

## A perspective Study on Lead Poisoning: Exposure, Effects and Treatment

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**Abstract:** Current studies focus on various aspects of lead 's poisoning, its distribution and interaction routes, adverse effects on human body and treatment procedures. Lead metal has been involved in human exercise from the past 6000 years. In ancient cultures, lead was applied in the production of kitchen utensils, food pantries and other decorative items. Lead poisoning in developing countries is considered as a major risk factor and its exposure routes may involve food, paint, soil, water and other lead containing products. The distribution of lead from blood to tissues takes 4 to 6 weeks. Lead is poisonous to humans and has the most damaging effects on hemopoietic system. Some of the visible effected systems are nervous, reproductive and excretory systems. Lead poisoning can be treated using chelating agents which undergo complexation with lead and are then excreted through urinary tract.

**Keywords:** Lead, exposure, toxic, detection, chelating agents.

### Introduction

Lead (Pb) is omnipresent and is among the earliest discovered metals (Flora, Gupta, & Tiwari, 2012). The uniqueness of lead, such as softness, high malleability, ductility and corrosion-opposition have led to its wide scale use in various industries such as motor vehicles, ceramics, polymers, etc. The use of free lead in our lives has in turn increased significantly. Lead is considered a powerful administrative chemical and is well known for its toxicity. The non-biodegradability of lead is the main source of its continued environmental persistence. Human exposure to lead arises from multiple sources such as lead petrol; industry processes such coal combustion. The concentration of lead greater than 5µg/dl is considered toxic (Cantor et al., 2019). In Pakistan the highest factors of lead exposure to children are use of aluminum utensils, and parents illiteracy (Rahbar, White, Agboatwalla, Hozhabri, & Luby, 2002), about 80% of children in country are having blood lead greater than 10µm/dl and this also depends upon the use of eye cosmetics like surma (Wright, Thacher, Pfitzner, Fischer, & Pettifor, 2005). Lead poisoning has been a topic of interest for many researchers but still the treatment methods are not well known. Lead toxicity is especially destructive and can have irrecoverable health effects. It has numerous effects on human body systems especially the central nervous, hematopoietic, pulmonary and renal system and results in severe disorders (Kalia & Flora, 2005). Severe toxicity is very rare and is linked to long term exposure. On the other hand, if blood lead level is reached to 1-40µm/dL it increases the systolic blood pressure (Spivey, 2007). If not handled in time, it could be much more serious. It is portrayed by constant vomiting, sleeplessness, delirium, seizures and coma. Other effects include kidney diseases, dental caries, and hypertension. Lead may cause hearing problem at blood level of 5 ug/dl, at 80 µg/dl it can

cause memory related issues and even death. Before 1985 permissible blood lead level was 40 µg/dl but in 1985 it was 25 µg/dl as recommended in USA (Manser, Khan, & Hasan, 1989).

Current studies were conducted to compile various aspects of lead's poisoning, its distribution and interaction routes, adverse effects on human body and treatment procedures.

### Route of Interaction and Effects

Lead is regarded as one of the biggest environmental pollutants. Lead pollution may be caused by the industrial lead as found in machinery i.e. lead motors or tubes, as well as metal reusing and foundries (Mañay, Cousillas, Alvarez, & Heller, 2008). The largest amount of lead is consumed every year by storage batteries and ammunition in the US (Guberman, 2011). Lead poisoning can be caused by exposure to dust, infected water, market products, air and soil. Gasoline containing lead is also related to lead poisoning (Lewis, 1985).

### Vocational Vulnerability

The root cause of lead poisoning is vocational exposure in adults. According to occupational safety and health development (OSHA) the safe lead levels in occupational areas are less than 40µg/dl. People may be subjected to lead at workplace, including munitions from irradiation shields, certain operating systems and dental X-rays etc. Lead miners, batteries and recyclers, fire instructors and plastics manufacturers, auto mechanics and glass manufacturers are also vulnerable to lead exposure. The parents which are exposed to lead at their work place can carry lead dust home and children are also exposed in this way. Occupational exposure is the cause of chromosomal abnormalities (Palus et al., 2003). Combined exposure of lead, copper and iron causes Parkinson's disease at exposure

for greater than 20 years (Gorell et al., 1999). The exposed women had abnormalities in menstrual cycle (Popovic et al., 2005), acute lead exposure causes kidney tubular damage (Loghman-Adham, 1997).

