A Clinical Chemistry Analyzer Evaluated by NCCLS Guidelines for Use in a Military Field Laboratory Unit

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In a previous comparison study of “dry chemistry” desktop analyzers, the ChemPro 1000 (Arden Medical Systems) was one of several instruments found suitable for field use. We have now evaluated the linearity, accuracy, and precision of the ChemPro 1000, according to NCCLS Document EP 0-P. We also compared results with those by the SMAC Technicon) and the Nova 9 (Nova Biomedical) for electrolytes, serum urea nitrogen, and ionized calcium in field and laboratory environments. The precision (CV) of the ChemPro was within acceptable ranges for dry chemistry desktop analyzers for all analytes tested. This instrument is a suitable and reasonable alternative to manual chemistry or to large, automated instrumentation in a field environment.

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The ability to perform fundamental chemistry analyses in the field is essential to the mission of a military medical laboratory unit. The standard manual chemistry methods require water-based reagents, which are bulky and difficult to transport and keep from damage during mobilization. The methodology is laborious and requires specially trained personnel. Current automated analyzers are impractical in a field setting. Recently, the development of “dry chemistry” desktop analyzers for physicians’ offices has allowed decentralization of some laboratory services to provide timely results for diagnostic or management decisions while the patient waits (1–5). Doos et al. (6) examined the suitability of several portable dry chemistry desktop analyzers in a mobile army field laboratory. In that patient-comparison study, all of the instruments tested were found to be “field suitable.” Although it did not have applications for all of the required analytes, the ChemPro 1000 (Arden Medical Systems, St. Paul, MN) was the instrument of choice because of its ease of use and low requirement for temperature-sensitive, fragile, or bulky consumables. We undertook the present study specifically to evaluate linearity, accuracy, and precision in a field laboratory setting, with the evaluation based on the guide-

Materials and Methods

The ChemPro 1000 is based on potentiometry, with ion-selective electrodes incorporated into disposable test cards. As many as four tests can be performed at once with use of one card: for example, the LYTES card is used to measure sodium (Na), potassium (K), chloride (Cl), and pH simultaneously, whereas the blood urea nitrogen (BUN) test is contained on a single card and requires mixing and a 2-min incubation. The instrument's performance and capabilities have been previously described (6).

Comparison studies for all analytes except ionized calcium were performed with the SMAC continuous-flow analyzer (Technicon Instruments Corp., Tarrytown, NY). ChemPro 1000 data for ionized calcium were compared with results obtained from the Nova 9 ion-selective electrode analyzer (Nova Biomedical, Waltham, MA).

The control material used in all studies was Clinical Chemistry Bovine Serum Control, Level I & II (American Dade, Div. of American Hospital Supply Corp., Miami, FL). This material is routinely used as a control for both the SMAC and Nova 9 instruments, and is compatible with the ChemPro system. It adequately spanned a useful range for each of the analytes tested in the study.

The method evaluation document from NCCLS, EP 10-P (7), is intended "to detect problems that are sufficiently severe to warrant immediate correction, referral to the manufacturer, or expanded investigation." The protocol involves collection of 45 data points at three concentrations in a specified order over five runs. A plot of labeled vs observed concentrations and some simple calculations allow a preliminary evaluation of nonlinearity, outliers, bias, and precision. More complex calculations are described that allow estimates in the form of t statistics for accuracy, precision, linearity, bias, carryover, and drift. We used the EP 10-P protocol in this study to compare data from the SMAC and the Nova 9 with data from the ChemPro 1000, as an aid in determining the suitability of the ChemPro instrument for a field environment. In addition, for linearity studies we used the high-concentration control material diluted with saline for each analyte during each phase of the study.

The study was conducted in three phases: Phase I, premobilization; Phase II, mobilization; and Phase III, postmobilization tests. During Phase I, the EP 10-P protocol was performed on the SMAC. Labeled values (x-axis) for the high- and low-concentration control materials were the previous month's means from the SMAC. The labeled values for the mid-concentration mixture were calculated.

During Phase II, a complete field medical laboratory unit was loaded onto trucks, convoyed for two days over 450 miles from Lexington, MA, to Gagetown, Ontario, and deployed at the mobilization site. The laboratory functioned for 10 days in a tactical field situation under varied environmental conditions. The EP 10-P study was conducted over five days for serum urea nitrogen, K⁺, and ionized Ca (Ca²⁺).

