HPA Compendium of Chemical Hazards

Lead

Key Points

Fire

- Reacts with hot concentrated nitric acid, boiling hydrochloric or sulphuric acid
- May cause explosions on contact with hydrogen peroxide or sodium, potassium or magnesium and their salts
- Use fine water spray and normal fire kit with breathing apparatus

Health

- Toxicity most frequently results from ingestion or inhalation and rarely from dermal or ocular exposure
- Harmful
- Metallic taste, severe abdominal pain, diarrhoea with black stools, vomiting, hypotension, muscle weakness, cramps, fatigue, abnormal liver function tests, acute interstitial nephritis are all recognised features following acute exposure
- Chronic lead exposure may lead to anaemia, headaches, irritability, tiredness, muscle weakness, paralysis, renal and hepatic injury and gastrointestinal disturbances
- In children, chronic exposure may lead to cognitive deficit, such as a decrease in IQ. Such effects do not exhibit a threshold
- Exposure to lead may cause spontaneous abortion, still birth or decreased birth weight, or cause fertility problems in males
- Inorganic lead compounds are classified as probably carcinogenic to humans by IARC

Environment

- Dangerous for the environment
- Inform Environment Agency of substantial release incidents

Prepared by S Bull
CHAPD HQ, HPA
2007
Version 2

Contents

GENERAL INFORMATION

INCIDENT MANAGEMENT

TOXICOLOGICAL OVERVIEW

Lead

General information

Key Points

Fire

- Reacts with hot concentrated acids
- May cause explosions on contact with hydrogen peroxide or sodium, potassium or magnesium and their salts
- Use fine water spray and normal fire kit with breathing apparatus

Health

- Toxicity most frequently results from ingestion or inhalation and rarely from dermal or ocular exposure
- Harmful
- Short-term exposure causes metallic taste, abdominal pain, sickness, loss of appetite, low blood pressure, kidney and liver damage
- Long-term exposure causes anaemia, headaches, irritability, tiredness, muscle weakness, paralysis, kidney and liver damage and stomach upsets
- In children, chronic exposure may lead to cognitive deficit, such as a decrease in IQ Such effects do not exhibit a threshold
- Lead exposure may cause miscarriages or still births or fertility problems in males
- Lead compounds are probably carcinogenic to humans

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Background

Lead is a naturally occurring element in the earth's crust. Much of the lead emitted into the atmosphere is in the form of inorganic salts. Exposure to inorganic lead occurs primarily through food and drinking water, although exposure via soil, dust, air and paint chips significantly contribute to the overall exposure.

The widespread occurrence of lead in the environment is primarily a result of anthropogenic activities. With the decline in combustion of leaded fuel and the phasing out of lead in pipes and paints, industrial emissions from mining, smelting, recycling or waste incineration are the major source of environmental lead.

Lead in water may result from industrial sources, but urban runoff significantly contributes to the total burden and solid wastes such as ammunition, leaded paints as well as industrial sources all contribute to the levels of lead found in soil.

Flaking paint, paint chips and powdered paint are major sources of lead exposure in young children. Other domestic sources of exposure include the contamination of food and drink from contact with utensils such as earth-glazed pottery.

Occupational exposure to lead and inorganic lead compounds may occur in a variety of occupations, including steel welding and spray coating, battery manufacturing or plumbing.

Most people are exposed to lead or lead compounds by eating or drinking contaminated food or drink, or breathing it in the air, such as from exhaust fumes, although the use of leaded fuel is declining. Children are mainly exposed to lead from eating soil.

The harmful effects that may occur from lead largely depend on how much people have been exposed to and for how long, therefore the amount of lead in the blood is often measured.

Eating food or drink or breathing in air contaminated with lead or lead compounds for a short period usually does not cause any ill effects. In rare cases nausea, vomiting, diarrhoea or kidney damage may occur.

If exposure continues for a long time people may become anaemic, lethargic and irritable or show other symptoms such as headache, muscle tremors, kidney or liver damage, nausea, vomiting or high blood pressure. Being exposed to lead for a long time can also affect both male and female reproduction, leading to miscarriage, stillbirths or premature births.

Children exposed to lead when in the womb or during the first few years of life due to eating paint chips containing lead, may have a lower IQ, behavioural problems or nerve damage. Children with high amounts of lead in their bones may have delayed growth.

Lead and its compounds are classified as probable carcinogens by the International Agency for Research on Cancer as lung, bladder and kidney cancer was seen in workers occupationally exposed to lead.

Production and Uses

Key Points

- Metallic lead is used in storage batteries, cables and in electronic equipment
- Inorganic lead salts are used in the production of pesticides, paint, ceramics, glass, plastic and rubber products

Metallic lead is used in storage batteries, cables, solders and steel products, ammunition, shielding systems from radiation and x-rays, circuit boards in computers and electronic equipment, and superconductor and optical technology. Inorganic lead salts are used in insecticides, pigments, paints, ceramics, enamels, glass, plastics and rubber products.

Frequently Asked Questions

What is lead?

Lead is a metal that is widely distributed in the earth's crust (soil and rocks), air and water. It is largely emitted into the environment as inorganic salts. Exposure to inorganic lead occurs primarily through food and drinking water, although exposure via soil, dust, air and paint chips significantly contribute to the overall exposure.

What is lead used for?

The use of lead in petrol, paint and pipes has now been phased out. It is now used in occupations such steel welding, battery manufacturing and plumbing and as part of glazings for pottery.

How does lead get into the environment?

