Sources and Toxicological Effects of Lead on Human

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ABSTRACT

Lead poisoning, also known as plumbism and saturnism, is a type of metal poisoning caused by lead in the body. The brain is the most sensitive. Symptoms may include abdominal pain, constipation, headaches, irritability, memory problems, infertility, and tingling in the hands and feet. It causes almost 10% of intellectual disability of otherwise unknown cause and can result in behavioral problems. Some of the effects are permanent. In severe cases, anemia, seizures, coma, or death may occur.

Exposure to lead can occur by contaminated air, water, dust, food, or consumer products. Children are at greater risk as they are more likely to put objects in their mouth such as those that contain lead paint and absorb a greater proportion of the lead that they eat. Exposure at work is a common cause of lead poisoning in adults with certain occupations at particular risk. Diagnosis is typically by measurement of the blood lead level. The Centers for Disease Control (US) has set the upper limit for blood lead for adults at 10 µg/dl (10 µg/100 g) and for children at 5 µg/dl. Elevated lead may also be detected by changes in red blood cells or dense lines in the bones of children as seen on X-ray.

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, state laws that ban the use of and national policies such as laws that ban lead in products such as paint, gasoline, ammunition, wheel weights, and fishing weights reduce allowable levels in water or soil, and provide for cleanup of contaminated soil. Workers' education could be helpful as well. 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. Chelation therapy in children is recommended when blood levels are greater than 40–45 µg/dl. Medications used include dimercaprol, edetate calcium disodium, and succimer.

In 2016, lead is believed to have resulted in 540,000 deaths worldwide. It occurs most commonly in the developing world. Those who are poor are at greater risk. Lead is believed to result in 0.6% of the world's disease burden. People have been mining and

using lead for thousands of years. Descriptions of lead poisoning date to at least 2000 BC, while efforts to limit lead's use date back to at least the 16th century. Concerns for low levels of exposure begin in the 1970s with there being no safe threshold for lead exposure

Keywords: Lead poisoning,

Introduction

The environment (waters, soils, and dust) contains different types of heavy metals, and these cannot be degraded. Different types of anthropic activities such as mining, smelting, and different kinds of industrial wastes are the main sources of heavy metals. Lead is a bluish-grey-colored heavy metal with low melting point. It can be molded easily into any shape and forms alloys with other metals (1). Lead toxicity is of prime concern in childhood because of environmental source in developing countries. Such poisoning occurs from different kinds of human-related activities such as painting of home, smoking-related activities, leaded petrol, contaminated food, and drinking water; smelting; and especially from the industries, which have been carrying out manufacturing processes (2-5). It is also found in human milk. Excessive exposure of the human body to lead results in disturbance of body function, which can be neurological, cardiovascular, hematologic, and reproductive. Blood containing high level of lead causes inadequate functioning of the central nervous system (CNS) and consequently leads to encephalopathy and edema that mainly affects the cerebellum. In pregnant women, high amount of lead in the body can cause miscarriage. Prolonged lead exposure was found to decrease potency of males (6)

Five micrograms per deciliter is endorsed as a reference (7-9)

An effort has been made to decrease the amount of lead in the occupational environment for the reduction of lead poisoning. Particularly in children, even a small concentration of lead has been reported to induce dyscognitive behavior. The CDC recommends testing for the presence of lead in the blood in all children at the age of 12 months and if possible, once more at the age of 24 months. Novel chelating agent is used for treatment if the BLL is 45 mg/dL or more(8).

Detection of lead poisoning

Lead poisoning is screened by determining the level of lead in fingerprick blood sample. Changes in the bones of the children can be detected using X-ray. There are techniques that have been used for the detection of lead poisoning in blood cells (10 mg/dL for adults and 5 mg/dL for children of the whole blood). Since children are in the stage of development, they are more susceptible toward lead poisoning. Wherever contamination is feasible, regular checkup and lead levels of blood have to be set (10-12).

