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LEAD POISONING, ANALYTICAL ASPECTS AND ITS MANAGEMENT

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ABSTRACT

Lead comes under the class of heavy metal poisons. Lead poisoning is preventable, though it continues to be a major cause of poisoning among children and adults. Sources of lead include dust, air, water, soil and some products of daily use. Acute poisoning is rare. Chronic exposure can harm a young child's growth, behavior and ability to learn. Most often, children get lead poisoning from breathing in or swallowing lead containing dust. Lead can also be passed from mother to baby during pregnancy. In adults, chronic poisoning involves mainly central nervous system, cardiovascular system and reproductive system. Diagnosis can be made by evaluating clinical signs and medical history with special inquiry into possible routes of exposure; by using X-rays; by qualitative as well as quantitative analysis of blood and urine for lead and related metabolites. Proper management is done by providing supportive care to the exposed and specific treatment using various chelating agents.

Key Words: Heavy metal, Exposure, Sources, Clinical Features, Diagnosis, Management, Treatment, Chemical Analysis.

INTRODUCTION

Metallic lead does occur in nature, but it is rare (Polyanskiy & Fillipowa, 1986). It is denoted by the symbol "Pb" with atomic number 204 and, a half-life of approximately 53,000 years. Lead has many isotopes, but only four of them are stable: ^{204}Pb, ^{206}Pb, ^{207}Pb and ^{208}Pb (Polyanskiy & Fillipowa, 1986). All the isotopes of lead, except ^{204}Pb, are the end product of a complex radioactive decay. Lead is bright and silvery when freshly cut, but rapidly tarnishes in air produce the dull luster. It is ductile, dense, very soft, and has poor electrical conductivity (Polyanskiy & Fillipowa, 1986; Thurmer et al., 2002; Tetreault et al., 1998). It is highly malleable but can be toughened by the addition of small amounts of antimony. This metal is highly resistant to corrosion.

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Lead does not evaporate. It gets into the air when lead containing materials are burnt. Lead comes into soil through broken-down lead paint, lead pipes, residues from lead-containing gasoline or pesticides, contaminated landfills; and, from industries such as foundries and smelters. Lead from the atmosphere or soil can end up in groundwater and surface water; and in this way into drinking water. The Australian Drinking water Guidelines and WHO allow a maximum 1µg/dL while in India maximum permissible level is 5µg/dL (Greene, 1993).

SOURCE OF LEAD

Lead is usually found mixed with other metals in ores, most abundantly with copper, and with zinc and silver (Holleman et al, 1985).

The main lead mineral is Galena (PbS), which contains 86.6% lead. Other lead compounds are Cerussite ($PbCO_3$) and Anglesite ($PbSO_4$) (Holleman et al, 1985).

Lead is widely used in the production of batteries, metal products [pipes and solder], ammunition and devices to shield X-rays (Gearhart et al., 2003).

Some lead compounds, e.g. lead chromate and lead carbonate are of bright colors, which are widely used in paints (Merrill et al, 2007).

Tetraethyl lead used to be added to gasoline (Seyferth, 2009).

It is commonly incorporated into herbal remedies such as Indian Ayurvedic preparations and remedies of Chinese origin (CDC, 2003).

Folk remedies like Azarcon and Greta, contain about 95% lead.

EXPOSURE OF LEAD

Occupational (Patrick, 2006)**:** Auto repair works, battery making ,glass manufacture, mining, plastics manufacture, ship building or ship breaking, smelting & refining, steel, welding & cutting, plumbing, pottery, printing, rubber industry, soldering (electronics) etc.

Domestic (Salvato et al., 2003)**:** House paint (Pearce, 2007), ceramic ware**,** colored picture books (comics)**,** contaminated flour**,** cosmetics**,** health foods**,** indigenous medicines**,** pencils**,** toys etc.

Environmental (Yu, 2005)**:** Automobile exhaust**,** drug abuse (glue sniffing)**,** soil**,** water etc.

