use of therapeutic monitoring in (future) multicenter studies and for interpretation of pharmacological data in clinical practice in patients on thiopurine therapy. In addition, exact storage conditions are often not mentioned in published reports; their omission may partly explain the current controversy concerning thiopurine metabolite research.

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Drug Monitoring and Toxicology (DMT)

To the Editor:

Tazocin is an injectable antibiotic preparation with broad-spectrum activity against aerobic and anaerobic gram-positive and gram-negative bacteria (1). Reported side effects that might prompt metabolic disease investigations include change in consciousness and encephalopathy (2, 3). We report 2 patients in whom interpretation of organic acid analysis was complicated by administration of tazocin.

Case 1 was a 56-year-old man admitted for routine aortobifemoral bypass graft surgery. Past medical history included peripheral vascular disease, hypercholesterolemia, and epilepsy. Postoperatively the patient developed an acute abdomen and at laparotomy required extensive small bowel resection to treat a mesenteric infarction. His subsequent course was complicated by heparin-induced thrombocytopenia. The patient further deteriorated, with a reduced level of consciousness (Glasgow Coma Scale 12/15), and was noted to have metabolic acidosis, with an increased anion gap of 27 mmol/L and a urine sample was sent for organic acid analysis by GC-MS (4). The results showed the presence of 4-ethyl 2,3-dioxo-1-piperazine, which was identified from a standard library (Fig. 1). This GC-MS peak was attributed to drug consumption, but its exact nature was not immediately recognized by the analyzing laboratory or other specialist laboratories consulted.

The 2nd case was a 67-year-old man admitted with a myocardial infarction. This patient underwent angioplasty, and subsequently developed left ventricular failure, hypotension, and acute renal failure necessitating intensive care. This patient had known severe peripheral vascular disease and developed osteomyelitis of his right foot, requiring right below-knee amputation. He developed a high anion gap metabolic acidosis (32 mmol/L) and a urine sample was sent for organic acid analysis. The presence of 4-ethyl 2,3-dioxo-1-piperazine was detected.

Each patient had been prescribed a number of drugs, but only tazocin was being given to both individuals. Tazocin is a combination of piperacillin sodium and the lactamase inhibitor tazobactam sodium. The structure of piperacillin is sodium (2S,5R,6R)-6-[(R)-2-(4-ethyl-2,3-dioxo-1-piperazine-carboxamido)-2-phenylacetamido]-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3,2,0]heptane-2-carboxylic acid, and it was this substance that was detected in the urine.

Tazocin has previously been reported to produce a peak in the β region in capillary zone electrophoresis, potentially simulating a small monoclonal protein (5). We observed that organic acid analysis by GC-MS of intravenously administered tazocin produced a peak. Although the presence of this tazocin peak is unlikely to result in

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an incorrect diagnosis, describing our finding may enable others noting such a peak to realize its identity more rapidly.

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False-Positive Rates for the Qualitative Analysis of Urine Benzodiazepines and Metabolites with the Reformulated Abbott Multigent™ Reagents

To the Editor:

In May, 2007, Abbott notified customers of the implementation of a new polyclonal antibody pool in the Multigent™ benzodiazepine reagent (supplied by Seradyn, Inc.) for use on their Architect™ chemistry analyzer. The new antibody pool demonstrated an increased analytical sensitivity for this screening method, which allowed detection of lower concentrations of individual benzodiazepines and their metabolites. Unfortunately, by increasing the sensitivity, Abbott decreased the specificity of this assay, resulting in an increased number of false-positive benzodiazepine results.

For the past 15 years, the clinical chemistry laboratory of the VA Boston Healthcare System has performed screening for benzodiazepines in urine by immunoassay. Before 2001 the toxicology laboratory confirmed every screen-positive benzodiazepine result by HPLC. Table 1 summarizes the historical benzodiazepine data in 2000, which shows that 94.6% of the screen-positive results were confirmed as positive. Because of the high confirmation rate, the laboratory altered its policy of automatically confirming every screen-positive result to a policy of confirming screen-positive benzodiazepine by clinician request only (1). This protocol resulted in a dramatic decrease of 95% in the number and costs of confirmation testing (1).

Table 1 also summarizes the recent VA Boston Healthcare System experience of using the reformulated Abbott Multigent benzodiazepine reagent (List no. 3L 39–20; Lot No. 49274M200 and higher). There was a significant increase to 25.1% in the screen-positive rate for patient samples tested for benzodiazepines in June and July 2007, compared to the historical screen-positive rate of 13.1%. Because the laboratory suspected that the new Abbott reagents were yielding false-positive benzodiazepine results, the toxicology laboratory performed HPLC confirmation testing for all screen-positive benzodiazepine results over the 2-month period and found a positive confirmation rate of 74.3%. The false-positive rate was 25.7%, which is 5 times the 5.4% false-positive rate obtained with the SYVA™ reagent used in 2000 (Table 1). During the 6-month period before the introduction of the reformulated benzodiazepine reagent, we had observed a screen-positive rate of 15.1% (1126/7476 screens) with the Abbott reagents, not unlike our historical rate of 13.1%.

We reviewed the medical records of patients (n = 37) from whom a total 50 randomly selected urine specimens were obtained that yielded positive screening results for benzodiazepines with the Abbott Multigent, but were negative with HPLC (false-positive results). Of the 50 false-positive results, 16 (32%), from 9 of the 37 patients, were found in patients on the medication sertraline (Zolof), a drug commonly used for depression, social anxiety disorders, posttraumatic stress and panic disorders, and obsessive-compulsive disorders. Sertraline is listed by Abbott in their package insert as a substance that commonly cross-reacts with and yields false-positive benzodiazepine screening results. Abbott also cites the possibility of high concentrations of oxaprozin yielding a false-positive benzodiazepine result, but none of the 37 patients were being prescribed this medication.

Because of the apparent high false-positive rate observed with the Abbott Multigent reagent, we proposed returning to the SYVA Emit benzodiazepine technology. A comparison of the Abbott/SYVA benzodiazepine reagents was conducted in our laboratory. Of the 50 randomly selected samples found positive by Multigent that gave negative results following HPLC confirmation, 47 of 50 screened negative by SYVA (94% concordance) and 3 of 50 gave positive screen results.

From May to July 2007, the toxicology section of the VA Boston Healthcare System, which performs all HPLC confirmation for all VA medical centers in New England, has analyzed a total of 1975 HPLC