Hyperbilirubinemia in Anicteric Blood?
Yu Chen,1,2* Lauren Graham,3 Ihssan Bouhtiauy,4 Gail Watts,1 and Mary Hamilton1

CASE DESCRIPTION
Plasma total bilirubin for a 65-year-old man was high [19.1 mg/dL (326 μmol/L)] on a Roche cobas 6000 analyzer. However, the specimen was anicteric and the icteric index was 1 (approximately 1 mg/dL or 17 μmol/L). A dilution study demonstrated nonlinear results. Direct bilirubin was measured as normal. The split specimen aliquots were further measured on analyzers from 5 different manufacturers (Table 1). The patient’s total protein and albumin were 93 and 34 g/L (reference intervals: 60–80 and 38–50 g/L).

QUESTIONS
1. What might cause artifactual hyperbilirubinemia in anicteric blood?
2. What strategies can be employed to deal with spurious increased bilirubin results?

The answers are below.

ANSWERS
The patient’s serum IgG, IgM, and IgA concentrations were 3.9, 0.1, and 39.2 g/L, respectively. Protein elec-
trophoresis revealed an IgA-λ paraprotein (38.3 g/L), a small Bence Jones λ in serum, and a prominent Bence Jones λ (27.3 g/day) in urine.

Table 1. Total bilirubin and direct bilirubin measurements for the 65-year-old man.

<table>
<thead>
<tr>
<th>Analyzer</th>
<th>Total bilirubin, μmol/L</th>
<th>Direct bilirubin, μmol/L</th>
</tr>
</thead>
<tbody>
<tr>
<td>Roche cobas 6000</td>
<td>326</td>
<td>3</td>
</tr>
<tr>
<td>Roche Integra 400</td>
<td>183</td>
<td>—</td>
</tr>
<tr>
<td>Roche Modular P</td>
<td>255</td>
<td>2</td>
</tr>
<tr>
<td>Abbott Architect c16000</td>
<td>9</td>
<td>9</td>
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<tr>
<td>Siemens Dimension EXL</td>
<td>5</td>
<td>1</td>
</tr>
<tr>
<td>Beckman DxC 600i</td>
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<td>2</td>
</tr>
<tr>
<td>Ortho Vitros 5600</td>
<td>10</td>
<td>9</td>
</tr>
</tbody>
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1 Department of Laboratory Medicine, Dr. Everett Chalmers Regional Hospital, Horizon Health Network, Fredericton, New Brunswick, Canada; 2 Department of Pathology, Dalhousie University, Halifax, Nova Scotia, Canada; 3 Department of Laboratory Medicine, Upper River Valley Hospital, Horizon Health Network, Waterville, New Brunswick, Canada; 4 Département de Biochimie, Réseau de santé Vitalité, Edmundston, New Brunswick, Canada.

* Address correspondence to this author at: Division of Clinical Biochemistry, Department of Laboratory Medicine, Dr. Everett Chalmers Regional Hospital, Horizon Health Network, Fredericton, New Brunswick, Canada E3B 5N5. Fax 506-452-5422; e-mail yu.chen@horizonnb.ca.

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IgG and IgM paraproteins have been suggested to interfere with total bilirubin assays, especially on Roche analyzers, by forming precipitants (1–5). In this case, IgA-λ and possibly Bence Jones λ involvement were indicated. To deal with pseudo-hyperbilirubinemia, naked eye examinations, spectrophotometric indices, different analytical measurements, and the clinical picture will be helpful (1).

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References