Burden of diseases from lead exposure

In 2016, the Institute for Health Metrics and Evaluation (IHME) estimated that worldwide 540,000 deaths and loss of 13.9 million healthy life, disability-adjusted life years (DALYs), due to lead poisoning were recorded. IHME also predicted that in 63.8% of cases of lead exposure, there was a liability to develop intellectual disability (13,14). Low- and middle-income countries were most commonly affected. It poses a continuous and serious impact on public health. This also adds to burden of these countries, which are already affected with other extensively familiar public health challenges. For a generalization of sustenance and capital rising, high number of DALYs associated with the exposure of lead may be used for the remediation of toxic waste (15,16).

Possible sources of lead exposure

Lead in paint

Until 1978, in every house, lead was used as common paint; later on, Consumer Product Safety Commission restricted lead in household paint. Before 1978, several buildings that were constructed had been painted with lead-based paints, and approximately, 74% of lead remains. Houses, which were built before 1950, pose a high chance of lead poisoning due to the use of lead-based paint. Exposure of children to lead paints through direct and indirect ways is common because of deferred maintenance and

living in old house. Ingestible lead dust may be hazardous. Old toys, furniture, and playground that are equipped with the lead-based paint have high lead content(18).

Lead in dust

Among children, common exposure source is the lead paint dust. Lead as dust is better and easily absorbed. Interior of the house can be contaminated with lead or lead dust due to damage to painted walls, and airborne exposure can occur due to fall out of lead. When painted surfaces such as windows or doors rub against each other, fine lead dust is formed, thereby contaminating the air. It can accumulate together on the surface of carpets, toys, and other objects, especially on the floors, which later affects the children since they have a high chance of putting their contaminated hands into mouth. A study in young children shows that amount of lead in house paint has a greater association with the BLLs than the quantity of lead dust in the house. Statistical analysis of 12 new studies has shown connection between lead in the dust to BLLs among children (age group: 6–36 months) and also a linear involvement between lead dust stacking and threat of possessing an elevated BLL (19-23).

Lead in water

Some old well pumps may have the possibility of being contaminated by lead. During the last two decades, measures have been taken to reduce the lead exposure through the use of tap water as per the safe drinking water act and a consequent Environmental Protection Agency Regulation (The Lead and Copper Rule) under the requirements of the 1986 and 1996 amendments. The formulation prepared for the consumption of infants with lead-contaminated water has a higher risk due to over intake of water as compared to their body size. If lead is suspected in plumbing, hot water taps should not be used and cold water taps should be flushed every morning for several minutes before use (20-25).

Lead in tableware

Lead may be present in pewter, brass, old, handmade, imported or poorly glazed ceramic dishes, and pottery. An acidic substance present in these pieces could act together with the glaze and increase the release of lead. Thus, the storage of acidic food such as tomato sauce, wine, orange, tomato and other fruit juices, and vinegar in glazed containers is more hazardous (26,27).

Lead in soil

The lead dust from the exterior of a house, which is painted with lead-based paint, can also combine with soil. It may cause problems to the workers during remodeling of the old house. The mixture of lead-contaminated soil can be stirred up by wind and may blow inside the house and surroundings. Metal smelting and battery manufacturing are other important sources of soil contamination by lead. This easily flows into the environment and thus easily mixes up with soil from the nearby homes. For children, lead-contaminated soil has high risk of elevated BLL (EBLL); however, the lead content of interior dust is of less importance. Children have a high BLL from exposure to play area soil and then from other locations (28-29).

Lead in folk medicines and cosmetics

Some folk medicines (greta, azarcon, and pay-loo-ah) may contain lead. These are frequently brought from Southeast Asia, India, Middle East, the Dominican Republic, or Mexico. These folk medications may contain high amount (approximately 90%) of lead. Various cosmetic products such as surma, kohl (alkohl), kajal, tiro, and tozali also contain a high amount of lead. Application of Kohl's results in successive ingestion of particles through hand-to-eye-to-mouth. Lead content of folk medicines and cosmetics is a vital predictor of the adult and children's risk for EBLL (30-32).

