronic exposure via food, antacids, or contaminated water.

Lead:

Lead is a tremendously poisonous metal that has caused widespread pollution and health problems globally due to its widespread utilization. In a dry environment, lead is displayed as a shiny silver metal with a slight bluish hue. Lead is classified as a carcinogen according to the Environmental Protection Agency (EPA). Anthropogenic activities like mining, manufacturing, and the combustion of fossil fuels have resulted in the accumulation of lead and its compounds in the environment, encompassing the atmosphere, water sources, and soil (24). Lead is utilized in the production of batteries, cosmetics, and various metallic products such as ammunition, solder, and pipelines, among other items. Major sources of lead comprise lead-based paints, gasoline, cosmetics, toys, household dust, contaminated soil, and industrial discharges. Exposure to lead can also happen through the consumption of water (25). The water distribution systems may contain lead and its blends, leading to water pollution with the adverse effects of lead; commonly known as lead poisoning, which can manifest either acutely or chronically.

Path of Human Exposure: Exposure to lead and its compounds can happen through breathing, swallowing, skin contact, or absorption from lodged or embedded lead-containing foreign objects. The main method of human exposure to lead generally involves swallowing or inhaling it.

Nephrotoxicity: Lead causes harmful impacts on all body organs, particularly on the kidney system. Acute lead-induced kidney damage leads to dysfunction of the proximal tubules, resulting in a Fanconi-like syndrome (26).

Chronic lead-induced kidney damage presents as hyperplasia, interstitial fibrosis, tubular shrinkage, kidney failure, and inflammation of the glomeruli.

Carcinogenicity: Lead, an acknowledged carcinogen, disrupts DNA repair mechanisms, genes that control tumor formation in cells, and the arrangement and sequence of chromosomes through the release of reactive oxygen species. It interferes with transcription processes by displacing zinc from specific regulatory proteins.

Hepatotoxicity: The detrimental impact of lead on hepatic cells is widely acknowledged. Exposure to lead heightens oxidative stress levels, leading to compromised liver functionality. The co-presence of organic solvents and lead induces liver damage due to their resemblances. Prolonged exposure to lead poses a potential toxicity risk to liver cells, leading to glycogen depletion, cell infiltration, and the potential development of chronic cirrhosis.

Immunological toxicity: Both sudden and prolonged exposure to lead trigger various detrimental effects on the immune system, eliciting diverse immune responses like heightened allergic reactions, susceptibility to infections, autoimmune reactions, and potentially cancer. Specific demographic groups are the heightened risk of lung, stomach, and bladder cancers linked to lead exposure (27). Exposure to lead stimulates the production of B and T-cells, alongside MHC activity, influencing cellular and humoral responses by regulating T-cell function, increasing susceptibility to autoimmune disorders and hypersensitivity reactions.

Cardiovascular toxicity: Exposure to lead, whether acute or chronic, triggers various abnormalities in human physiology. Chronic exposure to lead can result in conditions such as arterial rigidity, increased blood pressure, blood clotting, arterial obstructions, and heart issues by enhancing oxidative stress, reducing nitric oxide availability, increasing vasoconstrictor prostaglandins, disturbing the renin-angiotensin system, decreasing vasodilator prostaglandins, altering calcium signaling in vascular smooth muscle cells, heightening inflammation and endothelium-dependent vessel relaxation, and modifying the vascular response to vasoactive substances. Prolonged exposure also raises blood pressure levels.

Reproductive and developmental toxicity: Research conducted by the World Health Organization (WHO) has indicated that more than 10% of women are at risk of infertility due to exposure to heavy metals. Heavy metals like lead, cadmium, mercury, and other contaminants are frequently found in the environment and can cause reproductive issues.

Symptoms: Acute exposure might lead to symptoms like reduced appetite, headaches, hypertension, abdominal pain, renal dysfunction, fatigue, sleep disruptions, joint inflammation, hallucinations, and dizziness. Acute exposure commonly happens in workplaces and industries that use lead. Extended exposure to lead can result in conditions such as cognitive decline, congenital anomalies, mental disorders, autism, allergic reactions, learning difficulties, weight loss, hyperactivity, paralysis, muscle weakness, brain damage, kidney impairment, and potentially fatal outcomes.

