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A Review: The Toxic Effect of Lead on Human Health

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ABSTRACT
The periodic table highlights heavy metals, characterized by high density and atomic weight, which are prevalent in the biosphere and released through anthropogenic activities. Heavy metals can be classified as essential or non-essential, with the former being crucial for human metabolism, while the latter, including lead (Pb), poses significant health risks. Lead is a toxic metal which occur in the environment and found in some products. Lead, a non-biodegradable toxic metal, accumulates in environmental sources such as soil and water, primarily from human activities. It is associated with severe health consequences, particularly in children, leading to issues like developmental impairments and reduced fertility in adults. The detection of lead poisoning employs various analytical methods, with blood lead levels serving as the primary diagnostic tool. Treatment often involves chelation therapy to remove lead from the body and mitigate its toxic effects.

KEYWORDS: *Heavy metals, Lead, Non-biodegradable, Toxic metal, Developmental impairment, Toxic effects, Chelation therapy*

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INTRODUCTION

Heavy metals have large atomic weight and density, Due to which they constitute a significant chunk of the periodic table. Most are found in the biosphere, which includes rocks, soils and water. Commercial and industrial anthropological resources also release them into the environment (Mitra et al., 2022). Heavy metals are defined as natural metals or metalloids with an elemental density greater than $5g/cm^{-3}$ and an atomic number greater than 20 (Mathu et al., 2021). In environmental literature, metals and metalloid linked to toxicity, environmental pollution, and detrimental impacts on biota are sometimes called "heavy metals." Many definitions have been given to the phrase, most commonly in regards to density, relative atomic mass, and atomic number (Ali et al., 2017). Heavy metals are categorized as either necessary or essential heavy metals (Mo, Mn, Cu, Ni, Fe, Zn) or non-essential (Cd, Ni, As, Hg, Pb). Important metals like copper are essential to the human body's metabolism because they are needed for the production of hemoglobin and the breakdown of carbohydrates. However, cells may be harmed by high amounts of these metals (Kiran et al., 2022). In the vital physiological process, Traces of some critical heavy metals, like Co, Mn, Se, Zn, and Mg, are vital, but As, Pb, Hg, Cd, and Cu are well known for being hazardous. (Ali and Naima 2024).

Lead is a metal that is naturally found in comparatively small amounts and non-biodegradable. Lead levels in the atmosphere continue to rise due to human activities such as mineral extraction, production, and burning of fossil fuels. Lead is toxic to the human body in amounts throughout what is advised (Mitra et al., 2022). Lead is the most dangerous heavy metal in the environment. Among the main qualities that make it hard to quit using it are its gentleness, flexible nature, low conductibility, and resistance to corrosion; yet, because it is not biodegradable, its concentration increases in the environment and presents an increasing risk (Sani et al., 2021). Lead (Pb), a hazardous heavy metal, has no known biological function in the body, but its detrimental effects on health have made it a major global public health concern. The Advisory Committee on Childhood Lead Poisoning Prevention (ACCLPP) (2012) states that the top reference range value for children's lead blood is 5 µg per deciliter (µg/dL), which is also used as an advisory threshold for environmental and educational interventions (Riasatian et al., 2023). Known by its Latin name, Plumbum, which refers to "the liquid silver," and its symbol, Pb, lead is a chemical that is a member of the periodic table's carbon group. It was the first chemical to show particular types of toxicity and has an atomic number of 82 (Tahir and Alkheraije 2023). Due to its high immobility, high persistence in water and soil, and accumulation in the top 8 inches of the ground, the toxic non-essential heavy metal lead (Pb) is widely distributed and has a broad spectrum of detrimental effects on living things at the structural, biological, and biochemical levels (Henao and Herrera 2021). The human body is at risk from lead exposure at levels that are higher than optimal. Children are exposed to lead at higher levels. The earth's crust naturally contains less than 50 mg/kg of lead, according to reports, and geological processes that alter the Pb composition of silicates have an impact on this (Collin et al., 2022). Leaded gasoline, paint, lead bullets, plumbing pipes, pewter pitchers, storage batteries, toys, and faucets are the most prevalent sources of lead exposure. Inhalation and ingestion through food and water are the primary exposure mechanisms (Goyal et al., 2020). Painting, vinyl flooring, fluid, lead weights, lead shot, and contaminated vegetation growing next to smelters or highways are further sources of lead (Blakey et al., 2021). After exposure, blood lead levels level out about three months later.The liver and kidneys store the majority of lead, with the remainder being dispersed throughout the body, including the brain, adipose tissue, testes, heart, skeletal muscles, adrenal glands, pancreas, ovary, spleen, prostate, and spinal cord (Charkiewicz et al., 2020). Lead levels in the environment are acceptable-ranging between 0.10 and 0.30 µg m^{-3}.Pb concentrations in India's winters air were 1 µg m^{-3}, many times greater than the permissible limit (Raj and Das 2023). Before 1985, the acceptable blood lead level was 40 µg/dL; however, the United States approved a level of 25 µg/dL in 1985 (Chaudhari et al., 2020).

