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LEAD TOXICITY AND HEALTH EFFECTS -A COMPREHENSIVE REVIEW

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Abstract

Lead is a heavy metal with a low melting point and is bluish-gray, soft, thick, and malleable. It is frequently present in the environment at concentrations less than 50 mg/kg. Although Pb is often found in high amounts in nature, its presence in water is primarily attributed to human pollution and artificial activity. Pb is one of several elements, the effects of which can be harmful to human health and the environment. There are also concerns that Pb may be carcinogenic and harmful to humans. The biological half-life of Pb in the human body varies from 28 to 40 days in the blood to several years or even decades in the bone and other body tissues, and the danger associated with Pb poisoning is still unknown because of the wide range of clinical manifestations. Pb exposure has been linked to lung diseases, cardiovascular problems, neurological impact, renal impairment, reproductive toxicity, and potentially carcinogenic effects. Exposure time, diet, health status, age and general well-being can all play a role, in how individuals respond to lead poisoning. The FDA has set reference levels (IRLs) for exposure at 8.8 µg per day for women of reproductive age and 12.5 µg per day for adults. It can enter the body through either the digestive or the respiratory system. It is important to take steps to maintain a lifestyle that promotes preventive measures and enhances public health by ensuring regular monitoring of individuals who face frequent exposure to heavy metals, particularly Pb. To effectively monitor and prevent Pb exposure, it is crucial to establish comprehensive screening programs for high-risk populations and prioritize public health initiatives that focus on promoting healthy lifestyles and minimizing environmental pollution.

Keywords: ***Lead; Exposure; Heavy Element; Poisoning***

1. INTRODUCTION

Every year, almost 600 million people are affected by harmful conditions. Contamination of food with heavy metals is more likely to occur in polluted agricultural areas, causing widespread concern [1, 2]. Heavy metals are also predicted to contaminate more than 13% (or 0.24 billion hectares) of the world's arable land, as well as around 40% of lakes and rivers [2]. Lead (Pb) is a poisonous, malleable, and non-disintegrating metal that appears bluish-gray. Pb can exist in both organic and inorganic forms. Inorganic Pb is found in dust, dirt, old paint, and other consumer items, whereas organic Pb (tetra-ethyl Pb) is mostly found in leaded gasoline [3]. Both types of Pb are dangerous; however, organic Pb complexes are more toxic to biological systems than inorganic Pb [4]. Pb is the second most hazardous element, accounting for 0.002% of the Earth's crust [5], and has a natural concentration of less than 50 mg kg^{-1} [6]. According to [7], the unique properties of lead, such as softness, high malleability, ductility, low melting point, and corrosion resistance,

have been widely applied in a range of industries, including vehicles, paint, ceramics, and plastics. A recent study suggested that Pb (~29 ng/g diet) is essential for enzyme and cellular activities, especially during cell development, hematopoiesis, and reproduction [8]. Although lead occurs naturally, human activities have been recognized as the principal source of elevated lead levels in the environment [9]. Pb is released into the atmosphere as a byproduct of Pb mining, industries that employ Pb compounds or alloys, automotive emissions, and fossil fuel combustion [10]. Currently, people are exposed to Pb via soil dust particles that enter their homes and drinking water. It is considered carcinogenic (Group 2 B) to humans [11]. Lead primarily affects people via eating, with the human body absorbing 20-70% of ingested Pb, and children have a high Pb absorption capacity [12,13]. Pb is delivered to animals and plants via air, water, and soil [14].

Lead is easily absorbed by the human body. Once in the bloodstream, it circulates and accumulates in the brain, bones, teeth, and soft tissues (liver and kidney), causing chronic poisoning [15]. Lead levels should not exceed 0.01 mg/L, according to the World Health Organization [16]. However, this value is only 10 µg/dL in adults and 1.4 µg/dL in children [17, 18]. The biological half-life of lead in the human body varies depending on the exposure levels and individual characteristics, although it is estimated to vary between weeks and months. Excessive lead exposure is considered to disrupt biological systems, resulting in neurological, cardiovascular, hematologic, and reproductive disorders [19]. The purpose of this review is to explore the negative effects of lead on the human body. This study also discusses the causes and levels of lead contamination, emphasizing how exposure to lead in the environment varies over time.