PHARMACO-KINETICS OF LEAD

Absorption: Exposure to lead occurs by inhalation, ingestion and occasionally by skin contact. Lead is absorbed through mouth, nose, and eyes [mucous membranes] and through breaks in the skin. Tetra-ethyl lead passes through the skin (Patrick, 2006). Inorganic lead, found in food, paint and most lead-containing consumer products, are absorbed through inhalation and ingestion (Merrill et al., 2007). In adults, about 35–40% of inhaled lead dust deposits in the lungs and about 95% of that goes into the bloodstream. Of ingested inorganic lead about 15% is absorbed in adults, but this percentage is higher in children, pregnant women and people with deficiencies of iron, calcium or zinc (Karri et al., 2008). Children and infants absorb about 50% of ingested lead (Grant, 2009).

Distribution and excretion: The main body compartments that store lead are blood, soft tissues and bone; the half-life of lead is measured in weeks for blood, months for soft tissues and years for bone (Karri et al., 2008). The estimated half-life of lead in bone is 20–30 years and bone can release lead into the bloodstream, long after initial exposure is gone (Patrick, 2006). The half-life of lead in blood in men is about 40 days, but it is longer in children and pregnant women, as their bones are undergoing remodeling, which allows the lead to be continuously re-introduced into bloodstream (Barbosa Jr et al., 2005). Lead in teeth, bones, hairs and nails is bound tightly and not available to other tissues and is harmless. In adults, 94% of absorbed lead is deposited in bones and teeth. In children, only 70% is stored in this manner and 30% remain in free form in the blood stream, which may partially account for the more serious health impacts on children (Barbosa Jr et al., 2005). If lead exposure takes place over years, clearance is much slower, partly due to the re-release of lead from bone. Other tissues such as brain, spleen, kidneys, liver, and lungs also store lead to some extent.Lead is excreted from the body very slowly, mainly through urine. Small amounts of lead are also eliminated through the feces and very small amounts through hair, nails, and sweat.

Mechanism of action/toxicity: Lead has no physiological role in the body (White et al., 2007). Primary mechanism of lead's toxicity is its interference with the functioning of a variety of enzymes by binding to sulfhydryl groups (Pearson et al., 2003). It interacts with essential metals, working as cofactors of various enzymes, and displaces them (Dart et al., 2004). Among essential metals with which lead interacts are calcium, zinc and iron (Kosnett, 2006).

It mainly interferes with the activity of enzymes, delta-aminolevulinic acid dehydratase (ALAD), and ferrochelatase of heme synthesis (CDC, 2003; Fujita et al., 2002). ALAD converts delta- aminolevulinic acid to porphobilinogen. Lead interference with ALAD leads to accumulation of aminolevulinic acid, which is harmful to neurons (Kosnett, 2006). Ferrochelatase catalyzes union of protoporphyrin and Fe^{2+} to form heme. Its interference results in production of zinc protoporphyrin and development of anemia (Mycyk et al., 2005).

Lead creates reactive free radicals, which damage cell structures including DNA and cell membranes (Flora et al., 2008) It also interferes with the process of DNA transcription, with various enzymes that help in the synthesis of vitamin D and with enzymes that maintain the integrity of cell membrane (Dart et al., 200) This process may cause damage to RBCs leading to decreased lifespan and anemia (Casarett et al., 2007). Lead is harmful to developing immune system. It causes production of excessive inflammatory proteins which is a risk factor for asthma in children. On the other hand, it has also been associated with a decrease in activity of immune cells such as polymorphonuclear leukocytes (Casarett et al., 2007). Lead interferes with metabolism of bones and teeth; and alters the permeability of blood vessels by interfering with collagen synthesis. Lead also interferes with the normal metabolism of calcium in cells and causes intracellular accumulation (Chisolm, 2004).

ONSET AND DURATION OF ACTION

The time elapsing between the intake of lead and appearance of symptoms varies depending on individual and duration of lead exposure (Karri et al., 2008). Symptoms appear in child earlier than adult while some

people may have no symptoms. Symptoms usually develop over weeks to months in chronic exposure.

Fatal Dose and Fatal Period

The average lethal dose is said to be 10g/70kg for most lead salts, while it is 20g/70kg for Lead acetate (Pillay, 2005) and 100mg/kg for tetraethyl lead. Fatal period is variable. The large amount of lead can be fatal in 1-2 days while small amounts, taken for a long period, may not be detrimental.

Systemic Effects on Body

Lead has adverse effects on various organ system, mainly on central nervous system, renal system, cardiovascular system and reproductive system. Organic form of lead is more toxic than inorganic form due to its lipid solubility (Timbrell ed., 2008).

