Therapy 1855

AMBULATORY TREATMENT OF LEAD POISONING: REPORT OF 1,155 CASES

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ABSTRACT. Subjects with lead concentrations greater than 50 μg per 100 ml whole blood were referred to a municipal lead poisoning clinic for evaluation. Chelating agents were administered when two blood lead levels were more than 50 μg, or calcium disodium edetate (EDTA) provocative test yielded over 1,000 μg/l of lead in the urine in the succeeding 8 hours. Therapy was on an ambulatory basis. Patients with moderate encephalopathy were hospitalized. Intramuscular EDTA, oral penicillamine, or the two drugs in sequence were given to 582 patients in 1967 and to 573 patients in 1968. Clinical evidence of lead intoxication was present in 103 or 8.9% of the 1,155 patients. Several drug reactions to penicillamine were observed, but none to EDTA, and mortality dropped due to early detection and detoxification of subclinical cases of lead poisoning. *Pediatrics*, 46:389, 1970, LEAD POISONING, AMBULATORY TREATMENT OF LEAD POISONING, EDTA IN TREATMENT OF LEAD POISONING, PENICILLAMINE IN SUBCLINICAL LEAD POISONING.

In October 1966, the Chicago Board of Health initiated an extensive case-finding program to detect incipient lead poisoning in an estimated 150,000 children at risk in high incidence neighborhoods.[1] The test used was blood lead determination by atomic absorption spectroscopy. A specialized clinic was opened January 1, 1967 for the evaluation and treatment of all subjects found to have elevated blood lead values.

The undertaking burgeoned far beyond what was anticipated. Nearly 4,000 children with lead values of 50 μg per 100 ml of whole blood were detected during the first 2 years of the program and referred to the clinic for evaluation. Approximately 85% responded. An additional 1,500 children under 5 years of age were admitted to the clinic for lead values between 40 and 49 μg/100 ml. Satellite cases, physician referrals, and a pica-free group with severe iron deficiency anemia, hematocrits ranging from 12% to 25% as discovered by the screening test, comprised another 200 patients.

The structure of the clinic, guide lines used in case selection and treatment, and the results obtained are presented here.

THE LEAD POISONING CLINIC

The clinic occupies a wing in the Municipal Contagious Disease Hospital. It is staffed by a pediatrician, two registered nurses, one licensed practical nurse, an aide, a clerk, and an x-ray technician. During the summer the staff is augmented by a second physician and practical nurse. The clinic is open Monday through Friday from 8:00 A.M. to 4:00 P.M.

Clinic appointments are made by the head nurse, who reaches the parent by telephone whenever possible, by letter, through home visit by the neighborhood Urban Progress Center representative (UPC "rep"), or the district health nurse. All values over 80 μg are considered urgent and the parent is contacted immediately to determine whether the child has symptomatic lead poisoning. When a parent is unable or refuses to bring the child to the clinic, she usually gives permission to the UPC "rep"

(Received September 11, 1969; accepted for publication April 23, 1970.)

Supported in part by Children and Youth Project 601, Children's Bureau, Social and Rehabilitation Service, U.S. Department of Health, Education and Welfare.

M.J.O'C. was Commissioner of Health, City of Chicago.

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TABLE I

DIRECTIONS FOR THERAPY

Blood Lead Values	*Disposition*
60 μg or more in two samples	Intramuscular EDTA
50 to 60 μg in two samples	Oral penicillamine
40 to 50 μg in two samples	
if no longer exposed to lead hazard	Discharge
if exposure continues and	
EDTA provocative test is negative	Retest every 3 months
EDTA provocative test is positive	Oral penicillamine

to escort the child to the clinic for evaluation and treatment. Even if successive initial appointments were broken, eventually 90% of the children with lead values over 60 μg were brought to the clinic.

History, physical examination, and laboratory studies are completed at the initial visit. Five milliliters of venous blood are again submitted to the City Clinical Laboratory where lead content, hematocrit, G6PD, and hemoglobin electrophoresis are determined routinely on every sample. Urine is examined for sugar, protein, and cells. Urinalysis is repeated at every visit while the patient is receiving chelating agents. Roentgenograms are taken of the abdomen and wrists, and the wet films are interpreted to the parents.

If lead values are between 40 and 60 μg, a provocative test is performed with calcium disodium edetate (EDTA) based on the therapeutic dose of 50 mg/kg. A fraction of all urine excreted in the succeeding 8 hours is analyzed for lead content. Values over 1,000 μg/l are considered abnormal.[2] Mothers are provided with perineal bags for children not toilet trained to assist in collection of specimens. The aide instructs in proper application of perineal bags.

