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Some Improvements in Operation of the Technicon SMAC System

To the Editor:

In December 1977 a Technicon SMAC system for continuous-flow analysis was installed in our laboratory. Most of the initial problems were solved with the aid of Technicon staff, but several faults persisted which we had to overcome ourselves. Having attended a recent SMAC Users Meeting in Edinburgh, we were sufficiently encouraged to offer relevant details in print.

Because the SMAC system computer program is not readily amenable to alteration by the operator, it seemed desirable to introduce [only] changes that did not require any interference with the computer tape. Therefore, emphasis was placed on changes in the geometries of the various channels along with some reagent modification.

Creatinine: The creatinine channel, in particular, gave us much trouble, owing to within-sample variation. We found this to be due to the low absorbances in the normal range, resulting in minute changes in baseline being translated into large apparent concentration differences. Our solution to this was to decrease the volume of recipient stream by half, thereby both concentrating creatinine in the dialysate and prolonging its stay in the heating bath. Absorbances were about doubled by this procedure, and this proved to be adequate.

Cholesterol: It was a relief to get away from the nosy reagents of the Lieberman–Burchard method for cholesterol and substitute the enzymic procedure based on cholesterol esterase and cholesterol oxidase, where the hydrogen peroxide produced in the presence of horseradish peroxidase (EC 1.11.1.7) reacts with 4-amino-phenazone and phenol to produce 4-(p-benzoquinimonoimino)phenazine (1, 2). The Boehringer Mannheim CHOD-POD kit no. 148395 was used. However, the reagents for this assay are expensive, so we doubled the diluent fluid and for most assays with the SMAC was further diluted 1 in 4 with saline. The enzyme reagent was also diluted 1 in 4, resulting in an assay linear to 12 mmol/L and lowering the current cost to about 1 (2 cents) per sample. There is, therefore, no need to operate the enzymic cholesterol method for only a portion of each day because of cost. Screening of as many samples as possible for cholesterol content must be held to a very desirable feature.

Albumin: Bromcresol green (BCG) is now known to be unsuitable for use in albumin measurement because it is also bound to globulins. This problem is exacerbated in patients with low circulating albumin (nephrotic syndrome), where it is most important to know the true concentrations of this protein. Attempts to overcome this difficulty are usually based on shortening the exposure of plasma proteins to BCG (3), but recently Pinnell and Northam (4) introduced an automated assay for albumin, substituting bromcresol purple (BCP) for BCG. By doubling the concentration of BCP over that recommended and changing the wavelength to 600 nm, we found excellent correlation with results by an immunological method involving a laser nephelometer. Since this changeover, albumin concentrations of <20 g/L—a rarity with the BCG procedure—are frequently encountered, and all have correlated with the clinical condition of the patient.

Iron: The high ratio of sample to HCl–ascorbic acid reagent in the iron channel invariably caused precipitation of plasma proteins. The particulate matter first accumulated in the narrow orifice of the RAS valve (part 178-B482-01), causing disruption of the bubble pattern. On being dislodged, the sediment moved onto the membrane (H type), rupturing this. It was a frequent and expensive occurrence. The problem was overcome by adding the HCl–ascorbic acid reagent through an R.A. fitting (part 178-B482-02) with subsequent sample insertion by downward vertical flow through a T (part 178-G202-01) fitting. After about 200 samples it is necessary to disconnect the flow from the membrane inlet and use the wash mode for 5 min, to free the system of precipitate.

Sodium and potassium: These are measured by use of ion-selective electrodes; very frequently it was impossible to calibrate either channel with the reference serum. Examination of the recorder traces showed that during attainment of the plateau a spike frequently occurred, which the computer then rejected as unacceptable. The supplier recommends that the voltages on the electrodes be kept within ±0.1 V, but only when the setting was changed to 0.3 V on the potassium meter (155 lines on trace) and the sodium electrode also energized to 155 lines (there is no meter display on the sodium channel) were acceptable traces received. At that time the laboratory was in an old building, with frequent and irregular changes in electrical demand. When we moved to a new laboratory designed for heavy electrical consumption, it was possible to get satisfactory performances on both the sodium and potassium channels within the prescribed voltage limits. Other SMAC users may have occasional calibration problems with their electrodes, and inquiries about extra-laboratory demands on the electrical supply may prove useful.

With these various modifications the SMAC analyzer has behaved satisfactorily for the past year with no more than the usual minor problems with individual channels.

References

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Thiazides Do Not Affect Xanthine Excretion in Hereditary Xanthinuria

To the Editor:

In hereditary xanthinuria, xanthine oxidase (EC 1.2.3.2) deficiency results in low plasma and urinary concentrations of urate and high concentrations of its immediate oxypurine precursors, xanthine and hypoxanthine (1). The excessive xanthine excretion results in a tendency to recurrent xanthine stone formation, for which no specific treatment is available except long-term urinary alkalinization.

