IMPACT OF LEAD ON ENVIRONMENT AND HUMAN HEALTH –A REVIEW

Sandhya Kanupuru¹ and Dr. J. Pramoda Kumari²

¹,²Department of Microbiology, S.V. University, Tirupati, A.P, India.

ABSTRACT

The tanning leather industry, one of the most widespread industries, produce large amount of waste-water containing toxic pollutants which include heavy metals such as mercury, Lead, cadmium, selenium, copper, chromium, arsenic, pesticides and radionuclides that cause great environmental problems. The environment is under increasing pressure from solid and liquid wastes emanating from the leather industry. Pollution is depicted stepwise along the leather processing phases with a selected xenobiotic and contaminants. Toxic pollution due to Lead causes immense harm to humans which include physical and mental disabilities, reduced IQ, organ dysfunction, neurological disorders, cancers, reduced life expectancy, and in some cases, death.

The effluents must be handled carefully and should be treated before its reuse or disposal in water bodies. In recent years, the research for the removal of toxic metals has focused on new technologies rather than conventional methods like ion exchange, chemical precipitation, ultra filtration and so on which are expensive, need energy and can produce waste products that require careful disposal. One of the effective bioremediation methods is the biosorption, where the heavy metals like Mn, Cd, Cr, Cu, Zn and Pb detected in an industrial wastewater effluent can be biosorbed by fungi. Of all the heavy metals Lead plays a major role in affecting the human life of all age groups and the environment. Finance, health, and environmental agencies in recipient countries are responsible for setting their own development agendas to educate about the scope of Lead and other heavy metals within their countries in order to pursue international resources.

KEYWORDS: xenobiotic, tannery, effluent, bioremediation, biosorption.
1. INTRODUCTION

1.1 Lead

Plumbum (Pb), a chemical element in the carbon group otherwise known as Lead, is a soft and malleable metal, which is considered as heavy metal. It is grey-blue heavy metal found ubiquitously, which is poisonous to domestic animals and humans throughout the world.\[1\] It occurs in both organic (tetraethyl lead) and inorganic (lead acetate, lead chloride) forms in the environment.\[2\] Information on Lead’s poisonous ability can be traced back to the second century B.C., when Nikander, a Greek physician, explained the colic and paralysis associated with Lead ingestion. The previous reports of Lead toxicity occurred in Lead miners and wine drinkers. Workers in the metals trade remain an important risk group. Lead exposure remains one of the leading causes of workplace illness. In the United States, more than 320,000 American workers are occupationally exposed to Lead. It is a persistent metal that is still present in the environment, water, brass plumbing fixtures, paints, soil, dust and imported products manufactured with Lead.\[3\][4] Exposure to Lead mainly occurs through the respiratory and gastrointestinal systems. Absorbed Lead whether inhaled or ingested is stored in soft tissues. Lead is conjugated in the liver and passed to the kidney, where a small quantity is excreted in urine and the rest accumulates in various body organs, affecting many biological activities at the molecular, cellular and intercellular levels, which may result in morphological alterations that can remain even after Lead levels have fallen.\[5\] Lead toxicity is closely related to its accumulation in various tissues and interference with the bioelements that hamper several physiological processes.\[6\] Environmental exposures to Lead have increased toxic effects on various organs of the body. Research in humans and animals have shown that Lead has toxicological effect on the liver, bone, blood, kidney, lung, heart, brain and testis.\[7\][8][9][10][11][12] Lead mediated toxicities have been reported to include the induction of oxidative stress in tissues and organs which can lead to oxidative damage in two separate but related pathways. The first pathway is the generation of reactive oxygen species(ROS) and the second pathway is the depletion of antioxidants reserve through the generation of reactive oxygen species. Lead is reported to inactivate glutathione, an antioxidant by binding to its sulfhydryl moiety. Glutathione is a cysteine-based molecule whose antioxidant property includes quenching of free radical and is associated with drug and toxin metabolism in the liver.\[13\] Lead has also been shown to inactive enzymes containing sulfhydryl moiety like delta-aminolevulinic acid dehydratase and glutathione reductase as seen in Lead exposed animals.
1.2 Sources of Lead
Poor, urban and immigrant populations are at far greater risk of Lead exposure than the other groups in the United States. The general population is exposed to Lead through food, drinking water, soil, air and dust. Food and water are the major sources of exposure to Lead. In infants and small children, ingestion of soil and dust can also contribute importantly. Lead can be transferred to the infant from the mother in breast milk as reported by European Food Safety Authority in 2010. Lead paint is the primary source of Lead exposure which is a major source of Lead toxicity in children. Primary sources of residential Lead exposure for children and adults come from Lead dust in homes in environmentally polluted urban areas, Lead in soil or soot that can be tracked indoors and Lead-paint dust and chips in homes built before 19th century.

