

Osmometry Revisited

**A Practical Guide to Its
Clinical Use**

David H. Lobdell, M.D.



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It is now little more than a decade since the freezing-point osmometer moved out of the research laboratory to become part of the diagnostic armamentarium available at the community level. During the six years this instrument has been available at our hospital, it has been used thousands of times in diverse situations ranging from the monitoring of dialysates in the Renal Unit to the diagnosis of diabetes insipidus. The purview of osmometry has broadened considerably since then, prompting the present revision of this guide, which explains the freezing-point osmometer, the basic principles of "osmotic pressure" measurement and how serum and/or urine osmolality determination can aid in diagnosing and following a number of disease states.

The Osmometer

When a solute is dissolved in a solvent, four of the properties of the solution are changed in a roughly linear response to the amount of solute added: the freezing point is lowered, the boiling point is raised, the osmotic pressure is increased, and the vapor pressure is lowered. The resultant changes in these colligative properties are not proportional to the weight or change of shape of the dissolved particles, but only to their molal concentration (i.e., their number). When a mole of any non-ionic solute is dissolved in a kilogram of solvent, the freezing point of the solution is lowered a uniform amount; for water (the solvent in serum and urine) this is 1.86°C . A more marked depression of freezing point occurs when an electrolyte such as sodium chloride, which dissociates into ionic components, is added to the solution. In other words, the lowering of

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the freezing point is a function of the number of particles, molecules or ions in solution.

Osmolality, like freezing point depression, is also directly related to the concentration of free particles in a solution, as expressed by the formula

Osmolality = osmols/kg. solvent = on

where n is the number of particles dissolved in the solvent and o is the osmotic coefficient, a factor for correction of the observed osmolality to the ideal behavior of a solute.

For example, o NaCl is 0.93; one kilogram of water to which is added one mole of salt will contain $2 \times 0.93 \times 1$ mole = 1.86 osmols of sodium chloride. o for non-electrolytes such as glucose and urea is 1; since they do not dissociate, one mole equals one osmol (Osm). In biologic solutions, the milliosmol (mOsm) is used as a more convenient unit.

Osmolality, then, can be expressed as varying in a linear function with respect to the temperature change in $^{\circ}\text{C}$ of the freezing point. One osmol (1000 mOsm) of any solute lowers the freezing point of a kilogram of water by 1.86°C . As a corollary, the concentration of solutes in a body fluid can be conveniently measured by an instrument which will detect this temperature change. This is the function of the misleadingly-named freezing-point "osmometer." It does not measure osmolality or osmolarity or osmotic pressure directly, but actually a quite separate colligative property of solutions, and the result in mOsm/kg which the machine records is really a figment which would be a true osmolality only if biological solutions were pure aqueous solutions of salt. Purists will insist that the osmometer should be called a cryoscope and its measurements recorded in millidegrees rather than millimoles; they are correct, but it makes little difference what the instrument is called or how its readout is expressed so long as it supplies meaningful and superior data. This it does. The results obtained with the freezing-point osmometer correlate much better

with actual solute concentration than does any alternative method — e.g. electrical conductivity, specific gravity, or refractive index.

The osmometer, when stripped to bare essentials, consists of (1) a refrigerated bath to hold, supercool, stir and freeze body fluids, (2) an electric thermistor or probe which changes its resistance with temperature and is sensitive to 0.001°C, and (3) a Wheatstone bridge and galvanometer for translating temperature-related resistance change into calibrated units (mOsm/kg water). Following initial rapid supercooling (i.e., cooling below the freezing point) to a predetermined temperature, the sample is vibrated intensely for a moment, which produces heat of fusion as crystallization occurs. The temperature of the fluid then reaches an equilibrium plateau which is maintained for several minutes, during which time the temperature measurement is made by the thermistor. This plateau is slightly below the true freezing point, but by relating the unknown with standard solutions of known Osm concentration with which the osmometer is calculated, no specific correction is required. Duplicate determinations are always run, and must vary no more than 3 mOsm. The AI osmometer which we have used for the past six years requires only 0.2 ml of serum or urine.

