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Author (s): Ahmad Manan Mustafa Chatha[1], Saima Naz[2], Zaigham Abbas[3], Shafiq Ur Rehman[3]

Affiliation (s): [1]Government Sadiq College Women University, Bahawalpur, Pakistan
[2]The Islamia University of Bahawalpur, Pakistan
[3]University of the Punjab, Lahore

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Carcinogenic Effects of Lead (Pb) on Public Health

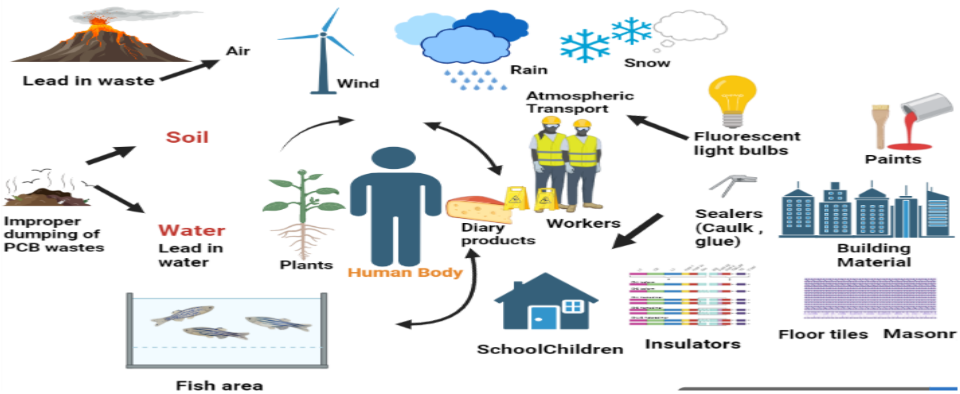
Ahmad Manan Mustafa Chatha[1], Saima Naz [2*], Zaigham Abbas[3], and Shafiq Ur Rehman[3]

[1]Department of Zoology, Government Sadiq College Women University, Bahawalpur, Pakistan
[2]Department of Entomology, Faculty of Agriculture and Environment, The Islamia University of Bahawalpur, Pakistan
[3]Institute of Microbiology and Molecular Genetic, University of the Punjab

ABSTRACT

Lead (Pb) is a potentially hazardous metal that penetrates the bones and blood as well as other major organs including the skin, liver, kidneys, and brain after being absorbed by the body. It is the most abundant heavy metal found in nature and utilized for a variety of industrial purposes. Lead is used in the manufacturing of bearings and printing fonts, as well as in the manufacturing of sulfuric acid, cable coverings, soldering products, guards in nuclear power stations, shields, vessels for radiation emitting materials, paints, ceramics, chemicals, and building structures. It is advantageous for physiological and biochemical processes in living beings in low concentrations. However, when it surpasses a specific threshold, it causes significant health issues. Lead is extremely persistent in nature and its continued use causes serious toxicological impacts, such as renal failure, carcinogenicity, high blood pressure, hematological effects, brain damage, reproductive system complications (in both men and women), bone screening, heart diseases, and liver damage. The available treatments, such as chelation therapy and other types of medicines, can help to reduce its adverse effects. The objective of this review is to delineate the adverse effects of lead on the human body, spanning from childhood to adulthood. Lead is a cumulative toxicant that affects multiple body systems and is particularly harmful to young children. The second major goal of this study is to define lead contamination and identify its sources and levels.

GRAPHICAL ABSTRACT



*Corresponding Author: saima.naz@gscwu.edu.pk

Keywords: chelation therapy, environmental pollutant, health effects, heavy metal, lead toxicity, non-biodegradable metal

1. INTRODUCTION

Lead (Pb) is the most dangerous contaminant in the environment. It is a natural constituent of the earth's crust having unique qualities, such as high flexibility, softness, low melting point, and ductility, all of which pose danger to human health in multiple ways. It is a durable metal present in various environments, including water, air, and soil. Its sources are diverse, originating primarily from or contaminating a wide array of products, such as paints, ceramics, water pipes, gasoline, solders, airplanes, cosmetics, x-ray machine protective layers, and hair dyes. It is regarded as a strong pollutant of a non-biodegradable kind that has been extensively studied [1]. Metals are distributed within the layers of the Earth's crust and their presence influences geographical changes and situational applications. The movement of metals in the environment governs their properties and various environmental factors [2]. Metals are necessary for the physiological and biochemical activities in living beings, if present in lower quantities. When metals reach a specific level, however, they have negative impacts on living beings that endure for a long time [3].