Lead in occupational sources

Occupational exposure is an important source of lead poisoning in adults. In the United States, >3 million employees are potentially exposed to lead in the factory due to working equipment (radiation protector, some surgical equipment, developing dental X-ray films processing to digital X-rays, and electronic fetal monitors) that involves lead-containing products. Workers who frequently come in contact with these kinds of equipment have higher chances of toxicity. People, who work in the lead-based zone, unintentionally expose their family to lead poisoning by carrying lead dust into their car,

their clothes, and bodies. Increasing amounts of lead in occupational sources have a strong correlation with the BLLs of adult (33-35).

Lead in metal costume jewelry

Lead poisoning in children has been most serious for the last decade. Children are encountered by lead toxicity from the metal costume jewelry containing lead. Charms are being manufactured without testing for lead. A high amount of lead (99.1%) is contained in charm and is considered dangerous as it raises BLLs up to three times the BLL seen in children (33).

Lead in toys

Toys and other useful goods for children are found with a high range of lead and pose lead poisoning threats. Maximum parents would not ever believe that their child's sports accessory set could have a high amount of lead. The Center for Environmental Health (CEH) discovered those lead toxic toys over the past few decades. CEH (since 2007) has carried out trial on thousands of toys for lead and has exposed abundant hazardous products. All sources of lead exposure are summarized in Table 1 (37).

Mechanism of lead poisoning

In the human body, lead toxicity occurs when the cell experiences oxidative stress [Figure 1]. Increased production of free radicals and overwhelming of antioxidant mechanism result in oxidative stress and consequential destruction. Antioxidant mostly protects the body and invalidates the generated reactive oxygen species (ROS). A tripeptide sulfhydryl group's glutathione (GSH) is the most important antioxidant-producing cell. In mammalian tissues, it is present in lesser quantity. It is a chief antioxidant for free-radical scavenging. ROS are stabilized by GSH which in turn converts to glutathione disulfide (GSSG) and with the help of enzyme glutathione-disulfide reductase, GSSG is reduced back to GSH. Lead binds to GSH's sulfhydryl group, inactivates GSH, and increases oxidative stress. Lead blocks the enzymes (□-aminolevulinic acid dehydratase [ALAD], glutathione reductase, glutathione peroxidase, and glutathione-S-transferase) activity and further reduces GSH levels. Inducing lead in a human body at high level causes destabilization of cellular membrane through lipid peroxidation, which can cause hemolytic anemia. Neurological toxicity of lead is due to an ionic mechanism barrier (BBB). Sodium ion concentration is also affected by lead toxicity; therefore, hampering cell-to-cell communication and uptake of neurotransmitters. Even in a very small amount, it can affect protein kinase C which is responsible for prolonged neural excitation and memory storage (38-40).

Sign and symptoms

At first, lead poisoning can be difficult or hard to detect because even people with high amounts of lead in their blood might seem to be fully healthy. Usually, signs and symptoms are not noticeable until unsafe concentration has accumulated in the body. According to the age of the patient, symptoms may vary [Table 2].

Toxicological effect of lead

Neurologic toxicity

Neurotoxicity means exposure of the entire body to lead toxic agents and the imbalance in the neurophysiological function.

