TETRAETHYL LEAD	ICSC: 0008

Date of Peer Review:
November 2003

Tetraethyl plumbane
Lead tetraethyl
TEL

CAS #	**78-00-2**	**$Pb(C_2H_5)_4$**
RTECS #	**TP4550000**	**Molecular mass: 323.45**
UN #	**1649**	
EC Annex 1 Index #	**082-002-00-1**	
EC/EINECS #	**201-075-4**	

TYPES OF HAZARD / EXPOSURE	ACUTE HAZARDS / SYMPTOMS	PREVENTION	FIRST AID / FIRE FIGHTING
FIRE	Combustible.	NO open flames.	Powder, water spray, foam, carbon dioxide.
EXPLOSION	Above 93℃ explosive vapour/air mixtures may be formed.	Above 93℃ use a closed system, ventilation.	Combat fire out of sheltered position.

EXPOSURE		**PREVENT GENERATION OF MISTS! STRICT HYGIENE! AVOID EXPOSURE OF (PREGNANT) WOMEN! AVOID EXPOSURE OF ADOLESCENTS AND CHILDREN!**	**IN ALL CASES CONSULT A DOCTOR!**
Inhalation	Convulsions. Dizziness. Headache. Vomiting. Weakness. Unconsciousness.	Ventilation, local exhaust, or breathing protection.	Fresh air, rest. Refer for medical attention.
Skin	MAY BE ABSORBED! Redness. (Further see Inhalation).	Protective gloves. Protective clothing.	Remove contaminated clothes. Rinse and then wash skin with water and soap. Refer for medical attention.
Eyes	Redness. Pain. Blurred vision.	Face shield, or eye protection in combination with breathing protection.	First rinse with plenty of water for several minutes (remove contact lenses if easily possible), then take to a doctor.
Ingestion	Convulsions. Diarrhoea. Dizziness. Headache. Vomiting. Weakness. Unconsciousness.	Do not eat, drink, or smoke during work. Wash hands before eating.	Rinse mouth. Give a slurry of activated charcoal in water to drink. Refer for medical attention.

SPILLAGE DISPOSAL	PACKAGING & LABELLING
Evacuate danger area! Consult an expert! Ventilation. Collect leaking liquid in sealable containers. Absorb remaining liquid in sand or inert absorbent and remove to safe place. (Extra personal protection: complete protective clothing including self-contained breathing apparatus.) Do NOT let this chemical enter the environment.	Unbreakable packaging; put breakable packaging into closed unbreakable container. Severe marine pollutant. Note: A, E, for preparations: Note 1 **EU Classification** Symbol: T+, N R: 61-26/27/28-33-50/53-62 S: 53-45-60-61 **UN Classification** UN Hazard Class: 6.1 UN Pack Group: I
EMERGENCY RESPONSE	**STORAGE**
Transport Emergency Card: TEC (R)-61S1649 NFPA Code: H3; F2; R3;	Fireproof. Separated from strong oxidants, acids. Keep in the dark. Ventilation along the floor. Store in an area without drain or sewer access.

IPCS
International Programme on Chemical Safety

SEE IMPORTANT INFORMATION ON BACK

TETRAETHYL LEAD — ICSC: 0008

IMPORTANT DATA

PHYSICAL STATE; APPEARANCE:
COLOURLESS VISCOUS LIQUID , WITH CHARACTERISTIC ODOUR.

PHYSICAL DANGERS:
The vapour is heavier than air.

CHEMICAL DANGERS:
The substance decomposes on heating producing toxic fumes. Reacts violently with strong oxidants, acids, halogens causing fire and explosion hazard. Attacks rubber, some forms of plastic and coating.

OCCUPATIONAL EXPOSURE LIMITS:
TLV: (as lead) 0.1 mg/m³; (skin); A4; (ACGIH 2003).
MAK: (as lead) 0.05 mg/m³; skin absorption (H); Peak limitation category: II(2); Pregnancy risk group: D; (DFG 2007).

ROUTES OF EXPOSURE:
The substance can be absorbed into the body by inhalation, through the skin and by ingestion.

INHALATION RISK:
A harmful contamination of the air can be reached rather quickly on evaporation of this substance at 20°C.

EFFECTS OF SHORT-TERM EXPOSURE:
The substance is irritating to the eyes, the skin and the respiratory tract. The substance may cause effects on the central nervous system, resulting in unconsciousness. Exposure at high levels may result in death. Medical observation is indicated.

EFFECTS OF LONG-TERM OR REPEATED EXPOSURE:
The substance may have effects on the central nervous system. May cause toxicity to human reproduction or development.