1.3 Properties of lead
Lead (Pb) is ubiquitous and one of the earliest metals discovered by the human race. Unique properties of lead, like softness, high malleability, ductility, low melting point and resistance to corrosion, have resulted in its widespread usage in different industries like automobiles, paint, ceramics, plastics, etc. This in turn has led to a manifold rise in the occurrence of free lead in biological systems and the environment.

2. Lead in the environment
The non-biodegradable nature of Lead is the prime reason for its prolonged persistence in the environment. Lead is found to be the most toxic element at all temperatures. Lead is a poison that affects virtually every system in the body, with no physiological value. Lead is a natural toxicant which affects a broad spectrum of species and persists in the environment and Lead is considered particularly a hazardous ecotoxicant. The effects of lead exposure on plants include inhibited plant growth, reduced photosynthesis and reduced water absorption. The environment is still the most common source of exposure to lead, despite the removal or sharp reduction of some of lead's most pernicious reservoirs in recent years.

2.1 Exposure to lead
Evaluation of lead exposed humans revealed that liver tissue is the largest reservoir of lead with respect to other evaluated organs and tissues. Lead was also found to accumulate in the kidney cortex and medulla of treated animals. Blood lead levels are more closely related to indoor dust exposure than to outdoor soil exposure. Lead exposure occurs mainly through the respiratory and gastrointestinal tracts. Approximately 30-40 percent of inhaled lead is
absorbed into the bloodstream. People may be exposed to lead and lead compounds via air and drinking water and through eating foods or swallowing dust or dirt that contains lead. Ingestion of contaminated soil and dust as a result of “hand-to-mouth” activities can be an important source of lead intake in some infants and young children. In the past, lead was an ingredient in some pigments and paints, which among other things, were used in toys, and these may be a further source of exposure.\cite{14} In addition, traces of lead are commonly found in coal, leading to diffuse release when it is burned domestically or industrially. Historically, the most important source of diffuse lead pollution in the general environment was from the use of alkyl lead as an additive in petrol.\cite{15} However, since 1998, Leaded fuel has been unavailable in the UK other than for a few specialist applications. The level of Lead in the blood is an indicator of recent environmental exposure i.e; for approximately the past 30 days as stated by World Health Organisation.\cite{16} Lead in bone is considered a biomarker of long-term exposure.\cite{17}

2.2 Lead in Soil

The sources of lead in the soil are diverse, including the burning of fossil fuels, mining and smelting of metalliferous ores, municipal wastes, fertilizers, pesticides, sewage sledge, pigments and spent batteries. Lead concentrations in soil are influenced both by underlying litho logical lead concentrations and by anthropogenic release of Lead.\cite{15} Lead was measured in top soils from England as part of a Department for Environment, Food and Rural Affairs (DEFRA)-commissioned project\cite{15} and the median concentration was 47 mg/kg with a range from 2 to >10196 mg/kg. Median concentrations of lead were 35, 57 and 166 mg/kg respectively in rural, semi-urban and urban areas. In urban areas, the minimum level of lead was 2.1 mg/kg and the 75th percentile was 322 mg/kg. Lead-contaminated floor, dust and soil contribute to lead intake during the first two years of life. In a pooled analysis of 12 epidemiological studies the loads of lead in floor dust (all less than 10 μg/ft² (107.6 μg/m²) were significantly associated with blood lead levels in children aged 6 – 24 months.

2.3 Lead in Air

Long-term monitoring has demonstrated a substantial reduction in environmental concentrations of airborne Lead in many countries following the phase-out of leaded petrol. According to the National Atmospheric Emissions Inventory, the main sources of lead emissions to the atmosphere in the UK in 2008 were metal production (mainly iron and steel) (63%), industrial combustion (9%) and residential, commercial, institutional and agricultural
combustion (7%). Atmospheric lead concentrations vary widely, but usually decline with increasing distance from emission sources. In the atmosphere, lead particles or aerosols are transformed by chemical and physical processes and are ultimately removed by dry and wet deposition to terrestrial or aquatic ecosystems.\textsuperscript{[14]} Children with lead dust or soil dust exposure can have blood lead levels as high as 90 μg/dL.

2.4 Lead in Drinking Water

The most common source of Lead in tap water is Lead pipe work installed before the 1970s, and non-approved solder used inappropriately in cold water systems. Homes built before 1986 may have Lead in pipes, fittings and solder; this lead can leach out of pipes and into drinking water. In certain cities, elevated Lead levels have also been found in school drinking water. Valves currently used in drinking water supply lines may also contain 5-7 percent leaded brass and constitute a significant source of Lead in the water supply. So Lead mainly leach from brass fittings (Drinking Water Inspectorate). Drinking water still accounts for approximately 10% to 20% of Lead exposure in children. Therefore Leadfree brass fixtures are to be used in pipes. A spate of kids are experiencing elevated blood Lead levels after being exposed to Lead in the city of Flint’s water supply as reported recently on 4\textsuperscript{th} October 2015.