***Central Nervous System*:** Lead affects both central and peripheral nervous systems (especially motor nerves) (Dart et al., 2004). Central nervous system effects are more prominent in children while peripheral nervous system effects are more prominent in adults (Bellinger, 2004). Lead damages cells in the hippocampus (Cleveland et al., 2008). Lead interferes with the release of neurotransmitters, mainly glutamate (important in many functions including learning) by blocking NMDA receptors. It also interferes with synapse formation in the cerebral cortex and organization of ion channels (Needleman, 2004). It causes the axons of nerve cells to degenerate and lose their myelin coats, reduces number of neurons and decreases neuronal growth.

Increased blood lead level in children has been correlated with decreases in intelligence, short-term memory, fine motor skills, nonverbal reasoning, attention, reading & arithmetic ability, emotional regulation and social engagement (Cleveland et al., 2008). Blood lead levels below 10µg/dL have been reported to be associated with lower IQ and behavior problems such as aggression, in proportion with blood lead levels (Guidotti et al., 2007). Blood lead concentrations above 10µg/dL are in danger of developmental disabilities (Meyer et al., 2003). Between blood lead levels of 5 to 35µg/dL in children, for each 1µg/dL increase in blood level, IQ decreases about 2–4 points (Brunton et al., 2007). Lead exposure in children is also correlated with neuropsychiatric disorders such as attention deficit hyperactivity disorder and antisocial behavior (Bellinger, 2004).

The brains of adults who were exposed to lead show decreased volume, especially in the prefrontal cortex on MRI (Stewart et al., 2006). High blood lead levels in adults are also associated with decreases in cognitive performance and psychiatric symptoms such as depression and anxiety (Shih et al., 2007). Amongst a large group of inorganic lead workers in Korea blood lead levels of 20–50 µg/dL were correlated with neuro-cognitive defects (Kosnett et al., 2007). An increase in blood lead levels from 50-100µg/dL has been found to be associated with persistent and possibly permanent, impairment of central nervous system function (Grant, 2009).

Lead encephalopathy is mainly found in children with exposure to tetra ethyl lead. It presents as vomiting, restlessness, headache, insomnia, hallucination, convulsions, coma and death. It is usually irreversible (Reddy, 2010).

Peripheral nervous system involves late in the course of toxicity, that too more in adults. There is degeneration of the nerve and atrophy of the innervated muscles. It mainly involves the fatigue-prone muscles. Extensors of the wrist are mainly involved, leading to wrist drop. Besides this, deltoid, biceps and anterior tibial muscle, leading to foot drop are also involved. Rarely, intrinsic muscles of eyes, hands and feet are also involved.

***Renal System*:** Kidney damage can occur at any level of lead in blood. The toxic effect of lead causes nephropathy and may impair function of proximal tubules leading to Fanconi syndrome. Lead poisoning inhibits the excretion of urate and causes a predisposition for gout (Wright et al.198). This condition is known as 'saturnine gout'.

***Cardiovascular System*:** Lead exposure is associated with high blood pressure due to vascular constrictions. It is also related to coronary heart disease, permanent arteriolar degeneration, heart rate variability and death from stroke (Navas-Acien et al., 2007). People who have been exposed to higher concentrations of lead may be at a higher risk for cardiac autonomic dysfunction on days when ozone and fine particles are higher in the environment.

Lead induced anemia is microcytic and hypochromic and in the chronic stage, it often changes to normochromic and normocytic. Basophilic stippling is seen in red blood cells are due to aggregation of RNA and ribosomes. It results from inhibition of 5 pyramidine neucleotidase, and the cells are unable to get rid of RNA degradation products with accumulation of ribosomes (Reddy, 2010).

Repro*ductive System:* Lead affects both, male and female reproductive systems. In men, above 40µg/dL, sperm count is reduced and changes occur in the volume of sperm, motility and morphology (Grant, 2009). Elevated blood lead level in pregnancy can lead to miscarriage between 3-6 months of pregnancy, low birth weight, prematurity and problems with development during childhood (Cleveland et al., 2008). Lead is able to pass through the placenta. A fetus is poisoned even in utero (Bellinger, 2005) when lead from the mother's bones is mobilized due to metabolic changes. It also excretes into breast milk. Blood lead levels in mothers and infants are usually similar. Increased calcium intake in pregnancy may help mitigate this phenomenon.