All patients are treated on an ambulatory basis, including those with mild encephalopathy. Sick children have 24 hour access to the clinic physician by using a telephone.

Patient observation varies from a minimum of 3 months to several years. The child is discharged when blood lead has fallen below 50 μg on two consecutive occasions at an interval of at least 1 month, and when his environmental hazard has been corrected. If his blood lead does not drop at any one visit as anticipated, he is recalled for an x-ray of the abdomen to check for radiopacities suggestive of recent lead ingestion.

INDICATIONS FOR THERAPY

An empirical concept of asymptomatic lead intoxication was evolved during the initial months of the clinic's operation. Increased exposure was assigned a value of 40 μg, and intoxication was given a value of 50 μg. Directions for therapy were established (Table I).

TABLE II

TREATMENT OF LEAD POISONING WITH PENICILLAMINE (CASE 1)

Date	*Blood Lead (μg/100 ml)*	*Hematocrit (%)*	*Comments*	*Treatment*
5–11	67	28	screening value	
5–16	58	27	x-ray: abdomen negative metaphyses 2 mm lines recalled for chelate therapy	bottle feedings discontinued iron 15 mg t.i.d.
6–5	64	32	landlord repaired apartment	PNC 125 mg b.i.d. for 28 days
7–11	57	37		PNC 125 mg b.i.d. for 28 days
8–8	39	39		PNC 125 mg b.i.d. for 28 days
9–10	40	38		PNC 125 mg b.i.d. for 28 days
10–28	32			discharged

TABLE III

TREATMENT OF LEAD POISONING WITH EDTA (CASE 2)

Date	*Blood Lead (μg/100 ml)*	*Hematocrit (%)*	*Comments*	*Treatment*
6–15	115	29	screening value	
6–19	130		x-ray: abdomen filled with particles 3 mm line at metaphyses	EDTA for 5 days fleet enema iron 15 mg t.i.d.
6–20			urine: 5,450 μg/l	
7–8	158			EDTA for 5 days
7–5			x-ray: many opacities in intestine	fleet enema EDTA continued
7–17	80		landlord repaired apartment	EDTA for 5 days
7–30	24		pica has ceased	
8–22	34			
10–8	48			
11–8	46	33	failed subsequent appointments	

THERAPEUTIC REGIME

Two chelating agents are employed, EDTA and penicillamine. Selection of the drug depends on the initial lead concentration. The drugs are not used concurrently.

EDTA is given in 5-day courses, 50 mg/kg, administered once daily. It is injected into the anterior thigh muscles, with 1 ml of 1% procaine added to the syringe. Urine is collected for 8 hours after each injection, and a 2 oz aliquot is submitted the following morning for lead analysis. Blood lead is determined the day treatment is initiated and again 1 week after the fifth injection. The 5-day course is repeated until levels drop to 60 to 70 μg/100 ml. Blood is tested every clinic visit, with the exception of the second through fifth day of a course of EDTA.

PNC is given orally in 4-week courses. The dose is 125 mg, two or three times daily, averaging 20 to 25 mg/kg. One-half the contents of a 250 mg capsule is offered in a palatable medium, such as juice, "pop," or

TABLE IV

TREATMENT OF LEAD POISONING WITH EDTA FOLLOWED BY PENICILLAMINE (CASE 3)

Date	*Blood Lead (μg/100 ml)*	*Hematocrit (%)*	*Comments*	*Treatment*
6–25	140		Value obtained at referring hospital	
6–28	94	27	x-ray: several particles in abdomen 1 mm line at metaphyses	bottle feedings discontinued iron 15 mg t.i.d. fleet enema EDTA for 5 days
6–29			urine: 17,600 μg/l	
7–11	69			EDTA for 5 days
7–12			urine: 12,800 μg/l	
7–25	64	37	apartment repaired	PNC 125 mg b.i.d. for 28 days
9–4	40			PNC 125 mg b.i.d. for 28 days
10–10	27			PNC 125 mg b.i.d. for 28 days
12–13	24	35		discharged

TABLE V

INITIAL BLOOD LEAD LEVELS OF PATIENTS TREATED IN 1967 AS COMPARED TO 1968

Year	40–69 μg	70–99 μg	100–219 μg	Total
1967	210	292	80	582
1968	383	165	25	573
Total	593	457	105	1155

jelly. Blood is tested for lead after 4 weeks and the drug continued until the level remains below 50 μg for two consecutive months. When prolonged treatment is required, PNC is given for 3-month periods, followed by a medication-free interval of 1 month. Patients with high initial lead levels who receive EDTA may be transferred to PNC when lead values drop to 60 to 70 μg range.