Lead predominantly gets into the environment as a result of industrial emissions from mining, smelting, recycling or waste incineration.

How will I be exposed to lead?

Most people are exposed to lead by eating or drinking food or drink containing lead. In addition, lead may be inhaled in lead-contaminated air, such as exhaust fumes. In children, the ingestion of flaking paint, paint chips or soil is the major source of exposure. People working in industries that use lead may breathe it in the air.

If there is lead in the environment will I have any adverse health effects?

The presence of lead in the environment does not always lead to exposure as you must come into contact with the chemical. Clearly, in order for it to cause any adverse health effects you must come into contact with it. You may be exposed by breathing, eating, or drinking the substance or by skin contact. Following exposure to any chemical, the adverse health effects you may encounter depend on several factors, including the amount to which you are exposed (dose), the way you are exposed, the duration of exposure, the form of the chemical and if you were exposed to any other chemicals.

Eating food or drink or breathing in air contaminated with lead or lead compounds for a short time usually does not cause any ill effects. In rare cases it may cause nausea, vomiting, diarrhoea or kidney damage.

Exposure over a long period may cause people to become anaemic, lethargic and irritable or cause headaches, muscle tremors, kidney or liver damage, nausea, vomiting or high blood pressure.

Can lead cause cancer?

The International Agency for the Research on Cancer classified lead and its compounds as probably carcinogenic to humans, as lung, bladder and kidney cancer was seen in workers occupationally exposed to lead.

Does lead affect children or damage the unborn child?

Children who are exposed to lead in the womb or during the first years of life may have a lower IQ, behavioural problems, nerve damage or delayed growth. The underlying assumption is that no exposure to lead is completely harmless. Being exposed to lead for a long time can also affect both male and female reproduction, leading to miscarriage, stillbirths or premature births.

What should I do if I am exposed to lead?

It is very unlikely that the general population will be exposed to a level of lead high enough to cause adverse health effects.

Lead

Incident management

Key Points

Fire

- Reacts with hot concentrated nitric acid, boiling hydrochloric or sulphuric acid
- May cause explosions on contact with hydrogen peroxide or sodium, potassium or magnesium and their salts
- In the event of a fire involving lead, use fine water spray and normal fire kit with breathing apparatus

Health

- Toxicity most frequently results from ingestion or inhalation and rarely from dermal or ocular exposure
- Harmful
- Metallic taste, severe abdominal pain, diarrhoea with black stools, vomiting, hypotension, muscle weakness, cramps, fatigue, abnormal liver function tests, acute interstitial nephritis are all recognised features following acute exposure

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Hazard Identification

Standard (UK) Dangerous Goods Emergency Action Codes[(a)]

UN		**2291**	Lead compound, soluble, n.o.s.	
EAC		**2Z**	Use fine water spray. Wear normal fire kit in combination with breathing apparatus*. Spillages and decontamination run-off should be prevented from entering drains and watercourses.	
APP		**-**		
Hazards	**Class**	**6.1**	Toxic substance	
	Sub risks	**-**		
HIN		**60**	Toxic or slightly toxic substance	

UN – United Nations number; EAC – Emergency Action Code; APP – Additional Personal Protection; HIN - Hazard Identification Number

* Normal fire fighting clothing i.e. fire kit (BS EN 469), gloves (BS EN 659) and boots (HO specification A29 and A30) in combination with self-contained open circuit positive pressure compressed air breathing apparatus (BS EN 137).

[a] Dangerous Goods Emergency Action Code List, HM Fire Service Inspectorate, Publications Section, The Stationery Office, 2004.

Chemical Hazard Information and Packaging for Supply Classification[a]

Lead compounds[b]

Classification	**Repr cat 1**	Category 1 reproductive toxin (developmental toxin)	
	Repr cat 3	Category 3 reproductive toxin (fertility)	
	Xn	Harmful	
	N	Dangerous for the environment	
Risk phrases	**R61**	May cause harm to the unborn child	
	R20/22	Harmful by inhalation and if swallowed	
	R33	Danger of cumulative effects	
	R62	Possible risk of impaired fertility	
	R50/53	Very toxic to aquatic organisms, may cause long-term adverse health effects in the aquatic environment	
Safety phrases	**S53**	Avoid exposure, obtain special instructions before use	
	S45	In case of accident or if you feel unwell seek medical advice immediately (show the label where possible)	
	S60	This material and its container must be disposed of as hazardous waste	
	S61	Avoid release into the environment. Refer to special instructions/safety data sheet	

[a] European Chemicals Bureau, Classification and Labelling, Annex I of Directive 67/548/EEC; http://ecb.jrc.it/classification-labelling/ (accessed 2/2007).

[b] Lead compounds with the exception of lead alkyls, lead diazide, lead azide, lead chromate, lead di(acetate) trilead bis(orthophosphate), lead acetate, lead (II) methane sulphonate, lead sulfochromate yellow, lead chromate molybdate, lead hydrogen arsenate and lead 2,4,6-trinitro-m-phenylene dioxide

Specific concentration limits[a]

Concentration	Classification
C ≥ 25 %	T, N; R61-20/22-33-62-50/53
5 % ≤ C < 25 %	T, N; R61-20/22-33-62-51/53
2.5 % ≤ C < 5 %	T, N; R61-20/22-33-62-51/53
1 % ≤ C < 2.5 %	T ; R61-20/22-33-52/53
0.5 % ≤ C < 1 %	T; R61-33-52/53
0.25 % ≤ C < 0.5 %	R52/53

[a] European Chemicals Bureau, Classification and Labelling, Annex I of Directive 67/548/EEC; http://ecb.jrc.it/classification-labelling/ (accessed 2/2007).