The ingestion of foods contaminated with lead and the inhalation of particles emitted by the combustion of materials that contain lead, such as household paint and gasoline, are the two main pathways of lead exposure. Inhalation is the most prevalent method of lead entry into the body with fumes and it plays the most important role in lead transfer. On the other hand, lead absorption via the cutaneous pathway is uncommon. Children are particularly vulnerable to lead contamination because of their frequent indoor and outdoor activities and interaction with items that may contain lead, such as furniture with lead coatings, toys, and paint chips [4].

Lead has a wide range of harmful impacts on human health. Most human bodily systems suffer negative health implications of lead exposure. Some effects are seen in those having a lower lead level in their blood, indicating modest exposure [5]. Lead has been shown to inflict oxidative damage by producing too many free radicals, as well as damage to cell membrane from the peroxidation of lipid that triggers inflammatory signaling pathways. The inflammatory response plays a critical role in negative consequences to health caused by lead [1].

After being absorbed by the circulatory system, lead attaches with erythrocyte constituents and then spreads to bones and soft tissues where it stays for many years. The lead stored in the bones outflows into the bloodstream causing lead poisoning. It poses an increased risk of asthma in children. Lead exposure may affect the concentrations of immunoglobulin E (IgE) in the blood, a key marker indicating allergy inducing diseases including asthma. With respect to neurodevelopment, lead is linked to learning difficulties as well as decreased focus in younger children. Other signs, such as neurobehavioral disorders, hearing problems, and muscular weakness may also develop as a result of lead poisoning, which has long-term effects on neurological, hematological, and renal systems. Memory loss, lack of concentration, sleeplessness, and disorientation are other side effects of long-term lead contamination [6].

This review article summarizes research on the association of lead exposure with provocative responses in respiratory, neurological, cardiovascular, digestive, and urinary diseases caused by toxicological impacts of lead.

2. MATERIALS AND METHODS

Searching terms including 'Pb', 'sources of Pb', 'Pb toxicity', 'routes of Pb exposure', and 'health effect of Pb toxicity' were used to target recent research for the most updated information. Science Direct, Research Gate, PubMed, Google Scholar, National Centre for Biotechnology Information, springer.com, and other academic weblinks were used to conduct a comprehensive search for literature based on the keywords. Furthermore, 35 review articles are carefully examined and 30 were found to be relevant, while the remaining were irrelevant as indicated in the flow chart diagram (Figure:1).

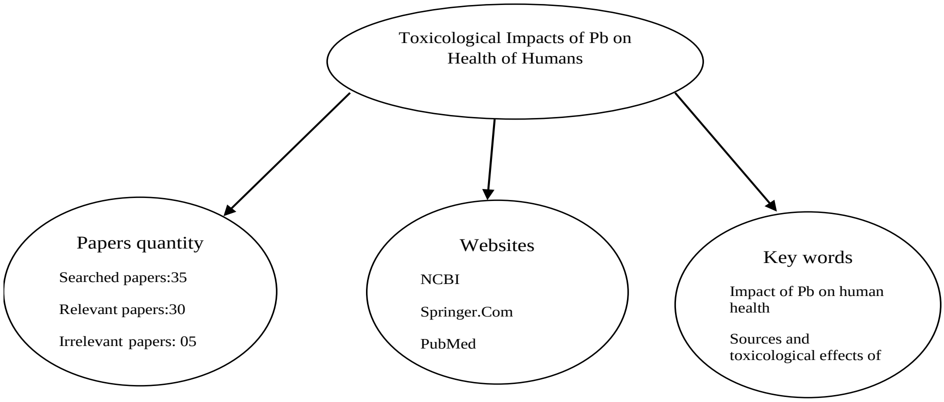


Figure 1. Flow Chart Diagram

2.1. Data Representation

Based on the primary goals of the current review, all relevant literature was thoroughly reviewed. Afterwards, the results gathered from all representative literature were retrieved and tabulated.