2. SOURCES OF LEAD

Lead-based paint is a significant source of Pb exposure, particularly in older homes built before the 1970s. The deterioration of lead-based paint can release lead particles into the air as dust or chips, posing health risks, especially to children who may ingest or inhale it [19]. Drinking water can still be a source of lead exposure when lead piping and plumbing exist, particularly in the presence of corrosive water [20]. Lead can leach into drinking water from lead pipes, solder, or fixtures, particularly in older plumbing systems and as a matter of fact, lead service pipes and lead-containing plumbing are still in use in many places [21]. Public health activities and infrastructural modifications are required to address the pervasive problem of Pb pollution in drinking water. Lead in soil can be built from a variety of sources, including previous use of leaded gasoline, lead-based paint, and industrial activity.

Contaminated soil increases the risk of Pb exposure, especially in metropolitan areas with a history of industrial activity or heavy traffic. Children playing polluted dirt may unwittingly consume lead particles, posing health risks [19]. Soil testing and remediation operations are critical for detecting and addressing Pb pollution in residential areas and playgrounds. Public awareness efforts and laws targeted at lowering Pb emissions and improving soil safety are critical for preserving human health and the environment. Consumer items, particularly those containing lead-based materials or coatings, pose a considerable risk of lead exposure [22]. Ceramics, pottery, toys, jewelry, and cosmetics may contain lead, especially if imported from countries with less severe rules [19]. Consumer products containing lead can cause health concerns, particularly for young people who may eat or touch them [23].

3. Exposure and Accumulation of Pb in the Human Body—Pathological Effects

The symptoms of lead poisoning differ based on the duration of exposure, type of food, and age and health status of the people exposed [24]. The effects of lead (Pb) on the body can be modified by interactions with other metals such as zinc, selenium, copper, iron, and manganese. These interactions are crucial because they can either increase or decrease the harmful effects of Pb in the body. Furthermore, tobacco smoke can operate synergistically with lead, dramatically increasing its effects on the body [25-27]. Lead is primarily absorbed through inhalation and ingestion, with inhalation being the primary route and swallowing particles contributing as a secondary pathway of absorption. It is distributed in the blood and accumulates in soft tissues (including the lungs, liver, kidneys, brain, spleen, and muscles) and bones, inhibiting the activity of sulfur-containing enzymes [28, 29]. The estimated proportion of lead taken into the lungs from the air is roughly 30-50% for adults, with the possibility of greater absorption rates (up to 95%). For very tiny and ultrafine lead particles, the digestive system absorbs approximately 10-44% of the lead, with the small intestine absorbing the majority of it. Pb may bind to both large-molecule proteins (e.g., albumin) and small-molecule proteins (e.g., metallothionein—MT) in the body, resulting in variable distribution and excretion [30,31]. Pb exposure can cause the development of a variety of diseases and pathologies in the body, including neurological, hematological, renal, cardiovascular, reproductive, skeletal, gastrointestinal, and immunological effects [32-39].

3.1 Neurological Effects

Lead exposure is well known for its negative effects on the neurological system, particularly in young adults whose growing brains are more susceptible to harmful effects. Pb concentrations over 0.8 µg/L in urine and 0.6 µg/L in blood may negatively damage the neurological system [40, 43]. Pb has been demonstrated to impair brain function by modifying neurotransmitter release, interfering with synaptic connections, and influencing cognitive processes [40,41]. Lead exposure in young people can cause cognitive impairment, learning difficulties, behavioral issues, lower IQ scores, and hyperactivity. Furthermore, lead can impair brain growth by interfering with calcium absorption, which is required for brain cell activity and synaptic connections [40]. The toxic effects of Pb are more damaging to children, who have rapid brain growth and a high rate of neural connections, making them more sensitive to Pb-induced brain damage. The neurotoxic effects of Pb, particularly in children, are well documented in the scientific literature [41, 42]. Lead-induced damage to brain areas such as the prefrontal cerebral cortex, hippocampus, and cerebellum can contribute to a variety of neurological disorders, including brain damage, mental retardation, behavioral issues, nerve damage, and possibly Alzheimer's disease, Parkinson's disease, and schizophrenia [43-46]. Research indicates that lead levels over 0.38 µg/L in blood and 0.1802 µg/L in urine can cause neurotoxicity [43].

