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CHRONIC LEAD POISONING

A REVIEW OF SEVEN YEARS' EXPERIENCE AT THE CHILDREN'S HOSPITAL, DISTRICT OF COLUMBIA

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THE purpose of this article is to review seven years' experience with the problem of chronic lead poisoning in infants and children in a large children's hospital, and to consider this experience in the light of previous reports.

BACKGROUND

Lead poisoning is still a significant cause of mortality and morbidity in children. Although only 19 cases were reported by Millichap and associates[1] in Great Britain in the 50 years ending in 1952, most American reports indicate a much higher incidence.[2-8] Without question the most important cause of chronic lead intoxication in children is ingestion of lead-containing substances. Scattered small epidemics of acute intoxication due to inhalation of lead fumes from burning storage battery casings have been reported.[9] Of the substances ingested by children, the most widely reported are paint from walls and woodwork and plaster.[1-5, 7, 8] Other sources are painted furniture and painted or lead toys. In earlier times, lead nipple shields and body powders containing lead were common sources.

In most reported series, the age range of children with lead intoxication is from 1 to 4 years,[3, 5-7, 10] the time of life when incidence is highest for all acute toxic ingestions. However, since only small amounts of lead can be absorbed and retained at one time, the abnormal appetite, or pica, to cause toxicity, must persist for several months.

The psychological background of the pica associated with chronic lead intoxication has been studied by several authors[5, 7, 10] who have observed that most of these children lived in blighted or slum areas where flaking paint and loose plaster were abundant. In addition, personal supervision was limited because of the necessity for working parents to be away from home, the large number of children in the families, and the parents' ignorance of the dangers of lead ingestion. Although most of the children were apparently normal in intellectual and motor functioning prior to illness, they were often emotionally unstable and harder to handle than their siblings. The mother-child relationship was frequently abnormal as manifested by the

mother's indifferent or punishing attitude toward the child, her encouragement of the child's oral activity as a substitute for maternal attention, and/or occasionally significant emotional problems in the mother herself.

Most authors have noted a higher incidence of symptoms from lead poisoning in the summer months.[3, 4, 5, 7] Two possible reasons are: (1) the effect of increased solar radiation on the skin producing in the patient more vitamin D, which presumably aids in the absorption of lead, and (2) more frequent dehydration and acidosis which mobilize lead from depots.

There seems to be little correlation between the incidence of lead poisoning and sex or race of the patient.

A survey of geographical distribution of plumbism in children is currently being made by Dr. Howard M. Cann of the Clearing House for Poison Control Centers of the U. S. Public Health Service.

Symptoms, when present, almost always relate to the gastrointestinal or central nervous systems.[1-6, 8] Among the frequent and significant symptoms are anorexia, vomiting, constipation, abdominal pain, irritability, convulsions, drowsiness, incoordination, and pallor. Less commonly reported symptoms include personality change, tremors, and diarrhea. A prodrome of minor gastrointestinal symptoms, such as constipation or abdominal pain, and central nervous symptoms, such as lethargy, may precede by as much as two weeks the onset of more serious symptoms of vomiting, coma, or convulsions. Although the symptoms of lead intoxication are obviously nonspecific, their association with a history of pica may prove quite significant.

There are often no abnormal physical findings, especially when there is no severe central nervous system disease. Among the most commonly observed objective signs are pallor, motor weakness, coma, convulsions, papilledema, hyperreflexia, and ataxia.[1, 3-8] Respiratory center depression[11] and diaphragmatic paralysis[1] have also been reported. Lead lines on the gums, which are common in adult plumbism, are quite unusual in children.[12]

The pathologic changes due to lead intoxication are in general rather nonspecific.[3, 5, 13, 14] The brain may show edema, punctate hemorrhages, gliosis, and focal necrosis, while the liver and kidney may show characteristic acid-fast intranuclear inclusions as well as renal tubular cell abnormalities. A frequent finding is degeneration of anterior horn cells. When tissues have been analyzed for lead content,[3, 7] the bones have contained the highest concentration, the liver and kidneys next; the brain, even in the presence of severe clinical encephalopathy, contained the least amount.

In one of our cases of fatal lead encephalitis previously reported by Rice and associates,[13] no lead was extracted from the brain although high levels were found in bone, liver, and kidneys. These findings suggest either that lead is not a direct toxic agent to brain tissue, or that the brain is so sensitive that even minute amounts can cause significant damage.

