Int. j. adv. multidisc. res. stud. 2025; 5(3):1410-1414

Received: 27-04-2025
Accepted: 07-06-2025

International Journal of Advanced Multidisciplinary Research and Studies

ISSN: 2583-049X

Exposure to Lead: Toxicity, Estimations and Prevention

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DOI: https://doi.org/10.62225/2583049X.2025.5.3.4466

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Abstract

Lead has been used by humans from time immemorial. The harmful effects of exposure to lead were recognized as early as second century BC. Exposure to lead has been frought with health hazards such as blindness, brain damage, renal illness, convulsions, and cancer. Lead toxicity is mostly due to distortion of enzymes and structural proteins, but this versatile toxicant also affects a variety of additional targets. The exposure to lead can be estimated by measuring blood lead levels. Various sensitive techniques are available for estimation of lead in the body fluids. High levels of lead can be treated with Lead chelation using the chelating agent that has a higher affinity for lead than calcium. The exposure to lead can also be controlled through various measures. Creating awareness about exposure to lead and implementation of control measures, both at community levels as well as individual level will help in reducing the harmful effects of lead.

Keywords: Lead Contamination, Public Health, Neurotoxicity, Renal Illness, Developmental Disorders, UNICEF Lead Report, CSIR-NEERI, Toxic Substances

Historical Account

The health hazard due exposure to lead have been recognized since the second century B.C., when Nikander, a Greek physician, who described incidence of colic and paralysis after ingestion of lead (Needleman, Herbert, 2004) [1]. Early victims of lead poisoning were primarily lead workers and wine consumers. Lead's sweetness made it beneficial in winemaking to balance the astringent flavour of tannic acid in grapes. Upper-class Romans consumed wine with high lead levels (up to 20 mg/liter). There has been speculation that lead poisoning contributed to the decline of Rome, with the Roman aristocracy's decreased fertility and rising rates of psychosis that are often cited as possible indicators of its impact. Colic outbreaks attributed to lead persisted in Europe until the 16th century, when Eberhard Gockel, a German physician, linked the episodes to lead contaminated wine. After detecting an outbreak of lead colic in his duchy, Duke Ludwig of Württemberg banned the use of lead in winemaking and imposed the death penalty on anybody who broke the law [1].

In recent times, the estimated 7 million tons of lead used in gasoline in the United States throughout the 20th century is still present in soil, air, water, and living creatures [2]. Globally, it is believed that modern man's lead exposure is 300 to 500 times higher than the background levels. According to a 1983 report by Britain's Royal Commission on Environmental Pollution, lead was widely disseminated by humans in the 20th century, making it unlikely that any section on the earth's surface or any form of life remains unexposed by anthropogenic lead [2]. According to an assessment by the US government's Agency for Toxic Substances and Disease, lead pollution from mining, paint, and smelting remains a significant environmental concern [3].

Lead Toxicity

Lead exposure is a significant health risk for workers in the metal trades, contributing to workplace illnesses. Acute lead poisoning at high levels can lead to health conditions such as blindness, brain damage, renal illness, convulsions, and cancer. Lead poisoning is sometimes misdiagnosed as a "aping disease" as it's symptoms resemble those of other common ailments. Toxic effects of lead differ across individuals and depend on multiple factors including environmental circumstances. Some individuals exhibit clinical symptoms at low lead levels, while others may remain asymptomatic even at greater levels of exposure. As of 2012, the Centres for Disease Control and Prevention (USA) have set the standard elevated blood lead level for adults to be 10 µg/dL and for children 5 µg/dL of the whole blood [4].

