

**Table 1. Electrolyte 2 Analyzer Results Compared with Those by Flame Photometry**

	Na	K
<i>Flame photometry</i>		
Mean, mmol/L	64.4	25.6
Range, mmol/L	28–112	10–50
<i>ISE</i>		
Mean, mmol/L	59.6	23.3
Range, mmol/L	27–105	9–47
n	36	36
p	<0.001	<0.001
r	0.988	0.992

and chlorhexidine gluconate (Hibitane), separately and together, and found that neither additive significantly affected values obtained with the Electrolyte 2 Analyzer. Results from the IL 501 were unaffected by Hibitane, but acidification rendered both sodium and potassium unreadable.

Thirty-six 24-h urine samples collected in the presence of Hibitane (200 g/L, 5 ml/L of urine) and subsequently acidified to pH  $\leq 2$  by the addition of concentrated HCl were analyzed with the Electrolyte 2 Analyzer and the flame photometer. I used Student's paired *t*-test to compare the results obtained by the two methods; correlation coefficients were obtained by using a least-squares method. Table 1 shows the results obtained. Correlation between the two methods was good, but the results differed significantly. Sodium results averaged 4 mmol/L lower by ISE than by flame photometry, and potassium results were 2 mmol/L lower.

A further 36 urine samples, obtained without additives and selected without conscious bias from in-patients at this Centre were analyzed by flame photometry and with the IL 501 Analyzer according to the procedure specified by the manufacturer (Table 2). For sodium, the two methods correlated well but the results differed significantly. For potassium the reverse was true: the results did not differ significantly, but the correlation was not as good.

Because of the poor results for potassium with the IL 501, I also tested urine specimens without dilution, with a different dilution factor, and with different diluents: de-ionized water; Tris, 50, 100, 200, 1000, and 2000 mmol/L, all at pH 8.0; imidazole, 10, 100, and 1000 mmol/L, all at pH 7.0; MgCl<sub>2</sub>, 200 and 1000 mmol/L; and a solution containing, per litre, 130 mmol of MgCl<sub>2</sub> and 24.8 mmol of Tris, pH 8.0. The highest concentration of Tris gave a sigmoid calibration curve. Taking into account both linearity of calibration and correlation with the results of flame photometry, the best results were obtained with the last-named diluent,

**Table 2. IL 501 Analyzer Results Compared with Those by Flame Photometry**

	Na	K
<i>Flame photometry</i>		
Mean, mmol/L	62.7	26.4
Range, mmol/L	24–133	9–69
<i>ISE<sup>a</sup></i>		
Mean, mmol/L	58.0	27.6
Range, mmol/L	25–120	8–80
n	36	36
p	<0.001	0.3 < p
r	0.988	<0.4
<i>ISE<sup>b</sup></i>		
Mean, mmol/L	59.0	22.6
Range, mmol/L	20–131	8–58
n	36	36
p	<0.001	<0.001
r	0.991	0.993

<sup>a</sup> Manufacturer's procedure: sample undiluted for sodium, diluted 10-fold for potassium. <sup>b</sup> Modified procedure: samples for both analytes diluted with equal volumes of Tris/MgCl<sub>2</sub> diluent as specified in text.

which was similar in composition to the diluent marketed by the manufacturer but used in different dilutions. Table 2 shows these latter results, which also differed significantly from those of flame photometry. For potassium the difference was close to zero at 10 mmol/L, but 10 mmol/L in the region of 50 mmol/L.

Contrary to my expectation, results obtained by flame photometry correlated well with results with the two ISE analyzers. This was, however, in agreement with other reports (1, 2). Evidently a small dilution sufficed to eliminate serious errors associated with ionic strength, pH, or ion-binding effects.

Both analyzers are simple and convenient to operate, if one considers their differences in sophistication and cost. The ionic strength and protein content of the urine samples were not measured, nor was the concentration of ammonium which is known, when high, to cause positive error with the potassium electrode (3).

I observed significant systematic errors with both ISE instruments, a feature that should be taken into account in interpreting data when strict accuracy is required. The fact that the procedures recommended by one manufacturer could be improved upon should also be noted.

I am grateful to Beckman Instruments International SA and Instrumentation Laboratory Inc. for loan of their equipment and to Dr. D. J. Reynolds for the flame photometric analyses.

**References**

1. Annan, W., Kirwan, N. A., Robertson, W.

S., et al., An evaluation of the Nova 1 ion-selective electrode analyzer for sodium and potassium determination. *J. Autom. Chem.* 2, 212–218 (1980).

2. Truchard, A., Hersant, J., Glikmanas, G., et al., Parallel evaluation of Astra 8 and Astra 4 multichannel analyzers in two hospital laboratories. *Clin. Chem.* 26, 139–147 (1980).