Almost all children with chronic plumbism have a significant anemia with associated basophilic stippling of the red cells and elevated reticulocyte counts.[1, 3, 5, 6, 8] The stippling and anemia are possibly due to the interference by lead with the incorporation

of protoporphyrin into hemoglobin.[15] A recent report of lead intoxication in adults[16] notes that the erythroblasts in the marrow show consistent but not pathognomic changes. It has also been suggested[17] that the stipples might consist of protoporphyrin (possibly combined with lead). Coproporphyrin III is almost always found in increased concentration in the urine of patients with chronic lead intoxication,[3, 4, 17-20, 23] and there is a definite relationship of urinary concentration of porphyrins to the stippled red cell count but not to the degree of anemia.

Lines of increased density in the metaphyses of the long bones as seen by roentgenography are almost always present in children with plumbism.[3-5, 8] These lines are not diagnostic nor are they areas of increased lead deposition; actually they are areas of differential calcification.[21] Other bones may also show "lead lines"; Keefer and Mokrohisky[22] point out that careful study of routine chest roentgenograms may suggest the proper diagnosis.

The laboratory tests which confirm a diagnosis of chronic lead poisoning are the demonstration of abnormally high levels of lead in the blood and urine; i.e., above 50 to 60 μg per 100 ml. of blood, or above 80 μg per 1,000 ml. of urine, or per 24-hour specimen of urine. In children, whose 24-hour volume of urine excretion may be as small as 100 to 250 ml., it is more realistic to calculate lead excretion per liter of urine per 24 hours. The degree of elevation of these levels does not correlate with the severity of illness.[1, 3, 4, 15, 19, 21, 23]

Although there are many factors from history, physical examination, and laboratory study which are suggestive of lead intoxication, there is no single pathognomonic finding. Children may have no symptoms although their blood or urine lead concentrations are definitely above normal. Such children might receive a diagnosis of potential, subclinical, or asymptomatic lead poisoning. The most significant data for establishing a diagnosis are a definite history of pica for lead-containing substances, suggestive signs and symptoms, anemia with stippling, "lead lines" on x-ray, increased lead and coproporphyrin levels in the urine, and increased lead concentration in the blood. The final diagnosis rests on the clinician's judgment after evaluation of the data at hand.

Prior to the late 1940's, treatment of lead intoxication was directed at shifting lead from the blood and soft tissues to the bones, whence it could be excreted more slowly and under controlled conditions. Such therapy included diets high in calcium, phosphorus, and vitamin D followed by citric and other organic acids. Since 1950, dimercaprol (BAL) has been used with equivocal efficacy and potential toxicity.[1, 3, 4, 8, 12, 19, 21] In 1952, Bessman and associates[24] and Belknap[31] reported on the use of calcium disodium ethylenediamine tetraacetate (versenate, edathamil, or EDTA), a safe and effective chelating agent which binds lead into a nontoxic complex which is easily excreted in the urine.[3, 18-20, 23, 30] There has been mention of potential toxic effects of EDTA on bone marrow[21, 31] and renal function[24, 30] but these effects may have been coincidental and certainly have not been consistently reported. Although blood coagulation is prolonged in vitro by EDTA,[32] we have found

no reports of clinical bleeding dyscrasias resulting from use of this drug in therapy of plumbism. EDTA is quite effective when administered intravenously or subcutaneously, and probably when given intramuscularly, but no final agreement has been reached regarding the efficacy of its oral use. The dosage is now generally accepted to be 30 to 75 mg. per kilogram per 24 hours, but in the first published work it was 0.5 Gm. 3 times daily, regardless of weight. Most authors now suggest a plan in which the drug is given for 3 to 5 days, discontinued during a 2- or 3-day rest period, and then given for another 3 to 5 days. Since EDTA apparently combines with lead only in body fluids and soft tissues, the purpose of the rest period between courses of treatment is to allow the lead in the bone to re-establish equilibrium with the lead-depleted soft tissues. Rieders and associates[26] suggest intravenous therapy once weekly on an outpatient basis; however, cumulative excretion studies by Chisolm and Harrison[19] show that 4 or 5 days are required for deleading soft tissues. During EDTA therapy of lead intoxication, urine lead excretion may be increased from 10 to 100 times the pretreatment level.[18, 20, 23, 30] Hardy and associates,[20] working with adults, showed that in three normal patients the increase was only 6 to 11 fold compared with rises of 20 to 30 times in three patients with plumbism. Another good index of successful therapy is the drop in urinary coproporphyrin excretion.[18-20]

