UNIVERSITY OF PENNSYLVANIA
PHILADELPHIA

THE SCHOOL OF MEDICINE

Laboratory of Pharmacology

September 20, 1943

Dr. Robert A. Kehoe
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University of Cincinnati
Cincinnati, Ohio

My dear Dr. Kehoe;

I wish to apologize for my apparent indifference to your letter of July 19, 1943. As a matter of fact I have been extremely interested in your comments and it was merely that when your letter came I was engaged in the rather hectic task of moving from Boston to my new position at the University of Pennsylvania which has so delayed my answer.

Your criticisms are most pertinent although I believe most of them were considered by us and only the necessary omission through condensation prevented our making most of the points more clear. This was probably a mistake, but perhaps I can satisfactorily answer many of your points.

First with respect to the diminution in lead concentration in the blood following citrate therapy, I should like to point out that our patients were seen for the first time at varying periods after their last exposure to lead, and that although our control periods may have been inadequate the likelihood that each patient would show a sharp drop in blood lead concentration immediately following citrate administration simply by chance is quite remote, as indeed our statistical analysis shows. I agree that it would have been desirable to carry a few patients through without citrate therapy and our only excuse for neglecting this is the paucity of clinical material available. As something of a substitute we have published in our preliminary report (enclosed) a group of patients treated at our hospital before the institution of citrate therapy. There is considerable difference between this group and the group of citrate treated patients.

Secondly, although it might have been interesting to determine lead intake in food and drink and admitting that this might vary within wide limits we did not consider such determinations necessary since we did not and cannot yet see why purely random variations such as these could be consistently altered by citrate therapy except by the possibility

which you mentioned that the increase in appetite following citrate would carry with it increased lead ingestion. Such a possibility presumes that citrate therapy has some efficacy in the treatment of plumbism but besides is definitely ruled out by the fact that our most striking increases in lead excretion occur immediately after citrate therapy is instituted and these tend to diminish while the increase in appetite is slower in appearing and is maintained. This same fact rules out the possibility that the increased lead excretion results from lead present in the administered citrate. I must take issue with you in your statements that alimentary lead excretion is negligible since I have evidence from radioactive lead given parenterally that the excretion of lead from the alimentary tract is appreciable. In the light of these considerations I cannot agree that our data on fecal excretion are worthless or that their statistical treatment is unwarranted, in fact our understanding of the function of statistics leads us to believe that their use permits a correct evaluation of chance variables such as the quantitites of ingested lead.

Your fears concerning our technique of taking aliquots of feces are needless. The procedure as published of acidulating and drying the entire collection and then taking an aliquot after thorough grinding and mixing is the accepted technique for such balance studies.

Your criticism of the absence of data on urine volumes is well taken. We did not include these data in order to save space and because there was no correlation between diuresis and lead excretion. Average 24 hour urine volumes before and after citrate therapy for each patient are as follows: C.C. 2328, 2380. A.R. 1585, 1896. R.R. 1860, 1713. H.C. 920, 950. J.W. 1230, 2030. J.N. 1461, 1380. A.B. 1714, 1845. B.C. 951, 1560. J.K. 1176, 1262. It is seen that J.W. the only patient who showed a decrease in urinary lead excretion during citrate exhibited a marked diuresis, while R.R. who demonstrated the most marked increase in urinary lead excretion experienced a slight fall in urinary volume.

I was rather distressed to find in the recent article by Bambach, Kehoe, and Logan on blood lead partition a somewhat disparaging reference to my study of the lead citrate complex ion which appeared to indicate a certain lack of understanding of my conclusions. You may be interested in seeing a copy of the letter which I sent to Dr. Bambach on this point.

Sincerely yours,

Seymour S. Kety, M.D.

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