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. What is the ideal collection tube for measuring the level of ammonia in blood? Is a tube containing EDTA suitable?

A.September 2021—*Importance of measuring ammonia.* Ammonia measurement is part of the differential diagnosis for hyperammonemia. Although ammonia is a normal by-product of amino acid metabolism, low plasma ammonia concentrations are caused by glutamine synthesis and urea synthesis in the liver.[1] An elevated level of ammonia suggests an abnormality in nitrogen homeostasis, most likely due to liver dysfunction.[2] Other possible causes of hyperammonemia include inborn errors of metabolism, gastric bypass, and drugs that have a direct effect on ammonia metabolism (e.g. valproic acid) or cause hepatotoxicity (e.g. acetaminophen).[3]

High concentrations of ammonia are toxic, especially to the central nervous system, and often manifest as encephalopathy, lethargy, vomiting, and seizures, among other symptoms.[1] When hyperammonemia is confirmed, prompt intervention is required to avoid long-term neurological damage. Further investigation is required to establish the cause of the condition.[1]

Methods used to measure ammonia. Although several methods can be used to measure ammonia, the most common are an enzymatic method (direct) and a microdiffusion method (indirect).[1,4,5] The enzymatic approach consists of reducing ammonia and alpha-ketoglutarate to glutamate by glutamate dehydrogenase in the presence of NADH or NADPH. The decrease in concentration of NADH or NADPH can be detected as a change in absorbance using reflectance spectroscopy.

In the microdiffusion method, ammonium ions are converted to gaseous ammonia in an alkaline environment in which free ammonia passes through a semipermeable membrane to an indicator layer (e.g. bromophenol blue). The color change in the presence of ammonia can be detected spectrophotometrically.

Considerations in sample handling. Whenever plasma ammonia results are elevated, sampling artifacts should be taken into account. Preanalytical errors are a main confounding factor in interpreting ammonia results. The following are recommendations for handling blood samples used to measure ammonia.

- Collect blood in an ammonia-free environment, avoiding exposure to air and water or to tubes contaminated with ammonia.
- Promptly centrifuge the sample to separate plasma from cell components. A hemolyzed sample is unacceptable because red blood cells contain high concentrations of ammonium.
- Measure the ammonia concentration within 15 minutes of collecting a blood sample, keeping the sample on ice until it is analyzed. (Maintaining the sample on ice delays spontaneous ammonia formation.)

- Freeze the sample if it cannot be processed within 15 minutes.
- Repeat the blood ammonia measurement if sample-handling errors are suspected.

Blood collection tube selection. Common practice is to collect a blood sample in an ethylenediaminetetraacetic acid or heparin tube to measure blood ammonia. There is no general consensus on the superiority of EDTA versus heparin as an anticoagulant in blood collection for measuring this waste product.[5-7]

Avoid using any tube that could be contaminated with ammonia. A serum sample in a tube with a clot activator (red top) is not acceptable because clotting increases ammonia production.[8]

Overall, plasma ammonia's sensitivity to temperature and time elapsed since collection are the major considerations when evaluating ammonia concentration in blood.[9-11]

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Sridevi Devaraj, PhD, DABCC
Medical Director, Clinical Chemistry and Point of Care Technology
Texas Children's Hospital and Pavilion for Women
Professor, Pathology and Immunology
Baylor College of Medicine
Houston, Tex.
Member, CAP Clinical Chemistry Committee

Izmarie Poventud-Fuentes, PhD
Fellow, Clinical Chemistry
Baylor College of Medicine
Houston, Tex.

Q. Is there a requirement to notify nursing personnel or doctors about each critical value obtained for a patient after the initial occurrence of the critical result?

A.CAP checklist requirement COM.30000 Critical Result Notification defines critical results as test results that may require rapid clinical attention to avert significant patient morbidity or mortality. Each laboratory may define its own critical values and critical results that pertain to its patient population. A laboratory may also establish different critical results for specific patient subpopulations (e.g. dialysis clinic patients, oncology patients, newborns). The policy may also define additional rules for critical result notification, such as notifications needed for additional critical test results obtained on a patient after an initial occurrence. Policies for reporting critical results should be approved by the laboratory director and allow for prompt patient-management decisions.

The CAP recommends that laboratories develop critical values and result notification policies in consultation with clinicians since clinicians are strongly discouraged from opting out of receiving critical result notifications. Developing clear-cut policies, coupled with educating staff about those policies, is the key to success.

Clinical and Laboratory Standards Institute. GP47: Management of Clinical- and Significant-Risk Results, 1st ed.; 2015.

Standard: Test Report. 42 CFR §493.1291(g). https://j.mp/CLIA_493-1291g

Trudy R. Darden, MA, MT(ASCP)
Manager, Accreditation Services
CAP Accreditation Programs
College of American Pathologists
Northfield, Ill.