During Phase III, after the return convoy, the EP 10-P protocol was run in a laboratory setting on the ChemPro 1000 for Na and Cl, and the data were assembled and compared.

Results and Discussion

Linearity studies with the ChemPro 1000 before mobilization demonstrated that the relation of readings to concentration was linear over the concentration ranges tested, which included the medically significant ranges for these analytes. Results from the same studies performed in the field and after mobilization were nearly identical, indicating that no adverse effects were produced by outdoor environmental conditions (dust), power failures, or transportation.

The EP 10-P document stresses the importance of visual inspection of a plot of labeled vs observed concentrations to detect outliers and qualitatively assess imprecision and linearity. We find that the impressions conveyed by such a plot are particularly useful if similar data generated by a familiar method are available. Thus by reference to plots such as those in Figure 1 for sodium, the ChemPro 1000 is less precise and more nonlinear than the SMAC. Whether the differences are clinically significant must be judged separately.

The nonlinearity observed in the plots of EP 10-P data for

![Figure 1](image-url)
sodium measured in the ChemPro 1000 and in the SMAC was not statistically significant in the EP 10-P data analysis. Conventional linearity studies of the ChemPro 1000, based on serial dilutions, produced straight lines for sodium and the other ChemPro analytes, confirming the EP 10-P analysis. The difference in precision seen on the plots was reflected in the CVs for the two systems calculated according to the EP 10-P protocol (Table 1).

Chloride determinations in the ChemPro 1000 were linear over the range studied, but a large and statistically significant bias existed at the low end relative to the SMAC, as was readily demonstrated by the graph of the EP 10-P data (Figure 2).

The method for ionized calcium as measured in the ChemPro 1000 appears to be imprecise, and exhibits a large bias at the low end relative to the Nova 9 (Figure 3). It is possible that environmental conditions and the inability to process the ionized Ca sample properly in a field situation introduced error. It was not possible to run a comparison study with the Nova 9 with the EP 10-P protocol because the Nova 9 was located in an acute-care laboratory where interruptions for analysis of urgent ("stat") specimens were frequent. Plots of ChemPro 1000 data for urea nitrogen and potassium revealed no significant bias or imprecision for either method.

An outlier is defined in EP 10-P as "a single point 'detached' from the main cluster of points at a concentration level," and detection of these is especially critical because such points can greatly affect the data, owing to the small number of samples. EP 10-P is not clear on the action required if one outlier is observed. Our practice has been to repeat the protocol for a sixth day, and eliminate the data from the day containing the outlier. If more than one outlier is observed at a given concentration, either the investigation should be broadened to collect more data to determine the cause or the points may be included in the experiment with the knowledge that the conclusions derived from the data may be affected by the outliers. By this definition, the three "detached" points for sodium by the ChemPro method might be considered outliers. If these points were excluded, the mean CV would be 2.6% rather than the 3.1% as shown in Table 1.

Table 1 summarizes the CVs for each analyte and instrument tested; the acceptable and medically allowable CVs for each of the analytes tested are also listed for comparison (8, 9). Acceptable CVs for desktop analyzers are suggested to range from 5% for most analytes to 10% for enzyme tests (9). Except for ionized calcium determinations, the performance of the ChemPro 1000 instrument was within limits acceptable for both traditional clinical laboratory methodology and desktop analyzers.

The ChemPro performed well in both field and laboratory environments. The time and skill required for instrument familiarity were minimal. Two problems were encountered in the field. The dusty surroundings accounted for occasional "self-test" failures, which were quickly and easily corrected by cleaning the card connector. Moreover, during several unexpected power failures, the current test sample results were lost, so the sample had to be re-assayed. The

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### Table 1. Summary of the Mean CVs for Each Analyte and Instrument Tested

<table>
<thead>
<tr>
<th>Instrument</th>
<th>CV, %</th>
<th>Medically allowable error</th>
</tr>
</thead>
<tbody>
<tr>
<td>ChemPro</td>
<td></td>
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</tr>
<tr>
<td>Na⁺</td>
<td>3.1</td>
<td>1.0</td>
</tr>
<tr>
<td>K⁺</td>
<td>2.6</td>
<td>3.0</td>
</tr>
<tr>
<td>Cl⁻</td>
<td>1.3</td>
<td>1.5</td>
</tr>
<tr>
<td>Urea nitrogen</td>
<td>5.0</td>
<td>8.0</td>
</tr>
<tr>
<td>Ionized Ca</td>
<td>6.1</td>
<td>?</td>
</tr>
<tr>
<td>SMAC</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Na⁺</td>
<td>0.8</td>
<td>1.0</td>
</tr>
<tr>
<td>K⁺</td>
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<tr>
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<td>Ionized Ca</td>
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<td>NA</td>
</tr>
<tr>
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<td></td>
</tr>
<tr>
<td>Ionized Ca</td>
<td>2.1</td>
<td>?</td>
</tr>
</tbody>
</table>

