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[Review article]

Lead toxicity due to paint and other industrial sources and contradiction in its toxicity studies

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ABSTRACT

Lead is one of the oldest known and most widely studied occupational and environmental toxins. Despite intensive study, there is still vigorous debate about the toxic effects of lead, both from low-level exposure in the general population owing to environmental pollution and historic use of lead in paint and plumbing and from exposure in the occupational setting. The majority of industries historically associated with high lead exposure have made dramatic advances in their control of occupational exposure. However, cases of unacceptably high exposure and even of frank lead poisoning are still seen, predominantly in the demolition and tank cleaning industries. Nevertheless, in most industries blood lead levels have declined below levels at which signs or symptoms are seen and the current focus of attention is on the subclinical effects of exposure. The significance of some of these effects for the overt health of the workers is often the subject of debate. Inevitably there is pressure to reduce lead exposure in the general population and in working environments, but any legislation must be based on a genuine scientific evaluation of the available evidences. We will discuss in this article about the various Mechanism of actions due to toxicity of the lead.

Keywords: Toxic metal, paint, reproductive toxicity, neurotoxicity, carcinogenicity, hypertension, renal function.

INTRODUCTION

Lead is a highly toxic metal found in the earth's crust. Because of its abundance, low cost and its physical properties, lead and lead compounds have been used in a wide variety of products including paint, ceramics, pipes, gasoline, batteries, and cosmetics. In most of the developing countries the battery industry is the principle consumer of lead of an estimated usage of 76% of the total primary and secondary annual production of lead .Lead is taken up by humans by ingestion and inhalation. Eating lead bearing paints by children and drinking of lead contaminated water are important sources of non-industrial poisoning. Lead absorbed in course of occupational exposure is superimposed on lead absorbed from other means which leads to increased body burden of lead. Exposure to lead can cause a variety of neurological disorders such as lack of muscular coordination, convulsions and coma. Lower levels of lead have been associated with measurable changes in children's mental development and behaviour [38]. These include hyperactivity; deficits in fine motor function, hand-eye coordination, and reaction time; and lowered performance on intelligence tests. Chronic lead exposure in adults can result in increased blood pressure, decreased fertility, cataracts, nerve

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disorders, muscle and joint pain, and memory or concentration problems. The effects of lead toxicity have been well established, with clear evidence of harm found in children whose blood lead levels are above 10 μg/dL and some evidence that harm may occur at lower levels [52],[30],[38]. A common source of lead exposure for children today is lead based paint and the contaminated dust and soil it generates [13];[29];[31];[32];[37];[42];[46]**.** A recent report of Toxics Link investigated a large number of paints available in India purchased in November-December 2006 for their lead content and found that most of the oil based enamel paints contained lead at levels above 600 parts per million (ppm). More than 60% of enamel paints contained lead higher than 5,000 ppm and the maximum content of 140,000 ppm was found in yellow enamel paint [28]. Ambient air concentration of lead during the operation of paint mixing, paint spraying may be at an average of 1.75 mg/m3 and 3.9 mg/m3 respectively [17] **.**Poisoning from lead-based paint has affected millions of children since this problem was first recognized more than 100 years ago [21]. Some of the developed countries have established limits on the lead content of paint e.g. US regulation of the lead content in new paints is 600 ppm. In many countries however there are apparently still no regulations on lead content of either new paint or paints in houses. This leaves the paint industry virtually unregulated.

PAINT AND ITS COMPOSITION

Paint is any liquid, liquefiable, or mastic composition which after application to a substrate in a thin layer is converted to an opaque solid film. Paint is used to protect, decorate (such as adding colour), or add functionality to an object or surface by covering it with a pigmented coating. Paint is composed of two basic ingredients: pigment and a binder; a solvent (thinner) is generally added to change the application characteristics of the liquid. In paint, the combination of the binder and solvent is referred to as the paint "vehicle." Pigment and additives are dispersed within the vehicle. The amount of each constituent varies with the particular paint, but solvents traditionally make up about 60% of the total formulation [28]. Typical solvents include toluene, xylene, methyl ethyl ketone (MEK), and methyl isobutyl ketone (MIBK). Binders account for 30%, pigments for 7% to 8%, and additives for 2% to 3%.