3. Chittenden, C., Application of ion-selective sodium and potassium electrodes for characterization of interferences using the Beckman Automated Stat Routine Analyzer (Astra). Astra Clinical Applications. Beckman Instruments Inc., Brea, CA, 1979.

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**Decreased Serum Alkaline Phosphatase Activity in Hypothyroidism: Possible Relationship to Low Serum Zinc and Magnesium**

*To the Editor:*

Low alkaline phosphatase (EC 3.1.3.1.) activity in serum has been reported in patients with hypothyroidism (1). The reason for this decrease is not precisely known. Here I describe a patient with severe hypothyroidism who had a low serum alkaline phosphatase that was probably related to low concentrations of magnesium and zinc in the serum. Some other interesting features of this case are also discussed.

A 74-year-old woman with idiopathic hypothyroidism, diagnosed five years earlier, was admitted to the emergency room in coma. Her temperature was 32 °C, pulse 48/min, and blood pressure 100/30 mmHg. Her other features characteristic of severe hypothyroidism included a puffy face, hoarse voice, enlarged tongue, and a coarse and dry skin. Results of cardiovascular, respiratory, and abdominal examination were normal. Neurological examination showed deep tendon reflexes to be absent. A diagnosis of myxedema coma was made.

Concentrations of some analytes in serum at admission were (per liter): sodium 116 mmol, potassium 2.5 mmol, chloride 80 mmol, total carbon dioxide 23 mmol, urea nitrogen 140 mg, and creatinine 10 mg. Serum enzyme activities (U/L) were: creatine kinase 1448 (normal 20–215), lactate dehydrogenase 307 (normal 90–210), and aspartate aminotransferase 91 (normal 5–35).

Serum albumin concentration was subnormal, 32 g/L (normal 35–50). Serum thyroxine concentration was 7 µg/L (normal 50–120), the free thyroxine index 0.3 (normal 2.2–4.7), thyrotropic hormone >40 int. units/L (normal <9). Data on serum phosphorus (normal =

**Table 1. Values for Zn, Mg, Alkaline Phosphatase (ALP), Thyroxin (T4), Phosphorus (PO<sub>4</sub>), and Creatine Kinase (CK) in Serum<sup>a</sup>**

Days after admission	Zn, µg/L	Mg, mg/L	ALP, U/L	T4, µg/L	PO <sub>4</sub> , mg/L	CK, U/L
0	390	10	31 (33) <sup>b</sup>	7	22	1448
3		17	69	85	6	1131
6	840	19	76	79	6	
8						270
12		22	112			

<sup>a</sup> Reference values as given in the text. <sup>b</sup> Measurement in parentheses made the next day.

25–45 mg/L), magnesium (normal = 18–28 mg/L), zinc (normal = 500–1200 µg/L), alkaline phosphatase (normal = 45–125 U/L), creatine kinase (normal = 25–215 U/L), and thyroxin during the hospital stay are shown in Table 1.

The patient was placed in the intensive care unit, where she was treated with intravenous thyroxin and steroids. She gradually improved and was transferred to a regular medical ward one week after admission.

This patient exhibited several interesting features. An association between low alkaline phosphatase and hypothyroidism has been reported previously (1), but the reason for it is not known. Here it occurred with low concentrations of zinc and magnesium in the serum. Both zinc and magnesium are necessary for optimal activity of alkaline phosphatase in serum (2), so the decrease in alkaline phosphatase could have been related to the subnormal concentrations of these cations. In harmony with this hypothesis, alkaline phosphatase activity became normal concurrently with zinc and magnesium. Furthermore, decreased serum alkaline phosphatase activity has been described in association with low zinc concentrations in patients who are receiving total parenteral nutrition (3) and in cases of hypomagnesemia (4).

Another interesting feature is the marked decrease in serum phosphorus after initiation of intravenous thyroxin therapy. This, to my knowledge, has not been previously reported. Thyroid hormone is known to stimulate adenosine triphosphatase (EC 3.6.1.3) activity, resulting in increased oxygen consumption by the cell (5). This increased oxygen consumption is accompanied by cellular uptake of phosphorus (6), which could lead to depletion of serum phosphate. This patient, however, demonstrated no clinically detectable abnormalities associated with hypophosphatemia, nor were any other factors known to cause severe hypophosphatemia present (7). The presence of hyponatremia and the increase in serum creatine kinase (EC 2.7.3.2) activity are well-established features of hypothyroidism (8).

