bility of a high-dose hook effect in the myoglobin assay.

**References**


**Table 1. Dilution test results for blood samples from two cases and a blood sample to which myoglobin was added.**

<table>
<thead>
<tr>
<th>Sample no.</th>
<th>Time between collection and first analysis, min</th>
<th>Ammonia concentration in first analysis, μmol/L</th>
<th>Time between analyses, min</th>
<th>Ammonia concentration in second analysis, μmol/L</th>
<th>Increase, %</th>
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<td>37</td>
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<td>457</td>
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</table>

**Measurement of Plasma Ammonia Is Affected in Patients Receiving Asparaginase Therapy**

*To the Editor:*

We recently observed a progressive increase in plasma ammonia concentrations in specimens from two patients that were being reanalyzed to confirm critical action value events (≥100 μmol/L). The initial analysis in one patient revealed an ammonia concentration of 163 μmol/L (Hitachi 917; Roche Diagnostics). Analyses at successive 20-min intervals revealed concentrations of 232, 292, and 315 μmol/L, respectively. Similarly, in another patient, the plasma ammonia concentrations were 209, 272, 351, and 383 μmol/L for the original and repeat measurements, respectively. Both patients’ medical records indicated that they were receiving antineoplastic therapy with asparaginase (ASNase).

The primary proteolytic activity of ASNase is the conversion of the amino acid asparagine to aspartic acid and ammonia. ASNase is also responsible for the turnover of the amino acid glutamine, although the $K_m$ for glutamine is 100 times higher than that of asparagine (1). ASNase is an important component of therapy for acute lymphoblastic leukemia (ALL). Its antineoplastic activity is thought to result from depletion of serum t-asparagine, which impairs protein synthesis and leads to delayed inhibition in DNA and RNA synthesis (1).

We then examined samples from a patient on ASNase therapy, tracking the time elapsed between sample col-
achieved. ASNase inhibitors such as drawn is one way this could be of ASNase immediately after blood is drawing. Adding specific inhibitors completely blocked after blood ammonia in these patients unless the true in vivo concentration of ammonia is impossible to determine. However, with our current method- patients receiving ASNase therapy. For this reason, it is important to monitor ammonia concentrations in patients receiving ASNase therapy. However, with our current methodology, it is impossible to determine the true in vivo concentration of ammonia in these patients unless the continuous production of ammonia as the result of ASNase activity is completely blocked after blood drawing. Adding specific inhibitors of ASNase immediately after blood is drawn is one way this could be achieved. ASNase inhibitors such as aspartic β-semialdehyde (ASA) and 5-diazo-4-oxo-l-norvaline (DONV) have previously been described in the literature (3), but they are not commercially available and, thus, not readily available to laboratorians. It is important to note that the determination of serum concentrations of asparagine and glutamine would also be compromised in these patients because these amino acids serve as substrates of ASNase.

Because our laboratory information system can access information on drug distributions from the pharmacy, we developed a feature that indicates to the operator, when plasma ammonia is ordered, whether ASNase was also dispensed. If so, the operator is required to contact the unit to determine whether the drug has been administered. The information is used to aid in the appropriate reporting of the plasma ammonia result.

It is clear from our observations that some ammonia production takes place in vitro, making the accurate measurement of circulating ammonia in patients receiving ASNase therapy nearly impossible. In the body, the liver usually removes ammonia by formation of urea. Toxic concentrations of ammonia could be reached if the liver’s capacity to remove ammonia is saturated. For example, Leonard and Kaye (2) reported severe encephalopathy with marked hyperammonemia in a child given ASNase for treatment of ALL. For this reason, it is important to monitor ammonia concentrations in patients receiving ASNase therapy. However, with our current methodology, it is impossible to determine the true in vivo concentration of ammonia in these patients unless the continuous production of ammonia as the result of ASNase activity is completely blocked after blood drawing. Adding specific inhibitors of ASNase immediately after blood is drawn is one way this could be achieved. ASNase inhibitors such as aspartic β-semialdehyde (ASA) and 5-diazo-4-oxo-l-norvaline (DONV) have previously been described in the literature (3), but they are not commercially available and, thus, not readily available to laboratorians. It is important to note that the determination of serum concentrations of asparagine and glutamine would also be compromised in these patients because these amino acids serve as substrates of ASNase.

The median elapsed time between collection and first analysis was 49 min, whereas the mean time between analyses was 12 min. A mean 24% increase in plasma ammonia concentration was observed between analyses. Interestingly, no increase in plasma ammonia concentration was seen on reanalysis of sample 2. We hypothesize that the endogenous ASNase substrates were depleted by the time of the first analysis because of the unusually long time that had elapsed before this sample was analyzed (180 min). The high concentration (457 μmol/L) in the first analysis was consistent with this interpretation.

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