Reduction of cerebrospinal fluid pressure by mechanical methods has generally been a last resort in treating lead encephalopathy. Techniques used with varying success have been lumbar puncture[1, 19] and craniotomy.[3, 6, 18, 21, 22, 33] Results of more recent work suggest that when no improvement is evident during therapy with EDTA, extensive surgical decompression of the skull can be lifesaving and may even reduce potential residuals.[33]

The prognosis for life in chronic lead intoxication apparently depends more on severity and duration of illness than on type of therapy.[19] The usual mortality figures range from 10 to 25 per cent[2, 3, 5, 8, 25]; the fatal cases almost invariably were those with severe encephalopathy. The residual neurologic damage from lead intoxication is as distressing as the mortality. Significant sequelae have been reported in from 25 to 75 per cent of cases and include paralyses, blindness, and organic brain damage, especially in areas of visual-motor function and language skills.[2, 5, 8, 10] There is a much higher incidence of severe sequelae after severe encephalopathy,[19] but, in general, residuals are best correlated with continuing pica and, hence, continued active disease.[7]

DEFINITION AND CLASSIFICATION

During the period 1950 through 1956, 43 patients were treated at Children's Hospital, Washington, D. C., because of chronic lead poisoning. No cases of acute lead poisoning, such as is caused by inhalation of lead fumes, have been observed.

In the present study the diagnosis of lead poisoning was made on the basis of abnormal blood or urine lead levels prior to treatment and/or any two of the three following abnormalities: (1) pica of presumably lead-containing material, (2) punctate basophilic stippling of red blood cells on smear, or (3) markedly increased transverse densities in the metaphyses

of the long bones by roentgenography. Determinations of urine and blood lead levels were originally performed by hospital research facilities under the direction of Dr. S. P. Bessman, and more recently by the D. C. Department of Public Health Laboratory. No qualitative or quantitative urine coproporphyrin or stool lead studies were done.

An attempt has been made to group the patients into the following arbitrary classes: asymptomatic, lead intoxication without encephalitis, mild encephalitis, and severe encephalitis. The asymptomatic patients were children who had no apparent sign or symptom of lead intoxication but, during study of families of patients with plumbism or during study for other symptoms, were discovered to have a significant accumulation of lead within their bodies. The patients with simple lead intoxication had anemia and gastrointestinal complaints such as cramps or constipation. The severe encephalitic patients had prolonged convulsions or coma for as long as 24 to 48 hours, while the patients with mild encephalitis had central nervous symptoms and signs not including those of severe encephalitis.

TABLE I. TYPES OF CHRONIC LEAD POISONING IN 43 INFANTS AND CHILDREN, 1950-1956, AT CHILDREN'S HOSPITAL, DISTRICT OF COLUMBIA

TYPE		NO. OF PATIENTS		PER CENT
Asymptomatic		12		28
Clinical symptoms without encephalitis		14		32
Encephalitis		17		40
Mild	8		19	
Severe	9		21	
Total		43		100

Table I shows that approximately 28 per cent of our 43 patients were asymptomatic and 40 per cent of the children had lead encephalitis. Obviously the proportion of encephalitis patients in any given series will color the mortality and morbidity of such a series and thus the effectiveness of therapy.

INCIDENCE AND ETIOLOGY

Distribution of cases according to age, sex, color, and season coincide, in general, with the patterns reported by other authors. The age group from 2 to 3 years contained 2½ times as many children as any other year, and the 1- to 3-year age group contained 75 per cent of the patients in this series.

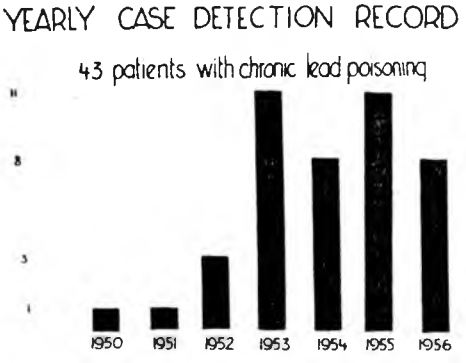

Fig. 1.—Annual incidence of lead poisoning at the Children's Hospital of the District of Columbia.

There was no significant difference in the sex incidence in this series, but a ratio of approximately 3 Negroes to 1 white patient reflects the fact that our clinic and ward population is predominantly Negro. Forty of the 43 patients resided in the District of Columbia. Thirty-eight of the 43 patients were diagnosed during the months of May through October. The recently increased yearly incidence of cases (Fig. 1) in all likelihood reflects our increased awareness and improved case finding. In 1952 and 1953, Dr. Bessman stimulated much interest at

Children's Hospital during his study of EDTA compounds and their value in therapy of chronic lead poisoning. In June, 1955, a Lead Poisoning Clinic was established, and in all probability our case finding will continue to improve.

