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Research Article

A Comprehensive Overview on Heavy Metal Poisoning: Toxicological Significances and Medico-legal Implications

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Abstract

Heavy metal toxicity poses a significant threat to human health, with varying acute and chronic manifestations depending on the metal involved. This study explores the toxicological profiles, few detection techniques, medico-legal relevance, and mechanisms of action of key metals, including arsenic, lead, mercury, cadmium, thallium, fluorine, copper, selenium, and iron in its discussion segment. Acute exposure to these metals often results in gastrointestinal, neurological, or systemic symptoms, while chronic exposure leads to long-term complications such as organ damage, neuropathy, or cognitive deficits. Analytical techniques like Atomic Absorption Spectroscopy (AAS), Inductively Coupled Plasma Mass Spectrometry (ICP-MS), and spectrophotometric methods enable accurate detection of metal toxicity. The medico-legal implications underscore their relevance in occupational exposure, environmental contamination, and intentional poisoning cases. Mechanistically, these metals disrupt cellular processes by interfering with enzymatic activity, oxidative balance, or essential metabolic pathways. This comprehensive overview highlights the importance of early detection and management to mitigate the health impacts of heavy metal exposure.

Keywords: Heavy Metal Toxicity; Acute Exposure; Toxicological Profiles; Medico-Legal Relevance

Introduction

Acute and chronic poisoning due to exposure to various chemical substances can lead to considerable morbidity and mortality. In cases of suspected intoxication, the examination relies on a thorough assessment of exposure history, physical examination, and laboratory evaluations. Heavy metals, including lead, cadmium, mercury, and metalloid arsenic, represent some of the most significant threats to human health. Typically, heavy metals are characterized by a density exceeding 5 g/cm3; however, a universally accepted definition is lacking. While their reactivity contributes to their potential toxicity, these metals also play vital roles in essential physiological functions. For instance, iron is crucial for oxygen transport, zinc is important for metabolism, and manganese and selenium are involved in oxidative stress defense. In contrast, elements like cadmium and bismuth lack recognized beneficial biological functions and are primarily regarded as toxic [1,4,5,12].

Most cases of poisoning arise from accidental exposures in environmental or occupational settings; however, chemical element poisonings can also occur as a result of suicide or homicide attempts. Metals like lead and mercury are more frequently associated with environmental exposure due to their prevalence in the surroundings. Conversely, arsenic and thallium are two elements commonly linked to criminal poisoning incidents. This underscores the necessity of obtaining a comprehensive history of the victim or patient in both clinical and forensic contexts for suspicion and presumptive diagnosis, with various aspects of intoxications being examined. This study aims to build upon that foundation by thoroughly exploring the pathophysiology, clinical manifestations, forensic characteristics, and potential exposure sources related to various elements. These include heavy metals such as thallium, lead, copper, mercury, iron, cadmium, and bismuth, as well as other elements like arsenic, selenium, and fluorine. Certain distinctive signs may indicate the presence of a specific element, facilitating the early identification of intoxication and the prompt initiation of emergency treatment or examination. As Paracelsus famously stated, "Poison is in everything, and nothing is without poison. The dosage makes it either a poison or a remedy" [13].

Materials and Methods

An online literature search was performed utilizing PubMed, Academia, Research gate, Scribd, Google Scholar, Elsevier, Springer and other search Engines, focusing on the source- natural and anthropogenic, signs and symptoms, medical history, physical examination, pathophysiology, and both clinical and forensic diagnoses related to heavy metal intoxications, specifically thallium, lead, copper, mercury, iron, cadmium, and bismuth. Additionally, other chemical elements such as arsenic, selenium, and fluorine were included in the search. The term "intoxication" was systematically combined with the aforementioned metals and elements, along with their associated clinical and forensic manifestations. To enhance the breadth of information, a thorough review of retrieved journal articles, governmental publications, and relevant books was conducted. This investigation encompassed literature in multiple languages, ensuring a comprehensive collection of scientific documents, including books, articles, and governmental resources, for this review. Each metal discussed in its entirety following introduction, nature, source, applications, exposure pathway into the body, effect produced, sign, symptoms and findings etc. providing a complete 360 degree picture to the reader of the present paper.

Thallium

Thallium (Tl) is a hazardous metal that was unintentionally identified in 1861 when a sulfuric acid plant emitted burning dust, revealing a vivid green spectral line that soon disappeared. Historically, thallium was primarily utilized as a rodent poison; however, due to a rise in accidental poisonings, many nations have prohibited its use for this purpose. Additionally, thallium's application in treating syphilis, gonorrhea, tuberculosis, and trichophytosis has been halted. Prior to 1930, thallium was employed in treatments for scalp ringworm because of its hair-removing properties, but the occurrence of pediatric fatalities led to the discontinuation of this method.

In contemporary applications, thallium is involved in producing green fireworks, imitation jewelry, optical lenses, semiconductors, low-temperature switching devices, and scintillation counters, serving as both a chemical catalyst and a pigment in artistic paints. The lethal dose of thallium is estimated to be around 10–15 mg/kg. In the medical field, it is utilized in myocardial perfusion scintigraphy and for identifying certain malignant tumors. Due to its swift distribution and absorption in the myocardium, small, nontoxic amounts of radioactive thallium are still employed today for diagnosing cardiac dysfunction.

Thallium salts are characterized by their lack of taste and odor, along with their capacity to dissolve completely in liquids. They are absorbed rapidly and can evade detection in standard toxicological screenings, making them particularly suitable for use in criminal poisonings. However, such incidents are relatively uncommon in many Western countries. Poisoning typically results from the ingestion of thallium salts, although there have been instances of exposure through inhalation of dust or fumes during smelting, skin absorption, and even overdoses related to cocaine and heroin use.

Once thallium enters the body, it is quickly distributed across various tissues. It binds to the Na^+/K^+-ATPase channel with a binding affinity ten times greater than that of potassium, disrupting its normal function. As thallium accumulates within cells, it interferes with the activity of several enzymes by attaching to sulfhydryl groups on the mitochondrial membrane, which hampers cellular respiration, disturbs calcium balance, and interacts with riboflavin and its derivatives. Furthermore, thallium's binding to glutathione inhibits its activation and the body's ability to metabolize heavy metals, leading to their excessive accumulation.

The prompt identification of thallium poisoning can be challenging because of the range of non-specific symptoms it presents. Early signs may include acute polyneuropathies, characterized by painful sensations in the hands and legs, especially in the soles of the feet, along with weakness primarily affecting the legs. Gastrointestinal issues such as vomiting, diarrhea, abdominal discomfort, or constipation also warrant consideration of thallium exposure. Additionally, later symptoms may involve hair loss and various skin conditions. Both peripheral neuropathy and gastrointestinal symptoms are among the initial indicators of thallium poisoning. The early dermatological manifestations are not unique to this type of poisoning and can include skin peeling with keratosis on the palms and soles, acne-like or pustular breakouts on the face, angular stomatitis, and painful inflammation of the tongue. The classic triad of symptoms typically develops within 2 to 3 weeks, featuring dermatological changes such as hair loss from the scalp and the outer edges of the eyebrows, while the eyelashes, pubic hair, and underarm hair may remain intact. Concurrently, transverse white lines on the nails, known as Mee's lines or Aldrich–Mee's lines, may appear. The acute hair loss is believed to result from thallium's interaction with cysteine sulfhydryl groups in hair, while dermatitis, Mees' lines, and neuropathy are likely consequences of a secondary deficiency in riboflavin.

