**DEFINITION**

There is no clear threshold at which lead becomes toxic. Impairment of cognitive function begins to occur at concentrations of whole blood lead greater than 0.48 µmol/L, even though clinical symptoms are not seen. In population studies, the relationship between lead concentrations and IQ deficits was found to be remarkably consistent, for every 0.48 µmol/L increase in blood lead concentrations, there was a lowering of mean IQ in children by four to seven points.

In New Zealand, lead poisoning is a notifiable disease if whole blood lead concentrations exceed 0.48 µmol/L. Interventions are required for all children with lead concentrations greater than 0.48 µmol/L.

**PREVALENCE**

In the USA, it has been estimated that 16% of children have blood lead concentrations in the neurotoxic range. Australian data indicate that 26-53% of children have lead concentrations >0.48 µmol/L. There has been only limited research in New Zealand on blood samples from the general population. In a 1975 Christchurch study of 170 pre-school children, 12.4% were found to have whole blood lead concentrations >1.45 µmol/L and 87% had concentrations of >0.5 µmol/L. However, some of the children in this study were selected because of known exposure to high environmental lead concentrations. In a sample of 579 Dunedin 11 year olds collected in 1986, 0.5% had lead concentrations >1.45 µmol/L and 49% were >0.5 µmol/L. The dentine lead concentrations of the deciduous teeth of 1,035 Christchurch children have been found comparable with similar studies from USA and UK. A 1994 pilot study of Wellington pre-school children found 11% had lead concentrations <0.5 µmol/L.

Lead poisoning has been labelled “one of the most common environmental paediatric health problems in the USA”. There is no reason to believe the problem is any less severe in New Zealand.

**PRESENTATION**

Clear clinical symptoms are unlikely when whole blood lead concentrations are <2.5 µmol/L. Lead has been called a “silent thief of children’s wits and futures”. Laboratory screening of young children thought to be at risk of lead poisoning is therefore the most reliable way of identifying cases.

In children with significant anaemia, whole blood lead concentrations underestimate soft tissue lead concentrations because more than 95% of blood lead is stored in red cells. In this situation, a corrected whole blood lead concentration can be calculated by multiplying the red cell lead by 0.33.

Signs and symptoms vary widely from individual to individual, depending on age and nature of lead exposure.

<table>
<thead>
<tr>
<th>Whole Blood Lead Concentrations</th>
<th>Symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.5 – 1.0 µmol/L</td>
<td>Asymptomatic or insidious decrease in IQ with impaired neurobehavioural development.</td>
</tr>
<tr>
<td>1 – 2.5 µmol/L</td>
<td>Decreased IQ, impaired neurobehavioural development, cognitive deficits, decreased play, decreased haemoglobin, irritability, aggression, sleeping less.</td>
</tr>
<tr>
<td>2.5 – 3.0 µmol/L</td>
<td>Anorexia, colic, vomiting, abdominal pain, constipation, hyper-irritability.</td>
</tr>
<tr>
<td>&gt;3.0 µmol/L</td>
<td>Vomiting, ataxia, decreased concentration of consciousness, coma, seizures, cerebral oedema, death.</td>
</tr>
</tbody>
</table>
PATHOPHYSIOLOGY

Lead is distributed into two tissue pools:

a) **Blood and soft tissue pool** – has relatively rapid turnover with a half-life of approximately 25 days. Lead in this pool accounts for the toxicity and can be removed by chelation therapy.

b) **Bone pool** – lead in this pool has a very long half-life (up to 20 years in adults) and is only slowly exchanged with lead in the soft tissue pool. Except in cases of extremely acute exposure, most of the body’s lead stores are held in the bone pool.

Up to 50% of the lead ingested by children is absorbed. Adults only absorb 5-10% of ingested lead. Gastrointestinal absorption is increased in iron or calcium deficiency. Lead is toxic because it binds to nitrogen, oxygen or sulphur within molecules and interferes with normal biochemical function.

