The Osmolality Adjustment in Urinalysis

HERVEY B. ELKINS, PH.D., LEONARD D. PAGNOTTO, and
MAX RICHMOND, Boston, Mass.

IN ASSESSING exposure to or absorption of toxic substances, urinalysis results are not consistent. For example, consecutive samples from the same worker may yield quite different findings, and samples from several workers with similar exposure may have widely varying contents of toxic element or metabolite. In industrial hygiene literature, it is not infrequent to find statements to the effect that "there is no relationship between individual excretion and exposure" to a given substance.[1]

The general implication of such statements seems to be that urinalyses are inherently unreliable as indices of absorption of toxic substances. While this may be true in some, if not in all cases, a number of other explanations of the reported variabilities of results are possible. Contamination of the sample or loss of the substance being sought (due to the decomposition of the urine sample) are frequent possibilities. In addition, many of the methods—especially those used in determining microgram and submicrogram amounts of toxic metals—are quite difficult, and in performing such analyses the best laboratories are not infallible. Even if the above difficulties are overcome and our assumptions regarding exposure are accurate, there are other factors which can affect the results of the urinalyses in such a way as to produce inconsistent findings.

When urinalysis results are expressed as parts per million, milligrams per liter, or in other units of concentration, they may be subject to great variation due to differences in water balance. Below are shown the lead concentrations in the urine of a lead-poisoning patient who was put on forced fluids.

Condition	*Lead (mg./L.)*
Forced fluids	
Test 1	0.035
Test 2	0.015
Fluids restricted	0.22

While the above is an extreme case, dilute urine samples are frequently obtained during routine procedures, and failure to compensate for this fact can lead to incongruous results. Measurement of rate of excretion by collection of 24-hr. or other timed samples is the classical method of correcting for variation in fluid balance, but the practical difficulty of securing reliable timed samples is a serious drawback to this procedure.

An obvious alternative is to relate the amount of the substance to some component of the urine other than water. For example, in the urine sulfate test for benzene exposure, the concentration of sulfate-conjugated phenols is related to the concentration of sulfate. Experience has shown that, in general, this compensates for variation in fluid balance, the urine sulfate ratios of similarly exposed workers being the same in dilute and concentrated urines.[2] Another component of urine which is sometimes used for this purpose is creatinine.

Aside from the use of timed samples, the most common method of correcting for variation in fluid intake is the specific-gravity adjustment.[3] This may be considered as relating the concentration of a single component to the total solid content of the urine. Some studies have indicated that values calculated with the specific-gravity adjustment are more consistent than those from timed samples, even when the latter are collected with unusual care.[6] Nevertheless, urinalysis results calculated according to the

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specific-gravity formula have also failed to be uniformly consistent. Consecutive samples from the same worker have shown considerable variation and samples from different workers with the same exposure have given even less consistent results. While a number of factors may contribute to this variation (one of the most interesting suggestions being that of the presence of natural chelating agents, in the case of heavy metals), it seemed plausible to suppose that specific gravity was not the best possible measure of urine concentration for this purpose.

At the suggestion of Dr. Edward Radford a study was made of osmolality as a substitute for specific gravity in adjusting urinalysis results.

Osmolality

What is osmolality? We have been unable to find the word in any dictionary, nor does it appear in any of several recent text books of physical chemistry. It is used in recent papers on renal physiology.

A number of properties of nonelectrolyte solutions (including vapor pressure, osmotic pressure, freezing point, and boiling point) depend on the solvent's molality—that is, the number of moles of solute per 1000 gm. of solvent (in our case, water). It is thus possible to determine the molality of a nonelectrolyte solution by measuring its freezing point. However, if electrolytes are present—as they are in urine and other body fluids—the depression of the freezing point and changes in other properties are greater than from an equal molal concentration of nonionic solute.

The term "osmolality" indicates the apparent molality of the solution, in terms of nonelectrolyte solute. It can be considered an index of the osmotic pressure, a property of great physiological importance. For example, it is believed that under conditions of dehydration the degree to which urine can be concentrated is determined by its osmolality. The specific gravity per se is unimportant. For this reason measurement of osmolality, rather than specific gravity, has been recommended in various kidney function tests, etc.[4]

As a practical test for measuring urine concentration, osmolality has both advantages and disadvantages in comparison with specific gravity—a property easily and rapidly determined by a very simple device, the urinometer.