Physicochemical Properties

CAS number	7439-92-1
Atomic weight	207
Chemical symbol	Pb
Common synonyms	-
State at room temperature	Solid
Volatility	Non-volatile at 20 °C
Specific gravity	11.3 at 20 °C (water = 1)
Flammability	Data not available
Lower explosive limit	Not applicable
Upper explosive limit	Not applicable
Water solubility	Insoluble in water, slightly soluble in alcohol.
Reactivity	Reacts with hot concentrated nitric acid, boiling concentrated hydrochloric or sulphuric acid. Attacked by pure water, but not tap water and weak organic acids
Reaction or degradation products	May cause explosions on contact with hydrogen peroxide or sodium, potassium or magnesium and their salts
Odour	Odourless

References[a,b,c]

[a] The Merck Index (14th Edition). Entry 5396: Lead, 2006.
[b] Lead (HAZARDTEXT® Hazard Management). In: Klasco RK (Ed): TOMES® System. Thomson Micromedex, Greenwood Village, Colorado (accessed 02/2007).
[c] The Dictionary of Substances and their Effects. Ed. S Gangolli. Second Edition, Volume 5, 1999.

Threshold Toxicity Values

Blood lead conc. ($\mu g\ dl^{-1}$)	SIGNS AND SYMPTOMS	
	ADULTS	**CHILDREN**
40 - 60	GI disturbances: nausea, vomiting, anorexia, constipation, abdominal cramps	
40 - 80	Reversible nephropathy: aminoaciduria, hypophosphataemia, glycosuria, interstitial nephritis	
48 - 120	Hypertension, tachycardia	
60 - 100		GI disturbances: abdominal pain, constipation, nausea, vomiting, anorexia, weight loss
100 - 300	GI disturbances: abdominal cramps, diarrhoea with black stools, vomiting and anorexia	Encephalopathy: irritability, poor attention span, headache, memory loss, tremor, ataxia, convulsions, drowsiness, malaise, coma, seizures, death

Reference[(a)]

[a] Agency for Toxic Substances and Disease Registry. Toxicological Profile for Lead, 1999.

Published Emergency Response Guidelines

Emergency Response Planning Guideline (ERPG) Values

	Calculated value (ppm)	Listed value ($mg\ m^{-3}$)
ERPG-1*	No data available	
ERPG-2**		
ERPG-3***		

* Maximum airborne concentration below which it is believed that nearly all individuals could be exposed for up to 1 hr without experiencing other than mild transient adverse health effects or perceiving a clearly defined, objectionable odour.
** Maximum airborne concentration below which it is believed that nearly all individuals could be exposed for up to 1 hr without experiencing or developing irreversible or other serious health effects or symptoms which could impair an individual's ability to take protective action.
*** Maximum airborne concentration below which it is believed that nearly all individuals could be exposed for up to 1 hr without experiencing or developing life-threatening health effects.

Acute Exposure Guideline Levels (AEGLs)

	ppm				
	10 min	**30 min**	**60 min**	**4 hr**	**8 hr**
AEGL-1†	No data available				
AEGL-2††					
AEGL-3†††					

† The level of the chemical in air at or above which the general population could experience notable discomfort.
†† The level of the chemical in air at or above which there may be irreversible or other serious long-lasting effects or impaired ability to escape.
††† The level of the chemical in air at or above which the general population could experience life-threatening health effects or death.

Exposure Standards, Guidelines or Regulations

Occupational standards

WEL	LTEL(8 hour reference period): No guideline value specified
	STEL(15 min reference period): No guideline value specified
ACTION LEVEL IN BLOOD[a]	25 μg dL^{-1} (woman of reproductive capacity)
	40 μg dL^{-1} (a young person)
	50 μg dL^{-1} (any other employee)

Public health guidelines

DRINKING WATER QUALITY GUIDELINE[b]	25 μg L^{-1} from 25th December 2003 until immediately before 25th December 2013. 10 μg L^{-1} on and after 25th December 2013
AIR QUALITY GUIDELINE[c]	0.5 μg m^{-3}
SOIL GUIDELINE VALUE AND HEALTH CRITERIA VALUES[d,e]	**Residential with plant uptake:** 450 mg kg^{-1} dry weight soil
	Residential without plant uptake: 450 mg kg^{-1} dry weight soil
	Allotments: 450 mg kg^{-1} dry weight soil
	Commercial/industrial: 750 mg kg^{-1} dry weight soil
	Provisional Tolerable Weekly Intake 25 μg kg^{-1} bw
	Blood lead concentration (used to derive soil guideline values) 10 μg dL^{-1}

WEL – Workplace exposure limit; LTEL - Long-term exposure limit; STEL – Short-term exposure limit

[a] The Control of Lead at Work Regulations, 2002. The Stationery Office, 2002.
[b] Interim Guidance on the Water Supply (Water Quality) Regulations 2000 (England) and the Water Supply (Water Quality) Regulations 2001 (Wales). Drinking Water Inspectorate, September, 2003.
[c] Air Quality Guidelines for Europe. World Health Organization Regional Office for Europe, Copenhagen WHO Regional Publications, European Series, No. 91, Second Edition, 2000.
[d] Department for Environment, Food and Rural Affairs (DEFRA). Soil Guideline Values for Lead Contamination, 2002.
[e] Department for Environment, Food and Rural Affairs (DEFRA). Contaminants in Soil: Collation of Toxicological Data and Intake Values for Humans. Lead, 2002.

