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November 1, 1938

Dr. Robert A. Kehoe
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Eden Avenue
Cincinnati, Ohio

My dear Dr. Kehoe:

Dr. Bowen has given me your letter dated October 11 for answer. I have delayed this answer until I should be able to obtain some information regarding which heavy metal sulphides were present in the hydrogen sulphide precipitate obtained from the urine of the patient studied. I now have some data upon this point, and am therefore prepared to furnish you with a summary of the results obtained in various laboratory analyses made by us. The following brief table contains the results of the urine analyses:

<u>Date</u>	<u>Mg. lead* per 1000 cc. urine</u>
1. August 29	0.83
2. September 24	0.59
3. October 8	0.11
4. October 21	0.12

*Lead determined by the Fairhall procedure, the sulphide precipitated may of course, contain certain other heavy metals sometimes present in urine.

The specimen obtained on October 8 was treated as follows. After the iodometric titration of the lead chromate precipitate the solution containing potassium iodide, thiosulphate and starch was acidified and re-precipitated with hydrogen sulphide. Simultaneously the "titration blank" (a control analysis carried from the stage of solution of the sulphides in nitric acid through the final titration with thiosulphate) was also treated with hydrogen sulphide. The precipitate from both specimens were submitted to qualitative spectroscopic analysis. The analysis was made by Dr. G. H. Cartledge of the Department of Chemistry of the University of Buffalo.

Bismuth was absent from both specimens. Copper was present in approximately equal amounts in both. Tin was present in approximately equal amounts in both, with possibly a very slight excess in the preparation from the urine. There was unquestionably more silver in the material precipitated from the urine than in the control, but the qualitative test was weak, and it seemed questionable whether that element was present in chemically determinable amount. The marked difference was in the amount of lead which the two precipitates contained. This element was present in such amounts in the material from the urine that it must have furnished by far the largest proportion of the heavy metals determined chemically.

Interpretation of these results seems somewhat difficult. The 0.1 mg. heavy metals (expressed as lead) recovered from urine at the present time is largely lead with a trace of silver. This heavy metal content is greater than that usually recovered by us from normal urine, (for in an analysis on a liter of mixed urine from diabetic patients carried out by us simultaneously with that of "specimen 3" 0.07 mg. was recovered, and our usual figures on normal urines are distinctly lower than this). It is perhaps a debatable question as to the cause of the higher values found earlier. We have kept an aliquot sample "specimen 3" which we will be glad to forward to you for analysis. Whether a study of this specimen will advance an understanding of the problem seems problematical.

The discussion of this case has been very interesting to me. My own criticism of the Fairhall method has been quite different from that upon which this discussion has hinged. I have felt, from general chemical considerations, from published results of quantitative spectrophalographic analyses and from conversations with chemists from hospital laboratories in which the more specific colorimetric lead determinations were in use, that recovery by the Fairhall procedure was probably somewhat low when only slight traces of lead are present. I have therefore, after consideration, not introduced on ^{epf} the more rapid colorimetric techniques because I was afraid the change in the nature of reports issued might be confusing to some of the people who were accustomed to "Fairhall results". My attitude in this respect was strengthened by the reaction to a finding of 0.03 mg. of lead in a 24 hour urine, which we duly reported on one occasion.

We have, of course, been aware that in certain instances heavy metals other than lead might lead to confusion, and have tried to avoid clinical errors of this sort by warning physicians to question the results in certain instances - specifically, to be sceptical of the interpretations of lead

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analyses when bismuth preparations were used in medication. Such data as is available upon the exposure to ^{and} metabolism and rate of excretion of, other heavy metals make it seem to me improbable that they can often significantly affect the findings. If they can do so it is a problem certainly worth study, and a problem which, in my opinion, cannot be answered easily and without a very extensive series of analyses.

There is really very little to say in conclusion. The interpretation of the findings in the specific case under discussion will differ, and should, I believe, to some extent be made in terms of the history and clinical condition of the patient. These the laboratory worker avoids when it is possible to do so, but he must, I believe, keep them in mind when he attempts to arrive at the significance of the results of his work.

Yours truly

Roger S. Hubbard

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Bio-Chemist

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