other infections (13%). Similar seasonal differences were described previously in a smaller series (3). In addition, we discovered a simultaneous course of TH in three sets of twins and two other sibling pairs (neither parent was affected). “Epidemic” incidence and familial occurrence strongly support a relationship of TH with viral, protozoal, or genetic predisposition for a unique response to any infection.

In our department of clinical biochemistry, ALP isoenzyme electrophoresis has been used for differential diagnosis of TH and organic hyperphosphatasemias. Over the last 8 years, ALP isoenzyme measurements were requested in 562 children under 5 years of age. We detected TH in 187 patients (33%) and hyperphosphatasemia of predominantly bone, intestine, or liver origin in 336 (60%), 21 (4%), and 18 (3%) patients, respectively. To our knowledge, we report the largest series of TH children that has been identified in one hospital. We conclude that TH cannot be regarded as a rare or exceptional syndrome (6) and that it belongs among the diagnostic tasks in present-day pediatric chemistry.

References

Fig. 1. Age distribution of 194 cases of TH.

Comparison of Single and Repeat Centrifugation of Blood Specimens Collected in BD Evacuated Blood Collection Tubes Containing a Clot Activator for Cardiac Troponin I Assay on the ACCESS Analyzer

To the Editor:
Cardiac troponin I (cTnI) has become a major marker in the diagnosis and monitoring of myocardial damage. On the ACCESS™ analyzer (Beckman Coulter), serum is the biological fluid compatible with both myoglobin and cTnI tests (1). However, residual fibrin (2) and microparticles (2) have been reported to interfere with one or more cTnI assays. Some of these interferences can be avoided with repeat centrifugation of the sample and/or the use of a clot activator (3). The BD Vacutainer™ Hemogard™ Thrombin glass evacuated blood collection tube (BD Thrombin) contains thrombin as a clot activator and may, therefore, obviate the need for repeat centrifugation of samples and the resulting delays in testing.

This open comparative study (without masking of phlebotomists, technicians, or investigators) was performed in the Laboratory of Biochemistry of the University Teaching Hospital Beaujon between August and October 1999. Its objective was to assess whether single centrifugation of blood specimens is adequate for samples collected into BD Thrombin tubes for the assay of cTnI on the ACCESS analyzer.

Patients with chest pain from the emergency department and patients with acute coronary syndrome from the cardiology intensive care unit were included. Samples were drawn in duplicate into BD Thrombin and BD Vacutainer Hemogard SST™ glass tubes (BD SST), the laboratory reference tube, whose sample is routinely centrifuged twice for this assay. Samples were centrifuged at 1300–2000g for 10 min at 10°C.

The first 64 results (cTnI range, 0–1.9 μg/L) included 10 (16%) above the threshold (0.1 μg/L). Results showed a random positive bias of the "BD Thrombin + single centrifuga-
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 analysis [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>
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<th>BD SST tube</th>
<th>BD Thrombin tube</th>
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<tr>
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**To the Editor:**

Transferin 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 ≈44% (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