SOURCES OF LEAD

Natural and man-made activities are the two main causes pollution from heavy metals (Goyal et al., 2020). Numerous natural and man-made factors contribute to the levels of lead present on Earth's surface. According to reports, Pb level in the earth's crust are less than 50 mg/kg. Natural mechanisms include geological processes that regulate the Pb composition of silicates (Collin and Venkatraman et al., 2022). The average amount of Pb in the soil is 14.8 mg/kg. Globally, Lead concentrations in surface soils have an average concentration of 10–67 mg/kg., with 32 mg/kg serving as the median. Igneous rocks have a Pb value of 10–25 mg/kg, while argillaceous sediments have a Pb content of 14–40 mg/kg. Seldom does it occur in ultramafic rocks and calcareous sediments at rates of 3.0–10 mg/kg and 0.1–8.0 mg/kg. Sedimentary rocks such as sand stones and shale had 21 Pb levels (22 mg/kg) (10 mg/kg) (Figure 1).

Most prevalent lead mineral is galena (PbS), among their minerals are cerussite, pyromorphite, minium, mimetite, and anglesite (Ashkan 2023). Smelting, refining, and mining are examples of human activities that can cause an increase level of amount of lead in the environment (Sangeetha and Umamaheshwari 2020). Leaded gasoline, industrial processes such as the casting and blazing of lead, art pottery, watercraft constructing, lead-based painting, lead-containing pipelines, battery recycling, grids, the arms industry, pigments, and book printing are some of the primary ways that humans are exposed to lead and its compounds (Sani et al., 2021).

LEAD POISONING

Lead poisoning, also referred to as plumbism, which is a hazardous ecological and occupational diseases that affect millions of people and children globally (Kianoush et al., 2014). Lead poisoning can occasionally be caused by lead ions used in ceramic coating that spill from acidic fruit juices (Wani et al., 2015). Reduced accessibility, more discerning eating patterns, or less sensitivity limit the risk of lead poisoning. Lead poisoning typically occurs when renovations are made to older properties that were painted with lead-based paint. Other sources of lead include vinyl flooring, fluid, lead weights, lead shot, lead fishing tackle, improperly disposed oily substances and batteries, and contaminated biodiversity growing beside smelting processes or roads (Blakley et al., 2020). Environmentally present lead can accumulate in growing plants or food processing facilities, causing lead contamination (Kianoush et al., 2014).