3.2 Hematological Effects

Pb exposure can have a major impact on the blood cell count and morphology. Lead poisoning can affect a variety of hematological parameters, including red blood cell (RBC), white blood cell (WBC), and platelet (PLT) counts as well as cell size and shape [47–49]. Lead exposure can reduce the RBC count, especially as the lead content and exposure time increase. RBC size tends to decrease when exposed to lead, with higher lead concentrations resulting in a more dramatic reduction [47]. Pb exposure can cause an increase in white blood cell counts, especially at higher Pb concentrations and for longer periods of time. This alteration in the WBC count indicates

a response to lead-induced immune disturbances in the body and leads to an increase in the PLT count, which may be associated with intravascular platelet rupture. An elevated platelet count can be a consequence of lead-induced thrombocytopenia and platelet proliferation [48, 49]. Furthermore, Pb exposure can cause anemia by inhibiting heme production and reducing red blood cell (RBC) survival. Lead overdose causes anemia, which is often hypochromic, normocytic, or microcytic with reticulocytosis. Lead can also block heme production enzymes, increasing blood and plasma levels of d-aminolevulinic acid (ALA) and free erythrocyte protoporphyrin (EP) [50].

3.3 Renal Effects

Pb exposure causes a variety of negative consequences in the kidneys, with both chronic and acute exposure resulting in severe damage [51]. Lead-induced renal consequences may manifest as glomerular and tubular alterations, resulting in proteinuria, nephrotic syndrome, and tubular dysfunction [34,52]. Chronic occupational exposure to lead or ingestion of lead-contaminated substances has been linked to an increased risk of renal dysfunction, chronic renal failure, hypertension, hyperuricemia, and gout [54, 55]. Furthermore, Pb exposure has been associated with kidney damage biomarkers, suggesting that even low-level environmental exposure may result in impaired kidney function [56]. Lead exposure can also cause anemia by interfering with heme production and decreasing red blood cell survival, resulting in hypochromic, normocytic, or microcytic anemia with reticulocytosis [57, 58].

3.4 Cardiovascular Effects

The cardiovascular consequences of lead exposure have been thoroughly examined, with findings indicating a strong link between chronic lead exposure and high blood pressure as well as other cardiovascular problems [59]. Epidemiological and clinical research has repeatedly linked lead exposure to hypertension (HTN) and a variety of cardiovascular diseases, including ischemic coronary heart disease, cerebrovascular accidents, and peripheral vascular diseases [60]. Several studies in experimental animals have shown that lead exposure causes hypertension. Furthermore, in vivo and in vitro studies have been conducted to investigate the effects of lead on the heart and vascular function, offering information on the processes by which lead exposure might cause cardiovascular illness. Lead exposure appears to be associated with higher blood pressure, which may contribute to clinical cardiovascular outcomes, such as cardiovascular mortality, coronary heart disease, stroke, and peripheral arterial disease. Notably, these correlations were detected even at very low blood lead levels, highlighting the need to identify and manage cardiovascular risks associated with lead exposure [60].

3.5 Reproductive Effects

Both men’s and women's reproductive health may suffer significantly as a result of lead exposure. Lead exposure in males has been linked to reduced libido, impaired spermatogenesis, and chromosomal abnormalities in sperms. Pb can lower sperm quality in terms of volume, density, motility, and shape [61]. It can also affect male reproductive hormone levels, including follicle-stimulating hormone, testosterone, and luteinizing hormone [62]. Prenatal lead exposure, even at extremely low levels, can be detrimental to both the mother and baby. Lead exposure during pregnancy has been associated to spontaneous abortion, intrauterine growth restriction, preterm birth, stillbirths, pregnancy hypertension, preeclampsia, and low birth weight [63–68]. Pb can pass through the placenta and damage embryonic development [69]. Pb exposure puts both men and

women at risk of infertility. Even modest levels of Pb exposure have been linked to negative reproductive outcomes. According to animal research, chronic lead exposure can diminish the weight of the body, testes, epididymis, seminal vesicles, and ventral prostate in men [70,71].

