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Is the 24-Hour Urine Sample a Fallacy?

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A study has been made of the use of 24-hour excretion (actual or projected) in comparison with the concentrations adjusted for specific gravity, as measures of exposure to lead, mercury, benzene, and trichloroethylene. It has been found that timed samples show a somewhat greater variation than values adjusted for specific gravity. When different individuals are considered, differences in body size affect the rate of excretion, as indicated by timed samples, to a certain extent. Other factors, however, appear to be of greater importance. The evidence presented, although not conclusive, suggests that the value adjusted for specific gravity is a better index of exposure than is the timed sample.

Introduction

THE LITERATURE of industrial medicine and industrial hygiene pays slight attention to methods of expressing urinalysis results. A few discussions of this problem, most of them limited to the element lead, have been published[1-3] but are largely ignored by workers with other metals, radioactive substances, solvents, and insecticides. Papers on these materials usually report findings on the basis of 24-hour samples, or, not infrequently, timed samples of shorter duration. When even short timed samples cannot be obtained, the results are ordinarly given as parts per million, microcuries per liter, or other unit of concentration in the urine, invariably accompanied by an apology for not using timed samples.

If we are dealing with averages, either procedure may lead to approximately equivalent results. In individual cases, however, especially when, owing to variation in fluid intake, the rate of urine excretion varies, the concentration of heavy metal, solvent metabolite, or radioisotope in the urine will also vary greatly. In such cases the rate of excretion is much more nearly constant than the concentration.

Ingestion of a pint of beverage may increase the flow of urine more than eightfold for a two-hour period. Our laboratory has received 24-hour urine samples that varied in volume from less than 350 ml to more than 3500 ml. Some authorities discount the importance of compensating for such variations, on the ground that they are so rare as to be unimportant. It has been our experience, however, that about 10% of the urine samples received are so dilute as to create a serious error if adjustment is not made. During a 12-month period, for example, more than 118 urine specimens with a specific gravity of 1.012 or less were submitted to our laboratory, for analysis for lead, mercury, phenol, trichloroacetic acid (TCA), or arsenic.

Adjusting for Specific Gravity

Twenty years ago Levine and Fahy proposed that variations in lead urine values be compensated by adjusting the concentration according to the specific gravity of the urine.

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TABLE I

Excretion of Several Industrial Poisons in Successive Samples of Urine

Substance	Duration	Number of Subjects	Average Percentage Deviation: 24-hr Sample (mg/24-hr)	Average Percentage Deviation: Adjusted Conc.[a] (mg/liter)
Lead	24 hr	19	11%	9%
Mercury	24	4	14	15
Uranium	16	1	35	38
Lead	4	63	20	15
Trichloroacetic acid	4	2	8	8
Weighted average			18	14

[a]Adjusted for specific gravity.

They suggested the formula:

$$\text{mg/liter (at Sp.Gr. 1.024)} = \frac{(\text{mg/liter}) \times 0.024}{\text{specific gravity} - 1.000}$$

where the left half of the equation is the value adjusted to a specific gravity of 1.024, and the actual specific gravity of the urine sample is used on the right side of the equation.

During a study of various facets of excretion of industrial poisons in urine, we have made a number of comparisons between values obtained by this procedure and those secured by use of timed samples. The customary procedure in problems of this sort is to collect successive urine samples from an individual and determine the extent to which the two values in question vary. We have done this with workers exposed to four different hazards, with the results shown in Table I.

The average deviation was, in general, less for long than for short samples. In the latter case the deviation was significantly less when the specific gravity adjustment was used than when timed excretions were considered. These deviations are notably lower than those obtained by Levine and Fahy[2] and, in the case of the timed samples, by Barnes.[1]

Further comparisons were made by obtaining urine samples from different members of groups of workers, all with similar exposures. The results are summarized in Table II. In the majority of cases, timed samples of six or eight hours, projected to 24 hours, were used. It was found that such samples were, in the main, more reliable than 24-hour samples, since, on questioning of the workers, the latter were frequently found to be incomplete. The results calculated on the basis of the specific gravity adjustment were more consistent than those based on the 24-hour excretion (projected or actual).

TABLE II

Variation in Excretion of Several Industrial Poisons within Groups Having Similar Exposures

Substance	Number of Groups	Average Percentage Deviation: 24 hr Sample (mg/24-hr)	Average Percentage Deviation: Adjusted Conc.[a] (mg/liter)
Lead	18	25%	19%
Benzene	13	30	21
Trichloroethylene	4	32	16
Dichlorobenzene	2	25	24
Weighted Average		27	19

[a]Adjusted for specific gravity.

