Accordingly, the displayed lactate concentration of the analyzer may differ from the true lactate concentration in plasma by a multiplication factor from 1 to infinity as the packed cell volume varies from zero to near 100%.

To validate the use of the calculated value in place of direct measurements, we measured plasma lactate concentrations by both methods in 97 blood samples in which the PCV ranged from 34 to 67%. For each blood sample, immediately after blood was drawn, we measured "estimated" and "true" plasma lactate concentrations. "Estimated" plasma lactate was determined according to the manufacturer's method and by correcting the displayed value with equation 2. "True" plasma lactate was obtained by promptly centrifuging blood at 1300 × g for 1 min and diluting a 100-μL aliquot of the supernatant fluid.

If the assay could not be done immediately after sampling, it was important to determine whether the well-known increase in lactate concentration with time was faster in whole blood than in diluted blood, or conversely. For this, we did 17 determinations of the changes of the plasma lactate concentrations: five with diluted blood at ambient temperature, four with dilute blood on ice, four with whole blood at ambient temperature, and four with whole blood on ice (in these two last cases, a 100-μL aliquot of blood was diluted with buffer just before each successive measurement).

For the 97 samples for which we measured both "true" plasma lactate concentration (x) and those corrected for hematocrit (y), the values ranged from 0.44 to 12.07 mmol/L. The average difference in the two groups of values was 0.835 (SD 0.062) mmol/L. Comparison in relation to zero by paired t-test gave: t = 0.568, p not significant. There was an excellent correlation (r = 0.953, p < 0.001), and the slope of the regression line was 0.992. We conclude that the established formula is a valid way to avoid the dilution error.

The increase in plasma lactate concentrations with time was expressed as a percent of the first measurement (Figure 1). The plasma lactate increase in diluted blood clearly exceeded that in whole blood [at 60 min, F(1,15) = 29.15, p < 0.001]. The increase in lactate after 60 min was 21% in whole blood on ice, 60.5% in whole blood at ambient temperature, and 332 and 394% in 10-fold diluted blood on ice and at ambient temperature, respectively. Within the first 10 min the lactate increase in both whole blood and in diluted blood on ice did not differ [at 10 min, F(2,14) = 0.16, p not significant]. However, the lactate increase in diluted blood at ambient temperature significantly exceeded that in the three other groups [F(3,13) = 18.95, p < 0.01]. This suggests that if one uses diluted blood that is promptly placed on ice, a maximum delay of 10 min may be acceptable in measuring plasma lactate concentrations.

Taking the present results into account, we conclude that the correction formula is especially useful in determining plasma lactate concentrations when the blood dilution volume may not exceed 100 to 150 μL (as, for example, samples obtained on the fetal scalp in utero by Salinger's method). Moreover, this measurement requires no preliminary centrifugation of the blood sample, which allows it to be done at the bedside. This method is the only one that, to our knowledge, allows the rapid, repeated determinations that are required when a therapeutic course has to be decided with the least possible delay (e.g. in human or newborn reuscitation or in obstetric monitoring).

The correction formula involves use of the packed cell volume. Often, it has been determined previously. Otherwise, it may be measured at the bedside (by microcentrifugation or by changes in resistivity), or an excellent estimate may be obtained simply by using a normal average value for PCV.

Finally, great care must be exercised during preparation of the blood samples. It is important for it to be kept on ice and it must be diluted only just before the 100-μL aliquot is injected into the measuring cell of the analyzer.

Fig. 1. Average increase of the plasma lactate concentrations in course of time under four conditions

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References

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Screening for Polymeric IgM: Some Overlooked History

To the Editor:
Krolowski et al. recently published a Letter in Chemical Engineering (25: 1673–1674, 1979) on a rapid screening technique for polymeric IgM. To set the record straight, I think a short historical review of this technique is in order. A very similar procedure was first reported by Butler et al. in 1961 (1) for the diagnosis of macroglobulinemia, at a time when specific anti-IgM antisera were not easily available. They used starch gel for their test, observing that polymeric IgM would not penetrate the gel, but did so after reduction with β-mercaptoethanol. One year later, Leder (2) published a technique involving the use of filter paper, in which the diagnosis of macroglobulinemia depended on observing a shift in electrophoretic mobility. In 1966, Neremberg published a variation of this approach (3), using cellulose acetate as the support and penicillamine as reducing agent. We tried this approach successfully in 1969 (4), and in 1970 we reported our findings in a larger study (5), showing that changes in electrophoretic mobility can also be demonstrated in some cases of IgG monoclonal gammopathy as well as in IgA monoclonal gammopathy. With the increased availability of specific antisera, this approach became obsolete, until rediscovered!

