PEDIATRICS, Vol. 44, No. 2, August 1969

American Academy of Pediatrics
Subcommittee on Accidental Poisoning
Prevention, Diagnosis, and Treatment of Lead Poisoning in Childhood

Lead poisoning in childhood must be approached as a chronic disease requiring comprehensive, long-term, medical and social management of the child and his family throughout the preschool years. This is because of the combination of poor housing containing lead paints, childhood pica, and personal-social deprivation. New sources of lead, such as general contamination of the environment from industrial and motor car exhausts, must also be considered. While diagnosis and therapy are important, the pediatrician's professional responsibility to his patient and community must include prevention. An effective program for the prevention and management of childhood plumbism requires the coordinated and sustained efforts of pediatricians; health department personnel; allied health professionals, such as medical social workers and child guidance workers; the executive, legislative, and judicial authorities of the community; and the community itself.

Medical surveillance of the health of young children is almost as urgent a requirement in the case of the asymptomatic child with pica and an increased body burden of lead as it is for the child suffering from plumbism. Through such surveillance, dangerous conditions in the environment of the child can be discovered and eliminated, and the care of the threatened child can be maintained until the threat has subsided. In this manner, the incidence of the disease can be reduced ultimately to the vanishing point; meanwhile, fatalities can be prevented, and the damage to the brain of poisoned children, which often follows in the wake of lead encephalopathy, can be greatly diminished. Pediatricians have opportunities through health programs in urban areas to develop preventive techniques and to contribute significantly to the prevention of lead poisoning among children. The elimination of the hazardous conditions in the affected urban areas involves economic considerations of large proportions and requires professional and public understanding of the problems and determination within the community to subordinate immediate financial considerations to human preservation. Freedom from this disease can be procured when enlightened citizens are prepared to pay for the elimination or rehabilitation of defective housing in neglected areas of the cities.

The disease occurs most frequently in the United States in children 1 to 5 years of age who live in deteriorated, pre-World War II urban housing. Prospective surveys in various cities indicate that 10 to 25% of such children have absorbed potentially dangerous quantities of lead and that 2 to 5% have clinical symptoms compatible with those of acute intoxication. Sporadic instances arise out of unusual sources. The prevalence of the disease in rural areas and smaller communities is unknown. Acute toxic episodes occur most frequently during the summer months. Acute encephalopathy is the most serious complication; although mortality from encephalopathy can apparently be reduced to less than 5%,\textsuperscript{3,4} at least 25% of the survivors sustain permanent damage to the central nervous system as manifested by seizures, mental retardation, specific learning defects, and behavioral disorders.\textsuperscript{5,6}

An enlightened approach to prevention, diagnosis, and comprehensive treatment requires an understanding of the causative factors. These include pica, cultural and be-
behavioral patterns in children, widespread environmental exposure to lead in deteriorated housing, and certain aspects of lead metabolism. For each patient seen, the pediatrician must devise a coordinated plan which gives due attention to each of these factors.

CAUSATIVE FACTORS

Pica

The term pica may be defined as the habitual, purposeful, and compulsive search for and ingestion of such nonfood items as clay, plaster, laundry starch, ashes, putty, string, paint chips, paper, dirt, crayons, yarn, matches, and cigarette butts. Most children and adults with pica tend to be highly selective; each exhibits a craving for only a few of the aforementioned items. The studies of Lourie and his associates indicate that nutritional deficiency is not an etiologic factor in pica as seen in children in urban slums. Their studies further indicate that as many as 50% of the children from both middle class and lower social and economic groups habitually ingest things that are not food. The onset of pica occurs usually at about 1 year of age, and the habit tends to disappear between 3 and 5 years of age. The child with pica often stimulates similar behavior in younger siblings. As many as 50% of mothers of children with pica also have pica themselves.

The interaction between child and mother is often the critical factor in the development of pica in children. Lourie suggests that it is useful to view pica as an oral fixation that serves for the relief of the child's anxiety in response to an absent or poorly functioning mother. Emotional difficulties in the mother are often associated with the child's pica. Maternal dependency is the pattern most commonly observed; such mothers often have a life history of despair, passivity, and inactivity, except during crisis. In such a family, pica often goes unobserved by the mother so that the child with plumbism may escape early detection. Some mothers, especially those who have moved from rural to urban areas, may accept pica as normal behavior in their child. Others actively but unwittingly promote orality in their child.

