exclude the possibility that positional effects also occur in mRNA analyses.

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References
6. Thomas von Kanel, Mircea Schneider, Javier Sanz, Sabina Gallati. Division of Human Genetics, University of Bern, Switzerland.

Table 1. HbA1c and related measurements over time.

<table>
<thead>
<tr>
<th>Date</th>
<th>Roche Tina-quant</th>
<th>Roche Integra</th>
<th>Tosoh 2.2 Plus HPLC</th>
<th>Serum glucose, mmol/L (mg/dL)</th>
<th>Patient fasting?</th>
</tr>
</thead>
<tbody>
<tr>
<td>April 1997</td>
<td>5.4</td>
<td></td>
<td></td>
<td>5.7 (102)</td>
<td>Unknown</td>
</tr>
<tr>
<td>November 2002</td>
<td></td>
<td></td>
<td></td>
<td>8.4 (152)</td>
<td>Yes</td>
</tr>
<tr>
<td>December 2002</td>
<td></td>
<td></td>
<td></td>
<td>8.6 (154)</td>
<td>Yes</td>
</tr>
<tr>
<td>February 2003</td>
<td>7.3</td>
<td>Not reported</td>
<td></td>
<td>7.1 (128)</td>
<td>Yes</td>
</tr>
<tr>
<td>July 2003</td>
<td>6.8</td>
<td>Not reported</td>
<td></td>
<td>7.9 (142)</td>
<td>Yes</td>
</tr>
<tr>
<td>October 2003</td>
<td>6.6</td>
<td>Not reported</td>
<td></td>
<td>6.9 (124)</td>
<td>Unknown</td>
</tr>
<tr>
<td>June 2004</td>
<td>6.4</td>
<td>Not reported</td>
<td></td>
<td>7.4 (133)</td>
<td>Yes</td>
</tr>
<tr>
<td>September 2004</td>
<td>7.0</td>
<td>Not reported</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>January 2005</td>
<td>4.8</td>
<td>Not reported</td>
<td>&quot;1.9&quot;a</td>
<td>7.7 (138)</td>
<td>Yes</td>
</tr>
<tr>
<td>July 2005</td>
<td>4.6</td>
<td>6.6</td>
<td>Not reported, &quot;2.7&quot;a</td>
<td>6.8 (123)</td>
<td>Yes</td>
</tr>
</tbody>
</table>

* The Tosoh HbA1c values that are in quotation marks were never reported. They represent the primary data from the analyzer but were accompanied by error flags.

Mislabeled Glycated Hemoglobin Results in a Patient with Hemoglobin SC Disease

To the Editor:

We encountered a 62-year-old man with hemoglobin (Hb) SC disease. Diabetes mellitus had been previously diagnosed in this patient on the basis of 2 increased fasting glucose values. During an 8-year period, his glycated Hb (GHb) was measured by 3 different methods (Table 1), each of which was affected differently by his Hb variants. The GHb results depended more on the method used than on the patient's mean blood glucose.

The patient’s GHb was measured initially (April 1997) by use of the Roche Hitachi Tina-quant immunoassay. In 2003–2004, we used the Tosoh 2.2 Plus, an assay based on HPLC, which produced chromatograms that were flagged as invalid, so we sent the patient's samples to a commercial laboratory, which used the Roche Integra immunoassay. In 2005, we again used the Hitachi Tina-quant method, which gave a GHb result of 4.8%. On the patient’s next sample (July 2005), we again used the Roche Tina-quant method, which gave a GHb result of 4.8%. On the patient’s next sample (July 2005), we again used the Roche Tina-quant method, which gave a GHb result of 4.8%.

The Roche Hitachi Tina-quant immunooassay is directed at the N-terminal portion of the Hb β chain. This method accurately detects glycated HbA, HbS, and HbC (1) and might be predicted to provide accurate values in this patient with SC disease. Although based on the same principle, the Roche Integra immunooassay exhibits significant interferences from HbS and HbC (1, 2), even when present in heterozygotes (HbAS, HbAC). Since the time of these determinations, the assay has been updated (3), but the original version is still widely used. In contrast, the Tosoh 2.2 Plus method measures HbA1c specifically and can be used in patients with HbAS (S trait) or HbAC (C trait) (1) because a substantial amount of HbA is present in these patients; our patient, of course, had no HbA.

From the patient’s fingerstick glucose records, we estimated (4) that his mean blood glucose was 6.7 mmol/L (120 mg/dL), a value higher than the 5.2 mmol/L (94 mg/dL) suggested by his Roche Tina-quant GHb results.

Although analytically accurate, the Roche Tina-quant GHb gave misleading results. The extent of Hb glycation depends not only on mean glucose concentration but also on the lifespan of the erythrocytes. The reference intervals (and the equations converting GHb to mean glucose) assume a normal erythrocyte lifespan, roughly 120 days. Patients with Hb SC disease typically have erythrocyte life spans of ~29 days (5).

In our case, none of the 3 GHb methods used provided clinically relevant data. With the Tosoh method, there was no HbA to measure; with the Roche Integra method, HbS and HbC were known to interfere; and with the Roche Hitachi Tina-quant, the result was misleading because of...
the patient’s shortened erythrocyte life span. SC disease is rare (0.017% prevalence in African Americans), but heterozygous Hb variants are not rare, nor are patients with altered erythrocyte life spans.

Analogous to Hb, other serum proteins, predominantly albumin, become glycated. So-called “fructosamine” is a rapid, relatively inexpensive, colorimetric assay whose value reflects short-term (2–3 weeks) glycemic control. This test is independent of Hb and can be used when the erythrocyte life span is altered (hemolysis and/or transfusion) or in the presence of Hb variants.

Laboratories should do a better job alerting physicians to the possibility of clinically significant interferences affecting GHb values, which should always be interpreted in conjunction with long-term fingerstick glucose records. For one thing, this can suggest when glycohemoglobin values are misleading. In addition, glycohemoglobin, as a surrogate for mean plasma glucose, cannot provide information on the number or severity of significant hypo- and hyperglycemic events. Laboratories should consider including in their GHb reports an indication of the method used, a disclaimer about potential interferences from Hb variants, and/or a note regarding the effects of altered erythrocyte life span.

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References