Normal Values

BLOOD: Normal serum osmolality generally falls into the range 275-300 mOsm/kg, with no significant sex difference. Only a small fraction of the serum constituents (about 0.85% by weight) determines osmolality. The serum electrolytes, particularly sodium, contribute about 275 mOsm, glucose and the non-protein nitrogenous substances less than 10 mOsm; the remaining constituents, including protein, exert negligible effect on freezing-point depression. Heparinized plasma samples can be substituted for serum, but other plasma anticoagulants may add measurable solute to the blood and make interpretation difficult.

There are several formulas which have been used to predict osmolality from the measured serum concentrations of the solutes which most influence osmolality in the healthy individual.

The one most often quoted is:

$$\text{Osm} = 1.86 (\text{Na}^+) = \frac{\text{glucose}}{18} + \frac{\text{BUN}}{2.8}$$

A simplification of the above which allows mental calculation is:

$$\text{Osm} = 2 (\text{Na}^+) + \frac{\text{glucose}}{20} + \frac{\text{BUN}}{3}$$

If only sodium and glucose are available, the following can be used:

$$\text{Osm} = 2 (\text{Na}^+) + \frac{\text{glucose}}{18}$$

The longest formula in print, one more complex than is actually necessary in view of the minimal contribution of calcium and magnesium ions to osmolality, is:

$$\text{Osm} = 1.85(\text{Na}^+) + 1.84(\text{K}^+) = \frac{\text{glucose}}{18} + \frac{\text{BUN}}{2.3} + 1.15(\text{Ca}^{++}) + 1.17(\text{Mg}^{++})$$

For the average individual, the calculated osmolality is somewhat lower than that measured by freezing point depression, the amount varying with the formula used. A significant difference (40 mOsm or more) implies the presence of a high concentration of solutes which do not normally contribute to serum osmolality and often constitute toxic metabolic byproducts of a serious disorder, such as lymphoma, metastatic cancer, liver failure, myocardial infarction, hemorrhagic shock, uremia, acute intoxications or various overwhelming infections. A measured osmolality 40 mOsm or greater than that predicted from the above formulas is thus of grave prognostic import, and usually presages death if it cannot be corrected by appropriate treatment.

In this regard, surgical research teams using the osmometer to monitor traumatic shock have shown that there is a

positive correlation between blood lactate levels in shock patients and the difference between measured and calculated osmolality; in situations where lactate levels are unavailable, the osmometer can thus provide equally useful information about the effectiveness of treatment. In one such study, a group of shock patients initially had elevated serum osmolalities averaging 350 mOsm/kg, with the differential between measured and calculated osmolality averaging 80 mOsm; patients successfully resuscitated manifested a fall in both values, while a progressive increase was noted in patients who ultimately expired.

It has recently been pointed out that the commonest acute cause of coexisting hyperosmolality and coma is excessive ingestion of alcohol. The measured serum osmolality in advanced drunkenness may be 100 mOsm/kg or more above that calculated from glucose, urea and sodium concentrations.

URINE: On a medium protein diet with an average content of salt, an adult excretes approximately 1200 mOsm of solute per day. Of this, urea comprises about 500 mOsm, and the three univalent cations Na⁺, K⁺, and NH⁴⁺ and their associated anions account for almost all the remainder. On an electrolyte-free and protein-free diet, excretion may fall below 200 mOsm per day, while on a high-protein diet with maximum ADH stimulation, the adult kidney can normally produce a urine with an osmolality which approximates that of the renal interstitial tissue at the tip of the medulla (1400m mOsm/kg), or about 1700 mOsm per day. The infant kidney is less efficient, with a maximum concentrating ability of about 600 mOsm/Kg.

It is misleading, then, to list one specific “normal” value range for urine osmolality, since solute output varies greatly with dietary intake.

Holmes used four groups of individuals to establish normal ranges, as follows:

1. healthy males — 392-1090 mOsm/kg
(767-1628 mOsm/24 hr.)
2. healthy females — 301-1093 mOsm/kg
(433-1146 mOsm/24 hr.)
3. convalescent patients — 273-896 mOsm/kg
(340-900 mOsm/24 hr.)
4. ward patients, house diet — 288-884 mOsm/kg
(261-900 mOsm/24 hr.)