Environment

The clear relationship between childhood plumbism and old, deteriorating urban housing is demonstrated by an investigation in Cleveland in which it was found that 27% of 801 children residing in old housing had absorbed abnormal quantities of lead and that 38% (4.7%) of these preschool children had symptoms of plumbism. Among the 105 comparable preschool children who lived in better housing, only three showed evidence of increased lead ingestion and none showed symptoms of plumbism. Comparable results using different parameters have been obtained in other cities. The usual location of leaded paints chewed by poisoned children are window sills, painted plaster, and walls. Common outside sources are painted door frames, fences, porches, and house walls. The interior woodwork, painted wallpaper, and painted plaster of houses built prior to 1940 and still in use may contain one or more layers of lead pigment paints that have never been removed. Lead pigments are still widely used in exterior paints. A few chips of such paint may contain 100 mg or more of lead. The safe daily intake of lead is estimated at less than 0.5 mg, although there is a difference in resistance to lead toxicity between, for example, males and females and adults and children. Studies in selected slum areas reveal that 50 to 70% of old houses contain dangerous quantities of flaking lead pigment paints on the painted interior surfaces. The physician should familiarize himself with the distribution of substandard housing in his area. The elimination of this hazard is within the province of local public health authorities and can be achieved through the adoption and enforcement of meaningful local regulations.

Metabolism of Lead

Lead intoxication in childhood usually results from the ingestion of lead. Repetiti-
tive ingestion (or inhalation) of small amounts of lead is usually far more dangerous than a single, massive exposure because such inorganic lead compounds are poorly absorbed into the body. Small amounts of lead are stored largely in bone over a period of time, and an excessive body burden of lead is only very slowly excreted. The studies of Kehoe show that at least twice as long a time is required to excrete an excessive body burden of lead as is involved in accumulation.

The biosynthesis of heme is exquisitely sensitive to the toxic effects of lead. Increased excretion of coproporphyrin (UCP) and δ-aminolevulinic acid (ALA) in the urine is virtually always found prior to the onset of clinical symptoms. The qualitative urinary coproporphyrin test (UCP) is perhaps best suited for clinic and emergency room use for the rapid, presumptive diagnosis of acute plumbism. This test should be available in all metropolitan hospitals serving high-risk urban areas, as it can be performed in a few minutes once urine is collected. The UCP test is almost always strongly positive when blood lead concentration exceeds 80 μg Pb/100 gm of whole blood in a toddler actively ingesting lead; however, at lesser concentrations of lead in blood, the UCP test is not sufficiently sensitive. For this reason, it is not ideally suited for mass screening techniques for the early detection of the child with asymptomatic increased lead absorption. Pending the wider availability of accurate blood lead determinations, the estimation of ALA in urine offers the best current technique suitable for mass screening. One serious limitation is the difficulty in obtaining random urine samples from young children, who are the ones at greatest risk. Preliminary data indicate that children actively ingesting lead whose blood lead concentrations are greater than 60 μg Pb/100 gm of whole blood can be detected by this technique with considerable accuracy, if 0.5 mg ALA per 100 ml of urine is used as the upper limit of normal for screening purposes. The determination of ALA in urine has been greatly simplified by the commercial availability of prefilled, disposable, ion-exchange resin columns. The detection of fluoresceins has been useful as a screening technique by those especially skilled in its use, but it does not appear to have the potentiality for widespread use in general hospital laboratories. Simplified techniques for ALA in serum and lead in hair are also under investigation.

### TABLE I

Laboratory Determinations Required for Diagnosis of Lead Intoxication in Children

<table>
<thead>
<tr>
<th>Test</th>
<th>Technical factors</th>
<th>Interpretation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Qualitative urinary coproporphyrin (UCP) test*</td>
<td>Peroxide-free ether required; test urine within 10 minutes after voiding.</td>
<td>Intense orange-red fluorescence (+++ or ++++) often associated with blood lead &gt;80 μg Pb/100 gm of whole blood and, therefore, is indication for immediate hospitalization and chelation therapy in symptomatic children even if all other presumptive tests negative. Test may give misleading negative results initially in moribund patients and severely iron-depleted children not regenerating heme. Moribund patients usually have glycosuria and other urine abnormalities.</td>
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TABLE I (Continued)