Treatment: Treatment options are scarce, with the only solution being removal from the source of exposure. Chelation therapy using EDTA is the standard medical approach for lead poisoning. Gastrointestinal decontamination (elimination of ingested lead using laxatives) is another method.

Cadmium:

Cd poisoning is a widely recognized global occurrence that results in numerous deaths annually. This hazardous heavy metal, known as Cd, is widely dispersed in the environment. Cadmium and its compounds have been classified as Group 1 carcinogens for humans by the International Agency for Research on Cancer. The impact of Cadmium spans various areas such as cellular growth, differentiation, and programmed cell death, which align with DNA repair mechanisms, the production of ROS, and the initiation of programmed cell death (28). Cadmium, a metal that gained significance in the 20th century, is a by-product of zinc manufacturing and can be present in different concentrations in soils, rocks, coal, and mineral fertilizers. Cadmium (Cd) exhibits a protracted biological half-life ranging from 17 to 30 years within the human organism. Empirical evidence indicates that dietary intake and cigarette smoke constitute the predominant sources of non-occupational cadmium exposure among the general population. Occupational exposure primarily arises from the inhalation of cadmium fumes in the cadmium-nickel battery manufacturing sector, as well as from the processes involved in the coating and plating of metals and the production of stabilizers utilized in plastics and paint pigments(29).

This element is utilized in a wide range of applications including batteries, pigments, plastics, and metal coatings, often used in electroplating procedures. The release of Cadmium into the environment naturally occurs through events like volcanic eruptions, erosion, river transportation, and human actions such as mining, smelting, tobacco consumption, waste incineration, and fertilizer manufacturing (30). The toxicological ramifications of Cadmium exposure can result in acute or chronic poisoning, particularly posing significant hazards to the renal system by accumulating in proximal tubular cells. Chronic exposure to lower concentrations may lead to cadmium deposition in the Renal, ultimately causing kidney disease, bone fragility, and lung impairment. Among smokers, tobacco stands out as the main source of cadmium intake due to the plant's ability to engross cadmium from the soil.

Human exposure to cadmium: Typically occurs through various channels such as consuming contaminated food, smoking tobacco, or working in environments tainted with cadmium, with smoking playing a significant role. Exposure can transpire through oral ingestion, inhalation of cadmium-laden fumes or dust, dermal absorption, ocular contact, and parenteral routes, among others.

Neurotoxicity: The neurological impact induced by cadmium is linked to the progression and prevalence of neurodegenerative conditions like amyotrophic lateral sclerosis, Parkinson's disease, Alzheimer's disease, and multiple sclerosis. Research indicates the harmful effects of cadmium on both the peripheral and central nervous systems, leading to disorders such as peripheral neuropathy, loss of smell, and disruptions in neurological functions. Moreover, the neurotoxic influence of cadmium extends to cellular mechanisms like differentiation, growth, and cell death, especially through neural cell apoptosis.

Nephrotoxicity: Resulting from exposure to cadmium is characterized by observable clinical symptoms like glucosuria, Fanconi-like syndrome, phosphaturia, and aminoaciduria. Direct interaction of cadmium with the proximal tubular epithelium significantly influences urine cadmium levels, leading to conditions like aminoaciduria, 32-microglobulinuria, and glucosuria, coupled with compromised renal tubular phosphate reabsorption. Prolonged exposure to cadmium can result in renal tubular acidosis, renal malfunction, and hypercalciuria.

Hepatotoxicity: Associated with cadmium predominantly affects the renal cortex and liver tissues in humans. Acute exposure to Cd leads to liver accumulation, contributing to various hepatic dysfunctions. Alteration of cellular redox balance by cadmium induces oxidative stress and hepatocellular injury, potentially causing liver failure and elevating cancer risk.

Cd, recognized for its toxic and carcinogenic properties, poses health risks related to conditions like kidney disease, bone disorders, and cardiovascular ailments (31). Moderate cadmium exposure is associated with conditions like hypertension, diabetes, carotid atherosclerosis, peripheral arterial disease, chronic kidney disease, heart attack, stroke, and heart failure. Studies conducted on the population of the United States have shown an increased risk of cardiovascular mortality connected to cadmium exposure.

Symptoms of cadmium: Exposure encompasses nausea, vomiting, abdominal pain, diarrhoea, headaches, flu-like symptoms, and throat swelling, often accompanied by tingling sensations in the hands.

