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Creatine Kinase Isoenzyme BB in the Serum of Renal-Disease Patients, Distinct from an Albumin-Like Artifact

To the Editor:

Aleyassine et al. (1) report that when creatine kinase (CK; EC 2.7.3.2) isoenzymes are determined, a natural fluorescent material is sometimes seen in the serum of patients with certain types of renal failure, which has an electrophoretic mobility like that for CK isoenzyme BB.

In our experience with a similar celulose acetate system (2) we have observed as many as four distinct bands in certain patients with renal failure. These bands correspond, when compared to a control marker, to CK-MM (the most cathodic), CK-MB, an albumin-like artifact, and CK-BB. The albumin-like band is distinct from both the CK-BB and the CK-MB bands. Furthermore, in the cellulose acetate electrophoresis system we use, the albumin-like artifact fluoresces yellow, as opposed to the blue fluorescence of the three CK isoenzymes. This technique may be somewhat more difficult than the Gelman "Super Sephrophere" system, but this distinct yellowish fluorescence is observed in the isoenzyme patterns of cardiac patients as well as those with renal failure. When CK-BB is present, it is visible as a distinct blue fluorescent band that is more anodic than the albumin-like artifact.

Galen and Van Lente have observed a similar phenomenon. In fact, Van Lente has developed a procedure for verifying the presence of CK-BB (3). He pre-incubates a portion of the patient's serum with anti-BB antibody. After electrophoresis the CK-BB, the artifact, and the CK-MM are seen in the untreated portion, but only the artifact and CK-MM are seen in the treated serum. This is consistent with our own observation that an albumin-like artifact fluoresces on the dried electrophoresed cellulose acetate plate without the application of detecting reagent. However, when the detecting reagent is used CK-BB may be observed in certain cases of renal failure as a band more anodic than the albumin-like artifact.

Evidently there are several artifacts that migrate with albumin and exhibit a natural fluorescence in cellulose acetate systems. One or more of these artifacts may be related to long-term hemodialysis. Whether these albumin-like artifacts migrate separately from CK-BB seems to depend on the method, system, temperature, duration of electrophoresis, and voltage used.

We believe that there is a distinct CK-BB band, not to be confused with either an albumin-like artifact or CK-MB, that is present in certain types of renal failure. Apparently not all electrophoretic systems are sensitive enough to demonstrate the appearance of this elusive CK-BB band as separate from the albumin-like artifact. We have observed that in a agarose system, CK-BB and the albumin-like artifact migrate together.

References


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Misinterpretation of Statistical Intercept Values

To the Editor:

Encouraged by the response to a recent note on the interpretation of correlation coefficients (1), we want to call attention to another common misinterpretation of statistics. When comparing a new technique or a new instrument with a reference method, it has become standard practice to report slope and intercept. The intercept is then taken as a measure of the offset between methods. This interpretation is not valid when the data are clustered about a central value far removed from zero. This is exactly the case in most clinical analyses where the data are distributed around a normal value. Moreover, the instruments are usually set or standardized at normal values, rather than at zero concentration. Regression of clustered data through the origin can yield grossly misleading results.

This argument is illustrated by data from an experiment in which three automatic electrolyte analyzers were compared on a routine basis, with use of clinical serum samples. Manual flame-photometric data were also obtained. These tests were part of a large study performed by Bio-Science Laboratories of Rockville Center, N.Y., and we thank Dr. Stanley Reimer for furnishing them to us. In this subset, the three automatic analyzers of various vintage (Photovolt Models PVA-4) are designated as A, B, and C, while the manual data are marked M. A summary of the conventional statistical evaluation for sodium concentration follows:

<table>
<thead>
<tr>
<th></th>
<th>r</th>
<th>Slope</th>
<th>s of slope</th>
</tr>
</thead>
<tbody>
<tr>
<td>A vs. B</td>
<td>.9967</td>
<td>1.024</td>
<td>0.016</td>
</tr>
<tr>
<td>A vs. C</td>
<td>.9917</td>
<td>1.035</td>
<td>0.026</td>
</tr>
<tr>
<td>B vs. C</td>
<td>.9873</td>
<td>1.002</td>
<td>0.031</td>
</tr>
<tr>
<td>A vs. M</td>
<td>.9716</td>
<td>0.980</td>
<td>0.046</td>
</tr>
</tbody>
</table>

* The symbol r is the correlation coefficient. Its proper interpretation has been discussed (1). The symbol s is the standard error of the estimate.

When comparing (e.g.) A vs. M, conventional wisdom prescribes that one express this relationship based on the slope and intercept values as A = 0.980M + 7.426. The frequent misinterpretation of such equations leads to useless and even misleading conclusions. First, a slope of 0.98 ± 0.05 gives no evidence that the relationship is other than 1.00. By taking 0.980 as the slope, a statistical scatter of a particular set of data is built into future evaluations as a permanent bias. Second, an intercept of 7.426 ± 6.3 is virtually useless in evaluating the offset between methods. The intercept at the origin can be dramatically different than the true offset. As a matter of fact, inspection of the raw data of this particular set indicated an offset of the order of 4–5 mmol/liter (which was traced to the method of standardization). Thus a nominal 7.5 mmol/liter with a probability of being between 1–13