A notable characteristic of acute thallium poisoning is the appearance of tapered or bayonet-shaped hair. This abnormality manifests as anagen hair with a tapered dystrophic root, along with darkened hair roots observable under a light microscope. In humans, this condition can be identified as soon as four days post-exposure to thallium and represents an optical effect resulting from the buildup of gaseous inclusions that cause light diffraction. This observation can serve as a significant indicator for diagnosing thallium poisoning prior to the development of alopecia.

Arsenic

Arsenic (As) is a widely distributed metalloid present in the Earth's crust and soil, with contamination primarily resulting from water runoff and leaching. Historical records indicate its use as far back as 400 B.C. by physicians in ancient Greece and Rome, and it continues to be utilized in traditional medicine practices in China and India. In contemporary Western medicine, arsenic has been employed to treat advanced African trypanosomiasis and acute promyelocytic leukemia. Additionally, it plays a role in mining (specifically smelting), the production of ceramics, agricultural pesticides, and in the electronics sector for semiconductors and lasers.

Arsenic exists in three oxidation states: elemental, trivalent arsenite, and pentavalent arsenate. While the elemental form is non-toxic, arsenite is significantly more toxic, possessing ten times the toxicity of arsenate. This metalloid can be found in three chemical forms: organic, inorganic, and arsine gas. Organic arsenic is generally low in acute toxicity, whereas inorganic arsenic and arsine gas are highly hazardous. Naturally occurring arsenic in seafood consists of non-toxic organic compounds like arsenobetaine, which can result in elevated arsenic levels in urine. Although most cases of acute arsenic poisoning stem from accidental ingestion of arsenic-laden pesticides, instances of suicide or homicide are less frequent. Nonetheless, arsenic is often regarded as a prevalent agent in homicides, earning it the moniker "Poison of Kings and the King of Poisons."

While arsenic can be absorbed through the lungs and skin, chronic exposure primarily occurs through the consumption of geologically contaminated water. Prolonged ingestion leads to accumulation in vital organs such as the liver, kidneys, heart, and lungs. Even after most arsenic is expelled from these organs, trace amounts can persist in keratin-rich tissues, including nails, hair, and skin.

Arsenic's interaction with sulfhydryl groups in specific tissue proteins disrupts numerous enzyme systems essential for cellular metabolism. The toxic dose of inorganic arsenic is roughly 0.6 mg/kg. In cases of acute arsenic poisoning due to ingestion, typical gastrointestinal symptoms arise, such as abdominal discomfort, nausea, vomiting, and severe watery or bloody diarrhea. These symptoms may progress to hypotension, heart failure, pulmonary edema, and shock, often resulting from cardiomyopathy, ventricular arrhythmias, and capillary dilation leading to fluid loss into third spaces. Generally, peripheral neuropathy manifests 2 to 8 weeks post-exposure, although it can occur within hours following a significant exposure. This condition presents as a bilateral and symmetric sensorimotor neuropathy, which may be mistakenly identified as Guillain–Barré syndrome. Chronic exposure to arsenic is linked to several cancers, particularly in the skin, lungs, liver, bladder, and kidneys, with increased incidence in groups exposed to arsenic through occupational or environmental means.

Elevated arsenic levels, whether from ingestion or inhalation, lead to acute arsenicosis symptoms, which the World Health Organization defines as a chronic health issue resulting from prolonged ingestion (at least six months) of arsenic exceeding safe limits, typically characterized by distinctive skin lesions, with or without internal organ involvement. Within 1 to 4 weeks, various skin manifestations can develop, ranging from raindrop pigmentation to fine freckles and spotted pigmentary alterations, as well as hypopigmented lesions on the trunk and limbs, alongside mild to severe diffuse hyperpigmentation or melanosis. While the pigmentation is most pronounced on the trunk, it can spread or diffuse, particularly affecting skin folds.

Macular depigmented areas can sometimes manifest on otherwise normal skin or against a hyperpigmented backdrop, a condition referred to as leucomelanosis. Mucous membranes, including the underside of the tongue and the buccal mucosa, may exhibit distinctive pigmentation patterns characterized by blotchy discoloration. Approximately five weeks following arsenic exposure, a transverse white line, measuring 1–2 mm in width, may emerge above the lunula of each fingernail, known as Mee's lines. This phenomenon results from disruption in the nail matrix and can be observed in both acute and chronic cases of poisoning, although it is not exclusive to arsenic. The most prevalent and initial cutaneous manifestation is melanosis. Hyperkeratosis of the palms and soles is regarded as a hallmark of chronic arsenicosis, typically developing after extended arsenic consumption. In research conducted by Rattner et al., it was noted that with a daily exposure of 4.75 mg, hyperpigmentation became evident after six months, while hyperkeratosis was observed three years later.

Lead

Lead (Pb), a heavy metal referred to in Latin as plumbum, meaning "liquid silver," has historically been associated with the terms plumbism and saturnism, which denote lead poisoning. It is believed that numerous Roman leaders may have suffered from lead toxicity, resulting in neurotoxic effects and infertility. The onset of the industrial revolution marked a significant rise in the use of lead-containing products, particularly in gasoline and lead-based paints. In England, a notable incident of lead poisoning occurred in 1700, linked to cider contaminated with lead, leading to severe abdominal pain among the affected individuals, a condition that became known as "Devonshire Colic." Benjamin Franklin documented the symptoms of lead exposure, including abdominal pain and peripheral neuropathy, in 1773. Although lead poisoning has not been entirely eradicated, its prevalence has gradually decreased in developed nations due to enhanced monitoring of both industrial and household lead exposure. Conversely, in developing countries, lead poisoning remains a significant issue and is recognized as one of the most common forms of occupational poisoning globally. The primary route of exposure is through inhalation; however, in cases of pediatric plumbism, the "pica syndrome" is often a prevalent factor.

The production of lead batteries, colored paints, lead compounds, and products made from rubber and glass can generate sufficient lead dust in the atmosphere to pose a poisoning risk. In the demolition sector, inhalation of lead oxide fumes can lead to toxicity. Members of gun clubs and their instructors are at an elevated risk of lead absorption due to exposure to lead dust and fumes from bullets and explosive materials. Additionally, the use of lead-based paints and the production of polyvinyl chloride (PVC) plastics also contribute to lead exposure, although the final products are considered safe.

Lead is a metal characterized by its electropositive nature, which exhibits a strong affinity for sulfhydryl groups. This interaction inhibits enzymes that depend on sulfhydryl groups, particularly those involved in intracellular calcium channels. Consequently, this leads to a reduction in heme synthesis, dysfunction in proximal renal tubules, and impaired osteoblast function. Additionally, lead influences the vasomotor responses of smooth muscle by affecting Ca2+-ATPase activity, potentially resulting in abdominal discomfort. Moreover, lead can compromise the blood-brain barrier's integrity by disrupting the intracellular connections within capillary endothelium. This disruption enhances capillary permeability into the central nervous system, leading to an increase in intracranial fluid levels. The presence of lead also impacts various neurotransmitters, including acetylcholine, γ-aminobutyric acid (GABA), and dopamine, triggering their unregulated release. This unregulated release can block N-methyl D-aspartate (NMDA) glutamate receptors and elevate protein kinase C levels.

