

Table 1. CSF Protein and Nephelos Reading Compared for Five Pooled Human Sera with Different Albumin/Globulin Ratios

Total protein	Albumin	Albumin/globulin ratio	$y(\text{protein}) = mx(\text{nephelos}) + c$
74	37	1.00	$y = 0.0212x + 0.0397$
68	36	1.13	$y = 0.0192x + 0.0342$
71	39	1.22	$y = 0.0190x + 0.0263$
74	41	1.24	$y = 0.0195x + 0.0119$
74	44	1.47	$y = 0.0174x + 0.0160$

fied by adding a precalibrated CSF protein scale, generated by use of a diluted commercial lyophilized quality-control serum.

We investigated the validity of using lyophilized materials to construct a precalibrated scale for this nephelometric assay. We found that analyses of serial dilutions of quality-control sera showed a linear relationship between nephelometric reading and total protein; however, for different quality-control sera the slope of the line varied. We also investigated dilute human serum, which has been recommended for use as a standard (2, 3), but analyses of dilutions of pooled normal human serum of differing total protein and albumin content gave results similar to those obtained with the quality-control sera (Table 1). Evidently results obtainable by the nephelometric method are a function of the calibration material used to generate the scale. It has been well documented that the results obtained for turbidimetric methods of CSF total protein estimation with sulfosalicylic acid depend on the albumin/globulin ratio (3-5). We have shown (Table 1) that if the albumin/globulin ratio of the standard material differs from 1.0 to 1.47, a 20% difference in CSF total protein results.

We consider that there are serious problems of accuracy associated with methods of standardization, both within an individual laboratory and between laboratories. A particular problem may lie in the assay of successive fluids from the individual patients whose CSF albumin/globulin ratios may be expected to alter as recovery ensues. We therefore consider that the nephelometric method for estimation of CSF total protein is not to be recommended for routine laboratory use.

References

- Murray, K. S., Measurement of total protein in cerebrospinal fluid with the Perkin-Elmer Amylase-Lipase Analyzer. *Clin. Chem.* 23, 1366 (1977).
- Gotelli, G., Weingartner, D., and Marton, L. J., Source of error in cerebrospinal fluid determination with the Du Pont Automatic Clinical Analyzer. *Clin. Chem.* 24, 173 (1978).
- Henry, R. J., Cannon, D. C., and Winkelman, J. W., *Clinical Chemistry—Principles and Technics*, 2nd ed., Harper & Row, Publishers, Inc., Hagerstown, MD, 1974, p 423.

4. Meulemans, O., Determination of total protein in spinal fluid with sulphosalicylic acid and trichloroacetic acid. *Clin. Chim. Acta* 5, 757 (1960).

5. Sethna, S., and Tsao, M. U., Protein level in cerebrospinal fluid. An evaluation of some methods of determination. *Clin. Chem.* 3, 249 (1957).

Bette C. Smith
L. A. Penberthy

Flinders Medical Centre
Bedford Park
South Australia 5042

Normal Range for Serum Sodium by Ion-Selective Electrode Analysis Exceeds That by Flame Photometry

To the Editor:

We wish to report our experience with a NOVA 1 Ion-Selective Electrode Analyzer for Sodium and Potassium (Nova Biomedical, Newton, MA) recently marketed in the United Kingdom by American Hospital Supply (U.K.) Ltd., Didcot, Oxon. An instrument supplied for a trial period in our laboratory produced results for plasma and serum sodium that differed significantly from those obtained by flame photometry.

In the NOVA 1, ion-selective electrodes measure sodium and potassium in whole-blood plasma, separated plasma or serum, or urine. A microprocessor automatically measures sodium and potassium in an aqueous standard with each specimen and performs a two-point calibration of the electrodes at 2-h intervals.

During a trial period of 14 days we evaluated the instrument by measuring sodium and potassium in serum and plasma and comparing the results with those obtained when the same samples were analyzed with a Technicon SMA 6/60 analyzer. The analytical precision of the NOVA 1, assessed by replicate analyses of a commercial control serum, was found to be acceptable. For 92 measurements each during 14 days, sodium values were 142.77 ± 1.15 mmol/L (mean \pm SD), with a coefficient of variation (CV) of 0.81%; potassium values were 3.92 ± 0.052 mmol/L (mean \pm SD), with a CV of 1.33%.