Health Effects

Major route of exposure[(a)]

- Toxicity most frequently results from ingestion or inhalation and rarely from dermal or ocular exposure.

Immediate signs or symptoms of acute exposure[(a)]

- Metallic taste, severe abdominal pain, diarrhoea with black stools, vomiting, hypotension, muscle weakness, cramps, fatigue, abnormal liver function tests, acute interstitial nephritis are all recognised features.
- Encephalopathy with headache, confusion, drowsiness, coma and seizures secondary to cerebral oedema may occur and is more common in children.

TOXBASE - http://www.toxbase.org
[a] TOXBASE: Lead, 2003.

Decontamination and First Aid

Important Notes

- Ambulance staff, paramedics and emergency department staff treating chemically-contaminated casualties should be equipped with Department of Health approved, gas-tight (Respirex) decontamination suits based on EN466:1995, EN12941:1998 and prEN943-1:2001, where appropriate.

Dermal exposure[(a)]

- Remove patient from exposure.
- Remove all soiled clothing.
- Wash all contaminated area thoroughly with soap and water.

Ocular exposure[(a)]

- Remove patient from exposure.
- Remove contact lenses if necessary and immediately irrigate the affected eye thoroughly with water or 0.9% saline for at least 10-15 minutes.
- Patients with corneal damage or those whose symptoms do not resolve rapidly should seek medical advice.

Inhalation[(a)]

- Remove patient from exposure.
- Ensure a clear airway and adequate ventilation.
- Apply other measures as indicated by the patient's clinical condition.

Ingestion[(a)]

- Remove patient from exposure.
- Ensure a clear airway and adequate ventilation.
- Consider gastric lavage if acute ingestion of lead or lead salts has occurred within 1 hour.
- Apply other measures as indicated by the patient's clinical condition.

TOXBASE - http://www.toxbase.org
[a] TOXBASE: Lead, 2003.

Lead

Toxicological overview

Key Points

Kinetics and metabolism

- Inhalation of fumes, mists or vapours or ingestion of food, drink or soil/dust are the main routes of exposure
- Absorption following inhalation is generally high (50-90%), depending on the particle size and approximately 5-15 % in adults (40 % in children) following ingestion
- Absorbed lead is distributed by blood to liver, kidney, bone and teeth
- The unabsorbed lead is eliminated through the faeces. That what is absorbed is mainly excreted in the urine

Health effects of acute exposure

- Lead is classically a chronic or cumulative toxin, hence few adverse health effects are observed following an acute exposure. Adverse effects caused by exposure to lead are considered not exhibit a threshold
- May cause GI disturbances (anorexia, nausea, vomiting, abdominal pain), neurological effects (encephalopathy, malaise, drowsiness), hepatic and renal damage or hypertension

Health effects of chronic exposure

- Chronic lead exposure commonly causes haematological effects such as anaemia, basophilic stippling or neurological disturbances including headache, irritability, lethargy, convulsions, muscle weakness, ataxia, tremors and paralysis
- In children, lead exposure may lead to cognitive deficits, such as a decrease in IQ, effects of which do not exhibit a threshold
- Renal and hepatic injury as well as GI disturbances may arise following occupational exposure
- Exposure to lead may cause spontaneous abortion, still birth or decreased birth weight, or cause sperm abnormalities in males
- Inorganic lead compounds are classified as probably carcinogenic to humans (group 2A) by IARC

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CHAPD HQ, HPA
2007
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Toxicological Overview

Summary of health effects

Lead is classically a chronic or cumulative toxin. Few adverse health effects are observed following an acute exposure at low dose levels [1]. Acute effects including GI disturbances (anorexia, nausea, vomiting, abdominal pain), neurological effects (encephalopathy, malaise, drowsiness), hepatic and renal damage and hypertension have been reported [1-3].

Chronic lead exposure may cause anaemia, basophilic stippling and decreased haemoglobin synthesis [4-6]. Neurological effects may also be observed such as fatigue, sleep disturbance, headache, irritability, lethargy, slurred speech, convulsions, muscle weakness, ataxia, tremors and paralysis. Epidemiological studies in children have shown an inverse relationship between blood lead concentrations above 10 $\mu g\ dL^{-1}$ and IQ. There is some evidence that even lower exposures are also harmful, and it is therefore assumed that there is no completely harmless level of exposure to lead [2].

Nephropathy and renal tubule dysfunction may arise following chronic lead exposure [5]. Hepatic damage has been reported only in a few cases following occupational exposure to lead [6]. Gastrointestinal disturbances such as nausea, vomiting, anorexia, constipation, abdominal cramps have also been observed in workers [1].

Chronic exposure to lead may cause adverse effects on both male and female reproductive functions [6]. Females may experience spontaneous abortion, stillbirths or low birth weight following occupational exposure before or during pregnancy [5], and in males reduced libido, low semen volume and sperm counts and decreased sperm motility may occur [1, 4].

Occupational exposure to lead has been reported to cause an increase in sister chromatid exchange and chromosomal aberrations, although such increases were not observed in environmentally exposed children [4].

Based on epidemiological and experimental data, the Working Group of the International Agency for Research on Cancer (IARC) concluded that inorganic lead compounds are probably carcinogenic to humans (group 2A) [7].

Kinetics and metabolism

Absorption of lead depends on the physical and chemical state of the metal, and is influenced by age, physiological status, nutritional status and genetic factors [4].