In conclusion, a decreased activity of alkaline phosphatase in serum in patients with hypothyroidism may be as-

cribable to low concentrations of zinc and magnesium serum. The activity of this enzyme could therefore serve as an indicator of the concentrations of these cations in serum. Also, serum phosphorus may markedly decrease after treatment of severely hypothyroid patients with intravenous thyroxin.

#### References

- Fraser, D., Hypophosphatasia. *Am. J. Med.* 22, 730–746 (1957).
- Chen, S. T., Alkaline phosphatase. *Front. Gastrointest. Res.* 2, 109–149 (1976).
- Ishikawa, A., Tsuchida, F., and Ishii, T., Clinical zinc deficiency during zinc-supplemented parenteral nutrition. *J. Pediatr.* 99, 339 (1981). Letter.
- Pimstone, B., Eisenberg, E., and Stallone, W., Decrease in serum alkaline phosphatase activity produced by magnesium deficiency. *Proc. Soc. Exp. Biol. Med.* 123, 201–203 (1966).
- Edelman, I. S., Thyroid thermogenesis. *N. Engl. J. Med.* 290, 1303–1308 (1974).
- Sterling, K., Milch, P.O., and Brenner, M.A., Thyroid hormone action: The mitochondrial pathway. *Science* 197, 996–999 (1977).
- Knochel, J. P., The pathophysiology and clinical characteristics of severe hypophosphatemia. *Arch. Intern. Med.* 137, 203–220 (1977).
- Spaulding, S. W., and Utiger, R. D. Hypothyroidism. In *Endocrinology and Metabolism*, P. Felig, et al., Eds., McGraw-Hill, New York, NY, 1981, pp 326–338.

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#### The Test-Assessment Chart

To the Editor:

The variance of the concentration, activity, etc. of any serum constituent of healthy individuals may be divided, following the suggestion by Van Steirteghem et al. (1), into three main components: (a) the intra-individual component of variance, reflecting the range within which a variable may fluctuate in one individual subject (within a certain period of time); (b) the interindividual component, determined by the scatter (i.e., differences) among many subjects;

and (c) the so-called analytical component, comprising all variations (or errors) in the preinstrumental and (or) instrumental phase of the analytical processes. Quantitative *a priori* information about all three types of variations can be a useful prerequisite for any competent judgment on a laboratory result.

Van Steirteghem et al. (1) showed three-dimensional representations of such data. Their figures, however, are not easily understandable with respect to critical relations such as analytical to intra-individual variations. In fact, a test may be more usefully assessed on the basis of the quotients of the three components of variance (rather than on the basis of their absolute values).

We therefore have recently proposed to graph (two-dimensionally) the ratios of analytical to intra-individual ranges (ordinate) vs the ratios of intra-individual to interindividual ranges (abscissa) (2). In this double-logarithmic plot the loci of constant analytical to interindividual variations are the “diagonals” (straight lines at an angle of -45°). A selection of test parameters is shown in this fashion in the “test-assessment chart” of Figure 1. It repro-

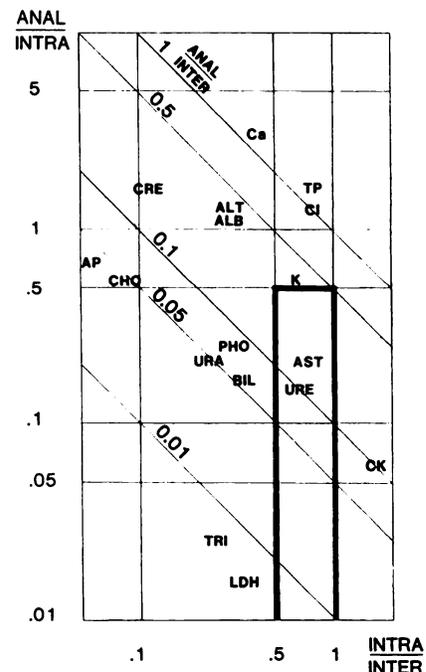


Fig. 1. The test-assessment chart: ratio of analytical to intra-individual variances (ordinate) vs the ratio of intra- to interindividual variances (abscissa), in a double-logarithmic net

The diagonal lines give the ratio of analytical to interindividual variances. Data from (1). Abbreviations: ALB, albumin; ALT, alanine aminotransferase (EC 2.6.1.2); AP, alkaline phosphatase (EC 3.1.3.1); AST, aspartate aminotransferase (EC 2.6.1.1); BIL, bilirubin total; Ca, calcium; CHO, total cholesterol; CK, creatine kinase (EC 2.7.3.2); Cl, chloride; CRE, creatinine; K, potassium; LDH, lactate dehydrogenase (EC 1.1.1.27); PHO, phosphorus, inorganic; TP, protein, total; TRI, triglycerides; URA, uric acid; and URE, urea nitrogen