LEAD INDUSTRIES ASSOCIATION

60 EAST 42ND STREET

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LEAD HYGIENE and SAFETY BULLETIN No. 12]

To the Members of the Lead Industries Association:

CHILDHOOD LEAD POISONING

Due to circumstances wholly beyond our control, including the untimely death of the principal investigator and the decision of his successor to continue the work under a grant from the U. S. Public Health Service, there has been great delay in completion of the study of childhood lead poisoning arranged for by the Lead Industries Association with The Johns Hopkins Hospital nearly six years ago.

Reports of the work have only now become available to us in the form of three reprints, all under the authorship of J. Julian Chisolm, Jr., M. D. and Harold E. Harrison, M. D., with the following titles:

"The Exposure of Children to Lead"

"Quantitative Urinary Coproporphyrin Excretion and Its Relation to Edathamil Calcium Disodium Administration in Children with Acute Lead Intoxication"

"The Treatment of Acute Lead Encephalopathy in Children"

A copy of the first of these reports is herewith. Attention is called to the summary and conclusions on page 955. Subject to limitations of supply, copies of the two other reports will be sent on request.

Manfred Bowditch

Manfred Bowditch
Director of Health and Safety

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THE EXPOSURE OF CHILDREN TO LEAD

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THE AVAILABILITY of a new and effective therapeutic agent has resulted in renewed interest in lead intoxication in childhood. Reports[1-4] emanating from various parts of the United States, indicate an increasing recognition of this disease, particularly in urban areas. While calathamil calcium disodium has proven to be of value in the treatment of acute episodes of plumbism, it cannot be used to prevent the toxic effects of prolonged excessive absorption of lead. In children as in adults, prevention of excessive exposure to lead remains the principal means of control.

A sound preventive program must be based upon adequate environmental data. The age incidence, seasonal distribution of the acute manifestations and concentration of cases among children residing in urban slum areas are well known.[5-7] Although the inhalation of lead fumes as a cause of plumbism in children has been reported,[8-9] it is believed that at present the ingestion of lead-containing paint flakes is the most common source from which children obtain excessive quantities of lead. The present report deals entirely with this latter type of exposure.

Data have been obtained upon the intensity of such exposure, duration of exposure and the seasonal factor in the production of lead intoxication in children. The "secondary" case rate among housemates of index cases has also been studied. Likewise, the relationship between the incidence of severe permanent damage to the brain and re-exposure to lead among survivors of an initial episode of acute lead encephalopathy has been examined. Observations were made upon the developmental status of affected children and the personal-social situations in which they developed lead intoxication. The purpose of this report is to present these data and to discuss the relative role which each of the several environmental factors may play in the production of lead intoxication in children. It is hoped that this may facilitate the implementation of adequate preventive measures.

CLINICAL MATERIAL AND DIAGNOSTIC CRITERIA

The clinical material was derived from the pediatric clinics of the Harriet Lane Home of Johns Hopkins Hospital and of Baltimore City Hospital. In all, 197 children exposed to lead, including 90 patients with acute lead encephalopathy, have been studied. All dwelled in the urban slum areas of Baltimore. Within this group, 50 children were personally studied by the authors. In these children, observations on developmental status and personal-social home situations were made. The study was conducted during the years 1952 to 1954, inclusive.

An important part of the present survey was the detailed analysis of exposure factors in nine households in which abnormal sources of lead were demonstrated. Within these nine environmental units, there were 9 index cases and 17 other children under 6 years of age who served as controls, or a total of 26 subjects with known exposure to lead. Among the 17 control subjects of this household-study group, the incidence of unsuspected "secondary" cases was determined.

Another group of 33 children were patients who were studied during and after hospitalization for acute lead intoxication or encephalopathy during 1952-1954. In addition, a review was made of all hospital records of chil-

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dren admitted to the above clinics during the previous 12 years and indexed as "lead poisoning" or "lead ingestion." Among these records, 138 contained sufficient information to establish and classify the clinical diagnosis according to the criteria listed below. These constitute 138 of the 197 subjects included in this report.

DIAGNOSTIC CLASSIFICATION. All subjects are classified in six clinical categories as follows:

Type I. Exposed-Normal. Subjects with a history of ingestion of materials suspected of containing lead or with evidence of radiopaque foreign materials in the gastrointestinal tract by roentgenography, were classified as exposed normals, if they had concentrations of lead in blood less than 0.06 mg/100 gm whole blood, absence of "lead lines" in roentgenograms of long bones, normal findings in examinations of the blood for an anemia which responded rapidly to the oral administration of iron, and no symptoms attributable to lead intoxication.

Subjects in this category were subdivided into two groups: a) those for whom exposure to lead was verified by analytic records giving the identification and lead content of the material ingested by the child and b) those for whom such analytic records were not available, although the clinical record indicated that a source of lead had been found in the child's environment.

Type II. Asymptomatic, Increased Lead Absorption. These subjects differed from the exposed-normal group in that they had elevated concentrations of lead in blood and roentgenographic evidence of storage of lead in the bones, without symptoms attributable to lead intoxication. Qualitative tests for coproporphyrin in urine were positive in some of these children.

Type III. Lead Intoxication (without Encephalopathy). The diagnosis of lead intoxication was made in children who had, in addition to evidence of increased lead absorption, several of the following manifestations: anemia resistant to iron therapy, increased urinary excretion of coproporphyrin, severe constipation, anorexia, hyperirritability, bizarre behavior patterns and intermittent vomiting. In the children of this group, there were no abnormal findings in the cerebrospinal fluid.

Type IV. Lead Encephalopathy, Mild. In addition to fulfilling the criteria for lead intoxication, the children of this group had abnormal findings in the cerebrospinal fluid and one or more of the following signs and symptoms: persistent vomiting, hyperirritability, ataxia, intermittent convulsions and somnolence or semistupor. Findings in the cerebrospinal fluid were considered abnormal if two or more of the following were present: increased concentration of protein, increased pressure and pleocytosis in the cerebrospinal fluid.

