December 29, 1933

Dr. I. M. Rabinowitch
The Montreal General Hospital
66 Dorchester Street, East
Montreal

Dear Dr. Rabinowitch:

I am pleased to have your letter of December 19th and I shall answer it as well as I can.

The evidence which we have that lead in the brain remains there for indefinite periods of time has come from two sources. First the study of experimental animals, especially those treated with tetraethyl lead in which there is a strong tendency for localization of lead in the central nervous system. I am sending you a reprint which shows the changes of distribution of lead in the tissues over a long period of time. You will note that the concentration of lead in the brain of these animals is as high after many months as it was found to be directly after the period of absorption. These animals were treated with every medicament which we have employed in attempts to aid lead excretion. Despite this fact the concentration of lead in the brain has remained high. The second evidence is in the form of observations on a few human beings who have been exposed heavily at one time to lead compounds. In one instance we have the opportunity of analyzing the brain as well as the other tissues some nine years after the cessation of occupational exposure. Analytical results in the tissues of the body in general were no higher than those which we have found in normal individuals, but the concentration in the brain was quite high. We are investigating the nature of the compounds in the brain which are formed by lead. Subsequently we shall have something to say about this matter. For the present it is perhaps just as well not to make any too broad statement.

In a number of instances we have found lead in the spinal fluid when tested spectrographically. We have not yet detected the presence of lead by chemical methods in spinal fluid in a quantitative way. We have not studied a sufficiently large number of cases to arrive at any important conclusions in this matter. However one thing appears to be reasonably certain and that is that there is no necessary relationship between the concentration of lead in the brain tissue and in the spinal fluid. There is one other matter about which I am willing to register a very considerable skepticism. Because of certain factors in experimental ob-

servations which have not been controlled, as discussed in one of our papers which recently appeared in the Journal of Industrial Hygiene, I am not convinced that we know very much about about the release of lead from the tissues in general. I am quite willing to accept the likelihood that acidosis, alkalosis, potassium iodide, phosphoric acid, etc., have a pronounced effect. On the other hand I do not regard these facts as proven. I think the whole field will have to be re-worked before we can arrive at any very satisfactory explanation of the mechanisms involved. Thus it seems to me entirely possible that the concentration of lead in the spinal fluid may vary from time to time within rather wide limits just as it does in the blood and just as it does also in the excreta. I do not think we know very much about the factors which produce these wide variations, and I do not think we shall know much about them until the whole study of lead metabolism has been reviewed in the most careful fashion. In saying this I do not wish to be destructively critical, but I am not convinced by our own data, which I believe to be as extensive as any that are available elsewhere. As a consequence of this feeling, I have said very little in published articles about the mechanisms of lead absorption and lead excretion.

I dare say you have seen our series of articles in the Journal of Industrial Hygiene but I am taking this occasion to send you a reprint together with the reprints which I previously mentioned.

I was glad indeed to talk to Dr. Dingwall. and I hope to have an occasion again to discuss with him and with you various aspects of this problem.

Cordially yours,

RAK:IS

Robert A. Kehoe, M.D.