niques for obtaining \( P \) values by means of the \( z \) statistic. In the general case of ROC plots for two different tests applied to the same set of patients, account must be taken of the correlation between the areas under each curve because, clearly, these are related. Zweig and Campbell discuss the importance of this aspect in their recent review (3).

In conclusion, we believe that the provision of such details would result in a more satisfactory presentation of ROC plot data published in Clinical Chemistry.

References

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Editor's Note: We encourage authors to follow these eminently sensible guidelines. We favor use of computer programs rather than the "cut-and-weigh" approach, to decrease concern about person-to-person variability. A reviewer points out that a majority of the deficiencies tabulated above for ROC curves were found in the older papers. For example, standard errors of areas under the curves and \( z \)-values were provided in no papers in 1992 but were in 90–92% of relevant full-length papers in 1994. Similarly, ROC areas were provided in 14%, 43%, and 62% of the papers published in 1992, 1993, and 1994, respectively. We shall expect all percentages to approach 100% in the near future.

Adjustment of Total Calcium with Results for BCP Albumin

To the Editor:

Ionized calcium assay is unavailable in many laboratories and impractical to perform on the numbers screened for disorders of calcium metabolism. Adjustment of serum total calcium for albumin concentration is widely practiced. Work suggesting that the procedure cannot yield a superior estimate of calcium status compared with total calcium (1) is refuted by more recent publications (2, 3). Increasingly aggressive management of mild primary hyperparathyroidism (4) makes it essential to avoid positive bias. However, since changing our albumin method to bromcreoul purpure (BCP), the most commonly used formula classifies 25% of samples as hypercalcemic. (Omitting the adjustment labels 20% as hypocalcemic.)

Most algorithms exploit the near-linear regression of total calcium on albumin, and reduce to the general formula

\[
[\text{calcium}]_{\text{adjusted}} = [\text{calcium}]_{\text{total}} + b(a - [\text{albumin}]_{\text{actual}})
\]

where \( a \) = "standard" albumin in g/L and \( b \) = slope of the regression line of total calcium on albumin.

Many laboratories reporting adjusted calcium use the arithmetically simple version (\( a = 40 \text{ g/L}, b = 0.025 \text{ mmol/L} \) without local validation. Laboratories not reporting adjusted calcium by default accept these constants disseminated in the literature and used by clinicians by adding 10 mg/L to total calcium for every 1 g/L albumin <40.

Published formulae are mostly based on bromcreoul green determinations of albumin, a method with variable positive bias (increasing at lower albumin values) relative to immunological reference methods and BCP (5, 6). A literature search found no algorithm based on BCP results. Additionally, none states confidence intervals or reproducibility of slope estimates. I attempted to derive more appropriate constants for BCP and incorporate additional information by gathering data from two hospitals with different case mixes over time.

Routine calcium requests are attached to nearly half of all urea and electrolyte samples received. The prevalence of disorders of calcium homeostasis in these samples will be low. This was exploited to derive regression data of calcium on albumin. Renal function profiles run on Hitachi 717 and 747 analyzers (Boehringer Mannheim, Mannheim, Germany) were retrieved from laboratory databases for five consecutive weeks and again at 5 weeks and 10 weeks thereafter. Second and subsequent results on a patient within each week were eliminated. No other a priori exclusions were made (e.g., by age, clinical condition, or source of sample). This yielded 300–500 samples per week from each hospital. To reduce the proportion of subjects with genuine (ionized) hypo- or hypercalcemia, I applied the following systematic exclusions: (a) subjects with creatinine >130 \( \mu \text{mol/L} \); (b) subjects with total calcium above the upper limit of the laboratory reference range of 2.15–2.55 mmol/L (previous work suggests that an increased total calcium has near 100% specificity for ionized hypercalcemia (2)); (c) samples identified on regression analysis as having an absolute standardized residual value >3 (this was always <2% of the samples). Regression lines were recalculated on the remaining data. The slope, \( b \), was then applied to the data, and the "standard albumin" was derived by iteration to minimize the number of individuals outside the reference range for total calcium.

Estimates of slope varied considerably from week to week (Fig. 1) but clustered around a value close to 0.011 for both laboratories. Both al-

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Fig. 1. Estimates of slope of total calcium on BCP albumin from two laboratories over time. Horizontal bars denote 95% confidence intervals.
In the Review by Watson and Scott entitled “Clinical utility of biochemical analysis of cerebrospinal fluid,” 1996;41:343–60, the total protein concentration in Table 1 should have been expressed in grams per liter (g/L), not milligrams per liter.

In the Case Report by S. Coyle, M.D. Penney, P.W. Masters, and B.E. Walker entitled “Early diagnosis of ectopic arginine vasopressin secretion,” 1993;39:152–4, in column 2, paragraph 3, page 152, and the title of Table 1, the concentration of hypertonic saline infusion should have been expressed as 50 grams per liter (g/L), not milligrams per liter.

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