October 11, 1952

Mr. Manfred Bowditch
Lead Industries Association
420 Lexington Avenue
New York City 17

Dear Manfred:

It appears that something in the nature of a tempest has developed, whether in a teapot or perhaps in some large receptacle, over the somewhat inadequate but well-intended information supplied to you by my friend and colleague, Doctor Robert Kotte, concerning some unfortunate results which attended the use of Calcium Disodium Versenate (5 cc ampules supplied by Riker Laboratories) in the treatment of two infants suffering from lead poisoning. Under the circumstances it seems best for me to clear the atmosphere by a statement of the facts, so far as I have them, since every one involved in the matter seems to be touchy, suspicious or otherwise upset. It even appears that I am suspected of sabotage in the matter, and of being constitutionally opposed to the development and use of specific therapy in lead poisoning, although I find it difficult to believe that anyone has seriously entertained any such idea. At any rate, while I am willing to do any required penance for my sins, I do not accept quietly indirect queries concerning my medical and scientific attitudes, and therefore in the not unalloyed role of peacemaker, I am prepared to accept the intermediate position which invites any blows intended for myself or others.

The situation, with respect to the use of EDTA in the treatment of lead poisoning came about here some months ago, when it was first suggested publicly that this agent might be useful. As is well known, I should think, I have had only a mild concern about the treatment of the usual case of lead poisoning in the adult, although we have subjected a number of types of therapy to rather rigid investigation. Moreover, I have inveighed, as vigorously as I know how, against the substitution of therapy for the preventive measures that are available and demonstrably effective, against industrial lead poisoning. On the other hand, I have been deeply concerned, for many years, over the serious problem of the development of adequate treatment for two types of lead poisoning which give rise to high incidence of fatalities, namely, lead encephalopathy in the infant and small child, and tetraethyl lead poisoning in the adult, which, if exposure is sufficient, is uniformly fatal. The former is a public health

problem of rather serious proportions, which, at present, is not wholly preventable, and which, therefore, requires and will continue, until it is solved, to require effective treatment.

When it appeared that EDTA might be useful, I obtained all of the information I could get, together with a supply of the material, and conferred with the group here in Cincinnati with whom I have collaborated for many years in the diagnosis of cases and in the study of the problem. I strongly recommended the use of the product in the treatment of selected cases of grave illness, and found complete agreement that the highly unfavorable prognosis justified the trial of the preparation. A means of following the cases, to determine the extent of the clinical benefits and to observe the effects upon the lead metabolism, was agreed upon, well before the time of year when such cases can be expected to reach their peak incidence. (We had somewhat in excess of twenty cases in 1951, with a mortality of about one third, and we are quite certain of seeing several serious cases, some of which are destined to be fatal, during the summer months of any year.) Meanwhile you (Bowditch) and Doctor Wheatley had been in more or less continuing communication with Doctor Kotte on the matter of lead poisoning as well as other types of illness among children, and we complied with your request to make such suggestions as we could for a form of report and an outline of procedures indicated for demonstrating the results of therapy. Our own procedure differed somewhat from that which was regarded as essential and that which could be carried out in certain other places, with particular reference to the analytical regimen. In this we followed our own counsel, since I have not been favorably impressed by the critique, or I should say, the lack of critique, on either the clinical or metabolic effects of the use of remedial agents in recent years in lead poisoning, because of the almost complete disregard of character and the known facts concerning the metabolism of lead in health and disease and the reliability of the methods required to establish the facts in the individual case, on the part of most of those who have undertaken such observations. Such methods were not available in the nineteen twenties, and there was no serviceable information on the subject until after the late thirties. There are such methods now and some data, but neither the methods nor the data have been taken seriously by more than a very few people. Consequently, I may be forgiven, perhaps, if I considered that it would be necessary for us to answer questions on the metabolic aspects of the matter for ourselves.

No suitable cases of lead encephalopathy among children were available for treatment until the late summer of this year, but two such cases appeared then, and treatment was initiated with EDTA in the Cincinnati General Hospital (I misinformed Lanza in an earlier letter, by saying that these were in the Children's Hospital). I was away at the time, but Doctor Kotte felt that it was wise to inform you (Bowditch) of what had occurred. The cases were not his own, and he had no direct or delegated

were desparately ill and several others required hospitalization and medical care. That there were no further fatalities may not be attributed to the beneficial effects of the use of EDTA, a supply of which was taken along, and further supplies obtained from Dr. Poole (whose accidental death, some days later has shocked all of us). However, the drug was well tolerated by these patients, and observations were made as well as they could be under the circumstances to determine the metabolic effects of the use of the drug in certain of these cases. (Some were treated with EDTA, others were not.) The analytical data on something over two hundred samples of blood and urine have not been obtained entirely, nor has it been possible to study them in relation to the therapeutic regimen, but all of these data will be available shortly, and they should show whether or not this agent is capable of influencing the behavior of tetraethyl lead and/or its decomposition products in the human body. It does not follow, of course, that these facts will have any important bearing on the problem of lead poisoning from inorganic poisoning, but they will have some significance, I hope, in relation to TEL poisoning.

We shall continue to make use of EDTA in an experimental study of the therapy of lead poisoning in the adult, and, in all likelihood, we shall be able to resume trial use in selected cases of lead poisoning in the child. Our experience, although as yet inadequately reported, fully justifies the position taken by the group that this preparation should not be distributed for general use, until such a time as adequate evidence can be obtained concerning its possible benefits and dangers. The incident and the hubbub about it also demonstrate clearly that the applicability of a proposed new remedy needs to be examined in an attitude of unhurried objectivity, rather than in an aura of enthusiasm based on theroretical considerations however exciting they may be.

I have given this letter as wide circulation as seemed necessary at this time. In view of the fact that I have gone somewhat outside my own professional province in reporting incomplete and inadequate information on patients who were not under my care, I must ask that this information be handled with appropriate professional discretion until the facts have been released by the responsible physicians.

Sincerely yours,

Robert A. Kehoe, M. D.

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CC: Dr. A. J. Lanza - Dr. Thomas L. Shipman - Dr. Harriet Hardy
Dr. Elston L. Belknap - Dr. George M. Wheatley