REVIEW ARTICLE

Lead and its Health Hazards

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ABSTRACT:
Metals are important source of pollutant toxicants which occur naturally in the environment. Now-a-days many metals have become essential to various biological processes and some level of human exposure is therefore unavoidable. Lead has been used by humans for at least 7000 years alone and in combination with other metals. It is highly toxic, ductile, malleable and easy to smelt. A wide range of adverse effects could be induced in human beings depending upon the dose and time period of lead exposure. Central nervous system of children is the most sensitive to lead effects while peripheral neuropathy, chronic nephropathy, and hypertension are the main concerns in adults. Other target tissues include the gastrointestinal, immune, skeletal, and reproductive systems. Effects on the heme biosynthesis provide a sensitive biochemical indicator even in the absence of other detectable effects. Present review is therefore written to provide comprehensive awareness regarding lead and its health hazards.

Keywords: Heavy metals, Lead, Human exposure, Health hazards, Toxicity, Prevention

INTRODUCTION:

The use of metals like lead, mercury, cadmium, arsenic etc. has played a crucial role in the progress and success of present civilization. Metals are important source of pollutant toxicants which are all naturally occurring in the human environment. Now-a-days many metals have become essential to various biological processes and some level of human exposure is therefore unavoidable. Thus essential metals are becoming toxic with increasing exposure. Worldwide toxic metals are being used for different purposes since hundreds of years such as Lead (Pb) that is said to be in use for at least 5000 years. It was employed in building materials, glazing ceramic pigments, and water pipes. Lead acetate during the Roman times was used to sweeten old wine, and some Romans might have consumed large amount of lead as much as one gram per day. Use of lead by human probably started prior to 2000 BC, at that time abundant supplies were obtained from minerals as a by-product of silver smelting. In 370 BC credit has been given to Hippocrates for the first description of abdominal colic in a man who extracted metals.[1]

Lead is also known as the horror mineral because it is associated with violence, lowered IQ, Attention Deficit Disorder, Attention Deficit Hyperactivity Disorder (ADHD) and other neurological diseases. It is a commonly distributed toxic metal with extensive uses in industry. Till 1970s lead was added to gasoline. The new gasoline has manganese in it instead of lead. It is also present in paints, lubricants, medications, cosmetics (i.e. lipstick) and inks. Books have been written on the toxicity of lead, which describe the lead related conditions from anemia to death.[2] The effects produced by the toxic metals also depend upon the half-life and elimination of the metals for example the biological half-life of lead in bone is 20-30 years. Thus continuous metal exposure may follow retention kinetics .The blood lead level in population of United States had elevated about 0.7-4.4 µg/dl in both genders with age limit of ≥1 to ≥60.[3] The main analytical problem in determining trace metals in blood contains lead levels and the data pertaining to lead levels in the population of United States has been reported by Center for Disease Control and Prevention (CDC). [4] This is clearly highlighting that the task is not easy at the level of technically advance country and in light of this one can think about the situation in our part of the world and in our country where heavy metals their toxicity and related complications are not addressed with due attention and there is paucity of documented literature. Present review is therefore written to provide comprehensive awareness regarding the sources, exposure to humans, health hazards, analytical techniques and measures to reduce if not prevent the problems caused by lead.

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METHODOLOGY:

Articles were collected and identified by using electron data bases Google Search, Google Scholar, Pubmed from 2000-2016. Keywords and phrases used were lead, heavy metals, toxic metal, lead toxicity, human exposure to lead, diseases caused by lead exposure. 200 articles were selected. Inclusion criteria was review articles, original articles, CDC and WHO reports. Exclusion criteria was articles related to animal studies, articles with heavy metals other then lead. Filters used were health hazards and human dangers. A total of 60 articles that met the inclusion criteria were included in this write up.

