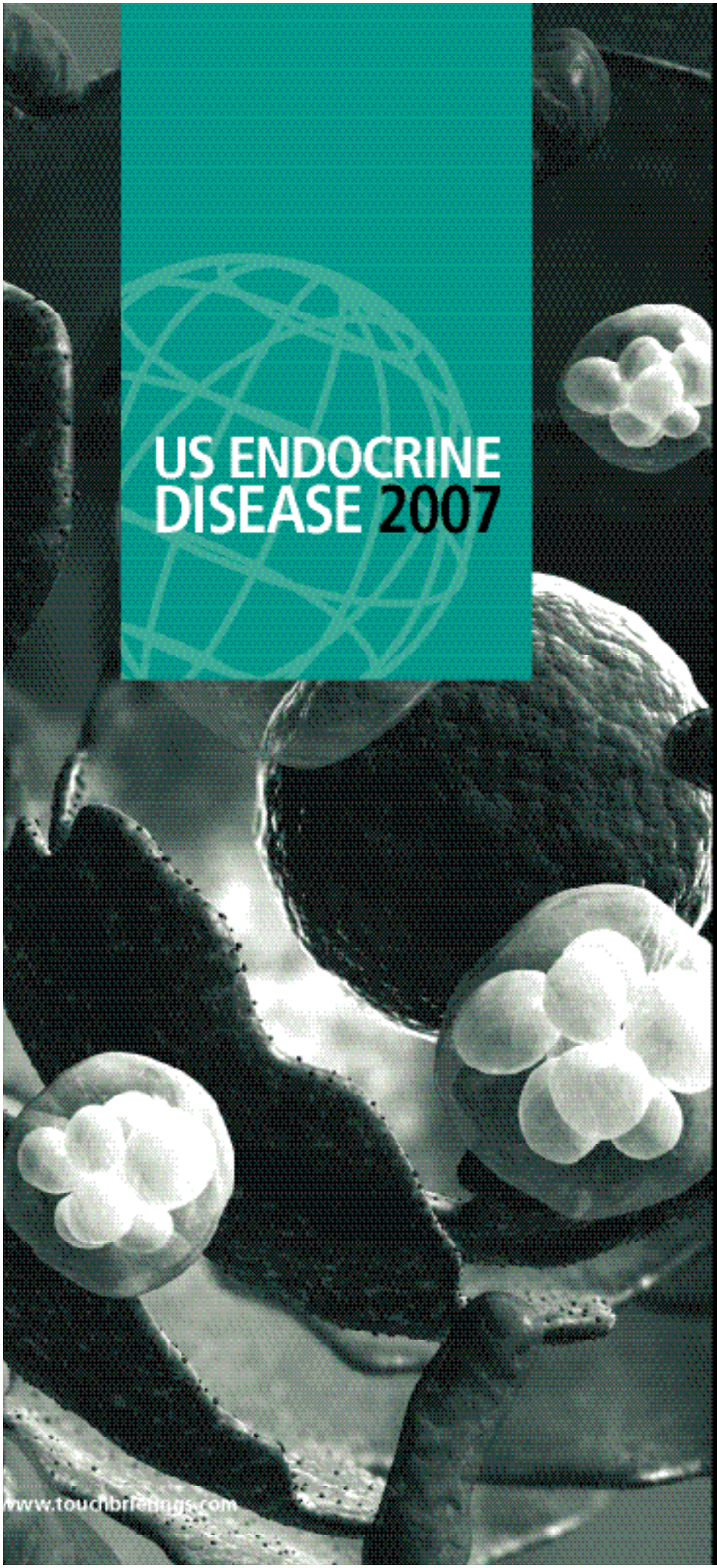

touch BRIEFINGS

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The Importance of Monitoring Blood Glucose

a report by
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It is estimated that diabetes, both type 1 and type 2, currently affects more than 195 million people worldwide. This figure is expected to rise to more than 330 million by 2030.[1,2] The rise in type 1 diabetes has been linked to changing environmental factors,[3] while the rise in type 2 diabetes is strongly associated with increasing rates of obesity.[4]

In people with normal glucose tolerance, blood glucose levels are automatically monitored and controlled by the body. After eating, the body releases enough insulin to keep the plasma glucose within a normal range that rarely rises above 7.8mmol/l (140mg/dl) and usually returns to pre-meal levels within two to three hours. In people with impaired glucose tolerance or diabetes, the body has little or no automatic control of blood glucose levels. After eating, they often experience extended periods of elevated blood glucose levels.

The chronic hyperglycemia of diabetes is associated with both micro- and macrovascular complications, which result in significant increases in morbidity and mortality. Improving glycemic control in diabetic patients has been shown to reduce these complications. Indeed, two large landmark randomized clinical trials, the Diabetes Control and Complications Trial (DCCT)[5] and the UK Prospective Diabetes Study (UKPDS),[6,7] confirmed the benefits of tight glycemic control in all patients with diabetes in terms of reducing the risk of macro-vascular complications.[8]

Measuring Glycemic Control

The level of glycated hemoglobin (HbA_{1c}) is the preferred standard for assessing glycemic control. HbA_{1c} values reflect the average blood glucose for the preceding three to four months. The upper normal limit for HbA_{1c} is approximately 6%. The American Diabetes Association (ADA) recommends an HbA_{1c} target of less than 7% in general, but suggests targeting an HbA_{1c} as close to normal as possible without causing significant hypoglycemia in individual patients.[9] Other guidelines are generally consistent with this recommendation, although the recommended HbA_{1c} targets differ slightly.[10–12]

However, there are limitations to monitoring glycemic control using only HbA_{1c}. As an integrated measure of fasting, pre-prandial, and post-prandial glucose levels, HbA_{1c} does not fully represent the risks that diabetic patients face on a daily basis, as it does not readily reflect the degree of glycemic variability that a patient may experience during a given day.[13–15]

