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 adenosine and Hcy was measured by its buffer. Conversion of SAH to adenosine and Hcy was measured by its buffer. At 3-DA concentrations ranging 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 (<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, cholesterol, creatinine, γ-glutamyltransferase, 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...
clinically significant at 2% for sodium; 5% for calcium, chloride, glucose, and potassium; and 10% for all other analytes tested (2). A statistical summary of all data is provided in Table 1 of the online Data Supplement.

On the Roche analyzer, heparinized plasma samples showed clinically significant decreases relative to serum samples for bile acids (−67%) and potassium (−6.0%). Clinically significant increases were seen for aldolase (+39%), ACE (+22%), and LD (+21%). According to the manufacturers’ assay package inserts, both serum and heparinized plasma samples are acceptable for ACE, aldolase, bile acids, LD, and potassium.

On the Vitros 950 analyzer, similar changes were seen in the concentrations reported for potassium (9.3% decrease) and LD (19% increase) in the plasma samples relative to the serum samples. In addition, mean total bilirubin results were 20% higher in the plasma samples on this analyzer. Both serum and heparinized plasma samples are acceptable for each of these assays according to the manufacturer’s assay information.

Concentration differences of comparable magnitude between serum and plasma samples were identified on both analyzers for potassium and LD. Lower potassium concentrations in plasma samples have been well described and are attributed to the prevention of clot formation with platelet rupture and potassium release (3, 4). Some reports have shown differences in LD values between serum and heparinized plasma samples (1), whereas others have not (3, 5, 6). Bakker et al. (7) initially reported an increase in duplicate errors in LD measurements on plasma samples, but this was later attributed to the method of primary tube sampling (8, 9). Falsely increased plasma LD concentrations may be caused by contamination with erythrocytes or platelets, which contain high concentrations of LD. Others have suggested that LD is falsely increased in the preparation of serum because of increased hemolysis and platelet release of LD with clot formation (7). Both sample types are acceptable according to the manufacturers of both instruments we tested. The fact that our samples were frozen before analysis may have contributed to release of LD from residual erythrocytes and/or platelets.

Other limitations of the current study are that a standard draw order was used for specimen collection and that first serum and then plasma samples were analyzed sequentially. Random collection and analysis orders are generally preferred, although in this case the standard non-randomized order is unlikely to have affected the results.

Two previous studies comparing heparinized plasma and serum found no difference for total bilirubin (1, 10), whereas a third study showed a difference that was statistically different but not clinically significant (3). We examined only low total bilirubin concentrations, using samples from healthy individuals, and found a clinically significant difference only for the Vitros 950 method. It is possible that the difference between serum and heparinized plasma samples with this method is a constant amount and that for samples with abnormally high total bilirubin, no significant difference would be seen. This hypothesis requires formal testing.

In contrast to a previous report (1), values for glucose concentrations were comparable between the two sample types on both analyzers. It has been suggested that glucose concentrations are lower in plasma than in serum as a result of a fluid shift from erythrocytes to plasma caused by anticoagulants (11). Our study demonstrates that serum and heparin plasma are comparable samples types. Separation of cellular components from serum or plasma should be performed within 60 min, as currently recommended (11).

Our data suggest that serum and heparinized plasma samples give results that differ enough to alter clinical decision-making in some assays, including several for which the two specimen types are considered equivalent by the assay manufacturers. For potassium, both serum and plasma reference intervals are readily available, and plasma is the preferred sample type. For the other assays, we recommend that only serum samples be accepted. Alternatively, separate reference intervals for plasma samples will need to be established.

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References

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To the Editor:

Hereditary persistence of α-fetoprotein (HPAFP) is an autosomal inherited disorder in which AFP is persistent in adult life. Since the description of the first case in 1983 (1), this clinically benign disorder has been reported in 11 unrelated families [Ref. (2) and references therein]. The molecular mechanism has been identified in four unrelated families (2–4). It has been related to a −119G>A substitution in the distal hepatocyte nuclear factor-1 binding site of the AFP gene promoter in three families (2–4) and to a −55C>A substitution in the prox-