Type V. Lead Encephalopathy, Severe. The encephalopathy was classified as severe if the patients either convulsed continually for a minimum period of 24 hours or remained comatose for a period of 24 hours or longer, or both.

The numbers of subjects in each diagnostic category were as follows:

I. Exposed-normal (with presumed lead ingestion)	41
(a) record of lead source available	14
(b) record of lead source not available	27
II. Asymptomatic, increased lead absorption	30
III. Lead intoxication without encephalopathy	10
IV. Lead encephalopathy, mild	46
V. Lead encephalopathy, severe	41
	185

The remaining 12 subjects of the total group of 197 children exposed to lead were normal control subjects in the household-study group who apparently had not ingested lead-containing materials.

METHODS OF STUDY

The intensity of exposure to lead was determined by measurement of daily fecal excretion of lead in all members of the household-study group under 6 years of age. Pooled 2- to 4-day collections of stools were made in the home in covered 1½ quart Pyrex casserole dishes supplied by the laboratory. Mothers were directed to have the child defecate directly into the casserole dish. In hospitalized patients quantitative collection of stools were made while the children were on metabolism frames.

Aliquots of the pooled 2- to 4-day stool samples were prepared for analysis by homogenization of entire samples in a Waring blendor in which the standard brass bearing was replaced by a cast iron bearing.[9] Duplicate aliquots were dry-ashed[10] and analyzed for lead by the mixed-color dithizone tech-

Cooper of Snyder.[19] All equipment was "de-leaded" with warm 20% nitric acid, followed by a thorough rinsing in "lead-free" water. "Lead-free" water was prepared by the passage of distilled water through an ion-exchange resin column.

The above method was entirely satisfactory for the analysis of lead in feces in specimens containing greater than 1.00 mg Pb 24 hr. As concentration of lead decreased below this value the insoluble matter present in some specimens caused increasing interference in the final extraction step. This interference was appreciable in many specimens containing less than 0.100 mg Pb 24 hr in which variations between pairs as great as twofold were encountered. The presence of iron in concentrations sufficient to interfere with the analysis occurred only in the stools of patients receiving iron medicinally. This was readily avoided by discontinuing the iron temporarily. Recovery of lead in feces by this method was 95 to 110%. The maximum allowable error from the mean of duplicates was ± 10% (0.100 to 1.00 mg Pb 24 hr) and ± 5% (1.00 mg Pb 24 hr or greater).

Tissues were quick-frozen and homogenized in the frozen state with mortar and pestle. They were then dried to constant weight at 105° C, frozen and re-homogenized. Analyses, in triplicate, of aliquots of this final homogenate were then carried out by the above method. Difficulties, resulting from low concentration of lead, were encountered only in the analysis of brain tissue in which variation from the mean of triplicates was ± 15%. In other tissues variation from the mean did not exceed ± 8%.

In all suspected cases of lead intoxication in children in Baltimore, samples of whole blood and of suspected environmental sources of lead were routinely analyzed for lead by the Baltimore City Health Department. Blood was analyzed by a wet-digestion dithizone technique utilizing a spectrophotometer for final color estimation.[20] Samples of paint chips, painted plaster, etc., were collected in the homes by a visiting public health nurse. The lead content was estimated by a semiquantitative technique[21] and reported qualitatively as follows:

Lead absent—less than 0.1% of lead
Trace of lead—0.1% to 1.0% of lead
Positive for lead—1% to 5% of lead
Strong positive for lead—greater than 5% of lead

RESULTS

In nine households selected for detailed study of exposure factors there were 9 index cases and 17 other ambulatory children less than 6 years of age, who served as controls. Of the nine index cases, four had acute lead encephalopathy, two had lead intoxication and three were classified as asymptomatic, increased lead absorption. Data on the intensity of lead exposure were obtained in this household-study group through the measurement of fecal excretion of lead before and after the removal of all identified sources of lead in the houses. By balance studies it has been shown by Kehoe and his associates[22] that fecal excretion of lead provides a good index of lead ingestion inasmuch as approximately 90% of ingested lead is excreted in the stool. Prior to the removal of identified sources of lead, stool samples were collected concurrently from control and affected subjects. Similar collections of stools from these subjects with lead intoxication were made in the hospital at least 1 week after the completion of therapy with calathamil calcium disodium and again upon return to their homes after the removal of all identified sources of lead. In all, 63 satisfactory pooled, 2- to 4-day collections of stools were obtained from 22 of the 24 ambulatory children under 6 years of age in eight of these nine households. Comparable stool samples were obtained from six children of physicians on the pediatric staff. These were classified as "nonexposed" controls. Stool samples were collected on admission to the hospital from seven additional patients with acute lead encephalopathy.

The subjects of the household study were classified according to the diagnostic criteria outlined. The results of the analyses of the stools for lead are presented in Table I. The results of similar determinations in "nonexposed" controls and additional patients with encephalopathy are included in Table I as a background for the evaluation of the household study group. All outputs of lead in feces were calculated from the

TABLE I

DAILY FECAL EXCRETION OF LEAD IN CHILDREN BEFORE AND AFTER REMOVAL OR ENVIRONMENTAL SOURCES OF LEAD*

Classification of Patients†	No. of Patients	No. of Specimens	Lead Output (mg/24 hr)		
			Mean	Median	Range
	Household Study Group				
Types III, IV and V					
At home during exposure	6	10	44.0	17.0	5.04 – 104.0
In hospital after therapy	5	15	0.304	0.150	0.054 – 0.630
Types II, III, IV and V					
At home after exposure	6	15	0.343	0.311	0.099 – 1.30
Type II					
At home during exposure	5	14	0.10	1.11	0.116 – 0.00
Household Controls					
At home during exposure	11	25	0.102	0.031	0.007 – 1.05
	Other Children				
Nonexposed controls**					
At home	6	6	0.192	0.137	0.010 – 0.173
Types IV and V					
During exposure‡	7	7	88.4	36.4	0.573 – 443.0

* The household study group has been divided according to both diagnostic classification and presence or absence of lead exposure, in order that the observed differences in fecal excretion of lead under these varying conditions can be seen. Each specimen represents a 2- to 4-day pooled collection of feces from the lead content of which is calculated the milligrams lead excreted per 24 hours. An average of two such specimens were collected from each patient during each period of observation relative to exposure.