In the general public, exposure to lead occurs primarily through the oral route, with some contribution from inhalation. In contrast, in the occupational setting, inhalation of inorganic lead in the form of fumes, mists, dusts and vapours is a major route of exposure. However, the toxicological effects are the same regardless of the route of exposure [8].

The absorption of particulate lead following inhalation involves the deposition of airborne lead particles in the respiratory tract and the absorption and clearance from the respiratory tract into the circulation [4]. Approximately 35 – 50 % of inhaled lead of particle size less than 1 μm is deposited in the lower respiratory tract, primarily in the alveolar tract, and 50 – 70 % of an inhaled dose is absorbed [2-4]. Higher deposition rates may occur with larger particles but this occurs in the upper respiratory tract and absorption occurs via the ingestion route [4]. Smaller particles of lead, such as those generated in exhaust fumes, are almost completely (>90 %) absorbed [4].

In adults, without occupational exposure, and in older children, lead absorbed by the gastrointestinal tract comes mainly from the intake of lead from food, drink and soil/dust. It has been estimated that children between 2 – 3 years of age ingest approximately 100 mg soil per day [4]. In adults, approximately 5 - 15 % of ingested lead is absorbed in the gut whereas in children and infants absorption may be as high as 40 % [2, 3]. Low levels of calcium, iron, copper, zinc or phosphorus in the diet or high levels of fat can increase lead absorption [2, 7].

Dermal absorption of inorganic lead compounds is generally quite low [4, 7]. One study reported increased levels in saliva and sweat following dermal exposure to inorganic lead, although blood or urine levels remained unchanged. It was postulated that the inorganic lead absorbed through the skin was transported in plasma and rapidly concentrated in sweat and saliva, without significant uptake by erythrocyes [2].

The route of absorption has little effect on the distribution of lead [4, 6]. The distribution of lead appears to be similar in adults and children, although a larger fraction of the body burden of adults appears in bone. Lead is transported primarily in the red blood cells bound to plasma proteins [6]. Absorbed lead is distributed by blood to mineralising systems (bone, teeth) and soft tissues (liver). The half life of lead in blood, soft tissue and bone is approximately 36 days, 40 days and 27 years, respectively [4].

Bone accumulates lead throughout most of the human life span but, at the same time, lead is mobilised from bone by remodelling [4]. In adults, approximately 94 % of the body burden of lead is in the bones, but only 73 % in children. Following chronic exposure, lead becomes deposited, in the form of insoluble lead phosphate, in areas of the skeleton that are rapidly growing, such as the radius, tibia and femur. Characteristic ‘lead lines’ may be seen on X-ray, and their width is related to duration of exposure [2].

Bone lead is readily mobilised to blood, the effect of which is most apparent in people with a history of occupational exposure and older people. Mobilisation of lead from bone to the more bioavailable maternal blood compartment is of importance in pregnant women and nursing mothers as it poses a risk for the fetus. Lead is readily transferred via the placenta from the mother to the developing fetus during pregnancy and accumulated in the bone. The concentration of lead in cord blood may be 85 – 90 % that of maternal blood, hence posing a risk for the fetus [4].

Inorganic lead is not metabolised, although conjugation with glutathione may occur. Organic lead may be metabolised to inorganic lead [1].

Approximately 90 % of ingested inorganic lead is eliminated unabsorbed through the faeces. Absorbed lead is primary excreted in the urine (75 %) and faeces (25 %), independent of the route of exposure. The rate of biliary excretion in humans is unknown [2, 6].

Sources and route of human exposure

Lead is a naturally occurring element in the earth's crust, mostly as the sulphide galena. Much of the lead emitted into the atmosphere is in the form of inorganic salts. In addition, combustion of leaded petrol yields predominantly inorganic forms of lead. Hence this report focuses on inorganic lead.

The main route of systemic exposure is predominantly via ingestion or inhalation. Exposure to inorganic lead occurs primarily through ingestion of food and drinking water, although exposure via soil and dust, air, and chipped leaded paint chips significantly contributes to the overall exposure [2-4].

The widespread occurrence of lead in the environment is primarily a result of anthropogenic activities. With the decline in combustion of leaded fuel and the phasing out of lead in pipes and paints, industrial emissions from mining, smelting or recycling are the predominant source of environmental lead [7, 8].

Lead in water may result from industrial sources, but urban runoff significantly contributes to the total burden. Depending on the pH of drinking water, temperature and residence time, lead may be leached from water systems such as from lead solder used for copper pipes as well as from old lead pipes, although this is less frequent due to the upgrading of water pipework [7].

Solid wastes such as ammunition, sewage sludge, leaded paints as well as industrial sources all contribute to the levels of lead found in soil. Measurement of soil samples in England and Wales was carried out and showed lead concentrations of between 3 and 16388 mg kg^{-1} with a median of 40 mg kg^{-1} [7].

Flaking, chipped or powdering leaded paint may be a major source of lead exposure in young children. Concentrations of up to 1-5 mg cm^{-2} have been reported in chips of lead-based paint. Exposure to lead from paint is usually confined to areas in the immediate vicinity of painted surfaces, and incautious removal of the paint can result in high localised concentrations of lead in indoor air [5]. Domestic sources include the contamination of food and drink from contact with utensils such as earth-glazed pottery or the use of herbal based remedies [1].

Occupational exposure to lead and inorganic lead compounds may occur in a variety of occupations, including steel welding and spray coating, battery manufacturing or recycling, radiator repair shops, plumbing and paint removal associated with building renovation. The Occupational Safety and Health Administration identified over 120 occupations in which workers may be exposed to lead [1].

