penate for these differences, Maas et al. (2) recommend that the ISE value should be multiplied by an appropriate factor to obtain the same result for substance concentration as that obtained by flame photometry for normal plasma. However, if the adjustment is to be made accurately, and applied to abnormal specimens, the influence of protein concentration must be taken into account.

We investigated this by analyzing a batch of serum specimens from hospital patients for Na⁺ and K⁺ with four direct ISE analyzers (Corning 614, Kone Microlyte, Nova 1, and Radiometer KNA-1) and by flame photometry. We used a different batch of sera for each ISE analyzer but the same IL 543 (Instrumentation Laboratory) flame photometer throughout. Analysis of reference sera (including National Bureau of Standards SRM 909) showed no consistent bias in the flame photometer results. Na⁺ concentrations in the specimens ranged from 110 to 160 mmol/L, total protein from 40 to 100 g/L. Specimens with evidence of hyperlipidemia were excluded.

The ISE–flame photometer differences in Na⁺ concentration were found to be linearly related to the total protein concentration in specimens in which the lipid concentration was presumed to be normal. Table 1 summarizes the results for the four instruments. The magnitude of the mean ISE–flame photometer difference varies with the instrument, but in each case it is significantly correlated with protein concentration. For these four instruments the slopes of the regression lines are similar but the intercepts are different. Others (3) have suggested that paraproteins may behave anomalously, possibly because they bind more water, but we found no evidence that results for such specimens differed significantly from the regression lines for total protein concentration.

It is therefore necessary to define the protein concentration of specimens for which the ISE–flame photometer difference will be zero. We suggest that the most appropriate protein value would be 70 g/L. From the slope of the regression line, a change of 10 g/L in protein concentration would produce a shift of approximately 1.4 mmol/L in plasma sodium concentration. Patients' specimens with total protein concentrations in the range 40 to 100 g/L would then be expected to show ISE–flame photometer differences of about ±4 mmol/L, ISEs could then be calibrated (or the calibration verified) for Na⁺ with an authenticated reference serum having a total protein concentration close to 70 g/L.

We also found a good correlation (r = 0.73) between the ISE–flame photometer differences for serum Na⁺ and K⁺, suggesting that both of these analytes are affected by the same factor, namely, the water content of serum. Levy (4) estimated the shift in serum Na⁺ concentration that would be expected from changes in serum water content for different protein and lipid concentrations. His data indicate that a change of 50 g/L in protein concentration would result in a shift of 5.7 mmol/L in measured Na⁺ concentration, which is close to the average shift (7.0 mmol/L) we found for these four instruments.

We therefore propose that all direct-reading ISEs should be adjusted so that they give the same values for Na⁺ in plasma or serum as those obtained by flame photometry at a total protein concentration of 70 g/L. Quality-control specimens used with ISEs should have a protein concentration near 70 g/L. The slopes of the regression lines for the instruments we have examined are similar; thus, all ISEs should then give the same results at other protein concentrations and with hyperlipidemic specimens, where the ISE–flame photometer difference may be much larger. The approach we have used provides a basis for relating results obtained by direct and indirect methods and for interpreting plasma Na⁺ concentrations in specimens with abnormal water content due to hyperproteinemia or hyperlipidemia.

<table>
<thead>
<tr>
<th>Table 1. Regression Statistics for Serum Na⁺ Differences at Different Protein Concentrations</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>No. of</strong></td>
</tr>
<tr>
<td><strong>samples</strong></td>
</tr>
<tr>
<td>Corning 614</td>
</tr>
<tr>
<td>Kone Microlyte</td>
</tr>
<tr>
<td>Nova 1</td>
</tr>
<tr>
<td>Radiometer KNA-1</td>
</tr>
</tbody>
</table>

*Correlation coefficient of ISE–flame photometer difference with total protein concentration; p < 0.001 for all r values.*

References


P. M. G. Broughton
S. C. H. Smith
B. M. Buckley

Wolfson Res. Labs.
Queen Elizabeth Med. Centre
Birmingham B15 2TH, U.K.

Problems with Transporting Serum to the Laboratory for Cryoglobulin Assay: A Solution

To the Editor:

Demonstration of cryoglobulin in a patient's serum is clinically important, both in diagnosis and in understanding the pathophysiology of the symptoms. Cryoglobulins are found in the serum of patients with multiple myeloma, with other B-cell neoplasms, and with conditions commonly accompanied by hypergammaglobulinemia, such as autoimmune diseases and chronic infections (1–3).

