appropriate control materials. The lower limit of detection for albumin by this method is 0.03 g/L. Electrophoresis of the random specimen and the 24-h urine collection (Figure 1B) on 10% cross-linked sodium dodecyl sulfate–polyacrylamide gel showed no protein of molecular mass similar to that of albumin in the random specimen. However, the sample from the 24-h urine sample obtained on the seventh day of hospitalization showed a well-defined band in the albumin region. Immunofixation electrophoresis (Figure 1A) also identified this protein as albumin. No monoclonal paraproteins were detected, but the presence of lysozyme and transferrin were demonstrated by immunofixation electrophoresis. \( \beta_2 \)-Microglobulin was not measured.

This case suggests that proteinuria with a transient decrease in albuminuria may occur in patients with similar constellations of medical problems (ischemic cardiac disease and diabetes mellitus) and drug treatment (1, 4). Data from 24-h urine collections and electrophoretic findings for comparison with subsequent urine specimens were not given in other reports (1, 4).

Our patient, however, showed continuing mild proteinuria (based on a urinary protein/creatinine ratio of 0.4 in both the random and the 24-h urine specimens) with a changing composition of urinary proteins. Albuminuria was initially undetectable by immunofixation in this patient, which differs from the findings of others (2). The apparent absence of albumin in this case of proteinuria may be a real but transient finding, possibly related to drug treatment, as suggested by previous reports (1, 2).

References

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Multilayer-Film Bromcresol Green Method for Albumin Measurement Significantly Inaccurate When Albumin/Globulin Ratio Is <0.8

To the Editor:

Recently we introduced in our "stat" laboratory a Kodak Ektachem 700XR analyzer (Eastman Kodak Co., Rochester, NY). Upon evaluating the chemistries, we observed significant discrepancies between our routine bromcresol purple (BCP) method for measuring albumin and the multilayer-film bromcresol green (BCG) method used by the Ektachem. Using orthogonal regression according to Bablok et al. (1), we calculated from results for 202 samples of unselected hospitalized patients the following regression line: \( [\text{Alb}]_{\text{Kodak}} = 0.925 \times [\text{Alb}]_{\text{BCP}} + 5.48 \) g/L \( (r = 0.93, S_{yx} = 2.2 \) g/L). Visual inspection of the graphical data revealed large discrepancies for albumin concentrations <25 g/L.

As is well known, BCG methods for measuring albumin in plasma do not always give accurate results, particularly for samples with a low albumin/globulin ratio, as in nephrotic syndrome, burns, and inflammations (2–4). The inaccuracy is particularly significant in methods involving long reaction times (>30 s). The Ektachem BCG-slide method has a reaction time of ~160 s, but was reported to yield satisfactory results in a pediatric population (5), and correlated well with a "fast reading" BCG method (6).

To verify our initial results, we analyzed a further 72 samples, selected to have albumin concentrations ranging from 10 to 50 g/L, and albumin/globulin ratios ranging from 0.26 to 2.5. We measured albumin concentrations with a rate immunonephelometric method (ICS; Beckman Instruments, Mijdrecht, The Netherlands), and compared these concentrations with those obtained with a BCP method (7) in routine use on a Hitachi...
717 analyzer (Boehringer Mannheim Diagnostics, Mannheim, F.R.G.) and the BCG slide method used on the Kodak Ektachem 700 XR (Generation 08). In addition we measured total protein in all samples by a biuret method (Hitachi 717) and calculated the albumin/globulin ratio.

The BCP method \( y \) correlated well with the ICS assay \( x \) \( (y = 1.033x - 0.52 \text{ g/L}, r = 0.994, S_{xy} = 0.78 \text{ g/L}) \), whereas the BCG slide system correlated poorly with the ICS method \( (r = 0.92, S_{xy} = 2.55 \text{ g/L}) \), showing a significant constant bias of 7.1 g/L and a negative proportional bias of 16% (slope = 0.845). Figure 1 shows the influence of the albumin/globulin ratio on the performance of the BCG slide. At low ratios there are large discrepancies between the Kodak and ICS methods. This led us to conclude that the BCG-slide method significantly overestimates albumin concentration in sera with an albumin/globulin ratio <0.8.

These findings underline the necessity of careful evaluation of new methods, and stress the superiority of BCP methods for the measurement of albumin in comparison with the widely used BCG-slide method.

References

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Investigators for Eastman Kodak respond:

To the Editor:
The letter by Leerink and Winckers continues the interesting debate over which dye-binding method is best suited for the determination of serum albumin. We recognize the limitations of the brom cresol green (BCG) approach, but point out that the lack of specificity they describe applies to all current BCG methods, not just the method on the Ektachem analyzer. When we developed the multilayer-film slide for albumin, we carefully considered the advantages and disadvantages of the BCG and BCP reactions. Finding no compelling performance advantage for BCP over a "fast" BCG method, we selected the more widely used BCG approach for the practical reasons discussed below.

When Leerink and Winckers brought their concerns to our attention, we investigated the performance of our albumin slides on 15 specimens with abnormally low albumin concentrations (15-28 g/L) and albumin/globulin ratios ranging from 0.38 to 0.96. We also used the Boehringer-Mannheim albumin/BCG method with the Hitachi 717 analyzer; the 10-s modification of the Doumas et al. BCG method (1), run on a centrifugal analyzer according to Corcoran and Dunn (2); and the Beckman rate immunonephelometric method (ICS). As our Figure 1 shows, all three BCG methods performed similarly. At albumin concentrations <30 g/L, results