In 2012, the Centers for Disease Control and Prevention in the United States set the threshold for lead levels in blood at 10 μg/dL for adults and 5 μg/dL for children. The primary symptoms observed in young children, who are particularly vulnerable, include irritability, decreased appetite, weight loss, learning and behavioral challenges, abdominal pain, vomiting, constipation, anemia, and renal impairment.

Key indicators of lead poisoning include abdominal pain, anemia characterized by basophilic stippling of red blood cells, blue-black deposits on the gums, and a lead line visible on joint radiographs. The blue-purplish lines on the gums, referred to as "Burton's lines," result from a reaction between circulating lead and sulfur ions produced by oral bacteria, leading to the formation of lead sulfide deposits at the interface of teeth and gums.

Fluorine

Fluorine (F) stands out as the most electronegative element and ranks as the thirteenth most prevalent element found in rock phosphates, minerals, and the Earth's crust in its ionic state. It plays a crucial role in the proper growth and development of various bodily organs, particularly bones and teeth. Consequently, it is recognized as one of the vital microelements necessary for the organism. Since 1945, fluoride has been introduced as a supplement in numerous public drinking water systems to combat dental decay. Over recent decades, its application in various forms and concentrations for the prevention of dental caries has seen a consistent rise due to its effectiveness. The US Centers for Disease Control has identified water fluoridation as one of the top ten public health achievements of the last century. Fluorine negatively impacts enamel formation by decreasing calcium levels in the matrix, which ultimately disrupts protease activity, hindering or halting protein breakdown within the enamel matrix. This impairment is influenced by both the duration and dosage of exposure. Such effects can lead to interruptions in enamel development and result in hypomineralization, characterized by increased porosity, which may manifest as white or yellowish spots on tooth surfaces. In the skeletal system, fluorine has an approximate half-life of seven years. About half of the fluoride integrates into hydroxyapatite crystals by substituting hydroxide ions, thereby modifying the structure and dimensions of these crystals. Additionally, fluoride appears to affect bone turnover by influencing the gene expression of the RUNX family transcription factor 2 (Runx2) and the receptor activator of nuclear factor kappa-B ligand (RANKL). It also impacts the expression of osteocalcin and osteoprotegerin while enhancing osteoblast activity.

Fluoride has increasingly been incorporated into dental care products and food sources, particularly through fluoridated water, leading to multiple avenues of fluoride exposure that are associated with a rise in dental and skeletal fluorosis cases. When fluoride concentrations exceed 1.5 mg/L (1.5 ppm) in drinking water, the risk of developing dental and skeletal fluorosis escalates. Nutrition plays a vital role in regulating serum fluoride levels, as certain ions like calcium, magnesium, and aluminum can reduce the bioavailability of fluoride. The prevalence of dental fluorosis is considered the most significant risk linked to community water fluoridation. First identified by Trendley Dean in 1937, dental fluorosis is a developmental disorder of the enamel caused by excessive intake and repeated exposure to small amounts of fluoride throughout all phases of tooth development. The severity of fluorosis is influenced by various factors, particularly the quantity and timing of fluoride exposure. Mild dental fluorosis is characterized by a white opaque appearance of the enamel, resulting from increased subsurface porosity. The initial signs include thin white horizontal lines on the tooth surface, accompanied by white opacities at the recently erupted incisal edge. These white lines align with the 'perikymata,' which are horizontal ridges on the tooth surface that correspond to the incremental lines in enamel known as Striae of Retzius. With higher fluoride exposure, these white enamel lines become more pronounced and thicker, and irregular cloudy patches along with thick opaque bands may develop on the affected teeth. As dental fluorosis worsens, the entire tooth may take on a chalky white appearance and lose its translucency. Prolonged or excessive fluoride exposure can impact deeper enamel layers, leading to a reduction in mineralization.

In severe instances, the presence of porosity, pitting, and brown discolorations associated with delicate enamel can often be observed on the tooth's surface. However, a definitive diagnosis of the condition should be established through a thorough patient history and should not be mistaken for other forms of discoloration or dental stains that exhibit a similar clinical appearance, such as the hypomaturation variant of amelogenesisimperfecta. The upper incisors are particularly susceptible to the effects of fluoride, likely due to exposure to air resulting from inadequate lip closure. Consequently, the incisal area may remain dry for extended periods, making any porosities more apparent. Furthermore, since the incisal edges and cusp tips lack a covering of dentin, any changes in pore volume in these regions will manifest differently than in other areas of the teeth. This can create the impression that the incisal section is more severely affected than the rest of the tooth surface, even though both areas may have similar levels of porosity.

Some researchers have reported cases of severe juvenile skeletal fluorosis, linking it to insufficient dietary calcium intake. Like dental fluorosis, skeletal fluorosis arises from prolonged exposure to elevated fluoride levels through ingestion or inhalation. The excessive accumulation of fluoride in bones and joints disrupts bone mineral metabolism, leading to bone resorption and abnormal calcium levels. While skeletal fluorosis is often asymptomatic, as the bones and joints weaken, patients may experience pain in the hands, feet, and lower back, along with muscle weakness, chronic fatigue, and painful joint stiffness during movement. Additional complications may include vertebral fusion, kyphosis with limited spinal mobility, flexion contractures in the lower limbs, and restricted expansion of the chest wall.

Copper

Copper (Cu) is a dense metal found naturally in various mineral forms, with chalcopyrite being the most prevalent and economically important. The classification of copper deposits is based on their formation processes. Porphyry deposits, typically located in the mountainous regions of Western North and South America, are linked to igneous intrusions and account for approximately two-thirds of the global copper supply. In contrast, deposits found in sedimentary rocks, such as those in the Central African Copperbelt and the Zechstein basin in Eastern Europe, represent about 25% of copper reserves. The unique properties of copper, including its malleability, resistance to corrosion, and excellent conductivity for heat and electricity, make it a preferred material for a wide range of applications across domestic, industrial, and advanced technology sectors. Presently, copper is utilized in civil engineering, power generation and distribution, the manufacturing of electronic devices, the production of industrial machinery and transportation vehicles, heating and cooling systems, telecommunications, motors, wiring, radiators, and frequently touched surfaces like brass doorknobs. Additionally, copper sulfate is widely employed in agriculture as a pesticide, in the leather industry, and in homemade adhesives, while its combustion is a common ritual among Buddhists and Hindus. Moreover, copper is a vital trace element in the human body, serving as a cofactor for numerous enzymatic processes, which underscores the importance of maintaining copper homeostasis. Excessive copper levels can lead to toxicity, primarily due to its ability to generate reactive oxygen species.

Copper toxicity, known as copperiedus, can arise from two primary sources: it may be congenital due to a metabolic defect or secondary due to factors such as excessive intake, heightened absorption, or diminished excretion linked to various pathological conditions. Secondary causes of copper poisoning can occur from the consumption of acidic foods prepared in uncoated copper cookware, exposure to high levels of copper in drinking water, the use of topical creams containing copper salts for burn treatment, environmental sources, or even in cases of suicide attempts, where the lethal dose ranges from 10 to 20 grams. Children are particularly susceptible to copper intoxication due to their attraction to the vibrant color of hydrated copper sulfate crystals. Symptoms of acute copper poisoning can vary widely and may include a metallic taste, nausea, vomiting, abdominal discomfort, heart failure, liver failure, kidney failure, intravascular hemolysis, and potentially death. Wilson's Disease, a genetic autosomal disorder affecting copper metabolism, is caused by mutations in the ATP7B copper transporter gene, with an incidence of approximately 1 in 30,000 to 1 in 100,000 individuals.