Health Effects of Acute / Single Exposure

Human Data

General toxicity

The systemic uptake of lead from different sources (air, water, soil, food) contributes to the total body burden of lead. Blood lead (PbB) concentrations are used as a measure of exposure, therefore, effects of lead are not described in terms of route of exposure but rather PbB concentrations [5].

Lead is classically a chronic or cumulative toxin. Few adverse health effects are observed following an acute exposure to relatively low levels [1]. If high enough exposure occurs then the primary symptoms of acute effects include GI disturbances such as anorexia, nausea, vomiting and abdominal pain. Malaise, convulsion, coma, encephalopathy, hepatic and renal damage and hypertension have also been reported [2, 3].

Haematotoxicity

Few haematological effects have been reported following acute lead exposure [6].

Neurotoxicity

In children, the most frequent neurotoxicological effect observed following acute exposure is encephalopathy, which occurs at PbB concentrations exceeding 300 $\mu g\ dL^{-1}$ although more subtle effects have been reported at 100 $\mu g\ dL^{-1}$ [1, 9]. Children with acute exposure to lead giving PbB concentrations of 45-50 $\mu g\ dL^{-1}$ did not show any deficits in IQ compared to controls [6].

Renal toxicity

Acute exposure to lead may lead to acute nephropathy during early stages of exposure, especially in children. Acute nephropathy is characterised by cytomegaly in proximal tubular epithelial cells and is manifested as aminoaciduria, hypophosphataemia and glycosuria. Morphological changes include the formation of nuclear inclusion bodies, mitochondrial changes and dysfunction of proximal tubules. Most effects are largely reversible [1, 6]. Effects on renal function have been observed at PbB concentrations of 40 $\mu g\ dL^{-1}$ [1]. Acute interstitial nephritis has also been reported at PbB concentrations of 40 – 80 $\mu g\ dL^{-1}$ [4, 9].

Cardiovascular toxicity

Acute exposure to lead leading to PbB concentrations of 48 – 120 $\mu g\ dL^{-1}$ has been reported to cause hypertension [1-3].

Gastrointestinal toxicity

Following acute lead exposure, gastrointestinal symptoms such as abdominal cramps, diarrhoea with black stools, vomiting and anorexia are most commonly observed in adults at PbB concentrations of 100 – 400 μg dL^{-1} although effects have been observed at concentrations as low as 40 – 60 μg dL^{-1} [1-3, 5]. In children, gastrointestinal disturbances including abdominal pain, constipation, cramps, nausea, vomiting, anorexia and weight loss occur at PbB of 60 - 100 μg dL^{-1} [2, 5].

Hepatotoxicity

Hepatic damage has been reported following acute exposure to lead although PbB concentrations at which this occurs were not stated [2, 3, 9]. The effects of lead on haem synthesis may alter function capacity of hepatic cytochrome P450 enzymes. In children with a urinary excretion of 500 μg per 24 hours, acute exposure to lead has been reported to inhibit hepatic cytochrome P450 enzymes [4, 6].

Delayed effects following an acute exposure

Following an acute exposure, lead-induced encephalopathy may take up to several weeks to occur and includes symptoms such as irritability, poor attention span, memory loss, headache, muscular tremor, ataxia, convulsions, hallucinations, drowsiness, malaise, coma, seizures and death [1, 9].

Health Effects of Chronic / Repeated Exposure

Human Data

Haematotoxicity

Lead exposure may lead to anaemia, due to reduced haemoglobin production and shortened life-span of erythrocytes. Reduced haemoglobin synthesis has occurred in adults and children at PbB of 50 μg dL^{-1} or 40 μg dL^{-1}, respectively [4-6] although inhibition of haemoglobin sufficient to cause clinically observable anaemia has been reported following exposure to 80 – 100 μg dL^{-1} lead [1, 3]. Basophilic stippling commonly occurs in erythrocytes due to the aggregation of ribonucleic acid [3].

Lead has a significant effect on haemoglobin synthesis as it inhibits δ-aminolevulinic acid dehydrogenase (ALAD) thereby decreasing haem synthesis, which leads to an increase in δ-aminolevulinic acid synthase. The activity of ALAD may be inhibited at PbB concentrations as low as 3 - 34 μg dL^{-1} with no threshold yet apparent. The activity has been reported to inversely correlate with PbB concentrations over the whole dose range [5, 8].

Neurotoxicity

Chronic lead exposure may lead to fatigue, sleep disturbance, headache, irritability, lethargy, slurred speech and convulsions at PbB concentrations of 40 – 120 μg dL^{-1} [3]. Muscle weakness, ataxia, tremors and paralysis may also occur [9]. Afferent nerves are not affected hence there is no loss of sensation or pain [3].

Neurobehavioural effects may be observed in lead workers with PbB concentrations of 40 - 80 μg dL^{-1}, including disturbances in reaction time, visual motor performances, hand dexterity, IQ and cognitive performance, anxiety and mood [1, 6].

Several studies have been carried out to investigate the correlation of behaviour and intelligence with lead exposure in children. Overall, most studies reported an inverse association with PbB and IQ in children, deficits being noted with a PbB concentration of 10 μg dL^{-1} and above although the lowest PbB concentration reported to cause such an effect was 5.6 μg dL^{-1} [2, 7]. Epidemiological studies suggest that an increase in PbB concentration from 10 to 20 μg dL^{-1} is associated with a deficit of 2 IQ points [10]. Children with chronically elevated PbB concentrations of 40 – 60 μg dL^{-1} commonly show signs of pallor, pica and irritability [2]. The Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment (COT) concluded that it was not possible to establish a threshold for the effect of lead [11].