Pigments

Pigments are insoluble solids, incorporated into the paint to contribute colour, texture or some other characteristics. Opaque pigments give the paint its hiding or covering capacity and contribute other properties (white lead, zinc oxide, and titanium dioxide are examples). Colour pigments give the paint its colour. Pigments may be inorganic, such as chrome green, chrome yellow, and iron oxide, or organic, such as toluidine red and phthalocyanine blue. The major lead containing pigments include white lead, red lead, leaded zinc oxide, chrome green, chrome yellow and chrome orange. Lead is present in these pigments as oxides, carbonates, hydroxides and chromates. Transparent or extender pigments contribute bulk and also control the application properties, durability and resistance to abrasion of the coating. There are other special purpose pigments, such as those enabling paint to resist heat, control corrosion, or reflect light.

Vehicles or Binders

Vehicles or Binders of paint are the material holding the pigment together and causing paint to adhere to a surface. In general, paint durability is determined by the resistance of the binder to the exposure conditions. Linseed oil, the most common binder, has been replaced, mainly by the synthetic alkyl resins. These result from the reaction of glycerol phthalate and oil and may be made with almost any property desired. Other synthetic resins, used either by themselves or mixed with oil, include phenolic resin, vinyl, epoxy, urethane, polyester, and chlorinated rubber.

Solvents

Solvents or thinners are used to adjust the consistency of the material so that it can be applied readily to the surface. The solvent evaporates, contributing nothing further to the film. Solvent most commonly used are naphtha or mineral spirits; turpentine is sometimes used but is very expensive. In paint manufacture, lead is found in the waste solvent-based paint sludge's which typically contain 27.5% pigment, 25% binders, and 47.5% organic solvents.

LEAD AND ITS PRESENCE IN PAINTS

Lead is a transitional element with the symbol **Pb** (Latin: *plumbum*) belonging to group IV **A** of the periodic table, has the atomic number 82 and relative atomic mass 207.2. It is a soft, malleable metal, also considered to be one of the heavy metals with a density of 11.3 g/cm3. Lead has a

bluish white colour when freshly cut, but tarnishes to a dull greyish colour when it is exposed to air and is shiny chrome silver when melted into a liquid [13]. Lead's low melting point (3270 °C), ductility, malleability and weathering resistance enables its use without the need for more complex equipment required for other metals. Metallic lead does occur rarely in nature. It is usually found in ore with zinc, silver and (most abundantly) copper, and is extracted together with these metals. The main lead mineral is galena (PbS), which contains 86.6% lead. Other common varieties are cerussite (PbCO3) and anglesite (PbSO4) [42]. It is used in building construction, lead-acid batteries, bullets and shot, weights, and is part of solder, pewter, and fusible alloys. In the past, lead was added to petrol in the form of tetra-ethyl lead (PbEt4) with an anti-knocking function; however, across the world this kind of petrol is currently being phased out for environmental and health reasons.

Lead in Paints

Lead-based paint is defined as any paint, varnish, stain, or other applied coating that has 1mg/cm2 (5,000 µg/g by dry weight or 5,000 parts per million) or more of lead. Lead based paints have disappeared from consumer sales for residential use in developed countries because of toxicity concerns. However, paint containing lead is still being used for certain industrial painting requirements [21]. Lead is added to paint for speed drying, increase durability, retain fresh appearance, and resist moisture that causes corrosion. Lead is used as pigment, with lead (II) chromate (PbCrO4, "chrome yellow") and lead (II) carbonate (PbCO3, "white lead") being most common. Lead chromates are often used to produce yellow, orange, red, and green paints. White lead (basic lead carbonate) is a superior paint pigment, has a high affinity for paint vehicles and a tremendous hiding power, widely replaced by Titanium oxide and Barium-Zinc-Sulfur combinations. For colour, lead pigments such as red lead and blue lead (lead sulfate with lead oxide, zinc oxide, and carbon) may be used industrially where corrosion protection and colour on metal is needed. Lead flake still finds use as an exterior primer and lead oleate may be encountered as a drier in paints.

