

CURRENT SURVEYS

Lead poisoning in childhood

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CHILDHOOD plumbism has features that distinguish it from the adult disorder in aetiology, presentation and prognosis. The prevalence of the condition has yet to be determined since, although not uncommon in urban paediatric units, it is likely that only severe cases are recognized. Since the sequelae include death and cerebral damage, it is important that children exposed to lead be identified and those with evidence of poisoning treated. The rational management of the condition depends upon an understanding of the metabolism and toxicology of lead in children together with a knowledge of predisposing factors.

Normal lead metabolism

In most communities the atmosphere and the diet contain small amounts of lead which are continuously inhaled and ingested. At least 90% of ingested lead is not absorbed so that the faecal lead content is an index of ingested lead. Adults normally excrete about 0.3 mg of lead per day from all sources (Kehoe, 1961a). Few estimates are available for children but children aged 24-35 months have a mean faecal lead excretion of 0.13 mg/day with an upper limit of normal of 0.18 mg (Barltrop & Killala, 1967).

Lead absorbed from the gut enters the circulation and 95% enters the erythrocytes. *In-vitro* studies with radioactive lead have shown that lead enters the cell but is not absorbed onto the cell membrane; equilibrium between plasma and erythrocyte lead is attained within 15 min (Barltrop, unpublished observations). Subsequently, lead is deposited in certain tissues notably liver, kidney and bone, whereas brain and skeletal muscle show minimal lead-binding properties.

The deposition of lead in bone proceeds at a slower rate than in liver and kidney, although the total amount deposited may ultimately be considerable. The net effect is that lead is transferred from the gut to the erythrocyte, transpor-

ted to the liver and kidneys where it is temporarily 'stored' and finally transported to bone where it is laid down with other minerals. Although bone lead is thought to be 'metabolically inactive' it may be released to the soft tissues again under conditions of bone resorption (Byers & Maloof, 1954). Since the blood lead concentration is the resultant of several equilibria, a high value may not indicate current ingestion and conversely a low value does not exclude a high whole-body lead burden.

Toxicology

Lead is a cumulative poison, so that toxicity is a function of both the magnitude of the dose and the rate of administration. Adult volunteers who ingested 1.0 mg of lead/day developed unacceptably high tissue levels after 48 months whereas 3.0 mg/day resulted in similar levels after only 4 months, i.e. a three-fold increase in the daily dose resulted in a twelve-fold potentiation of toxicity (Kehoe, 1961a).

In view of the different patterns of metabolic activity, it is unlikely that adult toxicity figures can be applied directly to children, even when differences in body weight are taken into account. Faecal lead studies on 2-year-old children with symptomatic poisoning suggest that this may result from the daily ingestion of 1-2 mg/day for 5-6 months (Barltrop & Killala, 1967).

Lead probably exerts its toxic action by combining with essential SH-groups of certain enzymes, for example some of those involved in porphyrin synthesis and carbohydrate metabolism. Lead has an effect on membrane permeability and potassium leakage has been demonstrated from erythrocytes exposed to lead (Cavagna & Beard, 1962). Renal tubular reabsorptive mechanisms are impaired in lead poisoning with leakage of phosphates, glucose and amino acids in the urine. Clinical manifestations cannot always be linked to the known

actions of lead however, for example, the cerebral oedema that accompanies the encephalopathy of plumbism is associated with minimal deposition of lead in cerebral compared with other tissues (Kehoe, 1961a, b).

Sources of lead

The commonest source of lead in childhood poisoning is the flaking paint found in the homes of families living in old, poorly maintained properties. Such flakes may be composed of multiple layers of paint applied over many years so that a significant amount of lead may be contained in a flake of small surface area (Fig. 1).

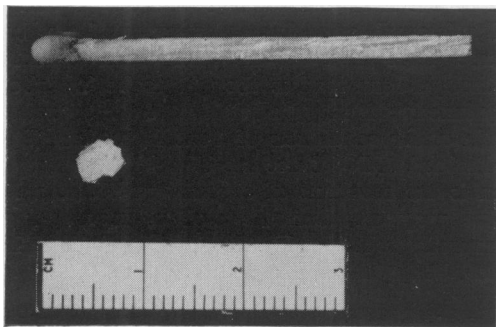


FIG. 1. A flake of paint, weight 10 mg, containing 1.0 mg of lead. Match and centimetre scale for comparison.

