

February 8, 1938

Dr. Kenneth Blackfan
Children's Hospital
300 Longwood Avenue
Boston, Mass.

Dear Doctor Blackfan:-

In accordance with the request in your letter of February 2nd, I am sending you two papers from the laboratory, one of which gives the details of our dithizone method and the other gives a rather detailed comparison of the dithizone and the spectrographic methods. You will note from the latter paper that the results obtained from the two methods are substantially the same. In fact the accuracy of the method of analysis is considerably more than the accuracy of our physiological interpretation of the results. This, I believe, will serve to answer your question as to whether the use of the dithizone method has modified my opinion as to the normal blood levels. The figures which I gave you in my letter of last June are, therefore, substantially correct. I may say that in some recent data on two experimental subjects followed over a period of months under laboratory conditions, the mean result in the blood was 0.032 mgs. per 100 grams of blood, with variations extending from 0.01 to 0.07. This, I believe, fairly represents the normal range of values.

Perhaps I should point out to you, however, that it is easier to recognize abnormal findings in the urine than it is in the blood. For example, we have recently studied several groups of workmen in lead trades in which the lead exposure was relatively small. These groups could readily be differentiated from each other on the basis of the urinary findings, but one did not find a significant statistical difference in the groups on the basis of their mean blood levels. To be still more specific, an unexposed group had a mean blood lead level of 0.038 mgs. per 100 grams of blood and a urinary level of about 0.04 mgs. per liter. A very slightly exposed group had a corresponding blood lead level of 0.045 and a corresponding urinary level of 0.08. The differences in the urinary values were statistically significant while the differences between the blood levels were not statistically significant, and therefore provided no basis for differentiation. As a matter of fact, we have found uniformly that where urine samples can be collected in such a way as to avoid any possible contamination, they

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are more useful for diagnostic purposes than any other type of biologic material.

I have always felt it necessary to be cautious in the acceptance of the diagnostic significance of any analytical results of a borderline type. Thus, if the blood findings are in excess of a tenth of a milligram per 100 grams of blood, one can be fairly sure of significant exposure. By the same token, if urinary results are correspondingly high, the interpretation is not difficult. My only point is that the urinary results in a given case are more likely to be definitely abnormal than are the blood findings. I am not quite certain as to the physiologic interpretation of this fact, but that it is a fact is without doubt. I personally like to have both blood samples and urine samples for analysis in most cases, and in some instances, especially those with recent exposure, I like to have fecal samples also. The latter are, of course, the least useful in most cases since it is very difficult to interpret the results of a single fecal analysis on account of the extreme variability of the lead content of the food material. In the case of children, however, on several occasions a diagnosis has been made possible by the discovery of paint-covered fragments of wooden objects in the stool.

Incidentally, before concluding, I should point out that in our experience, there is very little difference in the rate of lead excretion of children as compared to adults, whether under normal conditions or under conditions of lead exposure. I am not prepared to say that this is always the case, but so far we are not justified in differentiating children from adults with respect to rate of lead excretion.

Sincerely yours,

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Robert A. Kehoe, M.D.