Rare mutations that lead to a complete lack of ATP7B protein function can result in severe manifestations of Wilson's Disease. Over time, excess copper accumulates in the liver and brain, leading to complications such as cirrhosis, acute liver failure, and a range of nonspecific neuropsychiatric symptoms, including difficulties with speech, swallowing, tremors, coordination issues, and problems with concentration.

Copper accumulation in the cornea leads to the formation of the distinctive Kayser–Fleischer ring. These rings serve as one of the few critical diagnostic markers in clinical practice. First identified by Kayser in 1902, further investigations by Fleischer in 1909 expanded on this discovery. It wasn't until 1949 that Gerlach and Rohsrschneider confirmed that these rings were composed of copper. The Kayser–Fleischer ring exhibits a golden brown, green, or yellow hue around the corneal edge, resulting from copper deposits in Descemet's membrane. Typically, a slit lamp examination is necessary for accurate diagnosis, although in some cases, the rings can be seen without any special equipment. These rings are present in over 99% of individuals with neuropsychiatric disorders, yet only appear in 25–50% of those with liver disease or in pre-symptomatic stages. The ring often disappears with appropriate treatment, and its persistence or reappearance indicates uncontrolled copper levels.

In 1922, Siemerling and Oloff described a rare ocular manifestation of Wilson's disease known as the "sunflower cataract." They noted that the lens changes in patients with Wilson's disease bore resemblance to those caused by an intraocular copper-containing foreign body. The occurrence of sunflower cataracts is less frequent than that of Kayser–Fleischer rings, as they typically manifest in the later stages of the disease, and early diagnosis of Wilson's disease can reduce their prevalence. The sunflower cataract features a thin, central opacification located just beneath the anterior capsule, covering one-third to one-half of the anterior lens pole. This central opacification is surrounded by additional opacities arranged in a ray-like pattern, resembling the petals of a sunflower, which is how it got its name. It is important to note that the sunflower cataract is not classified as a "true" cataract.

Selenium

Selenium (Se) is a crucial non-metal chemical element that plays an essential role in various biological systems within the human body. As a vital trace element, selenium is a key component of over two dozen selenoproteins, which are integral to processes such as reproduction, thyroid hormone metabolism, DNA synthesis, and protection against oxidative damage and infections. Remarkably, the gastrointestinal tract absorbs a significant portion (80–95%) of water-soluble selenium compounds found in food. Once absorbed, selenium is processed by the liver and transported by selenoprotein P to various organs, with the highest concentrations found in the kidneys, liver, spleen, testicles, and skeletal muscles.

Despite its importance, selenium can be toxic, a fact that has been recognized in livestock for centuries, although the exact mechanisms remain unclear. In the early 1930s, a condition known as "alkali disease," characterized by hair and hoof loss, was identified as selenium toxicosis. Selenium has one of the narrowest margins between dietary deficiency (less than 40 μg/day) and toxic levels (400 mg/day), making it crucial to monitor intake levels for both humans and animals. The recommended dietary allowance for individuals aged 14 and older is 55 μg/day. Generally, a balanced diet that includes meat, grains, vegetables, and nuts provides sufficient selenium, eliminating the need for supplements.

Selenium-rich regions have been identified in places like South Dakota (USA), Venezuela, and China. While the mechanisms of selenium toxicity in cellular metabolism are not fully understood, it is believed that selenium can interact with glutathione to create reactive selenotrisulfides, leading to oxidative stress. This oxidative stress can damage cell membranes and macromolecules, ultimately compromising cell integrity and resulting in necrosis or cell death. Different forms of selenium can lead to varying levels of toxicity, such as the selenide form of selenious acid. Selenium experiences a fascinating triphasic elimination process that varies with its concentration levels. It accumulates in various organ tissues, and its gradual clearance mechanism contributes to the persistence of symptoms. This element finds its way into numerous commercial uses, heightening the risk of human exposure. It plays a role in solar energy, semiconductor manufacturing, and the production of electronics and ceramics. Additionally, selenium is incorporated into steel and copper alloys, utilized in photographic cells, and is essential in the creation of glass and paint. It also aids in rubber vulcanization, serves as a component in nutritional supplements, and is found in shampoos. Furthermore, it is combined with other compounds to enhance the polishing of metallic surfaces on firearms.

The ongoing discussion regarding selenium's potential protective benefits against cardiovascular diseases, myocardial alterations, and cancer has led to a surge in the popularity of dietary supplements containing selenium in various organic and inorganic forms. Unfortunately, manufacturing errors have resulted in dangerously high levels of selenium in some of these supplements. Instances of acute selenium poisoning can occur due to accidental ingestion or intentional self-harm. Common symptoms include severe irritation of the respiratory tract and mucous membranes, a metallic taste, nasal tingling, and rhinitis. In more severe cases, lung edema and bronchopneumonia may develop. Selenium dioxide (SeO2) can also cause skin erythema and necrosis.

Selenosis refers to the symptoms arising from selenium poisoning. When comparing acute and chronic forms of poisoning, chronic selenosis typically stems from the ingestion of organic compounds found in selenium-rich plants or animals, dietary supplements, or exposure to inorganic selenium in industrial settings. Most instances of acute selenium poisoning are linked to industrial mishaps, often through inhalation of selenium dust, fumes, or hydrogen selenide, which irritate the respiratory system.

Commonly reported symptoms include gastrointestinal issues, a metallic taste in the mouth, a garlic-like odor on the breath, hair loss or brittle hair, changes in nails such as red pigmentation and paronychia, diminished mental alertness, skin irritation, mucosal discomfort, and a condition known as "rose eye," characterized by swollen, pink eyelids. The distinctive garlic scent in breath and sweat arises from the formation of dimethyl selenide, indicating elevated selenium levels in the bloodstream. More severe cases can lead to musculoskeletal problems, nerve damage, liver failure, coma, and even death.

In regions where selenium levels in the soil are notably high, the most frequently observed symptoms include hair loss and nail abnormalities. Hair loss is attributed to the disruption of keratin's structural proteins, as selenium forms disulfide bonds that impair hair structure, leading to loss. Unlike hair loss caused by hormonal factors or alopecia areata, selenium-induced hair loss is widespread. Affected hair becomes dry, brittle, and easily breaks off at the scalp, often resulting in a rash and itching. Hair may also fall from other areas, such as the eyebrows, beard, armpits, and pubic region. New hair growth tends to be depigmented and lacks shine, while nails become fragile, often displaying white spots and longitudinal streaks.

