Filter Paper/Affinity Chromatography vs. Venipuncture/HbA_1 Ion-Exchange Chromatography

Determination of glycosylated hemoglobin (GHb) is widely used in clinical practice to monitor long-term glycemia in people with diabetes, and its use as a screening tool has also been investigated (1).

Several investigators have explored the feasibility of measuring GHb from blood samples dried on filter paper (2–7).The recent article by Slemenda et al. (8) compared a commercially available mail-in paper strip (filter paper) method (Evalulab, Palm City, FL) to what they refer to as a "standard" or "usual" method, specifically an HbA_1 microcolumn method (manufacturer not specified). However, the HbA_1 ion-exchange column methods are actually somewhat outdated; most clinical laboratories now use either specific HbA_{1c} ion-exchange or affinity chromatographic methods (9). (We must emphasize that there is nothing intrinsically wrong with the use of HbA_1 determinations but only that the method has serious well-recognized drawbacks compared with other methods, particularly with respect to specimen handling, storage effects, and interfering factors such as hemoglobinopathies.)

In their report, Slemenda et al. (8) conclude that both methods had adequate precision but that results differed when patients were ranked for glycemic control by the GHb results. There was a surprisingly low correlation between the two methods ($r < 0.80$).

We have shown an excellent correlation ($r = 0.97$) between results with affinity chromatography of fresh blood samples and filter paper–spotted samples, where the filter paper method was identical to that performed by Evalulab (3). In addition, there are previous reports by others of excellent correlations between ion-exchange/HbA_1 and GHb/affinity chromatography (10). Because Slemenda et al.'s actual data points are not shown, it is not clear whether their modest correlation may be due to a few outliers. There are also many factors that can interfere with HbA_1 methods but do not generally interfere with affinity chromatographic methods such as that used by Evalulab, e.g., abnormal hemoglobins. These factors were not discussed but could account for some of the discrepancies in GHb ranking between the methods. It would have been helpful if the authors had further investigated clinically significant discrepancies to determine which of the results was more accurate.

We do concur with Slemenda et al. that caution should be taken when comparing GHb data between methods. The fact that different methods can be measuring different glycosylated components, combined with the lack of reference standards, makes it difficult to compare results from different laboratories even when the same assay method is used at each location. The problem could be solved if standardization of GHb between laboratories were available (11).

RANDIE R. LITTLE, PhD
DAVID E. GOLDSTEIN, MD

From the Departments of Child Health and Pathology, University of Missouri School of Medicine, Columbia, Missouri.

Address correspondence and reprint requests to Randie R. Little, PhD, M263, Department of Pathology, University of Missouri School of Medicine, 1 Hospital Drive, Columbia, MO 65212.

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Reply

We appreciate the comments by Little et al. regarding our report on the relationship between these two meth-

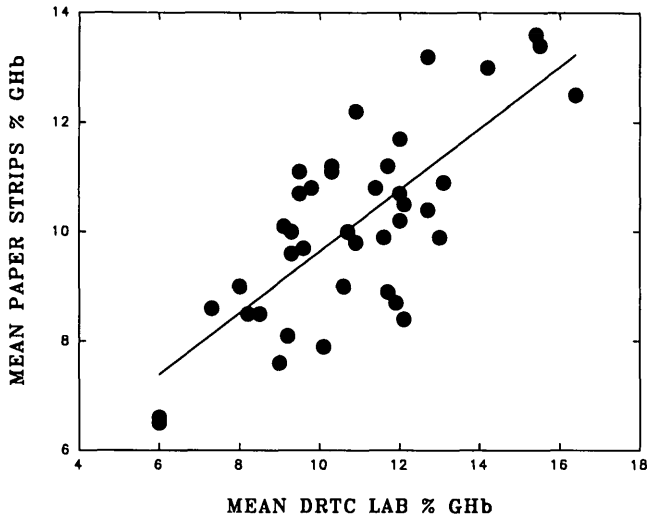

FIG. 1. Scatterplot of glycosylated hemoglobin (GHb) values (mean of four samples per subject per method). DRTC, Diabetes Research Training Center.

ods of assessing percentage of glycosylated hemoglobin. We, too, were somewhat surprised by the magnitude of the correlations, given the stronger correlations found by Little et al. (1,2).

Figure 1 addresses the issue of whether a few outliers accounted for the reported correlations. As is clearly shown, there are no especially influential points.

As mentioned in our original article, dividing the data into two groups (before and following a specific date) improved the fit but not the level found in the well-controlled within-laboratory experiments previously published (3). It should also be noted that the values shown in Fig. 1 are the mean of four measurements on the individual samples from each laboratory, thereby greatly reducing the influence of any single aberrant value on the reported correlation. Perhaps further between-method comparisons can resolve these differences.

CHARLES W. SLEMENDA, DrPH
S. EDWIN FINEBERG, MD
DAVID G. MARRERO, PhD

From the Department of Medicine, Diabetes Research Training Center, and the Regenstrief Institute for Health Care, Indiana University School of Medicine, Indianapolis, Indiana.

Address correspondence and reprint requests to Charles W. Slemenda, DrPH, Indiana University School of Medicine, Department of Medicine, Division of Biostatistics, Riley Research Wing, Room 135, 702 Barnhill Drive, Indianapolis, IN 46202–5200.

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Reply

We thank Dr. Kabadi for outlining the formidable difficulties of even considering any modification of the National Diabetes Data Group (NDDG) system of classifying the various syndromes of diabetes (1). It may appear to be inscribed in granite, but perhaps will turn out to be in limestone.

As Dr. Kabadi points out in his response to our two editorials, concern regarding the 1979 classification goes back many years (2,3). The main premise in revisiting the current classification is to underscore the need to resist the calcification of the classification. The NDDG produced a landmark classification that is far from being a rigid dogma. In fact, as long ago as 1980, the World Health Organization (WHO) Expert Committee on Diabetes Mellitus stated as one of their 10 recommendations "international standardization should be increased and directed toward diagnostic tests for diabetes and revised criteria for diagnoses, and a more rational classification of diabetes. . ." (4). Thus, it carries within its framework an inherent foresight calling for revisions to accommodate forthcoming information on the phases of diabetes and its heterogeneity. Any diabetes classification should be a dynamic structure reflecting and aiding our understanding of this puzzling group of disorders. The central issue today as we enter the 1990s is whether we can at least start structuring the diagnoses on the basis of etiology and pathology so that the phenotypic expression and severity of the various stages of each disorder become a secondary consideration. There is confusion and debate whether non-insulin-dependent (type II) diabetes equals non-insulin-dependent diabetes mellitus (NIDDM) and just what is meant by insulin-dependent diabetes mellitus (IDDM) as opposed to insulin-dependent (type I) diabetes. We need at least an etiologically based diagnostic framework to which the flood of advances in our understanding of the syndromes of diabetes can be related.

We have reviewed evidence that as many as a quarter of the patients responding poorly to oral agents actually have diabetes of autoimmune origin (3). Zimmett and King (5) point out that, in one third of patients ultimately diagnosed as having IDDM, the onset is after age 30 yr. We need prospective studies, both epidemiological and metabolic, of this group, which far outnumber those with conventional IDDM. As we learn more specifically to block the T-lymphocyte–mediated attack on the islets, there will be demand for more etiological diagnosis. As the demand for specific diagnostic tests increases, their cost should decline and will be trivial in relation to the long-term savings. Furthermore, taking into con-