Any adult value falling outside these ranges, when not explainable by diet, should lead to further study of the patient. In addition, one should always consider the urine osmolality in relation to the serum value; a high serum osmolality coupled with a low urine value, or a low serum value coupled with a high urine osmolality should also be considered abnormal. Normally, the ratio $U \text{ osm}/S \text{ osm}$ should exceed 1.0; after an overnight fast, the ratio should be 3.0 or greater. It approaches 1.0 in chronic renal disease, while diabetes insipidus or excretion of a large water load forces the ratio below 1.0.

Some Indications for Serum Osmometry

1. Differential Diagnosis of Hyponatremia and Hypernatremia

In every case with a significant elevation or decrease in serum sodium, serum freezing point determination should be performed for a more complete evaluation of the problem.

HYPONATREMIA The combination of a low serum sodium concentration and low serum osmolality indicates *dilutional hyponatremia*, which may follow intravenous administration of electrolyte-free fluids, or increased ADH release in traumatized patients, in those on prolonged positive-pressure ventilation and in the Schwartz-Bartter syndrome (q.v.). The same picture is noted in *non-symptomatic hyponatremia* (chronic cellular hypo-osmolality) associated with a variety of chronic diseases. Total body

sodium is normal. Because serum osmolality is depressed in proportion to the lowered serum sodium concentration, the ratio Na/Osm remains within normal limits (0.43 - 0.50).

In true *depletional hyponatremia*, with an actual decrease in total body sodium (such as may be seen in salt depletion from excessive sweating, gastro-intestinal loss, or following paracentesis), serum osmolality is not significantly lowered, since the fluid lost is usually iso-osmotic, and the Na/Osm ratio falls below 0.43. Hypertonic saline can be given to these patients with expected improvement; the serum sodium concentration will rise without any appreciable change in the determined osmolality.

The same situation prevails in *hyperlipemic pseudo-hyponatremia*; lipid does not enter solution and therefore does not affect osmolality, but it does occupy space and thus causes a spuriously low flame-photometer sodium reading coupled with a normal osmolality.

Hyponatremic congestive heart failure, uremia, and hepatic decompensation are often attended by a paradoxically high serum osmolality. In kidney disorders, the increased osmolality is presumably due to an elevated BUN, but in other diseases it must represent unanalyzed metabolic solutes. In such situations, the milliosmol concentration is of greater physiologic significance than the serum sodium, since body regulatory mechanisms are sensitive primarily to changes in total solute concentration. Intravenous administration of sodium to hyponatremic patients with marked derangement of kidney function and an elevated osmolality is usually not necessary, and in fact is hazardous since the total body sodium tends to be near normal.

HYPERNATREMIA Serum osmolality is usually increased in proportion to the elevation of sodium concentration from any cause, maintaining the ratio Na/Osm within normal limits. There are exceptions, however, and

sometimes the osmolality is lower or higher than would be expected from the sodium concentration alone. In Holmes' series of 59 patients with a serum sodium concentration above 150 mEq/L, a quarter had a measured osmolality less than 300 mOsm/kg, and a third exceeded 360 mOsm/kg. There was a much better prognostic correlation with osmolality than with sodium concentration; the problem was considered life-threatening when the osmolality exceeded 350 mOsm/kg.

2. Establishing Criteria for Hemodialysis

In patients with acute drug toxicity, acute renal shutdown, or liver failure, a significant discrepancy between the calculated and the measured osmolality can be considered a definite indication for dialysis, since the difference presumably represents an increase in potentially dialysable solute. In contrast, if measured milliosmol concentration is only slightly elevated above normal but specific gravity as measured by refractometry is significantly high, the molecules of toxic solute are too large to be dialyzed, and other means for clearing the circulation, such as exchange transfusion or plasmapheresis, should be considered.

3. Following the Course of Uremia

Chronic renal failure is an area where measurement of osmolality can replace routine electrolyte and blood nitrogenous component analysis, but it should be emphasized that this is a rational step only after electrolyte and BUN baselines have been established.