Mercury

Mercury, denoted by the symbol Hg, is a hazardous heavy metal that ranks approximately 67th in terms of natural occurrence among elements found in crustal rocks. It exists in the environment in three primary chemical forms: elemental or metallic mercury, inorganic mercury compounds, and organic mercury compounds, such as methyl, phenyl, and alkyl derivatives, each exhibiting distinct pharmacokinetic behaviors. The historical utilization of mercury can be traced back to around 1500 B.C., when the Chinese first extracted and employed a substance known variously as cinnabar, vermilion, or Chinese red. Aristotle is thought to have referred to mercury as "quicksilver," a name that persists to this day. Subsequently, the Mesopotamians named the planets after metals, with Mercury being the sole metal that retains its name as a planet. The metallic variant of mercury is also referred to as quicksilver or liquid silver, owing to its silvery, liquid form. For over three millennia, mercury and its compounds have been utilized for various medical purposes, including as cathartics, antiparasitics, treatments for syphilis, antipruritics, antiseptics, anti-inflammatory agents, diuretics, vermifuges, dental amalgams, and alternative therapies. In the 15th century, mercury was employed in Western Europe as a treatment for syphilis, which led to the saying, "two minutes with Venus, two years with mercury. Currently, more than 60 industries are exposed to mercury in the workplace, including those involved in the production of glass thermometers, neon lights, paper, paint, jewelry, insecticides, fungicides, batteries, barometers, chlorine, and caustic soda, as well as dental practices. Environmental mercury exposure primarily arises from coal combustion in power plants, leading to water contamination, and from the improper disposal of batteries, paints, lights, and other industrial materials. As fish consumption has risen and water pollution has increased, the environmental impact of mercury contamination in aquatic life has become a significant concern.

Mercury affects cellular functions by depleting thiol levels in mitochondria and binding to enzymes and proteins that contain sulfhydryl groups, ultimately leading to cell death through apoptosis. While there is some overlap in the clinical symptoms associated with different mercury forms, certain symptoms or combinations are more frequently linked to specific types. Consequently, the most commonly observed clinical syndromes for each mercury variant will be discussed individually.

Elemental mercury is a heavy, nonwetting liquid that is both volatile and lipophilic, capable of transforming into an odorless gas at room temperature, which can lead to clinical toxicity when present in significant quantities. It is one of the rare metals that exist in a liquid state at ambient temperatures. The vapor pressure of mercury increases approximately twofold with every 10 °C rise in temperature, meaning that heating it can greatly enhance both exposure and toxicity. These unique properties have allowed mercury to be widely used in various commercial products, including thermometers, barometers, thermostats, electronic devices, batteries, dental amalgams, and even some traditional home remedies.

The primary route of toxicity from elemental mercury is through inhalation of its vapors, particularly in occupational settings where improper handling, accidental spills, or inadequate ventilation occur. Additionally, the accidental breakage of mercury-containing items, like thermometers, can lead to exposure in residential areas. Even a small quantity of mercury from a thermometer can lead to poisoning in a heated indoor environment. Elemental mercury interacts with sulfhydryl groups on cell membranes, disrupting the production of proteins and nucleic acids, affecting calcium balance, and altering protein phosphorylation, which ultimately leads to oxidative stress and cellular injury. More than 80% of inhaled mercury vapor is absorbed and can quickly cross cellular membranes, including the blood-brain barrier and the placenta. The primary organs affected by elemental mercury vapor are the lungs and brain, with the kidneys being less impacted. In the human body, elemental mercury has a prolonged half-life of about 60 days. In contrast to the respiratory system, absorption through the gastrointestinal tract is minimal, and skin exposure typically has little clinical significance. Intravenous exposure to mercury is rare and usually occurs in situations of self-harm.

Acrodynia, derived from Greek meaning “painful extremities,” is also referred to as pink disease, Feer syndrome, or Feer-Swift disease. This rare condition primarily arises from exposure to elemental mercury, though it can also result from contact with phenyl mercury and mercury salts. It predominantly affects infants and children, who are often attracted to the shiny, metallic appearance of elemental mercury. When children come into contact with this substance through their skin, they may develop acrodynia.

The syndrome is characterized by several key symptoms: (i) autonomic disturbances such as excessive sweating, high blood pressure, and rapid heart rate; (ii) skin and dental manifestations including itching, a red rash, pink nail discoloration, inflamed gums, pink patches on the skin, mouth ulcers, and loose teeth; and (iii) musculoskeletal issues like muscle weakness and poor tone. The autonomic symptoms stem from mercury’s ability to disrupt the coenzyme S-adenosylmethionine, which in turn inhibits the enzyme catechol-o-methyltransferase, leading to increased catecholamine levels in the body. This rise in catecholamines can result in hypertension, sweating, and tachycardia, resembling the symptoms of a pheochromocytoma. Analysis of a 24-hour urine sample from affected individuals typically reveals elevated urinary catecholamines, although these levels are generally lower than those found in cases of pheochromocytoma.

The traditional triad of intention tremors, erethism, and gingivitis represents the primary symptoms associated with prolonged exposure to elemental mercury vapors. In addition to gingivitis, hyperpigmentation frequently manifests as a blue or black line along the gum line. Reports often highlight gingivitis and excessive salivation as the most common issues experienced. It is important to recognize that there is considerable clinical overlap between the symptoms of elemental mercury poisoning, particularly acrodynia, and those seen in Kawasaki disease.

Inorganic mercury

Inorganic mercury is comprised of mercuric and mercurous salts, with mercury sulfide (HgS), also known as cinnabar or vermillion, being the most prevalent. This compound is often utilized as a pigment. Mercurial salts have found applications across various sectors, including medicine as antiseptics (such as mercuric chloride), cosmetics, explosives, dyes, pigments, and antifungal agents in paints.

In contrast to its elemental counterpart, mercury salts are highly corrosive to the gastrointestinal tract, making ingestion the most frequent cause of poisoning. Additionally, inorganic mercury can be rapidly absorbed through the skin, leading to systemic mercury toxicity even from topical applications. Following the ingestion of mercurial salts, individuals may experience oral pain or burning sensations—known as stomatitis—along with gastrointestinal symptoms like nausea, vomiting, diarrhea, hematemesis, bloody stools, or abdominal pain. Severe toxicity can lead to colitis characterized by necrosis or sloughing of the gastrointestinal mucosa, as both the gastrointestinal system and kidneys are primary targets in acute inorganic mercury poisoning. Repeated topical application may result in hyperpigmentation, swelling, and a vesicular or scaly rash, with hyperpigmentation appearing as a gray-brown discoloration, particularly pronounced in the skin folds of the face and neck. Similar to elemental mercury, inorganic mercury exposure can also lead to acrodynia and erethism.

Organic mercury

The harmful effects of elemental and inorganic mercury have been recognized for centuries; however, the dangers posed by organic mercury have only recently gained attention, primarily due to significant environmental incidents that highlighted its toxicity. Methylmercury, a type of organic mercury compound, has been responsible for the highest number of poisoning cases and is the most common and hazardous form of mercury exposure outside of workplace settings. In the early 1900s, organic mercury compounds were utilized in various industrial and medical applications, including as preservatives, antiseptics, and seed treatments. Today, the primary route of organic mercury exposure for the general population is through the consumption of predatory fish, a phenomenon driven by biomagnification. Inorganic and elemental mercury, often released through industrial waste and pollution, are converted into methylmercury by soil and marine microorganisms. This methylmercury is quickly taken up by planktonic algae, which are then eaten by fish and other aquatic life, resulting in elevated levels of methylmercury in the tissues of larger predatory fish, such as tuna and swordfish.

Due to its high solubility, around 90% of organic mercury is absorbed in the gastrointestinal system. It swiftly penetrates the blood-brain barrier and the placenta, achieving concentrations in the brain that are three to six times greater than those found in the bloodstream. Pregnant women exposed to methylmercury have given birth to children afflicted with congenital Minamata disease, which is marked by symptoms such as spasticity, seizures, hearing loss, and significant cognitive impairment. The Food and Drug Administration recommends a safe daily intake limit of 0.4 μg/kg of body weight.