Indoor paint is responsible for 83% of the cases and in 64% of these the place of origin in the home is a window-sill or frame (Chisolm & Harrison, 1956) (Fig. 2). Other sources have included putty mixed with white lead, soil contaminated with lead (W. Orton, personal communication, 1967) and painted wall plaster.



FIG. 2. Window-sill chewed by a child in an adjacent cot. Paint in deep layers contained 50% lead. (Haringey Public Relations Department.)

Rare sources have included white lead dusting powders (Holt, 1923), retained intragastric metallic lead foreign body (Biehusen & Pulaski, 1956) and maternal milk contaminated by lead nipple shields (Ammaniti & Longobardi, 1962). Contaminated water supplies are a theoretical possibility (Crawford & Morris, 1967) and although childhood cases attributable to this must be rare in this country, examples have occurred abroad in families living near lead mines (Manhood *et al.*, 1960).

When heated, lead will vaporize and the fumes are extremely toxic. Byers (1959) describes a child who slept in a family printing shop and was poisoned by the fumes from a crucible of molten type-metal. More often, storage batteries burned as scrap or as fuel are responsible and deaths have even occurred in children living at a site remote from the burning (Travers, Rendel-Short & Harvey, 1956).

Pica

This term refers to the magpie (*Pica pica pica* (Linn.)), a creature with an appetite both capricious and voracious. Pica precedes most cases of childhood plumbism and may be defined as the ingestion of substances, other than medicaments, not normally regarded as food. It has been suggested that the activity may represent an attempt to fulfil a nutritional need such as iron deficiency (Lanzkowsky, 1959) but this has been disputed (Gutelius *et al.*, 1962). In fact pica is a common activity in young children which is probably a normal maturation phenomenon which occurs irrespective of race, social class or sex (Barltrop, 1966). Unless the ingested materials are known to contain lead a history of pica is of little diagnostic value.

Seasonal incidence

Most cases of lead poisoning occur during the summer months and this phenomenon has not yet been satisfactorily explained. There is some evidence from animal work that the toxicity of lead may be potentiated by ultraviolet irradiation (de Mello, 1951), by vitamin D administration (Sobell, Gawron & Kramer, 1938) and by a raised environmental temperature (Baetjer, Joardar & McQuarry, 1960). However, attempts to define the responsible agent in children have not yet been successful (Benson, 1962).

Clinical features

Children of both sexes aged 1-5 years are principally affected, with a peak incidence at 2 years of age. A history of several months pica for paint may be obtained during which the child

was asymptomatic. There are no specific features in childhood plumbism, the Burtonian blue line does not occur in children and peripheral nerve palsies are very rare. The symptomatology depends upon the degree of exposure which in turn is a function of the degree and duration of the lead ingestion. Four categories of exposure can be recognized and clinical features should be related to these (Table 1).

TABLE 1
Exposure and symptomatology

Grade	Description	Features
1	Normal exposure	None. Blood lead 0-36 $\mu\text{g}/100\text{ g}$.
2	Increased exposure	None. Blood lead exceeding 34 $\mu\text{g}/100\text{ g}$.
3	Symptomatic poisoning	Irritability, anorexia, constipation, pallor, vomiting. Blood lead usually exceeding 60 $\mu\text{g}/100\text{ g}$. Coproporphyrinuria.
4	Encephalopathy	Impaired consciousness, convulsions, coma, vomiting. Blood lead usually exceeding 80 $\mu\text{g}/100\text{ g}$. CSF protein and pressure raised.

There are no sharp divisions between the four categories and the rate of progression from one to the next is variable, although typically Grade 2 persists for several months, Grade 3 a few weeks and Grade 4 at most a few days. Cessation of exposure and the commencement of treatment may prevent and reverse the progression but the occurrence of encephalopathy in advanced instances of symptomatic poisoning cannot always be prevented.

Diagnostic aids

Since the features of childhood lead poisoning are so non-specific the clinical suspicion of plumbism must be confirmed by the application of certain chemical and other tests, before treatment is started.

The chemical determination of lead

(a) *Blood lead.* The cardinal aid is the determination of the blood lead. Values above 36 $\mu\text{g}/100\text{ g}$ whole blood are abnormal (Moncrieff *et al.*, 1964) but should be interpreted in the light of Table 1 before the case is assigned to a particular exposure group.