Thiazide diuretics decrease the urinary excretion and renal clearance of urate, resulting in hyperuricemia; this is believed to be mediated by thiazide-induced decreases in renal tubular secretion of urate (2). The effect of thiazides on urinary excretion of xanthine has not been previously studied in normal subjects, in whom urinary xanthine

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concentrations are too low to permit adequate evaluation. Subjects with hereditary xanthinuria provide an opportunity to study this effect of thiazides, which if similar to that on urate would make long-term thiazide treatment potentially valuable in preventing formation of xanthine stones.

We have studied the effect of short-term treatment with hydrochlorothiazide on xanthine and hypoxanthine excretion in a 50-year-old woman with well-documented xanthine oxidase deficiency, recurrent xanthine nephrolithiasis, and pyelonephritis. The detailed clinical and biochemical features of the patient have been reported previously (1, Case No. 3). At the time of the study she had moderate renal impairment, with a creatinine clearance of 50 mL/min, and was on a constant low-purine diet. After an adequate equilibration period, she was given 50 mg of hydrochlorothiazide orally twice daily for four consecutive days. We made 24-h urine collections before and after treatment, for use in measurement of xanthine, hypoxanthine, and total oxypurines (3). Table 1 shows our results, expressed as milligrams per gram of creatinine.

There was no significant change in either urinary total oxypurine or xanthine excretion, or in plasma xanthine or hypoxanthine concentrations. There was a small but insignificant decrease in urinary hypoxanthine.

The moderate renal failure in the patient might have contributed to the lack of effect of thiazides on the renal disposition of xanthine. An alternative explanation is that because xanthine has a higher renal clearance rate than urate (4), its renal disposition may be qualitatively or quantitatively different from that of urate, hence its different response to thiazide treatment.

### Table 1. Effect of Hydrochlorothiazide Treatment in Xanthinuria

<table>
<thead>
<tr>
<th>Mean g urinary excretion (and SE), mg/g creatinine, for daily hydrochlorothiazide dose of</th>
<th>0 mg</th>
<th>100 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Xanthine</td>
<td>95.9 (4.9)</td>
<td>129 (16.1)</td>
</tr>
<tr>
<td>Hypoxanthine</td>
<td>81.4 (24.7)</td>
<td>63.5 (6.5)</td>
</tr>
<tr>
<td>Total oxypurines</td>
<td>206 (33.1)</td>
<td>200 (19.7)</td>
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</tbody>
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* Mean of four 24-h values for each treatment

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Caveat in the Use of Serum Thyroglobulin Determinations for Monitoring Differentiated Thyroid Carcinoma

To the Editor:

In recent years, determination of thyroglobulin in the serum of patients with differentiated thyroid cancer after surgery and therapy with radioiodine has been advocated (1–4) as an index to success in treatment.

When this tumor marker is used for this purpose, a caveat should be heeded. Thyroglobulin concentrations may be normal in successfully treated differentiated thyroid cancer, but they may also be normal in differentiated tumors that have evolved into undifferentiated carcinoma (1, 5–8). Thus if serum thyroglobulin declines to normal or becomes undetectable after therapy, this may signify either control of a differentiated thyroid cancer or it may herald the transformation of a differentiated cancer into a rapidly growing and potentially fatal undifferentiated or anaplastic carcinoma.

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Immunocological and Electrophoretic Methods for Determination of Lactate Dehydrogenase Isoenzyme 1 Compared

To the Editor:

Diagnosis of acute myocardial infarction may be confirmed according to the criteria of Galen et al. (1), which include the presence of increased creatine kinase (CK; EC 2.7.3.2) MB isoenzyme and an LD1/LD2 ratio (by agarose electrophoresis) exceeding 1.0. Electrophoresis is ordinarily used to separate the five isoenzymes of lactate dehydrogenase (LD; EC 1.1.1.27). LD1 being the fastest moving (anodically) and LD5 the slowest. The increasing demand for such determinations makes more-easily performed methods desirable.

Immunocological methods for LD isoenzymes have recently been described (2–5), and Roche Diagnostics, Nutley, NJ 07110, has developed an immunochemical procedure kit for LD1 that combines the sensitivity and specificity characteristics of an antigen–antibody reaction with the rapidity of a direct, automated kinetic enzyme procedure.

Sera from patients in the critical coronary care unit were refrigerated at 2–8 °C and assayed for LD1 isoenzyme within 18 h. Total LD and CK were measured within 1 h with an acate discrete analyzer (DuPont Instruments, Wilmington, DE 19898). The upper