EXPOSURE TO LEAD AND ITS HEALTH EFFECTS

Lead is dispersed throughout the environment primarily as the result of anthropogenic activities. In the air, lead is in the form of particles and is removed by rain or gravitational settling. The solubility of lead compounds in water is a function of pH, hardness, salinity, and the presence of human material .Anthropogenic sources of lead include the mining and smelting of ore, manufacture of lead-containing products, combustion of coal and oil, and waste incineration. Many sources of lead, most notably leaded gasoline, solder in food cans, lead-arsenate pesticides, and shot and sinkers, have been eliminated or reduced due to lead's persistence and toxicity. Because lead does not degrade, these former uses leave their legacy as higher concentrations of lead in the environment. Plants and animals may bio-concentrate lead, but lead is not biomagnified in the aquatic or terrestrial food chain. The general population can be exposed to lead due to ambient air, foods, drinking water, soil, and dust [51]. Occupational hazards (for example, those experienced by painters, maintenance /renovation, and abatement workers who use unsafe paint removal practices) are the leading cause of elevated blood lead levels in adults. Ingestion of lead-contaminated surface dust is the most common pathway of lead poisoning in children. Though lead exposure is harmful to both adults and children, children are more susceptible, to the neurobehavioral toxicity of lead exposure because their nervous system is still developing, their absorption rates are higher, they have higher likelihood of engaging in hand to mouth practices and frequently spend time on the floor and on soil areas so they are more likely to be exposed to lead from paint dust, soil and water in their domestic environment [5]. Long term exposure to lead or its salts especially soluble salts or the strong oxidant PbO2 can cause nephropathy and colic-like abdominal pains. The most common metric of absorbed dose for lead is the concentration of lead in the blood (B-Pb), although other indices, such as lead in bone, hair, or teeth are also available The concentration of lead in blood reflects mainly the exposure history of the previous few months and does not necessarily reflect the larger burden and much slower elimination kinetics of lead in bone.

Lead in bone is considered a biomarker of cumulative or long-term exposure to lead because lead accumulates in bone over the lifetime and most of the lead body burden resides in bone. For

this reason, bone lead may be a better predictor than blood lead for some health effects. Epidemiological studies consistently show that effects in children are associated with B-Pb levels of about 100–150 µg/L. There are indications that lead is harmful even at B-Pb concentrations considerably below 100 µg/L; there may be no threshold for these effects. In many areas there have been major decreases in B-Pb levels in recent decades, mainly because of the phasing out of leaded petrol but also because of reductions in other sources of exposure [54].

The main target for lead toxicity is the nervous system, both in adults and children. Long term exposure of adults to lead at work will result in decreased performance in some tests that measure functions of the nervous system. Lead exposure may also cause weakness in fingers, wrists or ankles. Lead exposure also can cause small increases in blood pressure, particularly in middle-aged and older people. Lead exposure may also cause anaemia. At high levels of exposure, lead can severely damage the brain and kidneys in adults or children and ultimately cause death. In pregnant women, high levels of exposure to lead may cause miscarriage. High-level exposure in men can damage the organs responsible for sperm production [51]. Mortality in workers exposed to high levels of lead is increased, and adults who were poisoned by lead during childhood have increased blood pressure, which is a significant risk factor for cardiovascular diseases and mortality. Non-fatal mechanisms include renal effects; anaemia owing to the inhibition of several enzymes involved in haem synthesis; acceleration of skeletal maturation; alteration of hormone levels and immunity parameters; and encephalopathy (at high exposure) and various other diseases of the nervous system, among which cognitive and neurobehavioral deficits in children at low levels of exposure are of great concern. The health effects of lead exposure are summarized, together with routes of exposure, affected population groups and critical lead levels (B-Pb), in the Table below.

