

November 13, 1945

Mr. W. H. Abbitt,
Northwestern University,
Evanston, Illinois.

Dear Mr. Abbitt:

A few days ago Graham Edgar of Ethyl Corporation forwarded to me copies of an exchange of correspondence initiated by your letter of November 3. In suggesting that I reply Dr. Edgar has put me in a somewhat delicate situation. Nevertheless I shall give you my reactions to the suggestions in your letter.

First, as you are probably aware, Ethyl Corporation has sponsored a very great amount of investigative work in this Laboratory on lead compounds in relation to general problems of physiology, as well as to industrial and public health. By a combination of fortuitous circumstances I happen to be the chief advisor of Ethyl Corporation in practical medical matters and medical research, as well as the director of this Laboratory. It might sound a little selfish if, as their chief medical advisor, I were to say that in my opinion the best place for their medical research program is in the Kettering Laboratory of Applied Physiology. However, that in effect is just what I am saying, and I may as well be straightforward about it. The background of experience which we have had in the general approach to the problem, and in the physiological principles involved, is quite obviously greater than that of any other individual or group, and the technical facilities of the Laboratory in equipment and personnel are adequate for the task. Moreover, I think without being boastful it can be said that the things which you are endeavoring to undertake have been and are being prosecuted on a broad scale and require only to be extended by the same methods.

To be specific your item Number 1 has been carried out systematically over a period of the last fifteen years. By no means all of the data have been published, but much of the work has been boiled down and made available in illustrative form. The observations have been made not by one method but by several checked against the other, and there is no question of the essential accuracy of the methods and the soundness of the main conclusions arrived at.

Your item Number 2 has also been attacked on a rather comprehensive basis, and I am sure that more work has been done under the sponsorship of Ethyl Corporation in this field than has been done by all of the other combined laboratories who have worked at all

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in this field.

I say these things not to blow the horn of the Kettering Laboratory, for what we have been able to do in this field has been made possible through the generosity of Ethyl Corporation. There is room for other workers in the field, but I think I may say in all frankness that it is not to be supposed that Ethyl Corporation would or should sponsor other work of this type. This Corporation has already spent many thousands of dollars in work which has contributed toward the solution of a number of its problems, but which, also, has benefited industry in general. They are at liberty, of course, to arrive at their own conclusions, but I should be disposed to say that they have done more than their share in medical research along these lines.

Speaking as an investigator in this field, and for your information, I should like to point out to you that the answer to the problem represented in your project Number 2 has been obtained in large part. Not only do we know the geographical distribution of normal or incidental lead exposure on a substantially worldwide basis, but we are fairly familiar with the detailed distribution of lead in natural products, in the soil, in water, in vegetation, in natural food products and in processed foods. We have a pretty good idea of how much of the lead intake of the normal individual is modern in character and how much is of ancient and natural origin. We also know that there is no accumulation of excessive amounts of lead in the tissues of present day persons outside the lead trades. There are good reasons for the belief that such accumulations are less now than they were some centuries ago. May I suggest in all courtesy that you would be wise to review the literature of this subject before you embark upon extensive investigations. I gladly welcome the interest of other investigators in this field. I must point out, however, that in fifteen years of experience we have learned some of the general pathways that will have to be followed and have established methods of procedure that will be helpful to other investigators. I trust that some of the things we have found out so laboriously will not be overlooked by others, and that these things will not be rediscovered. I also hope that some of our original misconceptions will not be duplicated.

In connection with methods I would like to warn you against one of the ideas you have expressed. I have no doubt that the methods which you have developed are sound on the analytical side. On the other hand, the use of the very small samples of urine with which you are dealing is quite unsound from the physiologic viewpoint. May I warn you against proceeding on this basis in the study of industrial lead exposures. The biggest problem here is not analytical method, nor is the expense of the analytical work any very great obstacle to the conduct either of investigations

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or practical industrial control. The real difficulty is that of obtaining satisfactory samples of biological materials from exposed workmen. A small sample of urine obtained from an industrial workman is very likely to give information that is wholly misleading with reference to his lead exposure. This is a physiological problem, the main facts and principles of which have been worked out rather fully. In much of our work of this type we are employing the largest samples we can obtain rather than the smallest. We do this not because we like to handle large samples, but rather because physiological considerations have demonstrated to us that this is the only means by which we can obtain reliable information. We too use small samples of urine under certain circumstances in order to expedite delivery. However, in such instances we also obtain a sample of blood, the analysis of which enables us to avoid gross mistakes in the interpretation of the urinary findings. Samples of 100 ml of urine are variable in their lead content even when obtained from the same individual in different periods of the same day. The reason for this is that the lead concentration varies with the rate of water excretion via the kidney. There are other things that influence the rate of lead output, but this is one of the most important. For this reason the analysis of a few milliliters of urine no matter how precise, is very likely to be misleading. Thus it would require a series of analyses of such small quantities to obtain anything like a satisfactory indication of the general level of the urinary lead excretion of an individual. One could argue, of course, that all that would be required to correct this, would be to obtain a large sample from which a small portion would be taken for analysis. There are a number of difficulties here however, such as the following: (1) It is extremely difficult to avoid the contamination of samples of urine or of any other biological material with lead compounds from a great number of sources. For this reason the handling of such samples by any other than well trained persons is almost certain to result in contamination. Therefore, the collection of samples at a distance, or within the environment of an industrial plant is fraught with great difficulty and must be done in the simplest and most nearly fool-proof manner. We have struggled with this problem for many years, and have solved it. No one without actual experience has the slightest idea of the difficulties. (2) Urine as voided may be entirely clear and homogeneous. Frequently on standing even for short periods sediments settle out, or a flocculant precipitate forms. It is not possible to obtain a representative sample of such urine for analytical purposes, especially in relation to lead content, without acidifying so as to redissolve the flocculant material. This fact quite obviously makes it impossible to take a small sample from a larger volume in the field. One would be quite unwilling to accept a sample that had been handled to this extent by any other than trained personnel and in any other place than a properly equipped laboratory.

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I have no doubt that you are familiar with some of these matters, and certainly you would have an opportunity to find out about them by experience as we have. On the other hand, the field has now been developed to the point where analytical data on biological material have a very considerable significance. It is important, therefore, that earlier mistakes should not be repeated.

I should not wish you to feel that I am being unduly critical by proffering the comments above. Indeed, I repeat that there is plenty of work for all in this field of investigation. I think it is fair to say that we could be very helpful to almost anyone who is interested in work of this type. We are interested in your methods and I am sure we would be glad to exchange information with you on spectrographic problems in general. I have no doubt that you will be able to find financial support for your work, and in view of this feeling I should like to take this means of inviting you to visit us and to go over with us the many sides of this interesting technical problem as further background for the continuation of your own study. We are extremely interested in knowing where there are reliable laboratories to which work of this kind can be referred. It is highly advisable that laboratories of this type be available in many parts of the United States. Many industrial plants need services of this type. The great difficulty is that certain of the laboratories now engaged in this work lack either competent technical workers or persons familiar with the practical and physiological consideration. It is not enough that an analyst in this field should do a good job of analyzing a sample that is delivered to him. He must know that the sample so obtained is satisfactory and representative from the point of view of the situation that is being inquired into. Unless this is the case the analysis serves no useful purposes and actually leads to confusion. We should be glad to give you the assistance that would enable you to start on this work with assured precision.

Sincerely yours,

Robert A. Kehoe, M. D.

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C.C.: Dr. Graham Edgar

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