<table>
<thead>
<tr>
<th>Test</th>
<th>Technical factors</th>
<th>Interpretation</th>
</tr>
</thead>
<tbody>
<tr>
<td>X-rays</td>
<td>Use KUB technique; look carefully in rectosigmoid area for radiopaque fleas when rest of intestine appears negative.</td>
<td>Abdominal flat plate positive for radiopaque material in approximately 50% of symptomatic young children.</td>
</tr>
<tr>
<td>PA views of wrists and knees</td>
<td>Must be differentiated from growth arrest lines: “lead lines” at metaphyses are broad (&gt;2 mm) continuous bands of increased density whereas growth arrest lines appear as multiple narrow discrete lines; study films under bright light.</td>
<td>Interpret bone films with respect to child’s age:</td>
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<tr>
<td></td>
<td></td>
<td>A. &lt;2 yr: “lead lines” frequently absent in symptomatic children</td>
</tr>
<tr>
<td></td>
<td></td>
<td>B. 2-5 yr: “lead lines” usually present and may show “seasonal banding”</td>
</tr>
<tr>
<td></td>
<td></td>
<td>C. &gt;5 yr: “lead lines” rarely prominent.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Width of “lead lines” reflect duration of increased lead absorption but is unrelated to symptoms.</td>
</tr>
<tr>
<td>Hemoglobin, hematocrit,</td>
<td>Basophilic stippled cell count requires specialized technique not usually available in general hospital laboratories.</td>
<td>High usually &lt;10 gm; findings as in untreated iron-deficiency states, except reticulocytes often increased; basophilic stippled cell counts in peripheral blood of children too variable to be helpful, but basophilic stippling of normoblasts in bone marrow smears uniformly increased (&gt;50%) in plumbism in children and adults. Hematocrit required for interpretation of blood lead; since 90% of lead in whole blood is attached to red blood cell surface, correct blood lead data for very low hematocrits.</td>
</tr>
<tr>
<td>reticulocyte count, smear</td>
<td></td>
<td>Glycosuria (+ or ++) found in very chronic or very severe cases; very acute and severe cases often show proteinuria, hematuria, cellular casts, and leukocytes in sediment (important findings in critical patients if UCP test negative).</td>
</tr>
<tr>
<td>for morphology (basophilic</td>
<td></td>
<td></td>
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<tr>
<td>stippled cell count)</td>
<td></td>
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<tr>
<td>Urinalysis</td>
<td>UCP test takes precedence; use general reagents for reducing sugars (i.e., Clinist).</td>
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</table>

Specific Diagnostic Tests

| Whole blood lead              | Special lead-free needle, syringe and sample container must be used and often supplied by laboratory performing analysis; 10 ml lead-free B-D Vacutainer commercially available (Bectin-Dickenson). Draw enough blood (10 ml usually required) as insufficient samples may yield erroneously high results. | Normal unexposed children: 15-40 µg Pb/100 gm of whole blood |
|                              |                                                                                  | Mild symptoms may be present: 60-80 µg Pb/100 gm of whole blood |
|                              |                                                                                  | Symptoms may be absent but risk of encephalopathy great: >80 µg Pb/100 gm of whole blood |
|                              |                                                                                  | Result may be misleading (i.e., pretreatment values often within normal limits (>80 µg Pb/24 hours) in acute encephalopathy). Consider excretion >1.5 mg Pb/24 hours during first 24 hours of chelation therapy diagnostic of plumbism in symptomatic cases. |
| Urine lead output            | Use lead-free collection apparatus supplied by laboratory performing analysis. This test of limited value because quantitative 24 hour collection required in young children. |                                                                                  |
Fundamentally, the diagnosis of plumbism depends upon the demonstration of an excessive body burden of lead. In children, the most useful and direct index of this is blood lead concentration. Accurate determinations are a function of skill and experience, but they are essential and require both proper collection of samples and a laboratory experienced in blood lead determinations. Reliable results are not to be expected from laboratories in which only an occasional measurement of lead in blood or urine is made. At present, the ethylenediaminetetraacetate (EDTA) mobilization test for lead finds its application in research. Its interpretation is controversial. Interpretation of the various laboratory determinations required for diagnosis of lead intoxication in children is given in Table I.