Dimercaprol (BAL) is used only in patients requiring hospitalization for encephalopathy. It is given as intramuscular injections, 2.5 mg/kg every 4 hours for 5 days and is used concurrently with EDTA, 75 mg/kg, given in divided doses over 24 hours.

If opacities suggestive of lead are noted in the intestine on x-ray, the parent is given instructions to administer an enema packet (provided by the clinic) to the patient at home. EDTA is not withheld pending evacuation of the paint or plaster.

Iron deficiency anemia is frequently encountered and is almost invariably associated with prolongation of bottle feedings beyond infancy. It is treated with oral iron concentrates, 0.6 or 1.2 ml, equivalent to 15 to 30 mg elemental iron three times daily, elimination of bottle feedings, and decrease in milk to 1 pint daily.

CASE HISTORIES

Because of lack of guide lines for use of PNC in children with lead intoxication, an empirical method was devised, as illustrated by Case 1. This was an anemic but otherwise asymptomatic 17-month-old girl with a history of plaster ingestion. She drank five 8 oz bottles of milk daily. Laboratory findings and treatment are given in Table II. Delay in initiating deleading therapy was due to the mother's failure to keep earlier appointments.

Case 2 represents treatment with EDTA alone (Table III). This was a 27-month-old girl who continued to eat plaster from the walls for 2 weeks after the initial visit, when the apartment was repaired by the landlord. She remained asymptomatic even during the period of rising blood lead. Pica ceased a month after treatment began when the child learned to relate the painful injections to putting objects into her mouth.

EDTA followed by PNC for several months was the therapeutic approach utilized for most patients with initial lead concentrations above 70 μg. Case 3 was an 18-month-old boy referred from another hospital with a blood lead value of 140 μg. His twin sister's history paralleled his, although her lead concentration was only 66 μg. Both children ate crumbling plaster from the walls. They were "poor eaters," but drank six, 8 oz bottles of milk daily. Symptoms of lead poisoning were absent. Laboratory data and treatment are summarized in Table IV.

RESULTS

Comparison of Blood Lead Levels of Patients Treated in 1967 and 1968

The marked decline of lead values over 50 μg in the screened population, from 8.5% in 1967 to 3.8% in 1968, was reflected

TABLE VI

CLINICAL FINDINGS IN 1,155 PATIENTS JANUARY 1, 1967, TO DECEMBER 31, 1968

Data	1967	1968	Total	Percentage for 2 years
Patients treated	582	573	1,155	100.0
Pica for paint, plaster	458	443	901	78.0
Metaphyseal lines	459	494	953	82.5
Opaque material in gastrointestinal tract	205	202	407	35.2
Urine lead 1,000 μg/l	258	297	555	48.0
Symptoms of lead poisoning	71	32	103	8.9

in the lead values of patients treated with chelates (Table V). Comparison of blood values for the 2 years shows 372 (64%) of the patients had 70 μg or more in 1967, in contrast to 190 (33%) in 1968, although the number treated was roughly the same in both years. In the range of greatest hazard—between 100 and 220 μg—there were 80 patients (14%) in 1967 compared to 25 (4%) in 1968. Beginning August 1, 1967, more emphasis was placed on treating children with values between 50 and 60 μg, thus accounting for the increase in this area in 1968.

Seasonal Variation in Blood Lead Levels

During the period of this study, 676 (58.5%) of the patients were treated in the 4 months from June through September, and 479 (41.5%) were treated in the remaining 8 months of both years. There were 83 patients in the "off-season" in 1967 with lead values from 80 to 220 μg and 24 in 1968 with a range of 80 to 130 μg in the same period. The etiology of seasonal variation in blood lead levels remains obscure.

Clinical Findings in 1,155 Patients

Although blood lead values were lower in 1968 than in the previous year, there was a remarkable similarity in the number of children with pica and clinical findings in both years (Table VI). Pica was observed in 78% of the patients who had eaten paint, plaster, or putty. Radiopaque particles in the intestine, presenting a transitory clue to pica, were seen in 35% of the patients, as well as in many children whose tests were below the level requisite for chelate therapy.

Metaphyseal lines at the wrist and proximal femur, graded according to width in millimeters, were present in 82.5%; however, width of the line could not be correlated with symptoms, elevation of blood lead, or reported period of ingestion. Lines less than 1 mm were considered as negative; those of 1 mm in association with other findings as positive; lines of 2 mm were con-

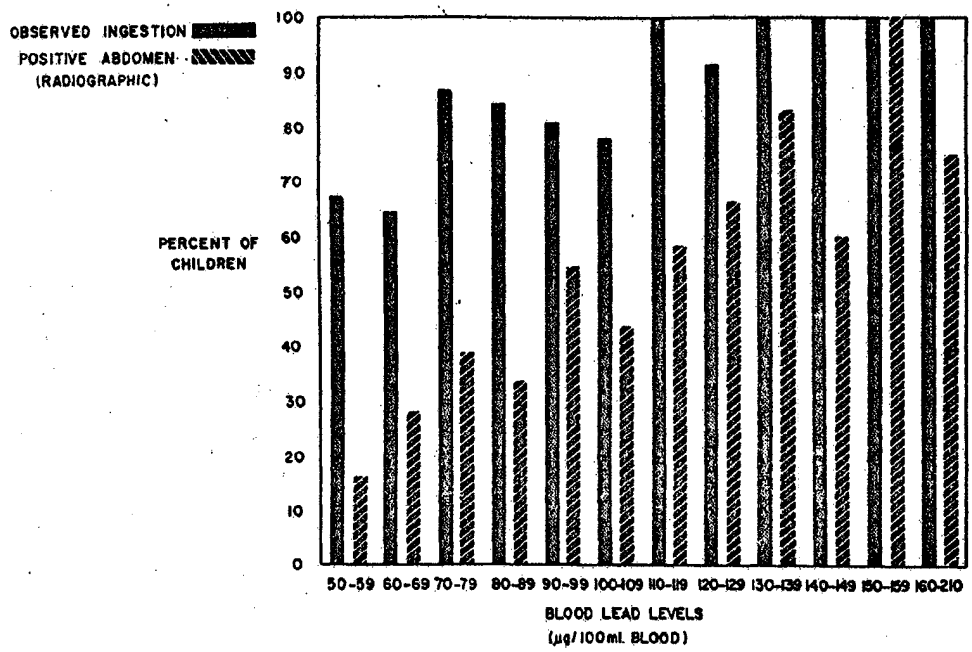

FIG. 1. Number of children observed to eat paint or plaster correlated with the number demonstrating abdominal radiopacities, at blood levels ranging from 50 μg to 210 μg.

TABLE VII

MANIFESTATIONS OF LEAD TOXICITY OBSERVED IN 103 PATIENTS

Symptom	*Instances*
Fatigue	2
Stupor	2
Ataxia	9
Gastrointestinal	12
Vomiting	28
Irritability	33
Drowsiness	38
Total	124

sidered as definite evidence of lead ingestion.

Urine specimens containing at least 1,000 μg/l of lead were submitted by 555 of the 608 patients who received EDTA. Data on urine lead for patients receiving PNC are not presented here because the number of dependable 24-hour collections was inadequate for meaningful evaluation.

History of Pica Compared to Abdominal Opacities on X-ray

Ingestion of paint or plaster was observed in 78% of all patients, the incidence rising from 65% in the 50 to 59 μg group to nearly 100% over 110μg (Fig. 1). Likewise, radiographic evidence of ingestion was noted at the initial visit of 17% in the 50 to 59 μg range, rising to 60% to 100% in 10 μg increments over 110 μg. The presence of particles in the gut on the day of evaluation was generally associated with a higher blood lead than the one obtained in the screening study.

TABLE VIII

AGE DISTRIBUTION OF 1,155 PATIENTS

Age (yr)	*1967*	*1968*	*Total*	*Percentage*
Under 1	1	1	2	0.2
1	192	217	409	35.4
2	215	212	427	36.9
3	102	83	185	16.0
4	48	42	90	7.8
5	17	13	30	2.6
6 and older	7	5	12	1.1

Manifestations of Lead Toxicity in 103 Patients

Symptoms of lead intoxication were encountered in 103 (8.9%) of the 1,155 treated children (Table VII). There were two manifestations of equal importance in 21 of those children. Drowsiness and vomiting was the most frequent combination. Convulsions occurred in three of the screened patients whose lead values were over 200 μg. They were hospitalized directly by the clinic pediatrician on being advised of the excessively high lead values. These children were not seen at the clinic.

