Assessing Metabolic Acidosis

To the Editor:

Kost et al. (1) recently reported the case of a 10-year-old boy with diabetic ketoacidosis in whom there was a discrepancy between the value for plasma bicarbonate calculated by the blood-gas analyzer (with use of the Henderson-Hasselbalch equation) and the value for TCO₂ measured in the laboratory. They were able to calculate that at the height of the acidosis the value for pK₁ is 5.49, differing markedly from the 6.1 used by the blood-gas analyzer. We are entirely in agreement with them that the most nearly accurate estimation of the bicarbonate concentration in plasma is obtained by directly measuring the TCO₂ in arterial blood. However, we cannot agree with their statement that the assumption of constant pK₁ is no longer tenable when therapeutic decisions are necessary for acid-base management. We maintain that the characterization of an acid-base disturbance provided by the calculated value for plasma bicarbonate, as measured in a blood-gas analyzer, is quite accurate enough for clinical purposes. We have shown this to be the case in the neonate (2), and we believe that in the case reported by Kost et al. the value for calculated bicarbonate served its purpose in demonstrating that there was a profound metabolic acidosis. The use of intravenous bicarbonate in the treatment of diabetic ketoacidosis remains controversial (3), but we think that most clinicians who use intravenous bicarbonate in these circumstances would prefer to titrate the bicarbonate infusion against a series of arterial blood-gas analyses, rather than expect to calculate a "once-and-for-all" dose aimed at a particular desired plasma bicarbonate concentration. The clinical situation is by its very nature unpredictable because of the interplay of the disease state and the therapy with insulin. Because the greatest deviations in pK₁ are likely to coincide with the extremes of disordered metabolism, the value for plasma bicarbonate calculated by the blood-gas analyzer should become more nearly accurate as the patient improves—and this was indeed what happened in the case reported by Kost et al.

References


P. R. F. Dear
M. J. Henderson
St. James's University Hosp.
Beckett St.
Leeds LS9 7TF, U.K.

Follow-up of Monoclonal Gammopathies in Asymptomatic HIV-Infected Subjects

To the Editor:

Monoclonal gammopathies (MG) have been described in AIDS patients (1, 2) and, more recently, in asymptomatic subjects infected with human immunodeficiency virus (HIV) (3-5). Because the prognostic value of finding MG in these subjects is not known, we followed up these asymptomatic subjects, to determine whether their outcome differed from that of seropositive subjects without MG. Both groups of subjects were under observation in our unit.

Eight HIV-seropositive subjects (positive by ELISA, with confirmation by Western blot) with MG (six IgG kappa, two IgG lambda) were seen semiannually over a mean period of 25.5 months (range 18-30). The subjects, ages 23-45 y (mean 33) were four homosexual men, two transfusion recipients, one female partner of a high-risk subject, and one subject without known risk factors. All subjects were asymptomatic for AIDS during the study period (stage II or III according to the criteria of the U.S. Centers for Disease Control). MG was identified by immunofixation and quantified by electrophoresis on cellulose acetate. Semestral observations included physical examination (lymph nodes) and laboratory tests for CD4 and CD8 lymphocyte count; p24 antigen; anti-core (p24 and p17) antibodies; erythrocyte sedimentation rate; concentrations of IgG, IgA, and IgM in serum (quantified by laser nephelometry); and serum protein electrophoresis to detect monoclonal bands. No subject received antiviral therapy before or during the study period. Table 1 gives, for each visit, the concentration of MG and the CD4 lymphocyte count of the eight subjects over the study period. We observed the appearance of MG in five subjects (they did not have MG at the start of the study and were retro-

Table 1. Monoclonal Gammopathies during the Follow-up of Eight Asymptomatic HIV-Seropositive Subjects