Treatment: The management of cadmium toxicity involves the monitoring of cadmium levels in blood, urine, hair, nails, and saliva. Individuals affected by cadmium toxicity necessitate interventions such as gastrointestinal tract cleansing, supportive care, and chelation therapy utilizing appropriate agents and nanoparticle-based remedies.

Arsenic:

Arsenic contamination has emerged from natural geological processes and human activities. Arsenic lacks both smell and taste. Inorganic arsenic is acknowledged as a carcinogen and can lead to skin, lung, liver, and bladder cancers. Groundwater pollution can also be caused by geological sources like arsenic minerals (32). Sedimentary and meta-sedimentary bedrocks present another source. Arsenic is released into the environment through various sources like paints, dyes, soaps, metals, semiconductors, pharmaceuticals, pesticides, fertilizers, and animal farming practices. These releases have significant implications for human health, including developmental abnormalities, neurological disorders, diabetes, and hearing impairments. The severity of the adverse health effects, including blood disorders and various cancers, is influenced by the chemical composition of arsenic, as well as the timing and extent of exposure. Many countries globally report instances of both acute and chronic arsenic exposure due to elevated levels of this element in drinking water sources, particularly groundwater (33). Research demonstrates heightened standardized mortality rates for various cancers like bladder, kidney, skin, liver, and colon in regions affected by arsenic contamination.

Human exposure to arsenic: Mainly occurs through the ingesting and inhalation of arsenic-containing foods. Dermal contact can also result in health problems, although to a lesser degree compared to ingestion or inhalation routes.

Neurotoxicity: Ingesting arsenic leads to cognitive impairment in the central nervous system, causing various neurological disorders like neurodevelopmental changes and an elevated vulnerability to neurodegenerative conditions. Arsenic poisoning also results in disruptions to synaptic transmission and alterations in neurotransmitter balance.

Carcinogenicity: The cancer-causing effects of arsenic are linked to epigenetic changes, DNA damage, and variations. The impact of arsenic exposure on cancer susceptibility is manifested through p53 protein expression, alterations in histones, DNA methylation, and diminished p21 levels. The mechanism involves arsenic binding

to DNA-binding proteins, thereby hindering DNA repair processes and heightening the risk of cancer development.

Skin toxicity: Toxicity induced by arsenic presents itself through various dermatological manifestations. These include hyperkeratosis, hyperpigmentation, and various types of skin cancer. Hyperpigmentation, a common alteration in the skin due to prolonged exposure to arsenic, is frequently observed. Additionally, arsenic exposure can initiate Bowen's disease, an early phase of skin malignancy. Hyperkeratosis, another consequence of arsenic exposure, typically manifests extensively on the soles and palms but can also affect other areas of the body. Lesions associated with hyperkeratosis and Bowen's disease have the potential to progress into invasive cancers.

Reproductive and developmental toxicity: Arsenic is identified as a reproductive toxicant in humans, leading to abnormalities in experimental animals, particularly. Affecting neural tube development. Inorganic arsenic negatively affects male reproductive functions by decreasing testicular weights, accessory sex organ sizes, and epididymal sperm count. It also disrupts testosterone levels, gonadotropin concentrations, and steroidogenesis. In females, arsenic consumption is linked to a higher risk of endometrial cancer (34). Exposure to arsenic during pregnancy disrupts endometrial angiogenesis crucial for embryo development, resulting in conditions such as endometriosis, subfertility, prematurity, sterility, and spontaneous abortions.

Genotoxicity: The genotoxic effects of arsenic manifest as alterations in deoxyribonucleic acid, including chromosomal abnormalities, mutations, micronuclei formation, deletions, and sister chromatid exchanges. Extensive research has been conducted to elucidate the genotoxic impact of arsenic, which involves the induction of oxidative stress and interference with DNA repair mechanisms are key outcomes of arsenic exposure. Despite its limited mutagenicity directly on DNA, arsenic enhances the mutagenicity of other carcinogens. Notably, human cell exposure to arsenic in combination with UV light demonstrates increased mutagenicity.

