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SYMPOSIUM

Biologic Variability in Plasma Glucose, Hemoglobin A1c, and Advanced Glycation End Products Associated with Diabetes Complications

R. David G. Leslie, M.D.,[1] and Robert M. Cohen, M.D.[2,3]

Abstract

Plasma glucose plays a key role in the complications of diabetes mellitus. Hemoglobin A1c (HbA1c) and circulating concentrations of advanced glycation end products (AGEs) are central to diabetes clinical care and pathophysiology. However, there is evidence for variation between individuals in the relationship of plasma glucose to both these measures and to specific complications. The glycation gap (GG) and hemoglobin glycation index represent tools for quantitating the variability in the relationship between plasma glucose and HbA1c useful for identification of underlying mechanisms. Recent evidence demonstrates the heritability of HbA1c, the GG, and AGEs, yet not of glycated serum proteins. There has been tremendous effort devoted to identifying the heritable basis of types 1 and 2 diabetes; however, studies on the heritable contributors to these mediators of glucose effect on complications are only beginning. New evidence for normal biologic variation in the distribution of glucose into the red blood cell (RBC) intracellular compartment and RBC lifespan in people with and without diabetes represent candidates for heritable mechanisms and contributors to the rise in HbA1c with age. Taken as a whole, genetic and mechanistic evidence suggests new potential targets for complications prevention and improvement in complications risk estimation. These observations could help tilt the risk–benefit balance in glycemic control toward a more beneficial outcome.

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Author Affiliations: [1]Centre for Diabetes and Metabolic Medicine, Institute of Cell and Molecular Science, St. Bartholomew's Hospital, London, United Kingdom; [2]Division of Endocrinology, Diabetes, and Metabolism, Department of Medicine, University of Cincinnati, Cincinnati, Ohio; and [3]Medical Service, Cincinnati Veterans Affairs Medical Center, Cincinnati, Ohio

Abbreviations: (ADAG) A1c-derived average glucose, (AGE) advanced glycation end product, (CGM) continuous glucose monitoring, (CML) carboxymethyl-lysine, (DirecNet) Diabetes Research in Children Network, (DZ) dizygotic, (eAG) estimated average glucose, (FOS) Framingham Offspring Study, (GG) glycation gap, (GSP) glycated serum protein, (HbA1c) hemoglobin A1c, (HGI) hemoglobin glycation index, (MZ) monozygotic, (NHANES) National Health and Nutrition Examination Survey, (RBC) red blood cell, (T1DM) type 1 diabetes mellitus, (T2DM) type 2 diabetes mellitus

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Corresponding Author: Robert M. Cohen, M.D., Division of Endocrinology, Diabetes, and Metabolism, University of Cincinnati Medical Center, 3125 Eden Ave., Cincinnati, OH 45267-0547; email address robert.cohen@uc.edu