One possible reason for this difference, which we considered, was body size. It seems logical to assume that a large man will inhale more dust or fume, and absorb and excrete more of the substance or metabolite, than a small man in the same environment. Our data on timed samples from lead workers have been split into two groups, consisting of individuals above and below average size. The results are given in Table III. As a measure of size we have used body surface area, as calculated from the tables prepared according to the formula proposed by Du-

TABLE III

Relationship between Body Size and Lead Excretion in Urine

Item	Body Size Group: Small	Body Size Group: Large
Number of subjects	39	35
Average body area, m^2	1.80	2.05
Lead excretion, mg/24-hr	0.154	0.193
Lead excretion,[a] mg/liter	0.174	0.180

[a]Adjusted for specific gravity.

bois.[4] The average exposures of the two groups are similar, if measured by the specific gravity adjustment, but the excretion per day is significantly higher for the larger men.

A different but consistent finding is obtained if our data on a group of men exposed to benzene are similarly treated (Table IV).

Table IV
Relationship between Body Size and Phenol Excretion of Subjects after Exposure to Benzene

Item	Body Size Group	
	Small	Large
Number of Subjects	6	4
Average body area, m^2	1.72	1.95
Phenol excretion, mg/24-hr	170.	176.
Phenol excretion[a], mg/liter	224.	179.

[a]Adjusted for specific gravity.

In this case the values adjusted for specific gravity indicate that the smaller men are on the average more heavily exposed than the large men. The rate of excretion per 24 hours, however, is slightly greater for the larger men.

If these findings are typical, it must follow that the total excretion of large men, based on volume adjusted for specific gravity, will on the average exceed that of smaller men. Our data on the average 24-hour urine excretion of various size groups are given in Table V.

Table V
Relationship between 24-Hour Volume of Urine Excreted and the Body Size of Subjects

Surface Area of Body, m^2	Urine Volume, liters/24-hr.[a]	
	Projected	Actual
1.25 – 1.69	0.82	0.62
1.70 – 1.79	0.98	0.86
1.80 – 1.89	0.96	0.84
1.90 – 1.99	1.01	0.87
2.00 – 2.09	1.03.	0.80
2.10 – 2.25	1.17	1.10

[a]Adjusted for specific gravity.

There is a marked difference in excreti[on] between the smallest and largest sizes; th[e] differences are less noteworthy in the inter[-] mediate groups. The projected values a[re] consistently higher than the actual valu[es] owing probably to diurnal variation in ra[te] of excretion—the samples that were proje[ct]ed were nearly all taken during the wo[rk] day, when excretion is generally at a high[er] rate than during the night.[5]

We also obtained samples from pairs o[f] workers who worked side by side or ha[d] similar jobs in the same work area. Com[-] parisons of urine excretion of different haz[-] ards from two such pairs are shown in Tab[le] VI.

As we might predict, the larger men show a significantly greater daily excretion, where[-] as the differences in the values adjusted for specific gravity are much less. In the cas[e] of foundry workers A and I, however, th[e] differences in daily excretion are much great[-] er than would be expected from the size dif[-] ferences, since, although A is a very larg[e] man, his coworker, I, is also well above aver[-] age size.

A similar picture can be obtained from paired workers of equal size, one of whom shows a high rate of excretion, and the other a low one. For instance, two molders and two pourers in the same foundry where A and I worked showed similar variation, although all were of about equal size, as shown in Table VII.

These differences bring out the fact that the 24-hour excretion, in terms of volume. adjusted for specific gravity varies greatly among individuals, regardless of differences in size, and only when averages are considered does size appear to be a significant fac[-] tor. There are undoubtedly several reasons for

Table VI
Excretion of Paired Workers

Worker	Body Area (m^2)	Hazard	24-hr Sample (mg/24-hr)	Adjusted Conc.[a] (mg/liter)
A	2.19	Lead	0.22	0.11
I	2.04	Lead	0.09	0.14
P	1.94	Benzene (phenol)	252.	152.
F	1.57	Benzene (phenol)	143.	119.

[a]Adjusted for specific gravity.

TABLE VII
Urinary Lead Excretion of Paired Workers of Equal Body Size

Worker	Body Area (m^2)	Job	24-hr Sample (mg/24-hr)	Adjusted Conc.[a] (mg/liter)
D	1.75	Molder	0.125	0.165
S	1.78	Molder	0.21	0.12
Ab	1.83	Pourer	0.29	0.22
T	1.89	Pourer	0.145	0.23

[a]Adjusted for specific gravity.