PHYSICAL PROPERTIES

Decomposes at >110 °C Melting point: -136.8°C Relative density (water = 1): 1.7 Solubility in water: very poor	Relative density of the vapour/air-mixture at 20°C (air = 1): 1.00 Flash point: 93°C c.c. Auto-ignition temperature: above 110°C

Vapour pressure, kPa at 20℃: 0.027 Relative vapour density (air = 1): 8.6	Explosive limits, vol% in air: 1.8-? Octanol/water partition coefficient as log Pow: 4.15

ENVIRONMENTAL DATA

The substance is very toxic to aquatic organisms. The substance may cause long-term effects in the aquatic environment. It is strongly advised that this substance does not enter the environment.

NOTES

Tetraethyl lead used as an anti-knock compound in gasoline also contains ethylene dibromide and ethylene dichloride as impurities. Depending on the degree of exposure, periodic medical examination is suggested. The relation between odour and the occupational exposure limit cannot be indicated. Do NOT take working clothes home. Card has been partially updated in January 2008: see Storage, Physical Properties.

ADDITIONAL INFORMATION

NAME

1.1 Substance

Tetraethyl lead and Tetramethyl lead

1.2 Group

Lead alkyl compounds

1.3 Synonyms

lead tetraethyl
lead tetramethyl
TEL
Tetraethylplumbane
Tetramethylplumbane
TML

1.4 Identification numbers

1.4.1 CAS number

Tetraethyl lead : 78-00-2

1.4.2 Other numbers

Tetraethyl lead : NIOSH TP4550000
Tetramethyl lead: NIOSH TP4725000

1.5 Brand names, Trade names

No data available

1.6 Manufacturers, Importers

No data available

2. SUMMARY

2.1 Main risks and target organs

The central nervous system is particularly sensitive to organic compounds of lead.

Poisoning due to organic compounds is a consequence of industrial exposure. Indirect exposure arises from environmental contamination. Humans can be exposed to lead from breathing air, drinking water, and eating foods that contain lead. A large number of occupations may be associated with risk of exposure to organic lead compounds, particularly the cleaning of gasoline tanks.

Some reports have associated the risks of repeated inhalation of leaded gasoline as a drug of abuse (Edmindster, 1985). Other possible source of exposure is skin absorption from gasoline burns.

Subclinical effects have been identified with sensitive methods used to detect cognitive and behavioral changes, especially in children. There are subtle neuropsychiatric, reproductive and renal effects of chronic low-dose lead exposure, children being particularly susceptible. The effects of low-dose of lead in adults remains to be cleared. Hypertension, gout, nephropathies, and neurotoxic manifestations may be related to lead exposure.

Organic compounds of lead have toxic properties which require precautions against both their percutaneous and respiratory absorption.

2.2 Summary of clinical effects

Poisoning by organic lead compounds presents mainly acute effects on the central nervous system. The chronic form of

this intoxication has been observed following prolonged and deliberate inhalation of leaded gasoline vapours ("gasoline sniffing") (Hansen et al, 1978). Poisoning may result from the absorption of a sufficient quantity of lead, whether briefly at a high rate or for prolonged periods at a lower

rate. Ingestion is not a significant occupational hazard. Respiratory and percutaneous absorption are the main routes of exposure.

Mild manifestations are: insomnia and nervous excitation, nausea, vomiting, associated with tremor, hyperreflexia, muscular contractions, bradycardia, arterial hypertension, and hypothermia.

Most severe cases present episodes of complete disorientation, mania, ataxia, hallucinations, exaggerated muscular activity, and violent convulsive seizures, which may terminate in coma and death.

In severe cases, muscle, hepatic and renal damage may occur. The clinical picture may persist for days and weeks. A rapid onset of symptoms after exposure indicates a poor prognosis. When the onset of symptoms is delayed for many days recovery is usually complete, but some neurological sequelae have been reported. Prolonged compulsive sniffing of gasoline has resulted in encephalopathy and death.

2.3 Diagnosis

Is based on history of exposure to lead alkyl compounds (occupational in most cases) and occurrence of nausea, vomiting and CNS symptoms: irritability, anxiety, restlessness and more severe disorders (tremor, confusion and seizures).

The laboratory studies to confirm the diagnosis are:

In blood: complete blood-count, whole blood-count lead level free erythrocyte protoporphyrin red cell delta aminolevulinic acid dehydratase activity.

In urine: 24-hour urine lead levels delta aminolevulinic acid and coproporphyrin

Sample collection: a 24-hour specimen of urine is preferable to a single specimen; the blood sample should be taken and stored in specially cleaned glassware.

2.4 First aid measures and management principles

- Remove the patient from further exposure, send for medical assistance.
- Remove and discard contaminated clothing.
- Exposed eyes should be irrigated with copious amounts of water.
- Wash skin with soap and copious amount of water.
- Control convulsions with appropriate drug regimen.
- In case of ingestion, unless vomiting is extensive, perform gastric lavage and administer a cathartic. If the

patient is obtunded, convulsing, comatose, insert an oro- or a naso-gastric tube and lavage after endotracheal intubation.

- Open and maintain at least one intravenous route.
- Administer intravenous fluids.
- Chelation is indicated only if blood levels are high. Penicillamine and calcium disodium edetate have been used and the increased urinary excretion of lead does not correspond with clinical improvement.
- In case of encephalopathy, BAL and edetate calcium disodium are indicated.

