An Evaluation of Ethylene Glycol-based Liquid Specimens for Use in Quality Control

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We investigated the analytical acceptability of ethylene glycol-based control sera by preparing sets of aqueous and ethylene glycol-based specimens that had added uric acid, calcium, creatinine, glucose, urea, sodium, and potassium. Ethylene glycol caused a significant systematic proportional bias in procedures involving dialysis, but had no discernible effect on methods not involving dialysis. The extent of bias was proportional to the concentration of ethylene glycol, was independent of protein concentration, and differed according to the type of dialysis system used. We conclude that ethylene glycol-based control materials can have useful applications in clinical chemistry, but caution must be exercised in their use with analytical systems that employ dialysis.

Additional Keyphrases: automated analysis • dialysis

Most serum-based reference, calibration, and control materials are lyophilized preparations that inherently have vial-to-vial variability of analyte concentrations because of imprecision in the volume dispensed by the manufacturer into the vials prior to lyophilization and in the volume employed by the user to reconstitute the specimens. In addition, losses of unstable components may occur during lyophilization or storage or after reconstitution. A stable liquid serum preparation has been described (1, 2) that contains about 30% (v/v) ethylene glycol and has color, clarity, and viscosity similar to that of human serum. The liquid serum is not subject to variations in concentration from imprecise dispensing and reconstitution volumes, and the ethylene glycol is said to serve as a bacteriostatic and stabilizing agent that results in a remarkable shelf life for the material at both freezer and room temperatures (2). The liquid serum was commercially available for several years (3), and a similar material recently has been marketed (4).

We were interested in evaluating a liquid serum preparation because of the relative ease with which interrelated specimens may be prepared. Sets of specimens having multiple quantitative interrelationships have been shown to have useful applications in clinical chemistry (5–12). The known relationships greatly facilitate method evaluations, and aid the detection and characterization of analytical problems. It is technically much easier to prepare interrelated specimens in liquid form than in lyophilized form, and liquid specimens are not subject to alterations of the established relationships that may occur with traditional preparations during the lyophilization and reconstitution processes. However, ethylene glycol might be expected to interfere with some analytical procedures; indeed, physico-chemical interference in the determination of osmolality, and of total protein by refractometry, is known to occur. We undertook a small study to ascertain whether ethylene glycol caused other, less obvious, analytical biases.

Materials and Methods

Preparation of Specimens

Preparation of interrelated specimens for studying the effects of ethylene glycol. We prepared a series of interrelated specimens that were identical except for the presence of either distilled water or 30% (v/v) ethylene glycol in the solvent matrices, as shown in Figure 1. Vials of a commercial lyophilized serum (MonTRol® I-X, Dade Division, American Hospital Supply Corporation, Miami, FL 33152) were reconstituted with distilled water, using 50% of the normal reconstitution volume, and combined. One volume of this concentrated base pool was diluted with 0.50 volume of aqueous diluent I (see below) to produce Pool B, and a second volume of concentrated pool was diluted with 0.50 volume of aqueous diluent II to produce Pool A. The aqueous diluents were prepared by dissolving weighed amounts of dried analytical grade sodium chloride, calcium acetate, potassium chloride, National Bureau of Standards Standard Reference Material (NBS SRM) urea, uric acid, glucose, and creatinine in distilled water and diluting to volume in a volumetric flask. Calcium, creatinine, urea, and glucose were included in Diluent I, while uric acid, sodium, and potassium were in Diluent II. Identical volumes of Pool A were placed in two volumetric flasks; one flask was diluted to volume with 80% ethylene glycol to produce Pool C, and the other was diluted with water to produce Pool D. The dilution volumes were chosen to result in a concentration of 30% (v/v) ethylene glycol in the final Pool C. Pool B was similarly diluted with either 80% ethylene glycol or distilled water to produce Pools E and F.

Pools C and F and Pools D and E were then combined in the proportions shown in Table 1 to produce two sets of interrelated admixtures. Aliquots were dispensed from the admixtures and stored at −20 °C for later analysis.

This procedure of specimen preparation resulted in two sets of specimens in which every specimen had the same amount of serum matrix, at a concentration close to that of normal serum. The two sets of specimens had identical gradients of

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the analytes of interest, and differed only in that one set contained 30% (v/v) ethylene glycol rather than water.