2.5 Lead in Rainwater and Groundwater

The unacceptable high level of Lead in rainwater is hazardous to human health. A comparison of the physico-chemical attributes of both rainwater and groundwater with WHO guidelines for domestic water reveals that rainwater contains Lead more than the stipulated maximum limit. The groundwater also shows marginal enhancement of Lead concentration. Consequently, edible vegetables show Lead which indicates quality impairment and bioaccumulation. So the toxic effects of excessive Lead levels in humans due to consumption of these vegetables include significant damage on the brain and heart related diseases in both adults and infants.\textsuperscript{[18]} On the basis of WHO (2006)\textsuperscript{[19]} specifications, the groundwater cannot be regarded as potable due to its high coliform counts, while the enhanced Lead concentration makes the rainwater objectionable. The environmental and health implications of the above include significant pollution of the atmosphere with respect to Lead and greenhouse gases.
3. Lead pollution and Human Environment—Occupational exposure

According to the Centers for Disease Control and Prevention (CDC), in 2003-2004, 94% of adults with identified Lead-exposure sources were exposed via occupational sources. The construction, manufacturing, and mining industries had the highest number of adults with elevated blood Lead levels. Adult occupational exposures have been tracked since 1994 through the CDC’s Adult Blood Lead Epidemiology and Surveillance program (ABLES). During this time a steady decline has been observed in occupational exposure-related blood Lead levels. In 2004 the number of people known to have occupation-related blood lead levels greater than or equal to 25 micrograms per deciliter was 7.5 per 100,000, a number that is expected to continue to diminish. As no safe blood Lead level in children has been identified, the Centers for Disease Control and Prevention (CDC) adopted a reference range for blood Lead based on the distribution of blood Lead in children of 1-5 years old. In 2010 the upper limit of this range was 5 micrograms per deciliter (µg/dL). The U.S. Department of Health and Human Services (HHS) and CDC are committed to eliminating this burden to public health. CDC aims to raise awareness about lead poisoning; Stress the importance of screening the children younger than 6 years of age who is at high risk and (preferably by ages 1 and 2) if they have not been tested yet; Highlight partners' efforts to prevent childhood Lead poisoning; and finally urge people to take steps to reduce Lead exposure.\[^{20}\] (CDC, 2014).

3.1 Household Environmental Risks and Health

The source of most Lead poisoning in children now is dust and chips from deteriorating Lead paint on interior surfaces. Lead paint dust, carbon monoxide, radon, pesticides and Volatile Organic Compounds are five common household pollutants that have the potential to cause humans undesirable health effects even at low dose exposure levels, such as those normally found in the home.\[^{21}\]

3.2 Hobbies

Exposure can also occur through activities like making stained glass, casting and ceramics, hunting, target shooting, remodeling and renovation, auto repair, or liquor distillation.\[^{22}\]

3.3 Toys

Chinese-made toys with Lead content occurred with alarming frequency in recent years. Concern over Lead paint used on toys has prompted several states to take action. In recent years, Maryland joined California and Illinois in regulating the level of Lead allowed in toys
marketed in the state. Even Children's jewellery has also been identified as a potential source of Lead exposure.

4. Dietary exposure to lead
Excluding accidental and occupational exposure dietary intake is considered the most important source of human exposure to heavy metals causing several health problems.\(^{[23]}\)

4.1 Infant formulae: potential risks from Lead in the infant diet and other Foods
The Food Standards Agency (FSA) has reported a survey of metals in complementary foods and formulae for infants, which were sampled during 2004 and 2005.\(^{[24]}\) All formulae sampled had Lead levels lower than the 20 μg/kg limit set by the European Commission (EC 1881/2006). Powdered formulae showed higher Lead levels (μg/kg as sold) than ready-to-consume infant formulae.

4.2 Complementary foods
As part of the FSA survey of metals in foods and formulae for infants, Lead concentrations were measured in samples of commercial infant foods sampled in 2004 and 2005. Values were approximately two-fold higher in breakfast foods, biscuits, cereal bars/rice cakes and rusk products than in the other foods tested. Recently both the European Food Safety Authority (EFSA) and the Joint FAO/WHO Expert Committee on Food Additives (JECFA) published evaluations of Lead. A conclusion was made that a provisional tolerable weekly intake (PTWI) of 25 μg/kg bodyweight (bw) previously established by JECFA may no longer be considered protective for health. In supporting their assessments, EFSA\(^{[25]}\) (EFSA, 2012) and JECFA (FAO/WHO)\(^{[26]}\) focussed on the extensive data that was available on the adverse effects in humans. The calculated benchmark doses (BMDs) and their lower 95% confidence limits for the effects of Lead are most likely to be relevant to dietary exposure in different subgroups of the general population.