- In cases of inhalation of vapours and fumes, symptomatic and supportive treatment are indicated. Ensure patient's airway and ventilation. Supportive measures include oxygen and artificial respiration.

3. PHYSICO-CHEMICAL PROPERTIES

3.1 Origin of the substance

Organic lead compounds include a number of common high-pressure lubricants (lead soaps) and the gasoline anti-knock agents tetraethyl lead (TEL) and tetramethyl lead (TML). TEL and TML are lipid-soluble liquids of high volatility and are prepared by chemical synthesis.

3.2 Chemical structure

Chemical name: Tetraethyl lead and Tetramethyl lead
Molecular weight: TEL: 323.45 TML: 267.3
Structural formula: $Pb(C_2H_5)_4$ $Pb(CH_3)_4$

3.3 Physical properties

Boiling point: TEL = 200 C (decomposes) TML = 110 C
Melting point: TEL = -136.8 C TML = -27.5 C
Flash point: TEL = 93.3 C TML = 37.7 C

Autoignition temperature:
Relevant density (20 C) : TEL = 1.653 TML = 1.99
Relative vapour density: TML = 9.2
Vapour pressure: TEL = 1 mmHg at 38.4 C
TML = 22 mmHG (25 C)

Solubility: TEL = soluble in benzene, ethyl alcohol petrol ether, gasoline and ethyl ether; insoluble in water.

TML = slightly soluble in benzene, ethyl alcohol and ethyl ether; insoluble in water.

Explosive limits: no data available.
Viscosity: no data available.
Relative molecular mass: no data available.
pH: no data available.

3.4 Other characteristics

3.4.1 Shelf-life of the substance

3.4.2 Shelf-life of the locally available formulation
3.4.3 Storage conditions
3.4.4 Bioavailability
3.4.5 Specific properties and composition

4. USES

4.1 Indications

Organic compounds of lead can be used as solvents for fatty materials and rubber. TEL and TML are liquid compounds of lead, which are miscible in all proportions with gasoline (and other organic solvents) and are available as "anti-knock" ingredients in gasoline fuel for the internal combustion engine (WHO, 1977; Budavari, 1989; Sax, 1989).

Alkyl lead compounds, the organic forms of lead, have

been in use as anti-knock additives in gasoline for almost 60 years. Use of these compounds (almost exclusively tetraethyl lead and tetramethyl lead) increased steadily up to 1973. A decline in consumption was started as more cars fitted with catalysts requiring lead-free gasoline have come into use (WHO, 1977).

4.2 Therapeutic dosage

4.2.1 Adults

4.2.2 Children

4.3 Contraindications

Workers may be exposed to organic lead compounds in a wide variety of occupations, including alkyl lead manufacture, gasoline processing, transportation, tank cleaning, filling station operators and garage workers. Both TEL and TML are absorbed through the skin and the respiratory tract. Ingestion is not a significant occupational hazard (WHO, 1977; ILO, 1983; Gosselin, 1984; Sax, 1989).

5. ROUTES OF ENTRY

5.1 Oral

Accidental or deliberate ingestion of alkyl lead compounds may occur, but is not frequent.

5.2 Inhalation

Inhalation of vapours of alkyl lead compounds should be considered as a major route of entry (ILO, 1983). It may occur in the occupational setting or as a result of "sniffing gasoline".

5.3 Dermal

Dermal absorption is an efficient route of entry for organic compounds of lead (ILO, 1983; Sax, 1989).

5.4 Eye

Not relevant.

5.5 Parenteral

Not relevant.

5.6 Other

Not relevant.

6. KINETICS

6.1 Absorption by route of exposure

Accidental or deliberate ingestion of alkyl lead compounds is not frequent. Inhalation of mists and vapours of alkyl lead compounds should be considered as the major route of entry.

Dermal absorption is an efficient process: organic compounds of lead are capable of penetrating the intact skin rapidly (Gosselin, 1984; Sax, 1989).

6.2 Distribution by route of exposure

Lead is distributed in man according to a three-compartment pharmacokinetic model. Blood and soft tissues represent the active pool and bones the storage pool. Lead is distributed to kidney tubular epithelium and to liver. There is redistribution by deposition in bone, teeth and hair. The long bones contain more lead and about 95% of the body load is stored in the skeleton. The largest part of circulating lead is bound to haemoglobin in erythrocytes, in which the concentration of lead is about 16 times greater than in plasma (WHO, 1977).

6.3 Biological half-life by route of exposure

The biological half-life of lead is extremely difficult to estimate (WHO, 1977). The half-life of lead in erythrocytes is 35 days; in soft tissues (kidney, liver and nervous tissue) the half-life is 40 days; the half-life in bone is 20 to 30 years (Ellenhorn, 1988; Garettson, 1990).