Main routes of lead exposure and critical effects identified with associated B-Pb levels for various population groups

Routes of Intake	Population Group (s)	Effects	Critical B-Pb Level (µg/l)
Placenta	Foetuses	Delays in neurological development	Probably no threshold
Mother's milk, inhaled air	Neonates and young children	- Inhibition of d-aminolevulinic acid dehydratase (ALAD) - Physical development	30-300 <70
Inhaled air, hand–mouth behaviour, ingestion	Children	- Decreased nerve conduction velocity - Cognitive development and intellectual performance - Hearing loss - Jaundice - Anaemia	 200–300 <100 <100 350 >200
Inhaled air, food ingestion	Adults	- Decreased ALAD activity - Blood pressure - Damage to renal function - Sperm count	30–340 <20 20–100 400–500

Sources: ATSDR (2005); Scientific Committee on Toxicity, Ecotoxicity and the Environment (2000)

MECHANISM OF TOXIC ACTION DUE TO LEAD

Lead poisoning results from the interaction of the metal with biological electron-donor groups, such as the sulfahydryl groups, which interferes with a multitude of enzymatic processes. Lead also interacts with essential cations, particularly calcium, iron, and zinc; it interferes with the sodium-potassium-adenosine triphosphate (Na+/K+ - ATP) pump; and it alters cellular and mitochondrial membranes, thereby increasing cellular fragility. Additionally, lead inhibits pyrimidine- 5'-nucleotidase and alters other nucleotide functions. Lead interferes with many enzyme systems of the body, thereby affecting the function of every organ. Clinical manifestations of lead toxicity include symptoms referable to the central nervous system, the peripheral nervous system, the hematopoietic system, the renal system, and the gastrointestinal systems. Children exposed to lead may experience devastating consequences because of the effects of lead on the developing brain. Lead can interfere with the synthesis of heme, thereby altering the blood concentration of enzymes and intermediates in heme synthesis or their derivatives. Thus lead poisoning can lead to accumulation of non heme iron and protoporphyrin – IX in red blood cells, an increase in delta aminolevulinic acid (ALA) in blood and urine, an increase in urinary coproporphyrin, uroporphyrin and porphobilinogen, inhibition of blood ALA-dehydrase (ALA-D), and an increased proportion of immature red cells in the blood (reticulocytes and basophilic stippled cells).

Reproductive toxicology

At very high blood lead levels, lead is a powerful abortifacient. At lower levels, it has been associated with miscarriages and low birth weights of infants [39]. Predominantly to protect the developing foetus, legislation for lead workers often includes lower exposure criteria for women of 'reproductive capacity'. The reproductive toxicity of lead on male lead workers has been studied but, to date, the results have been inconsistent [33]; [9]; [12]; [3];[49]. Some studies have shown reduced sperm count and motility, but there are few data showing an effect on reproductive capability. In addition, many of the studies have not taken into account potentially powerful confounding factors such as other occupational exposures (e.g. heat and solvents) or social factors such as alcohol consumption, smoking or the use of any medications. In addition, there was some evidence of deterioration of sperm chromatin in men with the highest concentration of lead in spermatozoa. Biological monitoring data failed to show any long-term effects of lead on sperm quantity or sperm chromatin [7].Current thinking is that significant effects on reproductive capacity are not seen below a blood lead level of ≥50 µg/100 ml, but blood lead concentrations of >40 µg/100 ml may affect sperm morphology and function [2].

