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LEAD POISONING IN CHILDREN: DIAGNOSTIC CRITERIA

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As the summer months draw near, it is reasonable to expect an increase in the number of cases of lead poisoning in children in many large cities throughout the Nation. This seasonal incidence has been repeatedly noted in studying the epidemiology of childhood plumbism.[1,2,3] The factors relevant to the increased summer incidence are not yet defined. Increased lead absorption caused by actinic rays of the summer sun[4] and increased heat of the summer leading to dehydration have been suggested.[5] Byers[6] feels that the summer incidence is a reflection of the greater chance of exposure to lead paint on the part of children playing outdoors, as compared to indoors. The seasonal variation in the occurrence of this disease should keep physicians alert to signs of lead poisoning in children in the summer.

That interest in this disease increases the incidence of diagnosed and reported cases has been borne out from the experience of cities such as Chicago, Cincinnati, Baltimore, and New York where interest and awareness concerning childhood lead poisoning are high. Where such interest does not exist cases may be frequently unrecognized.

A need for accurate diagnosis in childhood lead poisoning exists. Prognosis and institution of proper treatment depend to a great extent on the early and accurate diagnosis of this disease. Criteria for diagnosing cases of childhood plumbism have been formulated. The purpose of this communication is to present and discuss these criteria.

Diagnostic Criteria

In requiring a group or combination of conditions be present to make a diagnosis of a specific disease, there is a risk of missing some cases or erroneously diagnosing the entity in some cases in which it is absent, depending on the extent and specificity of the criteria set forth. The criteria listed below are based on selected collective experience with childhood lead poisoning and are designed to detect a minimum of false positive and false negative cases. After a reasonable period of carefully followed use these criteria will be revised, if necessary.

1. CLINICAL AND LABORATORY CRITERIA

A. Gastrointestinal Manifestations

One or more of the following:

1) Anorexia
2) Intermittent vomiting
3) Abdominal pain
4) Constipation

B. Central Nervous System Manifestations

One or more of the following:

1) Irritability
2) Drowsiness
3) Persistent vomiting
4) Incoordination
5) Convulsions
6) Coma
9) Papilledema
10) Paralysis of one or more cranial nerves
11) Elevated cerebrospinal fluid protein content
12) Cerebrospinal fluid pleocytosis

7) Weakness or Paralysis
8) Hypertension
13) Elevated cerebrospinal fluid pressure

C. Hematologic Manifestations
One or both of the following:
1) Hypochromic microcytic anemia
2) A significant degree of basophilic stippling of the red blood cells

D. Excessive Coproporphyrinuria

E. Urinary Findings
One or both of the following:
1) Glycosuria
2) Amino-aciduria

F. The demonstration of increased radiologic density at the metaphyses of long bones.

2. CRITERIA FOR LEAD ABSORPTION

The following findings present evidence for absorption of lead in quantities that are known to be capable of inducing intoxication.

A. The finding of a concentration of lead in the blood, as determined by a method of known high sensitivity and precision,[7] of 0.08 mg. per 100 gm. of whole blood or greater. Values of 0.06 - 0.08 mg. per 100 gm. of whole blood are indicative of abnormal absorption of lead, but often not a degree of absorption which is capable of inducing symptoms of intoxication. Repeat determinations are preferred.

B. The finding of urinary excretion of lead, as determined by methods of analysis of known high sensitivity and precision,[7] in amounts of 0.08 mg. or more per 24-hours [6,8] in patients not receiving treatment to increase lead excretion. Repeat determinations are preferred.

3. EXPOSURE TO A LEAD SOURCE

A confirmed history, by chemical identification of the source, of exposure to lead of such severity and of such duration as to be indicative of a dangerous degree of absorption.

Discussion

The child who is poisoned by lead will have taken in and absorbed dangerous amounts of lead. The presence of clinical and laboratory manifestations in such a child enables a diagnosis of lead poisoning

to be made.

Clinical and Laboratory Criteria – Manifestations included under clinical and laboratory criteria are non-specific, since any of these can be found in other illnesses. Even the increased radio-opaque areas or lines at the metaphyses of the long bones are not specific indications of lead absorption, for these radio-opaque lines are seen with other diseases, e.g., abnormal absorption and storage of other heavy metals and healing rickets. Such lines are not indicative of illness, but are so frequent in their occurrence in small children who are absorbing abnormal amounts of lead as to serve as warning. A child exhibiting this manifestation should be investigated carefully, with respect to the extent of his absorption of lead.

When any two of the criteria listed under clinical and laboratory criteria occur together with one of the criteria for lead absorption, a diagnosis of lead poisoning may be made.

Two or more of the clinical and laboratory criteria listed may be used to make a presumptive diagnosis of plumbism in children with early manifestations of increased intracranial pressure; such children require removal from the source of lead and emergency treatment. A delay in treatment while a blood or urine analysis for lead is being performed may be hazardous. Edathamil calcium disodium (calcium EDTA or edathamil) therapy can be instituted while blood or urine determinations are being performed. Treatment can be stopped if repeated lead analyses show the provisional diagnosis to be in error.

The central nervous system is frequently involved in children with lead poisoning. When involvement is such that abnormal cerebrospinal fluid findings (most commonly elevation of protein content) become manifest, the diagnosis of lead poisoning with encephalopathy may be made.[1]

Excessive coproporphyrinuria is a constant finding in acute episodes of lead intoxication, and can be demonstrated by a relatively simple qualitative test on freshly voided urine. Briefly, the urine is acidified to pH4 with acetic acid. Coproporphyrin is extracted immediately from the acidified urine into ether and then from the ether into 1.5 N. hydrochloric acid. Intense red flourescence of the hydrochloric acid layer when viewed under a Wood's light is indicative of an increased amount of coproporphyrin. Quantitative coproporphyrin determinations on 24-hour urine collections can also be performed.[9] These may be helpful in long-term management of patients.[10]

The coproporphyrinuria encountered in lead poisoning is incompletely understood, but derangement in hemoglobin synthesis and interference in prophyrin metabolism in tissues other then blood are probably underlying factors.[6]

Criteria for Lead Absorption – Once the suspicion of lead poisoning is aroused, the most important single consideration in the differential diagnosis is whether or not lead has been absorbed in quantities sufficient to induce illness. This can best be demonstrated by determining the lead content of the blood. The threshold value cited above, 0.08 mg. of

lead per 100 gm. of whole blood, is a critical one. Lead concentrations between 0.06 and 0.08 mg. per 100 gm. of whole blood are indicative of abnormal absorption of lead, but often not of a degree of absorption which is capable of inducing symptoms of intoxication.

Extensive studies have been made on the variability of the concentrations of lead in the blood and urine of adults and children, both under ordinary circumstances and under conditions of abnormal exposure to lead.[8,11-13] In a group of children between the ages of six months and four years, in whom there was no evidence of abnormal intake and absorption of lead, the average blood lead concentration was 0.027 mg. per 100 gm. of blood.[11] In a recent paper the upper normal limit of blood lead concentration in young children is stated to be 0.05 mg. per 100 gm. of blood.[12]

The appraisal of the significance of lead absorption by means of analysis of the urine is much more difficult and much less effective than that of analysis of the blood, especially with children. In young children there is a wide physiologic variation in 24-hour urinary volume. Factors such as dehydration and acidosis, often accompanying the acute episode of lead poisoning in children, can alter urinary lead output in the untreated patient, so that the amount excreted may fall within the normal range. The collection of an uncontaminated sample of urine from a young child for the purpose of lead analysis is usually difficult, extreme precautions being required to prevent contamination of the urine with lead.[6]

Administration of calcium EDTA to patients who have abnormal amounts of lead in their tissues is followed by a rise in urinary excretion of lead.[14,15] This increased lead excretion following edathamil administration has been suggested as the basis for a diagnostic test.[16] Patients receiving edathamil therapy should excrete 1.5 mg. or more of lead in the urine on any one of the first three days of treatment. This test, while by no means as satisfactory as that of the determination of the level of the urinary excretion of lead prior to any therapy, may be more practical than the collection and analysis of a 24-hour urine specimen from an untreated patient in those instances where a delay in therapy is hazardous.

Different methods for analyzing blood and urine for lead are available. A simplified procedure for the determination of lead in small samples of urine and blood has been reported.[17] This procedure requires only 2 ml. of blood where most determinations require 10 ml. The requirement of a smaller volume of blood is advantageous when working with children. Certain other analytical procedures are described in articles listed in a monograph published by the American Public Health Association.[7]

Glassware and other equipment used in the collection and analysis of blood and urine samples can and should be rendered free of any possible contaminating lead by rinsing with warm 20 percent nitric acid, followed by thorough rinsing in "lead-free" distilled water. Other special precautions must be taken in the laboratory to prevent contamination of the samples from lead-containing airborne sources during ashing and analysis.

Exposure to a Lead Source – Childhood lead poisoning, is in general a disease of poverty,[18] almost always found in areas of old, run-down housing. The source of lead is usually lead pigment paint applied and re-applied early in this century, to walls and fixtures which more recently have been neglected and allowed to fall into disrepair. These coats may be buried beneath other coats of paint, covered with wallpaper, or may cover wallpaper or plaster. With neglect the paint and painted wallpaper peel, and the painted plaster crumbles. Particles may then be picked and ingested by young children. Lead paint in good condition has been chewed off of surfaces also. An adequate safe substitute indoor paint was not made available until about 1940. Lead paint applied to outside surfaces has also been reported to be the source of lead in cases of childhood plumbism.[1,6]

Children's toys and furniture are not significant sources of lead unless repainted with lead pigment paint. Since 1955 the American Standards Association has recommended that only paints with a lead content of one percent or less may be considered safe for use on children's toys, furniture and in housing interiors.[19]

Other sources of lead should be kept in mind. Numerous cases of poisoning have occurred in both children and adults from inhalation of lead fumes[20] and exposure to ashes[21] resulting from the burning of lead storage battery casings for fuel, a practice sometimes resorted to by destitute families. Other sources of lead involved in childhood poisoning can be found in the medical literature, but in this country these sources play a relatively unimportant role. References to these are listed.[22-25]

In most cases of childhood lead poisoning, pica, the abnormal appetite for non-edible substances, is responsible for lead being taken into the body. Children, usually between the ages of one and five years, most often exhibit this abnormal appetite which may result from emotional *disorder*[26] or *nutritional deficiency*.[27] It has been shown that lead is retained in small amounts in the tissues of an adult with a daily intake of 1 mg. of soluble lead in addition to the normal daily dietary intake (0.2-0.4 mg. of lead).[28] Since lead pigment-containing paint peelings may contain 100 mg. or more of lead, the repeated ingestion of small amounts of these peelings is compatible with absorption and retention of dangerous quantities of lead in the tissues. This will eventually result in clinical manifestations of poisoning if the exposure is not interrupted.

A history of ingesting paint chips or chewing on walls or woodwork may or may not be obtained. Often such activity goes unnoticed or the amount ingested is considered insignificant by the parents. The history may be obscure, incomplete or fragmentary. The possibility of the existence of lead poisoning, therefore, must occur to the clinician from the nature of the illness itself, and he must be prepared to make a presumptive diagnosis in an acutely ill child without an elicited history of lead ingestion. Diagnosis (and therapy) must not be delayed because a source of lead is not readily demonstrable. The explanation of the origin of the disease, if it turns out to be lead poisoning, is often found after the fact.

A positive history of pica for paint and a roentgenogram of the

abdomen demonstrating radio-opaque material in the intestinal tract are valuable clues to the ingestion of lead. In New York City, blood lead analyses are performed on all children under the age of six years enrolled in the City Well Baby Clinics with a history of pica; young household siblings of these children are also examined in this manner.[29] The absence of these clues does not rule out the possibility of lead poisoning.

Exposure to a lead source may be confirmed by demonstrating that the source contains lead in excess of recommended limits. In children the history of lead exposure may usually be established by analyzing paint particles taken from the environment of the child and demonstrating excessive lead concentrations. The analytical procedure used should be an accepted one and should be performed by competent and experienced personnel.

Classification of Final Diagnosis – In making a final diagnosis involving a child exposed to lead, the following classification for diagnosis is recommended:

A. ASYMPTOMATIC INCREASED LEAD ABSORPTION

This diagnosis refers to the child who shows evidence of presence in the tissues and absorption of abnormally large amounts of lead, but who is asymptomatic. A source of lead, evidence of lead absorption, and increased radiologic metaphyseal density of long bones may be demonstrated.

B. LEAD INTOXICATION

1. Lead Intoxication Without Encephalopathy

Two or more of the clinical and laboratory criteria excluding central nervous system manifestations accompanied by abnormal cerebrospinal fluid findings, evidence for absorption of lead in dangerous quantities, and demonstration of a lead source enable this diagnosis to be made.

2. Lead Intoxication with Encephalopathy

Two or more of the clinical and laboratory criteria including central nervous system manifestations accompanied by abnormal cerebrospinal fluid findings, evidence for absorption of lead in dangerous quantities, and demonstration of a lead source enable this diagnosis to be made. This category may be subdivided, on the basis of severity of encephalopathy, into lead poisoning with mild and lead poisoning with severe encephalopathy. The latter group should include those patients who convulse and/or who are comatose for 24 hours or longer.1

The long-term prognosis of childhood plumbism (with reference to mental and neurological function) may depend upon the severity of the acute symptomatic episode. Therefore this classification should be of prognostic value.