CLINICAL FEATURES AND SYMPTOMS

***Acute lead poisoning*:** This is rare. Many reported cases of acute poisoning may actually be exacerbations of chronic lead poisoning when significant quantities of lead are suddenly released into the bloodstream from bone (Subhash et al., 2012). Only symptoms are metallic taste, dry throat, abdominal pain, nausea, vomiting, peripheral circulatory collapse, paraesthesias, depression, coma and death. In children, there may be cerebellar ataxia. Exposure to highly concentrated lead fumes can produce metal fume fever, an influenza-like reaction characterized by an acute self-limited neutrophilic alveolitis.

***Chronic lead poisoning*:** (Reddy, 2010; Wright et al., 1984; Navas-Acien et al., 2007; Grant, 2009; Bellinger, 2005; Subhash et al., 2012) Facial pallor especially circumoral is a characteristic feature of chronic lead poisoning and is due to local vasospasm. A stippled blue line over the gums, known as 'Burtoninan line', is seen due to deposition of lead sulphide granules. Lead sulphide is formed by the action of hydrogen sulphide formed by decomposed food in the mouth. Colic of intestine, ureters and uterus also occurs.

NORMAL/ REFERENCE VALUES

The current reference range of acceptable blood lead concentrations in healthy persons is less than 20µg/dL for adults (Tietz, 2006), and less than 10µg/dL for children (CDC, 2012) and pregnant woman (Ettinger et al., 2010). (table 1)

DIAGNOSIS (HPA, 2013; Khan, 2013; Marcus, 2013)

Diagnosis includes determining clinical signs and medical history with an inquiry into possible routes of exposure. It has been suggested that all children should be screened for blood lead levels on their 1st birthday and if possible at yearly intervals thereafter until they are 6 years old. If at any time the lead level is more than 20µg/dL, therapeutic intervention is indicated and if it exceeds 70µg/dL, it should be treated as a medical emergency (uspreventiveservidetaskforce.org, 2006). To investigate the sources of lead in the environment of children with elevated blood lead, a field portable X-Ray fluorescence analyzer can be very helpful. The current pediatric practice in the West is to first, measure the free erythrocyte protoporphyrin before carrying out a blood lead quantification. Urine levels of aminolaevulinic acid (ALA) can also serve as a sensitive indicator of lead poisoning. ALA excretion rises only when blood lead concentrations exceed 40µg/dL.

DIFFERENT INVESTIGATION IN CASE OF LEAD POISOINING

Blood Investigation

Complete blood count and peripheral smear: General and non-specific findings include low haemotocrit and hemoglobin values with normal total and differential cell counts. The peripheral smear may either be hypochromic or normochromic and microcytic. Basophilic stippling is usually seen only in patients who have been significantly poisoned for a prolonged period. Hypochromia and basophilic stippling are strongly suggestive of lead intoxication (Patrick, 2006) but their absence does not rule out lead poisoning.

Erythrocyte protoporphyrin (EP) levels: Exposure to lead also can be evaluated by measuring erythrocyte protoporphyrin (EP) in blood samples (Marcus, 2013). EP is known to increase when the amount of lead in the blood is high, with a delay of a few weeks. Thus EP levels in conjunction with blood lead levels can suggest the time period of exposure. If blood lead levels are high, but the EP is still normal, this finding suggests exposure was recent. However, EP level alone is not sensitive enough to identify elevated blood lead levels below about 35µg/dL. Due to this higher threshold for detection and the fact that EP levels also increase in iron deficiency, use of this method for detecting lead exposure has decreased (Patrick, 2006).

Blood lead level (BL) (Mycyk et al., 2005; Tietz, 1995)**:** Blood lead level can change rapidly in response to lead intake, even for short exposure periods. It usually has a linear relationship to intake levels. Blood lead levels reflect recent exposure or exposure over a period of up to 3 to 5 weeks. In individuals with high or chronic past exposure, BL usually under-represents the total body burden because most lead is stored in the bone and may be found at normal levels in the blood. However, during stressful circumstances, patients with a high body burden may have elevated BL because of release of lead stored in bone.