Symptoms: Symptoms of arsenic poisoning encompass abdominal pain, nausea, vomiting, diarrhoea, cough, chest pain, dyspnea, pharyngitis, arrhythmia, hypotension, paraesthesia in extremities, erythematous skin, garlic-like odour in breath and tissues. Prolonged exposure results in skin pigmentation, indurated patches, sore throat, and gastrointestinal disturbances.

Treatment: Chelation therapy, administered by a healthcare professional, involves the use of specific chemicals to remove arsenic from blood proteins. Another therapeutic approach is bowel irrigation. During treatment, monitoring of cardiac and renal functions is essential. Patients may also require oxygen therapy, intravenous fluids, blood transfusions, cardiac medications, or anticonvulsants.

Mercury:

Mercury, a hazardous heavy metal, is extensively found in the environment, with human primary exposure typically resulting from fish consumption or dental fillings. It is present in diverse forms, which include inorganic mercury consisting of Mercury exists in various forms, including forms of mercury, such as metallic mercury, mercury vapour (Hg0), mercurous (Hg2++), mercuric (Hg++) salts, and organic mercury compounds, exhibit distinct patterns of absorption and accumulation in bodily tissues (35). For example, methylmercury is efficiently absorbed through the gastrointestinal tract and distributed across various tissues, with a relatively lower ability to penetrate the blood-brain barrier compared to

elemental mercury. Nevertheless, once methylmercury reaches the brain, it undergoes demethylation to elemental mercury.

The toxic impacts of mercury are dependent on its chemical form, dosage, and exposure rate. Inhaled mercury vapour primarily affects the brain, whereas mercurous and mercuric salts predominantly influence the gastrointestinal lining and kidneys. Despite common symptoms such as fatigue, anxiety, and depression indicating low-grade chronic mercury exposure, they are seldom considered in the differential diagnosis (36). Methyl mercury tends to accumulate in body parts like the brain, liver, kidneys, placenta, and fetus, where a gradual demethylation process leads to the buildup of inorganic mercury.

Route of Human Exposure: Inhalation, ingestion, or dermal contact.

Nephrotoxicity: Acute mercury exposure can result in acute tubular necrosis in the kidneys, leading to symptoms like dyspnea, altered mental status, and abdominal pain. Conversely, chronic exposure can cause damage and necrosis in the par's recta of the proximal tubule, ultimately leading to tubular failure. Chronic mercury-induced kidney damage is characterized by elevated excretion of albumin and retinol-binding protein in urine, along with a nephritic condition associated with membranous nephropathy.

Carcinogenicity: The carcinogenic properties of mercury stem from its peroxidative characteristics, which generate ROS capable of activating signaling pathways that support tumour growth and the proliferation of malignant cells. Damage inflicted by ROS on cellular components such as proteins, lipids, and DNA is linked to the onset of cancer.

Cardiovascular toxicity: Recent findings have highlighted cardiovascular toxicity in conjunction with neurotoxicity, nephrotoxicity, and hepatotoxicity among individuals exposed to heightened levels of mercury. Studies have demonstrated correlations between increased levels of mercury in hair and elevated levels of oxidized LDL in atherosclerotic plaques, acute coronary events, and the advancement of atherosclerosis.

Skin toxicity: Skin toxicity attributed to mercury and its compounds is responsible for various dermatological conditions, including acrodynia (pink disease), a condition where the skin takes on a pink hue upon exposure to heavy metals like mercury. Individuals with tattoos containing red pigments such as cadmium sulphide and mercury sulphide may experience localized inflammation within a few months of getting tattooed (37). Symptoms of acute contact dermatitis from substances containing mercury encompass moderate swelling, scaling, vesiculation, and irritation, making mercury poisoning a common cause of dermatological issues.

Genotoxicity: Specific mercury compounds, recognized as agents that cause birth defects, particularly affect the development of the central nervous system. While there is still debate regarding the possible connection between mercury exposure and cancer development, some studies suggest that mercury exhibits harmful activity at the genetic level, while others do not support such claims of DNA damage.

Treatment: EDTA proves more efficient in eliminating lead, cadmium, nickel, and other toxic heavy metals. Chelating therapy, surgical removal of mercury, oxygen administration via a face mask, etc.

