

June 1, 1960

AIR MAIL

Dr. E. M. Rathus
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Division of Industrial Medicine
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William Street
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Reference: EMR:JG

Dear Doctor Rathus:

I hasten to reply at once to your letter of May 25, prior to my departure on a trip that will take me out of my office for a month, since otherwise there will be a long delay. In doing so I shall be brief since my time is short. This should not be taken to mean that my statements are arbitrary.

1. The range of concentration of lead in the urine of children in the U.S.A. differs but little from that of the adult in the U.S.A. In our experience the intake of lead in food and drink, on the part of the child, after being put on a mixed diet, is comparable to that of the adult, with due allowance for weight, and the "normal" metabolism of lead varies little from then on through life, subject, however, to variations in the composition and quantity of the diet.

It is likely that the infant whose diet is primarily and almost solely milk, has a low output of lead in the urine. We have very few data to demonstrate the facts, but in view of our knowledge of the lead content of milk and water, as well as the other components of the diet, there is little doubt about them.

The mean concentration of lead in the urine of different individuals varies (according to the diet) from around 0.02 to 0.03 mg. per liter, individual specimens of small volume ranging from a little less than 0.01 to a little more than 0.10 mg. per liter, depending largely but not solely upon ambient temperature and the throughput of water.

In the case of the infant and young child it is difficult to determine the facts with reference to the urinary excretion of lead because of the problems of sampling without contamination. The general run of hospital samples of the urine of small children, especially the females, are contaminated with lead in their collection and are not worthy of analytical investigation. For this reason many of the data in the literature are unreliable and must be ignored. Since it is so much easier to obtain uncontaminated samples of blood, an increasing reliance is being put upon determinations of lead in the blood. Moreover, for reasons that will appear later, the concentration of lead in the blood is much the more satisfactory indication of the lead content of the body. For these and other reasons, we rely almost wholly, for diagnostic purposes, on the lead in the blood of children, as distinguished from the lead

in the urine.

2. I do not accept the utility of Calcium Versenate (or any other chelating agent or medicament) as an aid in the diagnosis of "excessive lead absorption". The best of all possible means for the determination of the status of the individual, with respect to the quantity of lead in his body, is that of studying the level of concentration of lead in his blood, and the rate of excretion of lead from his body, under conditions which are not distorted by any therapeutic procedure. There is a normal (physiological) pattern of distribution of lead in the body, body fluids and excreta, which is clearly indicative of the burden of lead in the body. The moment you disrupt this pattern by any means, you obtain misleading results for analytical purposes. We do not have enough data under carefully controlled conditions to enable us to interpret the distorted effects of therapeutic procedures.

The foregoing statement answers the second part of your question #2. The answer is in the negative.

3. It is now possible to interpret the precise significance of the concentration of lead in the blood in relation to plumbism. At the onset of lead intoxication, the blood of both the child and the adult has somewhat more than 80 micrograms of lead per 100 grams of blood. Concentrations under that level, in our experience, are never associated with symptoms of intoxication. Concentrations above that level may or may not be associated with illness, but they must be above, if active symptoms are to be precipitated (symptoms persist sometimes after the blood level diminishes, but they never begin below that level).

It is not possible to derive similar conclusions or rules of thumb from various levels of lead concentration in the urine as determined by one or a few analyses. One must (1) be sure that he measures the current general level of the urinary lead excretion, and (2) that the renal excretion of lead has not been impaired. As for the latter factor, it is far from unusual, especially in the sick child, to find high concentrations of lead in the blood (concentrations in excess of 0.30 mg. per 100 grams), and low normal levels of lead concentration in the urine (0.01 - 0.06 mg. per liter). As the child survives and improves, it is not uncommon to find the lead in the blood dropping and that in the urine increasing until the normal relationships of the one to the other are restored. It is not possible, therefore, in a fair number of instances in the child, to employ the analytical findings in the urine for diagnostic purposes in relation to lead poisoning. The findings to which you refer in the first paragraph of your general text, after 3., are not remarkable in my view. However, I should like very much to know what was the lead content of the blood. If, as I suspect, it was in the range between 0.20 and 0.40 mg. per 100 grams, as it often is in fatal intoxication, your case would not be in doubt. I warn you, therefore, as I have undertaken to warn other investigators, that one should be prepared to investigate the lead content of the blood, especially in cases of childhood saturnism.

Incidentally, I do not consider that the findings in the urine following the administration of Versenate orally have anything much to do with the lead in the tissues of the body generally. Much of the lead in the urine following oral versene comes directly from the alimentary tract, where the versene contributed to its more rapid absorption. This form of therapy is not only useless, I think, but is actually contraindicated in most situations.

It will be found, I believe, that the use of versenate has a rationale when administered intravenously (can be given intramuscularly) in repetitive cycles, as a means of hastening the escape of lead from the body. Unless this is done for some time, it is of little value, since it results in only a little loss of lead (proportionately) from the body. It has very little curative value so far as I have been able to see, and its over-all beneficial effects have been very much magnified in the minds of physicians who know little or nothing about the quantitative relationships of the lead metabolism.

Sincerely yours,

Robert A. Kehoe, M. D.

RAK:ss