in regard to standardization and interference by lipemia, however, it should not be viewed, however, as a replacement for a standard assay of apoB. Any specimen found to have increased apoB by the EZ-HDL assay should be confirmed with a standard apoB test.

References


Latex-enhanced Immunoturbidimetry Allows D-Dimer Determination in Plasma and Serum Samples, Wolfgang Korte and Walter Riesen (Institute for Clinical Chemistry and Hematology, Kantonsspital, 9007 St. Gallen, Switzerland; *author for correspondence: fax 41-71-494-3900, e-mail Wolfgang.Korte@gd-ikch.sg.ch)

Quantitative D-dimer determination has become routine practice in patients evaluated for the presence of deep venous thrombosis or pulmonary emboli (1–3). D-Dimer concentrations below a certain cutoff specifically defined for each assay [500 μg/L for ELISA and comparable assays (3)] are considered sufficient evidence to exclude a deep venous thrombosis or pulmonary embolism if the pretest probability is low (4). In addition, D-dimer has been shown to be a reliable indicator of coagulation activation in disseminated intravascular coagulation (5) and malignancy (6). More recently, the relevance of the determination of D-dimer in arterial disease was evaluated (7), and it was shown that D-dimer is a very good predictor of recurrent acute coronary syndromes after a first event (8). There is also some indication that the amount of D-dimer generated correlates to some extent with the degree of atherosclerosis (9).

Fully quantitative D-dimer assays and their automation are recent improvements (10), and short turnaround times allow the routine use of such assays. Routinely, plasma is used for the D-dimer assays. Serum is believed not suitable because of the possibility of continued fibrinolytic activity, which (theoretically) could lead to a (falsely) increased D-dimer concentration. Here, we report that latex-enhanced immunoturbidimetric measurement allows the use of serum as a matrix for the measurement of D-dimer concentrations.

Samples were from patients who had a D-dimer test (from citrated plasma) ordered as well as available serum obtained during the same blood collection. The samples were selected without conscious bias during a 5-week period. Routine blood samples were collected with the Vacutainer® system (Becton Dickinson). For citrated plasma, blood (3.6 mL) was collected into 0.125 mol/L sodium citrate (0.4 mL). For serum, blood was collected into 10-mL tubes containing polystyrene granules. When the samples arrived in the laboratory, platelet-poor plasma was prepared from the citrated samples by centrifugation (1600g for 10 min at 22°C); serum was obtained by centrifugation (1500g for 6 min at 9°C). D-Dimer concentrations were determined using a latex-enhanced immunoturbidimetric assay (Tinaquant D-dimer on a Hitachi 917 analyzer; Roche Diagnostics). All D-dimer determinations from plasma and serum were performed according to the same routine protocol. D-Dimer concentrations were determined from both materials with three different methods of sample processing: (a) immediately after centrifugation (n = 33); (b) after incubation of the (centrifuged) original tubes at 4°C for 24 h (i.e., with the cell sediment/clot in place; n = 13); and (c) after incubation of

Table 1. Testing for significant differences between D-dimer concentrations measured in plasma and serum and with three different methods of processing.

<table>
<thead>
<tr>
<th>Processing</th>
<th>Immediate</th>
<th>24 h at 4°C</th>
<th>Supernatant, 24 h at 4°C</th>
<th>Immediate</th>
</tr>
</thead>
<tbody>
<tr>
<td>processing</td>
<td></td>
<td>24 h at 4°C</td>
<td>P for differencea</td>
<td></td>
</tr>
<tr>
<td></td>
<td>n</td>
<td></td>
<td>P for differencea</td>
<td></td>
</tr>
<tr>
<td>Median plasma D-dimer, mg/L</td>
<td>33</td>
<td>0.81</td>
<td>0.678</td>
<td>0.64</td>
</tr>
<tr>
<td>Median serum D-dimer, mg/L</td>
<td>33</td>
<td>0.77</td>
<td>0.760</td>
<td>0.72</td>
</tr>
<tr>
<td>R² for plasma vs serum</td>
<td>0.989</td>
<td>0.993</td>
<td>0.974</td>
<td></td>
</tr>
</tbody>
</table>