Urine Investigation (Reddy, 2010; Tietz, 2006)

Concentration of Aminolaevulinicacid (ALA): ALA concentration in urine is widely used as a measure of lead toxicity in workers who are exposed occupationally. For this purpose, colourimetric methods were employed previously, but today fluorometry (after separation by HPLC) is preferred. ALA level more than 5µg/dL indicates poisoning.

Urine lead level: If this is above 25µg/dL, it is a significant finding but it is unfortunately not very reliable.

Calcium disodium EDTA mobilization test: This test is done mainly in children to find out whether a child whose blood lead level is between 25-41µg/dL will respond to chelation therapy with a brisk lead diuresis. Children whose BL is more than 45µg/dL should not receive this provocative test. They should be referred for chelation therapy immediately.

Urine coproporphyrin level: Patient with lead poisoning usually excretes more than 15µg/dL of coproporphyrin in the urine.

Bone Investigation

X-ray fluorescence technique (amptek-xrf; Payne et al., 2010)*:* It is a sensitive method of detecting low levels of lead in the body. It is brief and non-invasive and carries low risk (localized skin dose of less than 0.01 Gy to an area of 1 cm^2). It is based on the specific atomic property of lead to emit characteristic X-ray upon stimulation induced by external irradiation. The stimulated radiation is monitored externally by a solid state detector and can be expressed in terms of lead concentration in the bone.

Radio-imaging (Khan, 2013)

a) Plain X-ray may show transverse lines in tubular bones. These are actually areas of arrested bone growth and may persist a long time after exposure ends. They are not seen in the early phase of exposure.

b) Plain abdominal X-rays may show radio-opaque flecks in cases of suspected lead containing foreign body ingestion (e.g. pica in children).

c) CT or MRI scans of the brain may be contributory in patients with symptoms suggestive of encephalopathy.

CHEMICAL TEST OF LEAD POISONING

The recommended methods of estimating blood lead level (BL) are: (US Department of Health and Human Services, 2007; Flanagan et al., 2008) Electrothermal Atomic Absorption Spectroscopy (EAAS), Anodic Stripping Voltammetry (ASV), Atomic Absorption Spectroscopy (AAS), Inductively Coupled Plasma Atomic Emission Spectroscopy (ICP-AES), X-ray fluorescence spectroscopy, Proton Induced X-Ray Emission (PIXE), Fast Neutron Activation Analysis (FNAA)

Atomic Absorption Spectroscopy (AAS) and Anodic Stripping Voltammetry (ASV) are the method of choice. In recent years, Inductively Coupled Plasma Mass Spectrometry (ICP-MS) has become the technique of choice in western countries owing to superior specificity and sensitivity.

1. Qualitative Test (Colour/Spot test)

(a) Hydrochloric acid Test

1. 1 ml of test solution is taken in a test tube.
2. One ml of dilute HCl is added to it.
3. A white precipitate is obtained which dissolves on boiling and reappears on cooling indicating the presence of lead.

(b) Potassium iodide Test

1. 1 ml of test solution is taken in a test tube.
2. One drop of dilute nitric acid and one ml of potassium iodide solution is added to it.
3. A bright yellow precipitate is obtained.
4. On boiling the contents, the precipitates dissolves out and on cooling golden yellow spangles are obtained. This indicates the presence of lead.

(c) Bicarbonate Test

1. A portion of the solution suspected to contain lead is spotted on a piece of filter paper and dried.
2. To it one drop each of dilute aqueous pyridine, and very dilute solution of sodium bicarbonate followed by one drop of 0.1 % gallocyanine is added.
3. A violet colored spot is observed, which confirms the presence of lead.

(d) Dithizone Test

1. Take 1 ml of extract (neutral or faintly alkaline) in a micro test tube.
2. Few crystals and then 2 drops of dithizone solution are added to it and shaken for 1 minute.
3. The green color of the reagent changes to red, indicating the presence of Lead.