Aluminium:

Aluminium, the third most abundant element discovered in the earth's crust, is naturally distributed in the atmosphere, soil, and water. The toxicity linked with Al is a key factor that restricts crop production in 67% of the acidic soil regions globally. Recent investigations into

environmental contamination have highlighted the significant threat posed by aluminium to humans, animals, and plants. Studies in environmental toxicology have suggested that aluminium has the potential to endanger humans, animals, and plants by triggering various diseases. Prolonged exposure to aluminium can induce oxidative stress in vital organs such as the brain, liver, and kidneys, thereby impacting the generation of free radicals and modifying the antioxidant capacities of enzymes (38).

Any interaction with aluminium holds the potential to disrupt or hinder various enzymes, leading to alterations in protein synthesis, nucleic acid function, and cell membrane permeability. Moreover, it can impact the levels of triglycerides in the bloodstream and their metabolic processes in the organism (39). Research findings have shown that aluminium promotes lipid peroxidation (LPO) while reducing the levels of glutathione (GSH), glutathione peroxidase (GSH-Px), glutathione S-transferase (GST), and catalase (CAT) activities in kidney tissue. The human exposure pathway to aluminium includes inhalation, ingestion, or dermal contact.

Nephrotoxicity: Involves an elevation in oxidative stress and lipid peroxidation that affect DNA and proteins, resulting in a decrease in GSH levels and the activities of GSH-Px, GST, and CAT. It also alters the functions of renal tubules related to p-amino hippuric acid transport, renal-tubular phosphate reabsorption, and sodium-water balance, inhibits Na+/K+ ATPase activity, and raises intracellular levels of free Fe+2, leading to oxidative stress.

Neurotoxicity: Neurotoxicity resulting from aluminium poisoning manifests as memory loss, tremors, uncontrolled movements, reduced coordination, muscle weakness, diminished curiosity, ataxia, speech impairments (such as dyspraxia, dysphasia, stuttering, and potential mutism), myoclonic jerks, severe convulsions leading to status epilepticus, changes in behaviour and consciousness levels like agitation, confusion, grand mal seizures, obtundation, coma, and potentially fatal chronic toxicity.

Symptoms: May include muscle weakness in proximal areas, bone pain, multiple fractures that do not heal, sudden mental status alterations, and early onset of osteoporosis.

Treatment: Chelation therapy is recommended for both acute and chronic aluminium poisoning cases, with deferoxamine mesylate being the only chelator proven to have positive effects in aluminium poisoning treatments.

Chromium: Chromium is widely distributed in various environmental sources like rocks, soil, animals, and plants. Its presence can be identified in solid, liquid, and gaseous forms. Chromium compounds exhibit significant persistence in sediments found in aquatic environments. Trivalent chromium is generally considered to have minimal harmful effects, especially when encountered in high contamination levels(40). The city of Kanpur is notably recognized for its significant tanning industry located in northern India. Residents inhabiting areas adjacent to tanning industrial operations face an elevated risk concerning their adverse health outcomes. The available human data regarding the toxicological implications of chromium Cr (III) in relation to oxidative stress and genotoxicity are exceedingly limited(41).

The toxicological effects of chromium, whether acute or chronic, are mainly associated with hexavalent compounds. Exposure to hexavalent chromium compounds can lead to notable toxic effects including dermatitis, Allergic skin responses, ulcers in mucous membranes, perforation of the nasal septum, asthma attacks, bronchial carcinomas, gastroenteritis, liver dysfunction, and kidney failure with reduced urine output can be caused by certain compounds like calcium chromate, zinc

chromates, strontium chromate, and lead chromates due to the considerable toxicity and carcinogenic attributes they possess are notable. Conversely, Chromium (III) assumes a crucial role as a dietary supplement, essential for both animals and humans, particularly in the realm of glucose metabolism (42). A diverse array of sources in the occupational sphere contribute to chromium exposure, encompassing materials like coatings, metal alloys, magnetic tapes, paint pigments, rubber, cement, paper, wood preservatives, leather tanning, and metal plating.

Route of Human Exposure: The pathway through which humans may encounter chromium involves several avenues, such as dermal contact, inhalation, and ingestion.