Optimal diabetes management involves control of fasting, pre-prandial, and post-prandial glucose levels. HbA_{1c} alone cannot be used to identify whether a particular patient's abnormal glycemic patterns are due to high fasting plasma glucose levels or high post-prandial plasma glucose levels. In fact, the relative contributions of fasting plasma glucose and post-prandial plasma glucose to HbA_{1c} vary according to HbA_{1c} levels, with post-prandial plasma glucose measurements becoming increasingly important as HbA_{1c} decreases toward target levels.[16]

Self-monitoring of Blood Glucose

Self-monitoring of blood glucose (SMBG) can help both patients and their healthcare professionals better adjust to therapy and assess the responses to therapy. Benefits of SMBG include the fact that patients can immediately assess the impact of an action on blood glucose levels and consequently undertake prompt interventions designed to counter the high or low blood glucose concentration. In addition, when adjusting oral agent or insulin doses, it is important to know the pattern of blood glucose values, i.e. when during the day the levels are high, in the targeted range, or low, since the design of the treatment regimen may differentially affect glucose concentrations at various times after drug ingestion or injection. SMBG can help healthcare professionals implement a treat-to-target approach, and it can help patients better adhere to treatment by showing them the responses they are having to their treatment.

The ADA recommends SMBG for all type 1 and type 2 diabetic patients being treated with insulin.[9] SMBG should be part of a total treatment regimen that includes diet, exercise, weight loss, and insulin or oral medications when indicated. The optimal frequency and timing of SMBG depends on many variables, including diabetes type, level of glycemic control, management strategy, and individual patient factors. Healthcare professionals will also need to modify SMBG regimens to accommodate changes in therapy and lifestyle. The ADA recommends that all diabetes

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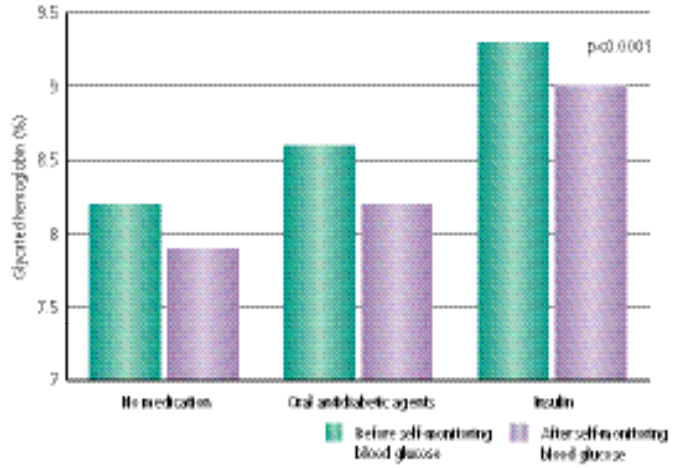
Figure 1: Relationship between Self-monitoring of Blood Glucose and Glycemic Control in Type 2 Diabetes Patients



Source: adapted from Karter et al.[18]

management programs should encourage at least daily monitoring. More specifically, it recommends that patients requiring multiple insulin injections should perform SMBG three or more times a day.[9]

SMBG can be particularly useful in certain circumstances, such as identifying hypoglycemic episodes. Often, fear of hypoglycemia can lead to a less intensive glucose management approach, resulting in suboptimal glycemic control. SMBG provides a means of identifying daily hypoglycemic events, allowing immediate treatment and/or modification of therapeutic regimens to allow tighter glycemic control.

Currently, there is a great deal of debate about the need for and frequency of SMBG for patients with non-insulin-treated diabetes. The debate is focused on the balance between the high and rising cost of blood glucose monitoring and the importance of the involvement and empowerment of people with diabetes in their own care. Currently, the ADA recommendations for SMBG in type 2 diabetes patients not being treated with insulin remain ambiguous: "The optimal frequency and timing of SMBG for patients with type 2 diabetes on oral agent therapy is not known but should be sufficient to facilitate reaching glucose goals."[9]

Self-monitoring of Blood Glucose and Glycemic Control

Although large clinical trials have yet to be conducted to assess the impact of SMBG on diabetes outcomes, recommendations for the use of SMBG in patients with type 1 diabetes are clearly defined.[9,10] Moreover, several studies have shown that treatment strategies involving SMBG are associated with improved glycemic control in both type 1 and type 2 diabetes.

In a longitudinal study from the Kaiser group, researchers studied more than 24,000 adult patients with diabetes in a large group-model managed-care organization.[17] They demonstrated that there is a relationship between SMBG and HbA_{1c} in type 1 diabetes patients (if they conducted glucose monitoring three or more times per day) and pharmacologically treated type 2 diabetes patients, irrespective of what pharmacological treatment they were on. SMBG performed at least once a day was associated with a lower HbA_{1c} than less frequent monitoring: type 1 patients who performed SMBG three or more times per day had a 1% lower HbA_{1c} than those who monitored less frequently or did not monitor. Type 2 patients who monitored once a day or more had a 0.6% lower HbA_{1c} than those who monitored less frequently. In this study, non-pharmacologically treated type 2 patients who conducted SMBG at any frequency had a 0.4% lower HbA_{1c} level than those not conducting it at all.

A more recent longitudinal study from the Kaiser group found that in patients who had previously not used SMBG, initiation of once-daily SMBG reduced HbA_{1c} levels significantly, regardless of treatment type (see *Figure 1*).[18] The study analyzed glycemic control among 16,091 patients initiating SMBG and 15,347 ongoing users of SMBG. Greater SMBG practice frequency among new users was associated with a graded decrease in HbA_{1c} (relative to non-users) regardless of diabetes therapy ($p<0.0001$). In the ongoing users group, changes inSMBG frequency among prevalent users were associated with an inverse graded change in HbA_{1c} only among pharmacologically treated patients ($p<0.0001$).

