Ghent University, Belgium. $^{77}$Se, $^{80}$Se, and $^{82}$Se were the isotopes monitored by this technique (reaction gas, CO; sample diluted 1 + 24; yttrium internal standard; quantification by standard addition) (3).

Representative selenium concentrations measured in Seronorm Level 1 and 2 serum samples are shown in Table 1. Considering the Level 1 sample, all values from the three analytical techniques agreed (within quoted uncertainty ranges) with the stated target value. Mean (SD) selenium concentrations for the Level 2 sample, however, were consistently higher than the target values: 161 (4) $\mu$g/L by magnetic sector ICP-MS, 152 (5) $\mu$g/L by DRC-ICP-MS, and 166 (17) $\mu$g/L by ET-AAS vs the suggested target value of 136 $\mu$g/L. A mean (SD) selenium concentration of 168 (17) $\mu$g/L was also obtained by magnetic sector ICP-MS analysis after microwave digestion of serum samples.

On the basis of our findings we propose that the selenium concentration in these batches of Seronorm Level 2 Trace Elements Serum may be inaccurate. We believe that a value of $\sim$150–165 $\mu$g/L may more closely reflect the true selenium concentration in these batches. We wish to make clear that we have no reason to doubt the quality of the initial certification process or the quality of the initial calibrating laboratories. Rather, we suggest that unknown factors such as aging, contamination, or changed manufacturing practices have caused these batches of this reference sample to differ from those originally prepared and evaluated.

| Table 1. Measured selenium concentrations in Seronorm Trace Elements Serum Levels 1 and 2. |
|---------------------------------|---------------------------------|
| **Isotope** | **Mean (SD) concentration, $\mu$g/L** |
| **Level 1** | **Level 2** |
| $^{77}$Se | 88 (3) | 168 (17) |
| $^{80}$Se | 83 (5) | 161 (4) |
| $^{82}$Se | 88 (9) | 166 (17) |
| **Mean (SD) concentration, $\mu$g/L** | **Level 1** | **Level 2** |
| **Stated Seronorm target: ICP-MS** | 83 (6)$^a$ | 136 (9)$^b$ |
| **Stated Seronorm target: ET-AAS** | 81 (3)$^a$ | 129 (8)$^a$ |
| **Ethanol addition method** | $^{82}$Se | 83 (5) | 161 (4) |
| **Microwave digestion method** | $^{82}$Se | 88 (3) | 168 (17) |
| **Confirmatory ET-AAS** | $^{82}$Se | 88 (9) | 166 (17) |
| **Confirmatory DRC-ICP-MS** | $^{77}$Se | 86 (3) | 152 (4) |
| | $^{80}$Se | 84 (2) | 150 (3) |
| | $^{82}$Se | 87 (2) | 153 (3) |

$^a$ Values supplied by the manufacturer, as measured by magnetic sector ICP-MS and ET-AAS.
$^b$ Values for stated Seronorm target are the mean (2 SD).

References

Editor's Note: Attempts to obtain comment from the manufacturer were unsuccessful.

Urinary Methylmalonic Acid Test May Have Greater Value than the Total Homocysteine Assay for Screening Elderly Individuals for Cobalamin Deficiency

To the Editor:
I read with interest the review on recommendations about total homocysteine (tHcy) determinations (1). In this review, the authors recommend screening individuals (>75 years) for cobalamin (vitamin B12) deficiency, using upper limits for tHcy of 16 $\mu$mol/L (folate-supplemented) and 20 $\mu$mol/L (non-supplemented). Use of the tHcy test for screening, however, may miss a large number of individuals with low levels of cobalamin deficiency (2).

We have recently published on the value of the screening test for tHcy of 16 $\mu$mol/L (folate-supplemented) and 20 $\mu$mol/L (non-supplemented) (3). The tHcy test may have greater value than the total homocysteine assay for screening because it allows the homocysteine thiolactone (tHcy) test to be used for diagnosis.

References

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number of seniors with significant cobalamin deficiency. In a urinary methylmalonic acid (UMMA) screening study of nonanemic elderly individuals age ≥65 years (2), 7 of 16 cobalamin-deficient individuals tested had tHcy <16.2 μmol/L. This group (n = 16) represented individuals with significant cobalamin deficiency with mean (SD) UMMA of 7.4 (4.8) mmol/mol creatinine (normal <3.6 mmol/mol creatinine) and tHcy of 18.6 (8.6) μmol/L. The deficiency of cobalamin is associated with a reported 2.6-fold increased risk for Alzheimer disease and/or atherothrombotic vascular disease causing heart attack or stroke (1, 3). Damage may be insidious and can occur before symptoms (3). In the above study (2), the authors used a normal UMMA value <4.7 mmol/mol creatinine, but today the criterion for normal UMMA is <3.6 mmol/mol creatinine, and thus an even greater number of UMMA-abnormal individuals would be missed by the tHcy test. 

In a study of nine total vegetarians (4), tHcy was normal in all, whereas the UMMA test was positive in seven of eight tested and serum MMA was increased in five of eight. UMMA concentrations decreased dramatically to normal in all individuals after they received cobalamin therapy. The UMMA test appeared to be more sensitive than the serum cobalamin assay in screening elderly populations (2) as well as in another study of vegetarians (5). In the vegetarian study population (n = 54), 83% (19 of 23) identified as cobalamin-deficient with the UMMA test had normal serum cobalamin concentrations. Individuals who received adequate cobalamin therapy had reduced UMMA values, suggesting that the UMMA test was effective for identifying early metabolic cobalamin deficiency.

The UMMA test appears to be the best candidate for a gold standard assay for identifying true tissue cobalamin deficiency (6). The serum MMA or tHcy tests have poor specificities and yield falsely high values in patients with renal insufficiency and other conditions (1, 2, 6). Unlike tHcy, the UMMA test does not show significant individual daily variation or sample instability in processing. The UMMA test requires only a 1-mL urine specimen, which is stable for at least 24 h at room temperature and for months if frozen. The UMMA test is similar in price to the tHcy test. Although the UMMA test may not be available at local hospital laboratories, it can be obtained at most large commercial laboratories. The UMMA test is noninvasive and relatively inexpensive, and the specimen can be sent through the mail unrefrigerated if the vial contains a preservative.

The UMMA test appears to meet the criteria for an acceptable screening test (1) and is the only cobalamin-deficiency assay that has been validated as a screening tool (2). The authors of the review (1) stress the importance of routine screening of the elderly, particularly because the US has initiated a program of folic-acid-fortification of flour, which may mask cobalamin-deficiency anemia and neurologic disease. Because of the high prevalence of cobalamin deficiency in senior populations, UMMA screening could spare many from permanent neurologic disability and fatal cardiovascular disease.

The UMMA test appears to be the test of choice for screening for cobalamin deficiency. It would be valuable to test this hypothesis with additional studies by comparing the UMMA test with other cobalamin assessment assays.

The author founded Norman Clinical Laboratory, Inc., which performs the UMMA test on clinical samples.

References

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