Preparation of specimens having an ethylene glycol gradient. Vials of a lyophilized serum (Chemistry Control Serum, Level I, Hyland Division, Travenol Laboratories, Inc., Costa Mesa, CA 92626) were reconstituted with 50% of the normal reconstitution volume and combined. The concentrated pool was supplemented with an aqueous diluent containing weighed-in amounts of analytical grade calcium acetate and NBS SRM-grade uric acid and glucose. One volume of this concentrated supplemented pool was diluted with 0.40 volume of distilled water, and a second one-volume portion was diluted with 0.40 volume of a decalcified solution of human albumin, 210 g/L. These pools were labelled pool N and Pool N–Alb, respectively. One volume of Pool N was diluted with ethylene glycol to a final concentration of 30% ethylene glycol (v/v); another one-volume portion of Pool N was similarly diluted with water. Two portions of Pool N–Alb then were diluted in an identical manner with either ethylene glycol or water. This procedure resulted in two aqueous pools, one of which was supplemented with albumin, and two 30% ethylene glycol pools, one of which was not supplemented with albumin. The two aqueous pools were mixed in the proportions shown in Table 2, to produce a set of linearly related specimens that were identical except for their concentration of albumin. The two ethylene glycol pools were mixed in the same manner as the aqueous pools (see Table 2) to produce a set of linearly related specimens that were identical to the aqueous set except for the presence of 30% ethylene glycol.

### Analytical Methods

We used the following methodologies: Technicon SMA 6/60® (Technicon Instrument Corp., Tarrytown, NY 10591). Sodium and potassium: flame photometry (13); urea nitrogen: diacetyl monoxime (13); glucose: glucose oxidase (14).

**Technicon AutoAnalyzer® 1.** Glucose: glucose oxidase (14); creatinine: alkaline picrate (15); uric acid: phosphotungstate (15).

**DuPont aca (DuPont Instruments, Wilmington, DE 19898).** Calcium: o-cresolphthalein complexone (16); creatinine: modified kinetic alkaline picrate (16); glucose: hexokinase–glucose-6-phosphate dehydrogenase (16); urea nitrogen: urease-glutamate dehydrogenase (16); uric acid: uricase kinetic method (16).

**Atomic absorption.** Calcium was determined by an automated procedure that employs the Technicon AutoAnalyzer I sampling and dialysis modules (17).
Manual flame photometry: Sodium and potassium were determined with the (IL) Model 343 instrument (Instrumentation Laboratories, Inc., Lexington, MA 02173).

Data Analysis

The specimens used in this study were designed to be linearly related so that a plot of analyte concentration (ordinate) vs. percent supplementation of the specimens (abscissa) should yield a straight-line relationship (6, 7, 11). The slope of the line may be known from the amount of analyte weighed-in during the preparation of the specimens. The best straight-line fit to the analytical data can be calculated by linear regression analysis, and the observed line can be described by its x-intercept and slope. The method's recovery of added analyte (PRA = Percent Recovery of Analyte) is calculated by the relation:

\[
PRA = \frac{\text{observed slope} + \text{known slope}}{100}
\]

Analytical biases are commonly categorized as proportional (only the slopes are affected), constant (only x-intercept affected), or combined (slope and x-intercept affected). Thus, by comparing the x-intercepts, slopes, and PRA's, we can identify the kinds of biases affecting the analyses of the interrelated specimens.

Results

Comparison of Specimens Prepared in Aqueous Solution and in 30% (v/v) Ethylene Glycol

Figure 2 illustrates typical results of analyses of the aqueous and ethylene glycol specimens for glucose. The nine interrelated specimens in each set were analyzed over a period of two weeks, but each aqueous specimen and the corresponding ethylene glycol specimen were always analyzed sequentially in the same analytical run. Thus, each set of corresponding data points (Figure 2) was obtained concomitantly, but the series of points along the line was obtained in many analytical runs over the course of two weeks. Graphs (not included here) of the data for the other six analytes were also nicely linear, and clearly revealed the absence (e.g., Figure 2a) or presence (e.g., Figure 2b) of analytical bias due to ethylene glycol. Table 3 summarizes these results, for each analyte, in terms of the x-intercept and slope of the best line fit of the data. We interpret these data as follows:

Glucose. Figure 2a and the data of Table 3 show that both the aqueous and ethylene glycol specimens were characterized by very similar x-intercept and slope values when analyzed with the DuPont ac(a). In addition, these slopes were close to the expected values, as the recovery of added glucose (PRA, Table 3) was 102.4%. Thus, ethylene glycol had no discernible effects on these analyses. Figure 2b and the data of Table 3 show that the aqueous specimens analyzed on the SMA 6/60 (glucose oxidase procedure) produced x-intercept, slope, and PRA values that were very similar to those of the DuPont ac(a) (hexokinase, glucose-6-phosphate dehydrogenase procedure).

