Hemoglobin Variants and Derivatives on A1C Measurement

Abnormal hemoglobin (Hb) variants (i.e. HbS, HbC, and HbE) and chemically modified derivatives (i.e. carbamyl-Hb) can cause interference and dramatically affect the results of A1C measurement. Such problems should be suspected whenever A1C results are out of keeping with results of self-monitoring of blood glucose. The Cholestech GDX™ System has virtually no interference from hemoglobin variants because the method uses boronate affinity chromatography to separate the glycated hemoglobin fraction from the non-glycated fraction.

Nearly 8% of African Americans carry the HbS trait and 2.3% carry HbC. In sub-Saharan Africa, prevalence of these two is up to one-third of all patients. HbE can be as high as 30% in Southeast Asia. HbF can reach 30% in individuals with hereditary persistence. Chemically modified Hbs may be chronically present in diabetic patients. Carbamylated Hb is the most commonly encountered of these.[2]

Because different laboratories use different methods, practitioners should familiarize themselves with the methodology of their local laboratory. Preferably a single laboratory should be used for all measurements for patients of a given physician to lessen confusion. The table below references some of the more common methods and the Hb variants that will cause interference with the measurements.

Methods	Interference (Yes/No)				
	Carbamyl-Hb	Hb C trait	Hb E trait	Hb S trait	Elevated HbF
Boronate Affinity Chromatography					
Cholestech GDX™[1]	**No**	**No**	**No**	**No**	**No**
Primus CLC 330™[2,3]	No	No	No	No	No
Abbott IMx®[2,3]	No	No	--	No	No
Cation-exchange chromatography					
Bio-Rad Diamat®[2,3]	Yes	Yes	No	Yes	Yes
Bio-Rad Variant®[2,3]	Yes	No	No	Yes	Yes
Menarini 8140[2,4]	Yes	No	Yes	Yes	No
Tosoh A1c 2.2 Plus™[2]	No	No	Yes	No	No
Immunoassay					
Bayer DCA 2000®[2,3]	No	No	No	No	Yes
Roche TinaQuant II®[2,3]	No	No	No	No	No
Roche Unimate®[2]	No	No	--	Yes	No

-- No Data Available

References
1. John WG. Glycated haemoglobin analysis. Ann Clin Biochem 1997; 34 (Pt 1):17-31.
2. Bry L, Chen PC, Sacks DB. Effects of hemoglobin variants and chemically modified derivatives on assays for glycohemoglobin. Clin Chem 2001; 47:153-63.
3. Goldstein DE, Little RR, Lorenz RA, Malone JI et al. Tests of glycemia in diabetes. Diabetes Care 1995; 18:896-909.
4. Roberts WL, De BK, Brown D, Hanbury CM et al. Effects of hemoglobin C and S traits on eight glycohemoglobin methods. Clin Chem 2002; 48:383-5.