Equally primitive methods of measuring freezing point are not sufficiently rapid or accurate for the purpose of measuring osmolality, and devices of some complexity and cost are commonly employed. We have used a Fiske osmometer,* containing a refrigerating unit and cooling system, and with a thermistor and Wheatstone bridge for accurate measurement of temperature. The device requires a 2-ml. sample, and reads directly in terms of milliosmols per 1000 gm. of water.

The data obtained by such a unit are more accurate than specific-gravity readings with a urinometer. For equally precise and rapid measurements of specific gravity, more expensive instrumentation providing close temperature control would be needed. The usual urinometer method also requires a rather large volume of urine.

Both specific gravity and osmolality are affected in the same way by changes in the fluid balance, being increased by dehydration and decreased by water diuresis. A plot of average osmolality against specific gravity (Fig. 1) shows a nearly linear relationship up to a specific gravity of about 1.027. Above this value, osmolality increases less rapidly than specific gravity.

The most important components of urine under normal conditions are urea and sodium chloride. The osmolalities of solutions of these compounds are much higher, in comparison with their specific gravity, than are those found in the average urine sample (Fig. 1). This reflects the presence of substances of higher molecular weight, which contribute more to the density of the solution than to its osmotic pressure.

The mean specific gravity of urine samples from workers as found by Levine and Fahy[3] is 1.024. At this specific gravity the average osmolality is about 0.9; at a specific gravity of about 1.027, an average osmolality of unity is reached.

Our results are only in fair agreement with those published by others. In comparison with specific-gravity results, Jacobson *et al.*[4] found markedly higher osmolalities in urine samples obtained from controls and patients than we found in workers. Holmes reported somewhat higher relative osmolalities in samples obtained from medical students, but lower values from patients with renal disease.[5] Neither of these

*Fiske Associates, Inc., Uxbridge, Mass.

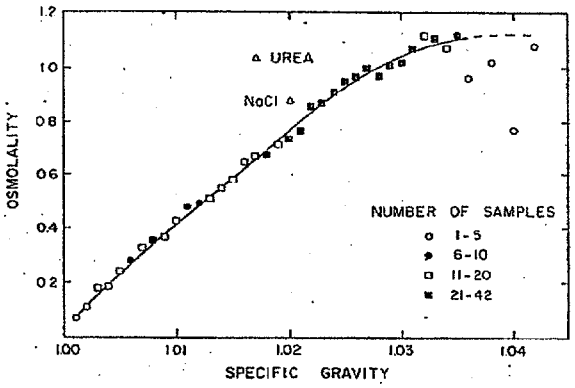

Fig. 1. Osmolality vs. specific gravity.

reports listed samples with specific gravities above 1.030, whereas our data include nearly 100 specimens with gravities between 1.031 and 1.042.

The discrepancy between our results and those of Holmes appears to lie in the specific-gravity measurements. For purposes of the specific-gravity adjustment,* it is important that the density of urine be related to that of water at the temperature of measurement, and our data are on this basis. Holmes' specific-gravity values appear to relate to water at 4° C.; i.e., they are essentially the same as the density and would average about 0.003 units lower than ours for the same samples.

For practical purposes we can consider that liters × osmolality = osmols, and mg./(L. × osmolality) = mg./osmol.

Below are shown data on 24-hr. and shorter timed samples, in terms of osmols per 24 hr., for individuals of different body size. Projected values refer to timed samples (6–12 hr.), calculated on a 24-hr. basis.

Av. surface area (*sq. m.*)	*Osmols/24 hr.* *Actual*	*Projected*
1.48	0.61	—
1.52	—	0.60
1.65	0.66	0.69
1.75	0.72	0.83
1.85	0.76	0.81
1.95	0.80	0.90
2.05	0.86	0.91
2.15	1.03	0.95
2.23	0.98	—
2.28	—	1.03

The average excretion per 24 hr. varies from 0.6 osmols for very small men and women

*Mg./L. adjusted = $\text{mg./L.} \times \frac{0.024}{\text{s. g. of sample} - 1.000} = \text{mg./Lg.}$