When a history of pica is sought in children with chronic lead poisoning, it is almost always found. In this series 40 of 43 patients had a positive history of pica although in 11 of these children pica was sought only in retrospect after other suggestive laboratory data became available. Of the 3 patients with no history of pica, the parents of 2 consistently denied any pica, while the chart of the third gave no indication that pica had been inquired about.

Twenty-one of these 43 infants and children were studied carefully by members of our psychiatry department[35] who felt that although hand-to-mouth activity is a normal phase of personality development, pica, or excessive appetite for nonedible substances, should be considered abnormal after 18 months of age. In these 21 patients the average age of onset of pica was 14 months, and the average age of initial hospitalization was 31 months. Other authors have speculated that at least 3 months must pass from the onset of pica to the onset of symptoms of lead poisoning. In this series an average of 17 months elapsed before hospital admission. Siblings of 43 per cent, and mothers of 10 per cent, of these children also had pica. It appeared that pica in these children resembled an addiction and was usually selective for a particular substance. In contrast, indiscriminate pica was seen in this series only in children with severe brain damage.

Paint, plaster, and newspaper were the materials most commonly ingested by these children, but facilities for testing lead content of these materials have not been available to us. As in other series, the paint was usually on common accessible indoor materials such as walls, woodwork, and furnishings. Lead nipple shields, imported cosmetics, and lead-painted cribs were not incriminated. The lack of appreciation of the significance of pica was most striking in several of the families in which the children were quieted and pacified by being placed beside the favorite plaster hole. The ignorance of the dangers of pica was not confined to parents and patients, for in one case a mother sought medical advice because of her child's pica and was advised to avoid conflict by permitting him to continue.

SIGNS AND SYMPTOMS

The symptoms and signs of lead poisoning observed in this series of 43 patients are summarized in Table II.

TABLE II. SYMPTOMS, SIGNS, AND DIAGNOSIS ON ADMISSION OF 43 INFANTS AND CHILDREN WITH CHRONIC LEAD POISONING

	NUMBER
Symptoms on Admission	
Gastrointestinal	27
Neurologic	22
Infection	18
Behavior problem	17
Ingestion (of any foreign material)	5
Other	4
Findings on Admission	
Infection	19
Neurologic abnormalities	17
Normal physical examination	10
Pallor	6
Vomiting	3
Allergic manifestations	2
Gum lines	0
Lead Poisoning Considered on Admission	
Yes	28
No	15

The majority of the asymptomatic group were suspected of lead poisoning by virtue of a history of pica or a report of basophilic stippling in a peripheral blood smear while the patient was being treated for an infection. Three children were first seen after ingestion of kerosene, aspirin, and furniture polish, respectively; because of a positive history of pica, further studies were carried out. One child was admitted to the hospital by the hematology service because of a chronic anemia which had been resistant to iron therapy for over a year; this child had a positive pica history. One child had a gait disturbance by history; increased metaphyseal densities on the roentgenogram aroused further interest in lead poisoning.

In the groups with symptomatic lead poisoning, symptoms were almost all referable to the gastrointestinal and central nervous systems. Gastrointestinal complaints included vomiting in 19, abdominal pain in 8, anorexia in 6, constipation in 3, and diarrhea in 2. Neurologic complaints included convulsions in 13, irritability in 10, other psychiatric or behavior disturbances in 7, and gait or walking difficulty in 4.

On the basis of physical findings these children could be separated into three major groups: those with infection as a primary problem (44 per cent), those with a variety of neurologic abnormalities (39 per cent), and those with entirely normal physical findings (23 per cent). Some of the children who were seen primarily because of infection also had neurologic abnormalities. The incidence of neurologic abnormalities observed was: convulsions in 8, coma in 5, marked irritability in 4, positive Babinski sign in 4, nuchal rigidity in 3, nystagmus in 2, lethargy in 2, hemiplegia in 2, optic neuritis in 2, and abducens nerve palsy, aphasia, spastic paraplegia, spastic extremity, central deafness, and intraocular ophthalmoplegia in 1 each. Six of the 43 children had marked pallor on admission which focused attention on the hematopoietic system. An observation that deserves particular emphasis was the absence of lead lines on the gums in all patients.

