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# A Review on Lead Toxicity and Its Adverse Effects on Human Health

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**ABSTRACT:**Lead toxicity is one of the most hazardous metal toxicities. It can enter the body through lead-based paint, dust, water, soil, tableware, and folk medicines. Environmental lead exposure is a global health concern in children. Acute or chronic lead exposure may cause reversible or even permanent damages in human beings. Occupational lead poisoning is still a health issue, particularly in developing countries. The majority of cases of lead poisoning are due to oral ingestion and absorption through the gut. Lead poisoning in adults occurs more frequently during exposure in the workplace and primarily involves the central nervous system. Lead is highly persistent in the environment and because of its continuous use its levels rise in almost every country, posing serious threats. Lead toxicity also affects neurotransmitter levels and causes severe health issues related to organ damage, some even leading to death. Lead poisoning is preventable. This includes individual efforts such as removing lead-containing items from the home, workplace efforts such as improved ventilation and monitoring, and nationwide policies such as laws that ban lead in products such as paint and gasoline, reduce allowable levels in water or soil, and provide for cleaning of contaminated soil. The major treatments are removal of the source of lead and the use of medications that bind lead so it can be eliminated from the body, known as chelation therapy. The main aim of this review article is to summarize lead toxicity detection, its sources, and its mechanism including various toxicological effects on human health.

**KEYWORDS:**lead toxicity, lead exposure, chelation therapy, human health.

## I. INTRODUCTION

Lead is an extremely useful metal but unfortunately has also proved to be a dangerous toxin, particularly for young children who are at a sensitive stage of their neurobehavioral development. It is now widely accepted that lead easily crosses the blood-brain barrier, that lead exposure can be detrimental even at extremely low levels, and that the adverse neurological effects of lead persist into older ages. Lead is a naturally occurring metal found in the earth's crust. It has a wide variety of uses in manufacturing due to its properties of being soft, malleable and corrosion resistant. Due to its non-biodegradable nature and continuous use, its concentration accumulates in the environment with increasing hazards. Human exposure to lead and its compounds occurs mostly in lead related occupations with various sources like leaded gasoline, industrial processes such as smelting of lead and its combustion, pottery, boat building, lead based painting, lead containing pipes, battery recycling, grids, arm industry, pigments, printing of books, etc. Lead is not required for human health and can be hazardous when taken into the body by swallowing or breathing in lead or materials contaminated with lead. Once in the body, lead circulates in the blood and can be stored in the bones. Infants and young children are especially sensitive to even low levels of lead, which may contribute to behavioural problems, learning deficits and lowered IQ [1]. The health effects from exposure to lead will depend on a variety of factors such as a person's age, the amount of lead they are exposed to and for how long, and if they have other health conditions. In pregnant women, high exposure to lead may cause miscarriage. Chronic lead exposure was found to reduce fertility in males [2]. Adults are most often exposed to lead if they work in a job which involves lead-based activities.

## II. SOURCES AND ENVIRONMENTAL EXPOSURE OF LEAD

Lead is used in the manufacture of batteries, metal products, paints, and ceramic glazes. Exposure to lead can occur from breathing contaminated workplace air or house dust or eating lead-based paint chips - or contaminated dirt. Lead is a very toxic element, causing a variety of effects at low dose- levels. The largest source of lead in the atmosphere has been from leaded "gasoline combustion, but with the phase down of lead in, gasoline, air lead levels have decreased considerably. Pharmaceutical companies have set a limit for maximum daily intake of lead as 1.0 µg/g, however

prolonged intake of even this low level of lead is hazardous to human beings. Occupational exposure also results in elevated blood lead levels. Increased blood levels are associated with delayed puberty in girls [3]. Other airborne sources include combustion of solid waste, coal, and oils, emissions from iron and steel production and lead smelters, and tobacco smoke. Lead was used in paint to add colour, improve the ability of the paint to hide the surface it covers, and to make it last longer. In 1978 the federal government banned lead paint for use in homes. Homes built before 1978 probably contain lead-based paint. Painted toys and furniture made before 1978 may also contain lead-based paint. Lead-based paint becomes a concern when it chips, turns into dust, or gets into the soil. Dangers from lead poisoning due to paint pigments mainly in children have sharply reduced the use of lead in paints. However old houses may still contain substantial amounts of lead paint [4].

