women who went on to develop pre-eclampsia (at 34 weeks of gestation) had sFlt1 values within the reference interval. This woman had abruptio placenta at delivery (36 weeks of gestation). In the remaining seven patients, the sFlt1 assay would have predicted preeclampsia a mean of 11.2 weeks (range, 6.5–16.5 weeks) before clinical onset. No significant difference was observed in mean (SD) serum creatinine concentrations (μmol/L) among the three groups [normal pregnancy, 52.5 (8.9); pre-eclampsia, 57.0 (14.9); isolated hypertension, 54 (16.6)].

Our findings confirm that the maternal serum sFlt1 concentration is markedly increased at delivery in women with preeclampsia and is measurably increased long before clinical onset (minimum of 6.5 weeks before onset). We emphasize the surprising lack of negative predictive value of a sFlt1 concentration within reference values in pregnancies complicated by abruptio placenta. We believe that measurement of sFlt1 could permit early management of at-risk women and could also help to identify women at risk of developing preeclampsia among patients presenting with gestational or chronic hypertension.

References

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3-Deazaadenosine, a Stabilizer of Whole-Blood Homocysteine Content, Does Not Interfere with the Single-Enzyme Homocysteine Assay while Totally Inhibiting the Enzyme Conversion Homocysteine Immunoassay

To the Editor:
Plasma total homocysteine (tHcy) is a risk factor for cardiovascular disease and possibly other diseases (1). Release of homocysteine (Hcy) from erythrocytes into the plasma before measurement remains a problem. The erythrocyte continues to carry methylation reactions at room temperature in whole blood, producing and exporting Hcy as an end product while the blood is waiting for processing or during delivery. Export of Hcy from erythrocytes into the plasma is temperature-dependent (2). At room temperature, the increase in plasma tHcy is ~1.0 μmol·L⁻¹·h⁻¹ (2). This corresponds to an ~10% increase per hour in a typical sample containing 10 μmol/L tHcy. Therefore, at present, the accuracy of Hcy measurements is compromised even when the plasma is separated within 1 h of sample collection (2). Hill et al. (3) studied the effect of temperature on the stability of plasma tHcy over a 72-h time course in blood collected into evacuated tubes containing either EDTA or 3-deazaadenosine (3-DA) and found that 3-DA is an effective stabilizer of plasma Hcy content. However, because 3-DA prevents Hcy production through competitive inhibition of the enzyme 5-adenosylhomocysteine hydrolase (SAHH), 3-DA interferes with popular assays of tHcy that are enzyme-conversion immunoassays based on SAHH (1, 2, 4).

We have previously developed a simple assay method for tHcy (5, 6) that uses a single and specific recombinant homocysteine α,γ-lyase (rHChYase), which produces the analyte H₂S from Hcy. The single-enzyme tHcy assay has received 510(K) clearance. The purpose of this study is to compare the interference of 3-DA on SAHH and rHChYase.

To determine the interference of...
3-DA on SAHH, we used S-adenosylhomocysteine (SAH) as a substrate at 50 μmol/L and 3-DA at 0, 50, 100, and 200 μmol/L in the assay buffer. Conversion of SAH to adenosyl and Hcy was measured by its subsequent conversion to H2Sb y sine and Hcy was measured by its buffer. Conversion of SAH to adenylic acid is unaffected by 3-DA at the concentrations needed to assay is completely interfered by the interference of 3-DA on SAHH, we used phenylenediamine hydrochloride as the chromophore (5, 6). When 3-DA was added from 0 to 200 μmol/L, the remaining activity decreased from 100% to 3.3% (Fig. 1). These results confirm the report of Woltersdorf et al. (4), who found highly significant interference by 3-DA, starting from 50 μmol/L, in the Abbott IMX Hcy assay, which is based on SAHH.

To determine the interference of 3-DA directly on rHCYase, we used 50 μmol/L L-Hcy with 3-DA at 0, 50, 100, or 200 μmol/L in the assay buffer. At 3-DA concentrations ranging from 0 to 200 μmol/L, the relative activity showed almost no change (1-4.5%), a striking contrast to the interference of 3-DA on SAHH (Fig. 1). For 10 plasma samples with and without 100 μmol/L 3-DA, measured with the rHCYase-based tHcy assay (5, 6), the mean (SD) tHcy was 10.4 (2.2) μmol/L with 3-DA and 10.6 (2.3) μmol/L without 3-DA. The concentrations measured by a HPLC tHcy assay (5, 6) were 10.7 (2.1) μmol/L with 3-DA and 10.8 (2.0) μmol/L without 3-DA.

We conclude that the SAHH-based assay is completely interfered by 3-DA at the concentrations needed to stabilize tHcy in whole blood, whereas the rHCYase-based tHcy assay is unaffected (5, 6). Thus, the remaining technical problem for routine and widespread tHcy measurement, the long-term storage of whole blood, can be solved with the use of 3-DA and the rHCYase-based tHcy assay.

Comparison of Serum and Heparinized Plasma Samples for Measurement of Chemistry Analytes

To the Editor:

Although serum and heparinized plasma specimens are considered equivalent for many assays, differences in results between these two sample types have been reported for several chemistry analytes. Significant differences between serum and heparinized plasma results have been reported for albumin, alkaline phosphatase, aspartate aminotransferase, calcium, carbon dioxide, chloride, creatinine, γ-glutamyltransferase, glucose, LD, potassium, phosphorus, sodium, total bilirubin, total protein, urea nitrogen, and uric acid were analyzed on both a Roche Modular P analyzer and a Vitros 950 analyzer. Additional assays for aldolase, α1-antitrypsin, amylase, angiotensin-converting enzyme (ACE), bile acids, direct bilirubin, ceruloplasmin, complement C4, complement C3, high-sensitivity C-reactive protein, creatine kinase, fructosamine, HDL-cholesterol, haptoglobin, iron, lipoprotein(a), lipase, LDL-cholesterol, magnesium, prealbumin, pancreatic amylase, phospholipids, transferrin, triglycerides, total iron-binding capacity, and unbound iron-binding capacity were performed only on the Roche Modular P analyzer. All reagents were from the instrument manufacturers unless otherwise stated in Table 1 of the Data Supplement that accompanies the online version of this letter at http://www.clinchem.org/content/vol50/issue9/.

Differences in the mean values for the two sample types were compared by paired t-test and were considered