Renal toxicity

Chronic exposure to lead leading to PbB concentration of 50 – 200 μg dL^{-1} may cause chronic nephropathy, characterised as a reduction in glomerular filtration rate, sparse nuclear inclusion bodies and irreversible atrophy of the proximal and distal tubules [5]. Proximal renal tubular dysfunction results in albinuria, aminoaciduria, glycosuria, phosphaturia and renal tubular acidosis [1, 6, 9]. Mortality following chronic nephropathy may occur at PbB concentrations exceeding 60 μg dL^{-1} [1].

Cardiovascular toxicity

Meta-analyses of epidemiological data have found a persistent trend in the data that supports a significant, albeit weak, association between PbB and blood pressure. The elevation in blood pressure was more pronounced in middle age rather than in the young [8].

Chronic occupational exposure to lead (> 30 μg dL^{-1}) has been reported to cause an elevation in systolic blood pressure, although other studies failed to reveal any significant differences. Diastolic pressures were unaffected by exposure to lead in some studies but others showed an increase in diastolic pressure in workers with PbB concentrations of 50 μg dL^{-1} [1, 6]. Reports noted that an increase in PbB concentration of 10 μg dL^{-1} produced a systolic increase of 5 mm Hg, whereas others showed that for every doubling of PbB concentration the systolic pressure increases by 1.5 – 3.0 mm Hg or 1.0 – 2.0 mm Hg in males and females, respectively [5].

Gastrointestinal toxicity

Following chronic lead exposure, nausea, vomiting, anorexia, constipation and abdominal cramps have been observed in workers with PbB concentrations of 100 – 400 μg dL^{-1} although effects have been observed at concentrations as low as 40 – 60 μg dL^{-1} [1, 3, 5, 6, 8]. Individuals may experience a metallic taste and excessive thirst [3].

Gastrointestinal disturbances also occur in children with a PbB of approximately 60 – 100 μg dL^{-1} [8].

Hepatotoxicity

Chronic exposure to lead may cause hepatic damage and mild hepatitis, although few cases have been reported. One individual with a PbB concentration of 203 μg dL^{-1} following an occupational exposure showed abnormal liver function tests and mild hepatitis upon autopsy, although few data were available [6].

It has been suggested that the effects of lead on haem synthesis may affect the functional capacity of hepatic cytochrome P450 enzymes to metabolise drugs. In children, decreased enzyme activity may occur with PbB concentrations of 44 μg dL^{-1}. Few data are available in adults [4].

Reproductive and developmental toxicity

Chronic exposure to lead causes adverse effects on both male and female reproductive functions [5].

Occupational exposure to lead before or during pregnancy resulting in a PbB of > 20 μg dL^{-1} has been associated with spontaneous abortion, late fetal death and stillbirth although one study reported a higher incidence of stillbirths in women with PbB concentrations of 10.6 μg dL^{-1} [5]. A decreased length of gestation may occur with PbB concentrations 12 – 23 μg dL^{-1} [4]. Low birth weight and reduced post-natal growth have also been reported with PbB concentrations of 10.4 μg dL^{-1} [1, 4, 9].

Occupational exposure to lead resulting in PbB concentrations of 40 – 50 μg dL^{-1} may be linked with reduced libido, low semen volume and sperm counts, increased abnormal sperm morphology and decreased sperm motility in males, leading to impairment of reproductive function [1, 4].

The most critical effects of lead toxicity occur in children exposed during fetal and/or postnatal development [1]. In children, encephalopathic symptoms and death may occur at PbB concentrations of 80 – 100 μg dL^{-1} [5]. Overt symptoms of the subencephalopathic central nervous system may occur at PbB concentrations of 40 – 60 μg dL^{-1}. Peripheral nerve dysfunction, detected by a reduction of nerve conduction velocity, can occur at PbB concentrations of 30 – 50 μg dL^{-1}. Non-overt neurotoxicity, such as cognitive (IQ) decreases, electrophysiological and neurophysiological deficits may occur in children at PbB concentrations of >10 μg dL^{-1}, although no clear threshold has been demonstrated [1, 5].

Lead may accumulate in areas that are rapidly growing, and in some cases, hypermineralisation of the radius, tibia and femur can be seen on X-ray. Children with PbB concentrations of 60 - 100μg dL^{-1} showed squint, foot drop and delayed growth [2].

Genotoxicity

Assessment of genotoxicity of lead in humans has focussed on the evaluation of lymphocytes from occupationally or environmentally exposed individuals as well as *in-vitro* studies using mammalian cells or microorganisms. In addition, chromosome aberrations and sister chromatid exchange, the significance of which is unclear, in lymphocytes taken from healthy individuals has been carried out [6].

Increased frequency in sister chromatid exchanges were seen in workers with PbB concentrations of 80 μg dL^{-1} although no change in frequency of sister chromatid exchanges was seen in workers with PbB concentrations of 49 μg dL^{-1} or environmentally exposed children with PbB concentrations of 30 – 63 μg dL^{-1} [4].

An increase in chromosomal aberrations was reported in workers with PbB levels ranging from 22 - 89 μg dL^{-1} although other studies reported that occupationally exposed workers with a PbB of 38 - 120 μg dL^{-1} or environmentally exposed children with PbB concentrations of 12 – 33 μg dL^{-1} did not have an increase in frequency of chromosomal aberrations [4, 6].