However, when we analyzed 84 specimens of heparinized plasma from hospital patients, the difference between the plasma potassium means for the NOVA 1 and the SMA 6/60 was +0.008 mmol/L, but the difference between the plasma sodium means was +5.6 mmol/L. For sodium, the differences ranged from 0 to 11 mmol/L in individual specimens.

These differences between the sodium values from the NOVA 1 and the SMA 6/60 were larger than either we or Nova Biomedical had expected. Specimens of serum and plasma from seven patients and six normal subjects were sent to Nova Biomedical in the United States, who confirmed the large sodium differences between ion-selective electrode analysis and flame photometric analysis, and excluded the possibility that the differences were due to any instrument or standardization error.

The wide range of sodium differences in patients' samples led us to investigate the comparison between NOVA 1 and the SMA 6/60 for normal serum specimens. Blood was collected from 22 members of the laboratory staff in apparent good health, allowed to clot for 1 h, centrifuged, and the serum was separated. The difference between the serum potassium means for the NOVA 1 and the SMA 6/60 was +0.049 mmol/L, and between the sodium means was +4.7 mmol/L. The differences in serum sodium in individual specimens ranged from +3 to +6 mmol/L.

The current edition of the NOVA 1 operating manual states that the values for serum sodium and potassium are similar to those obtained by other methods of measurement, such as flame photometry, and the sodium reference range quoted applies to sodium determined by flame photometry. Our results, obtained from normal serum samples, give the following ranges (mmol/L) for sodium and potassium (mean \pm 2SD):

	Na	K
SMA 6/60	137-144	3.5-5.0
NOVA 1	142-148	3.6-5.0

Our finding of a higher normal range for serum sodium confirms the finding of Patal and O'Gorman (1), who evaluated another ion-selective electrode analyzer (Space Stat 30; Orion Biomedical).

It is important that these differences between the ranges for normal values for sodium as measured with ion-selective electrodes and flame photometry be known, particularly in a laboratory where both types of instrument are used.

We have informed Nova Biomedical of our findings of a significant difference in values obtained for plasma and serum sodium when measured by ion-selective electrodes as compared to flame pho-

tometry. We understand that they intend to amend the NOVA 1 operating manual accordingly.

References

1. Patal, S., and O'Gorman, P., Evaluation of the Space Stat 30 Sodium/Potassium Ion Analyzer. *Clin. Chem.* 24, 1856 (1978).

**W. Annan
N. A. Kirwan
W. S. Robertson**

*Biochemistry Department
Royal Infirmary
Anlaby Rd, Hull HU3 2JZ, U.K.*

Another Case of Double Light-Chain Disease

To the Editor:

We read with interest the paper on "double light-chain disease" by F. R. Dalal and S. Winsten (1). This kind of myeloma seems very rare. However, we have had the opportunity to observe one case (2).

The patient, a 79-year-old man, presented with anemia, bone pains, and osteolytic lesions of the skull. The bone-marrow aspirate showed 75% plasma cells, with abnormal aspects. Standard electrophoresis of the patient's serum on cellulose acetate showed marked hypogammaglobulinemia with a distinct homogeneous band in the cathodic position. This band was a lambda light-chain M component. The trichloroacetic precipitation procedure indicated its urinary excretion to be 10 g/L (18 g/24 h). With concentrated urines an antiserum to Bence Jones proteins revealed two precipitation lines. The most anodic corresponded to kappa light-chain M component; the most cathodic one migrated to the same place as the serum M component and was of the same type: lambda light-chain. A urine sample was chromatographed on a DEAE A50 (Pharmacia, Uppsala) column to separate each protein. Then, with M. Fougereau and C. Schiff (CNRS, Marseille) we attempted the biochemical characterization of the components. By analytical separation of the peptides obtained on tryptic hy-

drolisis, and from the amino acid composition and determination of the NH₂-terminus residues, we concluded that the variable parts of these two light-chains were different. Unfortunately, as in the case reported by Dalal and Winsten, the patient died before immunofluorescence studies were performed.

References

1. Dalal, F. R., and Winsten, S., Double light-chain disease: A case report. *Clin. Chem.* 25, 190-192 (1979).
2. Gibaud, A., Schiff, C., Gibaud, H., and Fougereau, M., Caractérisation biochimique de deux protéines de Bence Jones isotypiquement différentes chez un même malade. *Lyon Med.* 236, 141-144 (1976).

**A. Gibaud
H. Gibaud**

*Laboratoire de Biochimie
Hôpital de Bellevue
Boulevard Pasteur
F 42100 Saint-Etienne
Loire, France*