In type 2 diabetes, it has been shown that meal-related SMBG within a structured counseling program improves HbA_{1C} levels.[19] More recently, a large epidemiological study that followed more than 3,000 patients over six years showed that SMBG was associated with decreased diabetes-related morbidity and all-cause morbidity in type 2 diabetes. This association was even seen in the subgroup of patients not taking insulin.[20] A recent meta-analysis reported that SMBG was associated an overall 0.4% reduction in HbA_{1c} levels ($p<0.0001$) in non-insulin-treated patients with type 2 diabetes.[21]

In many ways, the patient is the most important individual in the diabetes care team. They should be trained to prevent and treat hypoglycemia and to adjust their medication with the guidance of healthcare providers to achieve glycemic goals. The measures of glycemia that are initially targeted are the fasting and pre-prandial glucose levels. SMBG is a vital component in adjusting or adding new interventions and, in particular, in titrating insulin doses. To fully utilize the benefits of SMBG, patients must obtain readings at appropriate times during the day, recognize readings that are outside their target range, and take the appropriate action to improve glycemic control. The best way to achieve this is by having patients assemble a glucose profile by taking a series of measurements at different times on different days that encompass information from the fasting, post-prandial, and late post-prandial timeframes. These data are most useful if seven or eight measurements are captured within a given 24-hour period. This should enable the accurate generation of daily glycemic excursions, which will need to be addressed to obtain the best glycemic control possible. Patients should be especially encouraged to collect data following meals, since meal-based SMBG testing has been shown to facilitate improved HbA_{1c} levels.[19,22]

The levels of plasma glucose that should result in HbA_{1c} in the target range are between 70 and 130mg/dl for fasting and pre-prandial levels. If these targets are met but HbA_{1c} remains above the desired target, glucose levels measured 1.5–2 hours after a meal should be checked. They should be below 180mg/dl to achieve HbA_{1c} levels in the target range.

However, there are limitations to SMBG. These mainly relate to the inconvenience of having to take (multiple) measurements, discomfort of a finger-stick, cost of supplies, and the requirement for training and

education of patients and healthcare professionals about appropriate analysis and use of data.

New Guidelines for Management of Post-prandial Glucose

Until recently, an key recommendation for good diabetes management was to lower fasting or pre-meal blood glucose levels; however, recent studies suggest a link between post-meal glucose control and improved vascular outcomes in people with diabetes. In addition, epidemiological studies have shown a strong association between post-meal hyperglycemia, carotid intima-media thickness, and endothelial dysfunction, all of which are linked to cardiovascular disease.[23] Post-meal hyperglycemia is also linked to retinopathy[24] and cognitive dysfunction in the elderly.[25]

Opinions on post-prandial management targets vary among medical organizations and members of the medical community. Generally, the aim should be to reduce post-prandial glucose levels to as low as possible without risking hypoglycemia. The International Diabetes Federation (IDF) guidelines recommend that people with diabetes try to keep post-meal blood glucose levels to less than 7.8mmol/l (140mg/dl) two hours following a meal. The two-hour time-frame for measuring glucose conforms to guidelines published by most of the leading diabetes organizations and medical associations, although it should be understood that this is not necessarily the time-frame that defines the peak post-meal glucose excursions.

The IDF advises SMBG because it is the most practical method for measuring post-meal glucose and it allows people with diabetes to obtain 'realtime' information about their glucose levels. However, in patients with poor glycemic control, fasting plasma glucose is likely to more strongly affect overall glycemia.[16]

Conclusion

All healthcare professionals who help with the management of people with diabetes must have good working knowledge of SMBG tools and procedures. It is their responsibility to teach a number of skills to the patients so that the patient is equipped to undertake SMBG accurately. The skills that need to be taught include: selecting a glucose-monitoring system best suited to the individual's situation; instruction on correctly performing SMBG and recording glucose values; discussion and selection of mutually agreed target glycemic goals; making appropriate adjustments in diabetes care by using these results; and periodic reassessment of user technique and data use.[26]

> Self-monitoring of blood glucose (SMBG) regimens must reflect individual needs and healthcare professionals should modify SMBG regimens to accommodate therapeutic and lifestyle changes.

The optimal impact of SMBG is achieved only when the data obtained through monitoring are consistently applied in an individualized program of monitoring, assessment, reassessment, problem-solving, and decision-making. SMBG regimens must reflect individual needs and healthcare professionals should modify SMBG regimens to accommodate therapeutic and lifestyle changes. In addition, the healthcare professional will need to periodically review the monitoring program and data with the patient. ■

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The Accuracy and Interferences in Self-monitoring of Blood Glucose

a report by
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Diabetes mellitus affects an estimated 20.8 million individuals in the US, approximately 7% of the population. Diagnosed in only 14.6 million individuals, 6.2 million are unaware of their condition and remain untreated as a result.[1] Extensive research[2,3] has clearly shown that improved glycemic control can impede the development and progression of diabetic complications, but many patients with diabetes still do not achieve or maintain these glycemic goals.[4,5] In recent years, there has been a focus on self-monitoring of blood glucose (SMBG) as one modality that can help people with diabetes improve glycemic control.

The Benefits of Self-monitoring of Blood Glucose

The development of SMBG has revolutionized the management of diabetes by allowing patients to monitor glycemic responses to their diet, activity, oral medications, and insulin therapy. Indeed, SMBG has been shown to be associated with improved glycemic control in both type 1 and type 2 insulin-treated diabetes.[5,6] Although the role of SMBG in non-insulin-treated type 2 diabetes remains less defined,[7–9] a meta-analysis of studies that compared a diabetes management strategy with SMBG to one without SMBG has demonstrated the benefit of SMBG on glycemic control in non-insulin-treated type 2 diabetes patients.[10] Moreover, a large-scale study tracking the use of SMBG over a span of almost seven years showed an association between SMBG use and decreased diabetes-related morbidity and mortality in these patients;[11] this and other recent evidence supports the use of SMBG in non-insulin-treated type 2 diabetes.[12–14] SMBG profiles help healthcare providers (HCPs) better guide and plan individualized antihyperglycemic regimens and provide an educational feedback tool to inform patients of the effects of modulating their diet, physical activity, or intake of oral antidiabetic agents or insulin. Such active involvement in their care helps empower patients and has been shown to facilitate the achievement of glycemic targets.[8,15]

