caused by an unrelated gastrointestinal disorder. It has been said that severe vomiting is a feature of alkalosis with diabetic ketosis (3), but this is not always the case. In the case reported by Koett and colleagues, the alkalosis was attributed mainly to the electrolyte disturbance caused by thiazide diuretic therapy, with the mild vomiting only being a contributing factor. The major cause of the alkalosis may not always be so apparent and should be actively sought. The following case illustrates this point.

A 63-year-old man was admitted with diabetic ketosis. Diabetes mellitus had been diagnosed 17 months earlier and was treated with metformin, 500 mg three times daily, and carbohydrate restriction. He had been treated for three years with bendrofluazide, 10 mg daily, and potassium supplements, 24 mmol daily, for essential hypertension. Serum potassium measurements at clinic attendances over that period indicated adequate supplementation. Other medications were zotarol (80 mg) and methylprednisolone (1500 mg) daily. On admission he gave a three-week history of heavy glycosuria, and had lost 11 kg in weight over the previous three months. He denied nausea or vomiting and was not ingesting alkali in any form. He was clinically dehydrated and drowsy.

Biochemical studies revealed a blood glucose of 39.0 mmol/L, a serum potassium of 2.1 mmol/L, and serum urea of 12.9 mmol/L. Acid-base studies indicated a mild mixed respiratory and metabolic alkalosis; the hydrogen ion concentration was 30 mmol/L (pH 7.52), the standard bicarbonate (S) was 27.4 mmol/L (normal range 22–26 mmol/L), and the pCO₂ was 4.2 kPa (normal range, 4.7–6.0 kPa). Urine analysis showed 2% glycosuria (20 g/L), and ketones ++++, analyses performed with Clinistix and acetate tablets, respectively (Ames Co. Limited, Stoke Poges, Slough, Bucks., U.K.). After successfully treating the acute episode, we searched for the cause of his hypokalaemia and alkalosis and found Cush- ing’s syndrome. His plasma cortisol at 0900 h was 1790 nmol/L with a plasma corticotropin of 49 ng/L, and at 2200 h the plasma cortisol was 1710 nmol/L and the plasma corticotropin was 108 ng/L, not suppressed by dexamethasone. (Normal values for corticotropin are <10–80 ng/L). A chest roentgenogram showed a mass in the right lung, and we concluded that the patient suffered from carcinoma of the bronchus. He was treated with deep irradiation but died five weeks later. Permission for post-mortem examination was refused.

Alkalosis in patients with diabetic ketosis signifies dual pathology at least, i.e., diabetic ketosis and a second condition causing alkalosis, which overrides the acidosis of the former. In the case we report, the cause of the alkalosis was Cushing’s syndrome, the thiazide diuretic therapy possibly being a contributing factor. The Cushing’s syndrome might well have been overlooked in this case, had not a cause for the alkalosis been actively sought.

References

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Ed. note: The authors of the Case Report agree that “diabetic ketoacidosis” is not a discrete primary pathological entity and further say: “If we inadvertently implied this, it certainly was not intended. Throughout the text of our article we point out several possible pathophysiological and biochemical mechanisms which could theoretically interact and modify the usual laboratory expression of the uncontrolled diabetic patient. Our patient had a mixed metabolic and respiratory alkalosis, induced by diuretic therapy for hypertension and anxiety. Whether these secondary problems are completely extrinsic to the ‘primary disease process’ is debatable.”

Simultaneous Testing for Glucose and Total Reducing Substances in Routine Urinalysis

To the Editor:
Routine urinalysis in many pediatric hospitals includes tests for “true” glucose by a specific enzymic method and for total reducing substances with a modified Benedict’s reagent. The procedure is designed to screen for inborn errors of galactose and fructose metabolism, and will also detect pentosuria, reducing disaccharidurias, and in addition a wide variety of drugs and other compounds (1, 2). The procedure has been implicitly and explicitly recommended in both the pediatric and clinical chemistry literature (3–5). It is surprising therefore that it has never been critically evaluated in terms of yield of pathological results, generation of useful knowledge, and cost–benefit analysis. This Letter reviews 12 years of testing as related to these considerations.