(b) *Faecal lead.* The faecal lead content is indicative only of current lead ingestion and therefore has no place in the diagnosis of poisoning. A 24-hr faecal excretion of lead exceeding 0.18 mg by 2-year-old children indicates abnor-

mal ingestion and implies increased absorption, but this could be transient.

(c) *Urine lead.* The determination of urine lead has no advantage over blood lead in the diagnosis of poisoning. Increased excretion after the administration of EDTA (Whitaker, Austin & Nelson, 1962) or penicillamine (Ohlsson, 1962) may reveal a raised soft tissue lead, but these tests have no place in the diagnosis of the acute case when speed is essential.

Abnormal metabolism

The presence of abnormal amounts of soft tissue lead may be inferred from the demonstration of characteristic abnormalities of porphyrin metabolism. Lead interferes with several steps in the synthesis of haem from glycine and succinyl-CoA with accumulation of intermediates. The most convenient screening test is the estimation of urinary coproporphyrin III by comparison of the fluorescence of an acid-ether extract of urine with that of commercial mesoporphyrin IX standards (Benson & Chisolm, 1960). False positive results are not common in paediatric hospital admissions, about 2% of all cases (Bartrop, 1965) and levels seldom exceed 0.2 $\mu\text{g}/\text{ml}$ urine. The test can easily be made available for emergency work.

Other porphyrin abnormalities include increased excretion of delta-aminolaevulinic acid and increased free erythrocyte protoporphyrin. The various red cell abnormalities, basophilic stippling, hypochromia and transient fluorescence under ultraviolet microscopy (Whitaker & Vietti, 1959) are related phenomena of which only the 'fluorescyte count' has shown diagnostic value in paediatric practice.

Renal tubular dysfunction

The reabsorptive mechanisms of the renal tubular cells are impaired in lead poisoning with resultant glycosuria, phosphaturia and aminoaciduria. The urinary findings closely resemble those in the de Toni-Fanconi-Debré type of renal rickets and this has been described as an unusual sequel of lead poisoning (Caffey, 1938). The occurrence of glycosuria in the presence of a normal blood sugar is suggestive evidence of lead poisoning.

Radiological aids

These are of limited value in the diagnosis of lead poisoning. A plain film of the abdomen may indicate radio-opaque material in the gut suggestive of ingested lead paint (Fig. 3); however, this is not diagnostic, it gives no indication of how much lead has been absorbed and it may be negative if the paint is finely divided. Although



FIG. 3. Radio-opaque material in the gut of a child with pica for lead paint.



FIG. 4. Dense metaphyseal lines at the wrist of a child previously exposed to lead.

dense metaphyseal lines may be found in radiographs of the wrists or knees of children who have ingested lead (Figs. 4 and 5), it is seldom realized that these 'lead lines' are non-specific (Caffey, 1961) and may not appear until several months after exposure (Cooper, 1947). Negative skeletal radiographs do not therefore exclude the diagnosis of lead poisoning and the finding of 'lead lines' confirms only previous exposure and gives no information concerning soft tissue lead levels.

Cerebrospinal fluid

Lumbar puncture should be undertaken with extreme caution in children who have evidence of encephalopathy. The principal features are a raised pressure and protein content together with a moderate pleocytosis. The fluid is sterile and the glucose content normal.

Management

The three major objectives in management of lead poisoning are the prevention of further absorption, the removal of lead from the soft tissues and the prevention of recurrence.

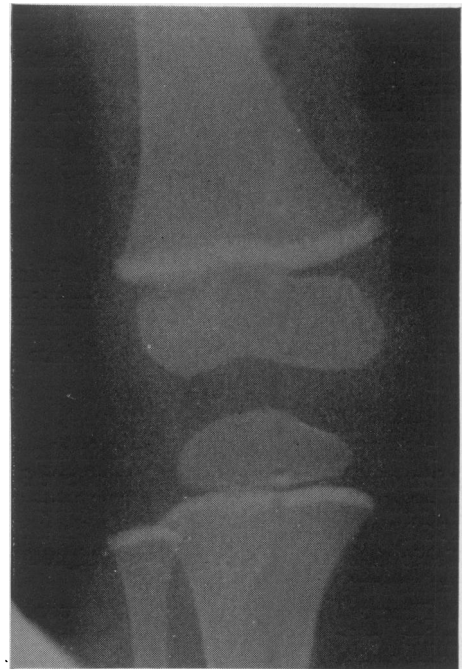


FIG. 5. Dense metaphyseal lines at the knee of a child previously exposed to lead.