4.3 Common food
The levels of Lead in most commonly consumed foodstuffs are generally low. Lead can accumulate in fish and shellfish and in addition can be found at higher levels in the offal (liver and kidney) of food animals. In a recent health risk evaluation conducted by EFSA in Germany the average Lead concentrations per main food group were highest for meat, followed by fish, vegetables and cereals. Lead intake from food was estimated to be 0.53 and 0.72 μg kg\(^{-1}\)bw and day for average and high-end consumers, respectively (German
A further source of Lead in the diet is from food containers containing Lead, e.g. storage in Lead-soldered cans, ceramic vessels with Lead glazes and Leaded crystal glass. Lead contamination of food arises as a result of environmental emissions, such as mining and the now diminished use of Leaded petrol. The European Food Safety Authority (EFSA) concluded that even low exposures to Lead in pregnant women, infants and children can adversely affect neurodevelopment. The International and European health-based guidance values for Lead exposure have been amended several times as new information has come to light. The UK FSA has recently warned consumers about the dangers of drinking clay based detox drinks as they are in Lead levels.

4.4 Home remedies, candy, Pica and contaminated food

Plants growing near the roads are mostly contaminated with Lead, mainly on their above-ground external surfaces. Vegetables near the roads contain 5-20 times more Lead than other vegetables. Several brands of candies that are imported from Mexico have been identified as having high levels of Lead. Lead contaminated candy produced in Mexico and transported across the border is available particularly in California, New Mexico, Arizona and Texas. Pica is described as a disorder usually characterized by the eating of one or more nonnutritive substances on a persistent basis for a period of at least one month by the Diagnostic and Statistical Manual of Mental Disorders. Commonly ingested substances include soil, clay, ice, baking powder, starch chalk, and paint. Although its prevalence is not known, pica is very common among young children and pregnant women.

4.5 Human breast milk

Lactation requires redistribution of maternal calcium with mobilization from bone stores. Generally up to 5% of bone mass is mobilized during lactation and Lead that has accumulated in this bone may be released into the blood and excreted in breast milk. However, as more than 90% of Lead in the adult human body is located in the bone, there can be real distribution of accumulated Lead from bone into plasma and subsequently into breast milk, during the periods of heightened bone turnover such as pregnancy and lactation.

5. Lead exposure: who's at risk?

Healthy People 2010, national health objectives promoted by the Office of Disease Prevention and Health Promotion at the U.S. Department of Health and Human Services, has set the goal of completely eliminating blood Lead levels of 10 µg per deciliter or higher in children by 2010 (Healthy People 2020 Objectives). One source of data in 2013 is the
Centers for Disease Control's (CDC's), Adult Blood Lead Epidemiology and Surveillance (ABLES) program that monitors laboratory reported elevated blood Lead levels (BLLs) among adults in 41 states.\(^{[31]}\)

5.1 Prenatal exposure
Lead exposure during fetal development may result from mobilization of bone Lead stored from past exposure into the maternal bloodstream and/or from direct elevation of maternal blood Lead levels caused by acute or chronic environmental Lead exposure during pregnancy. In utero Lead exposure is associated with impairment of postnatal neurodevelopment with an increased risk for developmental delay, lowering of IQ, and behavioral abnormalities.\(^{[32]}\)

5.2 Childhood Lead poisoning
HIV and AIDS, also reveals the dangers that old and poorly maintained buildings pose to children, who can easily ingest paint from walls and floors, putting themselves at risk for high blood Lead levels.

5.3 Pediatric Lead poisoning
The important pediatric exposures include elevated maternal blood Lead levels during pregnancy, breastfeeding, soil, food, or water contamination and excess Lead in toys. The use of Geographic information system(GIS) in environmental risk factor studies on childhood Lead exposure became a focus of research activity in the late 1990s. This prompted the CDC to develop a guideline for the use of GIS in childhood Lead poisoning studies in 2004 and lot of accomplishments have been made regarding this concern.\(^{[33]}\) To achieve this goal is conditional on the ability to develop strategies based on geographic areas.

5.4 Adult Lead poisoning
Lead poisoning causes some nonspecific signs and symptoms in adults such as abdominal pain, constipation, irritability, difficulty concentrating, and anemia. The kidney and cardiovascular systems are adversely affected by Lead exposure in adults.

6. Signs of Lead Toxicity
6.1 Symptoms in General and in Children
General symptoms include Blood Lead over 10\(\mu g/dl\), hypertension, increased nerve conduction velocity, tremors, upper extremity weakness and gingival Lead lines. In children
Symptoms are growth failure, aminoaciduria, language delay, behavioral change and abdominal pain. Gastrointestinal absorption of Lead is greatest in infancy. Infants absorb up to 50 percent of Lead ingested from food, water, contaminated dust, or soil, while adults absorb only 10-15 percent. Inorganic Lead (food, water, paint, toys, vinyl products) is minimally absorbed through the skin, but tetraethyl or alkyl-Lead (leaded gasoline), which is still legally allowed in aircraft, watercraft, and farm machinery, is well absorbed through the skin.

Colic is a characteristic early symptom of acute Lead poisoning following high exposures – for example, in the workplace. Other symptoms include nausea, vomiting, anorexia and constipation. High acute exposures also cause encephalopathy, both in children and in adults. However, because Lead accumulates in the body, adverse effects can occur from long-term dietary exposures at lower levels, insufficient to cause acute toxicity.