**Eatables**

Lead travels to body by food. It enters the food by the soil in which it is grown or the environment containing lead and may enter food web. As it enters in plants and animals which are consumed by humans it also enter the body by cookware used (Castellino, Sannolo, & Castellino, 1994). Moreover, children can also be poisoned by the commercial species used in food (Woolf & Woolf, 2005). The maximum limit for lead in eatables is 2.5mg/kg.

**Paints**

Lead containing products are colored and so used in paints; these lead compounds are major causes of lead poisoning (Gilbert & Weiss, 2006). Flakes of paint fall in floor and thus mix in the dust. As the children play on floor they are most exposed to this lead (Jacobs et al., 2002). Oils and paints, specifically of yellow and white colors are made of lead carbonate. They were used until zinc or titanium was introduced. The major cause of lead exposure are however leaded paints and dust (Mielke & Reagan, 1998).

**Soil**

Tetraethyl lead is added to gasoline which leads to soil contamination. The more polluted the soil then there would be more lead contamination. However, many other factors affect soil lead poisoning (Barltrop, Thornton, Strehlow, & Webb, 1975). Lead in soil is due to contamination by industries, gasoline residues, some fertilizers and paints. Although it is not a problem in non-gasoline countries but a major problem in under developed countries. The primary cause of lead in soil is dust from smelters (Schmitt, Philion, Larsen, Harnadek, & Lynch, 1979).

**Water**

Lead in atmosphere enters the ground and fresh water bodies. It also enters drinking water by pipelines or fixtures which are made of lead. Acidic water increases lead break down in pipes so pH of municipal water is increased to prevent corrosion (Crocetti, Barone, & Oski, 2004). Chlorine is replaced by chloramines due to less health effects (Maas, Patch, Morgan, & Pandolfo, 2005). Sometimes the stored rain water collected from domes contains lead (Rossi, 2008). The graph in Figure 1 concludes that the lead level in tap water is co-related to the lead levels in the children’s blood in that area.

According to Environmental Protection Agency (EPA), the limit for lead in water is 15 ppb (Renner, 2009). Figure 2 shows the levels of lead in different schools and cities of USA.

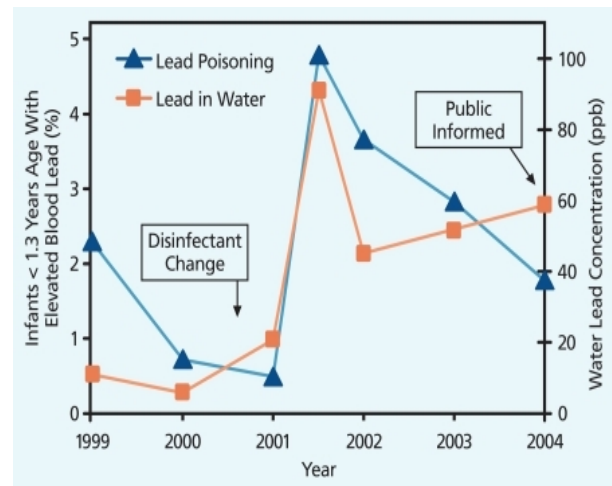


Fig. 1 Relation between blood lead level and level of lead in tap water of the area.

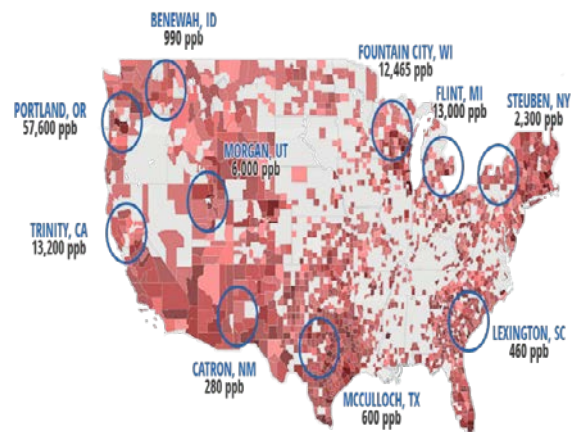


Fig. 2 the levels of lead (ppb) in different schools and cities of USA.