Prevention of absorption

Further ingestion is prevented by removing the child from the source of the lead, usually by admission to hospital. Unabsorbed lead in the gut is removed by means of a saline purge. Under no circumstances should oral EDTA be given since this may enhance absorption of lead from the gut and precipitate encephalopathy.

Removal of soft-tissue lead

Three drugs with metal binding properties are in common use for the removal of soft tissue lead. They all tend to form metal-drug compounds or chelates, which are relatively non-toxic, and are excreted in the urine.

(a) *EDTA (calcium versenate, versene)*. This is administered as the calcium disodium chelate in a dose of 50–75 mg/kg body weight/day (i.m. or i.v.) for 5–7 days. The course may be repeated after an interval of 48 hr but this has no advantages over oral penicillamine. The calcium compound is employed since the sodium compound can cause a dangerous diminution of plasma ionized-calcium and induce tetany (Foreman, 1961). Renal damage has been reported after the use of the calcium compound.

(b) *D-Penicillamine hydrochloride*. This drug is administered orally in a dose of 20 mg/kg body weight/day and may be used simultaneously with EDTA. The 'L' and 'DL' forms of the drug are significantly more toxic than the 'D' form and should not be used. The long-term administration of the 'D' form has induced the nephrotic syndrome so that it should be discontinued as soon as possible.

(c) *BAL (British anti-Lewisite, dimercaprol)*. This may be given by intramuscular injection in oil in place of penicillamine, for example to the unconscious or vomiting child, in a dose of 4.0 mg/kg body weight 4-hourly on the 1st day decreasing to 2.5 mg/kg body weight daily by the 4th day.

The duration of treatment with metal-binding drugs should be determined by the clinical and biochemical response to treatment. The blood lead may remain high for many weeks in spite of treatment and coproporphyrinuria may also persist. The total duration of metal-binding therapy is usually between 2 and 6 weeks. Some of the soft tissue lead will be deposited in bone during the period of treatment with metal-binding drugs; however, there are at present no certain means available to enhance this process. A high calcium diet has been claimed to increase deposition of lead in bone but more evidence is needed concerning this. In the present state of knowledge vitamin D should not be given, and

agents that promote bone resorption, such as parathormone, should be withheld.

Lead encephalopathy

The principal objective of treatment as in other encephalopathies, is the control of cerebral oedema. This is attempted by:

(a) the immediate intravenous injection of dexamethasone 1.0 mg/kg body weight and continuing this daily in dividend doses;

(b) restriction of fluid intake to maintenance levels for 24 hr;

(c) the use of dehydrating agents such as 30% urea 1.0 g/kg body weight or mannitol 2.0 g/kg body weight.

Further measures include hypothermia and, where indicated, anticonvulsants. Although surgical decompression has been used, it is accompanied by a high mortality (Greengard *et al.*, 1961) and is not recommended.

Prevention of recurrence

The child should not be returned to his former environment until the source of the lead has been chemically identified and has either been removed or made inaccessible. Surfaces coated with lead paint should be stripped and repainted with paint that does not contain added lead. Merely repainting the surfaces without preliminary stripping is inadequate since continued gnawing will uncover deep layers of paint with a high lead content (Fig. 2). It should be stressed that in this country the sale of 'indoor paints' containing as much as 1% lead by weight in the dried film is still permitted and that there are no regulations to restrict the use of such paints in the home.

Recurrence of pica for lead-containing materials can be detected by means of faecal lead measurements. Children who have survived lead poisoning remain liable to recurrences due to the release of bound skeletal lead during infections or during metabolic stress. This tendency to recurrence may persist for at least 1–2 years after the original ingestion. Children who have been poisoned should therefore have blood lead and urine coproporphyrin levels monitored carefully, especially during episodes of intercurrent infection.

Prognosis

Children with encephalopathy have a poor prognosis, with or without treatment and mortality rates of 14% (Chisolm & Harrison, 1957) and 23.5% (Byers, 1959) have been recorded. Permanent cerebral damage is a common sequel to poisoning and 30% of survivors have been so affected (Levinson & Zeldes, 1939) in spite of

treatment with chelator drugs (Bradley & Baumgartner, 1958). Cerebral damage may not always be overt and 94% of surviving children have been found to have psychological abnormalities when subsequently tested (Mellins & Jenkins, 1955). A high incidence (27%) of chronic nephritis in adults who had lead poisoning in childhood has been reported (Henderson, 1954).

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