June 5, 1964

Lewis M. Davis, M.D.
Greer, South Carolina

Dear Doctor Davis:

My attention has been called to a question of yours concerning lead poisoning in the May 4th issue of the Journal of the American Medical Association, and to the answer as given by Professor Martin I. Rubin, Ph.D. of Washington, D. C. I cannot suppose that the reply which you received was very helpful to you, if you were dealing with such a practical problem as is often presented by a patient or by anyone else who may have sought your advice. Moreoever, since one portion of the answer was misleading, I feel called upon to clarify the issue. In so doing I am not attacking Professor Rubin, who, after all is a chemist and can hardly be expected to have any very broad understanding of the physiological and clinical considerations involved in this matter. I am sharply critical of the person in A.M.A. headquarters who referred your question to a chemist, instead of a physician who is versed in the physiology of the metabolism of lead. I have written to both Dr. Rubin and the Editor in chief of the Journal. This was a most unfortunate incident, and it should not be repeated.

In order to answer your question satisfactorily let me say that the reliability of determinations of lead in the blood and urine depend entirely upon the facilities available for the purpose, upon the utter competence of the analyst, and upon the manner by which the samples are obtained for analysis. All of these are extremely important factors, since the analytical procedure must deal with exceedingly minute quantities of lead with a very high degree of accuracy. The result is that there are very few diagnostic laboratories that make any approach to reliability in this matter, and that one must know, in a very precise manner, whom to trust. Otherwise, he, as a physician, is much better off if he avoids any opinion based on such analyses, and depends entirely upon his clinical knowledge and judgment. It may be, in your area, that the laboratories of the State Health Department are equipped and staffed for this purpose, since lead poisoning still occurs with fair frequency in the industrial setting. Or you may have in mind some specific laboratory. If so, if you would so indicate, I can easily find out the facts. (We have been at this for a long time - longer in fact, than any other laboratory in the country, and we know most of the sources of reliable results.)

So much for this point. Let me say further to the point of your question, that the results of the analysis of the blood for its lead content are the most reliable evidence obtainable concerning the degree to which an individual under examination has absorbed lead, provided the interval of time, since the last period of exposure, is not too long. Lead is lost from the body following the termination of any period of unusual (as occupational) exposure to lead. When the blood and urine have reached the levels which are characteristic of the normal individual (with his normal content of lead) there is nothing that can be done to find out the quantity of lead which had been in the body previously. The evidence is gone, and it cannot be brought back again. Accordingly, one has to determine the facts during or in fairly close relationship in time (weeks) to the period of exposure.

Such information will never tell you whether the individual was ill or how ill he may have been, for the reason that there is no level of concentration of lead in the body that, of itself, demonstrates the existence of lead poisoning. The nature of the illness is determined by the clinical pattern of the disease -- symptoms and signs. If that is compatible with the characteristic pattern (or patterns) of the several forms of lead intoxication, the diagnosis can be made, provided one can find analytical evidence that potentially dangerous amounts of lead have been absorbed. It has been demonstrated clinically in large numbers of cases of actual and suspected lead poisoning that if the concentration of lead in the whole blood, as determined with a high degree of precision, is in excess of 0.08 milligram per 100 grams, the diagnosis of lead poisoning, made with good clinical judgment, may be accepted as fully confirmed. On the other hand, we have never seen a case of lead poisoning in an adult or infant, in which the concentration of lead in the blood (at the time of the exposure) was less than 0.08 mg. per 100 grams. This is a highly critical point in the concentration. Values above this, even up to 10 times this level are found in clinical poisoning, but similar values are also found in persons who are entirely well, but have sustained severe occupational exposure. Thus the high values in the blood, above the threshold, I repeat, mean absorption of lead, but not necessarily illness, while lower values, just below the threshold, mean definitely that not enough lead has been absorbed to produce illness.

The so-called provocative test (administration of the calcium disodium salt of EDTA) and the measurement of the response to it by the analysis of the urine, is an extremely variable affair. It is a purely empirical procedure, and in addition it is unpredictable, erratic and uninterpretable. The "rule of thumb" stated by Professor Rubin has come from several sources, none of whom had a sound idea of the physiology of the metabolism of lead. I condemn it unreservedly as a sleight-of-hand trick that has no basis in physiology. I am sure also, that unless it is carried out within a carefully coördinated team of medical and technical investigators, the results will be even more unreliable and erratic than is the thinking behind the procedure.

It may be that your question in the Journal had some problem behind it which I have not discussed. Should this be the case, I shall be pleased to hear from you further, for our work in this field, much of which has been published, is intended to aid our colleagues in dealing effectively with a problem which has been greatly confused for a long time.

Cordially yours,

RAK:vr

Robert A. Kehoe, M.D.