- **Lead Toxicity in Children**

Children are the most vulnerable to the effects of lead exposure due to their developmental immaturity, which can lead to lowered IQs, learning disabilities, impaired hearing, decreased attention span, hyperactivity, behavioral issues, and growth interference. These diseases can linger unnoticed for a long period, making them more dangerous. (Jannie Lincoln Kitman 2000) [3]. Children's developing organs make them more vulnerable to lead exposure [4]. Lead poisoning in children was identified more than a century back. The earliest reports of lead poisoning in children came from Brisbane, Australia [5]. These reports met with widespread scepticism about lead toxicity affecting children. Even though the phenomenon had spread rapidly, there was much uncertainty about attributing health issues to lead exposure. The rails were painted with white lead-based paint in residences built on piles with big wooden-enclosed verandas that acted as playgrounds for children. The lead paint was outlawed for domestic use in Brisbane in 1920. Lead poisoning in children was first reported in the United States of America in 1914 [2]. It was believed that acute lead poisoning led either to death or complete recovery with no residual effects. This notion was dispelled in 1943 with the first follow-up study in children who had recovered from acute poisoning but suffered from long-term deficits. According to a 2020 report by UNICEF and Pure Earth, half of India's children have increased blood lead levels. According to the report, up to 275 million children had blood lead levels over the WHO's intervention threshold of 5 µg/dL, with 64.3 million exceeding 10 µg/dL [6]. In 2022, CSIR-NEERI reported on the impact of Lead on Human and India's Response. The report corroborated with UNICEF statistics and made recommendations for lowering lead exposure in India (Pennington *et al.,* 2024) [7]. Safe limit of blood lead levels in adults is defined as 5 µg/dL (0.24 µmol/L) or below &, below 3.5 µg/dL (0.17 µmol/L) in children.

Ahamed, Maqusood, *et al.,* (2024) assessed the mean BLL and related risk factors for lead exposure in children (3-12 years) in Lucknow following the petrol lead phase-out program. When the data were compared to BLLs determined by the George Foundation among children in Mumbai, Bangalore, Kolkata, Chennai, Hyderabad, and Delhi, the results showed a decline in BLL in Lucknow children when compared to those reported from other cities in India when leaded petrol was used [8].

- **Lead Toxicity in Adults**

Lead is primarily stored in bone, raising concerns about its fate in older individuals when bone demineralizes. Elevated lead levels can also negatively impact cognitive functions in the elderly. After controlling for co-variates, older women (mean age 70.5 years) with blood lead levels above 8µg/dl performed worse on cognitive assessments and had shorter reaction times than women with levels below 3µg/dl [9].

Thomas Midgley Jr., a junior engineer at General Motors Research Corporation in Dayton, Ohio, reported to his employer, Charles Kettering, that he had discovered tetraethyl lead, a little-known chemical. Lead tetraethyl (TEL) is a combination of metallic lead and an alkyl series that reduces "knock" or "pinging" in internal combustion engines.

A large-cohort study among former workers using TEL (Tetraethyl lead) found a causal link between lead and dementia. Elevated bone lead levels were found to be associated with deficiencies in verbal and visual memory, as well as executive functions and manual dexterity in 535 subjects followed for an average of 16 years [10]. TEL (Tetraethyl lead) workers showed significant decrease in functions compared to controls at yearly intervals. The same researchers investigated the relationship between APOE genotype (located on chromosome 19q3) and bone lead levels. The results suggest that APOE genotype was a genetic risk factor for dementia, Alzheimer's disease, and cardiovascular disease (CVD).

The correlation between lead exposure and Alzheimer's disease highlights calls for more research into lead related dementia [10]. A 1992 follow-up study on participants from the second National Health and Nutrition Examination Survey (NHANES) (1976-1980) supports the claim that Lead exposure may also shorten life. Among 4292 participants higher lead levels (20-29 µg/dl) were associated with higher all cause death (46%) with 39% increase in cardiovascular mortality and 68% in cancer mortality.

Toxicology of lead

Lead is a divalent cation that binds tightly to sulfhydryl groups on proteins. Lead affects the majority of organs, but mostly the central nervous system. Lead toxicity is mostly due to distortion of enzymes and structural proteins, but this versatile toxicant also affects a variety of additional targets. Lead inhibits the development of the endogenous opioid system, a neurochemical system in the body that regulates pain, reward, and addictive behaviours [11]. It effectively cleaves the ribophosphate backbone of tRNA catalytically at specified locations.

Lead toxicity also stems from its ability to mimic and compete with calcium. In picomolar concentrations, lead competes with calcium for binding sites on cerebellar phosphokinase C, affecting neuronal signaling. Lead accumulates in mitochondria, causing swelling and deformation of the cristae. Uncoupled energy metabolism, inhibited cellular respiration, and altered calcium kinetics occur.

