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 monomeric (6). Two problems can arise in these situations: If a single monoclonal fraction is present, one may ask whether it is monomeric 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 monomeric 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 Krollkowski 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 validate the sample. 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 cuvets.

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 values 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 isoenzymes 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 Roberts 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 discriminately 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