The reader should be aware that a shift in electrophoretic mobility is a very poor criterion for identifying polymeric IgM, because non-IgM paraproteins can also be affected (5), but in general the
problem of heterogeneity of IgM arises in Waldenström macroglobulinemia, collagen diseases, and chronic liver diseases, for example, in which a variable proportion of the IgM might be monoclonic (6). Two problems can arise in these situations: if a single monoclonal fraction is present, one may ask whether it is monomorphic or polymeric; a shift in electrophoretic mobility after reduction will indicate the fraction to be polymeric, but the rarity of pure monomeric IgM fractions limits the usefulness of the test. More often—and this is true of all the above-mentioned situations—mixtures of monomorphic and polymeric IgM co-exist, and there would be a strong case for developing a method allowing the easy determination of the polymer/monomer ratio. The electrophoretic procedure described by Krolikowski et al. will not allow such a determination, because it is not quantitative.

References

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More Nearly Specific Fluorometry of Theophylline in Serum

To the Editor:
There is some chemical interference with the assay of theophylline by our fluorometric technique (1); this requires an additional step in the procedure to eliminate the interference. This step can be eliminated by adding ascorbic acid before the fluorescence measurement. In the modified procedure, addition of 2.0 mL of cupric sulfate reagent is eliminated; for it is substituted the addition of 2.0 mL of ascorbic acid solution (1 g/L, in 1 mol/L HCl, prepared weekly) into each tube. Mix, and transfer the solutions to rectangular sample cuvettes.

With this change, the assay is more specific because interference is eliminated, and it is also more sensitive and easier to do. Day-to-day precision (CV) for a concentration of 13 mg during 35 days was 6%. For mean concentrations of 20 and 30 mg/L it was 5%. Results correlate well with those by liquid chromatography and enzyme-multiplied immunoassay; total analysis time for a single sample is still the same: 10 min.

Reference

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Comments on a Case Report on Myocardial Infarction

To the Editor:
In their presentation of a case showing alleged discrepancy between electrocardiographic (EKG) and enzymic evidence for myocardial infarction, Borer et al. (1) choose to ignore a greater than twofold increase in total creatine kinase (CK) activity, which returned to an apparent baseline value two days after a peak value was reached.

It seems to me unreasonable to ignore increases in CK that do not exceed the upper limit of the reference interval. Using the authors' reference interval of 50-200 U/L, it can be seen that a normal individual who increases his hypothetical baseline value of 190 U/L by 10% would be considered to have enzymic evidence for myocardial infarction, while the patient reported a greater than 250% increase over baseline was interpreted as inconsistent with myocardial infarction in spite of temporally appropriate EKG confirmation. Changes in this patient's previously above-normal and rising lactate dehydrogenase (LD) activity were largely related to his primary disease (lymphomatoid granulomatosis) and its treatment; the failure, by a few units, of cardiac LD to reverse the LD1/LD2 ratio under these circumstances is hardly surprising.

The "reference" interval for CK is unusually broad, and compulsive adherence to its upper limit is likely to obscure the relationship of increases in CK to myocardial infarction [2]. Since CK determinations are usually multiple, as in the case presented, changes from baseline values (retrospectively or prospectively obtained) are likely to be as important or even more rewarding than simple normal/abnormal designations, especially when CK isoenzyme data are not available, or are inconclusive. Furthermore, CK isoenzyme values may not be as valuable as changes in total CK in borderline cases, for two reasons. First, 85% of myocardial CK is of the MM type (3) and, secondly, commonly used assays are so insensitive to minor changes in baseline activity that Roberta et al. (3) figure a five- to 10-fold increase over normal is necessary for detection.

Because skeletal muscle is the predominant source of normal CK activity, expression of CK activity as a function of muscle mass may permit definition or a more meaningful normal range. Creatinine values are a reasonably stable index of muscle mass, and exploration of CK/creatinine ratios would be a logical first attempt toward defining a reference interval that is more sensitive to detection of myocardial infarction.

References

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To the Editor:
[The above-cited] case report concluded that there was a discrepancy between the biochemical data and electrocardiographic changes in the diagnosis of myocardial infarction. In this age of extensive biochemical studies readily available for accurate diagnosis, several factors must be discriminatingly taken into account. Three crucial pieces of information were lacking from their report: CK-MB measurements, specific LD1/LD2 values, and the autopsy report.

According to a 1975 article by Galen et al. (1), firm diagnosis of myocardial infarction can be made when three or more of the following criteria are positive: elevated presence of CK-MB, LD1/LD2 > 1.0, classic acute clinical history, and positive electrocardiographic Q-wave. We propose that