Neurotoxicity

Much debate surrounds the potential effects of low-level lead exposure on young children. There is no doubt that subtle effect on child neuro psychological development can be seen at blood lead levels above ~20 µg/100 ml. Moreover, one recent US study has produced data suggesting effects below 10 µg/100 ml with no discernible no-effect level [14]. Studies have shown a slowing of sensory motor reaction time in male lead workers and some disturbance of cognitive function in workers with blood lead levels >40 µg/100 ml. Peripheral motor neuropathy is seen as a result of chronic high-level lead exposure, but there is conflicting, although on the whole convincing, evidence of a reduction in peripheral nerve conduction velocity at lower blood lead levels. The threshold has been suggested to be as low as 30 µg/100 ml, although other studies have not seen effects below a blood lead level of 70 µg/100 ml [15];[50];[45]. The clinical significance of reduced nerve conduction velocity is uncertain [6]. Subtle changes in neuropsychological function have been seen in inorganic lead workers. These effects are seen in visual/motor performance, memory, attention and verbal comprehension [25];[36];[10];[24]. These effects can be detected in workers with blood lead levels of >50 µg/100 ml, but it is claimed that sensory motor function is more sensitive than cognitive function and effects may be observed at blood lead levels as low as 40 µg/100 ml [48]. Many of these tests have been well performed and used non-exposed controls who had been well-matched for educational achievement. However, there are other variables that have not been adequately controlled, e.g. alcohol consumption or the incidence of hypertension and cerebrovascular disease. One interesting study has shown a subjective improvement in levels of tension, anger, depression, fatigue and confusion

following a significant improvement in occupational exposure and reduction in blood lead levels, but no significant improvement in the subtle neuropsychological test results [4]. There are no adequate data provided for drawing firm conclusions about the biological effects of current levels of exposure [23]. However, the findings are consistent associations of blood lead levels with test scores in executive abilities, manual dexterity and peripheral motor strength at blood lead levels as low as 18 μg/100 ml [44].

Carcinogenicity

The International Agency for Research on Cancer has concluded that the evidence for the carcinogenicity of lead and inorganic lead compounds in humans is inadequate [26]. Several large epidemiological studies of lead workers have found inconclusive evidence of an association between lead exposure and the incidence of cancer [1];[18]. In many of the studies there has been no attempt to deal with confounding factors such as smoking
and exposure to other potential carcinogens. A major study of a cohort of >4500 battery plant workers and 2300 lead smelter workers for the period 1947–1995 showed a significantly increased mortality from stomach cancer. However, based on closer analysis the increase did not appear to be related to lead exposure. There was also a small but significant increase in the incidence of lung cancer, but this could have been the result of
confounding from cigarette smoking or concurrent arsenic exposure [55]. A recent study from Sweden has suggested a slight excess of lung cancer in certain lead workers in a foundry but, to date, has not been able to determine whether this was due to the confounding effect of arsenic, which is a potent inducer of lung cancer [35]. There are therefore at present insufficient data for suggesting that lead compounds are carcinogenic in humans [27].

Hypertension

There have been interesting studies carried out in animals and in humans. It appears that in animals exposed to lead in drinking water, lead exposure affects the renin–angiotensin system, inducing sympathetic hyperactivity and increasing sensitivity to stimulation of cardiac and vascular β receptors and dopaminergic receptors [8];[53].There is also some evidence in humans that there is an association between low-level lead exposure and blood pressure, but the results are inconsistent [47]. There are inconsistent data for workers exposed to higher lead levels: a study of battery workers with blood lead levels of 40 ± 13 μg/100 ml showed a small but non-significant association between blood lead levels and blood pressure [41]. It is suggested that the failure to demonstrate increased blood pressure levels in some studies with high-level lead exposure may be due to a biphasic effect of lead on blood pressure. However, as in many other areas, it is possible that other confounders of raised blood pressure, e.g. obesity, cigarette smoking and alcohol consumption, might not have been properly considered in at least some of the studies. It is also obviously important that measurements of blood pressure are properly carried out using equipment that is properly calibrated and manned by appropriately qualified and experienced observers. Issues such as observer number preference and the impact of the actual measurement on the individual (white coat syndrome) must also be quantified. Recent studies suggest that it is possible that bone lead as opposed to blood lead is a better predictor of the risk of hypertension [11]. Another study among 220 lead industry workers showed a much stronger association between blood lead and hypertension in the 30% of the population who possessed a particular variant of the ATP1A2 gene [22].