Hepatotoxicity: The induction of hepatotoxicity by Cr (VI) manifests in liver impairment, displaying distinctive histopathological alterations like hepatocyte steatosis, parenchymatous degeneration, and necrosis. The repercussions of Cr (VI) hepatotoxicity entail heightened levels of (ROS) (43). Associated health detriments stemming from Cr (VI) exposure encompass occupational asthma, eye irritation, perforated eardrums, respiratory discomfort, renal and hepatic dysfunction, pulmonary congestion, upper abdominal distress, nasal irritation, respiratory tract malignancies, skin issues, along with teeth erosion and staining. Cadmium's influence on the renal and skeletal frameworks can be profound, possibly impacting bone mineralization through renal dysfunction or skeletal trauma.

Geno toxicity: Assessments carried out on chromium within yeast and animal cells have revealed a plausible risk of genotoxic and carcinogenic outcomes. Individuals engaged in mining and industries utilizing Cr are identified as a group at cancer risk. Studies have demonstrated that Cr (VI) possesses the capacity to trigger diverse structural alterations in genetic material. These modifications include DNA-protein complexes, inter-DNA linkage, and nucleotide chain breaks observed in both living organisms and cultivated cells.

Dermatological toxicity: Instances of immediate systemic and dermal hypersensitivity reactions have been recorded among individuals sensitive to chromium, primarily due to inhalation exposure(44).

Ocular Effects: Direct contact of the eyes with airborne mists, dust, or aerosols containing chromium compounds can result in adverse ocular consequences

Hepatic Effects: Workers exposed to chromium trioxide in chrome plating industries have reported severe hepatic ramifications associated with Cr (VI), including cellular irregularities, necrosis, lymphocyte and histiocyte infiltration, and heightened Kupffer cells.

Symptoms: Such as stomach discomfort, duodenal ulcers, gastritis, weight loss, anaemia, thrombocytopenia, stomach cramps, frequent indigestion, irregular heartbeat, disrupted sleep, and headaches have been documented. Presently, an established treatment for chromium toxicity is lacking. Fatal outcomes frequently occur in cases of acute poisoning, irrespective of the intervention administered. Typically, managing individuals with acute, high-dose chromium exposure involves providing supportive and symptomatic care.

Iron:

Iron stands out as the most prevalent transition metal present on the earth's crust. It plays a crucial role as a vital nutrient for various organisms, acting as a cofactor in numerous essential proteins and enzymes. Inadequate regulation can result in its involvement in

reactions generating radicals that can harm biomolecules, cells, tissues, and the organism as a whole. Historically, iron toxicity has received considerable attention, especially from paediatricians, as children are highly vulnerable to iron poisoning due to regular exposure to products with high iron content. Iron toxicities is characterized by four distinct stages(45). The initial phase, occurring approximately 6 hours post an iron overdose, presents gastrointestinal symptoms like gastrointestinal bleeding, vomiting, and diarrhoea. Ingestion exceeding 60 mg/kg can cause severe toxicity, leading to significant morbidity and mortality.

Human exposure routes: Encompass inhalation, ingestion, or dermal contact.

Cardiovascular toxicity: Research has explored iron as a potential risk factor for coronary artery disease. Elevated iron levels in the heart can impair its ability to pump adequate blood for the body's needs, potentially resulting in congestive heart failure. Hemochromatosis may lead to abnormal heart rhythms, also known as arrhythmias.

Carcinogenicity: The carcinogenic properties of iron are linked to its catalytic impact on the formation of hydroxyl radicals, inhibition of essential cell functions, and stimulation of cancer cell growth. In both animal and human studies, excessive iron build-up at specific body sites has been associated with the development of primary tumours.

Nephrotoxicity: The intravenous administration of iron can adversely affect healthy kidneys, with the potential nephrotoxic effects being more pronounced in the presence of active nephropathy.

Neurotoxicity: Studies have demonstrated that iron has the ability to oxidize DNA bases, and its accumulation in certain neurodegenerative disorders may contribute to increased oxidative damage to the genome and hinder its repair processes. Iron accumulation, particularly in the hippocampus and cortex, has been linked to neurotoxicity, occurring before detectable Alzheimer's disease lesions.

Hepatotoxicity: In instances of high doses or deliberate/accidental overdoses, iron can induce severe toxic effects, including acute liver damage.

Symptoms of iron: Poisoning includes injury to the gastrointestinal mucosa, leading to nausea, vomiting blood, abdominal pain, and diarrhoea, as well as dark and potentially bloody stools. Liver damage, which may become apparent days after ingestion, and a metallic taste in the mouth are also observed.