† Diagnostic Classification, see text for criteria.

** Nonexposed Controls: 14- to 35-month-old children of members of pediatric staff for whom there were no known environmental sources of lead.

‡ These seven patients admitted with acute lead encephalopathy were not members of household study group. Values shown are based upon total lead content of admission stool, divided by the number of days since the last previous fecal evacuation, in order to obtain mean daily excretion.

pooled collections as 24-hour outputs. In most subjects two pools of 2- to 4-day collections of stools were obtained during exposure. The data, therefore, represent approximately one "exposure-week" of observation in the various subjects. The term "exposure-week" is used, inasmuch as the samples were not always consecutive. On the first line of Table I are shown the outputs of lead during exposure of six patients with lead encephalopathy and intoxication. The mean output of lead in this group during exposure was 44 mg/day and the range was 5 to 105 mg/day. Three of these had acute lead encephalopathy. Their 24-hour outputs are calculated from the lead content of the first stool passed after admission to the hospital. All other stool collections during exposure were made in the homes. When these lead-poisoned children were removed from exposure to lead by hospitalization or, after discharge, by removal of all identified sources of lead from their homes, the daily fecal excretion of lead fell to normal values, approximately 0.3 and 0.5 mg. respectively (lines 2 and 3). On the fifth line of Table I, the mean daily output of the 11 control subjects in

TABLE II

Fecal Excretion of Lead*

Type of Subject	mg Pb/Day Mean	mg Pb/Day Range
Normal Children		
Premature nursing†	0.008	0 - 0.03
American Group I†	0.05	0.01 - 0.1
Present study	0.05	0.00 - 1.0
Industrial workers		
All types of exposure†	5.0	0 - 14.0
Severe exposure†	7.0	1.0 - 14.0
Lead Poisoned Children		
Present study	44.0	5.0 - 104.0

* In this table the daily fecal lead output of the normal and the poisoned children in the household groups are compared with similar data from the studies of Kehoe *et al.*[1-3] They determined the lead content of single fecal evacuations from children in a primitive Mexican community and in convalescent hospitalized American children. The only known source of lead for these children was that contained in their normal diet. They obtained similar determinations on exposed industrial workers. Despite the differences in sampling and analytic techniques, the fecal excretion of lead by the poisoned children apparently exceeds that of severely exposed industrial workers, while that of these household controls is of the same magnitude as that of normal unexposed children.

† Taken from data of Kehoe *et al.*: J. Indust. Hyg., 13:304, 1933.

the presence of exposure to lead was approximately 0.5 mg of lead daily. It can be seen that those children classified as asymptomatic, increased lead absorption (line 4) occupy an intermediate position between the poisoned and the control subjects. Thus, during exposure the poisoned children were found to be excreting approximately 50 times as much in the feces as the similarly exposed household controls.

The results shown in Table I may be compared with the studies of Kehoe *et al.*[1-3] on fecal excretion of lead under various conditions of exposure to lead (Table II). It can be seen that daily fecal excretion of lead in the control subjects of the present study is of the same order of magnitude as that of the normal children studied by Kehoe *et al.*[1] Even when allowance for differences in analytic and sampling technique is made, it is evident that the lead-poisoned children of the present study were excreting in the feces far greater quantities of lead than do heavily exposed industrial workers.

An unexpected finding of this household study was the discovery of five additional cases of unrecognized increased lead absorption and lead intoxication among the 17 control subjects. All of these unsuspected cases fell within the same age range as the index cases: namely, 12 to 35 months of age. No evidence of increased lead absorption or ingestion was demonstrated among the older housemates (Table III). Indeed, if the index cases are included, 14 of the 15 children aged 12 to 35 months in the nine

TABLE III

Household Study of

Distribution by Age of Unaffected Cases of Asymptomatic, Increased Lead Absorption and Lead Intoxication in the Absence of Nine Index Cases

Age Groups	Number of Subjects		
	Subjects at Risk	Asymptomatic, Increased Lead Absorption and Lead Intoxication	Normals
12 to 35 months	6	5	1
36 + months	11	0	11
Totals	17	5	12

$N = 0.05$

$P < 0.01$.

TABLE IV

LEAD CONTENT OF TISSUES OF CHILDREN DYING FROM ACUTE LEAD ENCEPHALOPATHY

Patient	Age (mos)	Time of Death*	Lead Content (mg Pb per kg tissue)				Total Lead Found in Soft Tissues (mg)	Output of Lead in Urine†
			Rib	Brain	Liver	Kidney		
R. McF.	48	22 hours	20.9	1.1	10.5	5.0	13.0	accurate
N. R.	24	14 hours	24.0	1.0	6.0.1	9.5	10.5	3.4
H. H.	60	3½ days	13.1	1.6	4.1	3.8	10.1**	4.6
L. D.	48	6 hours	10.0	1.7	–	–	–	0.6

* Time of death after institution of therapy with calcium disodium.

† Total output of lead in urine during therapy prior to death.

** Estimate of tissue, estimated lead content of which is approximately 3 mg.

households were found to be ingesting potentially toxic quantities of lead.