The above diagnostic classification is also suggested in order that children who are ingesting abnormally large quantities of lead and children with lead poisoning without encephalopathy will not be overlooked. Early diagnosis is essential for a good prognosis in this disease. Removal from lead exposure and therapy with calcium EDTA[15] will more often result in a favorable outcome if instituted early. Therapy with

calcium EDTA is not as effective once acute lead encephalopathy has occurred. This drug has not significantly reduced the 10–15 percent mortality rate from lead poisoning in children and seems to be no more effective than older measures in terminating the acute episode of encephalopathy.[30] However, there is some evidence suggesting that neurologic and mental sequelae associated with childhood plumbism, and especially with encephalopathy, may be reduced by the use of calcium EDTA.[30,31]

Those communities with active programs for the control of childhood lead poisoning, where only cases of lead encephalopathy and death are being reported, are undoubtedly missing numbers of early cases. Detection of these early cases is an important activity which should be undertaken by physicians, public health workers and poison control centers in communities where sources of lead may exist.

The Public Health Service offers consultation services and technical assistance to any community with a childhood lead poisoning problem. Case finding and prevention activities together with the institution of adequate diagnostic services are essential for controlling this problem.[2] For more details contact the National Clearinghouse for Poison Control Centers, U. S. Public Health Service, Washington 25, D. C.

Summary

Criteria to be used in diagnosing lead poisoning in children have been presented. Clinical and laboratory criteria, criteria for lead absorption, and exposure to a lead source are the three areas under which the diagnostic criteria fall. Two or more clinical and laboratory criteria coupled with one or both criteria for lead absorption enable a diagnosis of lead poisoning to be made. Although chemical identification of the lead source involved is important in arriving at a final diagnosis, treatment must not be delayed if the source is not readily demonstrated.

A classification for final diagnosis concerning the exposure of a child to lead is recommended. The importance of recognizing early cases of lead intoxication and even earlier asymptomatic cases in which increased lead absorption occurs is emphasized by the classification. Use of this classification should aid in establishing a long-term prognosis. Early diagnosis is necessary to reduce sequelae and mortality from lead poisoning in children.

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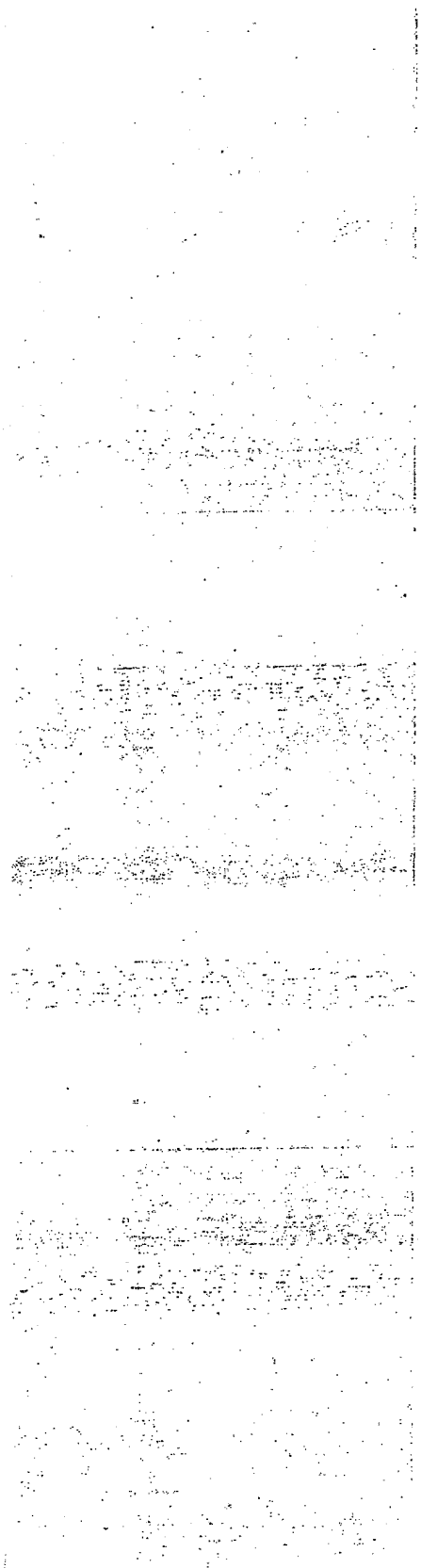

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