Appropriate use of SMBG will allow patients to identify, prevent or manage episodes of hypo- and hyperglycemia.[5] Furthermore, SMBG can help minimize fluctuations in blood glucose levels that have been shown to signal the imminent occurrence of severe hypoglycemia in 58–60% of cases[16] and may independently contribute to diabetic complications.[17] Increasing evidence of the benefits of SMBG has been associated with increased HCP and patient awareness about the importance of self-monitoring of blood glucose: 63.4% of all adult patients and 86.7% of those treated with insulin now carry out SMBG at least once a day.[18]

The Functionality of Glucose Meters

To date, the US Food and Administration Agency (FDA) has approved at least 25 commercially available glucose monitors[19] and the ADA reviews a number of them annually,[20] the majority of which use test strips containing either glucose hexokinase or oxidase chemistry.[21] The most common test involves obtaining a small blood sample (<1μL for many meters) through a finger prick and applying the sample to a test strip for a series of chemical reactions. The strip is then inserted into a meter that displays a measure of the glucose concentration, by a variety of means, including colorimetry, photometry, and electrochemistry.[22,23] Patients with diabetes can manually record these test results or utilize the meter's built-in memory and/or computer software.

Accuracy in Self-monitoring of Blood Glucose—Improving Patient Technique

Since patients and their HCPs rely on SMBG results to identify hyper- and hypoglycemia and modify treatment accordingly, it is important for glucose meter readings to be accurate and reliable. However, an ADA consensus panel reported that up to 50% of all SMBG readings may vary from their true value by more than 20%.[24] One study found that of 111 patients using glucose monitors, 53% were in compliance with ADA guidelines with SMBG readings showing less than 10% of variation, while 16% had SMBG readings that varied in excess of 20% of the control values. The performance of patients regarding SMBG was also evaluated using a checklist of steps deemed critical in the proper calibration and operation of their glucose monitors. The patients scored poorly in critical quality control, as many of which used improper techniques when collecting blood samples. Only one (0.9%) of the 111 patients scored perfectly on the evaluation checklist. In spite of the poor techniques and performance errors, a large proportion of glucose values obtained were still clinically acceptable.[24]

Despite the increasing simplification of blood glucose meters over the years, they are still not foolproof. Almost half of patients trained appropriately in SMBG can still obtain inaccurate readings through poor technique.[25] Patients of various ages and social classes have also been found to falsify their results, omitting high glucose readings, and recording extra results to indicate more frequent testing than in reality.[26] Such cases emphasize the importance and necessity of educating a patient in proper SMBG, not only in the technical aspects of correct usage and interpretation of a blood glucose meter, but also about the supporting role of SMBG in their antidiabetic regimens.

Many aspects can alter the accuracy of a glucose meter reading, including patient characteristics, variances in manufacturing of the glucose test strips, and interfering substances. Most importantly, the adequacy of training available to the patient will affect their ability to use the meter and, crucially, tell if they are using it correctly.[5,20,21,27]

Variances in the reactivity of the glucose test strips mean that some SMBG devices require the patient to enter a unique code to calibrate the meter. This is another aspect of the process that is open to error, and miscoded meters lead to an insulin dose error. However, certain newer meters have automatic coding, thus eliminating this potential problem.

In terms of patient characteristics, the cleanliness of the finger, the quality and size of the blood sample, and the technique used (for example in terms of wicking time in the well and complete filling of the well) can all influence the reading. Similarly, there are differences and variances in strip design and well size across manufacturers, and the cleanliness of the meter can also affect results. Some meters allow for these inaccuracies and others do not. Interfering substances are discussed below.[21,30]

Sources of Interference

Factors that cause erroneous readings on the blood glucose meters can be categorized into two groups: sugars and interfering substances. Cross-reactivity can occur between enzymes on the test strip and substances in the blood similar to glucose—such as maltose, galactose and xylose—while non-sugar molecules interfere by different methods.

Maltose, Galactose, and Xylose

Maltose is a disaccharide formed from two glucose molecules and is found in certain immunoglobulin products. Additionally, icodextrin used in peritoneal dialysis metabolizes to maltose. Galactose and xylose are found in certain foods, herbs, and nutritional supplements, and are also used in diagnostic tests. In clinical doses, these sugars can interfere with some blood glucose monitoring systems.[28] Inaccurate glucose readings can place a patient at risk for a number of complications, either masking hypoglycemia or giving false indications of hyperglycemia. In the past, some patients receiving products containing maltose, galactose, and xylose showed falsely elevated glucose readings, and were treated with aggressive insulin therapy as a result. However, the administration of this excess insulin caused these patients to suffer hypoglycemic shock or irreversible brain damage and death.[29]

In systems using test strips containing the enzymes glucose dehydrogenase (GDH), pyrroloquinolinequinone (PQQ), or glucose dye oxidoreductase, the maltose, galactose, and xylose sugars are mistaken for glucose and can lead to falsely elevated glucose readings. Currently, there are several commercially available glucometers and test strips that use this enzymatic chemistry, including the Freestyle family, first generation Ascensia® (Microfill), and the Accu-Chek® family. Accordingly, the FDA has recommended that physicians carefully review the labeling for both the glucose meters and the test strips to determine if the system is appropriate for use with maltose-containing parenteral products.[30] The FDA has authorized all manufacturers of maltose-containing products to warn about the potential interference with glucose monitoring systems.[30] Physicians should also extend these warnings of interference to patients taking galactose and xylose supplements, and take these factors into consideration when selecting a glucose monitor for a patient.