Routine testing with Clinistix tablets and Clinistix (both products of Ames Co.) was done according to the insert instructions. Urines found to contain a non-glucose reducing compound were forwarded to the special chemical division for identification of the compound by standard paper-chromatographic methods (6). The study group consisted of 147 539 admission urinalyses. Pentosuria and disorders of fructose metabolism were not encountered, nor was galactokinase (EC 2.7.1.6) deficiency. Two cases of galactose-1-phosphate uridylyltransferase (EC 2.7.7.10) deficiency were discovered, one which was also detected by the urine screening program and one that had apparently eluded it. However, classic galactosemia should not be considered as part of the potential yield in states where newborn screening is being carried out.

Ascorbic acid in one urine and cephalosporins in two additional urines were found to be the reactive compounds. The most common cause of a non-glucose reducing substance in urine was found to be lactose in six cases due to secondary lactase (EC 3.2.1.23) deficiency associated with diarrhea. A follow-up of three of these cases revealed a reversion to normal after treatment of the diarrhea. The yield of patients requiring medical attention or benefiting from the information was thus negligible. No new information was generated during the study period, although the discovery of a new metabolic disorder by virtue of the presence of a reducing metabolite in urine remains a possibility.

We have found that the procedure has considerable merit with respect to teaching of medical technologists, medical students, and house-staff physicians, because it encompasses the major pediatric mellitii. It provides a coherent framework within which a single objective finding can be related and extended to a meaningful discussion of laboratory tests, differential diagnosis, renal physiology, and benign and harmful genetic errors and their management. The procedure also lends itself well to teaching considerations of routine urinalysis, the chemistry of reducing compounds in urine, and the identification of unknown compounds.

The additional test is easily accommodated within an existing urinalysis structure without the need for additional personnel. Clerical work, usually
a check-off on the laboratory report, should not incur additional expense. The cost of the tablets would amount to about $250.00 per year for 12,000 admissions. It should be appreciated, however, that the disorders detectable by the test are indeed rare, and that the major justification for its use would appear to reside in the substantial academic benefits previously alluded to. This consideration alone, however, would seem to justify its continuance, particularly in teaching institutions.

References

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Evaluation of a Thrombin-Containing Blood-Collection Tube

To the Editor:

Recently Becton-Dickinson, Inc., Rutherford, NJ 07070, introduced an evacuated blood-collection tube containing 10 NIH Units of thrombin (Vacutainer Tube, no. 6528) for general use. In their literature (CLDS/78-1507-5), they recommend use of these tubes for the collection of blood from which serum samples are to be derived for use in emergency procedures because the thrombin causes clotting to occur within 2–3 min.

I undertook to see if the rapid clotting time or the thrombin additive would affect any of the following tests: Cl, K, Na, total carbon dioxide (CO2), urea nitrogen, glucose, protein, albumin, Ca, inorganic phosphorus, cholesterol, uric acid, creatinine, total bilirubin, alkaline phosphatase, lactate dehydrogenase (LDH), aspartate aminotransferase, and creatine kinase. I collected 40 pairs of serum specimens over a five-day period, both in Vacutainers with no additive (no. 6432) and the new thrombin-containing tubes. Each specimen was analyzed by continuous flow (SMA II; Technicon Instruments Corp., Tarrytown, NY 10591) for all tests except creatine kinase, which was analyzed with an acu (Du Pont Instrument Corp., Wilmington, DE) discrete analyzer. All methods on the SMA II were unmodified Technicon methodology, except cholesterol (enzymic; Bio-Dynamics/bmc, Indianapolis, IN) and glucose (glucose oxidase, bmc).

