November 1, 1967

Hugo Dunlap Smith, M.D.
Professor of Pediatrics
The Children's Hospital Research
Foundation
Elland Avenue and Bethesda
Cincinnati, Ohio 45229

Dear Hugie:

I have commented fairly extensively on the document which you sent to me yesterday, in two sets of sheets. One of these marked "A" gives some suggestions of mine for actual rewriting. The other marked "B" elaborates a bit on some of the faults of the document as I see them.

I hope my efforts to be helpful will serve your purposes. You are at liberty to use my comments in any way you choose. I'll be glad to discuss any of the points involved if you wish me to.

Sincerely yours,

Robert A. Kehoe, M.D.
Professor Emeritus of
Occupational Medicine

RAK:wp

enclosures

THE CHILDREN'S HOSPITAL RESEARCH FOUNDATION

EDEN AVE. AND BETHESDA

CINCINNATI, OHIO 45229

DEPARTMENT OF PEDIATRICS
COLLEGE OF MEDICINE
UNIVERSITY OF CINCINNATI

October 26, 1967

Dr. Robert A. Kehoe
Professor of Industrial Medicine
Kettering Laboratory
Eden and Bethesda Avenues
Cincinnati, Ohio 45219

Dear Dr. Kehoe:

This is the document about which I spoke to you and that we wish very much you will critique for us.

Many thanks.

Sincerely yours,

Hugo Dunlap Smith, M.D.
Professor of Pediatrics

HDS:ea

Enclosures

Lead intoxication in childhood is usually an acute disease which has manifested itself in active symptomatolgy following a brief (months) or somewhat prolonged (usually less than two years) period of abnormal absorption that has built up a dangerous body burden of lead. Symptoms varying in severity may persist until this body burden has diminished to essentially harmless levels. The onset of acute episodes occurs most frequently during the summer months in the Northern hemisphere, but it may occur at any time of the year when the rate of absorption of lead and the quantity of lead absorbed have reached dangerous levels. Approximately 25 percent of the survivors of acute lead encephalopathy sustain irreversible damage to the brain. If injury to the central nervous system is to be prevented or minimized, chelation therapy must be instituted promptly and, preferably, prior to the onset of major symptoms. It may be necessary to decompress the brain surgically in the more severe cases of encephalopathy in order to save the life of the patient or to prevent irreversible damage to the brain.

Intoxication results from weeks, months, or years of exposure of the child with pica to readily accessible sources of lead in his immediate environment, most frequently to household surfaces painted with lead-containing paints which may be chewed or sucked, or may yield flakes of crazing paint to exploring fingers and mouths.

Page 4, first sentence of Paragraph 2 is inaccurate and should be rewritten as follows or equivalent:

Daily or frequent exposure to lead through the ingestion of sufficient

A

quantities of paint or other lead-containing material (ranging from somewhat less than a milligram to ten of fifteen milligrams of lead per day) must continue for some time, over periods ranging from one month to two or more years, before a toxic or potentially lethal quantity has been absorbed into the body - - continue text unchanged to last sentence of paragraph - - Nevertheless, all children in the household less than 5 years of age should be investigated as to their absorption of lead or their symptoms of lead poisoning, whenever an index case is found.

Continue text, as is, to last paragraph on Page 4, which should be modified as follows: "The most valuable presumptive test in children is the determination of the content of Coproporphyrin III in the urine, by a method that has an established precision.

Continue without further change through Page 4 and Page 5. (I shall not comment on the therapy, since my experience is at second hand.) I regard the discussion of the relative merits of the use of BAL with EDTA as very dubious, especially the statement that BAL minimizes the possible toxic effects of chelation with EDTA (this flies in the face of what is known mechanistically about both, but if the emperical facts seem to justify these statements, I cannot gainsay them). I also think the statement about surgical intervention (of the right kind) should be queried. Moreover, I would guess that the analytical values indicative of danger, i.e., 100 micrograms of lead per 100 grams of whole blood, is an expression of an analytical method that has a larger error than that of certain other methods. I can see no justification for not regarding anything over 80 micrograms of lead per 100 grams of blood as clearly indicative of danger, if the determinations are equivalent in accuracy to our own. I always speak of the sensitivity and precision of the

A

analytical method in this relationship, since the error of some of the methods in certain hands is in excess of 20 percent. It happens that this is of considerable clinical importance. I agree however that children (and adults) may be asymptomatic with blood levels well in excess of 80 micrograms, or 100 micrograms, for that matter, and I would treat them for the prevention of illness.

