tient’s menstrual cycle could be interpreted as postovulatory luteal phase rather than follicular. Assuming a 2.2 μg/L positive bias with SST, our current laboratory follicular phase progesterone reference range of <1.6 μg/L could increase to <3.8 μg/L with SST. We recommend that all progesterone serum samples be collected in plain glass tubes until this SST interference problem is resolved. Our laboratory has notified Roche Diagnostics of this finding.

References

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A representative of Roche Diagnostics responds:

To the Editor:

The authors pointed out that falsely increased test results of the Elecsys® Progesterone assay may occur if gel separation tubes are used. This effect was not seen with other assays of the Elecsys reagent line. It may be directly related to the serum volume and the exposure time of the specimen to the tube. We have received similar feedback from others. Our own investigations could not fully elucidate the process that leads to the interference, but as the authors correctly concluded, it might be caused by one of the gel components.

To solve this interference, Roche Diagnostics started to develop a new assay at the beginning of 1998, named Elecsys Progesterone II, which entered the market in April 1999. The Elecsys Progesterone II will have completely replaced the Elecsys Progesterone by the end of June 1999. The Elecsys Progesterone II exhibits a new test design with respect to anti-progesterone antibodies and reagent composition and eliminates the interference caused by gel separation tubes. In conclusion, the authors’ investigations describe a not clearly understood phenomenon obtained for one Elecsys steroid assay that is no longer commercially available.

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More on Calcium Ion Activity Buffers for Coagulation Testing

To the Editor:

The partial thromboplastin time (PTT) test has been problematic over the years, in part because of the multiple reagent and instrument systems used for this measurement. However, preanalytic variables are also operative. Standardization of the prothrombin time (PT) with the International Normalized Ratio has been difficult, but the more complex PTT has not yet been standardized even to this extent. Part of the problem is the greater number of variables that affect the PTT compared with the PT (1).

An article by Rånby et al. (2) in the most recent issue of Clinical Chemistry provided a detailed study of calcium ion buffers used for the collection of blood specimens for the PTT. Because the PTT is the coagulation test of choice to screen for coagulation abnormalities and to monitor heparin therapy, any measures to improve the test would be most welcome.

Some years ago I, and others in my laboratory, became interested in the so-called preinstrumental variables of coagulation testing, which included the effects of the higher than necessary concentrations of citrate anticoagulants in specimens with increased hematocrits (3). We proposed using a lower concentration of citrate, i.e., 109 mmol/L (32 g/L) sodium citrate anticoagulant rather than the traditional 129 mmol/L (38 g/L) (4), for blood collection; this lower concentration currently is recommended. Subsequent work in our laboratory included investigation of the concentration of citrate anticoagulant (which Rånby et al. refer to as buffer) and its effect on the PTT, especially in connection with heparin therapy. We showed that the concentration of citrate ions does influence PTT results, especially at higher heparin concentrations (5). Therefore, it was with more than casual interest that I read the studies of Rånby et al. (2), who propose the substitution of isocitrate for citrate when collecting specimens for coagulation studies. A more “chemically correct” anticoagulant might well improve the diagnostic usefulness of the PTT, but several questions come to mind that would have to be studied before serious consideration is given to modifying the blood collection anticoagulants/buffers for coagulation testing.

Most laboratories use the same collection methods for both the PT and PTT. Because both tests are done on the same plasma sample, the effect of isocitrate anticoagulant on the PT would have to be studied. Although there is no reason to believe that isocitrate would adversely affect PT testing, careful comparative studies would have to be carried out.

More importantly, Rånby et al. opine that the revised procedure would be more sensitive to mild coagulation factor deficiencies. According to their statistical studies of comparative reference intervals, there were more mildly abnormal PTTs with the proposed anticoagulant/buffer. However, the effect of isocitrate on specific coagulation factor assays has not yet been studied. Nor have they reported the clinical correlation studies needed to confirm that these tests have correctly identified individuals with mild coagulopathies. Of course, an increased sensi-
tivity would be the hope of clinical as well as laboratory hematologists provided specificity is also acceptable. But until such investigations are performed, such conclusions would be premature.

Although the results of these studies are intriguing, they cannot yet be considered definitive. I hope that the group from Sweden and/or other investigators will pursue these leads. If the results are as anticipated, laboratories and manufacturers can consider filling future vacuum blood collection tubes with optimal amounts of isocitrate rather than the time-honored citrate anticoagulant.