Iron

Iron (Fe) stands as the most prevalent trace element within the human body, playing a crucial role in maintaining normal cellular functions and is recognized as one of the key minerals necessary for the body's homeostasis. This element is integral to various metabolic activities, including cellular respiration, the formation of myelin, the growth of neuronal dendritic trees, and the synthesis of DNA, RNA, and proteins. Furthermore, iron acts as a co-factor for numerous enzymes.

Iron poisoning, whether through deliberate or accidental ingestion, is a frequent occurrence, particularly among children, as iron supplements can resemble chocolate candies. Severe toxicity can arise from children consuming potent adult formulations, such as prenatal vitamins. In adults, the primary reasons for iron poisoning include suicide attempts and overdoses during pregnancy. Currently, iron overdose ranks as the second most prevalent type of overdose in pregnant individuals, with potentially serious repercussions. Additionally, iron toxicity can develop following multiple blood transfusions in the management of chronic conditions like thalassemia, sickle cell disease, and certain blood cancers. The serum iron level, assessed within 2 to 6 hours post-exposure, serves as the most effective laboratory evaluation, as rapid distribution of iron from the bloodstream to tissues may lead to a near-normal serum iron reading. When evaluated at its peak, serum iron levels below 350 micrograms/dL, between 350 to 500 micrograms/dL, and exceeding 500 micrograms/dL correspond to minimal, moderate, and severe systemic toxicity, respectively.

The regulation of metal absorption is crucial to prevent excess accumulation, as the body lacks a physiological mechanism to eliminate surplus iron. When iron is attached to transferrin, ferritin, or other transport and storage proteins, it remains unavailable for catalyzing free radical formation. In cases of iron overload, these proteins become overwhelmed, leading to transferrin saturation. This saturation results in an increase of free iron ions in the serum, which can be toxic to nearly all organs, causing tissue damage. Iron toxicity can be categorized into corrosive and cellular types. At the cellular level, excess iron disrupts metabolic processes in the heart, liver, and central nervous system. Free iron infiltrates cells and accumulates in mitochondria, interfering with oxidative phosphorylation, promoting lipid peroxidation, and generating free radicals, which can trigger anaerobic metabolism and ultimately result in cell death. Cellular injury often leads to metabolic acidosis. The corrosive nature of iron can also inflict direct damage to the gastrointestinal mucosa, potentially mimicking acute abdominal conditions. It is essential to recognize this clinical presentation as a potential sign of iron poisoning. Indicators such as leukocytosis, hyperglycemia, and metabolic acidosis can support the diagnosis of moderate to severe iron poisoning, although they are not specific.

The pathophysiology of iron poisoning was first outlined by Covey in 1954. This framework has since been adapted to encompass five distinct clinical phases. It is important to note that this progression may not be uniform across all individuals, and in instances of severe overdose, patients may present in a state of shock. The assessment of the stage of iron toxicity should rely on clinical symptoms and manifestations rather than the timing of ingestion.

In the initial phase, which typically occurs within 30 minutes to 6 hours post-ingestion, patients often display gastrointestinal symptoms including nausea, abdominal discomfort, vomiting, diarrhea, and the presence of blood in vomit or stool. The second phase, occurring between 6 to 24 hours, is marked by a period of relative stability, which may indicate either genuine recovery or the potential for clinical decline.

Stage III, which arises approximately 6 to 72 hours after exposure, is characterized by circulatory shock. During this phase, patients may experience a resurgence of gastrointestinal symptoms, shock, respiratory issues, and metabolic acidosis. Additionally, complications such as coagulopathy, liver dysfunction, heart muscle damage, and kidney failure can manifest.

In stage IV, occurring between 12 to 96 hours, hepatic necrosis may develop, indicated by elevated levels of aminotransferases and the risk of progressing to liver failure. Hepatotoxicity in this stage is associated with a mortality rate of 50% and is influenced by the dosage of iron ingested.

Finally, stage V emphasizes the aftermath of acute gastrointestinal injury, which may lead to scarring and obstruction in the pyloric region or proximal bowel, resulting in areas of stenosis. These late-stage complications are infrequently observed.

Cadmium

Cadmium (Cd), a heavy metal, is recognized as a widespread trace element and a significant environmental pollutant. This metal is among those that are not required for the physiological or biochemical functions of living organisms. Naturally, cadmium is found in ores alongside other metals such as zinc, lead, and copper. While the occurrence of chronic cadmium poisoning among industrial workers has decreased since the latter part of the 20th century, its compounds continue to be extensively utilized in various industries, despite growing awareness regarding the risks associated with prolonged exposure to cadmium. Presently, cadmium is employed in the manufacture of anticorrosive substances, serves as a stabilizer in polyvinyl chloride (PVC) materials, acts as a color pigment and neutron absorber in nuclear facilities, and is most commonly found in the production of nickel-cadmium batteries. Additionally, cadmium is a contaminant in phosphate fertilizers. When compared to mercury or lead, cadmium is more readily absorbed by plants from the soil, making its way into the food chain. Furthermore, the absorption process by plants is facilitated in conditions of low pH.

The hazardous nature of cadmium was initially noted in 1817 by Friedrich Stromeyer, particularly among workers in zinc smelting operations. In 1948, Friberg reported cases of emphysema and proteinuria in industrial employees exposed to cadmium dust, establishing a connection between cadmium exposure and kidney toxicity. Cadmium can be absorbed through the lungs, gastrointestinal tract, and skin, with cigarette smoking identified as a significant contributor to cadmium exposure. Smokers exhibit cadmium levels in their blood that are 4 to 5 times higher and in their kidneys 2 to 3 times higher than those of non-smokers. For non-smokers, dietary intake is the primary route of cadmium exposure, stemming from contaminated soil and water sources. In the liver, cadmium stimulates the synthesis of metallothionein. The resulting cadmium-metallothionein complex (Cd-MT) is easily filtered by the kidneys and reabsorbed in the proximal tubule, resulting in an extended half-life of approximately 10 to 30 years. This complex formation serves as a protective mechanism against the toxicity of free cadmium; however, with chronic exposure, the production of metallothionein can become depleted, leading to increased intracellular cadmium levels. This accumulation occurs in mitochondria and disrupts the respiratory chain at complex III. Over a lifetime, cadmium levels in kidney tubular cells tend to rise. The organs most impacted by chronic cadmium exposure include the kidneys, bones, and lungs, with about 50% of the accumulated cadmium stored in the kidneys, making them the primary site for long-term accumulation. Kidney damage is primarily indicated by elevated excretion of low molecular weight proteins such as β2-microglobulin and retinol-binding protein, as well as enzymes like N-acetyl-α-D-glucosaminidase. This condition, known as "tubular proteinuria," serves as a reliable indicator of proximal tubular injury.