As previously stated, many cases of uremia are characterized by a significant difference between the value for serum osmolality as calculated from the formula incorporating sodium, urea nitrogen and glucose levels and the value obtained by freezing point determination. This difference reflects accumulation in the blood of unmeasured metabolites. The serum concentration of sodium, which is responsible for most of its osmolality in normal people, in uremic patients may be lowered, normal, or increased.

There is a tendency for the lowest osmolality values to occur in those patients with lowered serum sodium, but the spread is quite wide; likewise, while there may be some correlation with the elevation in BUN, the spread again is quite wide. A uremic with low serum sodium and an increased concentration of unmeasured solutes may have a perfectly normal serum osmolality. Improper evaluation of the problem thus may occur, unless baseline electrolyte and urea nitrogen levels are obtained. However, once the serum electrolyte pattern had been established at a stable level, daily determination of serum osmolality may be the only laboratory work needed to follow the rate of solute retention and the progress of the uremia.

4. Hyperosmolal Non-ketotic Coma

The typical patient with this disorder is middle-aged or elderly and is admitted dehydrated, in semi-coma or coma with an elevated serum osmolality and a strikingly high blood sugar (usually 400 - 1000 mg/dl), but no ketoacidosis. The underlying diabetic state is almost always mild. This syndrome also has been described in non-diabetic burn patients receiving more than 300 gm carbohydrate per day over a prolonged period of time, in infants receiving incorrectly-diluted powdered formula, in acute pancreatitis, and following administration of glucocorticoids and diphenylhydantoin.

The coma in these patients had been explained as secondary to severe dehydration, owing to a shift of water from the intracellular to the extracellular compartment produced by the high blood glucose concentration and its resultant hyperosmolality. An osmotic diuresis then results in a hypertonic contraction of the extracellular fluid compartment, with water loss exceeding salt loss. Both compartments are thus water depleted. A major complication of the resultant dehydration is vascular thrombosis, especially of intra-abdominal vessels.

Serial determination of serum osmolality is a useful guide

in the replacement of the associated water deficit with hypotonic electrolytes, insulin, and glucose.

5. As a Guide to Solute Administration in Post-surgery Patients

This is perhaps the most valuable surgical application of osmometry, aside from the aforementioned monitoring of metabolic solutes in traumatic shock. Following surgery, the patient is in danger of being drowned in water or flooded with solutes. In the first few post-operative days, especially if there has been significant blood loss, there is increased ADH secretion with subsequent antidiuresis; osmolality of the serum will fall and that of the urine will rise. Overzealous water replacement during this period may lead to water intoxication and dilutional hypo-osmolality. On the other hand, prolonged administration of an isotonic saline solution (forgetting that there is insensible loss of water), prolonged tube feeding in neurosurgical patients, solute absorption from medicated dressings on burn surfaces, etc. may lead to hyperosmolality. The recent revival of interest in total intravenous hyperalimentation underscores the value of the osmometer in regulating solute administration; in our hospital, serum osmolality is monitored daily on hyperalimentation patients, with a view to maintaining the level below 300 mOsm/kg.

Some Indications for Urine Osmometry

1. Screening for Kidney Disease

Since renal tubular transfer activity is dependent upon the number of solute particles rather than their weight, osmolar concentration tests are more valid than those employing specific gravity determinations. While not always as informative as clearance studies, screening concentration tests can be quite valuable in infants or debilitated patients where multiple timed urine and serum samples may be difficult to obtain.

A simple and relatively comfortable test of concentrating ability is as follows (Fishberg):

The patient eats an early dinner, then has no more food or water until the test is finished at 9 a.m. The 10 a.m. and 11 a.m. specimens are collected and analyzed.

Normally, the urine osmolality in at least one of the specimens should reach a concentration of 850 mOsm/kg or greater; the failure to achieve this degree of concentration is generally regarded as a reliable indication of renal damage. In moderate renal dysfunction, osmolality may range between 400 and 600; severe damage may restrict concentration to less than 400 mOsm/kg.

