Ammonia is a toxic nitrogenous waste product that is normally processed by the urea cycle into urea.

Urea cycle disorders can be responsible for hyperammonemia and usually appear in childhood.

Hyperammonemia is a serious condition that must be urgently treated.

Ammonia testing is confounded by numerous preanalytical conditions. Residual platelets in plasma can cause large false increases of ammonia.

Control of preanalytical error is paramount to prevent treatment based on an incorrect laboratory result, as this can cause patient harm.

**References**


**Commentary**

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The case described by Orton et al. is of a young girl who presented with nonspecific complaints of headache and fatigue. One possible explanation for such symptoms is an inborn error in urea cycle enzymes, a group of rare disorders that more commonly presents acutely and in early childhood (1). Less commonly, chronic presentations with nonspecific symptoms can occur later in life (sometimes even in adults) and can be difficult to diagnose. Most cases also have various neuropsychiatric symptoms in addition to headache and fatigue, and the lack of these being described in this child make this diagnosis less likely. Plasma ammonia concentrations are the most common screening test for this condition, as well as for the similar hepatic encephalopathy that occurs in adults (2).

An experienced clinician often recognizes that laboratory results are inconsistent with the clinical picture, as happened in this case. Despite another clinician contacting the laboratory about apparently incorrect ammonia concentrations, it took a second inquiry from the clinicians caring for this child for the laboratory to complete a full investigation, leading to further complications of treatment in the patient and, presumably, large medical bills.

A good working relationship between clinicians and laboratorians is critical to optimal laboratory practice. The National Academies report on Improving Diagnosis in Health Care recommends such improved communication between clinicians and laboratorians (3). Clinicians

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expect that laboratory results accurately reflect the status of their patients but recognize that no test is perfect. Inquiries from clinicians should be looked on as a form of “quality control” and a chance for both the provider and the laboratory to improve their understanding of the issues that affect laboratory results. This can only result in better patient care and improved patient outcomes.

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References

Commentary
Sarah M. Brown*

When troubleshooting potential laboratory errors, the entire test system must be considered, including preanalytical steps. In this case, the authors had previously investigated analytical error associated with their ammonia assay after a community physician questioned results. The initial investigation, including review of QC, did not indicate analytical error. Although QCs are fantastic tools for evaluating the analytical performance of a test, they are not robust at identifying preanalytical errors. Alternatively, δ checks can be used to identify preanalytical errors. The δ checks are comparisons of results to previous results of the same analyte from the same patient. A δ, or significant change from a previous result, may indicate preanalytical errors. The δ checks are good for analytes that show little day-to-day variation, have low critical difference values, and have low intraindividual variation. Alternatively, tracers can be used to evaluate the entire testing system. A laboratory tracer undergoes all of the pre- and postanalytical steps. Tracers can uncover errors that standard quality controls and δ checks cannot, and are good for analytes that are not candidates for δ checks.

Ammonia is in analyte that is particularly susceptible to preanalytical error such as environmental contamination, improper tourniquet use, and hemolysis. Improper sample handling can also cause falsely increased ammonia. To prevent in vitro formation of ammonia from cellular metabolism, samples should be drawn on ice and plasma should be separated from cells immediately. Ammonia has wide intraindividual variation; concentrations can change with exercise and the amount of dietary protein. Ammonia can also show dramatic changes during the treatment of hyperammonemia.

This case highlights (a) the need to remove cells from plasma quickly and thoroughly before measuring ammonia and (b) how tracing back through an entire testing system can identify problems that would not be uncovered with routine quality assurance measures.

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