3.6 Skeletal Effects

Pb exposure can have a major negative impact on bone growth and health. Lead exposure can affect skeletal ossification, resulting in skeletal abnormalities and aberrant bone formation. Studies have demonstrated that lead exposure causes wavy fins, abdominal edema, stunted development, hyperplasia, and axial skeletal abnormalities in frogs [72]. Chronic Pb exposure can result in reduced bone mass, cortical and trabecular architecture, and mechanical bone quality. Animal studies have shown that Pb exposure alters the femur cross-sectional geometry and bone tissue material characteristics [73]. Pb exposure, particularly in young people, may increase the risk of developing osteoporosis later in life. Lead accumulates in bones and can be discharged during periods of rapid bone turnover, such as pregnancy, thereby increasing the body's exposure to Pb poisoning. Pb exposure can affect normal bone metabolism by interfering with calcium homeostasis and altering osteoblast and osteoclast activity levels. This can cause an imbalance between bone growth and resorption, resulting in skeletal deformities [74].

3.7 Gastrointestinal Effects

The gastrointestinal consequences of Pb exposure can lead to various symptoms and problems. Lead intoxication can cause gastrointestinal issues, such as constipation, diarrhea, vomiting, colic, low appetite, and weight loss [75]. Lead-induced colic can cause occasional vomiting, intermittent stomach discomfort, and constipation, with severe instances resulting in cramping and abdominal pain that may be misinterpreted as an acute abdomen or appendicitis. Children are more sensitive to lead absorption through the gastrointestinal tract, with up to 70% absorption compared with 20% absorption in adults. According to [34], iron and calcium deficiencies can enhance lead absorption in the gastrointestinal tract in both children and adults.

3.8 Immunological Effects

Pb exposure has been linked to changes in immunological function, potentially increasing the risk of autoimmune illnesses, infectious diseases, allergies, and cancer [77]. Pb exposure has been demonstrated to impact immune cell morphologies, hypersensitivity, and the balance of T helper cell subsets, with a specific focus on T helper 2 (Th2) cell development and Th1 cell proliferation. Occupational lead exposure has been associated with changes in circulating cytokines, leukocyte numbers, and immune cell types, indicating that lead has an immunosuppressive effect on the immune system [78,79].

3.9 Cell Cycles

Pb exposure has been demonstrated to have a major impact on the cell cycle, especially in human leukemia cells. The cell cycle is a tightly controlled process that governs cell growth and differentiation, and changes in cell cycle distribution can be linked to apoptosis and differentiation [80]. Lead nitrate exposure causes cell cycle arrest at the G_0/G_1 checkpoint in HL-60 cells. This arrest was marked by an increase in the G_0/G_1 cell population and a decrease in the S and G_2/M cell populations, indicating that lead nitrate induces cell cycle arrest at the G_0/G_1 checkpoint [81]. Gestational lead exposure has been demonstrated to upregulate cell cycle genes and decrease cell

cycle duration, resulting in increased proliferation and rod photoreceptor development in retinal progenitor cells [82]. Pb exposure has also been associated with DNA damage, cell cycle arrest, and apoptosis in human leukemia cells. The study discovered that exposure to lead nitrate caused DNA damage, resulting in cell cycle arrest and apoptosis, both of which are important cellular responses to genotoxic stress [81].

3.10 Carcinogenic Effects

Lead (Pb) is a recognized carcinogen that causes cancer in humans. The International Agency for Research on Cancer (IARC) has categorized lead as "probably carcinogenic to humans," citing ample evidence from animal studies and insufficient data from human research. Lead exposure has been associated with an increased risk of a variety of malignancies, including kidney, brain, lung, and hematological cancers [83]. Pb bioaccumulation in the body, particularly in the kidneys, increases the risk of developing renal cancer and can attach to proteins, increasing the risk of renal cancer through interactions with DNA in renal cells [26].

