Ambroxol medication and tested positive for Ambroxol in urine by the HPLC technique. Finally, we carried out a self-test. No LSD could be detected in a fasting urine sample of a volunteer who afterward took 5 mL of Mucosolvan® juice (Dr. Karl Thomae) equivalent to 15 mg of Ambroxol-HCL. Another urine sample was analyzed as being positive 90 min after ingestion of Ambroxol. The addition of 50 μL of Mucosolvan juice to the LSD-negative fasting urine also led to a positive result. Mucosolvan juice diluted with two parts of distilled water resulted in a positive LSD test as well.

Ambroxol is a widespread and frequently used concomitant medication for infections of the upper respiratory tract. Predominantly, Ambroxol is used in an outpatient setting. In Germany, no less than ~40 pharmaceutical companies distribute Ambroxol. Ambroxol is widespread in most parts of Europe as well as in Japan, but it is not admitted, e.g., in the United States of America and the United Kingdom.

Therefore, LSD drug screening with the homogeneous immunoassay CEDIA DAU LSD yields a high incidence of false-positive results, especially in winter. In conclusion, Ambroxol administration should be excluded when a LSD screening in urine is performed by CEDIA DAU LSD. Moreover, positive results should be verified by a more specific method, such as GC/MS or HPLC techniques.

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Modification of the Abbott Cyclosporine Monoclonal Whole Blood Assay

To the Editor:

Abbott Laboratories recommends that before every Cyclosporine Monoclonal Whole Blood Assay run on the TDx analyzer, a probe cleaning procedure be performed (1) to avoid an artifactual decrease of results in the first carousel position (2).

We asked whether non-use of this procedure significantly affected results for the sample in the first carousel position. In our study, the TDx analyzer underwent daily, weekly, and monthly maintenance, as recommended by the manufacturer. Between 15 and 20 samples were analyzed in each run, and the study was completed in a period of 2 months.

Fig. 1 shows the correlation and regression (Passing and Bablok method) found between the results obtained in the same run, in the first and any of the other carousel positions of the analyzer, for the cyclosporine A concentration in 70 whole-blood samples from liver and renal transplant patients. The difference between the means, although statistically significant ($P < 0.001$), is not clinically significant according to the
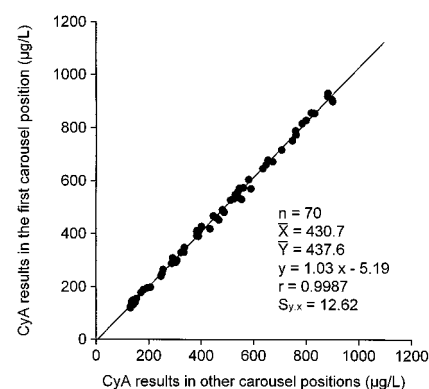

Fig. 1. Comparison of the values obtained in the first and any other carousel positions of the Abbott TDx analyzer, in the same analytical run, for the cyclosporine A (*CyA*) concentration in whole blood.

$$n = 70$$
$$\overline{X} = 430.7$$
$$\overline{Y} = 437.6$$
$$y = 1.03\,x - 5.19$$
$$r = 0.9987$$
$$S_{y \cdot x} = 12.62$$

criterion of Harris (3) and the therapeutic interval in our laboratory.

A CV of 2.5% was obtained using the method of replicates for the 70 pairs of values (interval, 120–929 μg/L; Fig. 1). This imprecision is similar to that found for 53 pairs of values, with a mean value of 445.1 μg/L (interval, 124–841 μg/L), obtained in the same run in other carousel positions, excluding the first position, for which a CV of 3.0% was obtained. In both cases, the CVs are similar to those reported by the manufacturer (1).

Given that the standard error of the estimate ($S_{y|x} = 12.62$) is less than the clinically acceptable error according to the criterion of Harris (3), a probe wash procedure appears unnecessary before each assay run. Each laboratory, however, should determine the impact on state, county, or other laboratory certification of changes to commercial procedures.

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Editor's note: A representative of the manufacturer warns about effects on laboratory certification of procedures that are contrary to the procedure provided by the manufacturer.

Method-specific Reference Intervals for Serum Anion Gap and Osmolality

To the Editor:

We wish to comment on reference intervals for the serum anion gap and osmolality. The serum anion gap, which is most commonly defined as AG = $Na-Cl-TCO_2$, traditionally has had a reference interval of 8–16 mmol/L with a mean value (i.e., mean of values used to determine its reference interval) of 12 mmol/L *(1, 2)*. In a recent report *(3)*, the stated reference interval for the anion gap was 12–16 mmol/L with potassium included in the calculation, approximately equivalent to 8–12 mmol/L without inclusion of potassium. This range of only 4 mmol/L appears to be too narrow for a healthy human population. Moreover, recent studies have shown that mean values for current analyzers often differ from the traditional value and may vary from 5.9 mmol/L for the Beckman Synchron to 12.4 mmol/L for the Nova analyzer *(4–6)*. Consequently, depending on the analyzer used, the serum anion gap reference interval may be as low as 2–10 mmol/L or as high as the traditional range of 8–16 mmol/L. We have also found marked interlaboratory differences in measurements by the same type of analyzer *(6)*. Thus, interpretation of the anion gap requires that each clinical laboratory determine its own reference interval.

The reference interval for serum osmolality also deserves study. One recent report *(3)* included a reference interval of 270–290 mOsm/kg. We believe this interval is inappropriately low, based on our duplicate measurements of serum osmolality by freezing point depression (Advanced Instruments Model 3MO osmometer) in 59 healthy volunteers of ages 20–60 years. Kolmogorov-Smirnov analysis indicated that we could not reject the hypothesis that the results were normally distributed ($P = 0.64$). The mean serum osmolality was 288 mOsm/kg, with a SD of 4.1 mOsm/kg, yielding a parametric reference interval of 280–298 mOsm/kg. The lowest and highest values measured were 280 and 298 mOsm/kg, respectively. Other published serum osmolality reference intervals based on freezing point depression measurements are 275–290 or 275–295 mOsm/kg in children and adults and 280–301 mOsm/kg in adults >60 years of age *(7, 8)*. Both analytical methodology and characteristics of the reference population, such as age, can contribute to differences in serum osmolality reference intervals. Again, the clinical laboratory must establish or at least verify the serum osmolality reference interval to aid in accurate interpretation.

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Capillary Electrophoresis in the Analysis of the Deletion/Insertion Polymorphism of the Angiotensin I-Converting Enzyme Gene

Capillary gel electrophoresis (CGE) in molecular pathology and genetics is an ideal instrument for fast, fully automated analysis. The number of reports dealing with the analysis of, e.g., PCR products, is continuously increasing. In this context, we noticed with interest the description of a CGE analysis of the angiotensin I-converting enzyme polymorphism by X.H. Huang et al. *(1)*. The CGE procedure is very similar to our communication published in 1996 *(2)*, but with our method, running times are substantially shorter: we have separation times of <10 min *(2)*. In general, modern CGE analysis of PCR products can easily be achieved in <10 min when there are such big differences in basepairs (100–300 bp) *(3, 4)*.

If Huang et al. *(1)* plan to screen a large number of samples for the angiotensin I-converting enzyme polymorphism by CGE, the use of a polyacrylamide-coated capillary and 0.6% hydroxyethylcellulose will increase their sample throughput by nearly 300%.

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