Lead has a binary effect on neurotransmitter release; spontaneous neurotransmitter release is increased, while induced release is reduced. δ aminolevulinic acid dehydratase is highly sensitive to lead. Inhibition of this enzyme causes an increase in circulation of aminolevulinic acid (ALA). ALA is a mild GABA (ɣ -aminobutyric acid) agonist that reduces GABA release through presynaptic inhibition. Increased ALA levels may contribute to behavioural issues in porphyria patients, as well as lead intoxication. Lead exhibits deleterious effects on the developing nervous system, particularly impacting immature astrocytes, myelin formation, and the integrity of the blood-brain barrier. This neurotoxicant impedes collagen synthesis and modifies vascular permeability. At elevated concentrations, lead induces cerebral edema and hemorrhage [12]. Fig 1 shows flowchart Illustrating the Pathways, Health Impacts, and Mechanisms of Lead Exposure and Toxicity in Children and Adults

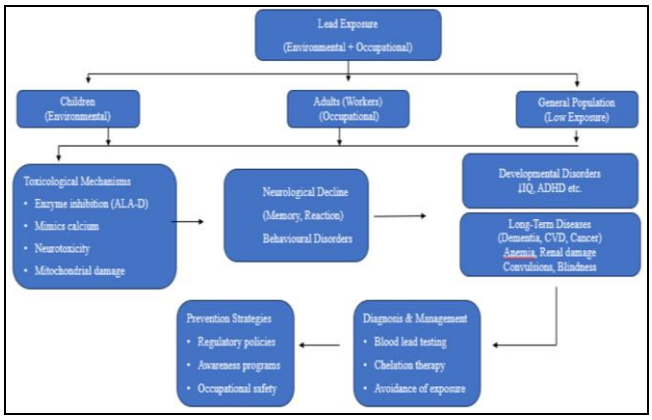

Fig 1: Flowchart Illustrating the Pathways, Health Impacts, and Mechanisms of Lead Exposure and Toxicity in Children and Adults

Occupational Exposure to Lead

Gupta *et al.,* (2024) estimated blood lead levels in adults from Guntur district, Andhra with and without occupational exposure to lead using A graphite furnace atomic absorption spectrophotometer. BLLs were noticeably greater in the occupationally exposed group compared with the unexposed population [13].

A cross-sectional study was conducted by Smita V. Patil (2019) in Western Maharashtra, India, on 70 petrol pump workers (PPW) and 70 automotive mechanics (AM) aged 20-40 who worked at petrol pumps and Car garages for more than a year and 70 healthy males with similar socioeconomic status as controls. BLL was measured using an Atomic Absorption Spectrophotometer (AAS). Occupationally exposed groups had significantly higher BLL levels compared to the control group. The study showed that lead and other heavy metal contaminants found in petroleum and exhaust fumes have a negative impact on health parameters. To improve worker safety, it is crucial to raise awareness of occupational dangers. Employees should implement personal safety precautions in the workplace for improved health.

Singh *et al.,* (2021) studied 120 individuals who were occupationally exposed to metals and 100 healthy controls who had no prior occupational exposure. Among the participants painters had higher blood lead levels [15].

Measuring Parameters of exposure to Lead

Several methods have been employed to detect elevated blood lead levels. Microscopic examination reveals alterations in blood cell morphology, and the absence of prominent dense bands in children's bones on X-ray imaging, indicative signs of lead poisoning. However, the primary diagnostic tool for assessing elevated body lead levels is the measurement of lead concentration in blood samples [4].

Measuring lead exposure, by analytical methods in the population inclusive of sensitive groups like newborns, children, and women in reproductive age, relies on detecting lead in biological samples, most often in blood. The most frequently employed techniques include Atomic Absorption Spectroscopy (AAS), Anodic Stripping Voltammetry (ASV), and Mass Spectrometry. Laser-based analytical approaches, such as Laser-Microprobe Mass Spectrometry and Laser-Induced Breakdown Spectroscopy (LIBS) offer superior detection efficiency and spatial resolution. However, they can be invasive and present challenges in quantification. Laser-Induced Fluorescence (LIF) provides highly sensitive detection by measuring the emission of photons from excited atoms, which enhances detection limits when coupled with LIBS. These analytical methods are of paramount importance in epidemiological investigations as they facilitate precise quantification of lead exposure while minimizing individual risk. Table 1 provides a comprehensive overview of these analytical techniques.