Glucose oxidase chemistry is specific for glucose, thus these test strips will not face interference from other sugars. GDH-nicotinamide adenine dinucleotide (NAD) test strips will also be free of cross-reactivity with other sugars as well.[29] As such, HCPs can recommend meters using these test strips to patients receiving maltose-, galactose- or xylose-based medications. GDH-flavin adenine dinucleotide (FAD) test strips react with xylose; therefore, patients with diabetes can safely use glucose meters with GDH-FAD test strips as long as they are not taking xylose supplements or xylose-containing medications. Currently, two systems using GDH-FAD test strips are FDA (protocol 510(K)) approved for use in the US. GDH-FAD test strips associated with the Ascensia Contour system do not cross-react with maltose, icodextrin, or galactose. However, GDH-FAD test strips used with the recently approved Glucocard X-Meter system have been associated with false elevation of glucose results when tested with galactose, lactose, maltose, maltotriose, and xylose, which resulted in the inclusion of a warning in the limitations section of the product's labeling to alert users. Overall, it is important to stress that both physicians and patients should carefully review the package inserts of all test strips. This will ensure that that type of glucose-testing system being used is appropriate for the patient.

Oxygen

In glucose oxidase test strips, oxygen acts as a competing electron acceptor. The corresponding reaction will vary depending on the pO_2 in blood samples. High partial pressure of oxygen (pO_2) (400torr) is most common in the critically ill, or in patients receiving oxygen therapy or undergoing surgery. These patients will show pronounced decreases in blood glucose level. Low pO_2 (40torr) is common in neonates or patients at high altitudes, in which glucose readings will be anomalously high. However, both situations are extremes, and unless the average patient prolongs exposure of their blood sample to air prior to testing (e.g. >15 minutes), the effect of oxygen should be negligible.[31,32]

Paracetamol

Paracetamol is the active metabolite in certain analgesics, is significantly oxidizable, and is known to interfere with glucose measurements.[33,34] Typical therapeutic levels (1–2mg/dl) are too low a concentration to have any significant effects,[35] but overdosing on paracetamol would be capable of inducing a clinically significant overestimation of blood glucose.[36,37]

Ascorbic Acid

Vitamin C is a potent antioxidant and easily oxidized. However, ascorbic acid is readily excreted in the urine and even large doses are quickly normalized within the body. Although ascorbic acid has the potential to interfere with results from glucose monitors,[34] normal levels (1–2mg/dl) are not at high enough concentrations to significantly affect the readings.[33]

Uric Acid

Uric acid is a natural by-product of purine catabolism. At normal levels, uric acid has an insignificant effect on glucose meter readings. However, poor clearance from kidneys or overproduction of uric acid can cause hyperuricemia. If oxidized, the uric acid can lead to falsely lowered values on glucose meters.[38]

Bilirubin

Bilirubin is a product of hemoglobin breakdown, and normal levels do not affect glucose meter readings in a significant manner. Bilirubin can be elevated in jaundiced neonates, or patients with liver disease, hepatitis, or

certain forms of anemia to create positive interference in meters using test strips with GDH-based chemistry.[39]

Hematocrit

Hematocrit counts vary depending on age and gender. Low hematocrit can be caused by a number of factors, such as anemia and sickle cell anemia, blood loss, malnutrition, or leukemia. In contrast, hematocrit can often increase under conditions of dehydration, but will normalize upon the restoration of fluid balance. Other causes of high hematocrit, though rare, include certain bone marrow disorders and tumors, lung diseases, and living at extremely high altitudes. Glucose meters are generally calibrated towards the normal hematocrit levels of 40–50%. Erythrocytes effectively act as a physical barrier affecting the diffusion rate of glucose in test strip chemistry; therefore, the hematocrit count is proportional to the rate of reaction in the test strip and inversely proportional to the meter signal, i.e. hematocrit above the normal range will give a lower glucose reading while hematocrit below the normal range will give a higher glucose reading.[35]

The Effect of Interference on Accuracy

Maltose, galactose, and xylose are likely the most serious causes of interference in glucose meters. However, the effect of these extraneous sugars on glucose readings can easily be negated with proper information and by choosing to only use meters that will not cross react with non-glucose sugars such as those using glucose oxidase or GDH-NAD test strips. In spite of the various interfering substances that can potentially confound the accuracy of glucose meters, these factors actually have little bearing in the average patient with diabetes.[28,33,35] To further emphasize this point, human misuse of the glucose meters has been found to be a more significant source of error than the instrument itself,[40] and even so, the majority of values can still serve as clinically acceptable indications of glycemic status.[24]

Conclusion

The increasing prevalence of diabetes illustrates the importance of proper disease management through successful use of SMBG. The glucose meters available on the market are similar in terms of functionality, yet vary in accuracy depending on multiple factors including variance in strip design and manufacturing, the patient's technique in testing and finger cleanliness, appropriate calibration of the meter with strip code, and the chemistry and cross-reactivity with interfering substances. When selecting the optimal glucose meter, not only must aspects from the patient's lifestyle and other health treatment regimes be taken into account, but also the glucose meter systems must also be assessed in detail to ensure the minimum risk of interference. ■

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Self Blood Glucose Measuring in the Non-insulin-requiring Diabetic Patient—To Test or Not to Test

a report by
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History

The initial patent for a practical glucose meter was issued in Elkhart, Indiana, in 1971, and the device has now evolved into a frequently used tool. The utility of finger-stick blood glucose testing using such meters has been solidly demonstrated in patients requiring insulin therapy; however, data are conflicting in non-insulin-requiring type 2 patients.[1] A systematic review of self blood glucose monitoring (SMBG) in type 2 patients not taking insulin concluded: "The overall effect of SMBG was a statistically significant decrease of 0.39% in glycated hemoglobin (HbA_{1c}) compared with the control groups. This is considered clinically relevant. Based on the UK Prospective Diabetes Study, a decrease of 0.39% in HbA_{1c} is expected to reduce risk of microvascular complications by 14%."[2] Davidson, on the other hand, in a counterpoint to this study, reviewed several trials and concluded that SMBG fails to reduce HbA_{1c} in type 2 patients not taking insulin and is therefore a waste of money.[3]