Renal function

Exposure to high lead levels can produce renal tubular damage with glycosuria and aminoaciduria (saturnine gout). Some studies have shown a linear correlation between serum creatinine levels and blood lead levels above 40 μg/100 ml while others have shown no effect below 60 μg/100 ml [34];[16];[20]. Other studies have found increased levels of *N*-acetyl-β-D-glucosaminidase and β2 microglobulin in the urine of lead workers, whereas other studies have not found such changes [40];[19]. Whether these are of any clinical significance, whether they represent minor cellular modifications rather than significant functional changes or irreversible renal damage or, interestingly, whether pre-existing renal impairment may lead to higher blood lead levels are still open to discussion. There are certainly no definitive data to suggest that current lead exposure levels lead to clinically significant renal damage. It has been suggested that these changes may be related to the cumulative lead dosage rather than the blood lead level and that measures of lead

accumulation such as bone lead levels may give a closer correlation.

Toxicokinetics

Although it is widely accepted that personal hygiene is the most important determinant of an individual's blood lead level, recent interesting information has shown that genetic polymorphism may also have an impact. In a study of almost 800 lead workers and 135 controls, it was shown that subjects with the vitamin D receptor B allele had significantly higher levels of lead in the blood and tibia than did those with the vitamin D receptor bb allele. In addition, subjects with the ALAD2 allele showed higher concentrations of lead in the blood but no differences in tibia lead or chelatable lead concentrations compared with subjects lacking this allele. It is believed that from this study it is confirm that the ALAD and the vitamin D receptor genes modify lead toxicokinetics [43]

CONCLUSION

Toxicity due to Lead is clearly evident due to various sources , and yet the measure of the toxicity is not achieved . So, the toxicity studies on lead is wide open for further discussion and many more studies can be conducted . Person who works in the industries which are subjected for lead products needs to assess and evaluate their health often by a proper procedure. In order to evaluate health risks in environmental and occupational exposures, the analysis for trace elements, e.g. lead, in biological fluids, is essential. Atomic absorption spectrophotometer (AAS) is one of the most widely used methods. Lead is best determined by atomic absorption spectrophotometer. This method produces a sensitive, practically noise-free determination with a working curve that is linear at least to 250 llg/dL blood or demineralised water. Lead absorption may be influenced not only by lead exposure but also by such factors as the subject's respiratory minute volume and the particle size and availability of the lead dust to which he is exposed. Blood lead concentrations can be related to many factors, such as age, smoking and drinking habits. Symptoms of chronic lead poisoning can be divided into six categories: gastrointestinal, neuromuscular, CNS, haematological, renal and others. The abdominal syndrome is a more common manifestation of a very slowly and insidiously developing poisoning. Symptoms of chronic lead poisoning often begin with general malaise, nausea and vomiting, colicky abdominal pain, constipation, vertigo, fatigue and headache. BLLs (Blood lead level) which can be easily monitored, can be reduced by chelating treatments, but the relatively large amounts of lead stored in the bone are subsequently mobilized slowly to raise BLLs even in individuals returned to a lead-free environment. Though lead poisoning can be treated with chelating agents, it appears that prevention of lead toxicity should be the primary goal. A short recapitulation of the main principles follows:

a- Substitution of lead by a less toxic substance.

b- Use of disposable coveralls, shoe covers and gloves.

c- A good quality filter mask is required.

d- There should be no eating, drinking or smoking in the work area.

e- Ventilation is required where there is any chance of lead being vaporized.

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