AETIOLOGY

In New Zealand, it has been estimated that the annual entry of lead into the environment amounts to 660 tonnes of lead from petrol and 440 tonnes of lead from ageing house paint. Lead from petrol was disseminated throughout the environment acting as a source of low concentration lead exposure for everyone. Lead from house paint is localised around each house and so is a potential source of high-concentration lead exposure for a few individuals.

Over 13 years (1982-1994), children have been admitted to hospital in Christchurch and Nelson with lead poisoning, 85% of these children were poisoned by lead in house paint. In 60% of cases, the poisoning was associated with home renovations. Infants appear to be particularly vulnerable because of their frequent hand-to-mouth activities. In the United States, 75% of lead poisoning in infants is due to lead paint, two-thirds of this is due to household renovations when dust is ingested or inhaled. The remaining third of lead paint-induced poisoning is due to the ingestion of chips of lead paint or paint-contaminated soil from around houses, often associated with pica.

Other sources of lead poisoning include lead-glazed pots, toys, folk medicines, industrial fumes, lead-piped water supplies in soft water districts and lead shot, either ingested or within the tissues.

Up until 1945, the principal pigment used to colour paint white, was lead carbonate or “white lead”. In the mid-1940s, 2,700 tons of white lead were used annually in New Zealand. Between 1945 and 1965, white lead was phased out in favour of titanium dioxide. The use of white lead in paint was banned in 1979. Paint produced after 1945 contained much less lead than before, and paint applied to houses since 1965 is unlikely to have a high lead content. It was estimated in 1984 that there were 251,000 timber-clad houses in New Zealand with lead paint on their walls. The oldest of these houses may each have 88 kg of lead pigment on the walls. Lead in the immediate home environment, is currently the main contributor to blood lead concentrations in New Zealand pre-school children. Natural weathering processes cause lead to be leached out of the paint into the soil around houses where it tends to remain. The lead in soil around houses poses a significant threat to children with pica.

During home renovations, especially when sandblasting is used, lead particles in a finely divided, readily absorbed form are produced. Absorption follows ingestion or inhalation. The normal hand-to-mouth activity of infants and toddlers is likely to result in toxicity if house dust contains a significant amount of lead. Lead ingestion should not exceed 5 µg/kg/day. A 10 kg infant would only need to ingest 5 mg of house dust daily containing 1% lead to develop lead toxicity.

Children who have severe lead poisoning, however, have usually ingested lead in a particularly concentrated form, such as paint chips. Children with developmental disorders are particularly prone to lead poisoning because of the increased duration of hand-to-mouth activity and higher incidence of pica.
INVESTIGATION

The diagnosis is based entirely on the measure of whole blood lead concentration. Blood for this specimen should be collected into a lead-free tube through skin that is not contaminated with lead. Other investigations may support the diagnosis and should be performed at initial assessment and sporadically during treatment. These are:

<table>
<thead>
<tr>
<th>Investigation</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Full Blood Count</td>
<td>This will classically show a hypochromic normocytic anaemia. In severe cases, there may be basophilic stippling or an increased reticulocyte count associated with haemolysis. No full blood count changes are seen in most mild or moderate cases of lead poisoning.</td>
</tr>
<tr>
<td>Radiology</td>
<td>X-rays of knees and hands may show metaphyseal lead lines resulting from an increase in the density of cartilaginous trabeculae with associated increased calcification. The width of these lines is proportional to the duration of exposure to lead. An allowance for the rate of bone growth needs to be made.</td>
</tr>
<tr>
<td>Erythrocyte Protoporphyrins</td>
<td>These are elevated in lead poisoning because of lead blocking the enzymes responsible for porphyrin synthesis. Following FEPS during treatment allows the biological effect of the lead on the individual to be monitored.</td>
</tr>
<tr>
<td>Serum Ferritin and Iron</td>
<td>Iron deficiency often coexists with lead poisoning and enhances lead absorption. Iron treatment should be withheld until after chelation if BAL is to be used.</td>
</tr>
</tbody>
</table>

MANAGEMENT

The single, most important step in the management of lead poisoning is to remove the child from the source of the lead. Sometimes this will mean leaving the family home until it has been detoxified.