Treatment: The treatment of iron poisoning typically involves whole bowel irrigation. In severe cases, chelation therapy may be necessary. Additional treatments may include rehydration, especially in cases of significant fluid loss due to vomiting and diarrhoea. In instances of difficulty breathing, the use of a breathing tube and ventilation machine may be required.

Chelating agents:

Chelating agents are substances utilized for the treatment of heavy metal poisoning through the process of binding with metallic elements within the human body, resulting in the formation of stable compounds that can be eliminated, primarily via the urine(46). The utilization of these chelating agents is crucial for the effective management of heavy metal toxicity, as they play a significant role in decreasing the metal accumulation in the body, thus alleviating symptoms and averting potential long-lasting harm. The selection of the appropriate chelating agent is contingent upon the particular metal implicated, the gravity of the poisoning, and the overall health condition

of the individual. (**Fig 5)** Chelating agents are specialized compounds employed in the treatment of heavy metal toxicity by binding to toxic metals, such as lead, mercury, and arsenic, to form stable, water-soluble complexes that are subsequently excreted via renal pathways. Common chelating agents include EDTA, dimercaprol, DMSA, and penicillamine, which serve to mitigate metal-induced damage to various organs and tissues, thereby facilitating detoxification and recovery processes.

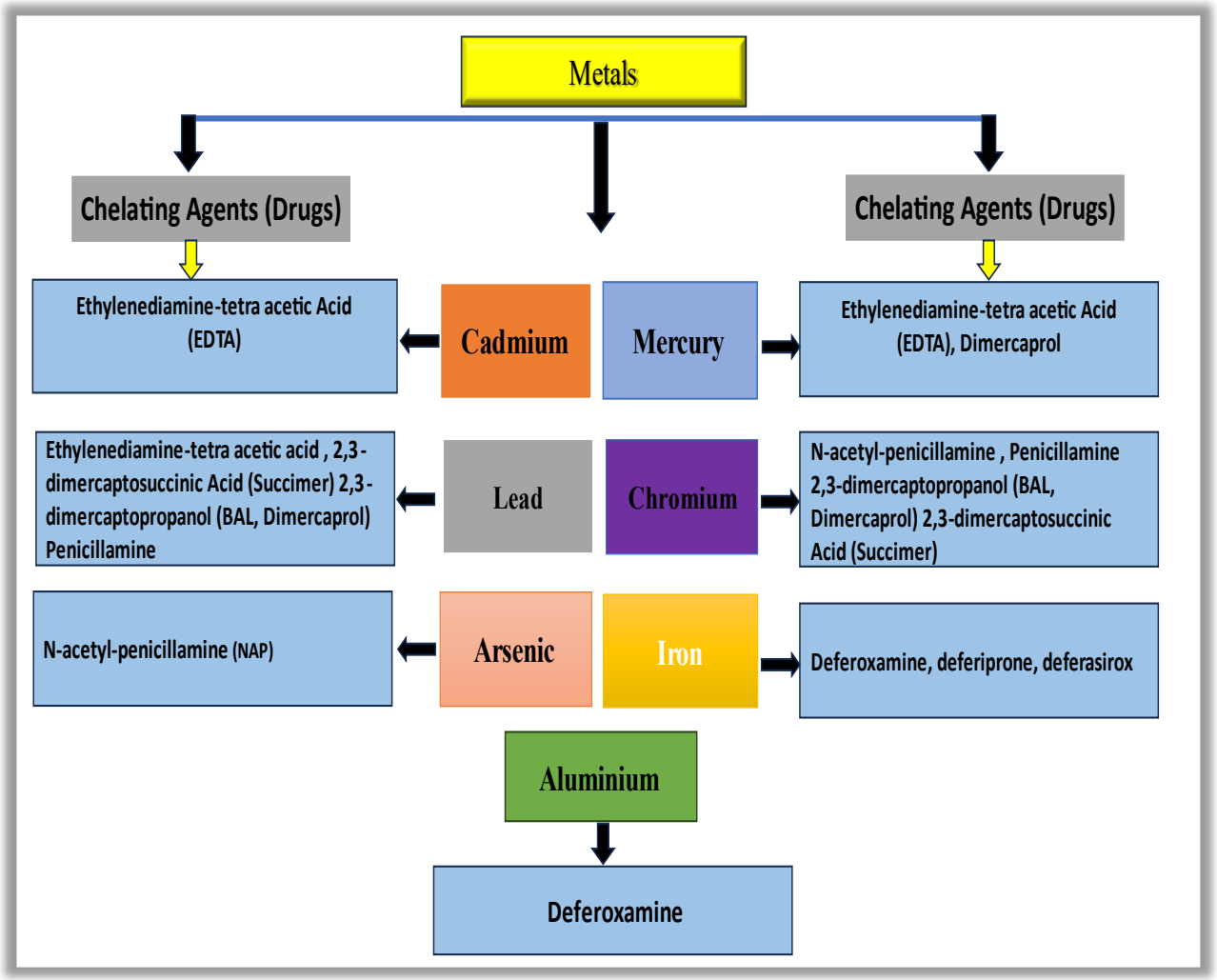

Figure 5: Chelating Agents Used for the Treatment of Heavy Metal Toxicity.

DISCUSSION

- The uncleanness of the environment, soils, and waters with heavy metals is a consequence of human activity. These metals are necessary in small quantities in our daily diet. However, in larger amounts, they can have reversible or irreversible and life-threatening effects.
- To effectively eliminate toxic metals from the human system, it is crucial to prevent their entry in the first place. This can be achieved by reducing exhaust and industrial pollution, among other measures. Additionally, heavy metals can enter our bodies through the ingesting of polluted food items.
- Techniques such as phytoremediation and intercropping can be employed to absorb and eliminate metal toxicity from soils, sediments, and waters. These techniques are effective in previous studies.

- The occurrence of heavy metals in soil is influenced by various factors, including pH, organic matter content, phosphorous levels, root zone, and the incorporation of chelating agents like (EDTA). Temperature variations also impact metal uptake by plants through their root systems.

Policy and Regulatory Framework for Managing Heavy Metal Pollution

