electrochemical: Yellow Springs Instrument Co., Yellow Springs, OH 45387) for assaying galactose.

For both fluorometric procedures, all reagents and standards were prepared as previously described (7). The manual assay requires 400 \( \mu \text{L} \) of Tris buffer (10 mmol/L); 600 \( \mu \text{L} \) of a solution containing \( p \)-hydroxyphenylacetic acid (50 mg/L) and horseradish peroxidase (EC 1.1.1.7) (10 mg/L); 160 \( \mu \text{L} \) of galactose oxidase solution (4.1 U/mL); and 400 \( \mu \text{L} \) of blank, standard, or sample filtrate. This mixture is incubated at 40 \( ^\circ \)C for 40 min, then mixed with 160 \( \mu \text{L} \) of 0.4 mol/L NaOH solution and the fluorescence is measured (317 nm excitation, 414 nm emission). The YSI was fitted with a galactose oxidase membrane and lactate buffer system (2). We used a 100 mg/L aqueous calibrator to define the assay range of 10–200 mg/L, a 10-fold increase in the manufacturer's claimed detection limit. No electronic modification of this model was necessary.

The inter- and intra-assay precision of all three methods was good, with respective CVs of 2.5–6.3% and 2.4–8.6%, the CVs being largest at the lowest concentrations. Analytical recoveries ranged from 95 to 105%. In comparison studies with patients' samples, MAN = 0.6 mg/L + 1.00 CF and YSI = 8.02 mg/L + 1.102 CF. There was an excellent intraclass correlation (3), 0.987, between the CF and MAN results; between the YSI and CF, however, this correlation was poor: 0.524.

Clearance of low concentrations of galactose from plasma is a measure of hepatic blood flow. To estimate clearance within \( \pm 5\% \), the accuracy of plasma steady-state during continuous infusion must be defined to within 2 mg/L. We found that overestimation of galactose by the YSI, which directly affected the intraclass correlation, resulted from a combination of factors: (a) less specificity of the galactose oxidase membranes, which was not totally correctable by subtraction of baseline values; (b) direct oxidation of interfering compounds at the platinum electrode, notably heparin flush and glycerol (plasma samples consistently gave positive readings across a blank membrane); and (c) operation at an inappropriately high sensitivity, thereby exaggerating the previous factors.

Evidently, either of the fluorogenic assays may be used for measuring low concentration of galactose, but the electrochemical detection system should not be used to measure values well beyond the manufacturer's specifications.

References

Naproxen Interference with the Ion-Selective Electrode in the RA-1000, Stephen P. Harrison (Dept. of Biochem., Bradford Royal Infirmary, Duckworth Lane, Bradford, BD9 6RJ, U.K.)

Salicylate interference with the bicarbonate ion-specific electrode in the RA-1000 (Technicon Instruments Inc., Tarrytown, NY) is well recognized (1) and often plays a serendipitous role in the unsuspected salicylate overdose. We recently analyzed a serum specimen from a patient admitted "overdose." The resulting bicarbonate value was flagged for interference. We assumed salicylate to be present and performed a screening test, using Trinder's reagent, which was negative. Analysis of the specimen in the SMAC (Technicon) gave a bicarbonate value 9 mmol/L lower than that in the RA-1000, and the raw data points obtained from the bicarbonate electrode showed an exaggerated fall in the electrode's response, similar to that seen with salicylate interference. Further enquiries into the patient's history showed that she had taken 25 g of naproxen (6-methoxy-a-methyl-2-naphthaleneacetic acid), a salicylate substitute, 4 h before the specimen was taken, the usual therapeutic dose being 500 mg. The structure of naproxen is quite different from that of salicylate and other previously reported interfering substances (2), which are generally single-ring structures.

Analysis of some serum pools containing various concentrations of naproxen showed a linear relationship between naproxen concentration and the result for bicarbonate ([bicarbonate] = 0.02[naproxen] – 2.07 mmol/L, \( r = 0.989 \)), with the flag present for all values >150 mg/L. The concentration of naproxen in the patient's serum was 600 mg/L, which compares favorably with 550 mg/L, the value obtained from the above relationship. Therapeutic concentrations of naproxen are not well documented, but at normal doses they probably do not exceed 80 mg/L (3), contributing less than 2 mmol/L to the result for apparent bicarbonate as measured in the RA-1000. However, arthritic patients on higher doses may attain concentrations that produce a flagged result, requiring the specimen to be analyzed by a different method.

Unfortunately, there is no quick screening method for naproxen, and its presence must be confirmed by more sophisticated methods.

References

\( \alpha_1 \)-Antitrypsin in Hyperlipidemia, P. M. Lutsky and J. Frohlich (Shaughnessy Hospital Lipid Research Group, Department of Pathology, University of British Columbia, Vancouver, BC V6H 3N1, Canada)

On electrophoresis, serum from some of our Lipid Clinic patients had apparently low proportions of \( \alpha_1 \)-globulin. We investigated this phenomenon. \( \alpha_1 \)-Antitrypsin (\( \alpha_1 \)-AT), the major constituent of \( \alpha_1 \)-globulin, is a major protease inhibitor in serum; its variants are well described (1). Cornicelli et al. (2) previously reported the simultaneous occurrence of heterozygosity for deficiencies of both \( \alpha_1 \)-AT and familial hypercholesterolemia, and suggested that the inheritance of these two defects was somehow linked.

Phenotypes of \( \alpha_1 \)-AT and the concentration of this protein in serum were determined in a prospective study of Lipid Clinic patients and healthy controls. The results showed

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