LABORATORY DATA

A summary of the pertinent laboratory findings is presented in Table III. Undoubtedly the two most helpful diagnostic procedures, other than lead determinations, were hematologic and roentgenographic studies. Hematologic studies on admission were abnormal in 37 of the 43 patients. The most common abnormalities were anemia (below 10 Gm. of hemoglobin) in 35 children, basophilic stippling in 29, and eosinophilia (above 5 per cent) in 23. Although hemolytic crises have been described, all of the patients with anemia appeared to have the typical peripheral blood smears and indices of iron deficiency. Punctate basophilia deserves comment. Not all children with lead poisoning showed stippled red cells; of those who did, one-third showed stippling only after repeated smears were examined. Obviously, it is of considerable assistance to have a properly stained and prepared blood smear, an unhurried microscopic examination by a trained observer, and the verbal or written statement from the clinician to the laboratory regarding the possibility of lead poisoning. It was striking that eosinophilia was

present in this series in 23 patients on at least one smear during hospitalization. Two children with eosinophilia had allergic histories, and two had stools containing ova and parasites. The remainder of these patients were not carefully studied in this respect. One might speculate on the possibility that these children with pica might also have ingested dirt which contained ova. The leukocytosis present in 13 patients was associated with infection, and did not correlate with severity of lead intoxication.

TABLE III. LABORATORY DATA OF 43 INFANTS AND CHILDREN WITH CHRONIC LEAD POISONING

	NUMBER	
I. Hematology		
Normal (on admission)		6
Abnormal (on admission)		37
Anemia moderate (8-10 Gm. Hb/100 ml.)	19	
Anemia severe (below 8 Gm. Hb/100 ml.)	16	
Leukocytosis (above 15,000/mm.^{3})	13	
Basophilic stippling—		
First Smear	20	
later smears only	9	
Eosinophilia and/or stippling	33	
II. Urine		
Normal		28
Abnormal		15
Proteinuria	8	
Glucosuria	5	
Pyuria	8	
Hematuria	2	
III. Blood Sugar		
Normal		2
Elevated		5
IV. Spinal Fluid		
Normal		10
Abnormal		16
Protein increased	15	
Cells increased	9	
Sugar increased	3	
Pressure increased (Pressure normal—3)	4	
V. Electroencephalogram		
Normal (No encephalitis)		10
Abnormal (All encephalitis)		7
Focal	3	
General	4	
VI. X-ray Study		
Long bone		37
Normal	3	
Abnormal	34	
Skull		10
Normal	6	
Abnormal	4	
Abdominal flat plate		3
Normal	0	
Abnormal (all encephalitis)	3	

Urinalyses were abnormal in slightly over one-third of the group, but the majority of specimens were collected after use of indwelling plastic catheters. Glucosuria was present in 5 children.

A variety of blood chemistry tests was performed, but not in a significant number of patients. Five of 7 children tested demonstrated elevated blood sugar levels. In this regard one child had 11 urine tests positive for sugar and 3 of 10 blood sugar determinations were elevated (300 mg. per 100 ml., 165 mg. per 100 ml., and 255 mg. per 100 ml.). In this child a trial dose of insulin produced a series of convulsions and coma.

Abnormal spinal fluid findings occurred primarily in the group with encephalitis, and spinal fluid was obtained after onset of convulsions or coma. In some cases the spinal fluid abnormalities caused confusion as to possible aseptic meningitis or encephalitis of viral or fungal etiology. Of the 17 patients with clinical evidence of encephalopathy, 12 had abnormal spinal fluid findings, 4 had normal spinal fluid findings, and 1 was not tested. The remaining 4 patients with abnormal spinal fluid all had clinical lead intoxication without neurologic signs or symptoms.

Electroencephalograms were performed in a minority of the patients.

In 7 patients, who clinically were considered to have lead encephalitis, there were focal or general abnormalities on the electroencephalogram. In none of the 10 patients designated as "asymptomatic" or "simple lead intoxication" was there any electroencephalographic abnormality.