Bismuth

Bismuth (Bi) is a trivalent metal that is categorized as a poor metal and shares chemical similarities with arsenic and antimony. Its name is believed to originate from the German term "wismuth," which translates to "white mass." As the least prevalent element in group fifteen of the periodic table, bismuth is relatively uncommon. It exists naturally as a monoisotope (209Bi) and is recognized as the heaviest stable element, with a theoretical half-life estimated at 1.9 × 10^9 years. Bismuth is primarily obtained as a secondary product during the extraction of lead, copper, and tin, typically found in ores such as bismuthinite (bismuth sulfide) and bismite (bismuth oxide). To date, no natural biological function for this metal has been identified. Historical records indicate that both inorganic and organic bismuth compounds have been utilized in medicine since the late 18th century. These compounds have been employed to treat various ailments, including skin disorders and war injuries, through topical applications (acting as astringents, emollients, and antimicrobials), as well as for syphilis via parenteral routes and orally for conditions like cholera infantum, peptic ulcers, and other gastrointestinal issues. Although the use of these compounds saw a significant decline with the advent of antibiotics in the 1980s, particularly for syphilis treatment, bismuth regained attention following the discovery of Helicobacter pylori, proving effective for numerous gastrointestinal problems. During World War I, bismuth iodoform paraffin paste (BIPP) was introduced as an antiseptic dressing, which continues to be widely used by maxillofacial surgeons and otolaryngologists. Additionally, BIPP is utilized in treating epistaxis. However, the use of bismuth iodoform paraffin paste can lead to neuropsychiatric symptoms, necessitating careful consideration of the patient's renal and hepatic health, as well as the wound's size and condition by healthcare providers.

Bismuth, upon entering the bloodstream, is disseminated throughout various tissues, exhibiting high concentrations and toxicity particularly in the kidneys and liver. In the kidneys, bismuth associates with a metal-binding protein in the proximal renal tubule cells, where it can remain bound for several months. Its toxic effects are primarily due to its strong affinity for sulfhydryl groups in essential enzymes, which disrupts their functions. Since over 99% of ingested bismuth is not absorbed, it is effective as a locally acting gastrointestinal agent. The small fraction that is absorbed is excreted unchanged through urinary and hepatobiliary pathways, although the exact contribution of each route remains a topic of ongoing research. Therapeutic use of bismuth compounds can result in serum concentrations ranging from 10 to 20 μg/L, with levels exceeding 50 μg/L indicating potential toxicity (normal levels are below 0.5 μg/L). Reported toxic effects associated with bismuth exposure include hepatitis, hepatic fatty degeneration, nephropathy, osteoarthritis, gingivostomatitis, colitis, and various neuropsychiatric symptoms.

Acute bismuth toxicity, typically resulting from a single high dose, primarily presents as nephrotoxicity, while chronic exposure to elevated levels of bismuth salts can lead to encephalopathy. A significant overdose of bismuth can cause reversible damage to the proximal tubules, culminating in acute tubular necrosis. This condition is characterized by proximal tubular dysfunction, known as Fanconi's syndrome, which clinically manifests as hypophosphatemia, hypouricemia, metabolic acidosis, renal glycosuria, and tubular proteinuria. Bismuth is recognized for inducing a reversible form of Fanconi's syndrome, which aligns with the progression of acute tubular necrosis. Various heavy metal poisonings, including those from bismuth, lead, and mercury, have been associated with reversible Fanconi's syndrome, in contrast to chronic cadmium exposure, which is linked to an irreversible form of the syndrome. Additionally, bismuth can penetrate the blood-brain barrier and interact with enzymes that play a role in oxidative metabolism, leading to decreased oxygen consumption and cerebral perfusion. This interaction may result in neuropsychiatric symptoms and encephalitis accompanied by brain lesions. Historical accounts have documented neurotoxicity associated with bismuth iodoform paraffin paste (BIPP) gauze, particularly following a notable outbreak of bismuth encephalopathy in 1970, which identified common symptoms of oral bismuth toxicity, including depression, anxiety, irritability, and potential mild incoordination. Over the years, clinicians have noted the emergence of additional neuropsychiatric symptoms following procedures involving BIPP gauze, such as malaise, insomnia, personality changes, ataxia, dysphonia, dysarthria, gait dyspraxia, myoclonic jerks—predominantly in the distal upper limbs—delirium, drowsiness, and even coma.

Discussion

This study underscores the toxicological significance of heavy metals, elucidating their acute and chronic effects, mechanisms of action, and medico-legal implications. The findings reaffirm that heavy metals such as arsenic, lead, mercury, cadmium, and others are potent toxicants capable of inducing a range of systemic and cellular dysfunctions. The acute symptoms often involve gastrointestinal distress, neurological impairment, or systemic shock, while chronic exposure manifests in debilitating conditions such as neuropathies, organ failure, and metabolic disruptions as depicted in table-1.

The study also highlights the critical role of advanced analytical techniques, including Atomic Absorption Spectroscopy (AAS) and Inductively Coupled Plasma Mass Spectrometry (ICP-MS), in detecting and quantifying these metals. The precision and reliability of these methods have significantly enhanced the diagnosis and monitoring of heavy metal toxicity. Furthermore, emerging techniques like X-Ray Fluorescence (XRF) and Neutron Activation Analysis provide non-invasive and high-sensitivity options for detecting specific metals like lead and thallium as shown in table-1.

From a medico-legal perspective, heavy metals have profound implications in cases of environmental contamination, occupational exposure, and deliberate poisoning. The historical use of arsenic and thallium in criminal poisoning cases underscores their forensic relevance. Moreover, chronic exposure to metals such as lead and cadmium, often through industrial sources, raises concerns about regulatory and preventive measures in public health.

The mechanisms of action of these metals reveal a common thread: their interference with critical cellular processes. Many of these metals bind to sulfhydryl groups or other essential biomolecules, inhibiting enzymatic activity and disrupting metabolic pathways. For instance, arsenic inhibits ATP production by interfering with cellular respiration, while lead disrupts heme synthesis and neurotransmitter signaling. Oxidative stress emerges as a central theme in the pathophysiology of heavy metal toxicity, highlighting the need for antioxidants in therapeutic strategies. Despite the comprehensive insights, there are limitations to this study. The variability in individual susceptibility to heavy metal toxicity due to genetic, nutritional, and environmental factors remains poorly understood. Further research is needed to explore the molecular basis of these variations and to develop targeted interventions. Additionally, advancements in detection techniques must continue to evolve to facilitate early diagnosis and minimize exposure risks.