References

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Metastatic Alveolar
Rhabdomyosarcoma with Increased Serum Creatine Kinase MB and Cardiac Troponin T and Normal Cardiac Troponin I

To the Editor:

We describe a 53-year-old man with metastatic alveolar rhabdomyosarcoma who had a massively increased creatine kinase MB (CK-MB) mass and index. The CK-MB increase was initially interpreted as evidence of myocardial infarction (MI), but the CK-MB remained increased. The patient had increased serum concentrations of cardiac troponin T (cTnT) and normal cardiac troponin I (cTnI). We theorize that tumor anaplasia caused malignant myocytes to express CK-MB and cTnT isoforms. Rhabdomyosarcoma release of both CK-MB and cTnT has not been described previously.

Serum CK and lactate dehydrogenase (LD) activities were assayed at 37 °C with the Hitachi 911 automated analyzer [Boehringer Mannheim (BM)]. CK-MB mass was measured with the Access (Beckman Instruments) immunoenzymatic assay. Serum cTnT was measured using a second-generation Elesys 1010 immunoassay (BM). Serum cTnI was analyzed using both the AxSYM (Abbott) microparticle enzyme immunoassay and the Opus Plus (Dade Behring) fluorogenic two-site immunoassay.

The patient presented to a community hospital with acute, bilateral leg weakness. He had a 3-week history of worsening thoracic back pain and lower extremity parasthesias, and 3 months earlier he had discovered a subcutaneous mass of his left foot. Foot x-ray at that time was unremarkable. The patient’s neurologic examination revealed that lower extremity motor power was decreased to 2+/5. He was unable to walk. His deep tendon reflexes were diminished, and his plantar responses were abnormal bilaterally. The patient was continence of urine but had anal sphincter laxity. He had decreased sensation below the nipples. Spinal cord compression was diagnosed. Computed tomography scan revealed a soft tissue mass that permeated the T2 vertebral body and impinged on the spinal cord. A left foot mass was also confirmed, and computerized tomography scan revealed a circumscribed soft tissue tumor, measuring 4 × 3.9 × 3.8 cm that surrounded the lateral fifth metatarsal. Core biopsies of both tumors revealed similar, round-cell neoplasms that were confirmed to be alveolar rhabdomyosarcomas by immunohistochemical and ultrastructural studies, with positive staining for vimentin, desmin, and muscle-specific actin. The patient underwent thoracic laminectomy. Postoperative neurologic function was unchanged.

The patient was treated with three cycles of doxorubicin and cis-platinum and then with spinal radiotherapy. Six months after his initial presentation, the left foot mass began to grow rapidly. The foot tumor was treated with radiotherapy, but within 1 month, the patient developed left inguinal lymph node metastases and deep venous thrombosis. He was readmitted to hospital where he developed an episode of atypical chest pain. An electrocardiogram revealed only nonspecific T-wave abnormalities. His serum CK was 336 U/L [reference interval (RI), 45–220 U/L]. His CK-MB mass was 150 μg/L (RI, 0–50 μg/L) with a CK-MB index of 45 (RI, 0.0–2.0). A cTnT of 0.95 μg/L (RI, 0.00–0.10 μg/L) and a cTnI of <0.5 μg/L on the Opus Plus [reference value, <0.5 μg/L] and 1.2 μg/L on the AxSYM (RI, 0.0–2.0 μg/L). There was no biochemical evidence of hepatic or renal failure. CK electrophoresis revealed increases of all CK isoenzymes (Table 1). Atypical CK variants were not present. A diagnosis of MI was maintained until serum cardiac enzymes, measured 3 days later, showed sustained increases. At this time, the patient had a CK of 334 U/L, a CK-MB mass of 195 μg/L, a CK-MB index of 58, a cTnT of 0.80 μg/L, and a cTnI of <0.5 μg/L (Opus Plus) and 0.8 μg/L (AxSYM). Serum LD was increased to 570 U/L (RI, 95–195 U/L). Considering the history of atypical chest pain, the equivocal electrocardiogram changes, and the sustained and dramatically increased CK-MB mass and index, a recent MI

Table 1. CK and LD isoenzyme electrophoretic fractionation.

<table>
<thead>
<tr>
<th>CK Isoenzymes (RI), μg/L</th>
<th>LD Isoenzymes (RI), μg/L</th>
</tr>
</thead>
<tbody>
<tr>
<td>CK-MM 130 (0–170)</td>
<td>LDs 334 (&lt;60)</td>
</tr>
<tr>
<td>CK-MB 106 (0–14)</td>
<td>LDs 758 (&lt;70)</td>
</tr>
<tr>
<td>CK-BB 25 (ND)*</td>
<td>LDs 318 (&lt;45)</td>
</tr>
<tr>
<td></td>
<td>LDs 45 (&lt;30)</td>
</tr>
<tr>
<td></td>
<td>LDs 45 (&lt;30)</td>
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</tbody>
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Total CK 261
Total LD 1500

* ND, usually not detected.