et al. did), we found a difference, both by t-test ($P < 0.01$) and by F-test ($P < 0.05$) between their serum zinc concentrations and those of the HIV-seronegative homosexual men. Furthermore, in contrast to the data of Buhl et al., we found no significant difference, by either t-test or F-test, in serum zinc concentrations between 23 HIV-negative heterosexual controls (mean 17.1, SD 2.7 mmol/L) and the 25 repeatedly HIV-negative homosexual men (mean 18.2, SD 2.0 mmol/L). Because their sample was relatively small, they may have noted spurious statistically significant differences. Our data prompt us to think that it is inappropriate to combine all HIV-seropositive, asymptomatic males together with those who are HIV seronegative.

Although we agree that serum zinc may be important as a cofactor in HIV-induced immunosuppression, we speculate that the decrease in serum zinc is a progressive event, occurring secondary to HIV infection. The implicit assumption by Buhl et al. is that homosexual men may be at further risk for the immunosuppressant effects of HIV, owing to an underlying zinc deficiency. Pifer et al. (3) have suggested that homosexual men may have a lifestyle-induced decrease in serum zinc that may augment any HIV-associated risk. However, this group also did not differentiate among asymptomatic men who were HIV seropositive or seronegative, and thus their conclusions are similarly difficult to interpret.

The cause of the progressive decrease in serum zinc that we have shown to occur is unclear and probably multifactorial in origin. It may result from inadequate intake of zinc-containing nutrients, but this decrease may be attributable both to overt malabsorption, seen in advanced HIV disease, and to subclinical malabsorption, which has been shown to occur (4), and which may be due to an HIV-induced enteropathy (5).

The search for potential cofactors in HIV disease is a challenging one. However, unless care is taken to analyze homogeneous groups, premature and potentially erroneous conclusions may be drawn. This is especially important as nutritional supplementation is frequently recommended to HIV-seropositive patients, often without a rational basis for this advice being observed.

References


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Diagnosis of Acute Myocardial Infarction When Skeletal Muscle Damage is Present: a Caveat Regarding Use of Creatine Kinase Isoenzymes

To the Editor:

Thompson et al. (1) describe their attempt to use creatine kinase (CK) MB isoenzyme (CK-2) for "diagnosing myocardial infarction when total CK is high." The patient population with high CK had skeletal muscle damage of various etiologies. The authors decided that the "most appropriate cutoff value for MB [was] >2% of total CK." Aside from the problem of defining "appropriate," the cutoff of 2% proved to be nonspecific: 13% of non-MI patients were positive by this criterion.

CK-2 has a predictably limited utility in diagnosing acute MI in patients who have evidence of severe skeletal muscle damage. In patients who suffer acute MI, serum total CK typically is about 1000 U/L, and peak CK-2, as measured by the same assay used by Thompson et al., is 8% of the total CK (2), or about 80 U/L (see Table 1). Corresponding typical values for severe trauma patients are 10 000 U/L for total CK and 100 U/L or 1% for CK-2. One can calculate that a patient who concurrently suffers MI and trauma of this degree will exhibit serum CK of 11 000 U/L and CK-2 of 180 U/L (calculated by addition of the respective values for each condition; Table 1). In such a patient, who (by definition) has had an acute MI, CK-2 is <2% of total CK and thus below even the low cutoff values that led to a 13% false-positive rate in the study of Thompson et al. (1).

The problem of detecting myocardial damage in patients with skeletal muscle trauma is of increasing importance. Heart donors are, commonly, victims of severe skeletal muscle trauma. Efforts are made to avoid transplanting damaged hearts but also to avoid wasting the (too) rare donor hearts. Reliance on serum CK-2 in prospective donors, especially on single samples, is replete with danger. The criterion of CK-2 >2% of total CK produces 13% false-positives (1), so use of this criterion could jeopardize the use of an unacceptably high proportion of available healthy donor hearts. This risk of organ wastage seems especially unacceptable when viewed in the context of a test that cannot reliably detect MI, as described in Table 1 and ref. 1.

I urge clinical chemists to interpret CK-2 results with caution in patients whose serum (total) CK is markedly increased. One approach is routinely to defer CK-2 analysis on such samples pending consultation with the requesting physician. This allows the pitfalls of interpretation to be discussed with the responsible physician, who usually appreciates the caveats and may then rely more heavily on the many other relevant diagnostic modalities such as electrocardiography, ultrasound, nuclear imaging, and cardiac catheterization.

References
