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PEDIATRIC LEAD POISONING

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To the physician not acquainted with pediatrics, childhood lead poisoning is at best an unfamiliar disorder; to the pediatrician, it is a treacherous disease in which the sequellae and fatality rates are disturbingly high, and of which the symptoms and signs are so commonplace and non-specific that initially the diagnosis may be easily overlooked. In some areas of the country it would appear that cases occur without being suspected. Accordingly, a review of the manifestations of pediatric plumbism and its differences from the adult disease is in order.

Clinical Manifestations

The signs and symptoms of lead intoxication among children chiefly involve three organ systems--the central nervous system, the gastro-intestinal tract, and the hematologic system. In the individual case, any one or all of the three systems may be affected. The symptom that especially should arouse the physician's suspicion is pica, or the ingestion of unusual substances, because, in the child, the route of absorption of lead is usually that of the intestinal tract. Although almost all children pass through a stage of oral exploration and chewing, this habit should have subsided by the age of 15 months and should never be of great intensity. Careful inquiry concerning the substances chewed is in order; for, when the history has been considered to be reliable, the child with lead poisoning has been found to have chewed on painted objects, plaster, wallpaper or putty for at least three months before clinical manifestations appeared (1). Despite the importance of pica as a historical signal, the diagnosis must not rest on a history of pica, since even careful questioning will uncover such a story in as few as 60% of cases at the time the patient is first brought for medical advice (2), and in a few instances the source of exposure never is discovered. On the other hand, since pica can provide the earliest warning of a future case of lead poisoning, inquiry concerning pica should be part of the history in every examination of a toddler aged child.

The most frequent hematological clue is the finding of a microcytic, hypochromic anemia. Regardless of its etiology, anemia indicated by less than 10.5 g. of hemoglobin per cu.mm. and associated with microcytosis and hypochromia is an almost invariable finding in lead poisoned children. Admittedly, iron deficiency anemia occurs so commonly in toddler aged children--in our hospital Lahey observed a 30% incidence in children in their second year of life (3)—that only a small portion of the children with such a blood

picture may be shown to have absorbed potentially toxic amounts of lead. Nevertheless, the observation of a microcytic, hypochromic anemia should raise the question of plumbism for investigation.

More than one explanation of the mechanism of the anemia in lead poisoning has been reported. In the adult, plumbism causes an interruption in the incorporation of protoporphyrin into heme (4). This, in turn, produces an appearance of the erythrocytes similar to those seen in iron deficient states, but with an increase in the free erythrocyte protoporphyrin, a normal serum content of iron, and a poor response to iron therapy in the absence of concomitant "de-leading" treatment. In addition to the interruption of porphyrin metabolism, an element of mild hemolysis may be considered to be due to an injury to the surface of the erythrocyte. Although in some children the hematologic findings indicate an interruption in the porphyrin metabolism (5), in the majority, the anemia will respond to iron therapy, thereby indicating coexisting deficiency of iron (2). The probability of lead intoxication, however, is increased if a hypochromic, microcytic anemia is associated with failure of response to iron therapy. Another piece of supportive evidence is the finding of stippling of the erythrocytes, but since stippling is observed in only 60 per cent of childhood cases, its absence should not discourage the diagnosis.

Among the gastrointestinal symptoms are recurrent vomiting, vague abdominal pain and constipation. Inasmuch as these are common pediatric complaints, a high index of suspicion is needed, if plumbism is to be recognized. Each summer, several toddler aged children with vomiting are seen two or three times in our Emergency Room before a diagnosis other than nonspecific gastroenteritis is suspected. In other instances, children are hospitalized for study of vague abdominal pains--not the board-like abdomen of adult lead colic--before the true diagnosis is considered. Constipation is a less common and less prominent symptom in the pediatric than in the adult form of the disease. Rarely the finding of black stools, in the absence of iron therapy, may be the result of the presence of lead sulfide. In contrast to adults, only the exceptional child with plumbism exhibits a lead line along the gums.

The most serious manifestations of pediatric saturnism are those resulting from cerebral involvement. These may vary from undue drowsiness to deep coma or repeated grand mal seizures. Sometimes the first clues are repetitive falling, clumsiness and ataxia; in other instances, convulsions cause the child to be brought for medical care. There is nothing especially characteristic about the convulsions, for they may occur with or without fever and may be focal or generalized; but when, in the course of a few hours,

the pattern of the seizures switches back and forth between right-sided, left-sided, and generalized, the possibility of plumbism deserves particular consideration. The physical examination under such circumstances may reveal papilledema, ataxia, lethargy, or seizures - with or without local paralyses and with or without reflex changes - and as such serves to confirm the involvement of the central nervous system but does not provide evidence concerning the etiology.