These results indicate that the two instrumental systems were similarly calibrated at the time of this study. However, the ethylene glycol-containing specimens analyzed on the SMA 6/60 produced a small change in x-intercept value and a relatively large change (−8.3%) in the slope value. It is apparent that ethylene glycol caused a substantial negative proportional bias in glucose analyses by the SMA 60/60 procedure.

Uric acid. As shown in Table 3, there is little difference in the results obtained with the aqueous and ethylene glycol specimens when analyzed with the DuPont ac(a) (uricase procedure). The PRA data suggest, however, that the DuPont ac(a) at this time was not calibrated to fully recover added analyte. The AutoAnalyzer I (phosphotungstate procedure, with six aqueous standards) shows a recovery of 101.7% of added analyte with aqueous specimens, but only 88.4% in the presence of ethylene glycol. As the x-intercept values are quite similar, the ethylene glycol clearly caused a negative proportional bias of −13.3% in the AutoAnalyzer procedure.

Creatinine. Results obtained with the aqueous and ethylene glycol specimens on the DuPont ac(a) (kinetic alkaline picrate procedure) show very good agreement. Also, these results agree well with those from the aqueous specimens assayed on the AutoAnalyzer I (alkaline picrate procedure, with six aqueous standards). The ethylene glycol specimens, however, when analyzed on the AutoAnalyzer, show a negative proportional bias of −3.8%.

Urea nitrogen. Table 3 shows that the results for urea are similar to those for creatinine. Ethylene glycol had a significant effect on the DuPont ac(a) procedure (urease–glutamate dehydrogenase) but caused a negative proportional bias of −4.8% in the SMA 6/60 procedure (diacetyl monoxime).

Calcium. Our atomic absorption procedure employs dialysis, but the standards are prepared in a decalcified human serum albumin matrix to compensate for the effects of serum proteins on dialysis (17). The data of Table 3 show that recovery of added calcium by this procedure was 101% with the aqueous set of specimens. However, ethylene glycol caused a negative proportional bias of −10%. The DuPont ac(a) pro-
Table 3. Evaluation of Effect of Ethylene Glycol (EG) on Analysis for Seven Analytes

