used for "SuperSTAT" bedside testing, as suggested by Ng et al. (1), this temperature bias must be taken into consideration. For example, mixing a sample by rolling the container between the palms should be avoided because this also will affect the sample temperature. Finally, the influence of different control-sample temperatures on precision (e.g., quality-control plots) should be stated explicitly by the manufacturer in the product information. Making this emphasis in product documentation will be helpful because the instrument is being marketed for use by nontechnical operators.

References

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An author of reference 1 responds:

To the Editor:

It is well known that ion-selective electrodes exhibit temperature sensitivity. However, in practice, the effect of sample temperature is small, at least for sodium and potassium measurements. This is partly because the sample temperature is usually between 25 and 30 °C after exposure to the collection tube and the instrument.

The variations of results from 25.5 to 30.4 °C found by Metzger and Kenny were well within the expected precision we had experienced with room-temperature specimens analyzed with the ChemPro-1000, i.e., CVs of 2.3–3.5% for potassium, and 0.6–1.7% for sodium. Furthermore, the small number of analyses at each temperature in their study makes it difficult to conclude that there is a significant bias in accuracy between 25.5 ± 0.5 °C.

Finally, it is clearly stated in the manufacturer's package insert that refrigerated specimens should be equilibrated to room temperature before analysis.

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More on Determination of Ionized Calcium in Blood with Ion-Selective Electrodes

To the Editor:

I read with interest the remarkable review of Bowers et al. (1) in which they report their success in offering ionized calcium determinations in serum as a routine service. I would like to emphasize a few points in relation to this subject.

As early as the late sixties, we were able to provide such a service with the first syringe-pump Orion equipment, especially for patients undergoing hemodialysis (2, 3). This success was made possible by the use of a particular standardizing protocol (4), using modified (frozen-stored) serum pools alternating with the unknown specimens in place of the aqueous standards recommended by the manufacturer. At the time we did not yet know much about residual liquid junction potential variations; this was our empirically found way to obtain stable readings and reproducible results. In fact, our main problem was in connection with the necessity of making the electrodes, a procedure yielding poor positive results.

In their section on Ca2+ analyzers, Bowers et al. include, along with apparatuses that were in use for several years in (advanced) laboratories, instruments that never worked—or only a few examples did. I think it unfair to those manufacturers who permitted the real progress in this field not to state straightforwardly the major contributions: first Orion with the syringe-pump from 1966 to 1974, then the SS-20 until the early eighties, which were the only reliable working machines on the market. Then from 1980 came the breakthrough from Radiometer with the first modern automat (ICA-1) and, in more recent years, the second series of the Nova Biomedical equipments (Nova-8). We personally tested unsuccessfully the Nova-2 (1979), AVL's Model 980, and the Kone Microlyte (1862).

Along with differences of calibrator matrix and reference electrodes, a major cause for differences in the final result for Ca2+ was the use in these instruments of various ion-selective sensors (without disclosing this openly to the user). One of our quality-control procedures was a monthly determination of Ca2+ on 20 members of our staff. In November 1978 the mean value of the measurements on our SS-20 jumped suddenly (Figure 1), and also became more stable. We interpreted this as an improvement in the electrode and reported it to the manufacturer, questioning if there had been a modification in the electrode preparation. The positive answer only came one year later when we learned that it corresponded to a switch from organophosphate to a neutral carrier exchanger. In the early eighties the existence of the chronobiological variability of Ca2+, shown by the crossing over of the Ca2+ and the 25-hydroxycholecalciferol curves, was recognized. A retrospective study showed that the apparent stability observed in 1975–79 was attributable to low sensitivity of the first neutral carrier electrodes, as opposed to the "instability" observed in 1977 and from 1980 on, which corresponded to a greater sensitivity.

The importance of pre-analytical errors (5) led us to impose blood sampling by our own departmental staff in clinical cases in which minor deviations of Ca2+ from "normality" are expected, as in early diagnosis of hyperparathyroidism. When Ca2+ results are urgently requested, one has to use heparinized blood. To avoid major changes by chelation, the concentration of sodium heparinate should not exceed 15 kilo-int. units per liter of whole blood (6), a value that can be increased to 50 by using calcium-titrated sodium heparinate (7). A non-negligible "dilution-error" might occur when an anticoagulant is used in an aqueous form, especially in small-volume samples from pediatric patients (8). The use of dry capillaries (Radiometer D-951 Clinitubes) or syringes (Radiometer B-129 Heparinized Blood Samplers) avoids this dilution error, but a "calcium-dilution" error, observed at low and high concentrations, may still persist.

The absence of an internationally recognized reference value system is definitely a drawback in clinical interpretation of Ca2+ results. The use of the pH 7.40-normalized Ca2+ value is certainly a way towards the definition of a simple (and possibly single) reference interval. Nevertheless, one has to keep in mind that such a pH "correction" is acceptable only as long as the calcium buffer capacity of the specimen serves as a function of pH is effectively well.

Fig. 1. Mean (20 healthy subjects) ionized calcium (1977–1982) and 25-hydroxycholecalciferol (1980–1982) in serum