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Semiannual test no.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>(204)²</td>
<td>(422)</td>
<td>(400)</td>
<td>(354)</td>
<td>(213)</td>
<td>(440)</td>
<td>(464)</td>
<td>(656)</td>
</tr>
<tr>
<td>2</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>(298)</td>
<td>ND</td>
<td>(510)</td>
<td>(370)</td>
<td>(350)</td>
<td>(420)</td>
<td>(467)</td>
<td>ND</td>
</tr>
<tr>
<td>3</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>ND</td>
<td>(311)</td>
<td>ND</td>
<td>(580)</td>
<td>(332)</td>
<td>(443)</td>
<td>(643)</td>
<td>ND</td>
</tr>
<tr>
<td>4</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>5</td>
<td>6</td>
<td>11</td>
<td>3.7</td>
<td>15+7²</td>
<td>15+7²</td>
<td>15+7²</td>
<td>ND</td>
</tr>
<tr>
<td>5</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>(210)</td>
<td>(412)</td>
<td>(300)</td>
<td>(530)</td>
<td>(240)</td>
<td>(310)</td>
<td>ND</td>
<td>ND</td>
</tr>
<tr>
<td>6</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>(220)</td>
<td>(240)</td>
<td>ND</td>
<td>(680)</td>
<td>(340)</td>
<td>(420)</td>
<td>(600)</td>
<td>ND</td>
</tr>
</tbody>
</table>

ND = not done.

¹CDC stage at start of and throughout study is listed in parentheses. ²Results shown are concentration (mg/L) or absence (—) of MG, with number of CD4 lymphocytes per microliter listed parenthetically. ³A second MG (IgG kappa) was detected at this testing.
spectively included); the disappearance of MG in three; and the appearance of a second MG (IgG kappa) in two subjects (patients D and E, last visit). Two subjects (C and E) were only recently HIV-infected, having been HIV-seronegative six months before the first visit. In all subjects of the study, no Bence Jones proteinuria was found. Also, there was no significant difference ($P > 0.05$) in mean CD4 lymphocyte count between these eight MG subjects and the 75 HIV-seropositive subjects followed in our center over the same period. The frequency of predictive markers of evolution towards AIDS—increased serum concentrations of $\beta_2$-microglobulin, neopterin (6), IgG, and IgA; increased erythrocyte sedimentation rate; reappearance of p24 antigen; and decrease of anti-core antibodies (7)—was not significantly ($P > 0.05$) greater in patients with MG than in those without.

MG was detected in certain subjects of our study who did not previously have this anomaly, proving the responsibility of HIV infection in the occurrence of this MG. The appearance or the disappearance of MG does not seem to have a prognostic significance in asymptomatic HIV-infected subjects. In our series, no different outcome appears in subjects with or without MG. The early finding of MG after seroconversion suggests that HIV may produce immunological disturbances in the first months of infection. Two evolving patterns can be distinguished for these MG: (a) the MG are transient in the HIV infection (their disappearance was observed in three patients), or (b) the MG persist, and a second component may appear (the two cases of biclonality in our series).

We conclude that the discovery of MG in asymptomatic HIV infected subjects does not indicate a poor prognosis and is not useful as a predictive marker of evolution towards AIDS.

References


Jean-Jacques Lefrere
Jean-Marius Fine
Micheline Marmeux
Patrick Lambin
Charles Salmon

Institut National de Transfusion Sanguine Rue Alexandre-Cabanel 75015 Paris, France

Preliminary Appraisal of a PR-EIA Kit for Quantifying Progesterone Receptors in Breast-Cancer Tissue

To the Editor:

Recently two reports in this journal evaluated an immunoenzyme assay for progesterone receptors (PR-EIA kit) distributed by Abbott Laboratories, Abbott Park, IL. Although Legros et al. (1) found no false positives for PR with the EIA method, in comparison with a dextran-coated charcoal assay (DCC), Smyth et al. (2) found eight of 34 cases to be falsely positive. In our laboratory we compared the DCC assay values of PR (multiple-dose titration assay and Scatchard plot analysis of data) (3) with PR-EIA results for tissue from 33 human mammary cancers and six serum samples from presumably normal human subjects. We used three PR-EIA kits from Abbott Laboratories, one of which was a gift from the manufacturer. We examined the influence of type of ligand—[$^3$H]R5020 vs [$^3$H]ORG2058—for labeling PR and of the presence or absence of 5 mmol/L sodium molybdate in the cytosol on results for PR measured by DCC vs EIA methods. As shown in Table 1, when we used 10 fmol of PR per milligram of protein as a cutoff limit for discriminating PR-positive from PR-negative tissues, two of the kits yielded an unacceptable number of false positives (of seven DCC PR-negatives, six were positive by EIA). The third kit performed better, yielding one false-positive out of five DCC PR-negatives. Neither the type of ligand used for the DCC assay nor the inclusion or omission of sodium molybdate altered the EIA results in relation to the DCC PR-negatives.

To determine whether the high degree of false positivity could be ascribed to antibody cross-reactivity with...