2. Quantitative Test

1. *Anodic Stripping Voltammetric measurements of lead*

10 ml ultrapure water and 1ml of acetate buffer (pH 4.6) is taken in polarographic vessel and then the measurement was started under the given parameters as in table 2. After this voltamogramme of the blank was recorded. 0.1 ml of the prepared sample solution was added to polarographic vessel and then voltamogramme of the sample solution was recorded under the same conditions. After the sample voltamogramme was recorded, 0.1 ml of 1 ppm standard of lead was added twice and then voltamogramme of the standard was recorded (Fig. 1 and 2). Finally the concentration of the metal was calculated by linear regression method (standard addition) using the following formula:

$$\text{Final Result} = \text{Concentration} \times \frac{\text{Cell Volume}}{\text{Sample amount}} \times \frac{\text{Multiplier}}{\text{Divisor}}$$

Where, Multiplier = Dilution

Divisor = Sample amount taken for preparation

2. Atomic Absorption spectroscopy (AAS) measured lead

***Stock Standard Solution*:** Lead, 1000µg/ml. Dissolve 1.598g of lead nitrate Pb $(NO_3)_2$ in 1 litres of 1% (V/V) HNO_3.

Operating Parameters

Instrument	AAS
Wavelength	217.00
Slit setting	1.0 nm
Light source	Hollow cathode lamp
Flame type	Air-acetylene flame. Oxidizing (lead, blue).

Operating current 5mA

Sensititvity: For the standard conditions described above, the sensitivity is about 0.20 µg/ml Pb for 1% absorption. A standard containing 6µg/mlPb will typically give an absorbance reading of about 0.10 absorbance units(about 34% absorption).

Linear working Range*:* for the standard conditions described above, the working range for Pb is linear upto concentrations of approximately 8µg/ml in aqueous solution.

Lamps: With multi-element lamps containing copper, the Cu 216.5 resonance line may interfere with lead determinations at the Lead 217.0 nm line. The lead 283.3 nm line should be used instead.

Flame Emission: The most sensitive emission wave length for lead is at 405.8 nm. A nitrous oxide, acetylene flame is recommended. Lead can also be determined at the 368.4, 283.3 and 261.4 nm wavelengths, but with reduced sensitivity. An air-acetylene flame may also be used with reduced sensitivity.

MANAGEMENT / TREATMENT OF LEAD POISIONING

General guidelines for management of lead poisoning are as follows (table 3 & 4):

Household remedies: (Greene, 1993; Weiss; Hughes, 2011)

1. Garlic can be used for detoxification in cases of chronic lead poisoning. It also has prophylactic effect.
2. Low dosage garlic pills or garlic pearls can be used on a daily basis.
3. Calcium has also been found effective in preventing the accumulation of lead in body tissues.
4. Aloe Vera juice may help remove lead from the digestive tract.

Pre-hospital management: (IARC, 2006; CDC-NIOSH; US Department of Labour-OSHA)

1. In case of skin exposure, wash exposed skin and hair with mild soap and water and rinse thoroughly with water. In case of eye exposure, flush eyes with plain water or saline. Persons with evidence of significant exposure should be transferred to a medical facility for evaluation.
2. Provide support to airway, breathing and circulation.
3. Exposed persons whose skin or clothing is contaminated with lead can contaminate rescuers by direct contact or through the release of inhalable dust. There is no serious risk of secondary contamination after clothing is removed and the skin is washed.
4. There is no specific antidote for lead poisoning. Pre-hospital treatment consists of supportive care and gastric decontamination. Chelation therapy is strongly recommended.

Hot Zone*:* Rescuers should be trained and appropriately attired before entering the Hot Zone. If the proper equipment is not available or if the rescuers have not been trained in its use, call for assistance or other properly equipped response organization.

Decontamination Zone*:* Patients who are able and cooperative may assist with their own decontamination. Remove and double-bag all contaminated clothing and personal belongings. Remove contact lenses if present without any additional trauma to the eye. If ocular pain or injury is observed, continuously rinse the eyes while transferring the victim to the critical care area**.**

Victim Removal**:** If victims can walk, take them out of the Hot Zone to the Decontamination Zone. Victims who are unable to walk should be removed on backboards. If these are not available, carefully carry or drag victims to safety.

ABC Reminders*:* Quickly access for a patent airway, ensure adequate respiration and pulse. If trauma is suspected, manually maintain cervical immobilization and apply a cervical collar and a backboard when feasible. Apply direct pressure to stop any heavy bleeding. Maintain adequate circulation.

Respiratory Protection: Positive-pressure, self-contained breathing apparatus (SCBA) is recommended in response situations that involve exposure to potentially unsafe levels of lead compounds.

