

MEDICAL DEPARTMENT
OCCUPATIONAL MEDICAL SERVICE

CAMBRIDGE 39, MASSACHUSETTS

December 7, 1964

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Dear Bob:

I was very much flattered to get the letter from you following my earlier one to Red Johnstone on the use of Calcium disodium EDTA. I think it curious that you and I have had such different experience in alleviating the same symptoms of lead intoxication. I am going to enclose a clinical study for which I was responsible that reports our favorable experience. We go on having this same experience with adult lead poisoning as reflected in reversal of hematological abnormalities and symptoms. I do not see a great number of cases these days and perhaps my experience is not the usual, but when I talk with my colleagues here locally who do see cases they appear to be having the same kind of experience that I am.

In the last letter of your first paragraph, you refer to children having further lead exposure as a reason for using this therapy. I think the same thinking needs to be applied to certain workers in lead-using industries. We find in this area that those men who start working in the storage battery industry enjoy it and go from one plant to the other and have continuing lead absorption. This is also true in a series of cases we have been seeing of men exposed to lead in the dismantling of structural steel bridges covered with leaded paint as well as in construction where leaded paint is used as a protection against weather. These men are sent from job to job, hired through their unions, and there seems to be no good way of controlling their lead exposures by the character of the work and method of hiring. It seems to me that in these individuals one has to tell the worker that he must change his job, and

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this of course is not always easy, in order to keep the body burden of lead small enough so that there are no detectable signs of intoxication even though lead absorption continues. I think this is a very practical problem not easily solved.

Now let me try to present my view of the use of the chelating agent for diagnostic purposes. Incidentally, I would appreciate reference to the "very considerable amount of evidence" that you speak of in the first line of your second paragraph. And I would certainly like very much to know whether or not there are any other references I should have of Dr. Tipton or others beyond that to be found in the January 1964 Archives of Environmental Health. In reading Tipton and others on this subject, I gather that the data are not final because of variation in analytic methods and lack of knowledge of lead in the human body in various parts of the world. However, from reading your letter it would appear that I am not adequately informed on this subject.

Then, I am very much interested in your remark that the pattern of distribution of lead does not change except in response to therapy with a chelating drug. Is it not necessary to take into consideration that the body itself makes a number of chelating agents as, for example, citrates. Some years ago before EDTA was available, I followed up the observation that one might use Sodium citrate to bring lead out of the body and I was able to do so with some success but nothing like the success that can be achieved with EDTA. I remember being told at the time that it would be difficult to assess the value of this procedure because of the fact that the body itself makes and uses the citrates as chelating agents. (Ref.)

I know very well your work on the normal lead content of the body. I wonder if you have any references on the determination of the body burden of lead in cases where there has been unusual lead absorption with or without intoxication. Your letter you can see is very interesting to me and brings out many of the questions that have occurred to me over the years in my study of the body's handling of lead. Let me hasten to say how modest my experience is, but this is no index of my interest in the matter.

Further, Bob, in thinking about distribution of lead in the body I am puzzled that you say that the behavior is so very predictable. Am I wrong in believing that lead and calcium behave in a similar fashion? Current knowledge certainly makes it clear that calcium is constantly on the

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move in the body and its precise rearrangement at any time in any place in the skeleton or in the urinary tract is determined by a number of factors that can differ under a number of circumstances. I had somehow thought that the same line of thinking was appropriate in consideration of lead body burden. Do help me out on this point.

I certainly would agree with you that the clinical use of calcium disodium EDTA as a diagnostic procedure is both empiric and pragmatic. However, I find it difficult to believe that once one has gained some experience it is not a useful tool. What has bothered me in the past is that conceivably if the kidney were damaged by any disease not easily detected, the diagnostic procedure might be of some harm. However, in talking with renal physiologists and in gaining experience where the maneuver seemed appropriate I have come to believe that the small diagnostic dose that we use is not harmful to the kidney.

In your discussion of the concentration in the blood with undisturbed body metabolism I think that you are really on my side in that it is quite impossible to be sure that the body metabolism is not being disturbed because of the many factors introduced during management of illness. In the Boston area, individuals who are not exposed to lead in industry will excrete with a single dose of EDTA .5 mg of lead per liter of urine with remarkable consistency. Now I certainly agree with you that one cannot interpret very closely the precise amount of lead that is excreted after a single dose of EDTA. However, there are generally other signs that can be put together with the amount of lead that is excreted after this single dose to make this a consistently useful diagnostic point. For example, I recently had a patient sent to me from one of the shipyards who had certainly been exposed in years gone by to leaded paint in his work. He had a number of complaints chiefly cough and shortness of breath but also weakness and easy fatigue. He did have evidence of emphysema and the question rose whether this was the only diagnosis. A single dose of EDTA showed that he excreted something of the order of .6 mg per liter of lead in urine. My opinion was that he did not have a lead body burden that would be any problem to him no matter what the changes in his metabolism might be. Like you, I find the over reading of lead absorption very troublesome and have thought that in this diagnostic procedure with EDTA it might be possible to develop sound evidence that could not be knocked over by an overenthusiastic lawyer or misinformed union steward trying to push a compensation case.

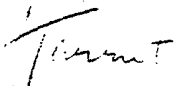
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I hope these rambling notes are of interest to you. I will certainly look forward to hearing from you again. I shall be most grateful for references that I can use to fill out my present file on this subject.

Sincerely yours,


Harriet L. Hardy, M.D.

HLH:ms

Enclosure

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