<table>
<thead>
<tr>
<th>Analyte</th>
<th>Instrument, specimen type</th>
<th>n</th>
<th>Slope</th>
<th>95% confid.</th>
<th>p</th>
<th>x-intercept</th>
<th>PRA</th>
<th>Slope bias (%)</th>
</tr>
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<tr>
<td>Glucose</td>
<td>aca, distilled H2O</td>
<td>18</td>
<td>20.72</td>
<td>0.41</td>
<td>-39.3</td>
<td>102.4</td>
<td>0.0</td>
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<td>Glucose</td>
<td>aca, 30% EG</td>
<td>18</td>
<td>20.73</td>
<td>0.24</td>
<td>-38.9</td>
<td>102.4</td>
<td>-8.3</td>
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<td>Glucose</td>
<td>SMA 6/60, distilled H2O</td>
<td>18</td>
<td>20.67</td>
<td>0.55</td>
<td>-40.9</td>
<td>101.9</td>
<td>0.0</td>
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<tr>
<td>Glucose</td>
<td>SMA 6/60, 30% EG</td>
<td>18</td>
<td>18.91</td>
<td>0.55</td>
<td>-42.3</td>
<td>93.6</td>
<td>0.0</td>
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<td>Uric acid</td>
<td>aca, distilled H2O</td>
<td>18</td>
<td>0.476</td>
<td>0.038</td>
<td>-99.4</td>
<td>93.3</td>
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<td>aca, 30% EG</td>
<td>18</td>
<td>0.489</td>
<td>0.033</td>
<td>-95.7</td>
<td>95.8</td>
<td>-8.3</td>
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<tr>
<td>Uric acid</td>
<td>AA, distilled H2O</td>
<td>18</td>
<td>0.519</td>
<td>0.021</td>
<td>-91.1</td>
<td>101.7</td>
<td>0.0</td>
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<td>AA, 30% EG</td>
<td>18</td>
<td>0.451</td>
<td>0.017</td>
<td>-93.6</td>
<td>88.4</td>
<td>-13.3</td>
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<tr>
<td>Creatinine</td>
<td>aca, H2O distilled</td>
<td>18</td>
<td>0.920</td>
<td>0.018</td>
<td>-18.9</td>
<td>97.9</td>
<td>+0.9</td>
<td></td>
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<tr>
<td>Creatinine</td>
<td>aca, 30% EG</td>
<td>18</td>
<td>0.929</td>
<td>0.014</td>
<td>-18.6</td>
<td>98.8</td>
<td>-8.3</td>
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<tr>
<td>Creatinine</td>
<td>AutoAnalyzer I, H2O</td>
<td>18</td>
<td>0.923</td>
<td>0.018</td>
<td>-18.3</td>
<td>98.2</td>
<td>-3.8</td>
<td></td>
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<tr>
<td>Creatinine</td>
<td>AutoAnalyzer I, 30% EG</td>
<td>18</td>
<td>0.888</td>
<td>0.020</td>
<td>-17.5</td>
<td>94.4</td>
<td>-6.0</td>
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<tr>
<td>Urea N</td>
<td>aca, distilled H2O</td>
<td>18</td>
<td>2.692</td>
<td>0.086</td>
<td>-61.7</td>
<td>96.2</td>
<td>-0.0</td>
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<tr>
<td>Urea N</td>
<td>aca, 30% EG</td>
<td>18</td>
<td>2.675</td>
<td>0.086</td>
<td>-62.1</td>
<td>95.6</td>
<td>-4.8</td>
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<td>Urea N</td>
<td>SMA 6/60, distilled H2O</td>
<td>18</td>
<td>2.793</td>
<td>0.126</td>
<td>-60.2</td>
<td>99.8</td>
<td>+0.3</td>
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<td>Urea N</td>
<td>SMA 6/60, 30% EG</td>
<td>18</td>
<td>2.660</td>
<td>0.145</td>
<td>-58.3</td>
<td>95.0</td>
<td>-10.0</td>
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<tr>
<td>Calcium</td>
<td>aca, distilled H2O</td>
<td>18</td>
<td>0.312</td>
<td>0.018</td>
<td>-113</td>
<td>104.0</td>
<td>+1.0</td>
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<tr>
<td>Calcium</td>
<td>aca, 30% EG</td>
<td>18</td>
<td>0.313</td>
<td>0.021</td>
<td>-112</td>
<td>104.3</td>
<td>+7.7</td>
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</tr>
<tr>
<td>Calcium</td>
<td>AA, distilled H2O</td>
<td>18</td>
<td>0.303</td>
<td>0.015</td>
<td>-107</td>
<td>101.0</td>
<td>-8.3</td>
<td></td>
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<tr>
<td>Calcium</td>
<td>AA, 30% EG</td>
<td>18</td>
<td>0.273</td>
<td>0.014</td>
<td>-109</td>
<td>91.0</td>
<td>-1.8</td>
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<tr>
<td>Sodium</td>
<td>IL, distilled H2O</td>
<td>18</td>
<td>0.507</td>
<td>0.024</td>
<td>-213</td>
<td>101.4</td>
<td>+1.0</td>
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<tr>
<td>Sodium</td>
<td>IL, 30% EG</td>
<td>18</td>
<td>0.512</td>
<td>0.025</td>
<td>-203</td>
<td>102.4</td>
<td>+7.2</td>
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<tr>
<td>Sodium</td>
<td>SMA 6/60, distilled H2O</td>
<td>18</td>
<td>0.494</td>
<td>0.027</td>
<td>-220</td>
<td>98.8</td>
<td>-8.3</td>
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<td>Sodium</td>
<td>SMA 6/60, 30% EG</td>
<td>18</td>
<td>0.530</td>
<td>0.041</td>
<td>-206</td>
<td>106.0</td>
<td>-1.8</td>
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<tr>
<td>Potassium</td>
<td>IL, distilled H2O</td>
<td>18</td>
<td>0.0502</td>
<td>0.0016</td>
<td>-89.0</td>
<td>100.4</td>
<td>+4.0</td>
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<tr>
<td>Potassium</td>
<td>IL, 30% EG</td>
<td>18</td>
<td>0.0493</td>
<td>0.0018</td>
<td>-87.0</td>
<td>98.6</td>
<td>-1.0</td>
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<td>18</td>
<td>0.0501</td>
<td>0.0027</td>
<td>-89.0</td>
<td>100.2</td>
<td>+4.0</td>
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<td>Potassium</td>
<td>SMA 6/60, 30% EG</td>
<td>18</td>
<td>0.0521</td>
<td>0.0027</td>
<td>-86.9</td>
<td>104.2</td>
<td>-8.3</td>
<td></td>
</tr>
</tbody>
</table>

* No. analyses.