**Lead-Containing Products**

Lead is present in some toys and cosmetics such as Kohl which comes from middle east and some parts of Asia and Africa (T. L. Guidotti & Ragain, 2007). Lead finds its way from herbal remedies from India and some Chinese remedies (Rossi, 2008). Ceramic glazing and improperly finished dishes can lead to leaching of lead into the food (Salvato, Nemerow, & Agardy, 2003). In some parts of the world, food containing cans contain the lead. When animals are hunted with lead bullets, lead is spread in their bodies. The bullets embedded in bones allow more spreading of lead, then those in muscles. People using these animals as food are also at risk (Fiorica & Brinker, 1989).

**Absorption of Lead**

Lead can invade in the body of a living being by several processes which include respiration through the lungs, by skin absorption, or by intake as food and then its digestion. The lead that is in the form of inorganic compounds can be absorbed all the way from respirator into the intestinal tract. The people who are working in lead rich environment are

exposed to lead and absorb it mainly by respiration (Philip & Gerson, 1994). Particle's size is the main factor influencing the absorption of lead by respiration. 30–40% of the respired lead is able to reach blood. The absorbing capacity by gut depends on the age and amount consumed. When an inorganic compound like that in paints was applied to skin little absorption was occurred whereas, in the case of organic components, the absorption is easy. The gastrointestinal absorption of lead in infants is greater than that that in the adults (Kostial, Šimonović, & PIŠONIĆ, 1971).

**Relation of Lead Retention with Calcium**

Retention of lead has an inverse relation with the presence of calcium in the body which means that if there is more calcium in the body then more lead will be accumulated and there will be less excretion. The reason for this is that both lead and calcium compete to bind with same binding site on a protein of intestinal layer of mucous which naturally binds the calcium. This allows less amount of lead to be excreted (Barton, Conrad, Harrison, & Nuby, 1978).

**Lead Distribution**

After the lead is absorbed in the body it is eventually distributed throughout the body. The distribution is mainly occurred through three components of the body which are blood, tissue and bone. 99% of lead in blood is accumulated in red blood cells whereas 1% makes home in plasma (Rabinowitz, 1991). However, this 1% is more harmful as it is significantly distributed to various organs like brain and lungs. The speed of lead transport is slow and takes 4 to 5 weeks (Philip & Gerson, 1994). The rate of distribution depends on blood flow. Approximately 95% of lead is present in bones as sulphate. The period of lead in bones is 30 years which increases with age. Lead may travel through placenta and is taken up by fetus after 12 weeks till development; lead concentration in umbilical cord is same as that in mother's blood. Table 1 demonstrates the lead exposure and its effects in two different aged groups of human beings.

Table 1 Lead exposure and its effects; "a" is based on body weight of 20kg assumption for 6 years old children; "b" is based on body weight of 60kg (Gerofke et al., 2018).

End point	Population group	Effects	µg Pb/L of blood	Corresponding lead exposure	
				µg/kgbw /day	µg/ person/day
Developmental neurotoxicity	Children	1% reduced IQ	12	0.50	10 <sup>a</sup>
Cardiovascular effect	Adults	1% increase systolic B.P	36	1.50	90.0 <sup>b</sup>
Nephrotoxicity	Adults	0% increase prevalence	15	0.63	37.5 <sup>b</sup>

**Excretion of Lead**

Lead that is in form of inorganic compounds can't be broken down whereas that as organic alkyl is oxidized by liver. The excretion of lead is almost negligible but most useful way is through the urinary tract. Figure 3 displays the mechanism of lead ingestion and transportation.

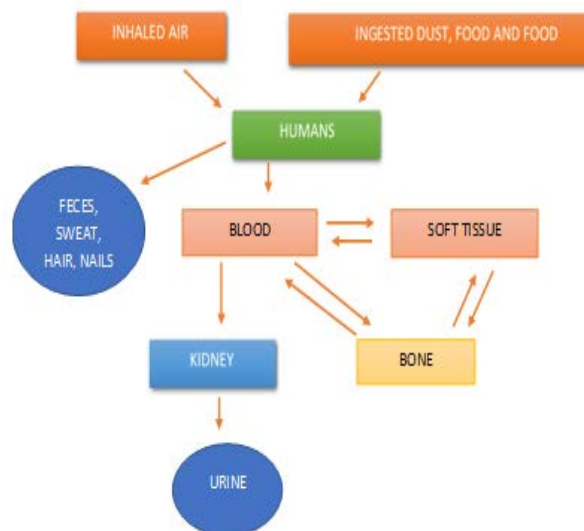


Fig. 3 Mechanism of lead ingestion and transportation.