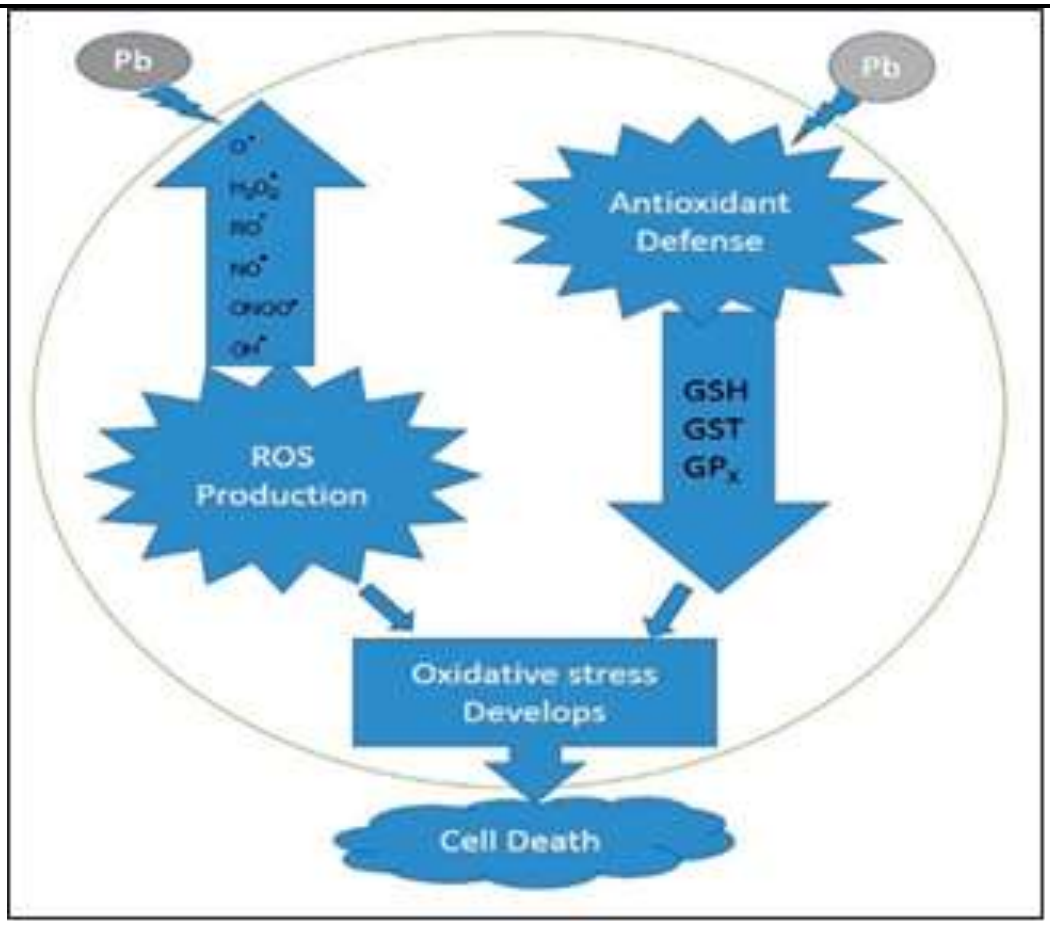


Table 1: Summary of sources of lead exposure

Sources of lead poisoning	Reason for poisoning	Citations
Lead in paint	Old buildings built before 1978 used lead-based paint	[15]
Lead in dust	Interior house dust contaminated with lead	[19]
Lead in water	Old well pumps still in operation contaminating lead	[21]
Lead in tableware	Old or poorly glazed ceramic dishes, pewter, brass, and pottery may contain lead	[23]
Lead in soil	Mixed lead-based paint with soil	[24]
	Lead also mixed with soil from mainly metal smelting and battery manufacturing factory	
Lead in folk medicines and cosmetics	Some folk medicines greta, azarcon, and pay-loo-ah contained lead	[16-25]
	Some cosmetics such as surma, kohl (alkohl), kajal, tiro, and tozali also contained lead	
Lead in occupational sources	Regularly working equipment (radiation protector, some surgical tools, developing dental X-ray films processing to digital X-rays, and electronic fetal monitors) that involves lead-containing products	[16]
Lead in metal costume jewelry	Metal costume jewelry (charm jewelry, costume jewelry, trinkets, and fashion jewelry) containing lead	[27]
Lead in toys	Toys and other useful goods for children found high range of lead	[28]

There are two main symptoms caused by such exposures; they are psychiatric disturbances and neurocognitive symptoms. It predominantly influences the CNS, generally the developing brain, and affects almost every organ system. Therefore, children suffer more from neurotoxic effects than adults and are at a greater risk [Table 3] of lead toxicity. An effective receptor N-methyl-D-aspartate is involved in the maturation of brain plasticity that occurs in brain organization; lead blocks this receptor and results in the interruption of

long-term potentiating and storage of newly learned knowledge. Lead easily crosses the endothelial cells at the BBB, which plays a significant role in brain fitness and is regularly compromised in disease. Blood lead concentration of children >10 □g/dL represents a higher risk for toxicity (20,22,30,29).