** PRA, per cent recovery of analyte.

Procedure (o-cresolphthalein complexone) was apparently calibrated somewhat differently, but there was no significant effect attributable to the presence of ethylene glycol.

Sodium and potassium. Ethylene glycol had little effect on either sodium or potassium analyses by flame photometry when performed with the IL 343 instrument. However, ethylene glycol caused a positive proportional bias of 7.2 and 4.0% in sodium and potassium analyses, respectively, when measured on the SMA 6/60.

Statistical significance of results. The differences in the slopes calculated for the aqueous and ethylene glycol specimens were statistically significant for all analytes. p values ≤0.20 are listed in Table 3, and highly significant differences were found for glucose, uric acid, creatinine, urea nitrogen, and calcium. p values for sodium and potassium were somewhat larger. However, in extended studies of sodium, 27 of 30 paired samples had higher values for the ethylene glycol specimen than the aqueous specimen, and three pairs had equal values. For potassium, 28 of 30 paired samples had higher values for the ethylene glycol specimen, and two pairs had equal values. Analysis of these data by the nonparametric sign test indicated that for both of these analytes there is a significant difference between the aqueous and ethylene glycol specimens at the p <0.05 level.

Effect of Ethylene Glycol Concentration

To further define the effect of ethylene glycol, we prepared a set of six specimens in which the specimens differed only in the concentration of ethylene glycol (see Materials and Methods). The specimens were analyzed for glucose (SMA 6/60), uric acid (AutoAnalyzer I), and calcium (automated atomic absorption, with dialysis). The results are summarized in Figure 3, which shows that as the concentration of ethylene glycol was increased from 0 to 40.8% there was a proportionate decline in the amount of analyte recovered. The degree of change caused by 30% ethylene glycol is in each case quite comparable to that observed in the initial comparisons (Figure 2 and Table 3).

Effect of Protein Concentration

All of the specimens in the preceding experiments had the same total protein concentration. To investigate the effects of ethylene glycol in the presence of changing protein concentration, we prepared two sets of specimens that had various amounts of protein (human albumin); one set contained ethylene glycol (30% by vol), the other a corresponding volume of distilled water (see Materials and Methods). The specimens were analyzed for uric acid, glucose, and calcium by the analytical procedures that had demonstrated bias (SMA 6/60, AAI, and atomic absorption with dialysis). The results showed that varying the protein concentration from 45 to 87 g/L had no discernible effect on the bias of the ethylene glycol specimens. The bias was constant at all concentrations of protein, and the average biases for uric acid, glucose, and calcium were -13.5, -7.1, and -9.8%, respectively. These biases were quite comparable to those observed in the earlier experiments. We conclude that the bias observed in the presence of ethylene
glycol is due entirely to the glycol and is unrelated to the protein content of the specimens, in the range of protein concentration of clinical chemical interest.

**Comparison of Dialysis Effect on the SMA 6/60 and AutoAnalyzer I Systems**

The results for glucose analyses of linearly related specimens with and without 30% ethylene glycol on these two systems are shown in Figure 4. Both systems were based on identical glucose oxidase methodology. The SMA 6/60 system shows a negative proportional bias of -7.2% for the ethylene glycol specimen set (good agreement with previously observed -8.3% bias, in Table 3); the AutoAnalyzer I system shows a bias of only -3.2%. Analysis of these specimens on the DuPont 6000 (not shown) showed no bias, with virtually identical analyses for both specimen sets. These results indicate that the degree of bias caused by ethylene glycol is dependent on the dialysis system used as well as on the analyte being determined.