Absorbed Lead is transported in the blood bound to proteins, predominantly in erythrocytes and also in plasma. It is then deposited in soft tissues and bone, where it tends to accumulate with age. Maternal bone is mobilised during pregnancy and lactation to meet the demands of fetal mineralisation and this leads to release of Lead from the bone. The kidney and cardiovascular systems are adversely affected by Lead exposure in adults. Neurotoxicity is identified at lower levels of exposure itself, and thus the developing brain appears to be more vulnerable than the mature brain. Calcium, iron and zinc deficiency have been associated with higher absorption of Lead. Lead usually enters the body through ingestion or through the inhalation of dust containing Lead particles or fuel exhaust. Absorption of Lead through the skin is far less efficient and it is a concern only in relatively rare situations. Inhaled inorganic Lead, when in sufficiently minute particles, can be completely absorbed through the respiratory tract.

6.2 Health hazards of Lead to animals and humans

The effect of biomagnification leads to serious health hazards for animals and humans. Lead poisoning occurs when a human being absorbs, through the air by inhalation or the food or other material by ingestion, substantially more lead than his body can excrete. The absorbed Lead enters the blood stream and accumulates in body tissue, particularly the bones, kidneys, and nervous system. The fetus, infant and child are especially vulnerable. Lead is a cumulative poison and once it is absorbed it remains in the body for months or years. Lead retention in vital organs can lead to renal disease, peripheral neuropathy, hypertension, gout, encephalopathy, and death. Lead can be stored in the bones for several decades. During
physiologic stress or immobilization, where an increase in bone turnover occurs, Lead can leave the bones and reenter the blood and soft tissues. Therefore, pregnancy, lactation, menopause, chronic disease, or calcium deficiency may increase the risk of lead toxicity. Subclinical Lead exposure may have effects on behaviour and intelligence. Evidence is that prolonged low-grade exposure to Lead may cause hyperactivity in children, learning difficulties and impaired brain function. Lead poisoning in children occurs at lower blood Lead levels than in adults. The age range of 1-5 years is the most critical. The pregnant woman and her fetus are highly susceptible to lead poisoning. Chronic exposure to Lead cause miscarriage and stillbirths.[17]

Lead toxicity is particularly an inconspicuous hazard with the potential of causing irreversible health effects. It is known to interfere with a number of body functions and it is primarily affecting the central nervous system, hematopoietic, hepatic and renal system producing serious disorders. Acute toxicity is related to occupational exposure and is a rare condition. But Chronic toxicity on the other hand is much more common and occurs at blood Lead levels of about 40–60 ug/dL. It can be much more severe if it is not treated in time and is characterized by persistent vomiting, encephalopathy, lethargy, delirium, convulsions and coma.

6.2.1 Lead Hazards for Pregnant Women and Children

Children with even slightly elevated blood Lead levels are at greater risk for significant neurobehavioral problems which extend through adolescence. Research has reported that elevated blood Lead levels in pregnant women, even those well below 10 micrograms per deciliter (Centers for Disease Control and Prevention's level of concern) can cause miscarriage, premature birth, low birth weight, and subsequent developmental delays in their children. Therefore elevated blood Lead levels during pregnancy are associated with an increased risk of preterm births and can increase the risk of spontaneous abortion.[38] Lead exposure can be especially harm during pregnancy, fetal development, and early childhood. Lead gets transmitted from mother to fetus through the placenta and an animal study by Gayer found that maternal and fetal blood Lead levels were nearly identical.C:\Users\Kritika\Downloads\4, Gardella C. Lead exposure in pregnancy: a review of the literature and argument for routine prenatal screening. Obstet Gynecol Surv 2001;56(4):231-8. - See more at: http:\www.nursingcenter.com\lncearticle?tid=820260 - P65 P66 5 The first pregnancy carries the greatest risk of Lead toxicity. Blood Lead levels
may actually increase in women during pregnancy as a result of increased mobilization of Lead from bones into the blood. Maternal bone is mobilised during pregnancy and lactation to meet the demands of fetal mineralisation, and this releases the Lead.

6.2.2 Effect of Lead on the developing fetus

Lead freely crosses the placenta and there is a strong correlation between maternal and umbilical cord blood Lead levels. In fact, the fetal blood lead level may be even greater than the maternal Lead level. An observational study and literature review by Shannon and colleagues found that at the time of delivery, infants' blood lead levels were, on average, 19% more than those of their mothers. Because of the incomplete blood-brain barrier, the effect of Lead on the fetus's central nervous system is greater during gestation and in the first 36 months of life than it is later in life.\[39\]

6.2.3 Risk characterization of Infants exposed to Lead

The potential risks from infants’ exposures to lead were characterized by margins of exposure (MOEs), calculated as the ratio of the BMDL of 0.5 μg/kg bw/day to estimated exposures from diet, soil and air. Calculated MOEs for dietary exposures in infants were generally >1, indicating that any risk from this source of exposure is likely to be small. A marginally low MOE (0.90) was calculated for high consumers of breast milk at ages 0-3 months, when the lead concentration in breast milk was taken as the highest that was recorded in a survey of UK women reported in 2004.

