Reference Interval for Phosphohexose Isomerase Activity in Aqueous Humor

To the Editor:

A solitary report in the literature suggests that determination of phosphohexose isomerase (PHI; glucose-phosphate isomerase, EC 5.3.1.9) activity in aqueous humor and serum may be a useful adjunct in the diagnosis of retinoblastoma (1). The aqueous humor/serum PHI ratio of 20 patients with retinoblastoma was compared with that for eight “controls” having intraocular diseases other than retinoblastoma, but the normal range of PHI activity in aqueous humor was not defined (1).

Establishing the normal range is obviously necessary to detect departures from normal in pathological conditions.

Collection of aqueous humor is risky and should not be done on completely normal persons. Because senile cataract is a part of the normal aging process, patients with senile cataract have been taken as “healthy” controls in establishing the normal range of aqueous humor lactate dehydrogenase (EC 1.1.1.27) activity (2).

We collected specimens of aqueous humor from 25 patients (14 men and 11 women; age range 50–80 years) with senile cataract who were otherwise healthy. The specimens were collected by limbal puncture (corneal side) at the time of cataract surgery. Venous blood specimens were also collected at the same time. PHI activity was determined in each specimen of aqueous humor and serum (3).

The mean (and SD) aqueous humor PHI activity was 7.8 (3.0) Bodansky units (BU), with a range of 2–15 BU. The distribution was nearly normal. Therefore, the normal range may be taken as 1.8–13.8 BU (mean ± 2 SD), which may be rounded off to 2–14 BU. This range actually covers 96% of the individual data in our sample.

The PHI activity ratio for aqueous humor/serum ranged between 0.10 and 0.50. The mean (and SD) was 0.32 (0.09). The distribution was almost normal. Therefore, the normal range for this ratio may be taken as 0.14–0.50 (mean ± 2 SD), which again covers 96% of our individual data.

References

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Salicylate Interference with Measurement of Acetaminophen

To the Editor:

A popular spectrophotometric assay for serum acetaminophen (used in the Rapid Stat kit; Lancer Division of Sherwood Medical, St. Louis, MO 63101) is based on ring nitration with nitrous acid (1–3). This method may yield erroneously high results in the presence of high concentrations of salicylate. Serum from a patient suffering from salicylate overdose, for example, showed 810 mg of salicylate (Du Pont act) and 69 mg of acetaminophen (Lancer Rapid Stat Kit) per liter 12 h post-ingestion, but gas-chromatographic analysis (by a commercial reference laboratory) indicated that this serum sample contained no acetaminophen.

The instructions with the Rapid Stat kit estimate the positive interference by salicylate as corresponding to 0.15 mg of apparent acetaminophen per liter for each 10 mg of salicylate that is present per liter. This value, used to correct the measured acetaminophen for the patient reported above, did not adequately account for salicylate interference. The value 0.15 appears to be based primarily on the observation (3) that 350 mg of acetylsalicylic acid per liter increased the apparent acetaminophen by 5 mg/L. In vivo, acetylsalicylic acid is rapidly hydrolyzed to salicylic acid, which thus accounts for 93–98% of the total circulating salicylate (4, 5). Interference from salicylates should therefore be based on salicylic acid, not acetylsalicylic acid.

Using the Lancer Rapid Stat Kit, we determined that 10 mg of salicylate per liter corresponds to 7.5 mg of apparent acetaminophen per liter, based on the mean for a 0.2–1.0 g/L series of aqueous salicylic acid standards. To validate this correction factor we sampled serum from patients on high-dose aspirin therapy who were taking no acetaminophen-containing products. We added known amounts of acetaminophen (0–80 mg/L) to these samples and determined salicylate and apparent acetaminophen concentrations. In all cases our corrected acetaminophen concentration was within 8 mg/L of the added amount. This value is within two standard deviations of the mean based on day-to-day precision studies (3).

Others have also reported the need for significant correction for salicylate interference in this colorimetric procedure. Rosenberg et al. (6) determined salicylate interference of 1.4 mg of apparent acetaminophen for each 10 mg of salicylate per liter in the original Glynn and Kendal procedure (2). Bessette and Calam (7) found that acetaminophen (mg/L) = 0.52 salicylate (mg/dL) + 7 for their modification of the Lancer Rapid Stat procedure.

We wish to alert others to the inadequacy of published values for salicylate interference in this acetaminophen assay, including the value indicated in the instruction for the Lancer Rapid Stat Kit. We would echo the recommendation of Rosenberg et al. (6) that each laboratory should determine its own correction for salicylate interference in this colorimetric acetaminophen determination.