I have rewritten the first page down to the second sentence of the second paragraph. The reasons for the changes and deletions follow:

1. Lead intoxication is not a chronic disease in the ordinary meaning of that term. Especially in children, but also in the adult, the onset of poisoning is essentially acute. It is the duration of exposure that is, so to speak, chronic. Time is involved in building up lead in the body to a toxic level, but when the level has been reached, and the onset is triggered by the appropriate stimulus, the illness is acute. The ~~combined~~ use of the term "chronic lead poisoning" is a semantic habit that should be discontinued.

2. Lead is not mobilized from bone by any mechanism that is now known, with the possible exception of bone disease that results in vertual disintegration of the skeleton within a comparatively brief time. There is simply no valid evidence that the more common of metabolic disturbances, including the intervention of intercurrent infections, results in any significant change in the metabolism of lead. The skeleton discharges lead in apparent compliance with its own metabolic activities in accordance with the laws of mass action. (The concentration of lead, in the bone, as compared with that of calcium, for example, is so slight as to be only proportionately, almost negligibly, effected by the usual metabolic disturbances of the body in sickness and in health.) ~~This idea~~ The contrary view was discredited years ago, and has continued in medical thinking, only because it was so authoritatively but mistakenly embedded there, before present methods of investigation were available. It is important that this fact be appreciated, especially by clinicians, since its persistence leads to misinterpretation of the causal background of the disease in the specific child, and also to mistaken therapeutic rationale, especially in matters of prevention.

3. I have added the statement about surgical intervention to the first paragraph for the reason that it should be thought of promptly in the salvaging of certain cases. Undue delay may result in loss of life or loss of cerebral competence.

B

4. I have eliminated the term chronic in Line one of the second Paragraph. It is better to say what one means, rather than to fall back on a much misused term in relation to plumbism. I have also - I think - improved the sentence by some additional words.

5. I would delete the statement in parenthesis in Line 10 from the bottom of Page 3. It is probably untrue. The figure in the case of the child is not known, but the value of 0.5 mg. per day is the upper limit of the safe daily dose of lead for the adult. In any case, nothing is contributed by this dubious statement, because of the necessity of introducing the factor of time into any level of daily dosage.

6. The statement about children in Cleveland, Ohio, on Page 3, Line 7 & 8, should be clarified. "May have plumbism" might be interpreted as meaning that one cannot determine whether or not they have. What is meant, I believe, is that they are in a dangerous environment, are absorbing lead at an abnormal rate, and may reach a dangerous level of absorption. Why not say "May develop plumbism" or "May develop plumbism, if they continue under their present conditions of exposure."

7. One may doubt that "bootleg whiskey," Page 4, Line 2, is significant in lead poisoning among children (in the age group under discussion). Since several other sources are omitted, this could be deleted from this discussion without loss.

8. On Page 9, the discussion of laboratory facilities, in my judgment is at fault. There is no good reason why at least one adequate laboratory cannot be established in any community of any size. This disease, generally speaking, occurs in communities large enough to have slums, although an occasional case may occur in smaller towns. Moreover, inquiry will serve to discover the existence of laboratories from which accurate analytical results can be obtained. This should indeed be done, rather than to put dependence upon a local inexperienced and ill-equipped laboratory. You will know what is appropriate to say in this connection, but some statement as to

B

a source of information about analytical laboratories might well be made.

9. Reference is made to the measurement of lead in hair (Page 9, Line 13, from top and Lines 8,9 & 10, from bottom). This should be deleted. There are no satisfactory data, nor are there likely to be, as to the physiological or toxic significance of lead in the hair. It is not even possible to distinguish between lead in and on the hair. This test has been "rediscovered" recently. It is just about as useful as the analysis of punched out plugs of skin, and it should not be sanctioned by presumably knowledgeable persons.