6.4 Metabolism

Alkyl lead compounds are transformed in trialkyl derivatives by dealkylation in the liver. TEL and TML are not the primary toxins but they are converted to triethyl lead and inorganic lead (WHO, 1977; Garettson, 1990).

6.5 Elimination by route of exposure

The rate of excretion of lead is low. Renal clearance of unchanged lead occurs essentially by glomerular filtration but at high levels some active tubular transport occurs. Urinary excretion accounts for 76% of daily losses, while gastrointestinal secretions for 16% and hair, nails, sweat and other routes for 8% (WHO, 1977; Ellenhorn, 1988).

7. PHARMACOLOGY AND TOXICOLOGY

7.1 Mode of action

7.1.1 Toxicodynamics

7.1.2 Pharmacodynamics

7.2 Toxicity

7.2.1 Human data

7.2.1.1 Adults

7.2.1.1 Adults (volunteer and clinical case data) The precise doses of the alkyl lead compounds responsibe for the effects are rarely, if ever, known. Patients with organic lead poisoning due to gasoline sniffing have been shown to have blood lead levels higher than 100 µg/dl (Keenlyside, 1984). A lead urine concentration of about 350 µg/dl is seen in severe TEL poisoning (ILO, 1983). The lowest reported lethal dose in man (LDL0) is 1470 µg/kg (Sax, 1989).

7.2.1.2 Children

No data available.

7.2.2 Relevant animal data

Tetraethyl lead:

Lowest toxic dose oral mouse: 11 mg/kg
LD50 oral rat: 1200 µg/kg
LC50 inhalation rat: 850 mg/m3
LD50 intraperitoneal rat: 850 mg/kg
LD50 intravenous rat: 14400 µg/kg
Lowest lethal dose skin dog: 547 mg/kg

Tetramethyl lead:

Lowest toxic dose oral rat: 112 mg/kg
LD50 oral rat: 105 mg/kg
LD50 intraperitoneal rat: 90 mg/kg
LD50 intravenous rat: 88 mg/kg
LC50 inhalation rat: 8870 mg/m3
Lowest lethal dose oral rabbit: 24 mg/kg
Lowest lethal dose skin rabbit: 3391 mg/kg
Lowest lethal dose intravenous rabbit: 90 mg/kg

There is no qualitative difference between the toxic effects of TEL and TML. However, the inhalation LC50 for tetramethyl lead is about 10 times greater than that for tetraethyl lead (WHO, 1977; Sax, 1989).

7.2.3 Relevant in vitro data

Biochemical studies of the respiration of brain slices incubated with inorganic lead compared with triethyl

lead (the active metabolite of TEL) have demonstrated a fundamental difference in the action of alkyl lead compounds on the brain (WHO, 1977).

7.3 Carcinogenicity

A study of workers manufacturing TEL revealed an excess of respiratory cancers (15 observed, 11.2 expected) and brain cancer (3 observed, 1.6 expected) but the evidence for carcinogenicity in humans is inadequate (IARC, 1987). Alkyl lead compounds have not been tested adequately: the evidence for carcinogenicity of organolead compounds in animals is inadequate (IARC, 1987).

7.4 Teratogenicity

No adequate animal studies exist of the possible teratogenic effects of lead (WHO, 1977).

7.5 Mutagenicity

TEL and TML did not induce mutation in bacteria (IARC, 1987).

7.6 Interactions

Interactions between lead and other environmental pollutants occur. Lead forms lead sulfate in both water and air in the presence of the sulfate ion (ATSDR, 1990).

7.7 Main adverse effects

8. TOXICOLOGICAL ANALYSES AND BIOMEDICAL INVESTIGATIONS

8.1 Material sampling plan

8.1.1 Sampling and specimen collection

8.1.1.1 Toxicological analyses

Not available

8.1.1.2 Biomedical analyses

Blood may be collected at any time. It is essential to avoid contamination: use only lead free needles, containers and stoppers; anticoagulant must be lead free. Urine can be collected at any time. A 24-hour specimen of urine is preferable to a single specimen. Avoid lead contamination from containers (ACGIH, 1986).

8.1.1.3 Arterial blood gas analysis

Not relevant.

8.1.1.4 Haematological analyses

Avoid lead contamination of samples

8.1.1.5 Other (unspecified) analyses

No data available

8.1.2 Storage of laboratory samples and specimens

8.1.2.1 Toxicological analyses

Blood and urine samples should be stored in specially cleaned glassware, and refrigerated as indicated for the specific method.

8.1.2.2 Biomedical analyses

8.1.2.3 Arterial blood gas analysis

8.1.2.4 Haematological analyses

8.1.2.5 Other (unspecified) analyses

8.1.3 Transport of laboratory samples and specimens

8.1.3.1 Toxicological analyses

Transport of samples should be done in refrigerated containers.

