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Dear Doctor Chisolm:

I was pleased to receive your letter of June 19, and only my preoccupation with pressing jobs kept me from replying promptly. I have been intensely interested in the work you and your associates have been doing, and in your publications. My interest is due in part, of course, to my general concern about the problem of lead intoxication, but it results to a considerable extent from the fact that lead poisoning in the child is frequently a lethal or seriously disabling disease (as distinguished from the current pattern in the industrially employed adult), and there is opportunity for a critical appraisal of therapeutic practice as well as theory. We have, as you know, collaborated with Hugo Smith, as we attempted to do years ago with a series of his predecessors, who did not remain with the job as he has. This has been an old problem in Cincinnati as it has in Baltimore.

I appreciate your comments, and I shall reply or remark upon them in sequence.

1. With respect to the duplication of samples of urine, we have little problem here in the Laboratory, since the suspended and settled material can always be dissolved by means of a lead-free reagent and the entire sample rendered homogeneous. Not infrequently, however, we encounter situations in which individuals have split samples without recognizing their inhomogeneous state. This can be very disconcerting, especially in a medico-legal situation, in which unfortunately, I am often involved. This is not the worst of the difficulties in this somewhat vexed field of professional activity, but it is not unimportant. I should be much interested in the device to which you referred for splitting the urine as it is voided. I do not remember having encountered any reference to it, but will review your publications with it in mind. If it has not been published, I'd be pleased to have a description, for it would be useful for experimental purposes.

2. With respect to the lead in the brain, I recognize the variability of the water content in relation to the gross weight of the fresh sample. We usually determine the dry weight of tissue samples

but I have not seen the necessity of employing it in the expression of our results. So far as the analytical procedure is concerned, it has given us no difficulty. While I recognize the considerable range in the variability, I have not found it to be a source of much concern, if for no other reason that we have found very few borderline results as between "normal" and abnormal findings. I have believed that we could differentiate the relatively low from the relatively high findings within the abnormal range on the basis of the history (when available in a reasonably satisfactory state), but more particularly, by means of the pattern of distribution in the other tissues. Perhaps I am reading into these results my own views of the descriptive physiology of the behavior of lead, but if so, my views came without prejudice from the data themselves.

3. As to my view of absorption of lead from the intestine at an accelerated rate in the intoxicated patient, I am not sure I understand you. Perhaps you will indicate the paragraph or sentence in which this idea appears to have been advanced. So far as I am aware, there are only three situations in which this or something akin to it occurs. (a) When an effective chelating compound is administered by mouth, the chelated lead in the alimentary tract may be absorbed in considerably increased quantity. (b) When the alimentary emptying time is delayed, as it often is in the lead intoxicated patient, the absorption of the lead that is in the alimentary tract (from the ingestion of lead previously from any source) occurs over a longer period of time. This can exert a significant effect upon the lead content of the tissues and body fluids. (c) When the concentration of lead in the alimentary tract is maintained at a relatively high level, there is a disproportionate increase in the rate of its absorption - that is, a larger percentage of the ingested is absorbed. This has been found to be the case too consistently in experiments in which known quantities of lead (in solution) have been taken with food, to be the result of variability (in absorption) among different experimental subjects. It is not a surprising phenomenon, but it is helpful to know that it is factual.

I have been interested in the apparently beneficial results of your use of BAL with EDTA in therapy. While I recognize that there are potentially beneficial mechanisms to account, hopefully, for such effects, I would not have anticipated any such outcome. I shall be glad to be convinced, and shall follow your experience and that of Smith and his group here. We are confronted here with a tragic disease, and I shall welcome any progress that may be made in its therapy, whether something specific and dramatic may be found, or whether we shall have to continue to content ourselves with small gains. As you may well understand, I am much more enthusiastic about the possibilities for out and out prevention,

on the one hand, and for the recognition of the problem in the earlier stages that are not so lethal or destructive, on the other.

Sincerely yours,

Robert A. Kehoe, M. D.

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