Use of complexing agents can increase the lead excretion and this is basic principle of treatment of lead poisoning. Gastrointestinal tract can also excrete lead as bile. Some minute amount may be excreted by skin as sweat and by nails but it is not a useful way of excretion. Also, the half-life of lead is as high as 10 years which allows it to be deposited.

**Effects on Various Organ Systems**

*Nervous System*

Nervous system is a major target of lead poisoning as compared to the other organ systems (Cory-Slechta, 1996). Nervous system is affected by age; the children are affected on the central nervous system while adults get effects on peripheral nervous system (Bellinger, Leviton, Allred, & Rabinowitz, 1994). Most basic symptoms include dull behavior and muscular tremor. As concentration increases the symptoms become severe like paralysis (Flora et al., 2012). When children are exposed to high lead level it effects their growth, cognitive behavior and hearing whereas too high exposure can even cause death (Cleveland, Minter, Cobb, Scott, & German, 2008). Early symptoms of lead poisoning include irritation, memory loss and dull attitude. As the brain of child is developing it makes it more prone to the effects of lead. Colic may also be caused by exposure to lead (Seppäläinen, 1984). Many studies show relation of lead concentration with intelligence (Council, 1993).

### Hematopoietic System

Lead negatively impacts the hematopoietic system by reducing hemoglobin formulation by inhibiting different main enzymes in the route of heme synthesis. Along with this it makes the cell membrane of red blood cells fragile hence decreasing their life span. These two effects cause anemia (T. Guidotti, McNamara, & Moses, 2008). This anemia is of two types, hemolytic anemia is due to high lead exposure and frank anemia is due to long time sufficient exposure (Vij & Dhundasi, 2009).

### Renal Effects

Kidney functioning is disturbed by high lead that is  $>60\mu\text{g/dl}$  but low concentrations up to  $10\mu\text{g/dl}$  can also cause significant damage (Grant, 2008). There are two types of kidney malfunctioning.

Acute nephropathy is described as disturbed tubular transport method and physical changes in epithelium of tubes occur together with nuclear aggregates having leaded protein. It does not lead to the presence of protein in urine but excretion of combinations called Fanconi's syndrome, which includes glucose, phosphates and amino acids.

Chronic nephropathy is much serious than acute because it can make the functional and physical changes irreversible. Glomerular and tubulointerstitial changes are characterized as a result of renal breakdown, high blood pressure and hyperuricemia (Rastogi, 2008).

### Cardiovascular Effects

Cardiovascular damage is very harmful and may cause problems like hypertension. Hypertension is caused by low lead concentration. In the case of cardiovascular damage lead poisoning is directly proportional to hypertension (Navas-Acien, Guallar, Silbergeld, & Rothenberg, 2006).

### Reproductive Health Effects

Lead has many negative effects both on the males and female reproductive system, as investigated by several studies on lab animals of both sexes (Infante & Legator, 1980). Men have commonly been shown to have reduced libido, anomalous spermatogenesis (decreased motility and total number), genetic damage, fertility problems, unusual prostatic performance and serum testosterone alterations. Females seem to be more prone to fertility issues, abortion, premature rupture of the membrane, pre-eclampsia, high blood pressure and untimely delivery (Flora et al., 2012) In addition, there may be direct impact on the developmental phases of the fetus (Saleh, El-Aziz, El-Fark, & El-Gohary, 2009).

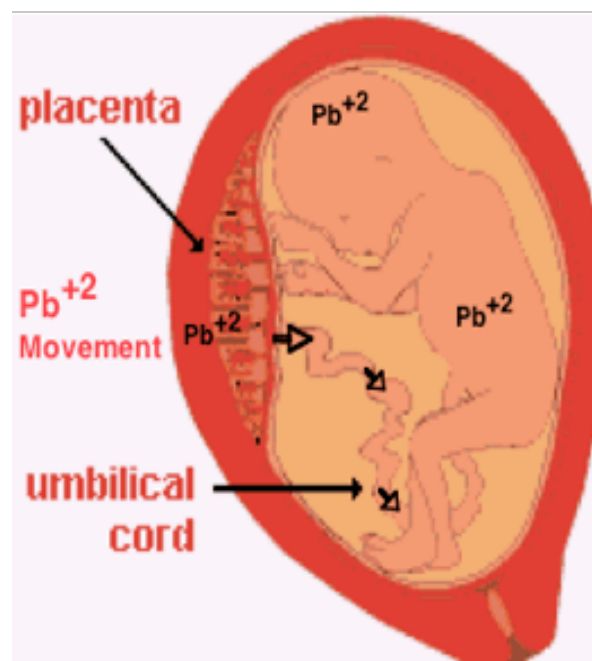


Fig. 4 Mechanism of lead transport from mother to fetus.