LITERATURE REVIEW:

Lead (Pb) occurs naturally in the environment. Lead (Pb) has been used by humans for at least 7000 years alone and in combination with arsenic and antimony. Lead (Pb) is a highly toxic, ductile and malleable metal that is easy to smelt. Lead occurs naturally in the earth's crust. It is also called as plumbum derived from Latin and is designated as Pb. Metallic lead (Pb) is resistant to corrosion and can combine other metals to form various alloys. Organo-lead compounds are dominated

by Pb4+. Inorganic lead compounds are used as pigments in paints, dyes, and ceramic glazes. Organo-lead compounds were used as gasoline additives. Lead is primarily derived from such human activities as mining, manufacturing, and burning fossil fuels that is found in all parts of the environment. Lead (Pb) has been a ubiquitous environmental pollutant, and is toxic even in low doses. Primary production and reprocessing of Pb is based on smelting, with substantial emission of metal fumes. Lead (Pb) toxicity exert impact on the nervous system, both in adults and children.[5] Lead alloys are used in batteries, shields from radiation, water pipes, and ammunition. Environmental lead comes mainly from human activity and is listed as a top toxic substance.[6] Lead toxicity problem has become more serious with the industrial expansion in the last two centuries, as evident from the Antarctic and Arctic ice core data showing presence of lead even in such far off places. The cognitive deficits, neurotoxicity, behavior disorders, growth problems, reduced heme synthesis and impaired hearing are reported as adverse effects of Pb. It has been observed that blood lead is associated with house dust concentrations of lead, the duration of time spent working in a closed workshop and the year in which the subject moved into that residence.[7,8]

Lead is not biodegradable and the concerns for ecotoxicity of lead are increasing. For instance, the leaded fish sinkers or pellets lost in the bottom of lakes and river banks can be mistaken for stone and ingested by birds causing adverse effects including death.[9] A primary source of lead exposure in children is lead-containing paint however major environmental sources of lead exposure is hand-to-mouth transfer of lead containing paint chips or dust from floors of older housing or from neighborhood soil among infants and toddlers up to 4 years of age.[10,11]

Pharmacokinetic characteristics: Lead absorption commonly occurs from lungs and depends upon vapor versus particle size and concentration. About 90% of lead particles are small and are readily absorbed through alveoli into blood. 99% of lead in blood binds to hemoglobin leaving only 1% for tissue distribution such as kidney, liver, skeleton and hair. The fraction of lead in bone increases with age from 70% of body burden in childhood to as much as 95% in adulthood, with a half-life of about 20 years however in blood lead half-life is about 30 days. Lead in trabecular bone is more labile and has a shorter turnover time than cortical bone. Lead released from bones may contribute up to 50% of the lead in blood, and is a significant source of endogenous exposure. Bone lead release may be important in adults with accumulated occupational exposure and in women due to bone resorption during pregnancy, lactation, menopause, and from osteoporosis.[12] Lead is eliminated via kidney and bile.

Sources of lead: There are many sources of lead in our environment.

(1) **Food Sources**

Agriculture lands near the industries and highways are at a greater risk of becoming contaminated by toxic metals. Even old house paint (Pb),sprays, insecticides and processes that involved fruits refining predispose human beings to metal toxicities. The food sources of lead are rice, milk, carrot, wheat, potato, calcium supplement, eggs, cocoa powder, smoked food, wine, beer, raisons etc.

(2) **Drinking water:** Contamination of water (wells and municipal water) by toxic metals is an important source of affecting humans. Pipes made of plastic, lead, copper and galvanized pipes can be an important source of water contamination particularly soft water contamination. The largest source of lead in drinking water occurs through leaching from lead-containing pipes, faucets, and solder, which can be found in plumbing of older buildings.[13,14]

(3) **Lead paint:** Lead carbonate [PbCO3/ Pb(OH)2)] was added to paints to speed drying, improve durability, and protect the surface from corrosion before 1978 when it was banned. All those who are concerned from manufacturing to use of lead containing paints are at increased risk but children are at particular risk from lead paints because they occasionally might eat paint chips. Lead paint can have a sweet taste, and babies and toddlers will often lick or suck window sills, crib bars, and other objects that may be coated with lead paint. Leaded dust from peeling, chipping, cracking or otherwise deteriorating lead paint will collect onto floors and other surfaces. Children touch the dust, and then put their fingers in their mouths.

(4) **Imported candies:** Lead has been found in candy and candy wrappers imported primarily from Mexico and Asia.[15]

(5) **Hobbies and art:** Some art supplies, such as artists' paint, still have lead in them. Some hobbies require the use of lead, such as stained glass, firing guns, making ammunition, and making fishing lures and sinkers.