1. Lead dust is the most common way that people are exposed to lead. Inside the home, most lead dust comes from chipping and flaking paint or when paint is scraped, sanded, or disturbed during home remodelling. Lead enters drinking water primarily as a result of the corrosion, or wearing away, of materials containing lead in the water distribution system and household or building plumbing. These materials include lead-based solder used to join copper pipe, brass and chrome plated brass faucets, and in some cases, pipes made of lead that connect houses and buildings to water mains. In 1986, Congress banned the use of lead solder containing greater than 0.2% lead, and restricted the lead content of faucets, pipes and other plumbing materials to 8.0%. Older construction may still have plumbing that has the potential to contribute lead to drinking water. Lead can be present in outdoor and indoor air. Lead in outdoor air comes mainly from industrial sources (e.g., smelters, waste incinerators, utilities, and lead-acid battery manufacturers). Wind-blown soil and road dust also may contain naturally occurring lead as well as lead from industrial sources, deteriorated paint, and the combustion of leaded gasoline and aviation fuel. Sources of lead in indoor air include outdoor air, suspended dust, and some hobbies (e.g., making stained glass objects using lead solder, shooting using lead bullets at indoor firing ranges).

Ayurveda is a traditional form of medicine practiced in India and other eastern Asian countries. Ayurvedic medicines are considered to be heavily contaminated with heavy metals. In one recent study the blood lead levels were evaluated in consumers of ayurvedic medicines. Of the 115 participants 40% were found to have an elevated blood lead levels of 10  $\mu\text{g}/\text{dL}$  or above and 9.6% had blood lead levels above 50  $\mu\text{g}/\text{dL}$  [5]. Recently a patient taking Chinese folk remedies was reported to suffer from dysplastic changes in erythroid precursors due to lead poisoning [6].

### III.MECHANISM OF ACTION LEAD POISONING

The precise mechanisms of action of lead on cellular metabolism remain largely unknown, despite the known effects of lead on porphyrin and heme biosynthesis that have been studied for decades. In fact, lead-induced alterations in porphyrin metabolism have long formed the bases of tests for the laboratory diagnosis of chronic lead poisoning. Lead induces an iron-deficiency-like response in developing erythrocytes, as evidenced by the same accumulation of zinc protoporphyrin, lead also induces a microcytic, hypochromic anaemia. Because iron must be in the reduced (ferrous) state before it can serve as substrate for ferro chelatase, inhibition of iron reduction by lead could explain the utilization of zinc as the alternative substrate. It is worth noting that acute lead toxicity may differ from chronic lead exposure by acting through multiple mechanisms. The mechanism of coproporphyrin resulting from lead poisoning is less clear. Increased coproporphyrin excretion is a very late response to lead exposure, which could argue against inhibition of coproporphyrinogen oxidase and suggest a more complex series of events. Moderate coproporphyrinuria as seen in lead poisoning has many etiologies, including a variety of toxic agents. Thus, coproporphyrinuria may be the result of more general cellular or tissue damage rather than inhibition of any specific enzyme. For these reasons, measurement of coproporphyrin excretion is no longer a test of choice for lead poisoning. Lilley et al. found that lead metal or lead nitrate solution, when placed on the skin, can be quickly absorbed and transported in the body [7]. The lead that was absorbed could be found in sweat and saliva, although was not detected in blood and urine. To prove that lead was transported through the body, Lilley et al. applied a high lead nitrate amount to the left arm of the volunteer. As a result, lead concentration was increased in the sweat sample on the right arm, which served as an evidence of lead being transported in the body. Another conclusion made from the study was that the rate of lead absorption through the skin increases with increased sweating of the skin. No increase in blood lead must have meant that lead does not get to the erythrocytes. Instead, it gets transported through the plasma and concentrates in the extracellular fluid pool, sweat and saliva. That is why workers who are occupationally exposed to lead have high levels of lead in sweat and saliva, but not in blood [7]. The only way lead can increase blood levels through skin is when being a part of organic molecules [8].

Although human body contains sufficiently large amounts of lead, moderately increased Pb concentrations become toxic from health point of view. The large affinity of  $\text{Pb}^{+2}$  to thiol (-SH) and phosphate containing ligands inhibits the biosynthesis of heme and thereby affects the membrane permeability of kidney, liver and brain cells. These result in either reduced functioning or a complete breakdown of these tissues since Pb is a cumulative poison.

#### IV. SIGNS OF LEAD EXPOSURE

##### Acute exposure

Acute lead poisoning is usually caused by a recent exposure to a high amount of lead. The symptoms may include, muscle pain, fatigue, abdominal pains, headache, nausea and vomiting, seizures, coma.

During acute poisoning, neurological symptoms may occur such as pain, weakened muscle power, sensory abnormalities, and occasionally brain inflammation, along with digestive system-related symptoms such as stomach aches, nausea, vomiting, diarrhea, and constipation. In instances where a large amount of lead has been ingested through the digestive system in a short period of time, the loss of a lot of water in the digestive system can cause shock, hemolytic action occurs, and symptoms such as anaemia may occur.