Lead poisoning can be either acute or chronic, rarely does acute lead poisoning occur. Fatigue, constipation, and abdominal colic are possible. Lead levels between 60 and 80 µgm/dL may cause peripheral neuropathy, and poor hematopoiesis that results in anaemia, renal tubular dysfunction, and decreased neurotransmission and neuronal cell death. At 80–120 µgm/dL, acute dementia with seizures, a state of unconscious and death may occur (Shukla et al., 2018). Lead poisoning occur in two forms either acute or chronic. Acute lead poisoning is rare. Abdominal colic, fatigue, and constipation are all possibilities. Peripheral neuropathy, impaired hematopoiesis leading to anaemia, renal tubular dysfunction, reduced neurotransmission, and neuronal cell death can all be caused by lead concentration between 60 and 80 µgm/dL. At 80–120 µgm/dL, acute dementia with seizures, coma- a state of unconsciousness, and death may occur (Pathak and Pal 2023).

Symptoms and signs of Lead Poisoning

Abnormal behaviour is one of the various symptoms of lead poisoning that differ from person to person, and exposure duration is a significant factor (Wani et al., 2015). Finding deceased animals is often the initial sign of lead poisoning. Affected animals may stop grazing when they exhibit symptoms of central nervous system (CNS) damage (www.cdfa.ca.gov). Organic lead may be more dangerous than inorganic lead since it is fat soluble and acts instantly (Timbrell, 2008). Additionally, research has demonstrated that there are no symptoms of lead poisoning even in cases where the body has high levels of lead.Acute symptoms and indications are caused by brief, strong exposures to lead, whereas chronic exposure typically shows up between weeks to months. Typical signs of chronic lead exposure include anaemia, headaches, fatigue, slurred speech, depressive symptoms, feeling dizzy, discomfort in the abdomen, lack of interaction, tingling and numbing in the extremities, anaemia, and short-term cognitive or attention issues(Sani and Amanabo 2021). Chronic exposure can cause numbness and tingling across the limbs, depression, nausea, and pain in the abdomen, loss of coordination, and short-term memory or focus loss (Patrick, 2006). Chronic lead poisoning also causes anaemia, impaired speech, headaches, fatigue, and sleep issues (Pearce, 2007). Children who have chronic poisoning typically act aggressively and won't play (Wani et al., 2015). Anaemia and neuropsychiatric symptoms such as migraine, decreased motor nerve impulse transmission, frustation and lack of attention and concentration issue are caused by blood lead concentration between 25 and 60 µg/dL instead. Adults with blood lead concent greater than 80 µg/dL may get abdominal colic, which is characterized by painful episodes (Sani and Amanabo 2021). Extremely severe symptoms, including migraines, drowsiness seizures, and coma, and signs of encephalopathy—a condition characterized by enlargement of the brain and increased pressure inside the skull—are caused by elevated blood lead levels surpassing 100 µg/dL (Henritig, 2006). However, these symptoms began to see in children's when their lead amount reach 70 µg/dL or more (Wani et al., 2015).

LEAD TOXICITY

Nearly every organ in the body is impacted by the extremely toxic element lead. The consequences of Pb poisoning in children are bad than in adults. Young children and infants are particularly susceptible to even low levels of lead, which can cause difficulties with learning, behavioural problems, and a reduction in IQ (Sani et al., 2021). People who are come in contact with extremely high concentration of lead (500–870 µg/L blood) may develop atrioventricular block, atrioventricular conduction abnormalities, and sinus node dysfunction (Charkiewicz and Backstrand 2020). More risk of miscarriage, premature birth of child, and low birth weight has been linked to occupational exposure in females that results in blood lead amount greater than 10 µg/100 ml. In one study, maternal blood lead concentration between 5 and 9 µg/100 m quadrupled the chance of spontaneous abortion (Gidlow 2015). Males experience a reduction in sperm volume and count, as well as changes in sperm motility and shape. (Wu et al., 2012). According to recent research, reduced libido, low quantity of semen and increased sperm amount aberrant sperm sturucture, and reduced sperm motility may all be associated with blood lead concentration in men more than 40 µg/100 mL, which could affect reproductive function (Gidlow 2015). The general environment has numerous causes of lead poisoning, especially in animals. These include soil and feed contamination from industrial pollution and agricultural practices. Additionally, animals that consume significant quantities of lead have been shown to perform poorly, become poisoned, and die (Assi et al., 2016). Lead poisoning affects the neurological, urinary, gastrointestinal, and genital systems in addition to the blood. Additionally, it is linked to teratogenesis, mutagenesis, and carcinogenesis in experimental animals (Sethy et al., 2020).