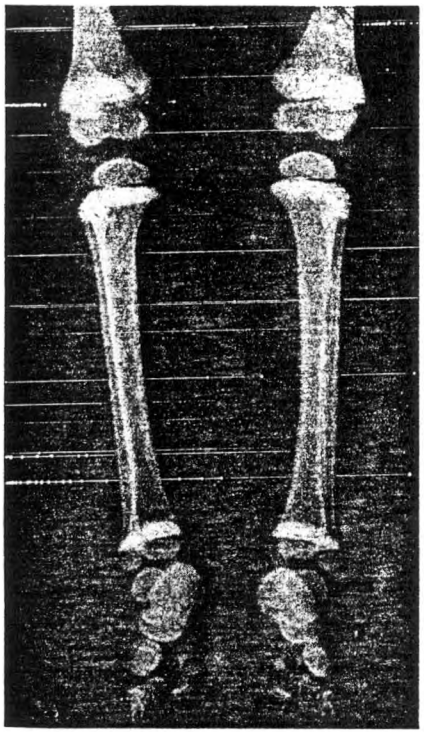

Fig. 2.—X-rays of the lower extremities of a patient with chronic lead poisoning, showing the increased densities at the metaphyses.

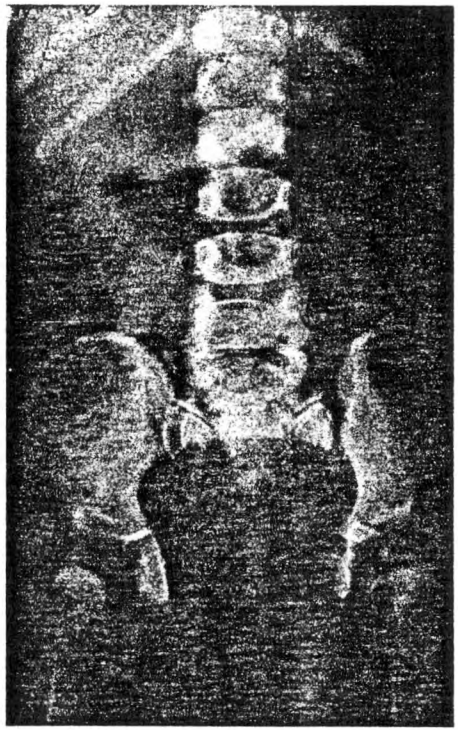

Fig. 3.—X-ray of the pelvis of a patient with chronic lead poisoning showing increased density of Ilian casts and ischia. Also note the density of the distal end of the right twelfth rib.

Roentgenographic studies, as mentioned previously, were of considerable assistance in establishing a working diagnosis. Increased metaphyseal densities can be seen in any of a variety of other diseases which cause a retardation of bone growth. Nevertheless, 34 of 37 long bone roentgenograms were interpreted as suggestive of heavy metal poisoning (Fig. 2). In this study, one chest roentgenogram, one pelvic roentgenogram (Fig. 3), and 4 skull roentgenograms demonstrated lines of increased density. In 3 children the presenting symptoms of vomiting, abdominal pain, or abdominal distention suggested a possible acute intestinal obstruction, but abdominal roentgenography revealed no evidence of obstruction. However, flecks of radiopaque material seen were felt to be fragments of lead-containing material (Fig. 4).

For the purpose of this study, a pretreatment blood lead level was considered suspicious in the range of 0.06 to 0.08 mg. per 100 ml., and toxic above this concentration; a pretreatment urine lead level was suspicious in the range of 0.07 to 0.15 mg. per liter per 24 hours, and toxic above

this range. Prior to treatment, 10 of 13 children tested had suspicious or toxic blood lead levels, and 15 of 20 children tested had suspicious or toxic urine lead levels. Only 5 of these 25 abnormal specimens were obtained from patients with encephalitis; this was because the first blood or urine sample from the majority of encephalitic patients was collected after EDTA therapy had already been instituted.

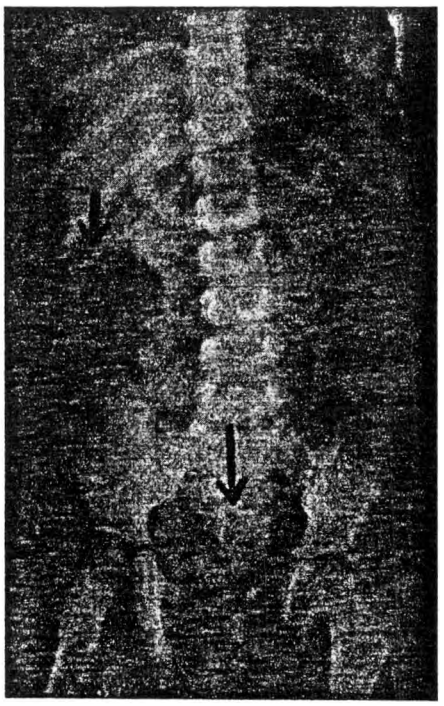

Fig. 4.—X-ray of the abdomen of a patient with chronic lead poisoning showing flecks of lead-containing material (paint) along the course of the intestines (arrows).