8.1.3.2 Biomedical analyses

8.1.3.3 Arterial blood gas analysis

8.1.3.4 Haematological analyses

8.1.3.5 Other (unspecified) analyses

8.2 Toxicological Analyses and Their Interpretation

8.2.1 Tests on toxic ingredient(s) of material

8.2.1.1 Simple Qualitative Test(s)
8.2.1.2 Advanced Qualitative Confirmation Test(s)
8.2.1.3 Simple Quantitative Method(s)
8.2.1.4 Advanced Quantitative Method(s)

8.2.2 Tests for biological specimens

8.2.2.1 Simple Qualitative Test(s)

Analysis of lead in blood is done by the wet chemical dithizone method.

8.2.2.2 Advanced Qualitative Confirmation Test(s)

8.2.2.3 Simple Quantitative Method(s)

Blood concentrations of lead are determined by atomic absorption spectroscopy. Lead in urine is analyzed after chelation and extraction by means of atomic absorption.

8.2.2.4 Advanced Quantitative Method(s)

8.2.2.5 Other Dedicated Method(s)

8.2.3 Interpretation of toxicological analyses

The concentration of lead in blood varies, in general, it is slightly elevated but in some cases of poisoning it is nearly normal. In cases of repeated gasoline sniffing the content of lead in blood is high. No close correlation exists between blood lead levels and the severity of intoxication. The urinary excretion of lead is increased markedly (Hansen, 1978; ILO, 1983; Gilman, 1990; Garrettson, 1990).

8.3 Biomedical investigations and their interpretation

8.3.1 Biochemical analysis

8.3.1.1 Blood, plasma or serum

Determination of whole-blood lead level. Determination of red cell delta-aminolevulinic acid dehydratase activity. Determination of free erythrocyte protoporphyrin.

8.3.1.2 Urine

24-hour urine lead level. Urinary delta-aminolevulinic acid. Urinary coprophyrin.

8.3.1.3 Other fluids

Lead in urine after calcium disodium EDTA mobilization test.

8.3.2 Arterial blood gas analyses

Not relevant.

8.3.3 Haematological analyses

Full blood count (red cells, white cell and platelet count). Determination of haemoglobin content and reticulocyte count.

8.3.4 Interpretation of biomedical investigations

In case of recent exposure or poisoning: whole-blood levels rarely exceeds 500 µg/L. Red cell delta-aminolevulinic dehydratase activity is inhibited (normal 30-60 IU). The concentration of protoporphyrin in erythrocytes may be increased (normal: 600 µg/L), but the results are inconsistent. In severe organic lead poisoning the concentration of lead in urine is rarely less than 3500 µg/L. The urinary delta-aminolevulinic acid (ALA-U) (normal: 4.5 mg/L) and the urinary coproporphyrin (CP-U) (normal: 150 µg/L) may be increased. The urinary lead excretion is increased by calcium disodium EDTA or D-penicillamine). Anaemia and basophilic stippling are uncommon. These findings occur in chronic exposure, as in gasoline sniffing cases, but the chemical and morphological abnormalities in blood

are absent in acute exposure (Beattie, 1972; ILO, 1983; Gilman, 1990; Garrettson, 1990).

8.4 Other biomedical (diagnostic) investigations and their interpretation

Serum creatinine, urinalysis, 24-hour creatinine and protein (evaluation of renal function). Serum creatine phosphokinase (CPK), lactic dehydrogenase (LDH) and serum glutamic oxaloacetic transaminase (SGOT): muscle and hepatic damage. Peripheral motor nerve conduction velocity (damage to peripheral nerves) only in cases of chronic exposure. Intelligence and personality tests: evaluation of psychological and neurological impairment. Electroencephalogram: in cases of lead encephalopathy (ILO, 1983; Garrettson, 1990).

8.5 Overall Interpretation of all toxicological analyses and toxicological investigations

Determination of lead in urine is the most commonly used indicator of lead organic exposure (ILO, 1983; Garrettson, 1990).

8.6 References

9. CLINICAL EFFECTS

9.1 Acute poisoning

9.1.1 Ingestion

Acute poisoning from ingestion is rare. In one case of massive ingestion of pure tetraethyl lead the initial signs and symptoms were related to increased intracranial pressure. The patient died 36 hours later with pulmonary oedema (Gosselin, 1984).

9.1.2 Inhalation

Inhalation is the most important route of absorption in the working environment. Inhalation induces sneezing, irritation of the upper respiratory tract and mild to severe systemic responses: insomnia, lassitude, nervous excitation, anxiety states, associated with tremors, hyperreflexia, spasmodic muscular contractions, bradycardia, vascular hypotension, and hypothermia. The most severe responses include complete disorientation with hallucinations, and facial contortions. Such episodes may progress to maniacal and violent convulsive seizures which may terminate in coma and death (ILO, 1983; Gosselin, 1984; Garrettson, 1990).

9.1.3 Skin exposure

Skin is a very important route of exposure, as alkyl lead compounds are easily absorbed through the intact structures. In contact with the skin they induce itching, burning and transient redness (ILO, 1983). In one case of massive skin exposure, a patient remained asymptomatic even though the urinary lead excretion was very high (Gosselin, 1984).