EFFECTS OF LEAD

Lead (Pb) is a more harmful metal that builds up in the body's blood, bones, liver, kidneys, brain, and skin after being ingested. Because Pb is poorly excreted by the body of humans, its detrimental effects on health can be both acute and permanent. Lead has been demonstrated to impact the immunological, gastrointestinal, endocrine, hepatic, and reproductive systems in humans (Charkiewicz and Usmani 2020). Lead has extremely harmful impacts on the environment, and even a small level of Pb can have negative physiological effects on plants. It lowers the water potential, modifies the membrane's permeability, and either inhibits or boosts plant enzyme activity. Most plants absorb lead in the following sequence: roots, leaves, stems, and seeds. Pb mostly prevents cations like K, Ca, Mg, Cu, and Fe^{+3} and anions like nitrates from entering (Bharti et al., 2021).

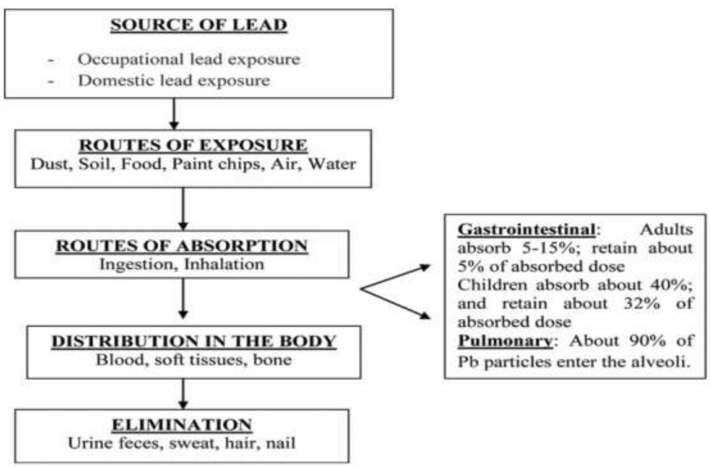

Figure 1: Diagrammatic representation showing sources and accumulation of lead

In animals, lead poisoning occur in two forms: acute and chronic. When animals are exposed to high quantities of lead in a brief period, acute lead poisoning develops (Pathak and Singh 2023). The most frequent cause of lead poisoning in ruminants is discarded lead-acid batteries because livestock can easily consume the lead and lead salts found in these batteries (www.cdfa.com). Chronic lead poisoning can occur when livestock are subjected to lower amounts of lead over time.Diagnosing chronic lead poisoning might be difficult since its clinical signs can be more subtle and ambiguous (Pathak and Singh 2023).The highest quantities of lead are often found in the bones and kidneys after prolonged exposure (Wani et al., 2015). Ataxia, hypoglossal nerve paresis, severe depression, muscular twitches, seizures, a coma death, and breathing problems are all symptoms of lead poisoning in cattle (Tahir and Alkheraije 2023).