6.3 Dangerous effects related to lead

The current CDC target blood lead level for children under the age of six is 10µg/dl. Children, and also the developing fetus, are especially susceptible to harm from exposure to lead because of their smaller size and their immature neurological system. Lead is a neurotoxin which affects both the central and peripheral nervous system. Multiple studies have shown a direct effect of lead exposure on IQ, attention, memory, learning disabilities, cognition, aggressive behavior and delinquency.\[40\][41][42][43] People with additional neurological impairments, such as seizure disorders and other neurological and psychiatric impairments, may also be at increased risk from exposure.
7. Effect of Lead on different parts of the body

Lead poisoning leads to damage of cardiovascular, renal, gastrointestinal, hematological and reproductive systems, as well as cause sub-cellular changes and neuro-developmental disorders, being the latter the most significant (UNEP).[44]

7.1 Effect of Lead on Nervous system

Direct effects of Lead on the nervous system may be classified as either morphological or pharmacological. Encephalopathy (progressive degeneration of some parts of the brain) is a direct consequence of Lead exposure and the major symptoms include dullness, irritability, poor attention span, headache, muscular tremor, loss of memory and hallucinations. More severe manifestations occur at very high exposures and include delirium, hypertension, lack of coordination, convulsions, impaired renal and thyroid function paralysis, coma, ataxia, vitamin D deficiency and preterm birth.[17] Fetus and young children are especially vulnerable to the neurological effects of Lead as the developing nervous system absorbs a higher fraction of Lead. The proportion of systemically circulating Lead gaining access to the brain of children is significantly higher as compared to adults. At higher levels, Lead can cause permanent brain damage and even death.[45] In children, Lead exposure has been associated with impaired verbal concept formation, poor grammatical reasoning, and poor command following on both standardized and in situ tasks. Lead exposure is particularly harmful in older adults of age 55 producing lower learning and memory scores. These individuals demonstrated decreased performances on verbal memory and visual memory tasks following Lead exposure.[46] The higher bone Lead level was associated with worse visuo spatial function, as measured with visual reproductions, embedded figures, and block design tasks than non exposed controls after a 22-year delay.[47] Grammatical reasoning difficulty was also associated with lead exposure in a study of adult lead workers.[48]

7.2 Effect of Lead on the Hematopoietic System

Lead poisoning cause anemia (both hemolytic and hemorrhagic), the mechanism of which occurs in two ways. A shortened erythrocyte lifespan and impairment of heme synthesis which causes increased concentration of protoporphyrin by inhibiting heme synthetase, the enzyme which combined protoporphyrin and iron to form heme. Lead causes inhibition of the enzyme δ-aminolevulinic acid dehydratase (ALA-D) resulting in a failure of utilization of δ-aminolevulinic acid which is excreted in increased quantities of urine[49] and finally Lead blood level measurement is one of the most important indicators to lead poisoning. The
combined effect of these two processes leads to anemia.[50] Zinc protoporphyrin (ZPP) is a compound found in red blood cells when heme production is inhibited by lead or by lack of iron. Measurement of zinc protoporphyrin in red cells has been used as a screening test for lead poisoning and for iron deficiency.

7.3 Effect of Lead on Renal system
Renal dysfunction occurs mostly at high levels of Lead exposure (>60 µg/dL) and damage at lower levels has also been reported (~10 µg/dL).[51] Abnormality of renal function causes acute nephropathy and chronic nephropathy which is characterized by glomerular and tubulo interstitial changes, resulting in renal breakdown, hypertension and hyperuricemia.[52] Inorganic Lead is not metabolized but it is excreted unchanged, primarily in the urine.

7.4 Effect of Lead on Cardiovascular system
Both chronic and acute Lead poisoning causes cardiac and vascular damage with potentially lethal consequences including hypertension and cardiovascular disease.[53]

7.5 Effect of Lead on Reproductive system
Lead causes a many adverse effects on the reproductive system in both men and women.

7.5.1 Effect of Lead on testis
It includes reduced libido, chromosomal damage, infertility, abnormal prostatic function, abnormal spermatogenesis (reduced motility and number) and changes in serum testosterone.

7.5.2 Effect of Lead on Female Reproductive system
Generally women are more susceptible to infertility, miscarriage, pre-eclampsia, pregnancy hypertension, premature membrane rupture and premature delivery.[54] During the gestation period, direct the influence of Lead on the developmental stages of the fetus has also been reported.[55]

7.6 Effect of Lead on Bone
The primary site of Lead storage in the human body are bones.[56] Turnover of bone tissue releases Lead back into the bloodstream and processes like pregnancy, lactation or menopause may increase blood Lead levels by speeding the bone tissue turnover. Lead in the body is measured with both blood levels and bone levels. Blood Lead levels are more reflective of acute exposure, whereas bone lead levels usually reflect cumulative exposure over time.[17] Lead gets stored in a person's bones for decades before being released into the
bloodstream or into soft tissues. It thereby causes further damage to that person's internal organs. The half-life of bone-deposited lead ranges from 20 to 30 years.

