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 the known facts concerning the metabolism of lead in health and disease and the character and 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

authority to obtain or to give out any detailed information, especially in the absence of the Chief of the Pediatric Service of the Hospital. He spoke, therefore, in general terms, feeling that it was best that every one concerned should know that caution should be exercised in the use of the material in the case of infants. It was this cautious warning of Dr. Kotte that precipitated the present situation. The correspondence with Dr. Kotte, which I regard as based on some impatience and misunderstanding, has troubled and offended him, as will be seen from his replies to the correspondence. His reaction would seem to me also to have resulted from some degree of misunderstanding, but he is a sensitive and honorable man, if perhaps somewhat inarticulate in spots, who would deeply resent any implication that he has been devious or anything less than completely straightforward in his dealings with his professional colleagues.

The essential facts about the two cases, which will require careful sifting by those responsible for the Service, as reported briefly to me, are as follows: Both children were dangerously ill, were hypertensive at the time the specific treatment was attempted, and both reacted badly to the test dose with further arterial and intracranial hypertension. The reaction was prompt and alarming, and while it may not have been due to the effects of the drug, it appeared to be. One of the children died in such unfortunate time relationship (I am not certain of the time interval) to the attempted therapy as to convince the resident staff that they do not wish to employ the drug in similar cases in the future. This fact also conditioned their reaction to giving out information that might bring serious criticism upon themselves and the Hospital, until such a time as the Chief of the Service had assumed responsibility for further action.

I have taken up the matter of furnishing the group with appropriate information on the results of the treatment of the two children, and I am assured that it will be forthcoming shortly. The Chief of Service has been away until recently. He has been heavily engaged in gathering up the loose ends of his work, and was not aware of the significance of the matter at issue until I explained it to him yesterday. (I have been out of town much of late, myself, and was too busy to go into it sooner.) In due course, therefore, the matter will be aired fully and reported in such manner as those responsible may determine. Meanwhile, one must recognize that care will be required in the treatment of small children who are dangerously ill of lead encephalopathy, if only to avoid obscuring the possible usefulness of a remedial agent.

More favorable news can be reported with reference to an experience with EDTA in the therapy of tetraethyl lead poisoning. A recent episode in Panama took one of my internist associates to Panama City, to assist in the treatment of some seventeen men, who had been poisoned because of failure to carry out the prescribed precautions for cleaning tanks in which leaded gasoline had been stored. Two of these men died before he arrived. Three others

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.

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

LEAD INDUSTRIES ASSOCIATION
420 Lexington Avenue
New York 17, N. Y.

MANFRED BOWDITCH
DIRECTOR OF HEALTH AND SAFETY

October 17, 1952

Mr. William G. Lussky
Vice President
Progress Paint Manufacturing Co.
Louisville 2, Kentucky

Dear Mr. Lussky:

I am extremely sorry that your inquiry of September 19th, received during my extended absence, has gone so long unanswered.

There is really no adequate reply to the question which you pose. White lead paint is unquestionably toxic, and while the majority of cases of lead poisoning in livestock which come to our attention involve ingestion of fresh paint from fences or farm buildings or from containers, paddles, etc. carelessly left about, there are enough reports of poisoning caused by the chewing of dried paint to render this a matter which cannot be wholly ignored.

It is my personal belief that authenticated cases of this last sort are extremely rare, but I would not attempt to say how much paint a given animal would have to ingest in a given time to be adversely affected.

Possibly Dr. Robert A. Kehoe, Director of the Kettering Laboratory, College of Medicine, Eden Avenue, Cincinnati 19, Ohio, could give you a more satisfactory reply.

Very truly yours,

MB:JG

cc (Blind) Dr. Kehoe

[redacted]

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