It has previously been observed that the level of lead in the blood or urine does not correlate well with the clinical picture, and such was our experience in this study. It had been thought that the first sample of blood or urine collected after the start of EDTA therapy might show a better correlation with the clinical picture, but this was not so (Table IV).

DIFFERENTIAL DIAGNOSES

Chronic lead poisoning was considered as a preliminary diagnosis in 28 of the 43 patients (65 per cent). Lead intoxication, like syphilis, sickle-cell disease, and infectious mononucleosis, can affect many systems and mimic many diseases. To illustrate this potential confusion in diagnosis, several examples might be offered. Three children were first thought to

TABLE IV. BLOOD AND URINE LEAD LEVELS BEFORE AND AFTER EDTA THERAPY OF CHRONIC LEAD POISONING

Blood Lead Levels
(mg./100 ml.)

	BEFORE EDTA THERAPY			DURING FIRST 24 HOURS OF EDTA THERAPY		
	0.02-0.06	0.06-0.08	>0.08	0.8-1.2	1.2-1.6	>1.6
Asymptomatic	1		3			1
Simple intoxication	1	1	2			1
Mild encephalitis		2	1		1	1
Severe encephalitis	1		1	1		2

Urine Lead Levels
(mg./L./24 hr.)

	BEFORE EDTA THERAPY			DURING FIRST 24 HOURS OF EDTA THERAPY			
	<0.07	0.07-0.15	>0.15	<0.7	0.7-1.5	1.5-2.2	2.2-3.0	>3.0
Asymptomatic	2	3	4		1	3	1	1
Simple intoxication	3	2	3	3		1	1	1
Mild encephalitis			2		2	1		1
Severe encephalitis			1	3		2		

have acute abdominal disease with possible intestinal obstruction; one child had a resistant anemia; one was treated as a diabetic. Poliomyelitis was diagnosed in another child with a spastic paraplegia resulting from chronic intoxication. It is of interest that children differ from adults with chronic plumbism in that the child's lower extremities are more commonly affected than his upper extremities.

MORTALITY AND PATHOLOGY

Three children (7 per cent) died (all with severe encephalopathy) after an average of 2⅓ days of hospitalization. Gross pathological diagnoses on one of these children[13] were edema and congestion of the brain, hepatic failure, pulmonary hemorrhage, and ascariasis. There were gross and/or microscopic changes in the liver, kidneys, and brain. Chemical analysis in this single case revealed the following lead concentrations (in milligrams per 100 grams of tissue): bone 9.96, kidney 0.8, liver 0.78, lung 0.10, brain 0.00. This reflects the previously noted poor correlation between clinical lead encephalopathy and chemical analysis of brain tissue. In the presence of marked anemia, the bone marrow of 2 children demonstrated marked erythroid hyperplasia.

THERAPY

This group of patients with chronic lead poisoning was treated with EDTA. No BAL was used. EDTA was given either intravenously or subcutaneously in the standard dosage of 30 mg. per kilogram per day; in the first 18 cases 0.5 Gm. was given 3 times daily regardless of weight. EDTA was given for 5 days, discontinued for 3 days, and then repeated for 5 days. In the present series no evidence of local or systemic toxicity from EDTA has been noted. In general, treatment has been dictated by the clinical status of the individual since the results of the chemical studies for lead were usually not reported for 1 to 2 weeks and then frequently did not correlate well with the severity of the symptoms. The most critical problem in therapy is the management of the child with lead encephalopathy who is in status epilepticus or coma. Craniotomy and reduction of spinal fluid pressure by repeated lumbar puncture have not been used consistently in our patients and we have too few data on which to base conclusions as to their efficacy. Intensive supportive nursing care, parenteral anticonvulsants, restricted parenteral fluids, and parenteral EDTA have been the mainstays of therapy. Oral EDTA has not been used in recent years because preliminary work showed very little promise.