7.7 Effect of Lead in Soft Tissue
Lead is stored in soft tissue. Autopsy studies show the liver to be the largest repository of soft tissue Lead (33%), followed by kidney cortex and medulla, pancreas, ovary, spleen, prostate, adrenal gland, brain, fat, testis, heart and skeletal muscle.\textsuperscript{[57][58]} Levels of Lead in soft tissue appear to be relatively constant during life thereby effecting the normal metabolic pathways of that particular soft tissue.

7.8 Effect of Lead on immune system
Immune modulation by heavy metals cause serious adverse health effects in humans. Lead has also been shown to worsen autoimmune conditions such as lupus in susceptible rodents and has been linked with an increased production of self-reactive antibodies directed against neural proteins.\textsuperscript{[59]}

8. Mechanism of Lead toxicity
8.1 Oxidative stress- Effect of Lead on Glutathione metabolism
Under the influence of Lead, the onset of oxidative stress occurs on account of two different pathways operative simultaneously; first is the generation of ROS, like hydroperoxides (HO\textsubscript{2}), singlet oxygen and hydrogen peroxide (H\textsubscript{2}O\textsubscript{2}) and second, the antioxidant reserves become depleted. Glutathione is a cysteine-based molecule whose antioxidant property includes quenching of free radical and is associated with drug and toxin metabolism in the liver. Lead inactivates enzymes like δ-amino levulinic acid dehydratase (ALAD), glutathione reductase (GR), glutathione peroxidase (GP\textsubscript{X}) and glutathione-S-transferase, which further depresses the glutathione levels.\textsuperscript{[34]}

8.2 Ionic mechanism of Lead toxicity
Ionic mechanism of action for Lead is due to its ability to substitute other bivalent cations like Ca\textsuperscript{2+}, Mg\textsuperscript{2+}, Fe\textsuperscript{2+} and monovalent cations like Na\textsuperscript{+}, affecting various fundamental biological processes of the body. Even in picomolar concentration, Lead can replace calcium, thereby affecting key neurotransmitters like protein kinase C, which regulates memory storage and long term neural excitation. It also affects the sodium ion concentration, which is responsible for a number of vital biological activities like generation of action potentials in the excitatory tissues for the purpose of cell to cell communication, uptake of
neurotransmitters (dopamine, choline and GABA) and regulation of uptake and retention of calcium by synaptosomes.

9. Lead in Ayurveda
Ayurveda is a traditional health care system which is originally practiced in South Asian countries. From 2000 to 2003 the CDC received 12 reports of adults with Lead poisoning associated with the use of Ayurvedic medicines and in 2004 a study published in JAMA reported that 13 of 70 Ayurvedic products produced in South Asia and sold in Boston-area stores contained potentially harmful levels of Lead. [60] Azarcon and Greta, used for the treatment of stomach ailments among some Mexican Americans, are brightly colored industrial powders that may contain from 70% to more than 90% lead.

10. Epidemiology
The Center for Disease Control and Prevention has identified 25 μg/dL as the lower bound for the range of concern for adult blood lead levels. Incidence of concerning blood Lead levels among adults were almost halved from 1994 to 2007, falling from 14.0/100,000 to 7.8/100,000. [61] According to the same study, occupational exposure was the primary source of lead exposure for adults, particularly in the battery manufacturing and mining industries. The risk was found to be higher among men than women because of occupational differences and there is no such gender difference found among children.

**Primary prevention** efforts focus on removal of Lead from the environment so that exposure cannot occur. **Secondary prevention** efforts are designed to minimize absorption of Lead and deposition in the mineralizing tissues, where it functions as a source of chronic exposure. **Tertiary prevention** reduces the morbidity due to Lead intoxication through chelation of Lead from the blood and soft tissues of an exposed individual. Chelation reduces the immediate toxicity associated with acute Lead ingestion, but it has limited ability to reverse the neurocognitive effects of chronic exposure. Therefore Primary prevention is the only way to reduce the neurocognitive effects of lead poisoning. [62]

11. Bioremediation of Lead
The effect of metals on the functioning of ecosystems vary considerably and is of economic and public-health significance. Consequently environmental awareness is growing among industrialists, consumers and legal constraints on emissions are increasingly strict thereby leading to a need for cost-effective emission control. The meander system used in the
Homestake Lead mine (Missouri) passes effluents containing Pb and other metals through channels containing cyanobacteria, algae and higher plants. Metals are removed from the water column with an efficiency greater than 99%. Fluidized beds of alginate and polyacrylamide immobilized algae, e.g. Spirulina platensis and Chlorella vulgaris have been used to remove a variety of metals, including Cu, Pb, Zn and Au, from mixtures for which different selective schemes have been devised. Heavy metals change the structure of the activated sludge micro fauna by modifying both cell density and species richness.

