splitless automatic injection system and flame ionization detector. The column used was a 25-m (007 series) OV-1701 fused-silica glass capillary column, 0.32 mm (i.d.) and 0.25-μm film thickness (Quadrex Corp., P.O. Box 3881, New Haven, CT 06525). A helium carrier-gas flow of 3.0 mL/min through the column was used with a column head pressure of 62 kPa (9 lb/in.2) and 30 mL/min makeup gas (22 mL/min through the split vent, 2 mL/min septum purge flow). A purge "on" time of 0.5 min was used to permit quantitative injection.

An initial oven temperature of 50 °C was maintained for 2 min, then changed to 200 °C at 16 °C/min. The column temperature was held at 200 °C for 0.5 min and then increased at 4 °C/min to 240 °C. The temperature was maintained at 240 °C for 0.5 min before being increased to 250 °C at 8 °C/min, with a final holding time of 10 min at 250 °C. The injection port temperature was 250 °C. The detector temperature was 300 °C.

Peaks were quantified with a Hewlett-Packard 3393 integrator and expressed either as micrograms of phytanic acid, pristanic acid, or hexacosanoic acid per milliliter of serum (with heptacosanoic acid used as the internal standard) or as a ratio of C26/C22 or C24/C22 fatty acids in serum. Identification of peaks was accomplished by co-chromatography with authentic fatty acid and phytanic acid standards and confirmed by gas chromatography–mass spectrometry.

The concentrations of hexacosanoic, phytanic, and pristanic acid measured in a series of control sera (Table 1) correlate very well with normal reference intervals previously reported. The method described has allowed us to diagnose several patients with a peroxisomal disorder. Examples of patient data obtained by this method are shown in Table 1. When used in conjunction with the previously published rapid assay method for pipenic acid (8), this method provides a rapid, relatively straightforward diagnosis of most peroxisomal diseases. We believe that our method is the only one described in which all of the metabolites essential to diagnose peroxisomal disease can be separated in one assay method and on one column.

We are grateful to Dr. Alf Poulose (Children's Hospital, Adelaide, Australia) for the mass spectral tracing of authentic methyl pristanate, which allowed us to confirm the identity of the peak from our GC tracing.

References

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Serum Zinc In Homosexual Men

To the Editor:

We read with interest the article by Buhl et al. (1), describing serum zinc concentrations in homosexual men, and we would like to comment on several points.

We have been studying the role of nutrition, and particularly of trace elements, as cofactor(s) in progressive HIV-induced immunosuppression. We determined serum zinc concentrations in over 200 subjects, grouped according to the CDC classification of HIV disease, and have shown that serum zinc decreases significantly in advanced HIV disease (2). Buhl et al. studied 19 HIV-seropositive homosexual men, two of whom had AIDS, suggesting that the 17 non-AIDS patients belonged to CDC groups II or III (asymptomatic without or with diffuse lymphadenopathy, respectively).

They found no difference in serum zinc concentrations in homosexual men who were HIV seropositive as compared with homosexual men who were HIV negative. In agreement with their findings, we found that the mean serum zinc concentration in 29 HIV-seropositive healthy homosexual men (CDC group II), 16.8 (SD 2.8) mmol/L, was not different from the mean value for serum zinc in 25 homosexual men who were repeatedly confirmed to be HIV negative over a six-month period (mean 18.2, SD 2.0 mmol/L). However, the mean value for serum zinc in 47 HIV-positive subjects with lymphadenopathy (CDC group III), 16.6 (SD 3.3) mmol/L, was significantly less than that in the repeatedly HIV-seronegative men (P <0.05). Comparison of variances (F-test) supported our finding that there was no difference in serum zinc concentrations between the seronegative homosexual men and seropositive group II subjects, whereas there was a difference between the seronegative men and seropositive group III individuals, with group III having a greater variance. Moreover, when we analyzed zinc concentrations in all asymptomatic homosexual men (n = 75), regardless of the absence or presence of lymphadenopathy (as Buhl
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 is typically 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 the even the low cutoff value 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


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Table 1. Values for Creatine Kinases in Sera of Patients after Myocardial Infarction and (or) Skeletal Muscle Trauma

<table>
<thead>
<tr>
<th>CK</th>
<th>CK-2, U/L</th>
<th>CK-2, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Myocardial infarction</td>
<td>1000</td>
<td>80</td>
</tr>
<tr>
<td>Skeletal muscle damage</td>
<td>10 000</td>
<td>100</td>
</tr>
<tr>
<td>Both</td>
<td>11 000</td>
<td>180</td>
</tr>
</tbody>
</table>