Cardiovascular toxicity

Lead can cause hypertension and affect blood vessels. Lead-blocked blood vessels can lead to immediate heart attack and death. Increasing BLLs significantly correlate with an increase in cardiovascular morbidity and mortality. Chronic and acute both types of lead poisoning can cause cardiac dysfunction and vascular damage. Recently, researchers have found an intriguing correlation between low blood leads concentration and cardiovascular toxicity, and recently, some studies suggest that low levels of lead may be associated with high blood pressure (40)

Hematologic toxicity

Due to lead toxicity, anemia is the classic clinical manifestation in erythrocytes. Young and iron-deficient children have more likelihood of developing lead-induced clinical anemia. A high amount of lead exposure in the human body causes hemolytic anemia. More than 99% of lead is distributed in red blood cells rather than plasma. Lead causes anemia by blocking the activity of ferrochelatase, aminolevulinic acid synthetase, and ALAD. Lead also inhibits enzymes related to heme synthesis. Heme is an oxygen-carrying moiety in hemoglobin, which consists of a porphyrin ring that holds iron ion in the center (44).

Nephrotoxicity

When lead affects the kidneys, medical experts call it “lead-related nephrotoxicity.” Due to lead exposure, nephrotoxicity occurs because lead is eliminated through the kidney. In the renal tubules, lead is absorbed by proximal tubular cells, and it binds to specific lead-binding proteins. These lead-binding proteins produce intercellular inclusions of proximal tubular cells (45).

Reproductive toxicity

Lead toxicity affects both the male and female reproductive systems. During the pregnancy, it crosses the placenta resulting in prematurity, intrauterine deaths, and low birth weight. Different in vivo study proves that constant exposure to lead may cause inhibition of menstruation, ovulation and follicular growth, delayed vaginal opening, and a decrease in frequency of implanted ova. Usually, BLLs of >40 □g/dl are more damaging to the human reproductive organs, sometimes, even at levels of <10 mg/dl lead can be dangerous (46).

Bone toxicity

A significant reduction in the bone calcium content upon lead intoxication has been observed. This decrease in calcium content may be because of the increased bone resorption. Lead is one of the risk factors for the development of osteoporosis by altering bone mineral metabolism. Osteopenia, osteoporosis, and osteomalacia with increased bone fragility in humans and experimental animals were observed because of lead exposure. Long-term exposure to lead damages different body tissues (47).

Toxicity in human cells

Overexposure of lead in the human body influences the activation of mitogen by raising the secretion of pro-inflammatory cytokines interleukin-6 (IL-6) and tumor

Table 2: Common symptoms in different age group

Age group	Signs and symptoms of lead poisoning	Citations
Newborn (ages 0-4 weeks), infant child (ages 4 weeks - 1 year), and toddler (ages 1-3 years)	Premature birth, lower birth weight, and slowed growth	[35]
Preschooler child (ages 4-6 years), school-aged child (ages 6-11 years), and adolescent (ages 12-19)	Learning difficulties, irritability, weight loss, tiredness or sluggishness, abdominal pain, vomiting, constipation, hearing loss, and seizures	[35]
Adults (ages 20-39) and young adult (ages 40-64)	High blood pressure, joint and muscle pain. trouble with memory storage, concentration, headache, abdominal pain, and sperm count decreases	[36]