Table 1: Comprehensive overview of analytical techniques to estimate lead

Analytical Method	Principle	Advantages	Disadvantages
Atomic Absorption Spectroscopy (AAS)	Vaporizes ionic lead and converts it to atomic state, and measures absorption of resonance from a hollow cathode lamp.	Method has high sensitivity and specificity; well-established in clinical chemistry and toxicology, making it a reliable method for detecting and quantifying trace elements including lead in biological samples.	Requires chemical degradation and advanced laboratory proficiency, necessitating skilled personnel and specialized equipment to ensure accurate and reproducible results [14].
Anodic Stripping Voltammetry (ASV)	Deposits lead ions on a mercury film electrode via reduction, then reoxidizes them for electrical monitoring, allowing for sensitive and selective detection of lead through anodic stripping voltammetry.	Pre-concentration step enhances sensitivity; simple equipment; cost-effective, making it a practical choice for on-site and routine monitoring of trace metal contaminants.	Mercury use poses environmental concerns; requires careful calibration for accuracy, highlighting the need for proper handling protocols and regular maintenance to ensure both safety and reliability of results [14].
Laser-Microprobe Mass Spectrometry	Uses a laser beam to desorb particles, which are analysed in a mass spectrometer, enabling rapid, high-resolution detection of elemental and isotopic compositions with minimal sample preparation.	High detection efficiency; spatial resolution; rapid analysis of surface and core layers, making it ideal for detailed compositional mapping and depth profiling in complex materials.	Destructive technique; uncertain elemental concentration quantification; low light-microscopy quality, limiting its applicability in scenarios requiring non-destructive analysis, precise quantification, or high-resolution imaging.
Laser-Induced Breakdown Spectroscopy (LIBS)	Ablates material with a laser pulse, creating plasma that emits light analysed for elemental composition, enabling rapid, multi-element detection with minimal sample preparation through laser-induced breakdown spectroscopy (LIBS).	Rapid analysis; non-contact method; suitable for various matrices, making it a versatile tool for real-time, in situ elemental analysis across diverse industrial and environmental applications.	Limited sensitivity for trace elements without combination with other techniques like LIF, which can enhance detection limits and improve analytical performance for low-concentration analytes [15].
Laser-Induced	Excites molecular targets with a laser	High detection sensitivity against dark	Limited to specific molecular targets and

Fluorescence (LIF)	beam and detects subsequent fluorescence emission, providing highly sensitive and selective analysis based on the unique spectral signatures of fluorescent compounds.	backgrounds, allowing for precise identification and quantification of low-abundance molecules even in complex or visually obscured samples.	requires complementary techniques for broader analysis, as it relies on the presence of naturally fluorescent compounds or the use of fluorescent tags to generate measurable signals [15].

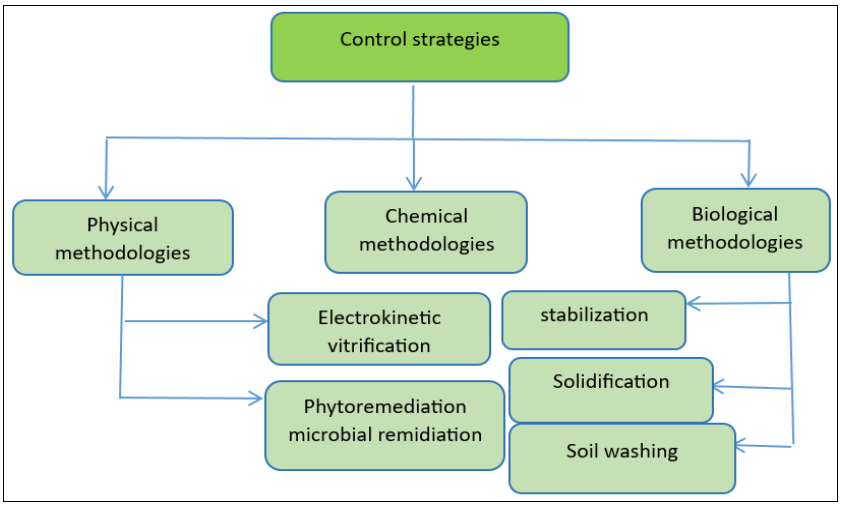

Fig 2: Illustration of various methods employed to mitigate the sources of lead exposure

Strategies for prevention of Exposure

Effective control measures can significantly mitigate lead exposure, thereby preventing its toxic effects (Fig 2). Heavy metal pollutants, notably lead (Pb), have a significant impact on the surrounding environment and the species that live in locations where they are created or released. As a result, several approaches are geared toward site-specific Pb remediation in order to effectively remove these pollutants. To minimize and alleviate harmful metal concentrations, a variety of strategies have been deployed, including physical, biological, and chemical approaches. Physical approaches, for example, provide potential remedies for Pb pollution, such as translocating the source of contamination, which involves removing pollutants from soil or water based on the concentration of the harmful metal [16].