(6) **Contaminated soil:** Another common source of lead is contaminated soil. Two possible sources of contaminated soil are leaded gasoline and industrial operations like smelters. While gasoline is generally no longer a major source of lead, decades of leaded gasoline left contamination in the soil next to roadways up to one-quarter of a mile from the road might be a source to expose children. They play on or near the floor and make their hands dirty. Often they put their fingers into their mouths. In addition urban environments in comparison to rural receive higher depositions of lead from vehicular emissions and are therefore at a greater risk. Similarly smelter operations also contaminate the soil and thereby expose the workers and the nearby land to a risk.

(7) **Jewelry:** Some jewelry is made of lead and can pose a danger to children if they put the jewelry in their mouths.

(8) **Lead at work:** Adults who work in industries that use lead (battery manufacturing, pipe fitting, firing ranges, demolition, glass production, smelting operations, etc.) should be careful not to bring lead home with them, shower and change clothes and shoes at work.

(9) **Dishware:** Imported glazed pottery and leaded

crystal may also be sources of lead.
(10) **Mini-blinds:** Vinyl mini-blinds exported by China, Indonesia, Taiwan and Mexico before 1997 contained lead, which was used to make them less brittle. Lead dust forms on the blinds, particularly when the blinds are exposed to sun and heat.
(11) **Lunch boxes:** There is evidence that some soft vinyl lunch boxes may contain lead in the lining.[16]
(12) **Herbal medicines:** Lead poisoning is reported to be caused by contaminated ayurvedic herbal products.
Effect of lead on Human Health: The effects of lead on human health can be summarized as in:
(A) **Children:** They may suffer from learning disabilities resulting in a decreased intelligence (decreased IQ), attention deficit disorder, behavior issues, nervous system damage, speech and language impairment, decreased muscle growth, decreased bone growth, kidney damage etc. The neurotoxicity of lead is of particular concern, because evidence from prospective longitudinal studies has shown that neurobehavioral effects, such as impaired academic performance and deficits in motor skills, may persist even after Pb blood levels have returned to normal. Although no threshold level for these effects has been established, the available evidence suggests that lead toxicity may occur at Pb blood levels of 10-15 mcg/dl or possibly less. High levels of lead are life threatening and can cause seizures, unconsciousness, and death.
(B) **Adults**: Multiple problems are related to high levels of lead in adults such as increase chance of illness during pregnancy, harm to a fetus including brain damage or death, fertility problems in men as well as women, high blood pressure, digestive issues, nerve disorders, memory and concentration problems, muscle and joint pain etc.
Thus a wide range of adverse effects could be induced in human beings depending upon the dose and time period of lead exposure. The central nervous system of children is the most sensitive to lead effects while peripheral neuropathy, chronic nephropathy, and hypertension are the main concerns in adults. Other target tissues include the gastrointestinal, immune, skeletal, and reproductive systems. Effects on the heme biosynthesis provide a sensitive biochemical indicator even in the absence of other detectable effects.The psychomotor tests or mental development indices, and broad measures of IQ are found to be the most sensitive indicators of adverse neurological outcomes and 2 to 4 point IQ deficit for each µg/dL increase in BLL within the range of 5–35 µg/dL with deficits in cognitive and academic skills could occur with BLL <5.0 µg/dL.[17]All these systems play a critical role in synaptic plasticity and cellular mechanisms for cognitive function, learning, and memory because lead affects virtually every neurotransmitter system in the brain, including glutaminergic, dopaminergic, and cholinergic systems. Diseases caused by lead are:
(1) **Anemia:** There is a significant negative relationship present between blood lead levels and hemoglobin percentage. Increased blood lead concentration may cause a decrease in hemoglobin percentage in some individuals. Increased blood lead concentrations also cause decrease in serum ferritin and body iron. It has been found that high dietary ferrous intake is associated with decrease blood lead concentrations.[18]
(2) **Heart diseases:** Lead and various other metals are also involved in producing an increase in cardiovascular diseases.[19] In this regard lead produced hypertension, coronary heart disease, stroke and peripheral arterial diseases. Lustberg and Silbergeld [20] investigated that the accumulation of toxic metals such as Pb in adults are associated with heart diseases, cancer and infertility. Further investigations about toxicity of these metals have shown that they produce atherosclerosis by increasing oxidative stress.[21]
(3) **Hypertension:** Lead cause hypertension.[22,23] Once the arteries become inflamed and brittle they become liable to rupture.Ca and fatty plaques prevents this rupture. The plaque in turn decreases the interior diameter of the arteries and increases blood pressure. The BLL and blood pressure has a weak, but significant association. The lead-induced hypertension and other cardiovascular diseases, is multifactorial including the pathogenesis (1) The endogenous nitric oxide and cGMP inactivation possibly through lead-induced reactive oxygen species; (2) The renin–angiotensin–aldosterone system changes and increases in sympathetic activity. (3) Alterations in calcium-activated functions of vascular smooth muscle cells including contractility by decreasing Na+/K+ ATPase activity and stimulation of the Na+/Ca++ exchange pump (4) A possible rise in endothelin and thromboxane.[24,25]
(4) **CNS diseases:** Increases in peak blood lead concentrations result in lower activity in the CNS. The existence of this effect is much greater than is currently believed.[26] A study has documented that Pb interacts with Ca-regulated enzymes such as protein Kinase C and causes oxidative damage.[27,28]
(5) **Reproductive diseases:** The population of women exposed to toxic metals either at work or in their home environment showed a correlation between high toxic metals levels in different biological specimen and the low birth weight of their children. Toxic metals cause premature birth, congenital malformation and even disturb production of chorionic gonadotrophin by the placenta and impair development of the newborn vascular system. There is evidence that statistical difference between mothers of healthy children compared to mothers of children with locomotor system malformation regarding toxic metal concentrations in various biological samples.[29]
(6) **Kidney diseases:** Lead can cause acute and chronic nephrotoxicity. The proximal tubular dysfunction caused by acute lead nephrotoxicity that could be reversed by treatment with chelating agents. Acute and chronic nephrotoxicity results in a characteristic microscopic change is the presence of intra-nuclear inclusion bodies (composed of a lead– protein complex) and appeared as a dense, homogeneous eosinophilic with hematoxylin and eosin staining. High level of lead in a relatively inert, non-toxic state was found in inclusion bodies

