Letters to the Editor should be typed double-spaced (including references) with conventional margins. The overall length is limited to five manuscript pages, including not more than one figure or one table.

Premature Degradation of Abbott TDx Reagents

To the Editor:

We have observed regularly decreasing digoxin values when examining our Levey-Jennings plots of quality-control (QC) specimens for digoxin (see Figure 1). Within 10 days after opening a new reagent kit, the results for QC samples decreased by 1 SD below the expected results. We observed this with four consecutive kits on two different TDx instruments (1, 2). Analysis of the measured digoxin concentration vs time since opening gave us the rate of decay. These slopes were significantly negative and similar for all four kits on both TDx instruments. The overall mean slope was \(-0.06\) (SD 0.02) \(\mu\)g/L per day (n = 10, \(P < 0.0005\)). The between-instrument variation, assessed by measuring the same QC material on the same day, showed no significant difference, 0.04 (SD 0.15) \(\mu\)g/L (n = 30, \(P > 0.15\)).

A prospective study confirmed these findings. We analyzed TDM “High” QC material (TDM Control; ICL Scientific, Fountain Valley, CA), using kit A twice per day on two TDx instruments for 10 days; kit B was used once every other day. Each kit was left open at 37°C for 1-2 h during each assay.

We calculated the rates of decay for each kit as measured by both TDxs. The slope for kit A was \(-0.05\) (SD 0.01) \(\mu\)g/L per day (n = 38); the slope for kit B was \(-0.02\) (SD 0.02) \(\mu\)g/L per day (n = 5). These slopes were significantly different (\(P < 0.0001\)) by analysis of covariance with a homogeneity of slopes model (SAS Institute, Cary, NC).

In a separate experiment, we assayed with a kit that had been kept closed at 37°C for over 72 h; the results were the same as with no heat exposure. Thus, we speculate that evaporation from kits left open on the instruments at 37°C is the major cause of reagent degradation. We advise laboratories that the accuracy of the Abbott TDx digoxin assay may deteriorate significantly within 7-10 days of opening a kit, as a function of use, but this deterioration can be limited by recapping the reagents as soon as the test is completed.

References


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N-Acetylcysteine Causes False-Positive Ketone Results with Urinary Dipsticks

To the Editor:

We used Chemstrip (Boehringer Mannheim) and Multistix (Miles Canada) dipsticks to test the urine of eight patients treated with N-acetylcysteine (NAC) for acetyaminophen overdose. We found that three urines gave false-positive ketone readings ranging from 4 to >10 mmol/L with Chemstrip, and five gave false-positive ketone readings ranging from 0.5 to >16 mmol/L with Multistix. When normal urines containing added NAC were tested, the detection limits for NAC detected by Multistix and Chemstrip were 0.3 and 0.6 mmol/L, respectively. The intensity of the false-positive color was proportional to the concentration of added NAC.

We used a ColorQUEST™ reflectance spectrophotometer (HunterLab, Fairfax, VA) with a small-sample port to measure the reflectance of the ketone pads on Chemstrip and Multistix dipsticks between the wavelengths of 400 and 710 nm. We used the Commission International de l’Eclairage (CIE) standard D65 light source at an observer angle of 10° for all measurements, excluding specular reflectance. The ColorQUEST calculated the CIE L*, a*, and b* color coordinates (1, 2) of the ketone pads. These coordinates describe how light, red, green, yellow, and blue a color is. We also calculated ΔE*, a measure of the total color difference (3, 3).

Urines with added NAC and urines from patients treated with NAC gave similar colors with the dipsticks (Figure 1), which suggests that NAC in the urine caused the false-positive results. However, because cysteine in urines also gave a color similar to that of NAC, we cannot exclude the possibility that cysteine, produced by the hydrolysis of NAC in the body, caused the false-positive reaction.