In four patients who died during an acute episode of lead encephalopathy, tissue content of lead was determined (Table IV). Three of the four patients died within 24 hours after the institution of therapy with calcium disodium. Total urinary output of lead prior to death varied from 2 to 5 mg. While it is not possible to estimate accurately the total lead content of the body from these data, the content of lead in soft tissues can be approximated. Aub *et al.*[3] and Kehoe *et al.*[4] have found in animals and in human necropsy material obtained from individuals dying within a few days or weeks after cessation of chronic exposure to lead that from one third to two-thirds of the total lead in nonskeletal tissues is contained in liver, kidney and brain. Skeletal stores vary greatly and reflect to a certain extent the duration of exposure. From the data in Table IV and those of the authors quoted, we may estimate total content of lead in soft tissues in these children as 20 to 100 mg.

In the entire series, records of identified sources of lead were available for 105 children. The location of these sources about the dwellings are shown in Table V. Of the 220 samples tested which contained greater than 1% of lead, only 4 were obtained from cribs and furniture. More striking is the fact that 110 of the 220 sources were window-sills and frames. Peeling wallpaper and crumbling plaster accounted for an additional 45 sources. For each of the 105 exposed children, from one to five different sources containing greater than 1%

TABLE V

EXTRANEOUS SOURCES OF LEAD*

Location	Lead Content	
	Less than 1%	1% or More
	Interior Sources	
Window-sills & frames	5	110
Interior walls		
painted paper	28	18
painted plaster	91	32
Door frames	1	13
Furniture	3	3
Cribs	3	1
	External Sources	
Door frames	5	10
Porches & house-walls	6	40
Fences & other walls	6	7
	Totals	
Interior sources	74	168
External sources	11	57
	85	225

* The distribution, by lead content and location, of the 310 identified possible environmental sources of lead to which 105 subjects in this series were exposed. These sources were identified by analysis of paint scrapings taken from the various surfaces in and about the houses which gave evidence of having been chewed. For each subject one to seven such sources were identified. For all 105 subjects at least one source containing greater than 1% of lead was found. For 100 of the 105 subjects at least one source containing greater than 5% of lead was found.

of lead were identified among the various items each child was thought to have chewed. For 102 of them there was at least one source containing greater than 5% of lead. The lead was contained in the paint on the surfaces. The paint was old and flaking and frequently contained many layers, one or more of which may have contained lead pigments in which the content of lead may have been 30 to 70% of the total solids in the paint.

An attempt was made to ascertain the duration of exposure likely to produce toxic symptoms. Maternal estimates of the duration of their child's ingestion of lead-containing materials frequently were either unobtainable or unreliable. The type of exposure, however, permitted an indirect estimate of the probable duration of exposure, if the following assumptions were made: a) the locations of the sources of lead required that the children be ambulatory in order to reach them, and b) exposure began at the time of ambulation, or at 12 months of age on the average. With these assumptions the probable duration of exposure could be estimated as the interval in months between the child's first birthday and the age at which the child was classified as asymptomatic, increased lead absorption, or clinical lead poisoning was discovered. When the data were analysed on this basis, no statistically significant correlation could be found between presumed duration of exposure and severity of disease (exposed-normal children excluded). Indeed, the data indicated that the presumed exposure was of similar duration in all diagnostic classifications manifesting increased absorption of lead, with or without symptoms.

An explanation for this became apparent when the seasonal factor was taken into account. Thirty two patients in the series developed acute lead encephalopathy prior to 2 years of age. The relationship between the seasonal factor and the presumed duration of exposure is shown for each of the patients in Figure 1, in which the month of the child's first birthday is joined by a bar with the month of onset of acute encephalopathy. The length of each bar, therefore, represents the assumed duration of exposure in months for each child. In the upper portion of Figure 1 the children passing their first birthday between May and September are shown. They were presumed to have been ingesting lead during some part of this 5-month summer period (when the peak incidence of acute lead encephalopathy occurs), yet they did not become ill until the summer of the following year as they approached 24 months of age. In the lower portion of Figure 1 are shown those patients reaching their first birthday during the winter months prior to April. They became ill during the first summer after the presumed onsets of ingestion. Reading from the top to the bottom of Figure 1 the probable duration of ingestion, therefore, becomes progressively shorter and approaches a minimum of 3 months. Within this group of 32 patients there was no statistically significant correlation between month of first birthday and severity of, or survival during, acute lead encephalopathy. Excluding December, the distribution of births by month in the group does not differ significantly from the monthly distribution of births in Baltimore for the years 1951 to 1953 inclusive, during which most of the patients were born. In this small group the peak in births during December, and the passage of the older infants through their first summer of ambulation without symptoms, suggests that 5 to 6 months of lead ingestion may elapse prior to the onset of acute lead encephalopathy.

The possibility that a minimum exposure period of 3 months is required, after which the advent of summer becomes the controlling factor in the production of symptoms, is also suggested by the following finding. In the entire group there were 14 children with unequivocal evidence of excessive lead ingestion including identification of at least one environmental source containing greater than 1% of lead, but with no evidence of increased lead absorption. Eight of these fourteen normal-exposed children

RELATIONSHIP BETWEEN MONTH OF FIRST BIRTHDAY AND MONTH OF INCIDENCE OF ACUTE ENCEPHALOPATHY

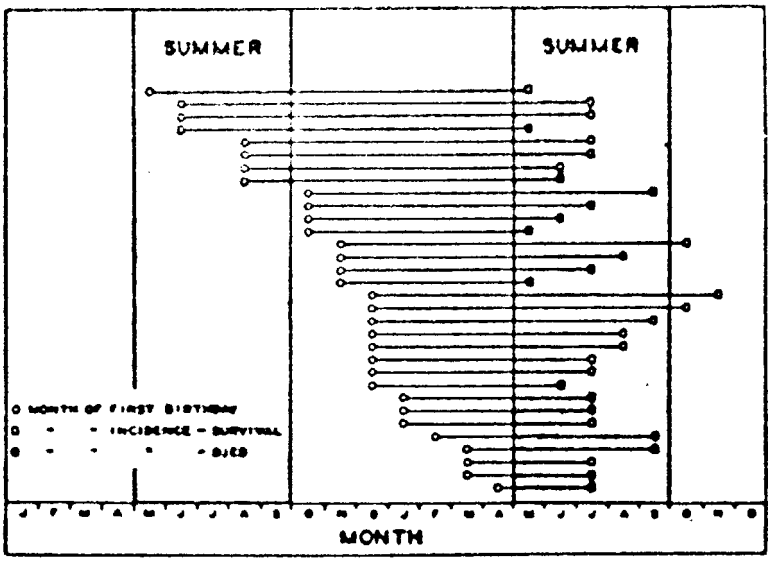

Fig. 1. In this graph the month of onset of acute symptoms for each of the 32 patients who developed acute lead encephalopathy prior to 2 years of age is shown on the right. On the left is the month of the child's first birthday. These points are joined by a bar. The length of each bar, therefore, represents the measured duration of lead exposure (in months) for each child. Twelve months of age was selected as the average age of ambulation. The nature of the exposure in this series required that the child be ambulatory in order to reach the sources of lead to be encountered. In this manner a relation between measured duration of exposure to lead and the seasonal factor in the production of symptoms can be demonstrated.

were less than 15 months of age. Conversely, among the 59 patients with encephalopathy, the youngest was 15 months of age.

Although these data on duration of exposure were indirectly deduced, they are supported by histories obtained from many parents, who stated that they had seen their children ingesting paint flakes or had found plaster particles in the child's stools since the time the child had begun to walk. It was also observed that among patients who survived an initial episode of acute lead encephalopathy and were re-exposed to lead, recurrent acute episodes of encephalopathy usually did not occur until the following summer.

An analysis of the occurrence of severe permanent damage to the brain among survivors of an initial attack of acute lead encephalopathy indicates the importance of continued environmental exposure to lead in increasing the incidence of central nervous system sequellae. In the entire series 61 survivors of acute lead encephalopathy were treated more than 12 months prior to evaluation of sequellae (therapy with citrate, 16 patients, therapy with BAL, 28 patients, and therapy with edathamil calcium disodium, 17 patients). Fifteen of the group were lost from follow-up. Forty-six of the sixty-one patients (citrate, 13 patients, BAL, 19 patients, and edathamil calcium disodium, 14 patients) have been

followed for 1 year or longer. Of these 46 patients, 14 were known to have continued ingestion of lead for periods of 2 months or longer, 4 had doubtful re-exposure and 25 had *no known re-exposure* to lead after the initial episode of encephalopathy. The incidence of sequellae in the survivors of acute lead encephalopathy was analysed, without regard to type of therapy during the acute phase, to determine whether there was any association between the occurrence of severe permanent residua in the central nervous system and re-exposure to lead. Presence of *one or more* of the following manifestations was considered evidence of serious permanent damage to the brain: severe mental retardation, recurrent convulsions and severe behavior disorder. Of the 21 survivors classified as having these "severe sequellae," 6 demonstrated one of these criteria, 3 had two and 12 fulfilled all three (Table VI). There is, statistically, a highly significant association between the occurrence of such "severe sequellae" and re-exposure to lead following recovery from mild encephalopathy (X_c = 14.30, $P < 0.01$). The correlation between sequellae and re-exposure to lead is more difficult to assess in the group surviving an episode of severe encephalopathy. Among the 20 severe cases, re-exposure was uncertain in 4. These four, all of whom had permanent residua in the brain, are omitted from Table VI. If these doubtfully re-exposed cases are considered as not re-exposed, X_c = 2.68 and $P > 0.1$ (re-exposure is not statistically significant). For the entire group of survivors of mild and severe encephalopathy there is no significant correlation between sequellae and the duration of acute encephalopathy, type of therapy during the acute phase or concentration of lead in blood after the acute illness. The loss of patients from follow-up does not vitiate the analysis. In survivors *not re-exposed* to lead there is no correlation between sequellae and age of incidence at the 18, 24, or 30-month levels.

DISCUSSION

The ages and seasonal distribution of symptomatic cases in this series are the same as those reported for children by various investigators.[5,6] Eighty-eight of the one hundred five cases of acute lead intoxication occurred during May, June, July, August, and September. Ninety of the one hundred five cases occurred in children between the ages of 12 and 36 months. It need only be re-emphasized here that homes in which the children of this series lived had several features in common: they were old and in varying states of deterioration and disrepair. In the homes visited,

TABLE VI

RELATION BETWEEN INCIDENCE OF SEVERE SEQUELLAE IN THE CENTRAL NERVOUS SYSTEM AND RE-EXPOSURE TO LEAD FOLLOWING RECOVERY FROM AN INITIAL EPISODE OF ACUTE LEAD ENCEPHALOPATHY

	Acute Lead Encephalopathy			
	Severe Cases[a]		*Mild Cases*	
	With Sequellae[b]	*No Sequellae*	*With Sequellae*	*No Sequellae*
Known re-exposure to lead	7	0	7	0
No known re-exposure to lead	8	6	0	17
	χ^2_c = 4.80, $P < 0.05$		χ^2_c = 11.33, $P < 0.01$	

[a] Four survivors of severe acute lead encephalopathy, who sustained sequellae but in whom re-exposure to lead was uncertain, are omitted from the table. (See text for discussion.)

[b] Sequellae = severe, permanent, residual damage to the brain (severe mental retardation, convulsive disorder, severe behavior disturbance).

crumbling, painted plaster or loose paint chips from walls, ceilings, door frames, window-sills, outside porches and fences were readily accessible to the hands and mouths of inquisitive small children. The data of the present study show the intensity of this type of exposure, but they cannot be applied directly to such questions as the minimal quantity of lead toxic for children or the maximal safe content of lead in liquid paint.

Among the environmental data presented, two factors stand out: the intensity of lead exposure provided by a small quantity of paint flakes and the role of the season in precipitation of acute lead encephalopathy.

The data in Table I on fecal excretion of lead may be utilized as a measure of the quantity of lead ingested by the various groups of subjects in the household study. The difference between the poisoned and the nonaffected children in these households does not require statistical analysis, for the mean daily fecal excretion of lead in the poisoned children exceeded, by 50-fold, that of the controls in which it fell within the normal expected range. In Table II it can be seen that the mean daily fecal output of lead by the lead-poisoned children (44 mg Pb/day) exceeded, by approximately sixfold, that of a group of severely exposed industrial workers (7.6 mg Pb/day) and, by elevenfold, that of workers in various trades in which exposure to lead is less severe. The groups of industrial workers chosen for comparison[14] were exposed to lead-containing dust, much of which is swallowed with the saliva. As in the children of the present study, the principal mode of absorption in these workers would be through the gastrointestinal tract. It has been pointed out that the occurrence of lead encephalopathy in adults has usually been associated with intense exposure.[15] The more frequent occurrence of encephalopathy in children as compared with adults may depend in part upon their more intense exposure rather than upon any inherent biologic differences between child and adu[illegible]

Lehman[16] recently reviewed the literature and concluded that the average daily ingestion of not more than 1.5 mg of lead is without harm. Kehoe *et al.*[17] have found that significant retention of lead in the tissues occurs when, in addition to normal dietary intake, adult volunteers are fed 2 mg of soluble lead (as lead acetate) daily. The data in Table I are in accord with these conclusions. Under the sponsorship of the American Academy of Pediatrics, the Committee on Hazards to Children of the American Standards Association studied the problem and recommends that paints may be considered safe for use on children's toys and furniture and housing interiors if the lead content does not exceed 1% of the total solids.[18] Paints and other surface coatings meeting this specification and those relating to other potentially toxic metals may be labelled: "conforms to American Standard Z 66.1-1955." It is essential to recognize that this recommendation applies only to the two or three layers of paint usually applied to a surface, not to multiple layers of paint as may be found in old deteriorated housing. As the number of layers increases or when a layer of paint containing lead pigments is added, the quantity of lead per unit area increases to the point where even a small flake may contain an excessive amount of lead. The magnitude of exposure to lead associated with the ingestion of a few small paint flakes is emphasized if we calculate the quantities of paint flakes necessary to yield the amounts of lead found in the stools of the lead-poisoned children: for example, 44 mg of lead would be equivalent to the ingestion of 0.88 gm or less of paint flakes containing 5% or more of lead, or to 4.4 gm of flakes containing 1% of lead. An example of the size and quantity of paint chips necessary to yield potentially toxic amounts of lead is shown in Figure 2.

In Table V the location and lead content of environmental sources of lead are shown. 102 of these 103 children were exposed to at least one source containing greater than 5% of lead. No case of lead intoxication has been found where the only

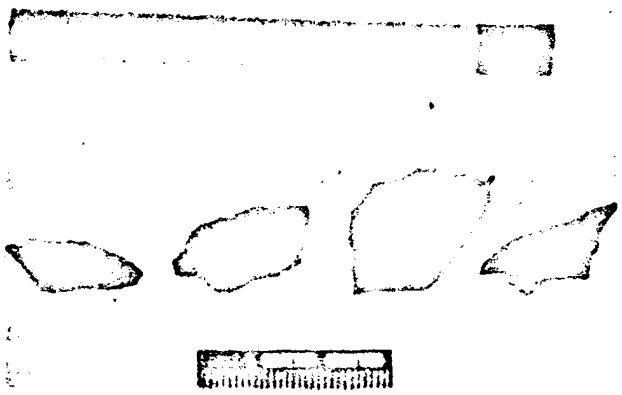

FIG. 2. Example of size and quantity of paint fragments containing a potentially toxic quantity of lead. Four small paint chips are shown with a cigarette for comparison of size. The aggregate weight of these fragments was 2.09 gm, they contained 234 mg (or 9.3%) of lead. With the fingernail they were easily removed from a door frame upon which a patient with acute lead encephalopathy was known to chew. His feces, which were obtained on admission to the hospital and 48 hours after the last previous fecal examination, contained 190 mg of lead. The mother stated that this child had been ingesting paint flakes almost daily from this and other sources (containing similar concentrations of lead) for approximately 10 months prior to hospitalization.

source of lead contained less than 1% of lead in the dried paint surface. The present data apply to old housing. Inasmuch as lead is presently used as a paint drier as well as a pigment, 1% of lead in total paint solids approaches the minimum consistent with a satisfactory house paint. It is conceivable that poor maintenance of modern housing with resultant accumulation of many layers of paints (containing as little as 1% of lead) on surfaces accessible to children may in the future constitute a hazard to small children.

Evidence has been presented which indicates that, after a minimum of approximately 3 months of this type of exposure, the advent of summer (in the presence of continued exposure to lead) is the controlling environmental factor in the precipitation of acute lead encephalopathy (Fig. 1). Although the mechanism of this phenomenon is not fully understood, experimental evidence has been obtained in animals which indicates that vitamin D and the actinic rays of the summer sun increase the absorption of lead from the intestine.[7] It has also been suggested that the increased heat of the summer leads to dehydration and acidosis in small children and in this manner may play a role in the production of encephalopathy.[8] In the present study no reliable data could be obtained concerning vitamin D intake in view of the sporadic use of vitamin D-fortified evaporated and fresh milk products by the subjects. Among the patients interviewed, a history of no vitamin D supplement during winter or summer was given by about half of the cases.

When the probable duration of exposure exceeded 3 months, no correlation could be demonstrated between increasing severity of disease and further monthly increments in exposure. This finding may be explained by the interplay of two other factors: the magnitude of lead ingestion observed in the household study group, and the seasonal factor in the precipitation of acute symptoms. It emphasizes the urgency during the summer months of the prompt removal of children manifesting asymptomatic increased lead absorption from such intense

exposure to lead. The data indicate that, in such a patient, acute encephalopathy may develop if exposure is permitted to continue but a few weeks longer.

Frequency of ingestion, is, of course, an important consideration. Long-term data obviously could not be obtained on this point. The data in Table I represent, at most, only 1 "exposure-week" in time. The repetitive ingestion of a few particles from one of the identified sources of lead several times during that week would be compatible with this data. Tissue contents of lead (Table IV) give an approximation of the amounts of lead which may be absorbed under these conditions.

The finding in the household study of five "secondary" cases among the six control subjects aged 12 to 35 months is significant. If confirmed, it indicates that a larger public health aspect of this disease exists in old housing areas than has heretofore been recognized. Furthermore, wherever an index case is found, his environmental contacts under 3 years of age should be submitted to careful clinical and laboratory examination.

Although the need for identification and removal of environmental sources of lead is well known,[1] a highly significant correlation between re-exposure to lead and the incidence of severe permanent sequellae in the central nervous system in survivors of an initial episode of acute encephalopathy has not previously been reported. This indicates that immediate and absolute prevention of re-exposure may, perhaps, be the single most important long-term factor in the eventual outcome in such patients. In our experience this has been satisfactorily accomplished only by burning the old lead-containing paint completely away or by transfer of the child to a new dwelling in good repair.

The term "pica" is frequently used in association with both lead poisoning and with mental defect in children. Thus, in the minds of many, plumbism and mental deficiency are frequently associated. This is not so with respect to the ingestion of other toxic substances, a single ingestion of which, suffices to produce symptoms. The want of toddlers in the 1-year age group to taste and eat a large variety of foreign material is well known and is considered to be a part of their normal behavioral pattern, at least for a short span of time.

In the present study all members of the household group were submitted to psychometric examination. Within this group no striking developmental deviations could be found between the affected and the non-affected members. In addition, 28 patients who were not re-exposed were psychometrically evaluated 1 year after recovery from acute lead intoxication and encephalopathy. The distribution of intelligence quotients on the basis of the revised Stanford-Binet Intelligence Scale, Form L, was as follows:

Intelligence Quotient	*Number of Patients*
60- 69	3
70- 79	3
80- 89	5
90- 99	9
100-109	5
110-119	4

These findings would agree with the concept that the ingestion of foreign material exhibited by these children was not a manifestation of mental deficiency, but that the ready availability of a highly toxic material in the environment was the important factor. This is certainly supported by the high "secondary" attack rate found among the control subjects of the household study.

If the assumptions are made that flaking, lead-containing paints are widely distributed in old housing, that there are large numbers of infants and toddlers living in such a physical environment and that normal as well as defective children may readily ingest amounts of lead sufficient to produce intoxication, the question arises: Why is lead intoxication not more prevalent than the numbers of cases presently recognized would indicate? Many cases of lesser degrees of intoxication may go unrecognized unless sought out (as indi-

cated by the incidence of "secondary cases") or may be the result of lesser ingestion. In still other children the duration of ingestion may be insufficient to produce overt signs of lead intoxication.

However, personal-social factors elicited in those subjects studied by the authors may, in part, account for the relatively greater ingestion of lead in the subjects of this report as compared with the larger population of children who may live in similar physical environments. With respect to maternal information concerning plumbism, mothers were asked if they were aware of their child's ingestion of paint or had heard of the danger of lead poisoning. Significant is the fact that 14 of 31 mothers, while aware of the danger involved, were not concerned because they considered the amount of paint flakes their child was eating to be insufficient "to hurt him." Such maternal statements are quite understandable in view of the preceding calculation that less than 1 gm of paint flakes may contain highly toxic quantities of lead. It is the repetitive ingestion of these minute quantities of such paint chips which leads to lead intoxication. If it is conceded that no mother can reasonably be expected to prevent this type of ingestion in the face of crumbling paint and plaster, it will be recognized that proper maintenance of *both interior and exterior painted surfaces* is probably the most important environmental factor in the long-term aspect of prevention of childhood lead intoxication.

The corrective efforts taken by the parents who attempted to curb the ingestion consisted largely of punitive measures which may be said, prima facie, to have been ineffectual. Only one had attempted to remove the source of lead. Common, likewise, was the lack of close parental supervision of the affected children. Thirteen of the thirty-three mothers were wage earners who worked at least several days of each week away from home. While away from home they left their small children with neighbors or in the care of older children. Six of the mothers had more than three children less than 5 years of age. They stated that in order to get various types of housework done, they shut the children in other rooms for short intervals, in these rooms sources of lead were found.

Several of the children in the hospital demonstrated an excessive desire for affection. From the point of view of the child, the ingestion of foreign material was an obvious attention-getting device in some, particularly in those who had been punished for it. Many others appeared to nibble inadvertently upon the window sills and door frames as they gazed out into the street. In these, boredom was apparently conducive to the lead ingestion, and may be attributable to the lack of an emotionally and intellectually stimulating environment. Many parents reacted by an overprotective attitude following their child's recovery from acute lead encephalopathy. They frequently sought advice about play activities for their child, the diminution in pica was often striking.

SUMMARY AND CONCLUSIONS

A study of some environmental, behavioral and social factors in the production of lead poisoning in children in an urban community has been reported.

Most significant among the environmental data presented were the magnitude of the exposure to lead *from repetitive* ingestion of small quantities of leaded-paint flakes, and the role of the seasonal factor (summer) in the precipitation of acute lead encephalopathy. The predominance of these two factors may explain the absence of any significant correlation between severity of disease and increments (beyond a minimum of 3 months) in the probable duration of exposure. It was concluded that a child without symptoms but having increased absorption of lead, recognized during the summer months, may progress to severe encephalopathy within a few weeks if the sources of lead are not promptly identified and eliminated.

The present studies demonstrate that exposure to lead may be intense in children

over 1 year of age living in dilapidated dwellings in which flaking leaded paint is readily accessible. The amounts of lead found in the feces of the poisoned children in the present study exceeded that found by others in the feces of exposed industrial workers. This suggests that the higher incidence of lead encephalopathy among children as compared with adults may, in part, result from their relatively greater exposure.

The importance of continued environmental exposure to lead in increasing the incidence of severe permanent damage to the brain among survivors of an initial attack of acute lead encephalopathy was demonstrated. The correlation between the occurrence of such sequellae and re-exposure to lead in patients recovering from mild acute encephalopathy was statistically highly significant. It was concluded that removal of lead from the child's environment is the only adequate protective measure in such cases.

The high proportion of children aged 12 to 35 months with average intellectual capacity found among cases of lead intoxication, and the high incidence of unsuspected cases found among 12- to 35-month-old housemates of the index cases demonstrate the importance of the environmental aspect of the problem in urban slum areas. This high incidence of "secondary cases" emphasizes the physician's obligation to examine carefully and promptly all environmental contacts under 3 years of age wherever an index case is found.

The developmental factors in the child and the social situations in the home which may intensify the ingestion of lead-containing materials were discussed. While the responsibility of parents to protect their children from environmental hazards is not denied, no mother can reasonably be expected to prevent the repetitive ingestion of a few paint chips when these are readily accessible. As lead is widely used as a paint drier, continued good maintenance of painted surfaces would appear to be more pertinent to the long range prevention of childhood plumbism than specific limitations on the content of nonpigment lead in fresh paint. The various environmental data all point to the conclusion that, where housing has been permitted to deteriorate, exposure to lead may be of such intensity as to outweigh such individual variables as mental retardation and emotional maladjustments in the child. Such intense exposure is a preventable hazard to normal small children, and, as such, constitutes a public health problem which may be more extensive than has heretofore been thought to exist.

Pending the wider availability of better housing, preventive measures will have to be adapted to individual home situations and to the available facilities within a given community. Basic to any preventive program are facilities for the prompt identification and removal of environmental sources of lead, as has been emphasized by others.[5-11] Equally important is a comprehensive social investigation of the home in order to evaluate the circumstances under which the child obtained toxic quantities of lead and to determine whether the identified sources of lead can be adequately removed, or whether a change of dwelling is required to prevent further dangerous exposure to lead.

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SUMMARIO IN INTERLINGUA

Le Exposition de Juveniles a Plumbo

Es reportate un studio de certe factores de milieu e morre in le production de inveneno-mento a plumbo in juveniles in un communitate urban.

Le plus significative del datos de milieu hic presentate es le magnitude del exposition a plumbo associate con le repetite ingestion de parve quantitates de squamulas de color a plumbo e le factor saisonal (i.e. le importantia del estate) in le precipitation de acute encephalopathia a plumbo. Le predominantia de iste duo factores explica possibilemente le absentia de un correlation significative inter le severitate del morbo e augmentos del probabile duration del exposition (ultra un minimo de 3 menses). Esseva concludite que un caso de asymptomatic augmento del absorption de plumbo que es revelate durante le estate pote progreder a severe encephalopathia intra alcun septimanas si le fonte del plumbo non es promptemente identificate e eliminate. Le diurne ingestion medie de plus que 1,5 mg de plumbo es potentialmente toxic. Un mediretate del matres interviewate esseva inconscie del facto que minuscule quantitates de colorante pote continer concentrationes toxic de plumbo.

Le presente studios demonstra que exposition a plumbo pote esser intense in juveniles de plus que 1 anno de etate qui habita domiciles derepute in que squamulas de colorantes a plumbo es facilemente accessibile. Le concentrationes de plumbo trovate in le feces del juveniles in le presente studio excedeva le concentrationes de plumbo trovate

per altere autores in le foces de exposite obrero industrial. Isto pare indicar que le plus alte incidentia de encephalopathia a plumbo inter juvenes in comparation con adultos es possibilemente in parte le resultato del relativemente plus alte grado de exposition.

Es demonstrate le importantia del factor de continue exposition a plumbo in augmentar le incidentia de severe lesiones permanente del cerebro inter superviventes de un initial attacco de acute encephalopathia a plumbo. Le correlation inter le occurrentia de tal sequelas e le re-exposition a plumbo in patientes convalescente ab leve episodios de acute encephalopathia essera statisticamente multo significative. Essera concludite que le eliminationes de plumbo ab le milieu del patiente es non solmente le sol adequate mesura de protection sed etiam un importantissime mesura therapeutic in le tractamento de tal casos.

Le alte proportion de juvenules de etates de inter 12 e 35 menses con capacitate intellectual morbe qui es trovate inter le casos de intoxication a plumbo e le alte incidentia de non-suspecte casos trovate inter lor condomiciliarios del mesme etates demonstra le importantia del aspecto ambiental del problema in areas urban de habitationes substandard. Iste alte incidentia de "casos secundari" accentua le obligation del medico de examinar caste- e promptemente omne condomiciliarios de minus que 3 annos de etate quandocunque un caso de intoxicamento a plumbo es trovate.

Omne le varie datos relative al milieu urban supporta le conclusion que in situationes in que on ha permittite un deterioration del conditiones domiciliari, le exposition a plumbo pote esser al intrinse que ille devenit un factor plus importante que variabiles individual, como per exemplo le retardation mental o le maladjustamento emotional del juvenules mesme. Tal grados de exposition a plumbo representa pro normal infantes e juvenules un hasardo que es preventabile. Illos constitue un problema de sanitate public que es possibilemente plus extense que lo que on ha previsemente supponite.