Skin Protection*:* Chemical-protective clothing is recommended because some lead compounds can cause skin irritation. Fully encapsulating, vapor protective clothing should be worn to deal with spills or leaks with no fire.

Hospital Management: (Pillay, 2005; Marcus, 2013; Peterson et al., 2004; Shannon, 2000; Menkes, 2006)

Acute poisoning: (Reddy, 2010) During acute poisoning following management should be followed:

1. Stomach wash with 1% sodium or magnesium sulphate
2. Use demulcents
3. Combination of BAL and Ca-EDTA
4. Penicillamine
5. 5 mg of 10% calcium chloride i.v. causes deposition of lead into bones, clearing it from the blood and relieving the symptoms,
6. Hemo-/peritoneal dialysis and
7. Symptomatic.

Chronic poisoning*:* Generally GRAEF protocol (modified version) is followed in case of chronic poisoning which is discussed below.

1. Mild poisoning (Blood Lead Level 20 to 35µg/dl): D-penicillamine 30 mg/kg/day in 3 divided doses. Start with

1/4th of the calculated dose. Double this after 1 week. Double again to full dose after 1 week. Continue this until the blood lead level falls to less than 15 µg/dl or 3 months have been completed.

2. Moderate poisoning (Blood Lead Level 45 to 75µg/dl): EDTA 50 mg/kg/day: When the blood lead falls below 40µg/dl, begin oral chelation.

3. Severe poisoning without encephalopathy (Blood Lead Level >70µg/dl): BAL 12 mg/kg/day. EDTA 50 mg/kg/day. Discontinue blood lead level when the BL falls below 40 µg/dl, but continue EDTA for 5 more days. Change to oral chelation subsequently which may have to be continued until the blood lead level falls below 15µg/dl or 3 months have been completed.

4. Severe acute poisoning with encephalopathy (Blood Lead Level >70µg/dL): This is a medical emergency, and the following measures must be undertaken immediately

i) BAL should be given

ii) Cranial CT scan to rule out cerebral edema. If there is cerebral edema,

iii) For seizures: Treat seizures with IV diazepam (Adult: up to 10 mg slowly, Child: 0.1 to 0.3 mg/kg slowly). Seizures from lead encephalopathy may be resistant to anticonvulsant therapy.

iv) Ca Na_2 EDTA 75 mg/kg/day IV infusion.

v) After the initial dose of BAL, repeat the same dose at 4 hourly intervals until blood lead level falls below 40µg/dl. Then reduce BAL to 12 mg/kg/day in 3 divided doses.

vi) Reduce Ca Na_2 EDTA to 50 mg/kg/day as the condition improves.

vii) Continue the above regimen until the patient is asymptomatic and can tolerate oral chelation with D-penicillamine or DMSA.

In addition to the modified GRAEF protocol, the following supportive measures must be instituted as applicable: (Pillay, 2005)

i) Thiamine 10 to 50 mg/kg is said to improve neurological manifestations of lead poisoning.

ii) In acute poisoning or in the event of radio-opacities in the GI tract on X-ray, stomach wash may be done.

iii) Lead colic usually responds to IV calcium gluconate.

iv) Correct iron deficiency, if present.

v) IV fluids to maintain specific gravity of urine below 1020.

vi) If intracranial pressure is high due to cerebral edema, administer mannitol or steroids as required.

vii) Organic lead poisoning is mainly managed symptomatically. Chelation is done only if there is production of inorganic lead in the body from organic lead.

viii) After one round of chelation therapy, allow an interval of 2 weeks and then estimate the blood lead level. Repeat chelation if necessary.

ix) And finally the sine qua non of treatment of heavy metal poisoning: remove the patient from the source of exposure.

