

December 23, 1965

James J. Chisolm, Jr., M.D.
Johns Hopkins Hospital
Baltimore, Maryland 21205

Dear Doctor Chisolm:

I am writing to ask a question concerning a statement which you made, or which I thought you made, at the Symposium on Lead in Washington, D.C. last week. The point is of considerably more than academic importance, and therefore I'd like to be sure of my ground. For one thing, if it was meant as I and others took it to mean, it was a flat contradiction of a statement of mine made in an earlier discussion in the same symposium. This, in itself, is not unduly disturbing, but it was taken up fairly sharply by Harriet Hardy. I didn't think it directly relevant to the specific matters under discussion, and therefore I did not enquire of you at the time or take issue with either your statement or that of Harriet. I expected to talk to you after the session, but this was not feasible.

The point is this. You seem to have said that acute infections in childhood plumbism resulted in the mobilization of lead and in the exacerbation of the illness of the child with lead poisoning. The question in my mind relates not to the intensification of the illness of the sick child which is altogether reasonable, but whether there is a recurrence of lead poisoning in the fully recovered child, and whether there is evidence that this may be due to the release of lead from its points of deposition or bonding in the body.

You are aware, no doubt, of the concept advanced by Aub and his associates at Harvard that the metabolism of lead is disturbed by a variety of factors including infections and disturbances in the metabolism of calcium and in the acid base equilibrium, etc. You may or may not be aware that this concept had its origin at a time when the analytical methods could be applied to the urine and blood, and when the loss

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of lead from the living body could be followed only by analysis of the feces. The facts so obtained were misinterpreted, and to make a long story short - the hypothesis that arose therefrom has since been shown to be untrue in practically all respects. As I stated at the Symposium, we have not found it possible to disturb the pattern of the distribution of lead in the tissues by any artificial means except one; namely - by the administration of certain chelating agents (BAL and EDTA). I believe from certain reported facts that certain severe forms of skeletal disintegration, as osteoporosis, for example, can release significant quantities of lead from the skeleton. I have no direct evidence that this is true. However, in a series of careful observation, we have never seen any quantitatively significant "mobilization of lead" in association with acute infections in the adult or infant, nor have we found any such effects in alcoholic bouts, general anaesthesia, or acute toxic or infectious illness. What I'd like to know, therefore, is whether you have real evidence that acute infections in childhood plumbism affect the metabolism of lead. That the course of illness is altered, I do not doubt, but is it fact, or assumption based on the assumptions of others, that the distribution of lead in the body is altered under these circumstances?

I am not arguing the case above, but am inquiring as to what you said and believe to be true. Our experience may not have covered all of the possible situations, and if it has not, I'd like to know more. I did not say that such things cannot occur, but that we had not observed any such thing after careful search. Valid answers cannot be given except on the basis of sound data. So far as I know, there are no such data in the literature.

I shall be most grateful to you if you will let me know your views. I am entirely confident that these are certain obscure biochemical phenomena, probably intracellular in character, that covert essentially inert (or inactive) lead into active (i.e., toxic) lead, and that this can occur with little or no changes in the distribution of lead in the tissues. I have no idea what mechanism is involved in this, beyond the likelihood that bound lead becomes free (ionic) lead.

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James J. Chisolm, Jr.

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With kindest regards.

Cordially yours,

Robert A. Kehoe, M.D.

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