CASE FOLLOW-UP

Follow-up of this group of patients is shown in Table V. It is important to note that one-fourth of the patients have been lost to follow-up. The persistence of pica, which would seem the crux of the problem, has unfortunately not been adequately followed, although our lead clinic is vigorously pursuing this problem now. In light of the thought that the severe neurologic residuals of lead encephalopathy might be due to repeated or continued poisoning, our series may be significant in that only 1 of 43 children went to a convalescent or lead-free home on discharge from the hospital. The other children returned to their parents and previous environments. It would

seem that safer housing for the entire family would be more feasible than the use of convalescent homes in preventing recurrent plumbism. This, of course, brings the problem into the realm of public health, sociology, and the law. We have seen recently that our social worker has been able to give affected families effective help in finding more satisfactory housing.

techniques.[35] As a result of those evaluations, the children were classified as having severe, moderate or no organic psychiatric residuals. It was the consensus of these workers that psychologic testing was the most efficient method of assessing mild to moderate degrees of organic brain damage. Three children were not tested psychologically, and on the basis

TABLE V. FOLLOW-UP OF 43 PATIENTS WITH CHRONIC LEAD POISONING

	ASYMPTOMATIC	CLINICAL SYMPTOMS NO ENCEPHALITIS	ENCEPHALITIS		TOTAL
			MILD	SEVERE	
Death	0	0	0	3	3
No follow-up	4	5	2	0	11
Follow-up	8	9	6	6	29
Pica continued	2	2	2	3	9
Pica stopped	1	4	2	1	8
Pica unknown	5	3	2	2	12
Well	5	8	3	0	16
Moderate residual	3	1	0	1	5
Severe residual	0	0	3	5	8

In this series of 43 patients, 3 children died and at least 13 others have moderate or severe neurologic and or psychologic residuals. Of the group of 17 children with encephalitis, 2 have not been followed, 3 are well, 9 have moderate or severe residuals, and 3 are dead. Forty-five per cent of the 29 children who survived and were followed up show residuals. This is a far grimmer picture than that painted by other recent reports[2, 5, 7, 8, 10, 19] and merits further study. The use of psychologic studies in this series may, perhaps, account for a part of the difference.

A group of 21 children who had recovered from lead intoxication were evaluated here on the basis of interviews with the parents, playroom sessions with the child, and by psychologic testing in the realms of intelligence, social maturity, and projective

of other studies it could not be determined whether they had no residuals or moderate residuals. Of the remaining 18 children, 8 had had encephalitis, and all had residuals (1 moderate and 7 severe). Of the 10 children who had had lead poisoning without encephalitis, 5 had moderate residuals and 5 had none. It is impossible, of course, to be certain how much of this brain damage is a result of the lead poisoning and how much may have preceded it. We know that one child was definitely retarded before the onset of his lead poisoning; 3 others had histories compatible with possible pre-existing damage, e.g., traumatic premature birth or bizarre autistic-type behavior. All 4 of these children fell into the group with severe residuals. Nevertheless, the residual morbidity resulting directly from chronic lead poisoning is truly shocking. The

variation between our results and those in the literature may suggest any of the following: (1) a difference in the population studied, (2) significant difference in therapy, (3) difference in the measuring devices and norms in the follow-up of these children, or (4) a combination of all these factors. We feel that the third alternative is the most plausible in the problem of plumbism.

The Lead Poisoning Clinic, which was established as a result of interest at this hospital in the problem of plumbism, is staffed by a team consisting of a pediatrician, a pediatric resident, a psychiatrist, a psychologist, and a social worker. The clinic provides a means of screening all pica cases, of standardizing in-patient therapy, and of better following patients discharged after treatment. When necessary, psychiatric assistance has been offered with greater parental acceptance of the team approach than of direct psychiatric referral alone. With psychiatric help, many of the parents are better able to handle their children's needs, and as the pica of these children becomes less of a problem, their lead intoxication tends to disappear.

SUMMARY AND CONCLUSIONS

The experience at Children's Hospital in the management of 43 children with chronic lead poisoning over a 7-year period is presented. The observed mortality of 7 per cent in 43 patients is significantly high even though it is an improvement over that noted in many previous reports. More important, the 45 per cent incidence of neurologic and psychiatric residual morbidity deserves serious consideration and further study. Chronic lead poisoning has become an increasingly significant problem as awareness of the diagnosis, treatment, and residuals has increased. Because lead encephalitis is an important killer and crippler of children, early diagnosis and therapy (with EDTA), as well as adequate and continued follow-up, are essential. The simple expedient of routine inquiry into the presence of pica will bring to light many cases of plumbism before they become symptomatic. Furthermore, counseling directed at cessation of pica seems to be an effective tool in prevention of continued lead poisoning. Perhaps even more important are the roles of the private physicians, public health authorities, and lawmakers in preventing the occurrence of this dangerous disease through education of the public, inspection and proper repair of substandard housing, and more stringent laws regarding lead-containing paints.

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