DETECTION OF LEAD

The amount of lead in the blood can be measured using a number of methods. Lead poisoning is frequently identified by the absence of thick lines in children's X-ray bones or by abnormalities in red blood cells that can be seen under a microscope (Sani et al., 2021). Among the methods for Pb_{2+} analysis that have been developed in the past ten years are reversed-phase high-performance liquid chromatography coupled with UV-vis or fluorescence detection, atomic absorption spectrometry (AAS), atomic emission spectrometry (AES), inductively coupled plasma mass spectrometry (ICP-MS), anodic stripping voltammetry, and others(Ding et al., 2010). The atomic absorption method, mass spectrometry, stripping voltammetry, inductively coupled plasma emission spectrometry, and others are instances of traditional methods of analysis. The methods selected are usually determined by the different samples, lead contents, and the detection limitations of analytical instruments (Wu et al., 2023). The primary method for identifying elevated amounts of body lead is the measurement of lead in blood samples; however, this method has the limitation of only detecting levels of circulating lead, not the amount of lead stored in the body. Lead poisoning is indicated by whole blood values of 10 μg/dL in adults and 5 μg/dL in children (Sani et al., 2021). All of these techniques are effective instruments for Pb^{2+} detection in terms of sensitivity and accuracy, but they are costly, time-consuming, and/or need specialized equipment. Thus, the creation of quick, easy, affordable, and accurate techniques for measuring Pb^{2+} with high sensitivity and selectivity (Ding et al., 2010).

According to recent research, an electrochemical method's excellent sensitivity, straightforward equipment, inexpensive manufacturing cost, quick reaction, and portability make it a valuable tool for detecting dangerous metal ions (Tu et al., 2021).

Colorimetric techniques on the basis of Gold nanoparticles with functionalization (Au-NPs) are appealing, practical, and capable of meeting these needs. High extinction coefficients, extremely distance-dependent optical characteristics, and colours produced by Au-NPs at nanomolar concentration make it possible to observe them using the naked eye without the use of sophisticated equipment (Ding et al., 2010).

TREATMENT OF LEAD

Chelation Treatment

The following list includes some typical chelating drugs used to prevent lead poisoning: (1) $CaNa_2$ EDTA, or calcium disodium ethylene diamine tetraacetic acid. (2) Penicillamine D, (3) DMSA, or meso 2,3-dimercaptosuccinic acid and Dimercaptopropane-1-sulphonate (DMPS) of sodium 2,3 (Sangeetha and Umamaheshwari 2020).

The Food and Drug Administration hasn't given D-penicillamine a license to treat lead poisoning. Therefore, its use for this indication should be regarded as exploratory. It is the only oral chelating agent that is sold commercially. It can be administered over many days. Up to 20% of patients receiving the medication may experience toxic adverse effects (Vijaya Kumar et al., 2012). Due to the possibility of serious adverse effects (such as clotting disorder, anaemia, urticaria, edema, aberrant liver activity, Stevens-Johnson syndrome, and nephrotic syndrome), D-penicillamine is utilized as a second-line oral chelating agent (Hon et al., 2017). Numerous antioxidants are used to protect against the toxicity of substances like lead and its byproducts. Through solubilization, a novel method known as antioxidant nanoencapsulation may enhance the cellular uptake and bioavailability of poorly soluble. When curcumin was encapsulated in a pluronic block copolymer, it released gradually and continuously and exhibited anticancer properties similar to those of free curcumin (Sani et al., 2021). The antioxidant qualities of flavonoids found in plants seem to be primarily responsible for the observed modification of the toxic effect of lead in crude extracts of numerous plants. Since lead causes toxicity in a number of organs, including the brain, kidney, and liver, antioxidants are currently thought to be important in the treatment of lead poisoning in humans (Sangeetha and Umamaheswari 2020).

CONCLUSION

Lead is non-essential and non-biodegradable heavy metal which bio-accumulates in the different organs of the body. Sources of lead are natural and human activity. Anthropological and human activity involves gasoline, paints, pottery etc. Lead is a heavy metal which cause toxicity in organisms because of its higher toxic in nature. Lead have similar biochemical properties to calcium which leads to its bio-accumulation in different organs of the body.Many treatment options are available today, including chelation therapy, nano-encapsulation, N-acetylcysteine (NAC), and many antioxidants that aid in the elimination of lead from the body. However, of them, chelation therapy is the most frequently employed.

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