4. Environmentally Degrading Effects of Lead

Lead is prevalent in the Earth's crust and is classified as a hazardous environmental contaminant owing to its poisonous qualities, persistence in the environment, and extensive pollution caused by human activity [84]. Pb is difficult to remove from the soil, where it is frequently injected via phosphate fertilizers (for example, superphosphates). The high amounts of lead (Pb) in water, air, and soil are mainly caused by industrial activities [85].

5. Accumulation of Pb in Tobacco Smokers

The bioaccumulation of lead (Pb) in tobacco users is a major concern because of the presence of this poisonous heavy metal in tobacco and its release into the smoke when cigarettes are smoked. Studies have indicated that tobacco smoke is a source of lead exposure, with smokers having greater levels of lead in their blood, lung tissue, and other tissues than non-smokers [86]. Tobacco cigarette brands vary in lead level, with typical values ranging from 3.05 to 3.51 µg/g dry weight. Cigarette smoke inhalation exposes smokers to lead and other harmful heavy metals, which can have long-term health consequences. The accumulation of Pb in tobacco users can contribute to a variety of health problems, including cardiovascular diseases, lung diseases, and other smoking-related illnesses [87].

6. Accumulation of Pb in Food

The accumulation of lead (Pb) in food crops is a serious problem for both food safety and human health. Cereals such as rice, wheat, and maize have been discovered to contain extremely high levels of lead. A study conducted in Bangladesh has found that vegetables such as cabbage, zucchini, sponge gourd, tesla gourd, okra, chili, drumstick, green amaranthus, papaya, and pointed gourd have 10-46 times greater Pb content than the maximum allowed concentration (MAC) of 0.10 µg/g [88]. Pb accumulates in food crops through a variety of pathways, including uptake from contaminated soil, particularly near roadsides, acid mining drainage areas, irrigation with untreated wastewater, adsorption of Pb in the roots and translocation to other plant parts, and soil-root interference, which leads to contamination [88,89]. The daily consumption of lead (Pb) can vary greatly, ranging from 0.007 to 3 mg, whereas the hazardous dosage of Pb ranges from 3 to 330 mg and the deadly dose ranges from 1.5 to 9 grams. The toxic levels of lead fumes vary from 2,600

mg/m³ to 2,900 mg/m³ per minute of exposure. Understanding the possible health hazards associated with lead exposure requires knowledge of these levels [90]. The absorption of lead (Pb) from the gastrointestinal system is controlled by both health status and food, and includes vital components such as iron, vitamins, polyphenols, and antioxidants. A well-balanced diet rich in these bioelements can help prevent Pb absorption and its harmful consequences. In contrast, a lack of physiologically active chemicals may enhance Pb absorption and accumulation in the body [91].Lead (Pb) exposure has been demonstrated to influence bones and cause calcium, protein, and vitamin D shortages [92]. This emphasizes the intricate link between dietary variables, absorption of hazardous metals, and overall health effects. Maintaining a diet rich in important nutrients and bioelements is critical for reducing the negative effects of Pb and other hazardous metals in the body. Adequate consumption of certain vitamins and minerals, including calcium, iron, and vitamin C, can help reduce Pb absorption. A diet rich in calcium and phosphorus decreases lead absorption even more, making plant calcium supplements particularly beneficial. Iron-deficient individuals absorb two–three times more lead (Pb) than those with adequate blood iron levels. Diets rich in vitamin C enhance iron absorption and may decrease lead absorption [93]. Children, particularly newborns and young children, consume a larger proportion of lead (Pb) than adults. This is due to their less diversified eating habits and increased hand-to-mouth activities, which result in greater lead absorption from multiple sources, such as polluted dust, soil, water, and food. Pb in food can originate from a variety of sources, including lead-plated plates, galvanized equipment, lead-containing stabilizers in polymers, and lead-based ceramics or glazes [94]. Furthermore, drinking water contains trace quantities of Pb owing to the use of galvanized pipes and solders in tap fittings. According to research, keeping food in enameled containers might increase Pb levels, especially in acidic liquids [95].