9.1.4 Eye contact

In contact with the ocular membranes organolead compounds induce itching, burning, and transient redness (ILO, 1983).

9.1.5 Parenteral exposure

No available data.

9.1.6 Other

Not relevant.

9.2 Chronic poisoning

9.2.1 Ingestion

Chronic poisoning by ingestion is not described.

9.2.2 Inhalation

No chronic form has been observed in a population exposed occupationally (ILO, 1983). Chronic recreational sniffing of leaded gasoline as a drug of abuse has led to neurological damage: tremors, exaggerated tendon reflexes, severe encephalopathy, and death (Hansen et al, 1978; Gosselin, 1984; Garrettson, 1990).

9.2.3 Skin exposure

No data available.

9.2.4 Eye contact

No data available.

9.2.5 Parenteral exposure

Not relevant.

9.2.6 Other

Not relevant.

9.3 Course, prognosis, cause of death

Illness resulting from acute episodes may persist for days or weeks, with intervals of quietude readily triggered into over-activity by any type of disturbance. Arterial hypotension and loss of body weight are common.

When the symptoms occur within in a few hours the exposure, an early fatal outcome is possible. When the interval is longer, the prognosis is better. Partial or recurrent disorientation and depressed circulatory function may persist for weeks. Residual damage to the nervous system has not been described.

Cause of death is direct damage to the brain (encephalopathy) involving capillary dysfunction, cerebral oedema, and interference with cerebral metabolism. In one case pulmonary oedema was described as terminal event.

Reported long term effects of chronic gasoline inhalation are body weight loss, muscular weakness, cramps, and neurasthenia. Recovery is complete and no evidence of neurological sequelae have been reported (Hansen et al, 1978; ILO, 1983; Keenlyside, 1984; Gosselin, 1984).

9.4 Systematic description of clinical effects

9.4.1 Cardiovascular

Acute : Arterial hypotension. Bradycardia.

Chronic: Arterial hypotension.

9.4.2 Respiratory

Acute : pulmonary oedema.

Chronic: not relevant.

9.4.3 Neurological

9.4.3.1 CNS

Acute: Insomnia, lassitude, muscle weakness, nervous excitation, anxiety, tremors, hyperreflexia. Disorientation, hallucinations, facial contortions, episodes of mania, convulsions. Encephalopathy with severe headache, convulsions, delirium and coma may occur.

Chronic: Disturbed sleep, headache, anxiety, irritability, intermittent stupor, generalized myoclonus, ataxia. Suicidal tendencies, psychosis, mania. Lead encephalopathy includes vertigo, ataxia, headache, insomnia, restlessness and irritability; delirium, tonic-

clonic convulsions, coma; increased intracranial pressure.

9.4.3.2 Peripheral nervous system
Acute and chronic: paraesthesiae, pain, muscle weakness.

9.4.3.3 Autonomic nervous system
Acute and chronic: not relevant.

9.4.3.4 Skeletal and smooth muscle
Acute and chronic: weakness and tremor; muscle damage is confirmed by elevated serum creatine phosphokinase (CPK).

9.4.4 Gastrointestinal
Nausea, vomiting, anorexia.

9.4.5 Hepatic
Transient elevation of transaminases.

9.4.6 Urinary

9.4.6.1 Renal
Proteinuria.

9.4.6.2 Other
Not relevant.

9.4.7 Endocrine and reproductive systems
Not relevant.

9.4.8 Dermatological
Itching, burning and transient redness of skin.

9.4.9 Eye, ear, nose, throat: local effects
Acute: conjunctivitis. Paroxysmal sneezing.
Chronic: not relevant.

9.4.10 Haematological
Acute: not relevant.
Chronic: erythrocytes with basophilic stippling are described in some cases. Anemia is uncommon and substrates of the haem synthesis, such as erythrocyte protoporphyrin may be normal.

9.4.11 Immunological
Not described.

9.4.12 Metabolic

9.4.12.1 Acid-base disturbances
Not relevant.

9.4.12.2 Fluid and electrolyte disturbances
Not relevant.

9.4.12.3 Others
Not relevant.

9.4.13 Allergic reactions
Not relevant.

9.4.14 Other clinical effects
Pallor of the face, loss of body weight in chronic exposure.

9.4.15 Special risks
There are no reliable data on the risk of spontaneous abortions and still births. Lead crosses the placenta and the fetal blood concentration at birth approximates that of the mother. Lead is also excreted in human milk in concentrations as high as 12 µg/L. Animal studies demonstrate that low-level exposure to lead during prenatal or postnatal life results in retarded growth.

(WHO, 1977; Hansen et al, 1978; ILO, 1983; Gosselin, 1984; Keenlyside, 1984; Ellenhorn, 1988; Garrettson, 1990).

