tion” combination when compared with “BD SST + double centrifugation” (P < 0.0001, paired t-test). Deming regression analysis yielded the following: slope = 1.16 [95% confidence interval (95% CI), 1.03–1.29]; intercept = 0.04 μg/L (95% CI, 0.02–0.06 μg/L). Table 1 shows the assay values of the six apparently false-positive results.

These results prompted a second phase, during which the BD Thrombin sample was also centrifuged twice. Nineteen additional patients were included. The difference between the results (cTnI range, 0.01–24 μg/L, 32% above threshold) was not statistically significant as analyzed by the paired t-test and the Deming regression [slope = 1.04 (95% CI, 0.93–1.14); intercept = −0.03 μg/L (95% CI, −0.08 to 0.02 μg/L)]. We conclude that a single centrifugation of collection tubes containing thrombin as a clot activator is insufficient to avoid false-positive cTnI results on the ACCESS analyzer. Repeat centrifugation eliminates false-positive results. The presence of thrombin in collection tubes does not significantly affect cTnI results by this assay. Roberts et al. (3) published similar results.

We thank Sanofi Diagnostics Pasteur (Marnes La Coquette, France) for providing the reagent, and BD France SA for providing the blood collection tubes.

References


### Table 1. Reference tube and BD Thrombin + single centrifugation discrepant false-positive cTnI results (μg/L).

<table>
<thead>
<tr>
<th>BD SST tube</th>
<th>BD Thrombin tube</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.000</td>
<td>0.38</td>
</tr>
<tr>
<td>0.052</td>
<td>0.172</td>
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<tr>
<td>0.083</td>
<td>0.104</td>
</tr>
<tr>
<td>0.000</td>
<td>0.131</td>
</tr>
<tr>
<td>0.103</td>
<td>0.189</td>
</tr>
</tbody>
</table>

To the Editor:

Transferrin saturation (TS) has been recommended for screening for hemochromatosis (1). It is widely available, and results may be increased even in young adults with hemochromatosis. The TS assay is a two-step assay with serum iron in the numerator and total iron-binding capacity, unsaturated iron-binding capacity (UIBC), or serum transferrin in the denominator. Serum iron/(serum iron + UIBC) equals the TS. In a previous study, we compared UIBC to TS as a screening test for C282Y hemochromatosis in a population of asymptomatic voluntary blood donors (2). Because blood donation could potentially affect iron status, we have reevaluated TS and UIBC in referred hemochromatosis patients and used first-time blood donors as control cases (n = 386, all wild type by C282Y genotyping).

“Discovered” cases refers to C282Y homozygotes found through pedigree studies, and “screened” cases refers to cases discovered during a population screening project in 5211 voluntary blood donors (2). The sample consisted of 78 male probands, 58 discovered men, 5 screened men, 26 female probands, 37 discovered women, and 11 screened women. All hemochromatosis patients and control cases had C282Y genotyping by RsaI restriction enzyme digestion (3). Homozygotes with a normal TS and ferritin (n = 5) were confirmed by direct DNA sequencing to exclude false-positive genetic testing (4).

Serum iron was determined by colorimetric analysis (Roche Diagnostics or Beckman Coulter). UIBC was determined on the Beckman Coulter LX-20 (Reagent 153-50; Diagnostic Chemicals Limited) or by adapting an existing assay to an automated microwell plate reader (Unimate 7 UIBC; Roche Diagnostics). TS by UIBC was directly compared with TS determined by immunochemical transferrin on the Beckman Coulter IMMAGE immunochemistry system (correlation coefficient = 0.986; n = 192). Between-run precision of UIBC was determined by measuring three levels of control daily for 31 days. CVs were 2.8–7.2%.

The diagnostic accuracy of UIBC and TS for the diagnosis of C282Y homozygotes was examined by ROC curve analysis with a program developed at this medical center (5). UIBC data were transformed to 1/UIBC for direct comparison to TS. The thresholds were determined from the ROC curves on the basis of the likelihood ratios [sensitivity/(1 – specificity)]. The areas under the curves were 0.96 (95% confidence interval, 0.94–0.98) for 1/UIBC and 0.96 (95% confidence interval, 0.94–0.98) for TS. Thresholds were 27 μmol/L (sensitivity, 88%; specificity, 99%) for TS and 27 μmol/L (sensitivity, 88%; specificity, 98%) for UIBC (Table 1). These thresholds are similar to those determined in the screening of 5211 blood donors in which the UIBC detected more C282Y homozygotes with fewer false positives and at a reduced cost (2).

These results raise the question

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### Unsaturated Iron-binding Capacity: A Screening Test for C282Y Hemochromatosis?

To the Editor:

Transferrin saturation (TS) has been recommended for screening for hemochromatosis (1). It is widely available, and results may be increased even in young adults with hemochromatosis. The TS assay is a two-step assay with serum iron in the numerator and total iron-binding capacity, unsaturated iron-binding capacity (UIBC), or serum transferrin in the denominator. Serum iron/(serum iron + UIBC) equals the TS. In a previous study, we compared UIBC to TS as a screening test for C282Y hemochromatosis in a population of asymptomatic voluntary blood donors (2). Because blood donation could potentially affect iron status, we have reevaluated TS and UIBC in referred hemochromatosis patients and used first-time blood donors as control cases (n = 386, all wild type by C282Y genotyping).

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stated in the title of this Letter. The cost of the UIBC assay in this study was estimated to be $1. It is intuitive that, using any cost-analysis system, the cost of the single-step UIBC will be less than the cost of the two-step assay using serum iron plus UIBC, total iron-binding capacity, or transferrin. In the less-common cases of hemochromatosis that are not associated with \textit{HFE} mutations, the disease is defined by iron overload, and thus both UIBC and TS would be expected to be abnormal. UIBC has been used successfully in other studies that screened for hemochromatosis without genotyping in all patients (6, 7). Therefore, UIBC, which has been used for large-scale population screening studies (8), appears to perform as well as TS as a screening test for hemochromatosis at a reduced cost.

### References

3. Adams PC, Chakrabarti S. Genotypic/pheno-

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