having acidic protein component composed of mainly with aspartic and glutamic acid residues with little cystine. Metallothionein is found on the outer surface of lead inclusion bodies and facilitates the transport of metal to the forming inclusion. Various heme containing enzymes are synthesized in the kidney. Their synthesis is affected by lead induced nephrotoxicity. This also affects Vitamin D metabolism leading to effects on bones and uric acid metabolism thus causing hyperuricemia, gout etc.[30,31]

(7) **Immunotoxicity:** Lead immunotoxicity might be a risk factor for childhood asthma [32,33] because IgE level was increased and inflammatory cytokines were found in lead-exposed neonatal rodents may be indicated an association between BLL and elevated IgE levels in children.[34]

(8) **Bones and Teeth:** Lead gets deposited in teeth and inhibits mineralization of enamel and dentine. It affects osteoblasts, osteoclasts and chrondrocytes by producing osteoporosis and delays in fracture repair. [35,36]

(9) **Other diseases:** Lead exposure increases the risk of various types of cancers including lung, brain, stomach, kidney, bladder cancers etc. [37,38,39] Severe deficiency and presence of essential trace elements in excess amounts both can affect the host response to combat pathogens especially the former increases the incidence, duration and severity of microbial infections. [40,41,42]

Analytical techniques for estimation of lead level: Biomedical analysis of toxic metals in biological samples like nails, blood, urine and hairs etc. is done because heavy metals concentration may give a picture for diagnosis of diseases.[43] Blood analysis give present status of metals load of body and it is usually found to be different than accumulation of metals in tissues. Whole blood analysis measures total metal levels that is present in the intracellular (within circulating blood cells) and extracellular (serum/plasma) fluids.[44] Blood circulation of various elements particularly the toxic ones is proportional to their depot-storage range properties which can be met by urine and hair testing.[45,46] Analysis of metals in urine is an important tool in diagnosis of various diseases and can be easily done along with blood analysis, as toxic metals may be deposited in various tissues like kidney, bone etc. without raising blood level. It has been observed that hair provides vital clues about body nutritional imbalances besides hair have simple matrix for analysis and almost ten times higher concentration as compared to blood and urine sample. Hairs are easy to collect, transfer and for storage in laboratory without any specific condition. Drug consumption and drug abuse and/or metabolite analysis in the hairs is commonly recommended. However hair cleaning before analysis is not an easy task because of endogenous and exogenous metal origin and removal is significant before analysis. Hairs may be contaminated by exogenous and endogenous sources of toxic metals. Human health research requires toxic metals to be monitored in all biological matrices. For organic and inorganic matrices, samples are dissolved and pretreated prior to instrumental analysis as in metal determination by atomic absorption spectrometry (AAS) requires a preliminary sample treatment.[47,48] In AAS sample preparation involve digestion, extraction and calibration by Certified Reference Material (CRMs) of analytes before the analysis of samples. Conventional sample preparation of organic materials for atomic absorption spectrometric analysis involves solubulization and or decomposition of the matrix typically achieved by wet digestion or dry ashing techniques using oxidative acids.[49] Different sample pre-treatments for metals have been developed for organic and biological samples. The direct sample introduction, as slurry sampling technique has also been used for pretreatment by avoiding the use of reagents and dilutions that can introduce contaminant besides no losses of volatile elements, safety of operation, short time duration and small amount of sample.[50]