S. No.	Metal	Acute Symptoms	Analytical Technique for Detection	Medico-Legal Importance	Chronic Symptoms	Mechanism of Action	Reference
1	Arsenic	Vomiting, abdominal pain, diarrhea, shock	Atomic Absorption Spectroscopy (AAS), ICP-MS	Frequently used in poisoning cases due to availability and delayed onset	Skin pigmentation, hyperkeratosis, neuropathy	Interferes with cellular respiration by inhibiting enzymes like pyruvate dehydrogenase; disrupts ATP production.	[22]
2	Lead	Abdominal pain, encephalopathy, anemia	AAS, ICP-MS, X-Ray Fluorescence (XRF)	Industrial exposure, chronic poisoning often seen in children	Neuropathy, cognitive impairment, renal damage	Inhibits heme synthesis, disrupts calcium signaling, and interferes with neurotransmitter release.	[27]
3	Mercury	Tremors, gingivitis, erethism	Cold Vapor AAS, ICP-MS	Poisoning from industrial spills, occupational exposure	Neuropathy, renal damage, cognitive deficits	Binds to sulfhydryl groups, disrupting enzyme activity and causing oxidative stress.	[14,32]
4	Cadmium	Nausea, vomiting, dyspnea, lung edema	ICP-MS, Graphite Furnace AAS	Industrial exposure, implicated in itai-itai disease	Osteomalacia, renal failure, respiratory damage	Causes oxidative stress, damages DNA, and disrupts calcium metabolism.	[24,39]
5	Thallium	Gastrointestinal symptoms, alopecia, neuropathy	ICP-MS, AAS, Neutron Activation Analysis	Historically used in homicides due to high toxicity	Peripheral neuropathy, vision loss, renal damage	Interferes with potassium-dependent processes, inhibits cellular respiration.	[12,14,18]
6	Fluorine	Nausea, vomiting, abdominal pain	Ion-selective electrode, spectrophotometry	Industrial accidents, water contamination	Skeletal fluorosis, joint stiffness, brittle bones	Forms strong bonds with calcium, leading to mineralization defects and enzyme inhibition.	[25]
7	Copper	Abdominal pain, hemolysis, jaundice	AAS, ICP-MS, Colorimetric assays	Poisoning from contaminated water or Wilson's disease	Liver damage, psychiatric symptoms, Kayser-Fleischer rings	Accumulates in tissues due to disrupted homeostasis, leading to oxidative damage and enzyme dysfunction.	[31,37]
8	Selenium	Nausea, vomiting, garlic breath odor	ICP-MS, AAS	Environmental exposure, dietary supplements	Hair and nail brittleness, peripheral neuropathy	Inhibits thiol-containing enzymes, causing oxidative stress and disrupting cellular homeostasis.	[44]
9	Iron	Vomiting, abdominal pain, hematemesis	Serum iron levels, Total Iron Binding Capacity (TIBC)	Accidental overdose in children, therapeutic overdose	Hemochromatosis, liver cirrhosis, diabetes	Catalyzes free radical formation via Fenton reaction, causing cellular damage and organ failure.	[22,25]

Table 1: Toxicological Profile, Detection Techniques, and Mechanisms of Action of Selected Heavy Metals.

Table-1 Below aims to summarize the findings of the present study in a concise manner.

Conclusion

Heavy metals are naturally occurring, dense elements that tend to accumulate in the environment, primarily as a result of human industrial activities, posing significant health risks to both humans and wildlife. Environmental contamination can affect air, water, sewage, seawater, and various waterways, leading to the accumulation of these metals in plants, crops, seafood, and meat, which can indirectly impact human health. Certain professions, such as those in the metal finishing industry and traditional glassmaking, are associated with a heightened risk of exposure and toxicity to specific heavy metals. The clinical manifestations of heavy metal poisoning are influenced by the particular element involved, the degree and method of exposure, the chemical and valence states of the compound (whether elemental, organic, or inorganic), as well

Bibliography

1. Agency for Toxic Substances and Disease Registry (ATSDR). "Toxicological profile for copper". Atlanta, GA: Centers for Disease Control (2002).
2. Agency for Toxic Substances and Disease Registry (ATSDR). "Toxicological profile for arsenic TP-92/09". Atlanta, GA: Centers for Disease Control (2000).
3. Arruti A., *et al*. "Evaluation of the contribution of local sources to trace metals levels in urban PM2.5 and PM10 in the Cantabria region (Northern Spain)". *Journal of Environmental Monitoring* 12.7 (2010): 1451-1458.
4. Beyersmann D and Hartwig A. "Carcinogenic metal compounds: Recent insight into molecular and cellular mechanisms". *Archives of Toxicology* 82.8 (2008): 493-512.
5. Bradl H. "Heavy metals in the environment: Origin, interaction and remediation". *Academic Press* 6 (2002).
6. Centeno J A., *et al*. "Environmental pathology and health effects of arsenic poisoning: A critical review". In R. Naidu, E. Smith, J. Smith, & P. Bhattacharya (Eds. Managing arsenic in the environment: From soil to human health (2005): 1-349.
7. Chang L W., *et al*. "Toxicology of metals". *CRC Press* (1996).
8. Duffus J H. "Heavy metals-a meaningless term?" *Pure and Applied Chemistry* 74.5 (2002): 793-807.
9. Fergusson J E. "The heavy elements: Chemistry, environmental impact, and health effects". *Pergamon Press* (1990).
10. Goyer R A. "Toxic effects of metals". In C. D. Klaassen (Ed. Casarett and Doull's toxicology: The basic science of poisons). McGraw-Hill Publisher (2001): 811-867.
11. Hamelink J L., *et al*. "Bioavailability: Physical, chemical, and biological interactions". CRC Press Inc (1994).
12. Harvey L J and McArdle H J. "Biomarkers of copper status: A brief update". *British Journal of Nutrition* 99.S3 (2008): S10-S13.
13. He ZL., *et al*. "Trace elements in agroecosystems and impacts on the environment". *Journal of Trace Elements in Medicine and Biology* 19.2-3 (2005): 125-140.
14. Herawati N., *et al*. "Cadmium, copper, and zinc levels in rice and soil of Japan, Indonesia, and China by soil type". *Bulletin of Environmental Contamination and Toxicology* 64 (2000): 33-39.
15. Kabata-Pendia A. "Trace elements in soils and plants (3rd ed.)". CRC Press (2001).
16. Morton W E and Dunnette D A. "Health effects of environmental arsenic". In J. O. Nriagu (Ed. Arsenic in the environment part II: Human health and ecosystem effects). John Wiley & Sons, Inc (1994): 17-34.
17. National Research Council. "Arsenic in drinking water". 2001 update (2001).
18. National Research Council Canada (NRCC). "Effects of arsenic in the environment". National Research Council of Canada (1978).
19. Nriagu JO. "A global assessment of natural sources of atmospheric trace metals". *Nature* 338 (1989): 47-49.

20. Patlolla A., *et al*. "Potassium dichromate-induced cytotoxicity, genotoxicity, and oxidative stress in human liver carcinoma (HepG2) cells". *International Journal of Environmental Research and Public Health* 6 (2009): 643-653.

21. Shallari S., *et al*. "Heavy metals in soils and plants of serpentine and industrial sites of Albania". *Science of the Total Environment* 1920.9 (1998): 133-142.

22. Stern B R. "Essentiality and toxicity in copper health risk assessment: Overview, update, and regulatory considerations". *Toxicology and Environmental Health A* 73.2 (2010): 114-127.

23. Sträter E., *et al*. "Pollution in coastal fog at Alto Patache, Northern Chile". *Environmental Science and Pollution Research International* (2010).

24. Sutton D J and Tchounwou P B. "Mercury induces the externalization of phosphatidylserine in human proximal tubule (HK-2) cells". *International Journal of Environmental Research and Public Health* 4.2 (2007): 138-144.

25. Tchounwou P B., *et al*. "Carcinogenic and systemic health effects associated with arsenic exposure: A critical review". *Toxicological Pathology* 31.6 (2003): 575-588.

26. Tchounwou P B., *et al*. "Arsenic toxicity, mutagenesis, and carcinogenesis—a health risk assessment and management approach". *Molecular and Cellular Biochemistry* 255 (2004): 47-55.

27. Tchounwou P B., *et al*. "Important considerations in the development of public health advisories for arsenic and arsenic-containing compounds in drinking water". *Reviews on Environmental Health* 14.4 (1999): 211-229.

28. Verkleji J A S. "The effects of heavy metals stress on higher plants and their use as biomonitors". In B. Markert (Ed. Plant as bioindicators: Indicators of heavy metals in the terrestrial environment) (1993): 415-424.

29. WHO/FAO/IAEA. "Trace elements in human nutrition and health". World Health Organization (1996).