March 11, 1936

Dr. L. Edward Gaul
100 East 59th Street
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New York

Dear Dr. Gaul:

I am very much interested in your letter of March 2nd and in your attempt to correlate various laboratory procedures with clinical data in relation to the problem of lead absorption and lead poisoning. I am very glad to express my own point of view as to the character of the problem.

As you doubtless know, we, in this laboratory, have been concerned with this problem for some time, and it is my opinion, after some ten years of study, that the essential facts are fairly clear in so far as their relationship to diagnosis is concerned. Some time ago I expressed myself in the literature on this subject, and I have had no occasion to alter my position materially. I believe that the industrial or medico-legal clinician is attempting to simplify the problem beyond the possibilities. It has been fairly well established, I believe, that the absorption of even considerable quantities of lead does not always result in illness or injury. On the other hand it seems fairly certain that lead poisoning does not occur unless lead absorption has taken place well above the average normal limits. We all ingest measureable amounts of lead daily; we all absorb lead; we all have lead in our tissues; and we all excrete lead. There is evidence that this has been the case for generations, and yet I do not believe there is any evidence that lead poisoning occurs from the absorption of the minimal amounts of lead which are present in food and beverages, commonly, and under the usual conditions of handling. In fact it seems clear that under these conditions of normal lead exposure, lead accumulation does not occur as a progressive phenomenon. From a clinical point of view, therefore, the study of a patient by means of analytical procedures, has as its purpose the appraisal of his recent exposure to lead compounds. If it can be shown that he has unusual amounts of lead in his tissues or excreta, then he has had unusual or abnormal exposure. Otherwise it must be assumed that he has not had such exposure, or that it occurred too far in the past to be detected by such means. The present analytical procedures are adequate to detect evidence of abnormal lead exposure, if employed soon enough after the cessation of exposure. We have shown that the magnitude of lead excretion

varies with the severity of the lead exposure and that when the lead excretion is within certain limits, cases of lead intoxication may be expected to occur among groups of people. Obviously, therefore, if the lead excretion of a patient is within these limits and if the clinical symptoms and signs are such as to correspond with what we know of lead intoxication, a diagnosis may reasonably be made. Paul Schmidt and his associates at the University of Halle apparently believe that lead intoxication is always present to some degree if the lead in the circulatory blood is above a certain level. This is not in accord with our experience. Suffice it to say at the moment that they have not proved their point. On the other hand it is quite clear that abnormal lead absorption can be demonstrated to have occurred through analyses of the blood. In some cases, at least, the same fact can be established by examination of the spinal fluid and in cases that come to autopsy, it is not difficult to establish the facts as to the magnitude of the lead absorption. However, all of these observations are dependent upon the examination of excretion or tissues before the absorbed lead has been lost from the body. We have shown quite conclusively that the lead content of the body diminishes progressively with the decrease or cessation of abnormal lead exposure. So far as our data go it is indicated that even after severe exposure, most of the tissues of the body resume approximately normal lead concentrations within a year to eighteen months of the cessation of exposure. An exception to this is the brain which retains lead in apparently an inert form for an indefinite period of time after its absorption in the brain substance. Whether or not this is always the case can not be said with certainty, but it appears that the brain alone of all the tissues of the body is capable of holding its content of lead for an indefinite period of time. This is not true of the skeleton and there is no evidence of which I am aware that it is true of any other tissue of the body. However not all the evidence is complete on this question. In any case, however, it must be recognized that the retention of lead by a tissue over a long period of time is not necessarily associated with injury or with intoxication.

It has been suggested by certain observations that lead may be retained in the skin as it is in the brain. We are unable to support this conclusion. Our data indicate that the skin is somewhat erratic in its behavior with relation to lead, and that there is no necessary relationship between the lead content of the skin and that of the body as a whole. It seems obvious to me that if one is to rely upon the analysis of a tissue in order to interpret the magnitude of lead exposure, one must select a tissue for examination which is fairly constant in its physiologic behavior, such as a bit of bone, or a living tooth. I am, therefore, very skeptical of the usefulness of skin analyses and particularly of analyses of very small sharply localized bits of skin. From the present available information, of which there is a great deal, we can safely rely upon a combination of blood and urine analyses in arriving at an appraisal of the recent lead absorption of a patient.

. E. Gaul

Since you have made mention of varying methods of analysis as a possible cause of confusion, I think I should express my opinion that this is the chief cause for conflict. Many methods have been used and for the most part the results have been published without reference to the sensitivity of the method employed. On the other hand, methods are now available which have been carefully and critically examined and tested, and which have been proven to yield results of high accuracy and uniformity. Thus the dithizone method properly handled and properly controlled will give very accurate information on certain materials; straight analytical procedures are quite satisfactory for certain other materials, and properly standardized spectrographic methods are very good indeed. I can say as a result of our own experience that it is now possible to employ various methods in parallel determinations, in such a way as to obtain almost perfect checks. Any one who works in this field should make a very careful study of methods and should be able to say for his published results just what they mean in terms of accuracy and sensitivity. Failure to do this in the present state of the matter is only to add to the confusion.

Perhaps you will gather from my somewhat lengthy discussion that I have very little confidence in any one laboratory procedure as the means of making a diagnosis. Rather one must have analytical results ofknown accuracy after which he must be able to interpret them in relation to the known physiological facts as to the behavior of lead. Obviously until we know the complete physiological background of lead, we may not obtain the correct answer in every case. In the main, however, we can rather easily obtain the answer to the question " has this patient had a recent (i.e. within the past few weeks or in some cases, months) abnormal exposure to lead compounds". I think this is the only useful information that can be obtained in the present state of our knowledge.

It is quite possible that I have not made myself entirely clear, for although my letter is somewhat long, there are quite a few points which are worthy of more discussion than I have given them. In as much as I visit New York rather frequently, I should be very happy to talk with you sometime about this problem, and since you have shown me the courtesy of asking my opinion, I make so bold as to put myself at your disposal for this purpose. If you would drop me a line and let me know when you would like to see me, we could probably arrange to get together at an early date.

Cordially yours,

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Robert A. Kehoe, M.D.

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