The management and mitigation of heavy metal pollution are governed by diverse regulatory frameworks worldwide, reflecting varying levels of industrialization, enforcement capacity, and environmental priorities. Internationally, conventions such as the Minamata Convention on Mercury and the Basel Convention on Hazardous Wastes set foundational guidelines for controlling heavy metal emissions and managing hazardous waste. Regionally, frameworks such as the European Union's REACH Regulation (Registration, Evaluation, Authorization, and Restriction of Chemicals) impose stringent controls on the use of hazardous substances, including heavy metals, across member states. In the United States, the Clean Water Act and the Clean Air Act regulate heavy metal discharges into water bodies and air, supported by state-level initiatives to monitor and remediate contamination. Similarly, countries like Japan and South Korea have enacted robust pollution control laws, bolstered by advanced technological interventions. In contrast, many low- and middle-income countries face challenges due to limited resources, weak enforcement, and lack of comprehensive policies, exacerbating health risks from heavy metal exposure. Globally, the effectiveness of these frameworks varies significantly, with developed nations demonstrating better compliance and outcomes compared to their developing counterparts. Strengthening global cooperation, knowledge sharing, and capacity building is essential to harmonize regulatory standards and enhance the management of heavy metal pollution across diverse environments.

CONCLUSION

Heavy metal contamination is a significant issue produced by human activity, particularly in developing countries. Industries like chemicals, energy, and communication are major contributors to this problem. Waste disposal and excessive fertilizer use also worsen the situation. It is crucial to raise awareness about the detrimental effects of heavy metals, their symptoms, and strategies for reducing contamination. Preventive measures, such as increasing awareness and controlling intake, are essential in addressing this issue. Ongoing research in epidemiology, public health, and clinical fields will further enhance our understanding and management of metal exposure and environmental contamination.

Collaboration between healthcare providers, students, scientists, academicians, environmental health departments, and employers is necessary to prevent human exposure to heavy metals. Chemicals and metals persist as ongoing concerns. The challenges associated with metals continue to persist despite the implementation of new control measures and increased enforcement of regulations. Nevertheless, valuable insights gained from past experiences may aid in mitigating the inevitable consequences of heavy metal utilization in the context of advancing industrialization, both in less developed and more developed nations worldwide. Advancing our understanding of the origins of toxic metals and their harmful properties can mitigate the introduction of undesirable materials into our body consequently lowering the likelihood of developing various illnesses.

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