Frequent Self Blood Glucose Measuring Is Expensive

The total Medicare/Medicaid expenditure for reagent strips, lancets, lancing devices, meters, batteries, and calibration solutions, etc., in 2006 was over $1 billion.[4] It makes little sense to spend this amount of money if there are no tangible positive results. A single finger-stick blood glucose measurement can cost as much as $1 retail; four tests a day can add up to nearly $1,500 per patient per year. So, where's the beef? There are studies and there are studies. In the clinic or the practitioner's office, what do we request of our patients and those paying for supplies? There are several criticisms of some studies included in reviews not showing efficacy, including:

- the 'study patient' effect—subjects in a control group are likely to have better outcomes than 'real-world' patients because of the attention of the study itself, so differential effects may be blunted;
- interventions in studies were heterogeneous;
- there was no use of SMBG data to effect change; and
- study and control groups had outcome-altering interventions.

The only randomized controlled trial to meet the *British Medical Journal*'s clinical evidence criteria found an insignificant HbA_{1c} reduction of 0.8% in SMBG subjects compared with 0.6% in non-SMBG controls.[5] Subjects in both arms of this trial had five meetings with a dietician over the six-month study.[6] In the real world, such intensive educational efforts are likely impractical and may be more expensive than frequent SMBG.

Self Blood Glucose Measuring Is Not Therapy

SMBG is a tool that can provide information to direct therapy or provide insight into behavior modification and medication adherence.[7] If the information is not used, it is worthless. Patients frequently indicate that meters and strips are sent by mail order with no instructions on meter use (outside of a manufacturer's instruction booklet) and no indication of when to test or what to do with the results. Worse yet, there are indications that some healthcare providers (HCPs) never look at meters or logs during clinic or office visits. Such practices might be metaphorically compared to recording the number of deaths from drunk drivers speeding on a stretch of highway, but doing nothing to alter it. To have a patient repeatedly test blood glucose and change nothing to correct poor control conforms to one definition of idiocy: continuing to do the same thing over and over while expecting a different outcome.

Rationale for Testing

SMBG as a means to improve glycemic control in type 1 patients and in pregnancy is well established and will not be discussed here. The rationale for patients with type 2 diabetes who have a change in therapy or who have started insulin therapy also receives little objection. It is in the group not requiring insulin therapy that the rationale for SMBG is questioned. American Diabetes Association 2005 standards indicate: "The optimal frequency and timing of SMBG for patients with type 2 diabetes on oral agent therapy is not known, but should be sufficient to facilitate reaching glucose goals. Patients with type 2 diabetes on insulin typically need to perform SMBG more frequently than those not using insulin."[8] Recommendations for 2007 indicate: "SMBG should be carried out three or more times daily for patients using multiple insulin injections. (Grade-A recommendation, i.e. based on clear evidence from well-conducted, generalizable, randomized controlled trials that are adequately powered…). For patients receiving less frequent insulin injections or oral agents or medical nutrition therapy (MNT) alone, SMBG is useful in achieving glycemic goals (Grade-E recommendation, i.e. based on expert consensus or clinical experience)."[1]

We must therefore revert to the truism brought to any clinical teaching situation: patients are different and there are different approaches to the therapy of the disease state. It therefore becomes the clinician's

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responsibility in diabetes to use whatever tools are available at whatever frequency necessary to achieve the best possible control of glycemia with the least risk of acute complications and at an economically feasible cost.

With the risks of retinopathy, cardiovascular disease, neuropathy, and possible amputation associated with uncontrolled glycemic levels, where is the line drawn in terms of healthcare expenditure? Perhaps the cost of long-term SMBG versus short-term usage has to be assessed from an alternate viewpoint. Although it is arguably expensive to fund SMBG, the value gained from monitoring and controlling blood glucose cannot be denied. After all, is it not more cost-effective, if not logical, to pay for the blood-testing apparatus than to pay for heart surgery and leg amputations?

Common Errors

A tool such as SMBG can contribute substantially to improved glycemic control if reasonably accurate and used appropriately. What if, however, the information is incorrect either because of technical inaccuracies or user error? Confounding issues related to blood glucose testing in the inpatient setting have been well elucidated.[9] In the outpatient setting, common errors in SMBG have been documented in observational studies.[10,11] SMBG data can be rendered inaccurate by several user errors, including:

- failure to store glucose strips properly;
- failure to set glucose meter codes to match strip codes;
- failure to apply sufficient blood on the meter's strip;
- failure to use control solutions;
- use of date-expired control solutions;
- use of date-expired strips; and
- failure to wash hands properly.

The frequency of user error relating to meter codes has been reported at approximately 16%.[10,11] In one study, exactly half of the patients were of Medicare age. As these patients are often challenged by cognitive and dexterity limitations and frequently have long-standing diabetes requiring insulin, therapeutic interventions based on such erroneous data can be destructive.

Recommendations

The Meter

The glucose meter should be accurate, easy to use, small, and convenient. Meters that do not require coding, are rapid and accurate, and require a very small amount of blood are preferred. The choice of meter should be a joint effort between the patient and the HCP based on the cognitive and physical limitations of the patient and the facility of the HCP to harvest the data, e.g. download capability. The choice should not be that of the mail order company or insurer. The number of meters available, some of which are downloadable (each having different software) and some of which are not, can be time-consuming and a daunting deterrent to HCP evaluation of the data.