3. RESULTS

3.1. Mechanisms of Lead Poisoning

There are different cellular, intracellular, and molecular mechanisms of lead neurotoxicity, such as the induction of oxidative stress, intensification of the apoptosis of neurocytes, interfering with Ca^{2+} dependent enzymes including nitric oxide synthase. Population studies have demonstrated a link between lead exposure and subsequent development of hypertension and cardiovascular diseases. Vascular endothelium is now regarded as the main target organ for the toxic effects of lead. It affects the vasoactive function of endothelium through the increased production of reactive oxygen species, inactivation of endogenous nitric oxide, and downregulation of soluble guanylate cyclase by reactive oxygen species, leading to limiting nitric oxide availability and impairing nitric oxide signaling.

3.2. Applications of Lead

Despite the fact that it is no longer widely utilized in many countries, it is still used in various industries, such as auto maintenance, battery production, recycling, refining, and smelting. Table 1 demonstrates how lead is used in many areas, such as factories, car businesses, radio stations, and hospitals.

Table 1. Applications of Lead

Sr.	Major Areas of Lead	Applications of Lead	Citations
1	Batteries	• Storage batteries that can be recharged. • Rechargeable storage batteries are used in light, airplanes, automobiles, electric vehicles, trucks, and tanks, as well as broadcasting stations.	[7]
2	Antiknock agent in gasoline	• Tetraethyl Pb (Tetraethyl lead (CH3CH2)4Pb) was discovered by Thomas Midgley in 1921 as a very effective and inexpensive antiknock additive for gasoline. • The octane levels of commercial gasoline are utilized. The higher the octane level, the greater the gasoline's anti-knock capabilities.	[8]
3	Insulation jacketing	• Sheathing the high voltage cables.	[9]
4	Radiation shields	• Radiation shields. • In hospitals when patients are screened with X ray, lead is used to protect them.	[10]
5	Ammunition	• Casting becomes easy due to the low cost of lead. • Lead can stop bullets from being deflected by wind and air turbulence due to high density.	[11]
6	Reaction tanks	• Lead can be easily oxidized into Lead oxide (PbO). The dense film of PbO covers the outer layer and prevents the deeper layer from being oxidized, thus makes lead resistant to degradation. • So, it is used to make reaction tanks and to make pipes.	[12]
7	Candles	• As a stiffener in some candles.	[13]

3.3 Effects of Lead Contamination on Living Organisms' Development

Table 2 depicts the consequences of lead contamination on living organisms' development including how it affects both male and female reproductive systems, resulting in miscarriages and other medical issues. It also has an impact on pregnant women, growing fetuses, and newborns who are breastfed.

3.4. Concentrations of Lead in Food Products

Table 3 illustrates the level of lead in several foods, such as milk, meat, poultry, cereals, and drinking water. This table also provides the lead content threshold in several foods.

Table 2. Effects of Lead Contamination on Living Organisms' Development

Sr.	Levels Affected during Organisms' Development	Effects	Citations
1	Reproductive system	On both male and female reproductive systems resulting in prematurity, miscarriages, birth weight (low), and developing problems in females.	[14]
2	Zygote	Zygote turns into a mass of cell without any differentiation.	[15]
3	Pregnant women	Risk of preterm births in pregnant women. Blood Pb level may increase in pregnant women due to the deficiency of calcium.	[15]
4	Embryonic development	Embryos with little cellular mass, lead toxicity to inappropriate skull and brain formation and they might be sterile as well.	[16]
5	Infants during breast feeding	According to the American Academy of Pediatrics, breastfed infants have a higher level of blood Pb as compared to the infants that are not breastfed.	[14]
6	Children 1-6 years of age	Even a low level of lead causes seizures, unconsciousness, and death.	[17]
7	Younger adults	Blood Pb level greater than 15 µg/dl causes nerve disorders, heart disorders, kidney failure, fertility problems, lower sperm count. and motility. However, Pb level below 10 µg/dl causes hypertension, essential tremor, decrease kidney functioning, and damage to central nervous system.	[18]
8	Later in life at age 40 and above	Lead toxicity leads to death because almost all vital organs lose their functioning.	[14, 18]