Laboratory Tests

Although symptoms and signs of hematological, intestinal or neurologic involvement occur in pediatric lead intoxication, none of these manifestations is diagnostic of the disease. We have observed repeatedly that the child with extensive pica but no undue absorption of lead, may have complaints identical to those of children with actual lead poisoning, with the exception that clear-cut signs of central nervous system disease do not occur in uncomplicated pica, but instead suggest the presence of lead encephalopathy. Accordingly, laboratory assistance is needed to pursue further the diagnostic inquiry. Unfortunately, the final proof that a child has assimilated sufficient lead within his soft tissues to have caused a potentially dangerous and toxic state can come only from time-consuming analytical studies of the content of lead in the blood, or less reliably, in the urine (6). Furthermore, suitable analytical facilities, including competent personnel, are not yet available in a great many communities. Therefore although not specific, several relatively simple and quick laboratory tests are in order pending the analytic results. Reference has already been made to the almost universal finding of a microcytic, hypochromic anemia. Whereas the presence of this anemia does not prove the diagnosis of lead intoxication, the absence of anemia makes the diagnosis unlikely (but does not exclude it). Stippling of the erythrocytes is also suggestive although not specific evidence; but since 40 per cent of our cases have not had this finding, its absence does not exclude the disease. Occasionally plumbism has been first suggested by the finding of eosinophilia; for the child who has ingested dirt and thereby acquired ascariasis or toxocarosis may also have chewed on lead-containing substances. In reverse fashion, a search for intestinal parasites is indicated for children diagnosed as having lead poisoning.

A very helpful sign is the observation, upon radiography, of radio-opaque flecks within the intestinal tract. This finding has been observed in 60 per cent of our cases, but may not occur if the child has been vomiting extensively, or has been removed from his exposure during the previous several days. Whereas so-called "lead lines" are

rarely seen in the gums of children, "lead lines" or lines of increased osseous sclerosis are commonly apparent at the ends of the long bones. Inasmuch as mild increases in density at zones of provisional calcification can result from other causes besides lead, more emphasis is placed on the "lead lines" if there are associated lines of increased density at the ends of the metacarpals, the phalanges, and the ribs, at the tips of the scapulae, or over the iliac crests. At times these roentgenographic changes have been the first indication that a child has been exposed to potentially toxic amounts of lead.

Additional support for a tentative diagnosis may come from the urinalysis. Although it is the exceptional patient in whom lead intoxication is manifested by Fanconi's syndrome of albuminuria, renal glucosuria, aminoaciduria, and phosphaturia (7), approximately 30 per cent of our patients have had either albuminuria or glycosuria, usually in only slight degree. A more healful finding is that of distinct coproporphyrinuria. When coproporphyrin has been present in large amounts in the urine, it has usually been related to the more severely ill and symptomatic cases (8). On the other hand, many asymptomatic instances of absorption of excessive and potentially toxic amounts of lead occur in the absence of coproporphyrinuria, and accordingly efforts to detect the earliest stage of lead intoxication must not rely on this test alone. A tentative diagnosis of plumbism is made if, in the presence of pica or other suggestive symptoms, any two of the following four tests are positive: anemia together with stippling; radio-opaque flecks in the intestinal tract; lines of increased density at the ends of the long bones, ribs, scapulae, and iliac crests; and coproporphyrinuria. These tests should be readily procurable in any hospital, clinic, or emergency room.

Once a tentative diagnosis is made, two further steps are undertaken. First, blood is drawn for a quantitative determination of lead, as a means of establishing whether the child has accumulated potentially toxic amounts of lead within his soft tissues–i.e., levels of 0.08 mg. Pb/100 g. of blood or greater. We do not generally ask for determination of lead in the urine of small children, since it is extremely difficult to avoid contamination when one is dealing with one-to-three-year olds, especially girls, and since a prolonged period of time is required for the collection of an adequate specimen. The second step, after the tentative diagnosis has been arrived at, is to include or exclude the possibility of encephalopathy. This distinction is based chiefly upon the presence or absence of an elevated level of cerebrospinal fluid protein. Accordingly, a lumbar puncture is done on any child with a tentative diagnosis of lead poisoning who has the least symptom or sign of possible cerebral involvement. That this definition of encephalopathy has been a useful one, can be seen from the fact that an increased cerebrospinal fluid protein was noted in all of our patients who had neurologic sequellae or who displayed severe mental re-

tardation after plumbism.

