

September 19, 1949

Dr. Rudolph K. Waldman  
Bureau of Industrial Hygiene  
1170 Main Street  
Hartford, Connecticut

Dear Doctor Waldman:

Your letter of September 8 has raised a question which I feel requires some considerable discussion.

I should not want to criticize severely the procedure of Levine and Fahy, as described in their article in the Journal of Industrial Hygiene and Toxicology. Actually, I saw the article before its publication and approved it, although I had some misgivings, since fully justified, concerning the application which would be made of their procedure. Actually, one should never, under any circumstances, attempt to interpret the lead exposure and absorption of an individual on the basis of an analytical result on one sample of urine. No manner of applying a correction factor or any other mathematical expression can ever make such a result satisfactory. The concentration of lead in the urine varies from hour to hour and from day to day in response to a number of factors, some of which are unknown. It is true that the largest physiological factor that we have been able to put our finger on is that of the volume of water voided within a unit of time. There are other factors which contribute to this, however, which make it unsafe to rely upon any calculation based on specific gravity or any other known factor. Therefore, it is necessary to have a number of small samples of urine, or one or more samples of large volume, or a sample or samples of blood, in arriving at the physiological status of the individual with respect to the current rate of lead excretion. In our practice, we require samples of blood with spot samples of urine in arriving at a conclusion. I would never express an opinion on less than one sample of urine in association with a sample of blood taken at the same time. Frequently the results are in agreement on these two materials, and under these conditions, interpretation can often be made. Even here, however, both results may be in that dangerous zone of *intermediate*

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magnitude which makes interpretation difficult, and under these conditions we always require additional samples before arriving at an interpretation. Under certain circumstances we require the collection of samples of urine of large volume. It is obvious that 24-hour samples cannot be collected under certain conditions. The alternative is to collect samples of large volume during periods in which the individual is not at work and while he is clean and free of the likelihood of contamination. This can often be done quite satisfactorily, as our experience over many years has demonstrated. I enclose herewith the kind of instructions we issue for the collection of various samples. When any part of this procedure is left to the worker or to a patient, we supplement the regular instructions with carefully worded advice. Under these conditions we usually get reliable samples.

We have been measuring the specific gravity ourselves for a number of years, and we have satisfied ourselves, as you appear to have done, that this observation cannot be used except to make a rough estimate of the significance of the dilution factor.

The primary value of collecting one sample of urine from each of a series of employees who are engaged in the same work, lies in the fact that variability can be dealt with mathematically, and that the group as a whole can be appraised fairly satisfactorily. Indeed, precisely the same kind of variability will be found if one obtains a corresponding number of samples at different times from the same individual. Thus, we use a number of analyses, whether on an individual or on a series of individuals, as a means of interpreting the severity of the lead exposure of a fairly uniform group of men. This is the only manner in which such analyses can be used in a trustworthy fashion. On the other hand, if you are trying to learn the status of an individual, you will have to analyze a series of samples, or else you will have to obtain both blood and urine at the same time. The blood does not show the high variability that is found in the urine, and therefore, if one is to analyze only one material, he should by all means employ the blood. Unfortunately, the range of variability in the blood is relatively small, in relation to various degrees of lead absorption, and therefore, one's interpretation is better if he has the results of the analyses of both blood and urine.

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Dr. R.K. Waldman

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I trust that I have made my position clear on this matter. The problem is not an easy one, and unfortunately, in the practical performance of the day's work, we are often put to the necessity of doing less than that which is required to yield sound and adequate information.

Sincerely yours,

Robert A. Kehoe, M.D.

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September 8, 1949

Robert E. Kehoe, M. D.  
Director  
Kettering Laboratory of Applied Physiology  
College of Medicine  
University of Cincinnati  
Cincinnati, Ohio

Dear Doctor Kehoe:

Our Department of Industrial Hygiene is concerned with the examination of body fluids from lead exposed workers. Because we very often notice that the specific gravity of the urines, especially of spot samples, varies considerably, we are using a correction factor according to the article "Evaluation of Urinary Lead Determinations" by Leo Levine and John P. Fahy, Division of Occupational Hygiene, Massachusetts Department of Labor and Industries, Boston, Massachusetts, which appeared in the Journal of Industrial Hygiene and Toxicology, Volume 27, January-December 1945, pages 217-223. I am writing to ask your opinion on this matter as I know that you have had extensive experience in evaluating lead findings.

It seems to me that the use of the correction factor according to specific gravity is justified only within certain limits, that is, so long as the specific gravity does not deviate too far from the average specific gravity (approximately 1.016 to 1.034). Extreme high or low specific gravities should be handled with precaution.

In our steady control of industrial workers, we use the following procedure of sample taking:

It is very difficult to obtain 24-hour specimens, therefore we distribute lead-free bottles to the workers which are used by them for voiding early morning urine at home. This precaution is taken in order to prevent any contamination with lead from work clothes or other sources in the factories. With only a few exceptions, the specific gravity of these urines does not vary much from the mean specific gravity. However, we also receive samples from doctors with private patients who are suspected of lead poisoning and it happens very often that specific gravity values of these urines are in the far extremes.

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We had, for instance, the following cases of suspected lead poisonings:

|     | <u>Lead Finding</u> | <u>Specific Gravity</u> | <u>Adjusted Lead</u> |
|-----|---------------------|-------------------------|----------------------|
| (1) | 0.086 mg./l. urine  | 1.004                   | 0.516 mg.            |
| (2) | 0.065 mg./l. urine  | 1.002                   | 0.780 mg.            |
| (3) | 0.130 mg./l. urine  | 1.002                   | 1.560 mg.            |

Not one of these three patients showed any severe symptoms of lead poisoning, whereas we found many cases where lead content ranging from 0.15 to 0.40 showed marked beginning plumbism.

We will appreciate your comments on this matter, which we would find very valuable from a man of your experience and ability.

Very truly yours,



RKW:rrp

Rudolph K. Waldman, Ph.D.  
Principal Biochemist

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