For the detection of kidney disease, suboptimal elevation of urine osmolality during fluid deprivation is superior to gravimetry, pyelography, PSP excretion, creatinine clearance, or determination of blood urea nitrogen. In fact, it may be the only clue to "silent" pyelonephritis in patients with negative bacteriologic urinary findings.

It should be understood that while tests of concentrating ability are quite sensitive, they are also rather non-specific and therefore are best used for screening or detection rather than for differential diagnosis of intrinsic renal disease. However, when paired with determination of the glomerular filtration rate, some narrowing of the field is possible. For example, concentrating ability is severely impaired while the GFR is only slightly decreased in medullary cystic disease, cystinosis, severe pyelonephritis, secondary amyloidosis, and the nephropathies of sickle cell anemia, potassium deficiency and hypercalcemia.

2. Following the Course of Intrinsic Renal Disease

As tubular function deteriorates during the end stage of chronic kidney disease or during severe acute tubular necrosis, loss of concentrating function causes solute concentration in the urine to approach that of the serum, so that the ratio $U \text{ osm} / S \text{ osm}$ is no longer greater than 1. This will be true even though urine output varies signifi-

cantly, as for example in the diuretic phase of acute tubular necrosis. Restoration of tubular function in the recovery phase of this disorder can be detected by a decided increase above 1 in the $U \text{ osm}/S \text{ osm}$ ratio.

The classic teaching that urine osmolality becomes "fixed" at the serum level in advanced chronic renal disease is erroneous. The majority of such patients exhibit urine persistently hyposmolar to their serum, even following the administration of Pitressin.

3. Calculating Osmolal and Free Water Clearances

Osmolal clearance is calculated from the familiar clearance formula $C = UV/P$, substituting serum osmolality for plasma osmolality, as follows:

$$C \text{ osm (ml/min)} = \frac{U \text{ osm} \times V \text{ (ml/min)}}{S \text{ osm}}$$

It can be seen from the above that when the ratio $U \text{ osm}/S \text{ osm}$ is 1, the amount of urine formed per minute equals the amount of serum which can be cleared of its solutes during that period. If urine osmolality is greater than serum osmolality, the volume of urine needed for clearance of the same solute load can be smaller; if $U \text{ osm}$ is less than $S \text{ osm}$, the minute volume must be greater than it would need to be if the urine were iso-osmolar.

Usually when the urine is hypo-osmolar to serum, an amount of "free water" (water in excess of that needed for solute clearance) has also been excreted. The equation for calculating free water clearance is

$$(C^{\text{H}_2\text{O}} = V - C^{\text{osm}})$$

$C^{\text{H}_2\text{O}}$ will be a negative value when the urine becomes concentrated by virtue of resorption of free water in the collecting tubules during fluid deprivation. The negative free water clearance is thus a quantitative measure of the concentrating ability of the kidney.

Clinically, osmolal and free water clearance studies have

been used to study a great variety of conditions affecting water and solute excretion, ranging from diabetes insipidus to split-function studies in renovascular hypertension. They appear to be of especial value in determining whether hyponatremia in congestive heart failure patients is on the basis of a low osmoreceptor setting, glomerulotubular imbalance, or sustained antidiuretic hormone secretion, thus allowing therapy to be tailored to fit the situation.

4. Differential Diagnosis of Polyuria

The triad of polydipsia, polyphagia, and hyposthenuria can be caused by a number of conditions. Although polyuria resulting from diabetes mellitus, nephritis, potassium deficiency or hypercalcemia is easily categorized by appropriate laboratory tests, the differentiation of diabetes insipidus (DI) from psychogenic polyuria (compulsive water drinking) requires osmometry.

In both DI and compulsive water drinking, the osmolality of the dilute urine ranges from 50 to 200 mOsm/kg and the ratio $U \text{ osm} / S \text{ osm}$ is therefore less than 1 (usually 0.2 - 0.7). A three-hour water deprivation will elevate the ratio to greater than 1 in a compulsive water drinker, but not in a patient with DI.

