otide showed a relationship with dietary riboflavin, neither were they related to EGRAC or plasma riboflavin. This supports the use of EGRAC, and, to a lesser extent, plasma riboflavin, as a marker of riboflavin status that reflects dietary intake.

We do not agree with the suggestion that the improvement in folate status in the folate-rich diet should have compromised riboflavin status, as it did in the folic acid supplementation period, because riboflavin intake after this intervention increased significantly from 1.45 ± 0.51 mg/day at baseline to 1.85 ± 0.61 mg/day (P <0.001). This is to be expected because the folate-rich cereals consumed are also good sources of riboflavin. We do, however, accept that a decrease in riboflavin intake might have contributed to the observed effect of folate supplementation on measures of riboflavin status.

The study design incorporated 4-month intervention periods without any washout period. Subjects were considered to have reached a “steady state” by the end of each intervention, and comparison was made between measurements at the end of each intervention; a comparison with baseline was also made at the end of each intervention; a comparison with baseline was also made before any intervention. Justification for this design was established on the basis of known characteristics of erythrocyte turnover, which is ~120 days. Concerns in this regard are fewer for riboflavin, which, unlike folates, readily enters circulating erythrocytes from the plasma. For this reason, and as has been known for many years, EGRAC is sensitive in the short term to dietary intake of riboflavin (4).

We do not accept the suggestion that we have underestimated the prevalence of riboflavin deficiency. The most common measure of riboflavin status in current use is EGRAC. It is accepted that there is a discrepancy between estimates of riboflavin deficiency through the use of EGRAC and estimates made from dietary intake, such as to suggest either an overestimate of bioavailability or an inappropriately low EGRAC threshold for normality. After using an established analytical method over many years, it is our experience, and that of others, that a cutoff value >1.4 more adequately reflects the distribution of values in a human population and has more functional relevance than a lower cutoff value (5–7).

References

Stuart J. Moat1*
Pauline A.L. Ashfield-Watt1
Hilary J. Powers2
Robert G. Newcombe3
Ian F.W. McDowell1

1 Cardiovascular Sciences Research Group
Wales Heart Research Institute
University of Wales College of Medicine
Cardiff, Wales, CF14 4XN, United Kingdom

2 Centre for Human Nutrition
Division of Clinical Sciences
University of Sheffield
Northern General Hospital
Sheffield S5 7AU
United Kingdom

Sample Preparation in Patients Receiving Uric Acid Oxidase (Rasburicase) Therapy

To the Editor:

With the advances in medicine and the development of newer therapeutic agents, the laboratory needs to be constantly aware of the potential analytical interferences from these medications. Here we demonstrate a potential analytical interference with a case report of a patient who received the recombinant uric acid oxidase Rasburicase (Sanofi-Synthelabo) and the sample handling requirements for uric acid analysis. Rasburicase is a potent uricolytic agent that catalyzes the enzymatic oxidation of uric acid to allantoin, a water soluble metabolite that is readily excreted by the kidney (1). It is used in the treatment and prevention of hyperuricemia, predominantly in patients with hematologic malignancies (1–5). The half-life of Rasburicase is estimated to be between 16 and 22 h (2).

A 28-year-old man presented with ascites to the emergency department at Sir Charles Gairdner Hospital, a tertiary teaching hospital in Western Australia. The patient was subsequently diagnosed with B-cell non-Hodgkin lymphoma 7 days postadmission. The day before commencement of the patient’s scheduled chemotherapy (day 8 of admission), he developed tumor lysis syndrome. The patient

*Address correspondence to this author at: Wales Heart Research Institute, University of Wales College of Medicine, Heath Park, Cardiff, Wales CF14 4XN, United Kingdom. Fax 44-29-2074-3500; e-mail: moatsj@cardiff.ac.uk.
had severe metabolic acidosis (9 mmol/L plasma bicarbonate; reference interval, 22–32 mmol/L), a plasma uric acid concentration of 1.59 mmol/L (270 mg/L; reference interval, 0.20–0.42 mmol/L (34–70 mg/L)), and a creatinine concentration of 97 μmol/L (11.0 mg/L; reference interval, 60–120 μmol/L (6.8–13.6 mg/L)]. Despite prompt resolution of the patient's metabolic acidosis with fluid hydration, he was transferred to the intensive care unit on day 12 of his admission because of respiratory failure and worsening renal failure. The patient's laboratory results confirmed ongoing tumor lysis, with plasma concentrations of 304 μmol/L (34.4 mg/L) creatinine, 1.13 mmol/L (190 mg/L) uric acid, 1740 U/L (reference interval, 125–250 U/L) lactate dehydrogenase, and 5.55 mmol/L (reference interval 0.80–1.40 mmol/L) phosphate; total calcium corrected to 40 g/L albumin was 1.62 mmol/L (reference interval, 2.25–2.60 mmol/L). Given the patient's substantial hyperuricemia, despite adequate fluid hydration and continuous veno-venous hemodialysis, he was given Rasburicase (9 mg intravenously; 0.15 mg/kg body weight) on the day of his intensive care unit admission (day 12) and, again, the following day (day 13). The patient's plasma uric acid concentration decreased dramatically to 0.52 mmol/L (88 mg/L) before his second infusion of Rasburicase on day 13 and became undetectable [<0.05 mmol/L (<8 mg/L)] on day 14 of his admission. The patient's renal function improved, and he was discharged on day 26 with a plasma creatinine concentration of 83 μmol/L (9.4 mg/L).