Table 1. Normal & Toxic levels of lead in Biological fluid

Matrixes	Normal level	Toxic level
Blood	1.9µg/dl for children 1.5µg/dl for adults	>10µg/dl for children >20µg/dl for adults
Urine	0.667µg/L	>25µg/dl

Table 2. Operating parameters for the determination of Lead by DPASV

Parameters	Description
Working electrode	Hanging Mercury Dropping Electrode
Calibration	Standard addition method
Number of replications	2
Drop size	4
Stirrer speed	2000 rpm
Mode	Differential pulse
Initial purge time	300 s
Addition purge time	10 s
Deposition potential	-1150 mV
Deposition time	90 s
Equilibration time	10 s
Pulse amplitude	50 mV
Start potential	-1150 mV
End potential	-700 mV
Voltage step	6 mV
Voltage step time	0.1 s
Sweep rate	60 mV/s
Peak potential Pb^{2+}	-380 mV

Table 3. Blood lead levels in adult and role of health care provider

Blood Lead Level (µg/dl)	Conditions	Management
10	Normal	
10-25	Some exposure occurred	Dietary and environmental management, follow up
25-40	Elevated Level	Active reduction of blood lead level, lab analysis, follow up
40-80	Seriously Elevated	Active reduction of blood lead level, lab analysis, follow up, chelation therapy if no response to conventional management
>80	Extremely Dangerous	Hospitalization and chelation

Table 4. Blood lead level in Child and role of health care provider

Blood Lead Level (µg/dl)	Conditions	Managements
5	Normal	
5-10	Not poisoned	
10-14	Mild Poisoning	Dietary and environmental management, follow up
15-19	Mild Poisoning	May need intervention
20-44	Moderate Poisoning	Active reduction of blood lead level, lab analysis, follow up
45-69	Severe Poisoning	May need chelation
>70	Life threatening	Medical emergency, Hospitalization and chelation

Figure 1. DPAS Voltamogramme of Pb obtained from standard addition technique with number of replications being 2. A) 0.1 ml sample in 1ml acetate buffer (pH 4.6) + 10 ml distilled water, B) A + 0.1 ml standard solution of Pb (1 ppm), C) B + 0.1 ml standard solution of Pb (1 ppm)

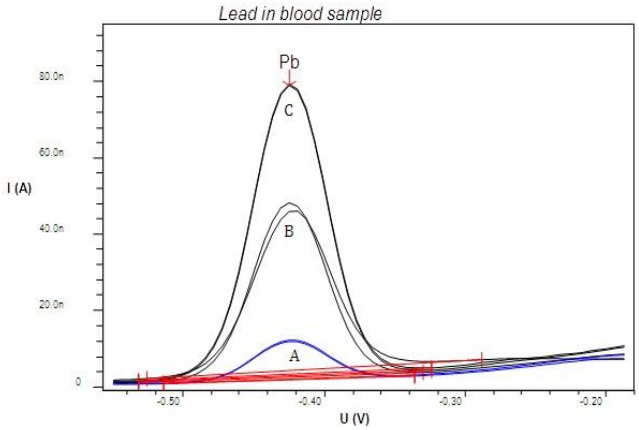
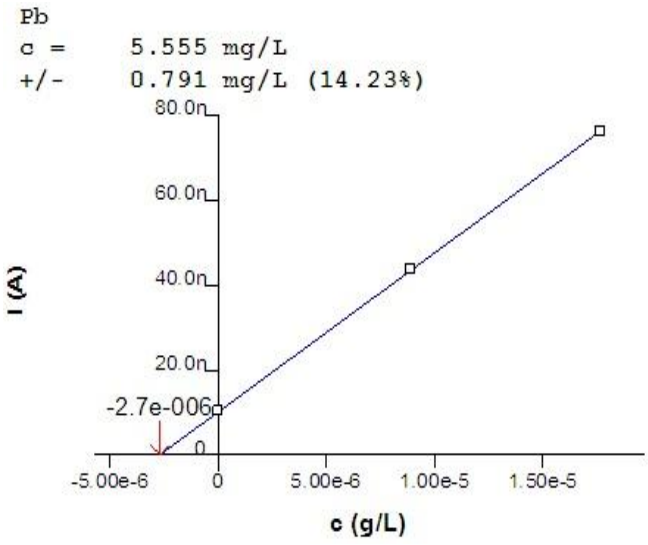


Figure 2. The calibration plot of Pb obtained from standard addition by DPASV technique



CONCLUSION

It is necessary avoid exposure of lead to common people. Following step should be taken to avoid lead poisoning:

- Wash hands thoroughly.
- Eat foods that are high in iron and calcium.
- Always supervise the children especially while playing.
- If using cold water, run the faucet for at least a minute before using.
- Wear protective equipment and clothing when working with known substance with lead content.

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