

UNIVERSITY OF CALIFORNIA

LOS ALAMOS SCIENTIFIC LABORATORY

(CONTRACT W-7405-ENG-36)

P. O. Box 1663

LOS ALAMOS, NEW MEXICO

IN REPLY
REFER TO:

H

June 29, 1955

Dr. Robert A. Kehoe
The Kettering Laboratory
University of Cincinnati
Cincinnati 19, Ohio

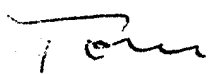
Dear Bob:

Thanks for your letter of the 24th. Harry Foreman told me only yesterday afternoon that he has nearly completed his final draft of the paper on the renal damage associated with prolonged administration of EDTA and he has agreed to send you a copy of this as soon as it is together in one piece. This will be primarily for your own information but we also hope that you will not hesitate to send back any comments which you may have. It appears to us that the injury to the kidney caused by EDTA is a form of toxicity rather unlike that with which we are usually concerned. Most toxic effects result from an actual chemical reaction between the toxin and some tissue component. In this situation, it would appear that the EDTA does not take part in any such chemical reaction but its presence apparently produces a local physical-chemical change producing an actual hydrops in certain cells. As I said, we have now observed this clinically in two human cases and I think that Harry has demonstrated the mechanism quite conclusively in rats.

As far as the use of EDTA in lead poisoning is concerned, I have had no first-hand experience and have depended on what I have learned from others. We have, however, had some interesting experiences with individuals who have absorbed significant amounts of either plutonium or americium. In these cases, we have known with reasonable accuracy the actual body burden as well as the expected rate of excretion in the absence of therapy. EDTA without any question increases this excretion so markedly that it is possible to eliminate a very significant percentage of this body burden which would not be eliminated otherwise. In these situations, of course, we are dealing with quantities of a microgram or less. We simply don't know how effective treatment would be in the case of a massive, perhaps fatal, overexposure. It is difficult to extrapolate these results to the lead problem. I have never yet been able to find out what actual body burden of lead is required to produce symptoms of plumbism. We know something about exposure levels and excretion rates but it seems to me that we still know comparatively little about retention. It's a great pity that there is not a suitable radioactive isotope of lead which would permit the study of this problem.

Very sincerely yours,

cc: M. Bowditch
H. Foreman
File


THOMAS L. SHIPMAN, M. D.,
Health Division Leader

*Rec letter 1/25/55 from
Rosenkitch & Dr. Kikuchi
Lansane, 6/24/55 filed in
lead in literature*

June 24, 1955

Dr. Thomas L. Shipman
Health Division Leader
Los Alamos Scientific Laboratory
P. O. Box 1663
Los Alamos, New Mexico

Dear Tom:

I appreciate your courtesy in writing to me about the Riker advertisement and the issues relating to it, and I am glad to have your expression of your attitude on the controversy, if that is the proper name for it. Insofar as I am concerned, it is not strictly speaking, a controversy. I have had occasion to speak for myself, and, in some sense, for two of the Councils of the A.M.A., and having spoken on a matter which concerns me deeply and relates itself to the wise and ethical practice of occupational medicine, I am finished with it, at least for the present. We are looking into some of the technical points involved in some experiments that may or may not be productive of real and pertinent information, and from that aspect the matter is unfinished, as it may well continue to be for a long time, but I, like yourself, refuse to engage polemics, which are both unproductive and unduly wearing.

In order to remove myself from what appeared to be developing into a pitched battle in which I never intended to engage, I wrote to George Maisson (of Riker) whom I have known for some time, explaining my position and pointing out to him and his associates the situation into which they were entering somewhat naively. Quite apart from the questions of utility and safety in connection with the procedure which they advocate - questions which require more answers than are now available - is the basic principle of using therapy as a substitute for the prevention of the absorption of potentially or actually dangerous quantities of lead. This, I am sure, from long and wide experience in the lead trades, is a stupid and immoral procedure. In the occasional instance, under appropriate conditions, under the management of a wise and capable doctor, this can be done, but as a general measure of prophylaxis it is brutal opportunism unworthy of a doctor of medicine or of a soundly sensitive owner or manager of a business. It makes me cringe in bitterness and shame at our ignorance and weakness of principle, that some of our colleagues are not only willing but enthusiastic panderers in this matter.

In the matter of the effectiveness of the preparation in the treatment of lead poisoning, the crucial evidence, in my opinion, will come from the study of the severe and often fatal cases of lead poisoning among children. We are

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in our third season of the use of the agent in that manner, and I believe that the regimen now in use will answer a number of the questions at issue in a fairly clear cut manner. If this is an average year, we shall have some twenty-odd cases within the next four months, of which under average conditions six to eight would die. Thus one does not need to draw conclusions from the degree of abatement of disagreeable but not critical manifestations of the disease, but can judge the issue (in time, if not at once) on the criteria of (1) survival and (2) sequelae. The arrangement between our staff and those of the Children's and the General Hospitals is such that these cases can be studied fairly well from both clinical and metabolic aspects. We have data on some twenty cases of varying types, and these data are being assembled for critical examination. This is a fairly elaborate task, and none of us who are involved have the time required to do it promptly, but we shall get it together eventually. Quite frankly, I am not too much impressed by the evidence now available in the literature on the treatment of lead poisoning, so far as I have had time and opportunity to examine it. One can be highly enthusiastic about the augmentation and the manner of the elimination of lead from the body. This is important, but it is not the important point. This can also be done fairly well by the administration of BAL. The real question is that of the influence of the agent on the course of the intoxication. Will it relieve the illness and will it save life? We seem to have some difficulty, even among supposedly realistic clinicians, in getting down to the basic question of the primary purpose of therapy. This is strange, especially in view of the experience with BAL, which does not indicate that this agent is beneficial. One would think that such experience would have promoted a healthy skepticism about the benefits of so-called deleading per se.

I am most interested in the renal damage to which you have referred, and I shall be concerned to know more about this as further information develops. The nature and the mechanism of the effect intrigues me, and if and when you learn more about it, I'll be glad to hear from you directly or through publication of the results.

Sincerely yours,

Robert A. Kehoe, M. D.

RAK:ef

C.C.: Mr. Manfred Bowditch

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