Glycation of Hemoglobin C in the Heterozygous State in Diabetic Patients

Nonenzymatic glycation of hemoglobin is usually quantified by the amount of HbA_{1c} after separation of hemoglobin isoforms. Glycation is known to occur for hemoglobin S (HbS) in patients with homozygous or heterozygous sickle cell disease (1,2). Hemoglobin C (HbC) results from the substitution of lysine for glutamic acid at position 6 of the β-chain and is found exclusively in negroid populations (Ghana, Burkina) with gene frequencies approaching 0.15 (3). We report here results for five diabetic patients in whom HbC could be observed in the heterozygous state. Using a semi-automated GHb analyzer system (MDMS Analyzer, Bio-Rad, Richmond, CA), separation of glycated HbC from total HbC is obtained (Fig. 1), and the HbA_{1c} values are not affected by HbC because its retention time is longer than HbA. The method is not really calibrated to give a quantitative measurement of glycated HbC; therefore, the percentage of glycated HbC was estimated by using the areas ratio. In these conditions, the five patients had HbC levels ranging from 28 to 37% of total hemoglobin. A significant correlation (r = 0.98) was found between the percentage of glycated HbC (8.7, 17.6, 8.9, 14.5, and 9.0%) and HbA_{1c} levels (7.3, 12.7, 5.9, 10.5, and 6.6%, respectively; normal range 4.0–5.8%) despite higher glycation rates for HbC with a mean HbA_{1c}: glycated HbC ratio at 0.73. This heterogeneity in glycation has been reported already by in vitro incubation of purified HbA and HbC with [^{14}C]glucose for 24 h at 37°C (ratio of 0.66) (4), whereas Aleyassine (5), using a combination of colorimetric and microcolumn chromatography methods, has found that HbC is glycated at a rate that is similar to that for HbA.

In short, our results prove that HbA and HbC are glycated to different degrees. The presence of higher concentrations of glycated HbC levels is suggestive of glycation at additional sites of the molecule caused by the existence of additional NH2 groups. This could be taken into consideration for clinical practitioners, considering the prevalence of such hemoglobin variants in a diabetic population and that interference problems occurred in GHb measurement by use of such methods as ion exchange or affinity chromatographies (6).

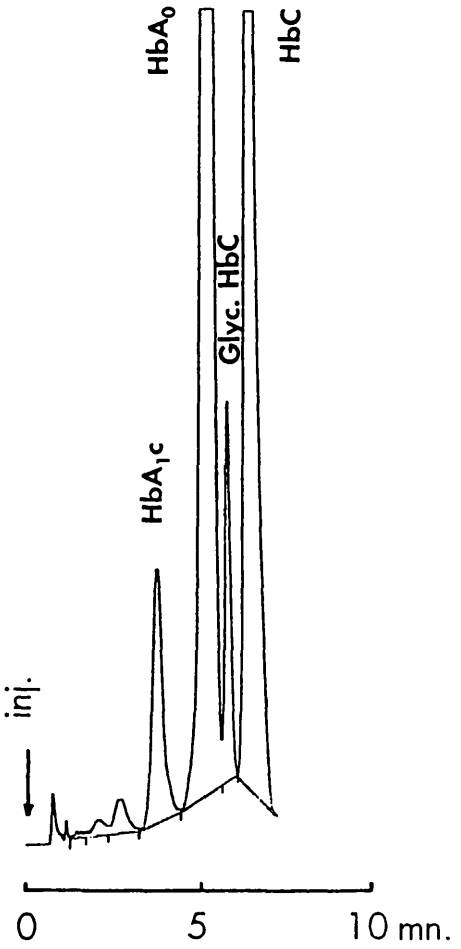

Figure 1—*Typical chromatogram from a diabetic patient with HbC trait.*

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References

1. Sosenko JM, Flückiger R, Platt OS, Gabbay KH: Glycosylation of variant hemoglobins in normal and diabetic subjects. *Diabetes Care* 3:590–93, 1980
2. Reid HL, Famodu AA, Photiades DP, Osamo ON: Glycosylated hemoglobin A_{1c} and HbS_{1c} in nondiabetic nigerians. *Trop Geogr Med* 44:126–30, 1991
3. Scriver CR, Beaudet AL, Sly WS, Valle D: *The Metabolic Basis of Inherited Disease*. 6th Ed. 1989, p. 2300–301
4. Tegos C, Rahbar S, Blume K, Johnson C, Beutler E: Glycosylated minor C, D, and E hemoglobins. *Biochem Med* 26:121–25, 1981
5. Aleyassine H: Glycosylation of hemoglobin S and hemoglobin C: *Clin Chem* 26: 526–27, 1980
6. Allen KR, Hamilton AD, Bodansky HJ, Poon P: Prevalence of hemoglobin variants in a diabetic population and their effect on glycated hemoglobin measurement. *Ann Clin Biochem* 29:426–29, 1992