It is important to regularly wash children's hands and improve their intake of calcium and iron. Youngsters should be discouraged from routinely placing contaminated hands in their mouths, as this increases the risk of lead poisoning. Vacuuming regularly and avoiding lead-containing items like blinds and jewelry will help reduce exposure. Replace lead pipes and plumbing solder in ancient residences to prevent lead contamination of drinking water. To address lead (Pb) pollution, contaminants in soil or water are managed by replacement based on their concentration, rather than by translocation from the source [4].

These strategies are more effective on a local scale. The main challenge with this strategy is ensuring safe and cost-effective dumping of contaminated soil or water. In vitrification, heavy metal contaminants in soil are melted by tremendous heat, resulting in Pb appropriation in a solidified mass. This procedure is expensive and not practical for vast regions although it provides a long-term solution to lead pollution as it cleans the soil and extracts the metal recycling. Table 2 gives the details of various methods employed to mitigate the sources of lead exposure.

Table 2: Details of various methods employed to mitigate the sources of lead exposure

Methods	Uses	Discovered by	Working principle
Electrokinetic method	Saturated soils and ground water	Ferdinand Friedrich Reuss [16]	Uses electrolysis and electrophoresis to clean soil and reduce pb contamination. No waste production, energy-efficient, time-saving
Electrokinetic soil remediation	Heavy metal-contaminated soil	Yalcin B. Acar and Akram N. Alshawabkeh [17]	Uses chemical agents and stable voltage to remove heavy metal from waste soil
Chemical stabilization	Soil and groundwater	-	Reduces bio-availability and flexibility of lead using liming, clay minerals, metal oxides, organic composts, and calcium magnesium phosphate
Bioremidiation	Waste management	George M. Robinson [18]	Converts harmful chemicals into less toxic metabolites
Phytoremidiation	Polluted soil and water	R L Chaney [19]	Uses plants to absorb, extract, and detoxify Pb; eco-friendly and cost effective
Rhizo-degradation	Plant roots	-	Lead is absorbed in plants roots aiding in soil detoxification
Phytoextraction	Root area to shoots or leaves	-	Contaminants are transported to above-ground plant parts for removal
Rhizo-filteration	Water and ground water	-	Plant roots absorb heavy metals from contaminated water sources
phytodegradation	Contaminated soil	-	Plants break down pollutants into non-toxic substances
phytovolatalization	Contaminated soil and air	Matt Limer and Joel Burken [20]	Plants absorb contaminants and release them in a less toxic form through transpiration
Specialized plant species	Pb-contaminated environments	-	Pistia statiotes and Ricinus communis accumulate Pb and help in soil remediation

Treatment for lead poisoning

Lead poisoning has been linked to cognitive deficiencies, especially in youngsters, highlighting the need for general reduction of exposure. The treatment for lead poisoning is dimercaprol and succimer. Both drugs bind to heavy metals in the body to treat poisoning. To treat lead poisoning, disodium calcium edetate, a calcium chelate of EDTA, is used as a chelating agent. Lead chelation occurs by exchange, as the chelating agent has a higher affinity for lead than calcium. This is then eliminated via urine, leaving behind harmless calcium. Treatment with succimer as chelation therapy in children exposed to lead can reduce blood lead levels and improve cognitive development.

Conclusion

The estimation of lead concentration in human whole blood has been extensively studied as a key indicator of lead exposure, particularly in occupational and environmental settings. Lead poisoning remains a significant public health concern, as it can result in a range of adverse health effects, including cognitive deficits, renal damage, and neurological disorders Lanphear *et al.,* 2018 [17]. Various analytical techniques, such as atomic absorption spectroscopy (AAS) and inductively coupled plasma mass spectrometry (ICP-MS), have been employed for the accurate and sensitive measurement of lead in blood samples [18]. The literature reveals that blood lead levels serve as a reliable biomarker for recent exposure to lead, making it an essential tool for monitoring and managing lead toxicity in at-risk populations [19]. With the availability of sensitive techniques available for estimating extent of exposure to lead, there is need for a comprehensive epidemiological survey to estimate exposure to lead at local and national level and among various professional groups at the risk of exposure..

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