Whenever a whole blood lead concentration >0.5 µmol/L is found in a child, the following steps should be taken:

1. The Health Protection Unit should be informed so appropriate environmental interventions can then be instigated.
2. All children in the household, children who visit frequently, and adults considered at risk should also be screened.
3. All cases should be discussed with a paediatrician.
<table>
<thead>
<tr>
<th>Class of Lead Poisoning (approx CDC category)</th>
<th>Whole Blood Lead Concentration (µmol/L)</th>
<th>Action taken by Paediatrician</th>
<th>Action taken by Health Protection Unit</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild (II)</td>
<td>0.5 – 1.0</td>
<td>Telephone advice to GP on follow-up.</td>
<td>Source tracing. Simple advice on reducing exposure to lead – usually by dust control measures.</td>
</tr>
<tr>
<td>Moderate (III)</td>
<td>1.0 – 1.9</td>
<td>Full outpatient medical evaluation as above and possible admission for treatment.</td>
<td>Home visit with detailed advice on reducing exposure to lead by dust control and household detoxification.</td>
</tr>
<tr>
<td>Severe (IV)</td>
<td>1.9 – 3.0</td>
<td>Full assessment and chelation treatment for many.</td>
<td>Home visit and sampling. Extensive advice on household detoxification. Possible evacuation of children to safe environment.</td>
</tr>
<tr>
<td>Life Threatening (V)</td>
<td>&gt;3.0</td>
<td>Immediate hospital treatment (medical emergency).</td>
<td>Maximal environmental interventions.</td>
</tr>
</tbody>
</table>

Whenever elevated blood lead concentrations are found, serial measurements of blood lead should be done so a trend can be established. Increasing concentrations demand more intensive environmental interventions.

ENVIRONMENTAL INTERVENTIONS

In most cases, the lead will have originated from house paint, very frequently associated with home renovations. For children without pica, house dust is usually the most important source of excessive lead absorption.

The following dust control measures have proven effective in lessening children’s absorption of lead from house dust:

1. Vacuum carpets at least weekly before damp cleaning.
2. Regular damp cleaning of all hard household surfaces with high phosphate detergent (most washing powders contain phosphates).
4. Regular careful washing of children’s hands, especially before eating and at bedtime.
5. Prevent access to obvious sources of lead e.g. peeling walls, paint dust, contaminated soil.
6. Leaving shoes at the doorway.
7. Wash children’s clothes and toys often, especially toys that are likely to be sucked or chewed.
8. Hose down outside paths near entrances.

Other household detoxification measures may include:

1. Scrubbing lead-painted surfaces with high phosphate detergent.
2. Sealing lead-painted surfaces with paint or chip board.
3. Vacuuming with high efficiency particle accumulator vacuum.
4. Removing topsoil and covering gardens in bark chip, pebbles, paving stones or grass.
As it is extremely difficult to detoxify houses once contaminated it is crucial that families are aware of the risks of lead toxicity from houses painted before 1965. Houses built before 1950 post the greatest risk to children. Advice from the Health Protection Unit should be sought before disturbing paint which may be lead-based.

Women of child-bearing age and children under 5 should not be present in a house while renovation involving lead-based paint is taking place. The Public Health Units provide a free service by which paint chips may be checked for lead and can supply a helpful leaflet on repainting.

When excessive lead absorption does not obviously arise because of house paint more through enquiries into hobbies, occupation and other sources of lead are needed.

DIETARY ADVICE

Children deficient in iron, calcium, zinc and ascorbate more readily absorb and/or retain lead from their diets. A diet rich in meat and dairy products should be encouraged. Any biochemical or clinical suspicion of deficiency is an indication for nutritional supplements e.g. iron. High fat diets increase lead absorption. Regular small snacks reduce lead absorption, as absorption is greater on an empty stomach.