Biological samples: The human biological samples which are used in analysis are blood, urine, nail and hair but estimation of lead in blood is the common one. Blood lead levels (BLL) test is used as a biomarker for human lead exposure [51]

Hairs: The characteristics of hair make them an attractive bio-monitoring substrate[52,53,54] Methods based on acid or alkaline digestion are commonly used. Samples are digested by addition of concentrated nitric acid in a beaker heated on a hot plate, after which hydrogen peroxide and nitric acids is added.[55]

Nails: Estimating the levels of toxic metals in nails is a common method of biological monitoring, diagnosis and assessment of metal exposures and their risks. Determination of toxic metals in finger nails has been assayed by atomic absorption spectrophotometry.[56,57]

Blood: Human Serum (5-10 ml) taken in a flask and added with 10 ml of concentrated nitric acid with digestion under gentle heating followed by cooling have been employed.[58] The diagnosis of diseases, intoxication and exposure to toxic metals is frequently evaluated by determining their concentrations in body fluids. When the analyses of whole blood were performed without sample digestion, the carbonaceous residues were generated in the graphite tube after several heating cycles.[59]

Urine: Determination of toxic metals in urine is used commonly in biological monitoring.[60]

PREVENTIVE MEASURES:

(1) Clean and safe drinking wáter from wells and municipal supplies

(2) Protect houses by avoiding lead containing paints & reduce lead dust

(3) Reduce dust levels in homes by:
Using a door mat to remove dirt from shoes before taking them off. Clean dust from underneath the matt frequently.
Taking off shoes before going into home. Even after scraping off dirt, shoes will track some dust and lead into home.
Keeping play areas clean. Frequently wash toys, pacifiers, stuffed animals and other objects young children put in their mouths.
Damping dust and damping mop the house at least

once a week as both are very effective at picking up dust.
Keeping sidewalks and porch free of dust and debris by using a HEPA vacuum if possible or simply by a broom[15]

(4) Healthy eating:
Washing hands before every meal and snack
Keeping children away from eating and chewing on non-food items such as paint chips, window sills, and dirt
Avoiding use of imported glazed pottery for food.
Eating foods high in calcium, vitamin C and iron. All these discourage absorption of lead.
Avoiding eating of lead containing candies
Avoiding eating of contaminated sea foods as fish, shrimps etc. being polluted by industrialized waste

(5) Lead testing: In blood samples usually but if required other samples as hairs, nails and urine may also be used to diagnose the features of toxicity.[16]

CONCLUSION:

Lead is a naturally occurring heavy metal. A wide range of adverse effects could be induced in human beings depending upon the dose and time period of lead exposure. Central nervous system of children is most sensitive to the effects of lead while peripheral neuropathy, chronic nephropathy, and hypertension are some of the main concerns in adults. Awareness regarding it`s exposure, health hazards and preventive measures should be disseminated through print and electronic media.

Government alone and or with NGOs should take measures to provide safe water supply for drinking, improve the hygienic practices in the living environmental conditions, ensure safety and control marine pollution, present industrial waste should be treated before drainage into sea, provide contaminant free fishery ,utilize mass, print and electronic media to educate people regarding healthy living, report to health officials in case of acute and chronic lead toxicity, monitor health parameters by employing health visitors etc.

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