Figure 4 shows that lead in mother's blood enter fetus through passive transport. Lead ions eventually cross the brain blood barrier leading to cognitive issues.

### Testing Lead Toxicity

#### Blood Lead

Measurement of blood lead is the preferred method for checking the childhood lead exposure. The rates of erythrocyte protoporphyrin are seen as indicating overexposure to lead in infants with blood fluids ranging between 0.48 and 1.20  $\sim\text{mol/L}$ . Accurate and consistent analysis of quite low-lead blood samples can be conducted if strict measures are to be noted at all phases to avoid the blood sample from exogenous lead contamination. Because blood lead is stored in red blood cells, low blood hematocrit correlated with lead poisoning anemia may cause undervaluation of lead exposure when measuring blood lead. Measuring lead in capsuled red blood cells has been pointed out to represent better the body lead. Although, the majority of research done depends on the blood lead concentration, which is the marker for lead exposure. Blood lead illustrates comparatively short-term visibility, likely during the previous 3-5 weeks. Table 2 shows blood lead percentages along with health risks.

Table 2 Blood lead percentages along with health risks.

Sr. no.	Blood lead percentage	Health effect
1	0-5	Usually background exposure
2	5-10	Take action
3	10-60	Cause for concern
4	60-100	Dangerous
5	100-120	Can be fatal



### Bone Lead

Of complete body about 90% lead is present in bones so effective method of measuring body lead is by bone lead. X-ray fluorescence is the safe and rapid way of measurement. The intravenous chelation measurement needs an 8-h urine collection which is difficult in kids.

### Biological Lead Sensor

Certain plants are used as tracers and indicators of the metal contents in soil as they take food and nutrients from soil. Plants near the road sides indicated more lead concentration as compared to those away from it. But the epiphytes such as several mosses that take their food from air are effective lead sensors. Spanish moss (*Tillandsia usneoides*) and Ball moss (*Tillandsia recurvata* L.) are examples of mosses which have ability to detect lead and other heavy metals in the atmosphere (Kostial et al., 1971).

### Treatment of Lead Poisoning

In the treatment of lead chelation therapy is one of the most effective technique, some of the commonly used chelating agents are dimercaprol (BAL), penicillamine, EDTA and DMS. These therapies are only considered when the level of toxicity is  $>40\mu\text{g/l}$  (Pediatrics, 1995). Current treatment is done by EDTA (Figure 5) and BAL in form of injections which is aided with penicillamine.

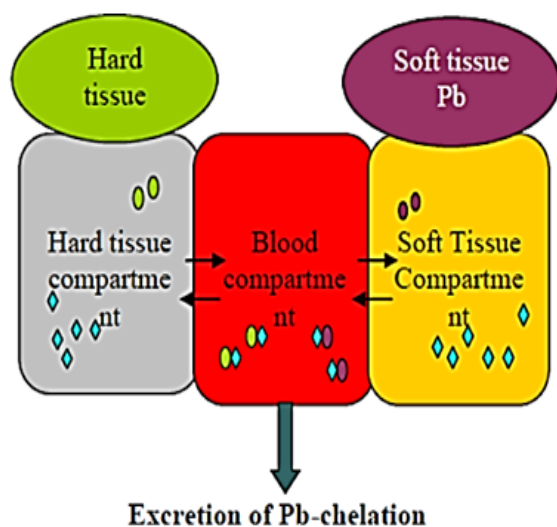


Fig. 5 Formation of Pb-chelates and their excretion.

EDTA has been mainly used for the treatment from past 40 years (Chisolm, 1992). This method of treatment is quite painful as it involves the use of injections; it also has some side effects as well like vomiting and headache. It may also cause urine toxification. Penicillamine however is not as good as others and also not suitable for people having penicillin allergies (Friedheim, Graziano, Popovac, Dragovic, & Kaul, 1978).