Table 3: Cognitive effects of lead neurologic toxicity

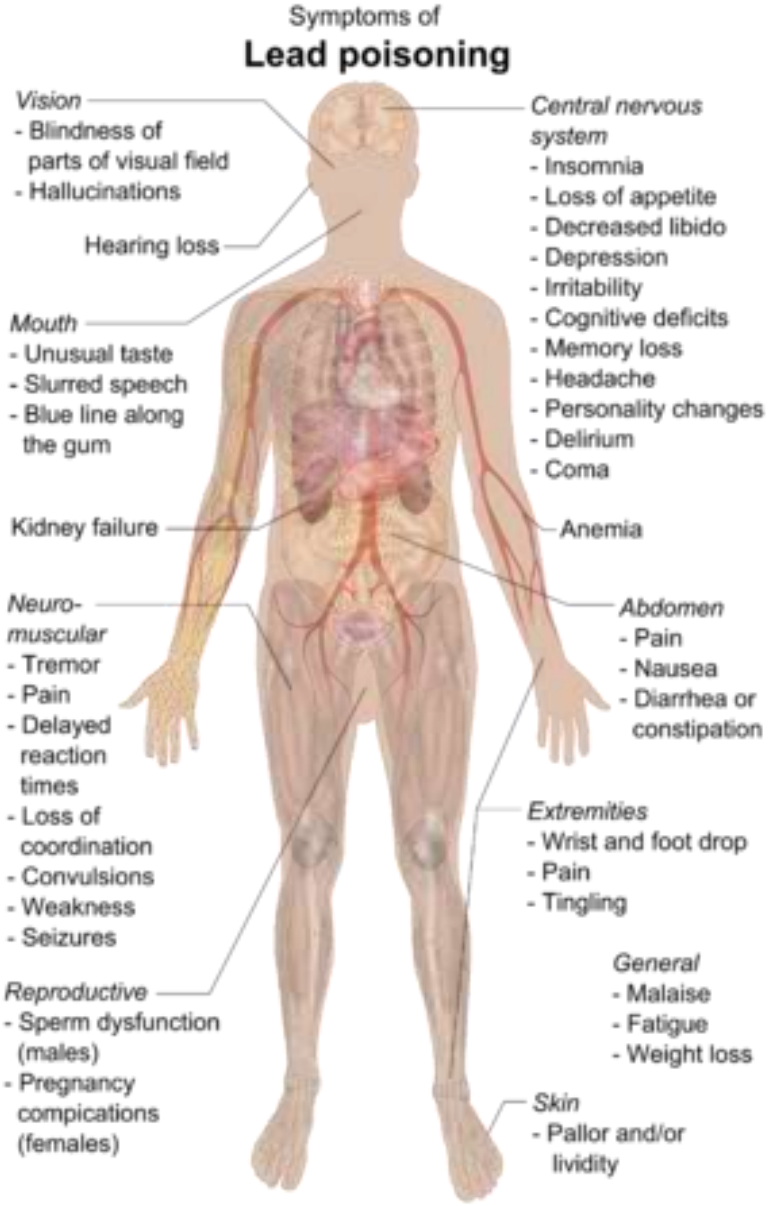
Cognitive parameter	Effect of lead toxicity	Citations
Intelligence	IQ decreases	[38,39]
Memory	Decreases learning ability, memory scores capacity, and other cognitive declines	[38-40]
Executive functioning	Decreases executive functioning abilities	[41]
Processing speed	Deficit processing speed	[38]
Language	Impede verbal concept formation, poor grammatical reasoning, and imperfect command	[42]
Visuospatial arts	Poorer copies of geometric figures and recalled visual patterns more weakly	[38]
Motor skills	Vasomotor coordination affected	[38-43]

IQ: Intelligence quotient

necrosis factor-α and chemokines IL-8. Major cellular functions such as expression of cellular metabolic enzymes, metallothionein expression, and protein kinase activity were affected by lead toxicity (48).

Prevention and treatment

In the United States, childhood lead toxicity prevention has taken a major concern in the public health for the reduction of blood lead concentrations in children. An excellent approach to lessen the lead toxicity is to suggest people, mostly uneducated people about CDC guidelines and by creating awareness about lead poisoning. Every parent should frequently wash their children's hands and prevent children from placing their hands in mouth habitually. It is suggested that every family should use cold water because hot water contains high amounts of lead. Vitamin C has antioxidant properties, which is capable of removing free radicals and alleviating oxidative stress. Therefore, the physician should suggest that taking Vitamin C containing food in the diet regularly because they minimize lead toxicity easily. A chelation therapy is a novel therapeutic technique for removing lead from the body. If BLLs are 45 mg/dL or greater chelation therapy can be recommended. Lead chelating agent has much more attraction toward lead than calcium and is excreted in urine (49-50).



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