**Discussion**

**Design of the Evaluation Specimens**

The specimens employed in this study were carefully designed to be identical in every respect except for the particular variable(s) under investigation, and to have to known quantitative relationships for the variable(s) (Figure 1 and Table 1). Because of the design of the specimens, a straight line having a known slope should be observed when the analytical results are graphed against the known composition of the specimens (Figure 2). In this way, the results from all systems evaluated may be compared to one another, as well as to known properties of the specimens. That is, the known properties of the reference specimen (rather than results obtained by a reference method) were used as the basis for comparisons.

The specimens also were designed to have informational redundancies that served to confirm that the specimens in fact had been prepared as they were intended to be prepared. For example, several analytes were included in each diluent (Figure 1), and consequently all of these analytes have identical values along the abscissa (% supplementation) when graphed as in Figure 2. Thus, the observation that the analytical results for all analytes were linear confirms that the aqueous and ethylene glycol sets of specimens did in fact have identical relationships, as planned. In addition, as corresponding pairs of the aqueous and ethylene glycol specimens were analyzed together, any differences observed may be attributed solely to the different matrices, and not to differences in analyte gradients of the sets of specimens, or to vagaries of the analytical system at the time of analysis.

**Effect of Ethylene Glycol on Clinical Chemical Assays**

Our experiments (Figures 2 and Table 3) show quite clearly that ethylene glycol can introduce significant bias in some analytical systems, while having virtually no effect in other systems. The systems affected by ethylene glycol share the common feature that dialysis is employed in the analytical procedure. Analyses for glucose, uric acid, creatinine, urea nitrogen, and calcium were subject to negative proportional bias when assayed in the presence of ethylene glycol in systems involving dialysis. Analyses for these same analytes were unaffected by ethylene glycol when assayed in systems not involving dialysis. In the case of uric acid, calcium, and glucose, the biases were -13.3, -10.0, and -8.3%, respectively; bias was dependent on the concentration of ethylene glycol (Figure 3) and independent of serum protein concentration.

In all cases the bias was directly proportional to analyte concentration (Figure 2 and Table 3) rather than constant at all analyte concentrations. Such bias is possibly due to an effect of ethylene glycol on the rate of dialysis of analyte. In most systems involving dialysis, dialysis ordinarily is far from complete and only a small fraction of total analyte is actually dialed and available for analysis. Under these conditions, small changes in solvent viscosity or osmolality, or in membrane permeability, should be expected to significantly affect
the concentration of analyte actually assayed in the recipient stream. A change in rate of dialysis should be expected to cause proportional biases, as were observed, and the effect should be expected to vary among dialysis systems that use different membrane configurations, as was observed (Figure 4).

Significance of Results

Liquid serum products containing about 30% ethylene glycol are now marketed for use in quality control (4) and for calibration of analytical systems (18). We did not use these products in our studies because the identical sets of aqueous and ethylene glycol specimens necessary for the study could not be prepared directly from the commercial products. Nevertheless, we believe our results are relevant for these products because the manufacturer's package insert lists assay values for a variety of analytical systems, and the biases (and lack of biases) evident in those data are quite comparable to those we observed.

Our results confirm that ethylene glycol-based specimens can have useful applications in many areas of clinical chemistry. Our evaluation procedure was quite rigorous, and we were unable to detect any significant bias attributable to ethylene glycol with any of the seven direct-chemistry procedures we studied. On the other hand, the usefulness of ethylene glycol-based specimens may be constrained by matrix effects in analytical systems that involve dialysis. We observed significant bias, clearly attributable to ethylene glycol, in each of the eight dialysis procedures we studied, and the degree of bias varied with the analyte and the type of dialysis system used.

To a large extent, the quality of clinical chemistry analyses is determined by the quality of commercial materials available to laboratories, and by laboratorians' understanding of the uses and limitations of those products. The occurrence of bias from the materials used in a commercial control or calibration material is, of course, not unique to liquid serum preparations. Most lyophilized quality-control and calibration sera have assay, or target, values assigned that also vary among methods or analytical systems because of the presence of nonspecific reactants, or interferences, in the products. These inadequacies of lyophilized products have not precluded their effective use because, with knowledge of the nature of the biases, various analytical ploys are used to compensate for the bias. It should be of more than academic interest to observe how laboratorians will compensate for some of the biases that are apparently inherent to these new liquid serum preparations.

References

16. Test Methodology Bulletins, PN 703700, PN 703708, PN 703709, PN 703723, PN 703701C, DuPont Co., Wilmington, DE 19888.