In the laboratory, we were surprised to obtain an undetectable uric acid concentration on day 14 of this patient's admission. Plasma uric acid analysis is performed by an enzymatic colorimetric assay (Hitachi 917, Roche Diagnostics) with a limit of detection of 0.05 mmol/L (8 mg/L). The between-run CVs of the assay are 1.1% and 1.2%, at mean concentrations of 0.23 mmol/L (34 mg/L) and 0.54 mmol/L (92 mg/L), respectively. Analytical interference was excluded by checking the sample for hemolysis, lipemia, and icteric indexes. The sample was reassayed to check for short sampling. The patient was not prescribed α-methyldopa, desferoxamine, or calcium dobesilate because, at therapeutic concentrations, these medications may cause artefactually low uric acid concentrations, as documented in the manufacturer's product insert. The patient did not receive ascorbic acid because high concentrations of this compound can interfere with peroxidase in the oxidative reaction of chromogenic reagents. We were unaware that the patient had received Rasburicase because the blood samples were sent to the laboratory as part of routine biochemistry testing. When the sample collected on day 13 was reanalyzed on day 14, the uric acid concentration was undetectable, instead of the expected result of 0.52 mmol/L (88 mg/L). This prompted
References

EeMun Lim
Peter Bennett
John Beilby*

Department of Clinical Biochemistry
PathCentre
The Western Australian Centre for Pathology and Medical Research
Hospital Avenue
Nedlands, Western Australia 6009
Australia

*Address correspondence to this author at: Department of Clinical Biochemistry, PathCentre, Locked Bag 2009, Nedlands, Western Australia 6909, Australia. Fax: 61-8-9346-3882; e-mail: john.beilby@health.wa.gov.au.

Clinical Capillary Zone Electrophoresis of Serum Proteins: Balancing High Sensitivity and High Specificity

To the Editor:
Capillary zone electrophoresis (CZE) is reported to be high (98.6%) and comparable to that of AGE (1, 5).

In a prospective study (2), we described three M-proteins with high pI values that migrated in the slow γ region on AGE but were not detected with Paragon. In addition, one high-concentration IgGα with a pI ≈7 that migrated in the mid-γ region on AGE was not separated by CZE. The Paragon has recently been upgraded [modified buffer, higher voltage (10.3 kV), more efficient cooling, adapted software (1.6.02)], and according to the manufacturer, this should have improved resolution of certain rarely occurring M-proteins. With the updated system, β-lipoprotein and fibrinogen were also resolved, which was not the case under earlier operating conditions.

The aim of the study was twofold: (a) we evaluated whether the upgrade enhanced resolution of previously unresolved M-proteins and in increased overall sensitivity; and (b) we evaluated whether the increased resolution affected specificity. One could hypothesize that because of the higher resolution, clinically unimportant heterogeneity in the γ-globulin zone will be observed more frequently.

To address the question of whether the upgrade increased resolution of previously unresolved M-proteins, we reanalyzed four sera that we described to contain a M-protein that could be separated by AGE but not by CZE (2). An additional similar sample with a M-protein migrating in the slow γ region with AGE but not with CZE was analyzed as well. Of the four post-γ-migrating M-proteins, one M-protein was detected with the new buffer system, one generated an error code, and two were missed. The high-concentration IgGα M-protein with a pI ≈7 that migrated in the mid-γ region on AGE (2) was not separated by CZE under software version 1.6.02 but gave an error code.

Collectively, the recently introduced new buffer system for CZE with the Paragon CZE system has a slightly increased sensitivity for detecting M-proteins that were previously missed. Some rare M-proteins...