*For comparison, the acceptable and medically allowable CVs for each of the analytes tested are listed (8, 9).*

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**Fig. 2.** Labeled vs observed values for chloride (mmol/L) with the ChemPro 1000

**Fig. 3.** Labeled vs observed values for ionized calcium (adjusted to pH 7.4), in mmol/L, with the ChemPro 1000
capability of battery back-up would be a desirable feature in these situations.

We thank Arden Medical Systems for the gratis use of the ChemPro 1000 and supplies; Martha Gearty for her assistance in coordinating this study; D.R. Misiano for allowing us the use of the Nova 9 at the Anesthesia Acute Care Laboratory, Massachusetts General Hospital, Boston, MA; and Dr. Sanford R. Kurtz, Director of Laboratory Medicine, Lahey Clinic, Burlington, MA, for the use of the SMAC and quality-control data. We especially thank Sandra L. Dusenbury, MT(ASCP), for technical assistance and suggestions in performing the EP 10-P protocol with the SMAC.

References

Estrogen and Progesterone Receptor Assays, by the EIA Method (Abbott), of Low-Speed Supernates of Breast-Cancer Homogenates

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Estrogen receptor (ER) and progesterone receptor (PR) assays were performed by solid-phase enzyme immunoassays (Abbott) on low-speed (2600 × g) and high-speed (100 000 × g) supernates of breast-cancer homogenates. The results were similar, indicating that ultracentrifugation is not essential for ER and PR assays with the Abbott kit.

Assay of estrogen receptors (ER) and progesterone receptors (PR) in breast-cancer specimens currently is still limited to laboratories that have an ultracentrifuge at their disposal. The introduction by Abbott Laboratories of solid-phase enzyme immunoassays for these receptors has simplified the receptor assays considerably in comparison with the ligand binding assay based on saturation analysis of the receptor with increasing hormone concentrations ($I_n$). For preparation of the cytosol, the tissue homogenate is centrifuged for 1 h at 100 000 × g according to the instructions issued with the Abbott receptor kits. In our experience with the ligand binding assay, results obtained with low-speed and high-speed centrifugations were not significantly different (unpublished observation). Here we present results that show it to be unnecessary to prepare the cytosol by ultracentrifugation. Receptor results obtained for cytosols prepared with a standard laboratory refrigerated centrifuge did not differ from results obtained for cytosols from ultracentrifugation.

Methods

The specimens for this study were not selected; instead, all specimens received for receptor assay within a certain interval were included.

Deep-frozen breast cancer specimens were pulverized with a microdismembrator (Braun). The resulting tissue powder was suspended in 10 volumes of pH 7.5 phosphate buffer. The homogenate was centrifuged either in a Beckman Ultracentrifuge L8-70 at 4 °C for 30 min at 100 000 × g or in a Hettich Rotanta refrigerated centrifuge at 4 °C for 60 min at 2600 × g. We removed the supernates with a Pasteur pipette, carefully avoiding the fat layer on the top and the sediment at the bottom. The protein concentration in the supernate was estimated by use of the Coomassie Blue dye-binding method (2). After suitable dilution of the supernates, ER and PR were estimated according to the protocols provided with the Abbott EIA kits.

Results

The mean results and the coefficients of variation (CV) for duplicate estimations of ER and PR in each of the high-speed and low-speed supernates of breast-cancer homogenates are shown in Tables 1 and 2. The correlations between the results for high speed and low speed are highly significant for both ER and PR (coefficient of correlation $r_1 = 0.98$ for 23 pairs of ER, $P_1 < 0.001$, $r_2 = 0.99$ for 25 pairs of PR, $P_2 < 0.001$, regression equation $y_1 = 0.99x_1 - 2.07$ for ER, $y_2 = 0.95x_2 + 1.17$ for PR). The results for low-speed and high-speed cytosol for all pairs are so close that in no case the classification into ER positive (ER > 4 fmol per milligram of protein) and ER negative (ER < 4 fmol per milligram of protein) or PR positive (PR > 10 fmol per milligram of protein) and PR negative (PR < 10 fmol per

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