Table 3. Concentration of Lead in Food Products

Sr.	Food Items	Threshold Content (mg/kg) Fresh Matter	Citations
1	Milk	0.02	[19]
2	Meat	0.1	[20]
3	Offal	0.5	[16]
4	Cereals	0.3	[21]
5	Fat & Oil	0.2	[22]

Sr.	Food Items	Threshold Content (mg/kg) Fresh Matter	Citations
6	Honey	0.1	[23]
7	Fruits	0.1-0.2	[24]
8	Drinking water	0.1	[20]
9	Tea	1	[25]
10	Apple	0.127	[26]
11	Pear	0.036	
12	Raspberry	0.111	
13	Strawberry	0.161	

3.5. Lead Induced Cognitive Effects

Table 4 depicts the brain toxicity of lead which has serious consequences for memory, motor ability, processing speed, and intellect, among other things. Lead poisoning reduces the learning ability, affects vasomotor coordination, and lowers IQ in those who are exposed to it.

Table 4. Lead Induced Cognitive Effects

Cognitive Parameter	Effect of Lead Toxicity	Citations
Memory	Learning ability decreases	[27]
Motor ability	Effects vasomotor coordination	[28]
Processing speed	Reduced processing speed	[29]
Executive functioning	Decreases executive functioning abilities	[30]
Intelligence	IQ decreases	[31]
Art in visual spatial skills	Geometric figures with poorer copies	[16]
Nerve conductance	Poor nerve conductance	[8]
Visual Patterns	Weak recalled visual patterns	[15]
Initiative functioning	Decreases executive functioning abilities	[18]

3.6. Biological and Non-biological Sources of Lead

Table 5 highlights the many lead sources, including biological and non-biological sources. Nutrition, water, and fish are biological sources, whereas dust particles, paintings, dirt, and cosmetics are non-biological sources.

Table 5. Biological and Non-biological Sources of Lead

Sr.		Agents of Lead	Intervention for Prevention	Citation
1	Biological Sources	Chocolates	With 0.07 micrograms per gram of lead, dark chocolate is the most dangerous. As a result, 50 grams of chocolate have 3.5 micrograms of lead, which is equivalent to the quantity of chocolate consumed once a day.	[15]

Sr.		Agents of Lead	Intervention for Prevention	Citation
2		Canned foods	The use of lead-soldered food cans has been discontinued by the FDA.	[11]
3		Snacks	Snacks inflict a significant amount of damage to children's bodies.	[8]
4		Water	To keep track of pollutants in the water, an annual public report should be produced.	[32]
5		Fishes	Mostly found in the liver and guts of most fishes, indicating that they avoid eating fish from polluted rivers.	[28]
6		Pica	Anxiety and obsessive-compulsive disorders should be addressed in people with pica.	[33]
7		Dust	Different initiatives have been launched to educate parents about home cleanliness in order to reduce blood Pb levels in children who have already been exposed. Vacuums should be utilized, although they are expensive.	[14]
8		Paint	Lead-based paints were used in old buildings built before 1978.	[18]
9		Table ware	Lead may be found in old and badly glazed ceramic dishes, pewter, brass, and pottery.	[34]
10	Non-biological Sources	Soil	Lead-based paints were mixed with dirt. Lead has been found also in the soil around metal smelting and battery production plants.	[35]
11		Folk medicines (indigenous medicine)	Lead was found in certain folk remedies such as, zircon and pay-loo-ah.	[32]
12		Cosmetics	Surma, kohl (al kohl), kajal, tiro, and tozali are among the cosmetics that include lead.	[36]
13		Occupational sources	Regulatory working equipment involves lead-containing items (radiation protection, surgical instruments).	[37]