TABLE VIII
Average Urinary Lead Excretions of Foundry Groups

Number in Group	Jobs	Average Body Area (m^2)	Lead in Urine mg/24-hr	Lead in Urine mg/liter[a]	Lead in Air (mg/m^3)
6	Melters and pourers	1.93	0.172	0.202	0.32
9	Molders	1.88	0.182	0.127	0.19

[a]Adjusted for specific gravity.

this, such as diet and kidney function.

It seems unlikely that there is a close relationship between the volume of air breathed or the amount of fume or vapor absorbed, and the rate of excretion of urine.

Our studies of these men, A and I, and S and D, included four investigations over a 14-month period. The findings were essentially the same in each case. If we postulate that these men, who had all worked for years in the foundry industry, have reached essential equilibrium so far as lead intake is concerned, this means that they are excreting about as much as is being absorbed. Since A and S are excreting nearly twice as much lead in the urine as are I and D, it must follow that they are eliminating less via other channels, if total absorption and excretion are the same. This means that the body burden of lead in A and S is no greater, and in fact is probably less, than that of I and D. That this may be so is suggested by the higher values adjusted for specific gravity of the latter men.

If we accept the above reasoning, the necessary conclusion is that milligrams of lead per liter, adjusted for specific gravity, is a better index of lead absorption than is milligrams per 24 hours. Further evidence favorable to this theory may be found in Table VIII. Based on 24-hour excretion, the exposure of the molders is slightly greater than that of the melter–pourer group. The values, adjusted for specific gravity, however, indicate a considerably higher lead absorption by the latter. In addition, the measurements of lead in air confirm the greater exposure of these men in comparison with the molders, who do not themselves handle molten metal.

In October 1963, blood samples were obtained from the melters and pourers and from others, including floor and platform workers and molders. Unfortunately, the foundry had been working only a few days a week during the summer, and lead levels were well reduced over those found during the winter and spring. The findings are summarized in Table IX.

The group averages confirm the greater exposure of the melters and pourers in comparison with the others studied. In the individual cases, workers A and S have higher blood leads than coworkers I and D, even though for the latter the values adjusted for specific gravity are higher. Pourer T, however, has a higher blood lead than Ab. But the differences in all cases are too slight to be conclusive.

One possible reason for the differences noted between the melter–pourer group and the molders lies in the higher temperatures to which the pourers are subjected. It is probable that loss of perspiration may be a major factor in causing the lower total excre-

TABLE IX
Urine and Blood Lead Values of Foundry Workers

Number or Identification	Job	Lead in Urine mg/24-hr	Lead in Urine mg/liter[a]	Lead in Blood mg/100 gm blood
6	Melters-pourers	0.153	0.171	0.059
7	Molders-platform workers	0.091	0.095	0.044
A	Platform worker	0.11	0.07	0.058
I	Platform worker	0.07	0.12	0.047
S	Molder	0.15	0.09	0.054
D	Molder	0.10	0.11	0.046
Ab	Pourer	0.23	0.18	0.055
T	Pourer	0.20	0.23	0.066

[a]Adjusted for specific gravity.

tion by these men in comparison with the molders, whose exposure to heat, as well as to fume, is somewhat less.

Conclusion

Although these data, in general, fall into the pattern indicated above, more study is needed, in particular, more blood lead determinations on men with higher exposures, before we are warranted in concluding definitely that the value adjusted for specific gravity is more significant than the timed sample. It seems likely that, if this conclusion is confirmed for lead, it will also apply to other elements and metabolites of organic compounds, although not necessarily to all such substances.

We do not intend to imply that the specific gravity adjustment is necessarily the best method of expressing urinalysis results. Kehoe has criticized both this method and the 24-hour sample as being physiologically unsound, but he does not suggest another procedure that will work for samples of all ranges of dilution.[6]

As between the timed sample and the specific gravity adjustment, however, we believe that the data we have favor the latter as providing the more meaningful results.

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Facts About Lead

The Lead Industries Association has prepared a booklet, *Facts About Lead and Industrial Hygiene,* which will be of interest to many persons in the areas of occupational health and industrial hygiene. A historical narrative of the facts and fallacies regarding lead poisoning is presented. This is followed by sections on the balance of lead in the body and the control of industrial exposures to lead in various forms. A section on safeguards and practical suggestions is also included. Copies of this publication may be obtained from the Lead Industries Association, Inc., 292 Madison Avenue, New York, New York 10017.