The Hickey-Hare salt-loading test is a more sophisticated method of differentiating DI from compulsive water drinking; it also provides osmolality data which differentiates central from end-organ DI. Essentially, a water diuresis is induced by hydration, and control observations are made on urine flow and osmolality. Then hypertonic saline solution is infused in amounts sufficient to elevate the serum osmolality and stimulate the osmoreceptor. Additional observations are then made of urine flow and solute concentration during and after infusion.

A recommended procedure follows: During the hour preceding the test, the patient is made to drink 20 cc of water per kilo of body weight. Urine is voided at 15 minute

intervals, and the test is started when the flow exceeds 5 cc/min. The urine is collected for two 15 minute periods and a blood sample is taken for serum freezing point determination; then, a 2.5 or 3 per cent sodium chloride solution is administered intravenously, at a rate of 0.25 cc/min/kg body weight over a period of 45 minutes (approximately 800 cc). A second serum osmolality is obtained. Urine collection is continued for 30 minutes after completion of the infusion. It is examined for volume, specific gravity, and osmolality.

Serum osmolality should be determined before and near the end of the infusion to make sure that an increase in osmolality sufficient to stimulate the osmoreceptors has been induced by the salt load.

The normal response (and the response of patients with psychogenic polyuria) to the salt infusion is a marked decrease in urine volume, a rise in urine specific gravity to well above that of plasma (S.G. 1.016 or greater) and an increase in urine osmolality up to 800 - 1200 mOsm/kg. This is usually evident less than thirty minutes after the infusion has been started.

In classical "central" DI, but also in nephrogenic "end-organ" DI due to lack of response of the renal tubules to the action of ADH, and in hypercalcemic polyuria, urine volume remains unchanged or may increase; in response to the salt infusion the specific gravity may rise, but not above 1.010. The urine osmolality does not significantly increase, and in any event remains less than that of the serum.

The test described above may be combined with Pitressin stimulation by administering intravenously 0.1 unit of aqueous Pitressin in 1 cc. of isotonic saline at the end of the procedure, and collecting urine for two additional 15 minute periods. This allows differentiation of classical DI from nephrogenic DI, since Pitressin will elevate the urine osmolality to 700 - 1000 mOsm/kg. in central ADH-defi-

ciency DI, whereas the osmolality in patients with end-organ DI will continue to be less than that of the serum.

The Hickey-Hare test may well be superseded by the procedure devised by Miller, which has the additional advantage of easily identifying partial defects in ADH secretion ("incomplete DI"), a not uncommon condition, but one formerly difficult to pinpoint.

The patient is deprived of fluid beginning at 6 p.m. the previous evening; if polyuria is too severe to tolerate such a long period of dehydration, fluid restriction is begun the morning of the test. Starting at 7 a.m., hourly urine specimens are voided and their volume and osmolality measured. When urine osmolality becomes fairly constant (less than 30 mOsm/kg change between specimens, a process which may take up to 18 hours), blood is drawn for serum osmolality, and 5 units of aqueous Pitressin is injected subcutaneously. A terminal urine osmolality specimen is collected 60 minutes later.

In normal persons and patients with psychogenic polyuria, urine osmolality is much greater after dehydration than is serum osmolality, and does not rise more than 5 per cent after the injection of Pitressin. Patients with "incomplete DI" secondary to limited hypophyseal stores of ADH are also able to produce a urine hyperosmolal to blood after dehydration, but exhibit a greater response to Pitressin in terms of urine osmolality increase (9 per cent to 67 per cent in one series). In patients with full-fledged central DI or nephrogenic DI, urine osmolality remains much less than blood osmolality after dehydration; after Pitressin, urine osmolality rises more than 50 per cent.

5. Differential Diagnosis of Oliguria of Sudden Onset

In dehydration, the scanty, concentrated urine will possess an osmolality greater than 800, and a sodium concentration less than 10 mEq/L.

In early acute glomerulonephritis or in glomerular hypoperfusion resulting from circulatory shock, the urine sodium

concentration remains low — below 30 mEq/L— while urine osmolality exceeds serum osmolality. The degree to which urine osmolality exceeds serum osmolality appears to have some value in prognosticating whether or not a patient in circulatory shock will develop lasting renal injury. In one series, a ratio $U \text{ osm}/S \text{ osm}$ below 1.5 pre-saged progressive renal failure, while a ratio exceeding 1.5 made the likelihood of kidney damage remote.