Sr.	Agents of Lead	Intervention for Prevention	Citation
14	Metal costume jewelry	Lead-containing metal cosmetics and jewelry (charm jewelry, costume jewelry, trinkets, and fashion jewelry)	[38]
15	Toys	Toys and other children items were found to contain a high level of lead.	[39]
16	Sandhor	By avoiding low-quality sandhor	[27]
17	Utensils	Since the amount of lead in locally made utensils is 922 times higher than in commercially produced utensils, local utensils should be avoided.	[12]
18	Cigarettes	Cigarettes have lead contents ranging from 1.33 to 3.61 g g1 dry weight, with an average of 2.46 g g1. In branded cigarettes, there is a smaller quantity.	[14]
19	Pipes	A visible presence of 2.5% lead is discernible on the moist surface of pipes.	[37]

4. DISCUSSION

Based on its environmental resilience and transportability, lead is a hazardous metal that is toxic and causes significant environmental contamination. Lead is non-biodegradable which is the main cause for its persistence in the environment. It is used in a variety of industrial and mining operations due to its unique physical and chemical characteristics. Persistent lead exposure, at lower levels, is a common health issue, particularly among low-income populations and ethnic minority groups [40, 41].

Lead absorbed by inhalation or ingestion is deposited in soft tissues. The liver has the greatest quantity of lead at about 33%. Another study suggests that cholestrogenesis (biosynthesis of cholesterol) as well as phospholipidosis of tissue is accountable for the minor cellular impact of lead, therefore, cellular processes play a role in hepatic symptoms associated with lead toxicity [42]. The cardiovascular system, renal system, neurological system, skeletal system, hematological indices, immunological parameters, pulmonary system, gastrointestinal system, reproductive system, and the endocrine system are all affected by lead as a chronic toxicant. Sensitivity to the detrimental effects of lead is also determined by an individual's genetic make-up [40, 41]. Multiple metabolic processes are harmed by lead including calcium inhibition and protein reactions. Lead enters the body and replaces calcium, interacting with biological components and disrupting their optimum functioning. It also lowers the function of various enzymes by altering their structure and inhibiting their activities, while fighting for binding sites with required cations. The major mechanism of lead poisoning is oxidative stress which causes alterations in the content of fatty acids in membranes. Lead has also been linked to changes in gene expression [22]. Hematopoietic system, renal system, and hepatic functions are all drastically reduced in children exposed to it. Children of industry employees have an immensely increased amount of lead poisoning [43].

4.1. Recommendations

There is no point at which lead exposure has no negative consequences; no degree of lead exposure is acceptable. As a result, measures and regulations are required to avoid exposure. It is recommended that the parents should teach their children how to avoid inadvertent lead intoxication. A variety of antioxidants should be utilized to remove lead from the body. There are a variety of therapeutic options available these days. It is far preferable to avoid direct contact with pollutants and, therefore, avoid future effects. Medical diagnosis, health knowledge, and proper medical treatment can all help to minimize lead poisoning. As a result, the hygiene approach is critical to prevent the effects of ambient lead pollution and should be implemented globally. Environmental measures are required to repair the known sites of lead pollution but they are also important to evaluate or explore new (potential) sources of health risks.

4.2. Conclusion

The impact of lead on human health was examined in this review. Lead exposure has a variety of physiological, biochemical, and behavioral consequences. The cardiovascular system, peripheral and central neurological systems, hematological system, and certain organs including kidneys and liver are among the most hazardous. It causes anemia, carcinogenicity, harm to both male and female reproductive systems, kidney damage, heart illness, brain damage, raised blood pressure, liver damage, and adverse impact on children's cognitive capacity and behavior. The quantity of lead in the environment has increased because of human activities. Failure to keep the amount of lead under control would result in serious difficulties in the future. The good news is that lead level in the body may be reduced using a variety of treatments now in use. Chelation treatment, nano-encapsulation, and N-acetylcysteine (NAC) are the most important. There are other medications that can help to decrease the impact of lead on the body. Due to variations ranging from hereditary factors to the environment and food, treatment techniques are not equally successful for everyone. Engineering solutions may be beneficial in reducing lead exposure in the workplace. The government should organize seminars to spread awareness about the damaging impacts of lead on human health, provide essential preventative and remediation tools via radio and television, and take steps to reduce the levels of lead in the environment.

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