9.5 Other

Not available

9.6 Summary

10. MANAGEMENT

10.1 General principles

Treatment is symptomatic in the acute stages of poisoning and chelation therapy is indicated only if inorganic lead levels are high. In case of ingestion of organic lead compounds or exposure to vapours, it is mandatory to decontaminate the patient and remove him from further exposure.

In case of chronic poisoning, prevent further exposure and treat symptomatically. Individuals with blood lead levels > 600 µg/L must be removed from the work place.

General supportive treatment is based on: maintenance of clear airway and respiration, control of convulsions, reduction of cerebral oedema, and eventually chelation therapy, if indicated.

The treatment of organic lead poisoning is mainly symptomatic: in acute phase, the drugs of choice are diazepam to control convulsive seizures, and mannitol and steroids to reduce cerebral oedema. In cases of chronic poisoning, chelation therapy with calcium disodium edetate (EDTA), penicillamine, dimercaprol (BAL) or succimer will promote the excretion of the inorganic lead produced from the metabolism of organic lead. Chelation therapy is indicated in all symptomatic patients and patients whose blood lead levels exceed 700 µg/L.

In case of chronic poisoning, prevent further exposure and treat symptomatically. In adults with blood levels up to 1000 µg/L, combined treatment with intramuscular BAL and intravenous EDTA for 5 days is indicated. Interrupt treatment for 2 days and start EDTA if blood lead levels remain high (>1000 µg/L). Then penicillamine should be given for 3 - 6 months (20 mg/kg/day oral route). Note that some problems may arise in the use of chelators (see 10.6)

10.2 Relevant laboratory analyses

10.2.1 Sample collection

Blood and urine should be collected at any time. It is essential to avoid contamination: needles, containers and anticoagulants must be lead-free. A 24-hour urine specimen is preferable.

10.2.2 Biomedical analysis

Lead in blood and urine. Red cell delta-aminolevulinic acid dehydratase activity. Free erythrocyte protoporphyrin. Urinary delta-aminolevulinic acid. Urinary coproporphyrin. Full

blood count (red cells, white cells, platelets; haemoglobin and reticulocyte count). Electroencephalogram (ILO, 1983; Gosselin, 1984; Ellenhorn, 1988; Garrettson, 1990).

10.2.3 Toxicological analysis

Not available

10.2.4 Other investigations

Not available

10.3 Life supportive procedures and symptomatic/specific treatment

In case of severe poisoning, make a proper assessment of breathing, circulation and neurological status. Maintain a clear airway and aspirate secretions from airway. Start artificial respiration at the first sign of respiratory failure. Administer oxygen if cyanosis is present. Correct dehydration.

Analgesics may be necessary to control abdominal pain.

If the patient is obtunded, convulsing or comatose, insert an oro- or nasogastric tube and lavage after endotracheal intubation.

If the patient is convulsing, administer diazepam 0.1 mg/kg IV. Coma or convulsions may indicate increased intracranial pressure; mannitol, steroids and hypothermia, and referral to a neurosurgical unit, may be necessary.

Administer intravenous fluids. Monitor vital signs. A successful outcome has been achieved with sustained supportive therapy in association with persistent, vigorous sedation (ILO, 1983; Garrettson, 1990).

10.4 Decontamination

In case of ingestion, provided convulsions are not imminent, induce emesis or perform gastric lavage. In general, emesis is not induced if the product solvent is a petroleum distillate.

Gastric lavage may be performed if emesis fails, but bearing in mind the risk of imminent convulsions.

In cases of inhalation, the management is symptomatic and supportive: remove from exposure and maintain the airway and ventilation. Supportive measures include oxygen and artificial respiration.

Skin - remove all contaminated clothing and wash the skin and hair.

Eyes - extensive irrigation with water or saline should be performed.

10.5 Elimination

Chelation therapy will promote the excretion of inorganic lead produced by the metabolism of organic lead through

urine. A good urinary output is mandatory. Haemodialysis is indicated in case of impaired renal function.

10.6 Antidote treatment

10.6.1 Adults

There are no antidotes for tetraethyl lead, tetramethyl lead or triethyl lead (Garrettson, 1990). Lead chelators may be used only to promote excretion of inorganic lead produced by the metabolism of organic lead compounds.

Calcium disodium edetate (CaNa2EDTA): 1 to 2 g daily (non-convulsing or comatose) patients 2 to 4 g daily (convulsing or comatose patients), in two divided doses intramuscularly or IV in saline infusion,

slowly, for 5 days.

Dimercaprol (BAL): 2.5 to 4 mg/kg/dose intramuscularly
every 4 hours, for 48 hours; then, every 6 hours, for 48 hours; and every 6 to 12 hours for more 7 days.

Succimer could also be used.

D-penicillamine: 250 mg 4 times daily for 5 days. Doses in long-term treatment should not exceed 40 mg/kg/day.