References
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Diagnostic Specificity of Serum Myoglobin Radioimmunoassay for Acute Myocardial Infarction is Improved by Using Age-, Sex-, and Race-Specific Reference Ranges

To the Editor:

Many investigators have demonstrated that myoglobinemia is an early quantitative index of acute myocardial infarction (AMI) (1); others find it to be less specific than serum creatine kinase (EC 2.7.3.2) isoenzyme MB (CK-MB) (2, 3). We demonstrated that serum myoglobin concentrations are sex-, age-, and race-related and suggested that the specificity of the test might be improved by using different reference ranges according to age, sex, and race (4). The reference range arbitrarily set to be the tolerance limits for coverage of at least 99% of the population with 95% confidence, determined from data on 292 apparently healthy subjects, was 18-63 μg/L (generalized reference range). In contrast, if the data were grouped according to age, sex, and race, the upper limits of reference ranges varied from 40 μg/L (20-50 years, female, black) to 91 μg/L (20 years, male, black) (4).

We studied 55 patients admitted to the coronary care unit of our medical center: 31 white (19 men, with two ≤50 years, and 15 women, with three ≤50 years) and 24 black persons (16 men, with four ≤50 years, and eight women, with three ≤50 years). Diagnosis of AMI was based on the clinical setting plus diagnostic electrocardiographic changes, myocardial scintigraphy, or serum CK-MB concentration, or some combination of these. Blood samples were routinely drawn 0, 6, and 12 h after admission. The mean peak myoglobin concentration (± one standard error of the mean) for 20 patients with AMI was 306 (53) μg/L, compared with 51 (8) μg/L for 35 patients without AMI. Diagnostic classifications based on peak serum myoglobin concentrations are shown in the following tabulation:

<table>
<thead>
<tr>
<th>No. patients</th>
<th>Age-, sex-, race-specific reference ranges (4)</th>
<th>Generalized reference range (18-63 μg/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>With AMI</td>
<td>19 ± 1 20</td>
<td>20 0 20</td>
</tr>
<tr>
<td>Without AMI</td>
<td>4 ± 31</td>
<td>7 28 35</td>
</tr>
<tr>
<td>Total</td>
<td>23 ± 32</td>
<td>27 28 55</td>
</tr>
</tbody>
</table>

Sensitivity, specificity, and positive predictive values of the serum myoglobin concentrations were 95%, 89%, and 83%, respectively, when the age-, sex-, race-specific reference ranges were used; and 100%, 80%, and 74%, respectively, when the generalized reference range was used.

The only falsely negative patient was an 80-year-old black man whose myoglobin concentration was 64 μg/L at the time of admission (reference range 18-91 μg/L). This value decreased to 38 and 32 μg/L, respectively, 6 and 12 h after admission, which suggests that this patient had in fact had an AMI sometime before his admission.

Of four patients with a falsely positive test by both reference ranges three had muscle trauma—a condition known to cause an increase in serum myoglobin concentrations. The other patient, a 57-year-old white woman, had myoglobin concentrations of 267 μg/L at 6 h and 33 μg/L at 48 h after admission; the corresponding values for total CK were 243 and 75 U/L, respectively (reference range: 0-80 U/L). CK-MB was not detected. No electrocardiographic changes suggestive of AMI were observed. No myoglobin scintigraphy was performed. This patient was admitted to the coronary care unit for ill-defined epigastric pain. Chronic obstructive pulmonary disease was also present. The remaining three falsely positive patients were black men with peak myoglobin concentrations of 91, 90, and 68 μg/L, respectively, which are negative when the reference range of 18-91 μg/L specific for black men is used, but are positive when the generalized reference range of 18-62 μg/L is used.

Thus the results of our study with a limited number of coronary care unit patients indicate that the specificity of myoglobin RIA can be improved, especially among black men, by using different reference ranges specific for age, sex, and race, and that the diagnostic efficiency of myoglobin RIA compares favorably with that of serum CK-MB reported recently by Witherspoon et al. (5). However, more data are needed to determine whether serum myoglobin RIA with age-, sex-, and race-specific reference ranges is as useful as serum CK-MB in early diagnosis of AMI.

References

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IL 1303: Viscous Specimens Can Cause Problems

To the Editor:

We would like to call attention to a problem in the analysis of arterial blood gases in specimens of extremely high viscosity. Such specimens will apparently go through the visible pathway of the IL 1303 (1) but will trigger an error code, SAMPLING ERROR. Such error messages, in our experience, have frequently been spurious and therefore may prompt the technologist to disregard the message. The specimen, run again, will reproduce the same numbers, and corresponding control specimens will run correctly. We describe a case that illustrates that acceptance of such results may be dangerous.

The patient in question presented with polycythemia secondary to dehydration and hypoxia. The patient’s hematocrit concentration was 72%. The whole-blood viscosity was much above normal (4.338 Pa-s at 37 °C).

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