Carcinogenicity

The standardised mortality ratios for cancers of the respiratory tract, digestive tract and kidney were increased from 1 to 2.5 in workers in lead production and battery plants who had PbB concentrations of 40 – 100 μg dL^{-1} [1]. A follow-up study did not show a significant elevation in death rate due to cancer [5, 6].

An increase in overall cancer incidence and in the incidence of lung cancer was observed in workers with a PbB concentration of 21 μg dL^{-1}. A subsequent study of the same cohort showed an increase in nervous system cancer in workers with a PbB concentration of 29 μg dL^{-1} [6].

A meta-analysis of case control and cohort epidemiological studies of battery or smelter industries found a significant excess risk of overall cancer, lung and bladder cancer. No PbB concentrations were given and no corrections for confounders were made due to lack of available data.

In order to evaluate the potential carcinogenicity of lead, the Working Group of the International Agency for Research on Cancer (IARC) considered epidemiological evidence from occupational studies of highly-exposed workers. Cancers of the lung, stomach, kidney, brain and nervous system were evaluated. Based on the available data, the Working Group concluded that there is limited evidence for the carcinogenicity to humans following exposure to inorganic lead compounds [12]. In considering the genetic and related effects of exposure to lead, the Working Group discussed the mechanistic aspects of lead as a potential carcinogen. They concluded that there is little evidence that lead interacts directly with DNA. The genetic effects of lead appear to be mediated in part by the modulation of reactive oxygen species and the interaction with proteins, including those involved in DNA repair. This may result in mutation, cell proliferation and changes in gene expression, all of which may contribute to a carcinogenic response following chronic exposure. The Working Group reached the evaluation that inorganic lead compounds are probably carcinogenic to humans (group 2A) [12].

Animal and In-Vitro Data

Genotoxicity

Pregnant mice exposed to lead nitrate (12.5 – 75 mg kg^{-1}) on the 9^{th} day of gestation showed chromosomal aberrations in the form of deletions at all doses administered in both maternal and fetal cells, indicating that prenatal exposure to lead may induce genotoxic changes in the fetus [6]. There was no treatment effect on sister chromatid exchange in lymphocytes or number of micronuclei in bone marrow erythrocytes obtained from rabbits treated with up to 0.5 mg lead acetate. Monkeys orally exposed to 1 or 5 mg lead showed an increase in chromosomal aberrations, although statistical significance was not reached. Other studies showed that only animals receiving a calcium deficient diet showed several chromosome aberrations [6].

Lead chloride was shown to be mutagenic in *Salmonella typhimurium* TA102 without S9 activation, but was non-mutagenic in three other strains with and without metabolic activation.

Carcinogenicity

The kidney is the primary site for tumour formation in rats and mice. However, at high concentrations tumours in the pituitary gland, adrenal gland, thyroid gland, prostate, lungs and nervous system have also been reported in rodents exposed to lead compounds [5]. The kidney tumours are generally assumed to be produced by a non-genotoxic mechanism and therefore to exhibit a threshold [7].

Carcinogenicity studies have been carried out in rodents with lead acetate, lead subacetate and lead phosphate. Renal tumours were observed in both female and male rats, a greater incidence occurring in male rats, at concentrations of lead exceeding 10 mg kg^{-1} per day [1]. Animal data led the Working Group of IARC to conclude that there is sufficient evidence for the carcinogenicity in experimental animals following exposure to inorganic lead compounds [12, 13].

References

[1] World Health Organisation (WHO) (2000). Safety evaluation of certain food additives and contaminants. WHO Food additives series No 44. WHO. Geneva.

[2] International Programme on Chemical Safety (IPCS). Lead. Monograph for UK PID. London.

[3] International Programme on Chemical Safety (IPCS). Lead, inorganic. Poisons Information Monograph PIM 301.

[4] International Programme on Chemical Safety (IPCS) (1995). Inorganic lead. Environmental Health Criteria 165. World Health Organisation. Geneva.

[5] Risk Assessment Information System (RAIS) (1994). Toxicity profile for lead. Chemical Hazard Evaluation and Communication Group, Biomedical and Environmental Information Analysis Section, Health and Safety Research Division.

[6] Agency for Toxic Substances and Disease Registry (ATSDR) (1999). Toxicological Profile for Lead. US Department of Health and Human Services. Atlanta, US.

[7] Department for Environment Food and Rural Affairs (DEFRA) and Environment Agency (EA) (2002). Contaminants in Soil: Collation of Toxicological Data and Intake Values for Humans. Lead. R&D Publications. TOX 6.

[8] Agency for Toxic Substances and Disease Registry (ATSDR) (2005). Toxicological Profile for Lead. Draft for public comment. US Department of Health and Human Services. Atlanta, US.

[9] National Poisons Information Service (NPIS) (2003). Lead. TOXBASE®.

[10] Department of the Environment Transport and the Regions (1998). Lead.

[11] Committee on Toxicity of Chemicals in Food Consumer Products and the Environment (COC) (2003). COT2003/02. COT statement on a survey of metals in infant food.

[12] International Agency for the Research on Cancer (IARC) (2004). Inorganic and organic lead compounds. IARC monographs on the evaluation of carcinogenic risks to humans. Vol 87. Lyon.

[13] International Agency for the Research on Cancer (IARC) (1998). Some metals and metallic compounds. Lead and lead compounds. Vol 23. Lyon.

This document will be reviewed not later than 3 years or sooner if substantive evidence becomes available.