

## A Review of Variant Hemoglobins Interfering with Hemoglobin A1c Measurement

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### Abstract

Hemoglobin A1c (HbA1c) is used routinely to monitor long-term glycemic control in people with diabetes mellitus, as HbA1c is related directly to risks for diabetic complications. The accuracy of HbA1c methods can be affected adversely by the presence of hemoglobin (Hb) variants or elevated levels of fetal hemoglobin (HbF). The effect of each variant or elevated HbF must be examined with each specific method.

The most common Hb variants worldwide are HbS, HbE, HbC, and HbD. All of these Hb variants have single amino acid substitutions in the Hb  $\beta$  chain. HbF is the major hemoglobin during intrauterine life; by the end of the first year, HbF falls to values close to adult levels of approximately 1%. However, elevated HbF levels can occur in certain pathologic conditions or with hereditary persistence of fetal hemoglobin. In a series of publications over the past several years, the effects of these four most common Hb variants and elevated HbF have been described.

There are clinically significant interferences with some methods for each of these variants. A summary is given showing which methods are affected by the presence of the heterozygous variants S, E, C, and D and elevated HbF. Methods are divided by type (immunoassay, ion-exchange high-performance liquid chromatography, boronate affinity, other) with an indication of whether the result is artificially increased or decreased by the presence of a Hb variant. Laboratorians should be aware of the limitations of their method with respect to these interferences.

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**Abbreviations:** (ADA) American Diabetes Association, (GHB) glycated hemoglobin, (DCCT) Diabetes Control and Complications Trial, (Hb) hemoglobin, (HbA1c) hemoglobin A1c, (HPLC) high-performance liquid chromatography, (IFCC) International Federation of Clinical Chemistry (RM) Reference Method, (UKPDS) United Kingdom Prospective Diabetes Study, (NGSP) National Glycohemoglobin Standardization Program

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