In acute tubular necrosis, urine osmolality typically is lower than that of the serum, and the sodium concentration in a spot specimen will usually be greater than 30 mEq/L.

6. Guiding Potassium Replacement in Hypokalemic Patients

Restoration of depleted body potassium by intravenous solute administration customarily is monitored by sequential determination of serum potassium, although serum levels do not necessarily reflect cellular potassium content; a hypokalemic patient can be returned to a normal serum concentration, yet his cells may still be potassium-depleted. Determination of urine osmolality is helpful by virtue of the fact that low cell potassium impairs renal concentrating ability by producing a reversible tubular nephropathy. Adequate replenishment of cell potassium will be reflected by a return of urine osmolality from a Pitressin-resistant hyposthenuria to a normal range.

Osmometry is probably a valid guide to potassium replacement only when the deficit has been of short duration, as in post-surgical patients; the kidney of chronic hypokalemic nephropathy associated with long-standing potassium depletion, such as is found in ulcerative colitis or chronic diuretic overdosage may take as long as three weeks to regain its normal concentrating ability after body potassium has been replenished. In this situation, while osmometry can be of value in following the functional recovery of the damaged kidney tubules, it would be hazardous to depend upon it as an index of body potassium requirements.

Occasionally, hypokalemic patients will be found not to exhibit urine hypo-osmolality. This indicates that there has been a temporary shift of potassium out of the blood compartment, resulting in a low serum potassium concentration, but that the tissues are nevertheless adequately supplied with this cation.

7. Diagnosis of Schwartz-Bartter Syndrome

Inappropriate production of ADH or an ADH-like substance in the face of reduced serum osmolality may be associated with poorly-differentiated bronchogenic carcinoma, mediastinal tumors, myxedema, porphyria, expanding intracranial lesions, and following cranio-cerebral trauma. Certain medications (e.g. Vincristine, sulfonyl-ureas, ethacrynic acid and furosemide diuretics) are known to induce a reversible form of this syndrome.

ADH-mediated water retention accentuates the hypo-osmolality of the serum and produces a persistent hyponatremia, while making the urine inappropriately hyperosmolar and elevating its sodium concentration to over 25 mEq/L.

For the diagnosis of inappropriate secretion of ADH to be valid using these criteria, renal and adrenal functions must be normal and the patient must not be receiving a fluid overload.

Selected References

1. Weisberg, H.F.: Osmolality, ASCP Commission on Continuing Education Critique CC-71, 1971. Emphasizes physiochemical background of osmometry. Good bibliography (123 references).
2. Holmes, J.H.: Measurement of Osmolality in Serum, Urine, and Other Biologic Fluids by Freezing Point Determination. Pre-workshop Manual on Urinalysis and Renal Function Studies, ASCP Commission on Continuing Education, 1962. One of the pioneer papers concerning clinical application of osmometry, and still very useful.
3. Boyd, D.R., et al.: Utilization of Osmometry in Critically-ill Surgical Patients. *Arch Surg.* 102:363, 1971. One of a number of papers emanating from a group which promotes the use of osmometry in day-to-day management of traumatized and post-surgical patients.
4. Dormandy, T.L.: Osmometry. *Lancet* 1:267, 1967. Not very clinically oriented, but British, and therefore delightfully written.
5. Miller, M., et al.: Recognition of Partial Defects in Antidiuretic Hormone Secretion. *Ann. Int. Med.* 73:721, 1970. An important paper outlining cryoscopic identification of surprisingly common partial abnormalities in ADH secretion. See also Editorial, *Lancet* 1:531, 1971.
6. Takasu, T., et al.: Mechanisms of Hyponatremia in Chronic Congestive Heart Failure. *Ann. Int. Med.* 55: 368, 1961. For the cardiologist, valuable in distinguishing between and managing the three distinct varieties of hyponatremia which may complicate chronic heart failure.



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