The Patient

The diabetes patient should be thoroughly instructed in the proper operation of the meter. Meters requiring fewer steps facilitate ease of teaching and learning and may lead to increased accuracy of test results. In addition, those instructions should be periodically reviewed and competency demonstrated. Information obtained from SMBG should be reviewed by the HCP, preferably using downloaded meter data. Downloaded blood glucose data are very useful in detecting glucose trends to effect therapeutic changes. As patients are infrequently evaluated in the clinic/office, the patient must be instructed how to act on the blood glucose information. Specific instructions are needed relating to frequency of testing and timing, e.g. post-prandial testing. Type 1 patients, pregnant patients, those starting insulin therapy, and those with changing therapy require multiple tests daily. Stable type 2 patients who are at glycemic goal will likely require less frequent testing. Post-prandial tests in this setting are especially useful for patient education. It is also important to spot trends of progressive β-cell deterioration and the need for accelerated therapy.

The Healthcare Provider

Regardless of how well a patient performs SMBG, the results are useless if the HCP overlooks the data. If the HCP shows little to no interest in the information, patients will feel less inclined to adhere to SMBG. Conversely, HCPs who take the time to look over the data and log books and educate patients about the importance of SMBG readings will not only benefit the patient, but will also positively reinforce their SMBG performance and adherence.

Summary

The worldwide epidemic of diabetes is producing unacceptable human suffering. This in turn produces economic losses from direct costs and lost production. Therapeutic endeavors must be directed to attenuation of this effect. A cure is not on the horizon; the best tools available to HCPs are those that reduce risks and delay or prevent disease progression. In type 2 patients, therapeutic approaches must be progressive, reflecting the gradual loss of β-cell function. SMBG is the singular, immediate, accurate measure available to the patient allowing therapy adjustment. With appropriate education, the patient and healthcare team can adjust therapy to approach glycemic goals. The value of testing, not simply the cost, must be appreciated by patients, HCPs, and the healthcare system. Prevention or delay of complications and improvement in daily symptoms and quality of life are priceless. As with all tools employed to alter disease states, the use of SMBG must be individualized. The frequency of testing must be geared to outcome goals set by the healthcare team and the patient. ■

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Barriers and Behaviors in Blood Glucose Monitoring

a report by
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"The relatively infrequent and uneven inclusion of behavioral and social science principles in diabetes care has limited the effective use of new knowledge gained from biomedical clinical trials. A focus on biomedical intervention without integration of behavior and social science principles into clinical care severely limits the impact of biotechnology and biomedicine."[1]

As this quotation suggests, the integration of blood glucose monitoring into overall patient care occurs at the intersection of biomedicine and behavior, and requires considerable behavioral medicine expertise on the part of diabetes care providers. Accordingly, we should discuss what is known about patient adherence to blood glucose monitoring, characteristics of adherent and non-adherent patients, the controversial relationship between blood glucose monitoring and glycemic control, and behavioral medicine interventions to promote adherent self-monitoring of blood glucose (SMBG) and improved glycemic control.

Levels of Adherence to Self-monitoring Blood Glucose

We derive considerable encouragement from the recently reported findings from the Centers for Disease Control and Prevention (CDC), which indicate a substantial and steady increase from 1997 to the present day of the number of US citizens with diabetes who self-monitor their blood glucose at least once a day.[2] According to this report, the SMBG objectives of 'Healthy People 2010' have already been achieved. However, while the CDC findings appear to provide evidence of important gains in SMBG adherence, we observe that adherence to SMBG measured as an absolute frequency—e.g. once a day, as in the case in the CDC report—may result in estimates that are not always related to the actual SMBG requirements of patients with diabetes.

Vicenze et al.,[3] among others, have pointed out that an adherence to SMBG measured in terms of the proportion of the recommended SMBG frequency (absolute frequency ÷ healthcare provider stipulated frequency) may provide the most meaningful assessment of SMBG adequacy and result in lower estimates of adherence. Measured in relation to the proportion of patients adhering to the SMBG frequency recommended by the American Diabetes Association (ADA), in a sample of 44,181 respondents and with an 83% response rate[4] it was stated that 60% of those with type 1 diabetes and 67% of those with type 2 diabetes reported SMBG frequencies lower than recommendations. At this juncture, we note that the prevalence of SMBG appears to be improving in the US over time, that SMBG adherence adequacy may be most meaningfully evaluated in relation to recommended—not absolute—frequency of monitoring, and that whatever population trends may develop, in terms of the physician–patient encounter SMBG adherence is individually variable and differs within individuals across time and circumstance, and should be continuously monitored in relation to the patient's health status.

Factors Influencing Self-monitoring Blood Glucose

A multiplicity of studies have identified the determinants of SMBG frequency. For example, the recent CDC report[2] presents multivariate findings to indicate that less well-educated patients, those without health insurance, those whose therapy is less intensive, and males have a substantially reduced likelihood of performing daily SMBG. Other research echoes this pattern of findings[4] and indicates that for those with type 1 diabetes, male sex, ethnic minority status, low income level, smoking, and being <65 years of age are independent predictors of less-frequent SMBG. For those with type 2 diabetes, male sex, ethnic minority status, lesser education, language barriers, higher cost of out-of-pocket strip expenditures, longer duration of diabetes diagnosis, smoking, and excessive alcohol consumption are independent predictors of lower-frequency SMBG.

In addition, research has identified psychological factors that are related to lower-frequency SMBG, including lower levels of self-esteem, self-efficacy, and competence, and higher levels of anxiety, depression, and perceived painfulness of monitoring procedures.[3,5–9] Environmental factors associated with SMBG infrequency, including lifestyle interference and inconvenience of SMBG, lack of parental involvement (for SMBG frequency for adolescents with type 1 diabetes), and lack of family support (for SMBG frequency for adults with type 2 diabetes), have also been identified.[3,10,11]

In summary, adherence to SMBG appears to be meaningfully linked to a number of patient characteristics, ranging from time since diagnosis to