CHELATION THERAPY

Chelating agents competitively bind lead, removing it from biologically active molecules. Once bound, the chelating agent and the lead is excreted primarily in the urine. The blood and soft tissue pool of lead is rapidly depleted reducing biochemical evidence of lead toxicity and may reduce neurotoxicity. The bone pool is largely unaffected so, on completion of each course of the treatment, the soft tissue pool is ‘restocked’ with lead from the bone pool. Rebound of concentrations therefore occurs and multiple courses of treatment are frequently needed. Chelating agents can greatly enhance the absorption of lead from the gastrointestinal tract so drug therapy may be dangerous unless the child is removed from lead exposure.

There is no international consensus as to which asymptomatic children with elevated lead concentrations should receive chelation therapy.

Oral chelation therapy will lower blood concentrations for children with lead concentrations between 1.0 – 1.9 µmol/L but long term effectiveness and benefit is uncertain. There is almost universal agreement that chelation therapy is indicated for children with concentrations >2.0 µmol/L. For children in the intermediate range of 1.5 – 2.5 µmol/L, clinical judgement should be applied. The following factors should lower the threshold for chelation therapy in an individual child:

- children under 2 years
- children with rapidly rising concentrations
- when there is evidence of biochemical toxicity (lead lines, increased FEPs, anaemia)
- when elevated concentrations persist for 2-3 months despite removal from lead exposure.
Treatment of Lead Poisoning without Encephalopathy

(when whole blood lead concentration is <3.5 µmol/L)

A.

<table>
<thead>
<tr>
<th>Step</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Administer succimer at 30 mg/kg per day for 5 days, followed by 20 mg/kg per day for 14 days (see oral chelation therapy section below).</td>
</tr>
</tbody>
</table>

Or

B.

<table>
<thead>
<tr>
<th>Step</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Commence a dextrose saline infusion at an appropriate maintenance rate. Give 2 hours prehydration. Free fluids should continue orally, as well as full maintenance fluids throughout treatment period to ensure a good diuresis.</td>
</tr>
<tr>
<td>2</td>
<td>Calcium disodium edentate is added to the burette to give 25 mg/kg/dose as a 2-hour infusion every 12 hours, 10 doses in total.</td>
</tr>
<tr>
<td>3</td>
<td>Screen urine daily for blood and protein (nephrotoxicity).</td>
</tr>
<tr>
<td>4</td>
<td>Check electrolytes on days 1, 2 and 5 of treatment.</td>
</tr>
</tbody>
</table>

**Side effects:** Ca EDTA is nephrotoxic so should never be used without adequate urine flow. An alternative treatment should be used if nephrotoxicity occurs. Hypocalcaemia, fever, rash.

**A rebound in lead concentration occurs over 1-3 weeks following treatment, so frequent measurements of lead concentration are required until a trend can be established.**
Treatment of Lead Poisoning with Encephalopathy

(when whole blood lead greater than 3.5 µmol/L)

Lead encephalopathy is a medical emergency and should be managed in an intensive care setting. It is diagnosed by finding any one of the following: coma, seizures, bizarre behaviour, ataxia, apathy, incoordination, vomiting, decreased conscious concentration of subtle loss of recently acquired skills in the presence of an elevated whole blood lead concentration, usually >5 µmol/L. As significant delay often occurs before a whole blood lead concentration is available, circumstantial evidence of lead toxicity such as basophilic stippling of red cells, lead lines at knee metaphyses or Fanconi syndrome should be sought when the diagnosis is considered. It is preferable to commence treatment before a definite diagnosis is made, than to delay.