Except for Cl, K, Ca, and LDH (Table 1) the results from a plain tube and a thrombin-containing tube were identical. Poor correlation coefficients and large differences in population means were observed in these four tests. For Cl, the higher values for the thrombin tubes can be attributed to the rapid separation of the serum from the cells, which would prevent further uptake of Cl by the erythrocytes as compared to a tube with no additive (1). In the case of K and LDH, slight (non-visible) hemolysis could account for the observed differences (2). For Ca, the difference may be due to the rapidity of clotting.

Unfortunately, the four tests that show poor correlations are tests that are important on an emergency basis. Table 2 gives histogram data for the differences between the plain and thrombin-containing tubes. In a large percentage of cases, the observed differences are large. One must consider these differences in the light of the emergency situation in which such tubes would be used. I believe that the ability to eliminate the clotting time factor in hastening an urgent test justifies the difference

<table>
<thead>
<tr>
<th>Test</th>
<th>Units</th>
<th>No. pairs</th>
<th>P mean</th>
<th>T mean</th>
<th>Diff.</th>
<th>m</th>
<th>b</th>
<th>R²</th>
<th>Sᵧₓ</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cl</td>
<td>mmol/L</td>
<td>37</td>
<td>105.0</td>
<td>107.8</td>
<td>-2.78</td>
<td>0.963</td>
<td>6.64</td>
<td>0.692</td>
<td>2.69</td>
</tr>
<tr>
<td>K</td>
<td>mmol/L</td>
<td>41</td>
<td>4.24</td>
<td>4.36</td>
<td>-0.11</td>
<td>0.870</td>
<td>0.67</td>
<td>0.739</td>
<td>0.26</td>
</tr>
<tr>
<td>Ca</td>
<td>mg/L</td>
<td>40</td>
<td>88.0</td>
<td>90.6</td>
<td>-2.62</td>
<td>0.948</td>
<td>7.12</td>
<td>0.841</td>
<td>2.87</td>
</tr>
<tr>
<td>LDH</td>
<td>U/L</td>
<td>37</td>
<td>206.5</td>
<td>226.9</td>
<td>-20.38</td>
<td>0.989</td>
<td>22.63</td>
<td>0.965</td>
<td>16.66</td>
</tr>
</tbody>
</table>

Abbreviations: Diff.: average difference (Plain-Thrombin), m: slope, b: intercept, R²: correlation coefficient, Sᵧₓ: standard error of the estimate.

Table 2. Histograms of the Differences between Plain and Thrombin-Containing Tubes

- **A. Calcium, mg/L**
  - -8.5: 2.50
  - -7.0: 5.00
  - -5.5: 20.00
  - -4.0: 7.50
  - -2.5: 27.50
  - -1.0: 17.50
  - 0.5: 12.50
  - 2.0: 5.00
  - 3.5: 0.00
  - 5.0: 2.50

- **B. Chloride, mmol/L**
  - -7.9: 5.41
  - -6.8: 2.70
  - -5.7: 8.11
  - -4.6: 2.70
  - -3.5: 35.14
  - -2.4: 13.51
  - -1.3: 10.81
  - -0.2: 10.81
  - 0.9: 8.11
  - 2.0: 2.70

- **C. Lactate dehydrogenase, U/L**
  - -48.4: 10.81
  - -40.8: 5.41
  - -33.2: 8.11
  - -25.6: 18.92
  - -18.0: 16.22
  - -10.4: 29.73
  - -2.8: 2.70
  - 4.8: 5.41
  - 12.4: 0.00
  - 20.0: 2.70

- **D. Potassium, mmol/L**
  - -0.76: 4.88
  - -0.62: 2.44
  - -0.48: 4.88
  - -0.34: 9.76
  - -0.20: 14.63
  - -0.06: 41.46
  - 0.08: 12.20
  - 0.22: 4.88
  - 0.36: 2.44
  - 0.50: 2.44