Sequelae

A host of residuals have been reported and serve to emphasize the importance of prevention. Besides a 25 per cent fatality rate among those with encephalopathy, the most serious sequelae involve the brain. Recurrent convulsive seizures, with both focal and generalized electroencephalographic abnormalities occurred in 40 per cent of our patients with prior encephalopathy, and an additional 20 per cent had paralyses or other significant neurological deficits. Intellectual ability, as reflected by intelligence quotient, may be impaired following the disease. Five or more years after their original illness, children with encephalopathy have been found to have an average I.Q. of 80 (range, 58 to 104), while the average I.Q. in those who had had lead poisoning without encephalopathy ranged from 75 to 117, and averaged 87. In contrast, the average I.Q. of 98 was recorded both for controls and for a group that had had pica without lead poisoning (9). Behavior problems, poor discipline, inadequate interpersonal relationships, inability to comprehend the abstract (10, 11), increased incidence of acute poisonings, and late chronic nephritis (12) are among the other reported residuals of plumbism among children.

Chisolm and Harrison (1) stress that the severity of residuals may be correlated with the duration of the exposure to lead and with the incidence of recurrent episodes of exposure. Their findings suggest the need not only for prompt interruption of the exposure to lead and the early removal of lead from the body, but also for prolonged vigilance to ensure that re-exposure does not occur. In the past five years, 19 per cent of the 229 instances of excessive lead absorption documented among children in Cincinnati have been recurrent episodes. The level of lead in the blood of most of these children has been only just above the upper normal limit, but is still indicative of continued or recurrent exposure. It should be remembered that far smaller quantities of lead must be absorbed to maintain a toxic level than to achieve it.

Epidemiology

Preventive efforts require a knowledge of the situations in which lead intoxication is likely to occur. As has been stated, the disorder occurs primarily among toddler aged children, 90 per cent of the cases occurring in children between 15 and 36 months old. If one member of a family is found to have plumbism, all the siblings between one and five should be carefully checked since there is a 33 per cent incidence among siblings (1). A preponderance of non-whites merely reflects the population residing in the older,

more disheveled dwellings in the impoverished areas of our cities from which virtually all cases of pediatric plumbism come (13). Interior surfaces within buildings in these areas have, over the years, received numerous coats of paint, many of which contained lead, and with the influx of an economically poor population, the walls and ceilings have fallen into disrepair, providing a readily available source of exposure for any inadequately supervised toddler who, due to a variety of poorly understood factors, continues to explore with his mouth.

Although the habit of pica may be present in any season of the year, and although the ingestion of lead usually persists for at least three months before potentially toxic levels of lead accumulate in the body of the child, symptomatic lead poisoning among children is confined almost entirely to the hotter months of the year, late April through September (1). Various theories for this seasonal incidence have been proposed, but as yet no satisfactory explanation had been obtained (14, 15). Extremely infrequent instances of symptomatic saturnism have occurred in the winter months; the majority of these cases were also unusual in that they resulted from respiratory rather than intestinal route of absorption, having followed the burning of automobile battery casings.

Treatment

The treatment of lead poisoning in children falls into four main categories: the elimination the source of abnormal exposure to lead, the hastening of the removal of lead from the body, the symptomatic therapy for lead encephalopathy, and the prevention of re-exposure to lead. That the therapy is not so effective as one would wish, is apparent from the statistics of morbidity and mortality which have already been mentioned. Once a presumptive diagnosis has been made, the first step is to stop any further exposure to lead. Generally, this is best achieved by removing the child from the environment in which he has obtained the lead. Although occasionally the mildest cases may be transferred to a different home or sent to a convalescent home, most children are hospitalized. To prevent the absorption of such lead as remains in the intestine, laxatives and repeated enemas are given. Over the years, many drugs have been used in attempts to remove lead from the soft tissues either into the bones or from the body. The only effective chemical agents have been British Anti Lewisite (B.A.L.) and the disodium calcium salt of ethylenediamine tetra-acetic acid (E.D.T.A.). Because of its greater effect on the removal of lead and because of a reportedly lower rate of sequelae (2), E.D.T.A. has been used in preference to B.A.L. Even with the use of E.D.T.A., four or five days are required for the removal of only 25 mgm. of lead, on the average, whereas the soft tissues

of a child with saturnism may contain as much as 50 or even 100 mg. of lead (2, 16). A serious drawback to the use of E.D.T.A. is that an exacerbation of symptoms, especially those of encephalopathy, may occur during the first 24 hours of the therapy. Attempts to avoid this difficulty through careful cleansing of the intestine before initiating the drug therapy, through the use of small doses initially, and through the restriction of fluid and electrolyte intake have been disappointing. Currently, following the suggestion of Chisolm (17), we are using B.A.L. together with E.D.T.A. in the following regimen:

