Q&A column

Editor: Frederick L. Kiechle, MD, PhD

Submit your pathology-related question for reply by appropriate medical consultants. CAP TODAY will make every effort to answer all relevant questions. However, those questions that are not of general interest may not receive a reply. For your question to be considered, you must include your name and address; this information will be omitted if your question is published in CAP TODAY.

Q. Please describe the contemporary significance and use of osmolality testing in the clinical laboratory.

A. April 2019—Osmolality testing aims to quantify the number of osmotically active particles per unit mass of solution, often reported in milliosmoles per kilogram. In biological fluids, it is reported in millimoles per liter. Freezing point depression osmometry is the preferred method for measuring osmolality in the clinical laboratory since, unlike vapor pressure osmometry, its results are not influenced by atmospheric temperature.[1] There are clinical applications for measuring the osmolality of serum, urine, and stool. The principal osmotically active solutes are sodium, chloride, potassium urea, and glucose. In nondisease states, urine osmolality corresponds to urine specific gravity. The ratio of urine to serum osmolality is normally about 1:3.

Serum and urine osmolality are used for the diagnostic workup of sodium disturbances and polyuria, while stool osmolality can help distinguish etiologies for chronic diarrhea. Serum osmolality also has some utility in testing for intoxication. In the context of hyponatremia, urine osmolality distinguishes between primary polydipsia and other entities, such as the syndrome of inappropriate antidiuretic hormone secretion.[2] When correcting hyponatremia using isotonic saline or a similar infusate, frequent monitoring of plasma and urine osmolality is critical to ensuring that the rate of correction is appropriate and the risk of osmotic demyelination syndrome is minimized.[2] In the workup of polyuria, after excluding diabetes mellitus, urine and serum osmolality guide the differential diagnosis between diabetes insipidus and other entities.[1] Urine osmolality aids in the distinction between water diuresis, which is seen in diabetes insipidus, and osmotic diuresis. If it is equivocal, the water deprivation test can be used to increase serum osmolality and facilitate more definitive test results.[2] Urine and plasma osmolality are measured every few hours during the water deprivation test to clarify the diagnostic picture and monitor for potentially clinically detrimental fluid imbalances. Stool osmolality is occasionally directly measured when factitious diarrhea (created by adding water or other hypotonic fluids to a stool sample) is suspected. In the case of factitious diarrhea, stool osmolality is lower than serum osmolality.[1]

In the context of toxicology testing, an increased serum osmol gap (the difference between calculated and measured osmolality) may suggest the presence of otherwise unmeasured osmotically active substances, including volatile alcohols. While direct testing for the more common alcohols is generally readily available, the osmol gap may support a clinical suspicion for intoxication while more definitive laboratory workup is pending.

Measurement of serum, urine, and stool osmolality plays a key role in the diagnostic workup and monitoring of several clinical conditions. Although in some settings its utility and practicality are limited by the availability of alternative testing, such as direct ethanol testing in the setting of suspected intoxication or urine specific gravity to estimate renal concentrating ability, osmolality measurement remains the best test in certain clinical scenarios.

1. Rifai N. Tietz *Textbook of Clinical Chemistry and Molecular Diagnostics,* 6th ed. St. Louis, Mo.: Elsevier; 2018.
2. Goldman L, Schafer AI. *Goldman-Cecil Medicine,* 25th ed. Philadelphia:

Elsevier Saunders; 2016.

Sammie Roberts, MD,
Department of Pathology
University of Colorado School of Medicine
Aurora, Colo.
Former member, CAP ClinicalChemistry Committee

Sridevi Devaraj, PhD, D(ABCC)
Professor, Pathology and Immunology
Baylor College of Medicine
Director, Clinical Chemistry and
Point of Care Testing
Associate Director, Microbiome Center
Texas Children's Hospital, Houston
Member, CAP Clinical Chemistry Committee

Q. When a result is outside the analytical measurement range, the sample is processed by dilution. If the result of that dilution is found within the AMR, it is then multiplied by the dilution factor and reported. Should we include a comment on the report saying the result was obtained after dilution?

A. For results greater than or less than the analytical measurement range, a numeric result must not be reported unless the sample is processed by dilution, a mixing procedure, or concentration to obtain a value that falls within the AMR. The result must be within the AMR before it is mathematically corrected by the concentration or dilution factor to obtain a reportable numeric result. Although the laboratory is required to retain testing records, including mathematical corrections, there is no requirement to include a comment on the patient report indicating that a result was obtained after dilution.

1. Medicare, Medicaid, and CLIA programs; laboratory requirements relating to quality systems and certain personnel qualifications. *Fed Regist.* 2003;68(16):3712. To be codified at 42 CFR § 493.1282(b)(1)(ii).
2. College of American Pathologists. CHM. 13710 Diluted or concentrated samples. In: Chemistry and toxicology checklist. Aug. 22, 2018.

Joel Graff, MBA, MT(ASCP)
Senior Technical Specialist
Laboratory Accreditation Program
College of American Pathologists
Northfield, Ill.