

**ABSTRACT****Blood Testing And Monitoring For Type 2 Diabetes Control**

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Diabetics currently manage their disease by a combination of daily self-monitored blood glucose (SMBG) measurements with assessment of glycated hemoglobin (A1c) levels every 3-6 months. A number of recent reports question the efficacy and relevance of frequent SMBG monitoring for the millions of type 2 diabetics not taking insulin (Brownlee and Hirsch, 2006; Saudek et al., 2006). For type 2 diabetics, who make up 80-90% of the diabetes population, the role of SMBG and frequency of testing are not clear, especially in diet-treated patients. The A1c test is acknowledged worldwide as the gold standard of diabetes management and predictor of diabetic complications, but to date it is not accepted as a reliable screening or diagnostic tool for diabetes (Saudek et al., 2006). Due to the lifespan of the erythrocyte, an A1c measurement represents a weighted mean of glycated hemoglobin over a 3-4 month period, which, in certain instances, fails to correlate with accepted diagnostic criteria: fasting plasma glucose levels and/or oral glucose tolerance testing. The influence of variability in the erythrocyte lifespan, e.g., with diabetes, requires more study and the value of monitoring A1c in predicting or preventing microvascular disease in type 2 subjects is not strongly established (Jeffcoate, 2004).

Over the last 15 years there have been many reports published which describe the use of serum protein indicators for the assessment of glycemic status over a period intermediate between SMBG and A1c (every 2-4 weeks), specifically fructosamine (FA) and glycated albumin (GA), owing to their 14-20 day half-life in serum. The kinetics of A1c, fructosamine, and glycated albumin in response to blood glucose dynamics have been studied by Tahara and Shima (1995) and have been found to reflect the weighted mean of the preceding plasma level for 100, 40, and 30 days, respectively. Glycated serum proteins (FA, GA) were found to be more predictive by multivariate analysis of the standard deviation of mean glucose levels than was A1c in a study of both type 1 and type 2 patients who performed regular self-monitoring of

glucose over a 12-week period (Beisswenger et al., 1993). Kurashita et al. (1992) recommended both A1c and GA as accurate measures of maternal glucose metabolism during pregnancy, but reports by Narayanan (1991) and Hicks et al. (2001) recommended FA and GA for gestational diabetes monitoring. When compared to A1c and GA, however, fructosamine was found by Shima et al. (1989) to be a poorer predictor of borderline diabetes and glucose tolerance test results.

The fructosamine assay, which measures all glycated serum proteins, has provided an easily automated and thus inexpensive assessment of intermediary glycation. A diabetes screening project by Carter et al. (2000) measuring SMBG and FA in a workplace population of 277 demonstrated a 15% increase in diabetic detection due to the addition of fructosamine. A larger, more recent study by Lindsey et al. (2004) employing FA monitoring demonstrated glycemic improvement, but no improvement in the quality of life in the diabetic subjects. The fructosamine assay was originally colorimetric and iterations of the test have suffered through reports of inaccuracy and unreliability when compared to SMBG or A1c. The measurement of glycated albumin, which represents 80% of plasma proteins, has been reported as a more reliable intermediate index by virtue of the fact it measures a single plasma protein and is subject to fewer interference factors than the colorimetric-based FA assay. Further, Schleicher et al. (1993) demonstrated that GA measurements, unlike A1c and FA, are inherently compensated for albumin concentration and thus relatively independent of high and low blood albumin states. Additionally, glycoalbumin formation is not a surrogate but a principal avenue leading to diabetic complications, such as nephropathy (Bundschuh et al., 1992; Cohen et al., 1995; Chen et al., 2000). Recently glycated albumin has been shown to induce superoxide generation in cells (Yoo et al., 2004), which leads to free radical production, pathologic sequelae, and deleterious complications, such as retinopathy (Monnier et al., 2006).

A well-established intermediate index would be advantageous for assessing the millions of type 2 patients who exert poor diabetic control, as well as gestational diabetics and perhaps the geriatric patient who wishes to reduce the number of SMBG fingersticks (Survey, 2005). To date, however, GA measurement has been confined to specialty laboratories and is relatively expensive. The time is right for a reliable test for intermediate glycation that rapidly processes a drop of patient blood and displays a GA percentage in a point-of-care or over-the counter product. Such a GA index will serve as a reliable indicator of diabetes management, filling the void between SMBG and A1c and might also serve as a screening or diagnostic tool, especially in the instance of type 2 prediabetes.

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