a Difference between processing immediately after centrifugation vs processing after incubation of the centrifuged sample in the original tube (with clot and cell sediment present) for 24 h at 4°C.
b Difference between incubation of the centrifuged sample in the original tube (with clot and cell sediment present) for 24 h at 4°C vs incubation of the original supernatant (with clot and cell sediment removed) for 24 h at 4°C.
c Difference between incubation of the original supernatant (with clot and cell sediment removed) for 24 h at 4°C vs processing immediately after centrifugation.
D-dimer concentrations is of interest. However, the use of serum samples are available but where measuring D-especially important for clinical studies in which only applicable to a routine setting. These results may be tion with the immunoturbidimetric method used here is phlebotomy, suggesting that serum D-dimer determina-

Fig. 1. Linear regression between plasma (independent variable) and serum (dependent variable), with the 95% confidence interval.

The correlation for the detection of D-dimer concentration from the two different materials was calculated by linear regression analysis, and testing for differences was performed using the Mann–Whitney rank-sum test (SigmaStat; SPSS).

No significant differences between median plasma and serum D-dimer concentrations were detected (Table 1). Close agreement between plasma and serum was seen (Fig. 1). Plasma samples processed immediately after centrifugation yielded slightly (but insignificantly) higher D-dimer concentrations (mean serum/plasma ratio, 0.946; 95% confidence interval, 0.888–1.004); similarly, the other two processing methods also showed no differences in the resulting concentrations (see Table 1). Plasma- and serum-derived concentrations in relation to the usual cutoff (0.5 mg/L) were concordant in all samples (Fig. 1).

Plasma samples are the standard matrix for the quan-
tification of D-dimer. We show here close agreement of D-dimer concentrations determined from citrated plasma samples and serum. These results thus differ from earlier published comparisons. In earlier studies, an ELISA format was used, and although the concordance between plasma and serum was good (11, 12), it was not good enough to allow replacement of plasma by serum. Thus, all available kits for D-dimer measurements suggest using plasma as the standard matrix. Of specific interest is that these results were from samples obtained through routine phlebotomy, suggesting that serum D-dimer determination with the immunoturbidimetric method used here is applicable to a routine setting. These results may be especially important for clinical studies in which only serum samples are available but where measuring D-dimer concentrations is of interest. However, the use of serum for D-dimer determinations needs to be evaluated and validated in a clinical study setting before such results can be used for the exclusion of deep venous thrombosis or pulmonary embolism.

Prof. W. Riesen is a member of an advisory board to Roche Diagnostics.

References


New Approaches to Cyclosporine Monitoring Raise Further Concerns about Analytical Techniques, David W. Holt,2 Atholl Johnston,2 Barry D. Kahan,3 Raymond G. Morris,4 Michael Oellerich,5 and Leslie M. Shaw 6 (1 St. George’s Hospital Medical School, London SW17 0RE, United Kingdom; 2 St. Bartholomew’s & The Royal London School of Medicine & Dentistry, London EC1M 6BQ, United Kingdom; 3 University of Texas Health Center, Houston, TX 77030; 4 The Queen Elizabeth Hospital, Woodville, South Australia 5011, Australia; 5 Georg-August-Universität, D-37075 Göttingen, Germany; 6 University of Pennsylvania Medical Center, Philadelphia PA 19104; address correspondence to this author at: Analytical Unit, St. George’s Hospital Medical School, London SW17 0RE, UK; fax 44-20-8767-9687, e-mail d.holt@sghms.ac.uk)

Of late there has been a re-evaluation of therapeutic drug monitoring (TDM) strategies for optimizing cyclosporine