Fig. 1. The CIE L*, a*, b* coordinates, describing the color developed on the ketone pads after reaction with NAC, acetoacetate, or urine of a patient treated with NAC. Chemstrip results were evaluated with 20 mmol/L acetoacetate in urine control (A); normal urine containing 12 mmol/L NAC (B); and urine from a patient (C). Multistix 10 SGs were reacted with urine controls containing 20 mmol/L acetoacetate (R) or NAC (G); normal urine containing 12 mmol/L NAC (M); and urine from the same patient as above (O). The numbers in parentheses beside the symbols represent the L* coordinate.
NAC (20 mmol/L) and acetacetate (20 mmol/L) added to normal urine gave almost identical purple colors with Multistix (ΔE* = 2.9). On the other hand, Chemstrip gave a redder and less blue color with NAC than with acetacetate (ΔE* = 10.2) (Figure 1). Inexperienced observers would find it difficult to distinguish between these two colors.

Gordon-Smith et al. (4) report that one can distinguish false-positive ketone reactions from a true ketone reaction by adding a drop of glacial acetic acid to the ketone pads. The acid will cause the color produced by sulfhydryl groups to fade in 60 s. However, we found that acetic acid is effective only at low concentrations of NAC. At NAC concentrations >10 mmol/L, the color on Chemstrip did not completely disappear in 3 min, and the Multistix turned brown.

Mesna (sodium 2-mercaptoethanesulfonate) (4-6), captopril (7), and other drugs containing free sulfhydryl groups (6) are known to give false-positive ketone readings with urinary dipsticks. NAC, which also contains a free sulfhydryl group, gives false-positive ketone test results when added to urine specimens (6). The urinary concentration of NAC administered during cancer chemotherapy is unlikely to be great enough to interfere with dipstick ketone tests (8). However, the following calculations explain how we obtained the false-positive ketone test results for urines from patients treated with NAC for acetaminophen overdose. A 70-kg patient undergoing the recommended NAC treatment (9, 10) would ingest 93 g of NAC and excrete about 6 g of it in three days (9). The concentration of NAC excreted in the urine would therefore be about 5–6 mmol/L—enough to give a strongly positive ketone reaction with both Multistix and Chemstrip.

Hepatic necrosis is the primary adverse effect of acetaminophen overdose. False-positive ketone readings caused by NAC in urine could, therefore, lead to misdiagnosis of ketois associated with liver failure, possibly followed by unnecessary investigations or inappropriate clinical management.

References

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Comments on the Proposed Revision of the Oral Glucose Tolerance Test

To the Editor:

Schwartz et al. (Clin Chem 1990;36:125–8) criticize the "standard" 100-g glucose tolerance test and suggest that use of a modified solution with different diagnostic criteria, based on results for fewer blood samples (taken at 0, 30, 60 min after the glucose load) will allow faster and more nearly accurate diagnosis of diabetes or impaired glucose tolerance. However, these conclusions are not supported by the results they presented. First, they administered 100 g of glucose as the "standard" test, whereas the current recommendation of the National Diabetes Data Group (1) and the World Health Organization (2) is to use a 75-g dose for adults, which reduces the incidence of nausea associated with the test. Further reducing the dose, as Schwartz et al. suggest, would reduce this side effect, but would also decrease the reproducibility and sensitivity of the test (3).

Secondly, their comparison of the blood glucose profile in nondiabetic subjects with that in overtly diabetic patients is of no use for choosing the best diagnostic criteria. They don’t present the profile obtained with the "standard" dose, which should be similar. The actual recommendations (1, 2) for interpreting the results make use of the blood glucose concentration. The choice of these criteria is based on clinical studies that showed that microvascular disease was rare in persons with 2-h plasma glucose values <11.1 mmol/L(4, 5). Schwartz et al. showed no clinical evidence that their version of the test would be a better predictor of complications than would the recommended version, particularly in borderline cases. In fact, in the overtly diabetic patients they studied, a much simpler way to make the diagnosis would have been to repeat the fasting plasma glucose determination. A second result >7.8 mmol/L would have been diagnostic of diabetes.

Finally, Schwartz et al. made an error in the description of the specimens they analyzed. Plasma, not serum, samples are obtained with the grey-top Vacutainer Tubes. These specimens are not interchangeable, because plasma glucose values can be 5.1% lower than serum values (6).

References

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Two of the authors of the article in question respond: