0.57 U/L, \( r = 0.997 \). Two patients' sera (a and b) were each assayed seven times in the same run. The mean (SD) and CV were as follows: (a) 1.61 (0.02) U/L, 1.4%; (b) 21.47 (0.08) U/L, 0.4%.

Two pooled specimens of above-normal acid phosphatase serum were prepared, stabilized as above, and stored at -20°C. During a 13-day interval, six aliquots of each pool were assayed by the DMA/704 test. The mean (SD) and CV were as follows: low pool, 1.27 (0.06) U/L, 4.3%; high pool, 12.70 (0.83) U/L, 5.0%. Commercial lyophilized serum controls (no. 3110–34 and no. 3111–34; Fisher Scientific, Orangeburg, NY) were stabilized as above, stored at 4°C, and assayed nine times during 21 days. The mean (SD) and CV were as follows: low pool, 1.45 (0.10) U/L, 6.9%; high pool, 6.89 (0.35) U/L, 5.1%. Sera with acid phosphatase values of 75 and 0 U/L were mixed in various proportions and assayed by the DMA/704 test. The linear-regression statistics \( y = 0.011x \) as follows: slope = 1.0004, intercept = -0.011, \( r = 0.9999 \). Therefore the relation between concentration and instrument reading in the DMA/704 method is linear to at least 75 U/L.

Assay of 27 patients' sera in the range 0.0 to 2.5 U/L (aca method) by both methods showed that the DMA/704 test has a high-normal value limit of approximately 1.7 U/L, based on the aca high-normal-value limit of 0.8 U/L. Finally, in our hands the calibration of both the "test" and the "blank" channels on the Hitachi 704 has been stable for at least two months (the same lot number of DMA reagents being used).


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Lactate Dehydrogenase Isoenzyme 6 in Serum of Two Patients with Severe Pre-Eclampsia

To the Editor:

Electrophoresis of lactate dehydrogenase (LD; (S)-lactate:NAD+ oxidoreductase, EC 1.1.1.27) isoenzymes in serum occasionally reveals an additional LD band, not representing an LD isoenzyme linked to autoantibodies and migrating cathodally to LD5, designated LD6 (1–5). Although some studies (2–4) suggest that the additional band represents alcohol dehydrogenase (ADH; EC 1.1.1.1), another report (5) suggests that the additional band is in fact a true lactate-dependent dehydrogenase isoenzyme. Recent studies have shown that two additional bands migrating cathodally to LD5 may appear in the serum of some critically ill patients (6, 7).

We have recently seen two patients whose serum LD electrophoreograms displayed an additional band migrating cathodally to LD5.

1. A 22-year-old primigravid woman was hospitalized in the 33rd week of gestation because of a blood pressure value of 170/110 mmHg. In the 38th week of gestation the aspartate aminotransferase (ASAT), alanine aminotransferase (ALAT), and LD activities in her serum increased to peak values of 474, 375, and 1332 U/L, respectively; concomitantly, the platelet count decreased, 16 × 10^9/L being the lowest value observed. Coagulation data showed increased fibrin degradation products (FDP; range 10–40 mg/L) and a prolonged bleeding time. The patient showed demonstrable edema and complained of nausea, headache, and epigastric pain, for which she was treated with analgesics and antihypertensive drugs. A cesarean section was performed and a healthy premature male infant was born.

2. A 30-year-old secundigravid woman was hospitalized in the 34th week of gestation because of headache, nausea, and a blood pressure value of 165/126 mmHg. Three days after admission, her blood-pressure value increased further and she complained of severe epigastric pain. Serum ASAT, ALAT, and LD activities increased to peak values of 572, 336, and 1659 U/L, respectively; concomitantly, her platelet count decreased, 8 × 10^9/L being the lowest value observed. Coagulation data showed increased FDP (range 40–80 mg/L) and a prolonged bleeding time. A cesarean section was performed and a healthy premature male infant was born.

For both subjects the serum LD isoenzymes were separated by electrophoresis on agarose gels and stained with the color reagent from Corning (Palo Alto, CA). The electrophoreogram of LD isoenzymes of serum of both patients displayed an additional band migrating cathodally to LD5 (Figure 1). Investigation of the substrate specificity of the additional band in the serum of both patients proved that it was a true lactate-dependent dehydrogenase isoenzyme (LD6).