**DIAGNOSIS**

Early diagnosis depends upon early identification of the high-risk child, the high-risk parent, and the high-risk dwelling. The child is a toddler with exaggerated oral activity. The parent is a mother with inadequate resources, either physical or emotional, to cope with her family's needs. The dwelling is a neglected housing unit with lead flakes within reach of a small child's grasp. The persistence of pica resulting in the ingestion of lead-pigmented paint chips for a period of 3 months or longer leads to the insidious onset of clinical symptoms and eventually, if not interrupted, to encephalopathy with frequent, permanent brain damage. Characteristically, clinical manifestations develop over a period of 3 to 6 weeks. Commonly, the child first exhibits progressive anorexia. He becomes less playful, less alert, and hyperirritable; this may be interpreted as a behavior disturbance. Careful observation may reveal developmental regression. The child may also become clumsy and even frankly ataxic. Many patients have an associated microcytic, hypochromic anemia resulting from deficient dietary intake of iron. During this early phase of illness, vomiting may occur intermittently. Brief self-limited convulsive episodes may also occur. Constipation and abdominal colic generally are not observed in a small child, but vague abdominal pain or discomfort are often present. If early lead intoxication is not recognized at this point and the child continues to ingest lead, acute encephalopathy may occur at any time, especially in the summer.

The fulminant form of encephalopathy develops precipitously in a period of 1 week or less. Vomiting becomes increasingly frequent, persistent, and forceful; it tends to occur within one half hour after the ingestion of food or fluid. The child's apathy and unwillingness to play progress to drowsiness and stupor, interspersed with lucid or hyperirritable episodes. Even at this point, the mother may interpret these symptoms as recurrent, severe temper tantrums. Finally, alterations in the state of consciousness progress at an even more rapid pace to coma and convulsions. Neurologic manifestations such as paralysis or weakness most commonly occur postictally. The clinical picture described here tends to develop more rapidly and acutely in children under 2 years of age. In older children, recurrent, but less severe, episodes are more likely and may suggest some degenerative cerebral disorder. In preschool children, lead poisoning must be considered in the differential diagnosis of behavior disorders, convulsive disorders, and mental retardation. Lead encephalopathy must be included in the differential diagnosis of tuberculous meningitis, viral encephalomyelitis, and other causes of acute, increased intracranial pressure. The peripheral neuropathy of plumbism is usually seen in older children and tends initially to affect dorsiflexion of the foot, producing foot drop.

Since the clinical manifestations of plumbism are nonspecific, the diagnosis depends upon an appreciation of the causative factors, a high index of suspicion, and the performance of definitive laboratory procedures as outlined in Table I. In the child with symptoms suggestive of plumbism, provisional diagnosis and the decision
to hospitalize the patient and institute chelation therapy promptly must be made at the time of the first clinic visit. One must bear in mind that the mothers of children with plumbism are likely to be “crisis oriented”; as such, they are likely to be unobservant, to miss scheduled clinic appointments, and not to return until the child is moribund. It is unusual for all of the listed laboratory tests to be positive in a given patient. Hence, there is a need for multiple procedures.

The diagnosis of acute lead encephalopathy can usually be made on the basis of clinical observation without resort to lumbar puncture. Some authorities believe that lumbar puncture should be avoided unless absolutely necessary for differential diagnosis. Because of the massive cerebral edema found in acute lead encephalopathy, lumbar puncture may entail a grave risk of herniation of the cerebellum. Cerebral edema may develop so rapidly that the classic signs of increased intracranial pressure (retinal hemorrhages, papilledema, and so forth) may not have developed at the time lumbar puncture is contemplated. In any case, if lumbar puncture is attempted, the smallest amount of fluid should be collected, dropwise, and never allowed to spurt out; 1 ml of cerebrospinal fluid is more than sufficient. In acute lead encephalopathy, the fluid shows normal sugar content, mild pleocytosis, and a moderate increase in protein content. Attempts to obtain fluid by ventricular tap are not warranted and usually fail.