Table 1. Comparison of Osmol and Adjusted Volume Excretion

Surface area (*sq. m.*)	*Osmols/24 hr.*	*Adjusted vol./24 hr.* (*L.*)
1.50	0.60	0.65
1.65	0.68	0.74
1.75	0.77	0.86
1.85	0.78	0.88
1.95	0.85	0.95
2.05	0.88	1.00
2.15	0.99	1.06
2.25	1.00	1.15

Table 2. Lead in Dilute and Concentrated Urine Samples

Nature	*S. g.*	*No.*	*Lead found* *mg./osmol.*	*mg./Lg.*
Dilute	< 1.010	26	0.19	0.22
Concentrated	> 1.029	10	0.26	0.18

(weight. about 120 lb.) to about 1 osmol for men over 6 ft. and weighing over 200 lb. This means that the value "mg./osmol" will usually be greater than "mg./24 hr." except when the subject is a very big man. A similar relationship was found for total solids excretion, as measured by the specific gravity adjustment.[6] In Table 1 daily specific-gravity adjusted volumes (Lg)* are compared with osmols per day for the different size groups. "Actual" and "Projected" values are combined for the purposes of this comparison.

In general, excretion calculated as liters adjusted to 1.024 specific gravity exceeded that calculated as osmols by about 10%. In individual cases "osmols/day" frequently equalled and occasionally exceeded slightly "adjusted volume (liters)/day."

This means that the term "mg./osmol" will on the average exceed "mg./Lg." by about 10%. A marked difference exists between dilute and concentrated samples, however, as shown in Table 2.

Adjusted for osmolality the average values are slightly lower in dilute samples and significantly higher in concentrated urines than are the specific-gravity adjusted values. In individual cases the differences may be much greater. In Table 3, listing findings in lead workers, a number of samples of high specific gravity

*Adjusted volume = actual volume × $\frac{(\text{s. g.} - 1.000)}{0.024}$

TABLE 3. SAMPLES OF HIGH SPECIFIC GRAVITY

No.	S. g.	Lead found		Av. for co-workers
		mg./osmol.	mg./Lg.	(mg./Lg.)
1	1.033	0.39	0.31	0.30
2	1.034	0.24	0.17	0.30
3	1.034	0.45	0.30	0.30
4	1.035	0.16	0.13	0.14
5	1.036	0.10	0.05	0.07
6	1.038	0.16	0.09	0.18
7	1.040	0.09	0.04	0.17

are shown, together with the values adjusted both to osmolality and specific gravity. The averages for the co-workers (employes in the same work area and with occupations similar to those of the subject worker) are given for purposes of comparison. In all cases the osmolality adjustment yields a higher result, sometimes more than twice the specific gravity value.

Several of the urine samples of high specific gravity gave a positive test for sugar, and in all such cases the osmolality was relatively low. It seems highly probable that in such cases the specific-gravity adjustment gives too low a value. Whether the osmolality adjustment gives a result that can be substituted directly for the specific-gravity value is open to question, but it appears to be a logical procedure.

Comparison of the consistency of results calculated by both specific-gravity and osmolality adjustments yielded no clear-cut conclusions. Samples analyzed for lead and trichloracetic acid seemed slightly more consistent when the specific-gravity adjustment was used than when calculated on the basis of osmolality, while the reverse was true for samples analyzed for mercury phenol and hippuric acid.

In determining osmolality it is desirable that the sample be reasonably fresh and that no acids be added. The osmolality is greatly increased by small amounts of strong acids, such as are sometimes added to keep heavy metals in solution when the sample cannot be refrigerated.

Summary

For the purpose of adjusting urinalysis results, a study was made of urine osmolality as a substitute for, or supplement to, specific gravity. The data indicate that, while osmolality has certain theoretical advantages, essentially the same results are obtained as with specific gravity—except in the case of extremely dilute or very concentrated samples, or samples containing sugar or large amounts of other substances of high molecular weight.

Department of Labor & Industries
286 Congress St.
Boston, Mass.

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PREVALENCE OF TUBERCULOSIS

About three million deaths are attributed to tuberculosis annually and some fifteen million people living in newly emerging nations are capable of transmitting tuberculosis according to a report of the 18th International Tuberculosis Congress held in Munich during October, 1965.

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