Many articles and reviews concerning cryoglobulinemia exhort caution in handling the specimen: it should be drawn in a prewarmed syringe and maintained at 37 °C while being transported to the laboratory (4). Unfortunately, little guidance has been provided as to just how to do this. Some say to place the sample close to the body, such as under an armpit, in a pocket, or worse! Aside from the aesthetic problems with this approach, samples from patients with potentially highly contagious diseases should not be so handled. Another approach has been to place the tube containing the specimen in a cup of water at 37 °C for transportation to the laboratory. Again, this entails considerable subjectivity. Some individuals will measure the temperature of the water, or take it from a water bath controlled at 37 °C, but too often they simply use the hot-water tap. Aside from such variation in the initial temperature, the insulation provided by the typical Styrofoam cup is not satisfactory.

We observed that many specimens for cryoglobulin assay are at room temperature by the time they reach our laboratory. Thus, we have devised a simple procedure for specimen transportation, using a thermos bottle filled with sand at 37 °C. This approach can
keep the temperature of a sample constant for intra- or even interhospital transportation.

As shown in Figure 1, the temperature stability in this simple device is considerably better than in water at 37 °C, even under well-controlled conditions for the latter. To determine the effects of using this method on the quality of the specimens received for cryoglobulin assay, and, more importantly, on the yield of positive samples, we recorded the temperature of and final results for all specimens received for cryoglobulin analysis during four months. During this interval we received a total of 120 such specimens, 73 in sand (in a thermos), 43 in water (in a Styrofoam cup), and four that were kept in the axilla or in the palm during transport. The temperatures of the samples at the time of receipt differed considerably, the respective mean temperatures for sand- and water-transferred samples being 36.1 °C (SD 2.5, range 31.5–41) and 30.7 °C (SD 2.7, range 25.0–35). Of the samples received in sand, nine (11%) were positive for cryoglobulin, and of those in water, two (5%) were. The hand-carried samples were not found to have cryoglobulin.

Quantification of serum cryoglobulins is a time-consuming and expensive procedure, but it can have considerable clinical relevance. This simple transportation device improves the chances of receiving a specimen that is useful for laboratory study.

References


Fig. 1. Temperatures of water under various conditions of transportation for 1 h
Almost no change in temperature of the water was seen when it was placed in sand at 37 °C in a thermos bottle (closed circles), but there was a marked, rapid decline in temperature of samples maintained in a Styrofoam cup with either sand at 37 °C (open circles) or water at 37 °C (triangles). Even the temperature of a sample placed in water at 37 °C in a thermos (open circles) declined 2 °C during 1 h. Ambient temperature: 25 °C

More on a Case of Methanol Poisoning: Error In a Procedure

To the Editor:

We would like to comment on a paper (1) that dealt with the accidental ingestion of methanol by an infant. In the study, an eight-month-old infant ingested at least 3.5 g (109 mmol) of methanol. The authors report that serum methanol concentration 8 h after this ingestion was 9.7 mmol/L (310 mg/dL) and the formate concentration was 23 mmol/L in the blood. By 21 h after the ingestion, the blood formate was reportedly about 32 mmol/L. They conclude that "despite the increase in formate to 22–24 times the adult reference limit by 21 to 32 h after the ingestion, no abnormalities of the infant's eyes were noted at approximately 55 h."

This interesting case bears further comment. It would appear to us, after a close examination of the data presented in their Figure 1 and with the information given concerning the ingestion by the infant, that the values for blood formate are extraordinarily high and that the authors' conclusions may be based on a possible calculation error. We have made the following calculations, based on the authors' information. We do not know the weight of the infant, since it was not mentioned in the article, so we assume a weight of 10 kg. Blood disappearance curves published by several authors indicate that methanol and formate distribute uniformly to body water (2–8). Therefore, if a 10-kg infant ingested 3.5 g (109 mmol) of methanol, a value for blood, extrapolated to zero time, would yield a methanol concentration in serum of about 15 mmol/L. This is approximately what would have been obtained by extrapolating to zero time the data in Figure 1 of Shahangian et al. (1).

If all of the methanol were instantly and completely metabolized to formic acid and distributed to body water, the maximum concentration of formic acid in blood at zero time would be 15 mmol/L. At 21 h after ingestion, the patient had a value for methanol in serum of 3.4 mmol/L, and the total amount of methanol in the infant's body should be 24 mmol. Thus during the first 21 h, 85 mmol of methanol would be eliminated from the body. If we assume that all the methanol eliminated during this period had been first oxidized to formate, then a maximum of 85 mmol of formate would be formed from methanol. If we further assume that none of the generated formate was oxidized to carbon dioxide during this time, we would have a maximum value for serum formate of about 13 mmol/L. But we know that formate is metabolized and excreted, thus the actual concentration of formate in the serum should be markedly lower than 13 mmol/L. Therefore, we believe that the authors made a substantial (possibly 10- to 100-fold) error at some stage of their analysis. Accordingly, their final conclusion drawn is based on lower values for formate than they report. The reason they observed no ocular toxicity may be that formate concentrations were very low during the period of measurement.

References

8. Yant WP, Schrenk HH. Distribution of methanol in dogs after inhalation and administration by stomach tube and subcuta-