##### Chronic exposure

If a person is exposed to smaller amounts of lead over a longer time period, chronic (long-term or ongoing) lead exposure may produce symptoms such as, irritability, lack of energy, loss of appetite, learning disabilities, behavioural problems, poor school performance, poor coordination, impaired growth. Chronic lead poisoning may also manifest as a grey color in the skin or a blue line in the gums, known as the Burton line. Aside from these symptoms, an increase in vision deformities. Lead exposure has been found to increase risk of numerous conditions that may have adverse effects on nervous system function, including hypertension, renal insufficiency, thyroid metabolism, vitamin D deficiency, and premature birth.[14] .

##### Lead exposure in pregnancy and children

Exposure of an embryo in uterus to lead increases the possibility of premature birth and low birth weight. As the body size of children is smaller than that of adults and lead is more quickly absorbed, they are more vulnerable to lead poisoning. Additionally, because babies crawl on the floor and suck on various objects, they are more readily exposed to lead. There is consistent evidence that the risk for spontaneous abortion is increased by maternal exposure to high levels of lead (*e.g.*, occupational exposures)

##### Effects on Respiratory System

Recent studies have suggested an association between blood lead levels and childhood asthma. Although, blood lead levels are not significantly linked with a diagnosis of asthma, the higher blood lead levels may culminate to a more severe form of asthma in children. (due to eosinophilia and elevated immunoglobulin E levels). [19]

##### Male Reproductive Effects

Recent reproductive function studies in humans suggest that current occupational exposures may decrease sperm count totals and increase abnormal sperm frequencies. In men, there is sufficient evidence that BLLs  $\geq 15$   $\mu\text{g}/\text{dL}$  are associated with adverse effects on sperm or. It is unclear how long these effects may last in humans after lead exposure ceases.

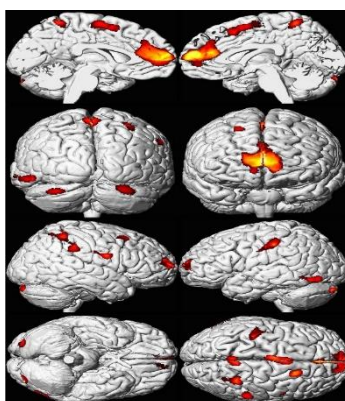
##### Cancer

EPA has classified elemental lead and inorganic lead compounds as Group 2B: probable human carcinogens, revised in 2011. This classification is based in part on animal studies, which have been criticized because the doses of lead administered were extremely high.

##### Effects on Brain

Exposure to lead wreaks havoc in the brain, with consequences that include lower IQ and reduced potential for learning. But the precise mechanism by which lead alters nerve cells in the brain has largely remained unknown. New research has used high-powered fluorescent microscopy and other advanced techniques to painstakingly chart the varied ways

lead inflicts its damage. Lowered intellectual scores have been most commonly noted in children following lead exposure. In reviewing paediatric cross-sectional studies on intellectual deficits following lead exposure, 3-point decrements in IQ have been noted when blood lead concentration increased from 5 to 20  $\mu\text{g/dL}$  and 5.3-point decrements in IQ when blood lead concentration increased from 5 to 50  $\mu\text{g/dL}$  [12]

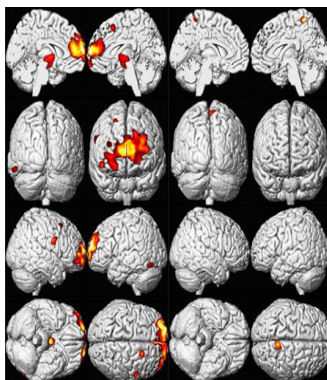


The brains of adults who were exposed to lead as children show decreased volume, especially in the prefrontal cortex, on MRI. Areas of volume loss are shown in colour over a template of a normal brain.<sup>[20]</sup>

#### Lead Exposure a Bigger Threat to Boys Than Girls

The female hormones estrogen and estradiol may help protect against lead's harmful effects on the frontal areas of the brain, according to the findings published recently in the Journal of Environmental Health.

"The study supports existing research suggesting that estrogen and estradiol in females may act as neuroprotectants against the negative impacts of neurotoxins," study author Maya Khanna, a psychology professor at Creighton University, said in a university news release.



Sex Influences Brain Volume Loss Associated with Lead Exposure (Males left and Females right) [20]

### V. EVALUATION AND DIAGNOSIS OF LEAD EXPOSURE

#### Urine Analysis

Detection of urinary coproporphyrins is also a biomarker of lead toxicity by virtue of lead effect on heme biosynthesis. High levels of urinary coproporphyrins are usually indicative of severe cases, although, high levels of lead can also be detected in the body in the absence of coproporphyrins. [16]