Age Distribution

Seventy-two percent of the patients were almost equally divided between 1- and 2-year-olds. Sixteen percent were 3-year-olds and 7.8% were 4-year-olds. An older sibling of 5 or 6 years occasionally followed the example of a younger one in picking plaster off the wall. Persistence of pica for paint and plaster was not observed in children older than 5½ years, although several children between age 5 and 7 had a residual lead burden from previous ingestion high enough to warrant chelate therapy (Table VIII).

Number of Patients Treated with Each Chelate Regime

Each patient was treated by one of three chelate regimes: PNC, EDTA, or both used in sequence (Table IX). PNC was used as the sole chelating drug in 47% of the patients, all of whom had a lead content under 70 μg. EDTA alone was used in 13% of the patients. In 39% therapy was initiated with EDTA then continued with PNC after the blood lead had decreased to the 60 to 70 μg range.

Complications Due to Use of Chelates

There were no significant complications from the use of EDTA. Drowsiness was noted occasionally in the afternoon following the initial one or two injections. This

condition apparently was not related to concentration of blood lead. Transient hematuria appearing in one specimen only was observed in six patients. No infections occurred at injection sites. A tender, nonsuppurative nodule developed in one child but disappeared in a few days.

Reactions to penicillamine were few but tended to be more serious than to EDTA. Several patients experienced vomiting or diarrhea, although not simultaneously, but nearly all were able to resume the drug after a few days' interruption. About 0.5% developed pruritic urticaria. In two patients, the eruptions resembled erythema multiforme and erythema annulare and were accompanied by high fever. A third child had generalized angioedema without proteinuria. All children with dermatologic complications responded well to oral antihistaminics and withdrawal of the drug. Most PNC complications occurred in the first week or two of medication. However, one child entered another hospital with a 2-week history of progressive edema after taking PNC for 3 months. Proteinuria was present and a diagnosis of nephrosis, possibly due to PNC, was considered. She had a spontaneous diuresis shortly after entering the hospital and was discharged without a renal biopsy.

Although chelation therapy was not withheld while the gut was emptied of radiopaque material, no aggravation of symptoms or increase in blood lead was noted. Febrile illness was not observed to produce an increase in blood lead or to precipitate acute encephalopathy.

Venous samples were obtained more than 20 times in some patients during the course of treatment, but no instance of thrombophlebitis was encountered.

Complications Due to Asymptomatic Lead Poisoning

The effect of lead in producing mental retardation in asymptomatic patients has yet to be thoroughly evaluated. Delay in the appearance of speech beyond the third birthday and behavior problems were present in about 1.5% of the patients studied; however, some of these children were slow to achieve early developmental objectives before the onset of pica. No gross neurological defects or nonfebrile seizures developed in any patients up to the time of discharge from the clinic. Several parents of seemingly "asymptomatic" patients reported improvement in behavior and language ability after a course of therapy. This indicates the difficulty in recognizing deterioration in a chronic disease such as lead poisoning.

TABLE IX

NUMBER OF PATIENTS TREATED WITH EACH CHELATE REGIME

Chelate	*1967*	*1968*	*Total*	*Percentage*
Penicillamine	252	295	547	47.4
EDTA	112	42	154	13.3
EDTA—Penicillamine	218	236	454	39.3
	582	573	1,155	100.0

Recurrence

Recurrent ingestion, as established by history obtained from the mother, by repeat x-rays of the abdomen, and by secondary rises in blood lead levels, was observed in 3% of our patients. None developed symptoms of intoxication before treatment was reinstituted.

CONCLUSION

In the 6 years from 1960 through 1965, during which time some screening for lead poisoning was carried out in the city's infant welfare clinics utilizing coproporphyrinuria for case detection, 1,081 cases were reported with 110 deaths.[3] In 1966, when public health and volunteer workers canvassed the high-risk neighborhoods to aid in securing urine specimens,[4] recorded cases rose to 320, with seven deaths.[5] Following the introduction of blood lead testing as the screening method late in 1966, there were 1,336 cases reported in the 2-year period 1967 and 1968, with 17 deaths. The impact of the program became quite evident in 1969 when reported cases

dropped to less than 450 with one death.

During the period of this study, 1,155 (86.5%) of all 1,336 lead poisonings reported in the city were treated in the clinic. The rest were treated either as in- or outpatients at other hospitals in Chicago. Encephalopathy as a complication of lead poisoning is not specifically reportable in Illinois. However, the consensus of the resident staffs of those teaching hospitals that formerly saw the majority of patients with lead poisoning admitted as emergencies, indicated that encephalopathy has greatly decreased in incidence. As one resident put it, "The lead picture has changed."

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