<table>
<thead>
<tr>
<th>Step</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Control seizures and treat shock with careful intravenous rehydration so overloading is avoided. Oral fluids should not be given.</td>
</tr>
<tr>
<td>2</td>
<td>Give BAL 4mg/kg/dose as deep I.M. injection 4-hourly. (BAL may cause vomiting, hypertension and tachycardia).</td>
</tr>
<tr>
<td>3</td>
<td>Four hours later, Ca EDTA is commenced 25 mg/kg/dose as a 2-hour infusion every 12 hours, 10 doses in total. This must only be started if adequate urine flow is established (&gt;0.5 mL/kg/hr). Ca EDTA concentration in parenteral fluid should not exceed 0.5%. So to allow adequate fluid restriction longer infusions or intramuscular injections (extremely painful mix with lignocaine) may be given.</td>
</tr>
<tr>
<td>4</td>
<td>Meticulous fluid and electrolyte management is required, as raised intracranial pressure is usually present even in the absence of classical signs. Once shock is treated, fluids should be restricted to minimal basal requirement to maintain normal electrolytes with a urine output of 0.5-1.0 mL/kg/hr.</td>
</tr>
<tr>
<td>5</td>
<td>Five days chelation treatment is usually given using both agents. Electrolytes, renal and hepatic function should be monitored daily throughout treatment.</td>
</tr>
<tr>
<td>6</td>
<td>A second course of chelation therapy may start 2 days after completion of the first following the same protocols based on lead concentrations.</td>
</tr>
</tbody>
</table>

Oral Chelation Therapy

Succimer (2,3-dimercaptosuccinic acid) is a water-soluble derivative of BAL. It has a high affinity for lead, arsenic and mercury and is absorbed orally, forming metal complexes which are eliminated in urine. Succimer produces a more effective plumburesis than Ca EDTA or BAL and reports suggest fewer side effects. It is becoming the first line drug for the treatment of asymptomatic lead poisoning. Experience with Succimer is however limited. Succimer is not recommended for children with levels >3.5 µmol/L due to lack of experience and the theoretical risk that it may increase lead mobilisation into the brain.

Succimer is administered orally, but has a foul odour of hydrogen sulphide, causing compliance difficulties, and offensive urine and stools. Only 100 mg capsules are available; the contents of the capsule may be given with a small amount of soft food or a fruit drink for children who cannot swallow capsules. Children may need to be hospitalized for the initiation of therapy to monitor for adverse effects and institute environmental abatement. The dosing schedule is 10 mg/kg/dose, 12-hourly, for a further 14 days as an outpatient. If more courses are required, a minimum of 2 weeks between courses is preferred, unless blood lead concentrations indicate the need for immediate re-treatment. Patients who have received therapeutic courses of CaNa2EDTA, with or without BAL, may be treated with Succimer after an interval of 4 weeks.
Side effects have included nausea, diarrhoea, appetite loss and a dramatic but usually transient increase in serum alkaline phosphatase. During treatment evaluate liver function regularly.

CHILDREN ARE NEVER DISCHARGED FROM HOSPITAL UNTIL A RELATIVELY LEAD-FREE ENVIRONMENT CAN BE ASSURED.

Screening

Lead poisoning is more common than other child health problems for which screening already occurs in New Zealand. Some states in the USA have organised screening of all children for lead poisoning. At present, no plans exist for population-based screening in New Zealand. Screening targeted at children with the greatest risk of having elevated lead levels can however be done as part of normal child health care. The group selected for targeted screening could include any child whose parents give a ‘yes’ answer to any one of these questions.

DOES YOUR CHILD:

• Live in or regularly visit a house with peeling or chipping paint built before 1965? This could include a day care centre, pre-school, the home of a baby sitter or relative.
• Live in or regularly visit a house built before 1965 which is being renovated or has been renovated within the last 2 years? Any disturbance of pre-1965 paint should qualify, even carefully performed de-leading work.
• Have a brother, sister or playmate with significantly elevated lead concentrations? (<0.5 µmol/L)
• Live with an adult whose job or hobby involves exposure to lead?
• Regularly chew non-food items or eat soil which might be contaminated by lead?
• Risk lead exposure from industrial activities e.g. lead smelting, mining, battery recycling?
• Have unexplained intellectual disturbances or behavioural problems? This particularly applies to problems of sudden onset.

In Wellington in 1994, the main risk factor for elevated lead concentrations in pre-school was living in a house more than 50 years old that had had existing paint removed within the last 2 years. Elevated lead concentrations were found in 57% of children living in these circumstances.
REFERENCES

14. Russel CF. Disaster management or project management: Managing lead paint

For further information please contact Susan Grant or Trevor Walmsley, Trace Metal Laboratory, CHL. Ph: 03 3640 317, Fax: 03 3640 320.