### VI. DIETARY MANAGEMENT

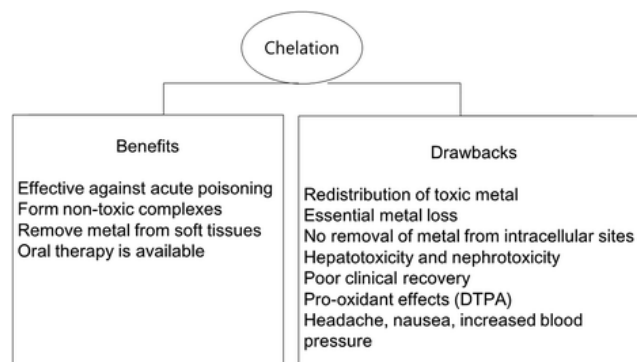
Antioxidants are effective in decreasing and treating the oxidative stress-induced toxicity of lead. Antioxidants used in the alleviation of lead toxicity include vitamins, flavonoids, and herbs. Gurer et al. investigated how an antioxidant (N-acetylcysteine) and a chelator (succimer) could treat the symptoms of lead poisoning in rats [9]. In the study, 344 rats were given lead acetate in their drinking water for five weeks. The next step was to remove lead-contaminated water and replace it with either NAC or succimer. At the end of the experiment, RBC levels were measured. The group of rats that was treated with lead had induced oxidative stress, evidenced by lipid peroxidation through the increase of malondialdehyde content and G6PD, as well as decrease in GSH.

Vitamin C (ascorbic acid) is the most widely studied antioxidant capable of removing free radicals. Unsurpassed in its ability to bind to and remove lead, vitamin C is highly effective at alleviating lead toxicity. As vitamin E improves lead-induced memory impairment, it has been recommended as good for preventing lead-induced health problems with appropriate dosing. Natural polyphenolic compounds, flavonoids are abundant in fruits and vegetables. Like other antioxidants, flavonoids prevent oxidative stress by binding with heavy metal ions and preventing free radical chain reactions. Quercetin is abundant in fruit, vegetables, and tea. It has a stronger antioxidant effect than vitamin C or E. An antioxidant that can be used in the treatment and prevention of oxidative stress-induced disease,  $\alpha$ -lipoic acid is found in foods like carrots, beets, and potatoes. Inexpensive and with few adverse side effects, herbs are being used clinically with effect. However, as the treatment period is very long, their use is limited to prevention rather than treatment of symptoms of lead exposure.

### VII. CHELATION THERAPY

In This treatment, a medication given by mouth binds with the lead so that it's excreted in urine. Chelation therapy might be recommended for children with a blood level of 45 mcg/dL or greater and adults with high blood levels of lead or symptoms of lead poisoning. Chelation involves introduction of one or more agents that bind with lead and facilitate its excretion. Recommended chelation agents include oral meso-2,3-dimercaptosuccinic acid (DMSA) and intravenous or intramuscular ethylenediaminetetraacetic acid (EDTA). Encephalopathic individuals with severe, acute lead toxicity are usually treated with intramuscular dimercaprol, either alone or in combination with EDTA. Both cessation of lead exposure and chelation effectively lower blood lead levels, reducing pharmacological effects of lead, but they show no therapeutic benefit against morphological changes [13]. Chelating agents continue to be the mainstay of treatment for lead poisoning which forms complexes with lead, prevent its binding to cell constituents and, being hydrophilic. These drugs are metabolized and are eliminated in the urine. [17] The most widely used chelating agents are Dimercaprol, also known as British Anti-Lewisite (BAL), Calcium Disodium ethylenediaminetetraacetate (EDTA), and Succimer (2,3-meso-dimercaptosuccinic acid or DMSA) [18]

- EDTA chelation therapy. Doctors treat adults with lead levels greater than 45 mcg/dL of blood and children who can't tolerate the drug used in conventional chelation therapy most commonly with a chemical called calcium disodium ethylenediaminetetraacetic acid (EDTA). EDTA is given by injection.



Benefits and drawbacks of chelation therapy

## IX. ADVANCED MEASURES

A recent study on a cohort of workers occupationally exposed to lead found that worker's cohort treated with N-acetylcysteine (NAC) showed a significant reduction in the blood lead levels. Additionally, all groups receiving NAC showed a significantly elevated activity of glutamate dehydrogenase. Further, the treatment with NAC normalised the level of homocysteine and decreased oxidative stress. It can thus be concluded that NAC could be as an alternative therapeutic agent for chronic lead toxicity in humans. [15]

## X. CONCLUSIONS

Many studies have been conducted on harmful health impact of lead but still Despite its toxicity, lead has been widely used by humans for many centuries. As a result of its use, lead poisoning has been an old but persistent problem. The accumulation of knowledge about main sources of lead along with its detection, pathways of absorption, and oxidative effects contribute to treating and preventing lead intoxication cases. The accumulation of knowledge about main sources of lead along with its detection, pathways of absorption, and oxidative effects contribute to treating and preventing lead intoxication cases This study have been conducted on health problems caused by low-level lead exposure and cronic exposure on human health .

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