Letters to the Editor should be typed double-spaced (including references) with conventional margins. The overall length is limited to five manuscript pages, including not more than one figure or one table.

Reference Intervals for the Kinetic Angiotensin Converting Enzyme Assay

To the Editor:

Buttery (1) asks why, with use of basically the same method [furylacryloyl-L-phenylalanylglycylglycine (FAPGG) as substrate], there are differences in the published reference intervals for angiotensin converting enzyme (ACE, EC 3.4.15.1). In particular, he cites differences between ours (2) and that of Neels et al. (3) and asks whether an incorrect differential millimolar absorptivity (the difference in absorbance between 1 mmol/L solutions of substrate and product, referred to as "AA" by Buttery) is responsible. The differential absorptivity of FAPGG changes greatly with respect to wavelength and, as pointed out (4), may, even at the same nominal wavelength, be different in different instruments depending on the particular characteristics, such as the bandpass of the instrument. We measured the differential absorptivity at the wavelength and with the instrument we used to do the analyses and are therefore sure that the correct differential absorptivity was used. What, then, could explain the differences?

The differences in the reference intervals are, as pointed out (2), at least partly explicable on the basis of the different substrate concentrations used (0.9 mmol/L as opposed to 0.75 mmol/L). When FAPGG is used as substrate in ACE measurement, it is not possible to use concentrations greatly in excess of its K_m (0.3 mmol/L), because to do so would lead to unmeasurably high absorbances. At substrate concentrations not greatly in excess of the K_m for an enzyme, the activity of the enzyme is substrate dependent. Buttery found no effect of substrate concentration on ACE activity. This contrasts with our findings (2) and those of Ronca-Testoni (4).

We agree that the situation where there are different reference intervals is not desirable. The answer is to agree on standard conditions for ACE measurement with FAPGG as substrate. We suggest using a substrate concentration of 0.8 mmol/L, a wavelength of 340 nm, and with the correct differential absorptivity being established for each instrument.

References

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A New Analytical System for Assessing the Protease–Antiprotease Imbalance in Intensive-Care Medicine

To the Editor:

Activation of plasma prokallikrein and the plasma antiproteases inhibiting active kallikrein (C1 esterase inhibitor, antithrombin III, and α2-macroglobulin) can help in the diagnosis and therapeutic monitoring of intravascular coagulation, septic shock, and acute respiratory distress syndrome. In fact, several authors have considered prokallikrein activation to be the primary factor in such acute complications, often seen in intensive-care medicine.

Although enzymatic methods involving chromogenic substrates are now available for these quantifications, they remain relatively unknown and unused in emergency and intensive-care medicine, because they are considered time consuming and impracticable. To improve this situation, Behringwerke (Marburg, F.R.G.) has developed a new analytical system, the "Chromotimer," which quickly performs individual coagulation and fibrinolysis tests. The Chromotimer uses reagents for chromogenic and turbidimetric methods, and measures the time to attain a specified increase of absorbance (0.1 A), rather than the increase of absorbance, as in a classic spectrophotometer.

Using the new Chromotimer system, we quantified prokallikrein and two plasma antiproteases—C1 esterase inhibitor and antithrombin III—with chromogenic substrates purchased respectively from Kabi Vitrum (COA-SET prokallikrein; Kabi, Stockholm, Sweden) and Behringwerke (Behringrom—antithrombin III, Behringrom—C1-inactivator). We adapted to the Chromotimer the manual methods proposed by these manufacturers. The results were expressed as the percentage of activity in a pooled specimen of normal plasma. The methods are analytically reliable. For four levels of activity (25, 50, 75, and 100%), within-run and day-to-day CVs ranged between 5% and 10%. The lower limit of detection (mean +3 SD of 20 measurements of a deficient plasma) was respectively 14% for prokallikrein, 8% for C1 esterase inactivator, and 5% for antithrombin III. Our results for 50 samples collected from patients in the Intensive Care Unit (pancreatitis, burns, septic shock, and myocardial infarct) correlated well with those measured with the classical chromogenic method (y = 1.05x - 0.74 and r =