**TREATMENT**

**Initial Therapy**

Immediate and permanent separation of the child from the sources of lead in his environment is essential for any child with an excessive body burden of lead. It is best to treat all symptomatic children as potential cases of acute encephalopathy and hence to begin treatment immediately before the results of the quantitative determination of lead in blood and urine are known. Where blood lead concentration exceeds 80 µg Pb/100 gm of whole blood, the risk of encephalopathy is great, even in asymptomatic children, so that such children should also be hospitalized and treated promptly. The highest reported survival rates in the treatment of acute lead encephalopathy are those reported by Coffin, *et al.* and by Chisolm. Both authors have followed the same general plan of therapy, which includes (1) the use of BAL and CaEDTA in combination, (2) restriction of parenteral fluids to basal requirements and minimal estimates for replacement of deficits resulting from vomiting and dehydration, (3) prompt institution of chelation therapy with no attempt to evacuate residual lead from the bowel by enema, and (4) judicious use of mannitol to promote initial diuresis in dehydrated patients and to ameliorate cerebral edema. The use of steroids for the relief of cerebral edema is controversial. Experimental evidence in animals suggests that steroids may enhance the renal toxicity of EDTA. For this reason, some recommend that steroids not be used. Surgical decompression for relief of increased intracranial pressure is clearly contraindicated. Where blood lead concentration lies between 60 and 80 µg Pb/100 gm of whole blood and there is hematologic evidence of lead toxicity but no clinical symptoms, EDTA gives satisfactory results. Preliminary information indicates that d-penicillamine given orally after lead is evacuated from the bowel may prove equally satisfactory. At present, d-penicillamine is considered an investigational drug when used in the treatment of lead intoxication.

**Long-term Therapy**

Long-term care is essential and, in many ways, is both the most difficult and the most important aspect of treatment. The first precept is: no child ever returns to a leaded house. This aspect of therapy requires the coordinated efforts of public health authorities to effect the removal of hazardous lead sources, assistance for the mother in her quest for safe housing, and, increasingly, mobilization of the community.
It has also been reported that patients maintained on oral d-penicillamine therapy during the first 3 to 6 months of convalescence do not experience toxic relapses during intercurrent infections. Phenobarbital and/or diphenylhydantoin sodium (Dilantin) are generally adequate for the control of seizure disorders that may follow lead encephalopathy. Recurrence of seizures without recurrent lead ingestion is usually indicative of a lapse in anticonvulsant medication. Both seizures and behavioral disturbances tend to abate during adolescence. Behavioral abnormalities resulting from central nervous system injury following lead intoxication can be greatly intensified by a persistently abnormal mother-child relationship.

**PREVENTION OF CHILDHOOD LEAD INTOXICATION**

The development of health programs in the poverty areas of most of the large cities in the United States offer an excellent mechanism for the institution of mass procedures for early recognition and prevention of childhood lead intoxication. To be effective, these programs must be supported by a local health department with appropriate personnel and laboratory at its disposal. Accurate blood lead determinations should provide the basis of any mass screening technique. Pending improvements in the analysis of lead in blood, the urine ALA test of Davis and Andelman and the analysis of lead in hair, which are currently under study, offer the best substitute for the purpose of mass screening. Further experience with both of these techniques is needed before a final evaluation of them can be made. For early detection, efforts should be concentrated on children 12 to 18 months of age. Each abnormal test calls for thorough clinical evaluation of the patient and, at the very least, a confirmatory blood lead determination.

In the absence of mass screening programs, early recognition depends upon identifying the child with pica and his dependent, depressed, overwhelmed, or unaware mother. Suspicion of lead poisoning and indications for blood lead analysis and other laboratory tests include: (1) pica in the child by history or observation either in the clinic or house; (2) symptoms of plumbism as outlined previously; (3) nutritional anemia, especially after 12 months of age; (4) aberrant behavior; (5) developmental delay, especially in speech development. Parental indications that increase the risk of lead poisoning in the child include (1) a working mother who finds it difficult to account for her toddler's activities during her absence; (2) the arrival of a newborn infant and possible lack of attention to the toddler; (3) depressed, psychotic, or alcoholic mother; (4) history of pica in the mother or previous children of the mother. In short, lead poisoning should be suspected when there is any evidence of lack of mothering of a toddler residing in a dilapidated, pre-World War II house. Hopefully, the elimination or proper rehabilitation of substandard housing, and the rebuilding of the inner core of our cities, will eliminate childhood lead poisoning as it is now seen. Until this is done, pediatricians responsible for the care of children residing in hazardous areas must be ever alert to this problem. This paper is offered as a guide to the essential ingredients of an effective program.

**REFERENCES**


PREVENTION, DIAGNOSIS, AND TREATMENT OF LEAD POISONING IN CHILDHOOD

Pediatrics 1969;44;291

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