Both patients suffered severe pre-eclampsia with liver involvement and a low platelet count. In such patients intravascular fibrin deposition in the hepatic sinusoids can cause obstruction of blood flow and result in epigastric pain (8–10). The severity of the disease seems to correlate with such laboratory measures as reductions in platelet count (11) and increases in serum LD activities (12, 13). The appearance of LD6 in the serum of both patients coincided with peak values for serum ASAT, ALAT, and LD activities and with the concomitant occurrence of clinical signs characteristically seen in patients with severe pre-eclampsia. LD6 disappeared from the serum of both patients coincident with a decrease in serum ASAT, ALAT, and LD activities and with a general improvement in their clinical condition.

LD6 has been detected in serum of patients with various clinical conditions (1–5). In two cases, LD6 was detected in liver tissue obtained at autopsy of patients who died during their hospitalization (5). These same authors detected LD6 in liver tissue from ran-
domly selected autopsy cases. The lysosomal and microsomal fractions most clearly showed the additional band in the electrophoretogram representing LD6. Another report (14) also suggests the mitochondrial origin of LD6.

Our findings indicate that the appearance of LD6 in the serum of patients with severe pre-eclampsia with liver involvement suggests mitochondrial damage of liver tissue. The appearance of LD6 in the serum of such patients may be a biochemical marker for evaluating the severity of the pre-eclamptic crisis, because it appears together with clinical signs characteristically seen during these crises.

References

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Usefulness of the Fructosamine Measurement for Monitoring Diabetic Patients

To the Editor:

Suohon et al. (1) recently evaluated the correlation of glycated serum proteins, glycated albumin, HbA₁c, and serum fructosamine with the 24-h blood glucose profile in pregnant insulin-dependent diabetic (IDD) patients, concluding that fructosamine assay may not be a valid measure of integrated glycerina in these patients. These authors correlated the indices of integrated glycerina with results of a single 24-h blood glucose profile in IDD patients who exhibited quite a large excursion of blood glucose concentration (postprandial blood glucose 2.5–16.0 mmol/L, mean blood glucose on the day of testing 4.4–10.9 mmol/L). They suggest that the single profile is representative of daily blood glucose concentrations in these patients. However, examination of their data (Figure 3 in I) shows a consistent decrease in HbA₁c and other indices, at least in two of the four patients shown, thus pointing to changes in glycemic control during the study. Therefore, relating the indices of integrated glycerina to an arbitrarily chosen 24-h blood glucose profile may not be valid. Furthermore, in patients b and d shown in their Figure 3, serum fructosamine paralleled and indeed predicted changes in HbA₁c in patient b the increase in fructosamine on day 15 was paralleled by the increase in HbA₁c 25 days later. In patient d the decrease in serum fructosamine observed at day 15 was paralleled by a decrease in HbA₁c at day 45. Patient a exhibited a parallel decrease in serum fructosamine and HbA₁c throughout the monitoring period. Notwithstanding problems with the specificity of fructosamine assay, the lack of data on blood glucose in this longitudinal experiment doesn't allow conclusions as to the clinical superiority of any of the tests used.

Fructosamine concentration is dependent on the concentration of albumin in the serum (2), whereas both glycated albumin and glycated serum proteins as measured by affinity chromatography remain unaffected by albumin concentration. This can, at least in part, explain discrepancies between fructosamine and the other two tests. We observed a high rate of discrepancies between fructosamine and HbA₁c results, particularly in IDD patients (3, 4). These two tests reflect different periods of glycemic control and, for this reason if for no other, they cannot be regarded as substitutes for each other.

A lot remains to be learned about the specificity of the nitroblue tetrazolium reaction used in the fructosamine test. We have to learn even more about the clinical interpretation of the combined measurement of glycated hemoglobin and other short-time indices of integrated glycerina. This can only be done in a longitudinal study where the most important endpoint, blood glucose profile, is repeatedly measured over periods at least equivalent to the half-life of longest-lived protein studies (HbA₁c) and where these data are subsequently related to changes in the indices of integrated glycerina.

References

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