October 25, 1950

Dr. W. I. R. Thompson,
Boots Pure Drug Company Limited,
Nottingham, England.

Dear Doctor Thompson:

When I was in England some weeks ago I came upon information indicating that your company had developed a stabilized product, BAL glucoside, which might be available for use. On this account I called up and through Miss Antill obtained information from one of your associates (Mr. Brown) to the effect that if I would write to you, I should be able to find out about the status of the situation and whether or not the material is available for clinical use or clinical trial. Having returned home only recently and having gotten some other urgent matters behind me, I hasten to follow out this advice and to seek some information from you.

Our problem arises in connection with the experimental study of the lead metabolism. You may or may not be familiar with our work in this field, but in the course of these investigations we had occasion to try BAL in the treatment of a series of acute cases of lead intoxication. By acute cases I mean acute episodes of colic. So far as we were able to establish the administration of BAL, up to tolerance, was of no avail in reducing the severity of the colic or in shortening the period of illness and disability. On the other hand, the effect of the administration of BAL on the lead metabolism was profound though brief, and inasmuch as we have never been able to induce any such changes by any other means, we were intrigued with the possibility that presented itself. It occurred to us that if a less toxic preparation of this type could be used, and given repeatedly so as to maintain a sharp increase in the urinary excretion of lead, we might be able to "delead" persons who had absorbed appreciable quantities of lead, and thus be able to return them to their work in a much shorter time than would be safe otherwise. Quite apart from these practical considerations, which I shall not discuss in detail, we might hope to learn a number of things about the lead metabolism, from the careful study of patients. The published work on BAL glucoside suggested that this preparation might answer our purpose, but we were unable in this country to obtain the help of any of the persons who had been concerned with any work of this sort during the war. The chemists who were familiar with the preparation of BAL, who might have been expected to give competent advice and help in the synthesis of the glucoside, had been scattered, and were engaged in other work. Some correspondence with some of our English colleagues, failed to provide any answer to our problem. We were loath to embark upon the chemical studies that would give us some expertness in this field, since we felt we would have a rather long term of work in acquiring the skill and know-how

necessary to this end. It was with considerable interest, therefore, that I heard of your interests in this direction. In order that you may be familiar with this aspect of our work, I am sending you a reprint of a brief article in which our preliminary observations have been described, just in case you have not seen it. I think there is little question that the effect of BAL on the blood is to release lead from the red blood corpuscles or otherwise to bring it out where it is available for distribution into the tissues and excretion. In any case, as you probably know well, the lead concentration in the blood drops precipitously for a period of some hours, and the excretion of lead in the urine is greatly amplified, in some instances as much as thirty fold. Within something like eight hours after the administration of a single dose of BAL, this situation reverses itself, and the only apparent effect is that the body has lost a larger quantity of lead than would have been lost through the normal avenues of excretion. We should like very much to follow this matter over some period of time during and after the administration of a preparation which could be given in effective dosage repeatedly.

Any information which you could give me as to the availability of this preparation, as to the length of its stability and as to the safety in its administration will be greatly appreciated. If there is any question about the safety of the material, or if its stability is in doubt and is in need of being tested by animal experimentation or otherwise, we can, of course, follow your advice. The Laboratory is well equipped with able chemists, although none of my associates have had any experience with the synthesis or stabilization of any of the thiol preparations.

In case you are interested in our investigations of the lead metabolism, I should be glad to send you reprints of the published work available. Unfortunately a large proportion of our work carried out over the period of the last several years has not been summarized and published in detail, partly because of our preoccupation with other matters, and partly because the work is still under way. We have virtually completed the story of ingested lead, in such a way as to know what we need to know about the absorption, distribution, storage and excretion of such lead. We are now engaged in the story of inhaled lead, and this work is of particular interest, we think, because it has been carried out in controlled and essentially balanced experiments on human beings.

Any information or advice you can give me on this general subject will be greatly appreciated. We should be glad to purchase such quantities of any presently available preparation, as we may require in our work.

Cordially yours,

Robert A. Kehoe, M. D.

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