11.1 Phytoremediation of lead
Traditional methods of remediation of Lead contaminated sites include a variety of physical, thermal and chemical treatments.
1. Phytoextraction - the use of plants to remove contaminants from soil.
2. Phytovolatilization - the use of plants to make volatile chemical species of soil elements.
3. Phytostabilization - the use of plants to transform soil metals to less toxic forms, or to reduce mobility, but not remove the metal from soil.

12. Prevention of Lead induced toxicity
Guidotti and Ragain\textsuperscript{[63]} proposed a three-way measure as preliminary preventive approach towards Lead toxicity which includes Individual intervention, Preventive medicine strategy and Public health strategy.

12.1 Antioxidants protect from Lead induced oxidative stress
Generally, an antioxidant can prevent lead toxicity in three ways.\textsuperscript{[64]} By inactivating the generated ROS at molecular level thereby terminating the radical chain reaction i.e chain breaking. By chelating the Lead ion and preventing further formation of ROS by chelating Lead and maintaining it in a redox state, which leads to its incompetency to reduce molecular oxygen. Antioxidants are broadly grouped according to their mechanism of action: primary or chain breaking antioxidants\textsuperscript{[65]} and secondary or preventive antioxidants.\textsuperscript{[66]} Common primary antioxidants include tocopherol, flavonoids, and ascorbic acid. Secondary antioxidants includes low molecular weight polyphenols. Natural antioxidants can be categorized into enzymatic and non enzymatic antioxidants. Enzymatic antioxidants include SOD, CAT, GP\textsubscript{X}. Non enzymatic antioxidants such as flavonoids, carotenoids, minerals, vitamins, \textit{etc.} are constituents of many fruits, vegetables, grains nuts and some meats.\textsuperscript{[67]} The role of vitamins (B, C and E) has been found to be extremely significant and competitive in fighting the
toxicological manifestations of Lead poisoning. These vitamins chelate Lead from the tissues along with restoring the pro or antioxidant balance.\textsuperscript{[68]}

12.2 Lead Prevention and Intervention
As preventive education and early intervention are critical in reducing the toxic effects of Lead on children, educators should become familiar with the resources and services for families identified in Lead Prevention and Intervention: Resources and Services for Parents."
As educators work closely with children and families, they are likely to know of a family or child in the community who may be at high risk for exposure to environmental Lead and who has recently been identified as having an elevated blood Lead levels. Educators must have knowledge about these resources in order to provide or direct families to them, and to refer families to appropriate medical, social service, public health and housing services. Educators should review the Department of Public Health (DPH) screening data and map indicating the rate of screening by town. In towns where compliance has been low, school districts should encourage provider and parent compliance with necessary mandated screening requirements.

12.3 Current Approach to minimize Lead poisoning by different Organisations worldwide
12.3.1 Scientific Advisory Committee on Nutrition (SACN) and The Centers for Disease Control (CDC)
Currently Lead poisoning is the foremost environmental health threat to children in the United States. One of the most important tools for mitigating human impact to streams, rivers and lakes is water monitoring. Monitoring solutions help to prevent the introduction of contaminates and helps enforce environmental policies. Monitoring regimes, along with progressive environmental policies help to mitigate the human impact to natural waters and natural ecosystems to improve the quality of life.

12.3.2 The Global Alliance to Eliminate Lead Paint (GAELP)
GAELP organized the first International Lead Poisoning Prevention Week on October 2013\textsuperscript{[69]} along with Environmental Protection Agency EPA, WHO, CDC and UNEP with an intention to raise awareness worldwide about Lead poisoning and strengthen actions to eliminate the use of Lead in paint. The campaign theme was “Lead-Free Kids for a Healthy Future”.
12.3.3 World Health Organisation (WHO)

WHO is currently developing guidelines on the prevention and management of Lead poisoning, which provide public health authorities, policy-makers and health professionals with evidence based guidance on the measures that they can take to protect the health of children and adults from lead exposure. WHO is organizing International Lead poisoning prevention week of action with an objective to state that though Lead poisoning is entirely preventable, yet lead exposure is estimated to account for 0.6% of the global burden of disease, with the highest burden in developing regions.\[^{70}\]

12.3.4 European Food Safety Authority (EFSA)

Recently on October 12\(^{th}\), 13\(^{th}\) and 14\(^{th}\) 2015, EFSA conducted a conference in Milan on shaping the future of food safety to discuss on several issues related to food safety.

REFERENCES


27. German LExUKon project. Food Additives and Contaminants - Part A Chemistry, Analysis, Control, Exposure and Risk Assessment, 2014; 31(6).


60. Saper RB et al., Heavy metal content of ayurvedic herbal medicine products. JAMA, 2004; 294(23): 2868-73.