### 2,3-Dimercaptosuccinic Acid

2,3-dimercaptosuccinic acid (DMSA) is also known as succimer; it is a heavy metal chelating agent used to treat heavy metal poisoning like lead, arsenic and mercury. It is an oral drug which may form stable and soluble complexes which are easily excreted through urine. It does not have any notable side effects and can even reverse the metabolic issues due to lead poisoning like heme synthesis. Some of the side effects are vomiting and nausea. The dose given to children for a week is 10mg/kg after eight hours; the dose is decreased to the gap of 12 hours after a week (Mann & Travers, 1991).

### EDTA

EDTA chelation method is used from past 40 years for effective removal of heavy metals from the body. Mainly it's complex of calcium; calcium disodium EDTA is used. The calcium ions are replaced by lead and this complex is excreted with urine, as it is soluble in water. Following the treatment with EDTA toxicity symptoms like nausea and abdominal pain are disappeared. It is a very effective form of treatment as the body comes to its normal state within 2 to 3 days of treatment. It increase urine lead extraction manifolds, thus allowing an effective treatment (Wegelius & Harjanne, 1956).

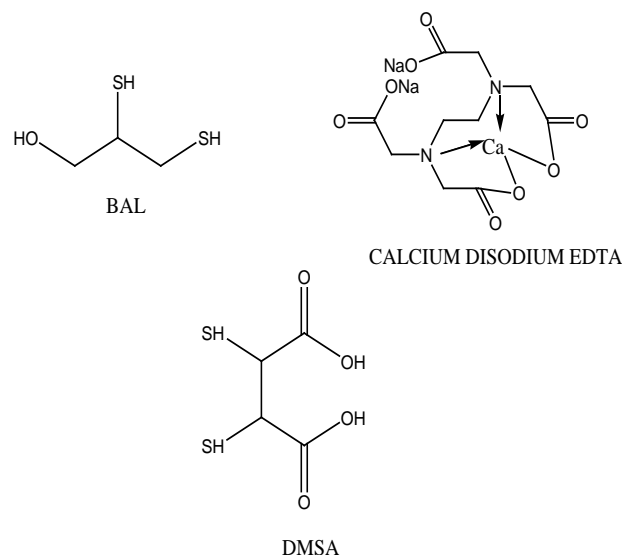


Fig. 6 Structures of BAL, EDTA and DMSA.

### Dimercaprol

Dimercaprol is also called BAL. BAL stands for British anti-lewisite. It was used in world War 2 in order to prevent deaths of soldiers from lewisite. Lewisite is the arsenic based chemical used in war. BAL has been used from 60 years for effective treatment of heavy metal poisoning. It is also used to treat Wilson's disease (Vilensky & Redman, 2003); it can be used to treat lewisite intrusion within one hour

of contamination. It was tested against lewisite burns in rat and showed the excretion of arsenic in urine. In humans BAL is placed on the skin or is rubbed in underarms; this does not show an effective excretion but when repeated can be used to obtain sensitivity (Peters, Stocken, & Thompson, 1945). It forms soluble, non-toxic and stable complexes which are excreted (Pediatrics, 1995). Figure 6 displays the structures of BAL, EDTA and DMSA.

## Conclusion

Above review concludes that even though lead is among the oldest discovered metals but the hazardous effects are maximized after the wide variety of lead uses in almost all fields of life from food to medicine. It has no essential function in human body but once ingested it is almost unable to be excreted naturally because of its long half-life, so is stored in the body. It may cause serious health issues which are sometimes irreversible. The maximum limit for lead in eatables is 2.5mg/kg. The levels of lead in blood are related to water levels of lead of that area. Almost 30–40% of the lead respired is able to reach blood whereas approximately 95% of lead occurs in bones as sulphate. It increases the systolic blood pressure blood when reaches 1-40µm/dL and kidney functioning is disturbed by high lead that is >60µg/dl. All major organ systems of the body are likely to be affected by lead toxicity like hematopoietic, renal, nervous and cardiovascular systems. Detection procedure involves X-ray fluorescence. Measurement of blood lead is commonly used for detection but bone lead measurement is effective because 90 percent of body lead is present in the bones. After detection treatment may be carried by chelation therapy.

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