Problems with chelators:

- oral chelators may promote lead absorption from the gastrointestinal tract.
- the chelator-lead complex is nephrotoxic; urine output must be monitored.
- chronic chelation therapy with EDTA or penicillamine promotes loss of essential metals.
- intra/muscular injection of EDTA is painful; multiple sites should be used.
- BAL may cause local pain, nausea, vomiting; hypertension has been reported after BAL therapy. Antihistamines may be administered.
- D-penicillamine may cause alteration of taste, neutropenia, allergic rashes, aplastic anaemia, nephropathy and hepatitis (Gosselin, 1984; Noji & Kelen, 1989; Gilman, 1990; Garrettson, 1990).

10.6.2 Children

There are no antidotes for tetraethyl lead, tetramethyl lead or triethyl lead (Garrettson, 1990). Lead chelators may be used only to promote excretion of inorganic lead produced by the metabolism of organic lead compounds.

Calcium disodium edetate (CaNa2EDTA): 50 mg/kg/day in two divided doses (non-convulsing child) or 75 mg/kg/day in two divided doses (convulsing child)

intramuscularly of IV in saline infusion, slowly, for 5 days.

Dimercaprol (BAL): 2.5 to 4 mg/kg/dose intramuscularly every 4 hours, for 48 hours; then, every 6 hours, for 48 hours; and every 6 to 12 hours for more than 7 days.

Succimer could also be used.

D-penicillamine: 20 to 40 mg/kg/day (maximum 1 g/day) may be given for 3 to 6 months.

10.7 Management discussion

Chelation therapy is effective in removing only inorganic lead. The role of chelating agents in acute organic lead poisoning is controversial.The risks of chelation include depletion of essential metals due to rapid mobilization and, after oral administration, impaired absorption from the gastrointestinal tract. Good therapeutic results with chelators have been reported in cases of chronic exposure

(gasoline sniffing). The efficacy of chelators in organic lead encephalopathy has recently been established (Hansen et al, 1978; Gosselin, 1984; Gilman, 1990; Garrettson, 1990).

11. ILLUSTRATIVE CASES

11.1 Case reports from literature

Four men cleaned a tank which had held leaded aviation gasoline. Exposure was followed shortly by illness in which mental symptoms were prominent. Blood lead levels were raised to 645 to 925 µg/L. Lead was found predominantly in the lipid blood fraction. Urinary coproporphyrin was slightly raised in one case. Erythrocyte protoporphyrin was slightly raised in the three more severe cases. Blood delta aminolevulinic acid dehydratase activity was markedly reduced. Urinary lead excretion was increased by D-penicillamine administration. All men recovered in a few weeks (Beattie et al, 1972).

Several cases of organolead compound poisoning associated with gasoline sniffing presented with lead blood levels higher than 1000 µg/L. Signs of organic lead poisoning, mostly neurological symptoms, have been detected in children and adolescents who had been sniffing gasoline for periods ranging from 6 months to 5 years. Blood delta aminolevulinic acid dehydratase activity was reduced. Treatment with chelating agents resulted in symptomatic improvement (Keenlyside, 1984).

Over 3 years, 62 persons burned by gasoline flame were admitted to a burns unit. Increased mortality associated with gasoline burns led the authors to question the influence of lead in this problem. Urinary lead and coproporphyrins were measured in 18 persons burned by gasoline. The levels were elevated above the normal or safe limits in 14 (Wood et al, 1968).

11.2 Internally extracted data on cases

Not available

11.3 Internal cases

12. Additional information

12.1 Availability of antidotes

To be completed locally.

12.2 Specific preventive measures

Occupational exposure:

- use protective clothes (including shoes).
- the protective clothes and shoes must not leave the plant.
- avoid skin contact with lead vapours.
- avoid contact of lead with oxidizers (such as perchlorates, peroxides, permanganates, chlorates and nitrates) and chemically active metals (such as potassium, sodium, magnesium and zinc) since violent reactions occur.
- insist on personal hygiene: do not smoke, do not eat, do not drink in contaminated environment.
- eating facilities must be separated from working area.
- face and hand coverings should be made of impermeable material.
- medical surveillance programme for lead: pre-employment and pre-placement examination, periodical examination,

clinical tests, record-keeping and health education.
- immediate cleaning up of spills. Floors can be wet with a fine spray to avoid stirring up dusts.
- storage receptacles should be kept covered to reduce fumes and dust.
- measurement of lead air levels (ILO, 1983; Glenn, 1987).

Non-occupational exposure:

- avoid gasoline sniffing.
- control of lead emissions in air (ATSDR, 1990).

12.3 Other

In the 1980s it was considered that about 90 percent of airborne lead was derived from the exhaust gases of motor vehicles. In many countries a decrease in the use of lead in petrol has been associated with reductions in the air lead concentrations of urban areas (UNEP, 1984).

Concern over improving the quality of the environmental by lowering the lead content in gasoline and the control of the occupational exposure decreased average blood levels of the population in the USA by nearly 50% (Goyer, 1990).

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