mmol/L on the OPTI would thus be <1 per 20,000 (0.005%) pediatric samples submitted in a typical (non-tertiary) institution.

In adults, hyperammonemia is similarly rare but typically far less severe. In 3 studies of liver failure patients, involving 129 acute and chronic cases (9, 10), mean plasma ammonia concentrations were 49 to 172 μmol/L. Valproate-induced encephalopathy has led to ammonia concentrations up to 140 μmol/L (11). In 2004, in 4 unusual cases of emergency room—treated adult hyperammonemia, maximum ammonia concentrations were 103, 133, 300, and 500 μmol/L, the last in a patient under high-dose fluorouracil chemotherapy (12). Hence we expect the occurrence of OPTI potassium bias >0.5 mmol/L to be extremely rare in adult samples.

The Clinical and Laboratory Standards Institute (CLSI) Guidelines for interference testing (13) suggest a high ammonia test point of 80 μmol/L, which was measured on the OPTI during its development and revealed no offset in reported potassium. Because no significant bias was seen in potassium at ammonia concentrations <300 μmol/L, we (the developers/manufacturers) considered this method to be interference free. The OPTI has been marketed globally for 8 years, and we have received no previous complaint, query, or observation concerning ammonia interference with potassium measurement.

As part of our risk assessment, we included the possibility of incorrect clinical action based on an erroneous high potassium reported by the OPTI. We consulted an independently contracted expert (Professor Alan Plummer, Emory University School of Medicine) who believes it is possible, but extremely unlikely, that harm could come to a patient if the ammonia interference problem with the OPTI were not known by the clinicians treating the patient. In his opinion, ammonia concentrations >500 μmol/L are very rare, and if they do occur, he doubts any clinical remedy to normalize the potassium would occur before the measurement was repeated, most likely on a different analyzer. If the institution had only the OPTI analyzer, then a repeat falsely increased potassium concentration would be found, and if no other tests were obtained (e.g., electrocardiogram), it is possible the patient could receive potassium-lowering medications (e.g., insulin), which could lower potassium to clinically dangerous concentrations. Professor Plummer said he considers this scenario to be extremely unlikely because virtually all such patients would be in intensive care units and monitored very closely.

In short, we acknowledge that plasma ammonia concentrations can exceed 400 μmol/L. We thank the authors for their study, and regardless of the rarity of the extremely high ammonia concentrations that produce potassium interference, we have since included a warning statement within our Operator’s Manual and will modify our protocols to include medical opinions concerning pathological test ranges of potential interferences, above and beyond those recommended by the CLSI Guidelines.

References

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Preparation of Uric Acid Standard Stock Solution

To the Editor:

For measurement of uric acid in serum, calibrators of known concentration must be prepared in a suitable solvent. Uric acid is virtually insoluble in water or common organic solvents, but it can be dissolved in basic solution such as aqueous solutions of Li2CO3 (1), KOH (2), NaOH (3), and ammonium hydroxide (4, 5). Siekmann (4) used ammonium hydroxide as the solvent for dissolving uric acid at a molar ratio of ammonium hydroxide to uric acid of ~120:1. Ellerbe et al. (5) used ammonium hydroxide as the solvent for dissolving uric acid at a ratio of ammonium hydroxide to uric acid of 1.7:1. In addition, Ellerbe et al. (5) showed that uric acid is stable in ammonium hydroxide at a molar ratio of 1.7:1.

We are working to develop a new definitive method for serum uric acid by use of HPLC-isotope dilution mass spectrometry (HPLC-ID/MS). We prepared a stock standard solution of uric acid in 1 mmol/L ammonium hydroxide at a molar ratio of 1.7:1, according to Ellerbe’s method. But uric acid was...
not dissolved completely after several hours to several days. We changed the concentration of ammonium hydroxide from 1 mmol/L to 2 mmol/L. We again prepared a standard solution of uric acid at the same molar ratio of 1.7:1 with this concentration of 2-mmol/L ammonium hydroxide. With this ammonium hydroxide concentration, uric acid dissolved completely in a few minutes. The standard solution was stable at least 3 months stored in a well-stoppered brown, all-glass container at −20 °C. Ammonium hydroxide was selected because it was suitable for mass spectrometric analyses and also because uric acid was stable in the ammonium hydroxide solution. We therefore recommend the use of 2 mmol/L ammonium hydroxide, not 1 mmol/L ammonium hydroxide or other basic solutions, to prepare uric acid standard solutions.

References

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Plasma Aldosterone: Comparison of a New Automated Assay with a Standard Extraction Method

To the Editor:
A variety of clinical conditions present with an abnormality in aldosterone concentration. Primary hyperaldosteronism (PHA), long considered a rare cause of hypertension (<2% of the hypertensive population), has in the past decade been suggested to be present in 3%–32% of hypertensive patients (1). Although commercially available reagent sets have made it technically easier to measure plasma aldosterone concentration (PAC) for PHA analysis, these methods are often time-consuming and limited to small throughput, with reported problems arising with their application to assay PAC from patients with chronic renal failure (CRF) (2–4).

We previously validated a new automated method for measuring direct renin (5), and because there was little, if any, information on the evaluation of a similar method for aldosterone, we applied this automated