7. Prevention and Monitoring of Lead Poisoning

Individuals with specific health issues, such as renal illness, chronic bronchitis, emphysema, rhinitis, osteoporosis, osteomalacia, anemia, liver damage, and hypertension, or those who smoke frequently, should not work in lead-exposed workplaces. Preventive actions should be adopted to encourage healthy health habits, such as reducing smoking, practicing rigorous personal cleanliness, and boosting staff knowledge of lead exposure. Employers should also take steps to reduce lead emissions in the workplace so that the daily concentration levels are not exceeded. These preventive measures are critical for protecting the health and well-being of those working in workplaces where lead exposure is a concern [96].

Gastric lavage and the delivery of disodium phosphate (4-8 g in a glass of water) are the recommended therapies for acute oral poisoning, particularly when lead (Pb) exposure is involved. These treatments function by binding to any Pb that has not been eliminated from the body, thereby decreasing absorption and possible toxicity. Gastric lavage is a technique that involves washing the stomach with water or saline solution to eliminate ingested contaminants including lead. In contrast, disodium phosphate may bind to Pb and other toxins, allowing them to be removed more easily [97]. It is crucial to highlight that chelating medicines, which are commonly used to remove heavy metals such as lead from the body, are not indicated as therapies for acute oral poisoning due to the danger of kidney damage. Chelating drugs can bind to lead and other metals, but they can also injure the kidneys if administered incorrectly or in large quantities [98]. Chronic lead (Pb) poisoning is generally treated symptomatically, with the goal of treating symptoms and problems rather than eliminating the toxin itself. Pb contamination is mostly generated by high vehicle

traffic, fossil fuel combustion, mining, metallurgical activities, and sediment removal [99]. Certain substances, such as polyphenols, melatonin, carotenoids, l-carnitine, and coenzyme Q10, can be utilized to attenuate the negative health consequences of lead exposure [53]. These compounds may reduce Pb absorption and toxicity in the body. Another method for reducing Pb and other heavy metal pollution is phytoremediation, which involves the accumulation and removal of these toxins using plants or nanoparticles [76]. Phytoremediation is less costly, more effective, and ecologically benign than other remediation techniques. Additional tests, including a complete blood count, prothrombin time determination, and liver function tests, can be used to estimate the quantity of Pb in the bodies of exposed people. These tests assist in determining the level of Pb exposure and its effects on various body systems [100].

8. CONCLUSION

Lead (Pb) is one of the most dangerous metals that people may be exposed to, especially in professional settings and natural environments. Inhalation, ingestion of contaminated foods and drinks, and skin absorption are the most common routes of exposure. Pb accumulates in the body over time, with some estimates indicating that it can persist for up to 30 years. Pb exposure can cause epigenetic modifications that lead to the development of malignancies, chronic illnesses, and other pathological conditions. Chronic Pb exposure in humans may induce carcinogenesis. Other effects of lead include oxidative stress and increased reactive oxygen species (ROS) production, which are typically counterbalanced by enzymatic antioxidant defenses, such as superoxide dismutase (SOD), catalase (CAT), and glutathione peroxidase (GPx), as well as non-enzymatic antioxidants, such as glutathione (GSH), vitamin C, and vitamin E. Adequate dietary intake of important micronutrients, such as zinc (Zn), iron (Fe), and calcium (Ca), can help prevent lead absorption and toxicity. Individuals who are occupationally exposed to heavy metals such as lead require regular monitoring to preserve their health, adopt effective preventative measures, and improve public health outcomes. People at risk of lead poisoning, such as metallurgists, mechanics, farmers, plumbers, and firemen, should undergo complete diagnostic tests to identify PbB levels and probable neurotoxicity. This enables the early diagnosis and control of lead exposure, thus reducing its negative consequences on health.

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