September 28, 1953

Messrs. Frank Austin and Donald Ostrow
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Gentlemen:

I regret that the pressure of preparation for an extended trip abroad has made it impossible for me to answer your letter of August 18 earlier. Many items of unfinished work still remain behind me as I leave today, but I cannot be guilty of neglecting your questions completely despite the fact that I cannot answer adequately.

The diagnosis of lead poisoning is covered adequately, I believe, in the booklet and reprint which I send you, but the therapy is a different story. Let me comment briefly on various aspects of the matter for such use as it may be to you. There is so little in the literature on recent aspects of the matter, that my comments may seem to lack documentation, but that will have to be as it may. On certain issues we shall have to wait for more information, since the answers are not available. Therefore, all of us must be patient and try not to arrive at conclusions until the facts are obtained.

First, let me say, with emphasis, that the processes of "deleading" per se constitute an invalidated form of therapy. Those advocated years ago on the basis of the alleged parallelism of the lead and calcium metabolism, are not possible to achieve, since the hypothesis of the parallelism is incorrect, insofar as it relates to procedures for "storing" lead, on the one hand, and "mobilizing" it on the other. The hypothesis was elaborated before methods of analysis were adequate - as applied to urine and blood - to demonstrate its inapplicability. The metabolism does not work that way at all, for indeed lead and calcium are almost certainly in competition for the phosphorus linkage, so that the one interferes with the other under suitable conditions. Thus the lead may be in the process of absorption and deposition when the calcium is being released and excreted, and vice versa.

Second, the release of lead from certain tissues of the body may be accomplished in some measure both by BAL and EDTA, but this, in

itself is not necessarily good therapy. It is interesting in relation to mechanisms, and therefore important experimentally. However, the matter of real and sustained clinical improvement is a wholly different matter. BAL releases lead from the blood (erythrocytes) very rapidly so that excretion, mainly via the urine, is greatly but briefly increased. There is no evidence that any "mobilization" from the skeleton occurs, and it appears that any such action is slight and of secondary importance, if it actually occurs at all. The real problem, however, is the clinical situation, for not only is there no good evidence that the use of BAL brings about clinical improvement, but there is some that seems to prove that it may precipitate more serious illness. (This has not been our experience, but I cannot ignore certain observations of others.)

In the case of EDTA, also, increased excretion of lead occurs. From sketchy data, I think it safe to say that the pattern of the behavior of the lead complex with EDTA is different from that of BAL, but wherein it is different is not clear to me. There is some suggestive evidence that clinical improvement occurs in response to it, but I have not seen convincing evidence in sufficient volume. I am not prepared to accept the apparent improvement of ordinary types of industrial lead poisoning as anything other than mildly suggestive, while the outcome, in the case of childhood encephalopathy, has not, so far as I know, been established with sufficient certainty. In any case, we have had enthusiasm about various types of therapy before only to see them discarded. We need an effective therapy that will save life. (You are probably aware that the death rate among infants and children is 25 to 30 per cent.) If it will not do this, it is not good enough. We can eliminate lead poisoning from industry with our present knowledge, and this ought to be done. I am not even slightly interested in a palliative treatment of lead poisoning that will encourage industry to continue in the belief that lead poisoning is not much of a problem, since it is readily and successfully treated. Certainly we as physicians want to be as effective in all therapy as we can. But let us not lose our equilibrium and forget where the problem of industrial lead poisoning resides.

This is not an ample discussion of these matters from your viewpoint, I am sure, but it is the best I can do at this time. I hope I shall have an opportunity later to talk with one or both of you.

Sincerely yours,

Robert A. Kehoe, M. D.

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