B.A.L. 4 mgm./Kg/dose intramuscularly every 4 hours for 5-6 days

E.D.T.A. 12.5 mgm./Kg/dose intramuscularly, mixed with procaine, also every 4 hours for 5-6 days

The first dose of E.D.T.A. is given concurrently with the second dose of B.A.L. Before initiating this therapy, one should make certain that the child is voiding well. Thus far, too few patients have been managed with the combined therapy to yield any reliable impression of its value.

Children whose blood contained markedly elevated levels of lead-greater than 0.10 mg. Pb/100 g. and those with persistent coproporphyrinuria following the first course of E.D.T.A., should have one or more additional five-day courses at five-day intervals. All children should have the lead content of their blood determined after the lapse of at least two weeks after their last course of E.D.T.A., this time interval having permitted some redistribution of lead from the skeleton into the soft tissues (this process is usually far from complete in two weeks).

If the symptoms, signs, and spinal fluid protein indicate the presence of encephalopathy, symptomatic treatment for a swollen and distorted brain is in order. In an effort to reduce cerebral edema, 1 to 1.5 g. of urea per Kg., as a 30 per cent aqueous solution has been administered at 8 to 12 hour intervals, with conflicting reports as to the results (18). No untoward results of this therapy have developed in our hands, but if, within 6 to 8 hours, distinct improvement in the frequency of seizes, depth of coma, or signs of severe cerebral edema does not ensue, radical craniectomy is undertaken without further delay to provide cranial decompression (19). We believe that such surgical intervention may save an occasional life, but that the brain has usually been irreparably injured. When craniectomy is performed, it should be followed by measures to prevent so-called Cushing's ulcers of the esophagus, stomach, and duodenum. For this purpose, slow gastric drips of milk, antacids, and anticholinergic drugs are advised.

The final step in management is to prevent re-exposure. In cooperation with the Public Health Department, the home should be made "lead free" or a new home found before the child is returned to his family. Social service and psychiatric consultation should be held in order to rectify any inadequacies of supervision, discipline, or emotional climate that might have contributed to the pica. Although only infrequently does it abort the pica, therapy with iron should be prescribed to remedy the co-existent iron deficiency anemia. Perhaps the most vital step of all is to continue to observe the child frequently after discharge, drawing blood for lead analyses at three or four month intervals in order to be certain that unrecognized and untreated re-exposure does not occur.

Summary

To summarize, lead poisoning is a treacherous disease because in early childhood its clinical manifestations are commonplace and not specific for plumbism. The intoxication develops gradually, requiring persistent ingestion of lead-containing substances usually over a period of at least three months. Then, chiefly during the hot summer months, acute manifestations may develop indicating involvement of the central nervous, gastro-intestinal, or hematologic systems. For early recognition of the disease, a high index of suspicion and judicious use of four laboratory tests--blood examination for anemia and erythrocytic stippling, roentgenograms of the long bones for "lead lines," plain x-rays of the abdomen, looking for radio-opaque flecks within the intestines, and a urinalysis especially checking for coproporphyrinuria--are essential. If any two of these four tests yield positive evidence, a tentative diagnosis of plumbism should be made, blood should be obtained for a precise analysis of lead, and the possibility of encephalopathy ruled in or out. The search for cases of saturnism should be chiefly among 15 to 36 month old children residing in the older, more impoverished areas of the city, where the interior walls and ceilings of the houses, having in the past been repeatedly painted are now in poor repair. Patients once treated must be watched closely for recurrences, and siblings of children with lead poisoning ought to be carefully checked for the disease. Treatment, which regrettably does not prevent either a fatality rate of 25 per cent if encephalopathy is present, or a high incidence of neurologic and behavioral sequelae, includes the termination of the exposure to lead, hastening removal of lead from the body through the use of E D.T.A. and B.A.L., symptomatic therapy for encephalopathy, and the prevention of re-exposure to lead. Having stressed when to suspect pediatric lead poisoning, how to diagnose it, and how to treat it, I should like to conclude by stating that being entirely a man-made disease, it should be totally preventable!

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