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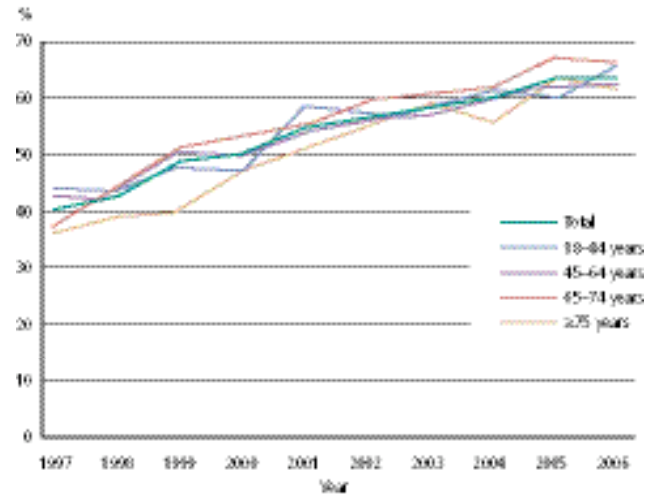
Figure 1: Estimated Basic Rate of Daily Self-monitoring of Blood Glucose Among Adults with Diabetes



Figures adapted from the US age group–behavioral risk factor surveillance system, 1997–2006.[2]

Table 1: Continuing Support for Maintenance of Intervention and Behavioral Change

Behavior change interventions should involve:

- well-validated behavioral science intervention models;
- collaborative identification of the self-care challenge;
- collaborative goal-setting for achievable outcomes;
- collaborative problem-solving;
- contracting for change;
- rewarding success; and
- continuing support for maintenance of interventional and behavior change.

Emotional support interventions should include:

- screening for diabetes-related emotional distress;
- providing ongoing informal emotional support; and
- referring treatment of significant emotional difficulties.

Source: Fisher and Glasgow, 2007.[1]

depression to family support, which may present in the clinical setting. A systematic assessment of patient adherence to SMBG and patient characteristics robustly linked with adherence levels in the research literature, coupled with targeted intervention support to address challenges to adherence, may be explored as means for promoting SMBG at an appropriate frequency.

Is Self-monitoring Blood Glucose Linked with Glycemic Control?

A demonstration of the relationship of SMBG frequency with glycemic control is an obvious and controversial matter for the promotion of SMBG as an important element in diabetes management. On the one hand, observational studies often show no relationship of SMBG with glycated hemoglobin (HbA_{1c}) levels, especially for non-insulin-treated diabetes patient populations,[12–14] and some research suggests that high-frequency SMBG added to the scenario may be related to distress, worry, and depression for non-insulin-treated diabetes patients,[13] although other studies show that SMBG is associated with increased wellbeing and reduced depression.[15]

However, from a critical perspective it is extremely important to note that observational studies of the relationship between SMBG frequency and glycemic control may be problematic from the methodological and statistical points of view. Specifically, it seems quite plausible that, in observational research, diabetes patients with poor glycemic control may monitor frequently (as a consequence of their poor glycemic control and in an effort to remedy this situation), and it seems equally valid that diabetes patients with poor glycemic control may monitor infrequently (which contributes to their poor glycemic control). Similarly, it seems credible that diabetes patients with good glycemic control may monitor frequently (and thereby achieve good glycemic control) or infrequently (as they do not perceive a need to do so). Accordingly, observational studies may show no relationship between SMBG and glycemic control because SMBG frequency may be related to both good and poor glycemic control.

Given the problematic nature of observational studies of the relationship between SMBG and glycemic control, we may seek clearer evidence concerning the causal link between SMBG frequency and glycemic control in intervention studies, which successfully improve SMBG frequency and that consistently show improved HbA_{1c} levels.

Welschen et al.[16] carried out a systematic review of six randomized, controlled trials conducted to evaluate the effect of SMBG in type 2 diabetes patients not using insulin. "The overall effect of SMBG was a statistically significant decrease of 0.39 in HbA_{1c} compared with control groups. This is considered clinically relevant … expected to reduce risk of microvascular complications by ~14%."[16,17]

At this point, it would seem prudent to exercise caution in interpreting observational studies showing no relation between SMBG and glycemic control, and to carefully consider the results of randomized controlled trials showing that improved SMBG may be causally related to improved glycemic control. At the same time, implicit in the analysis of the findings concerning SMBG and glycemic control, it would be sensible to emphasize the role of patient education concerning actions to be taken when SMBG results show high blood glucose levels in an attempt to exploit the full value of SMBG for glycemic control.

Can Interventions Improve Self-monitoring Blood Glucose?

Given evidence that SMBG may result in improved glycemic control, and that SMBG levels are often suboptimal, convincing evidence that clinical interventions may result in improved SMBG is exceedingly important. To this end, it is encouraging to note that meta-analytic reviews as well as a multiplicity of individual intervention studies demonstrate success in improving SMBG frequency. For example, a meta-analysis of self-management training trials by Norris et al.[18] showed positive effects of interventions on knowledge, frequency, and accuracy of SMBG, as well as on dietary habits and glycemic control, at six-month follow-up intervals.

However, at the same time evidence for maintenance of change beyond six months was inconsistent and thought to be related to regular reinforcement and collaborative intervention approaches, as opposed to a top-down didactic approach. We note that numerous individual intervention trials have demonstrated success, including research showing that counseling and SMBG device introduction improved HbA_{1c} over a six-month follow-up.[19] Other observations include:

- automated telephone reminders and nurse follow-up of problems increased SMBG, self-care (foot, weight), and dietary adherence, and lowered HbA_{1c} over a 12-month follow-up;[20]
- provision of a blood glucose 'Owners Manual' increased SMBG and improved HbA_{1c} over a six-month follow-up;[21]
- a Stages of Change model-based intervention improved SMBG compared with usual care;[22]
- a motivational interviewing intervention improved SMBG, dietary adherence, and glycemic control over a four-month follow-up;[23,24] and
- an computer-based patient education study showed improved HbA_{1c} and increased physician adherence to treatment guidelines.[25,26]

According to Fisher and Glasgow,[1] successful interventions to improve diabetes self-management should involve both behavioral interventions (to teach effective self-care strategies) and emotional interventions (to address problems such as depression, which may interfere with self-care). Suggested elements of behavior- and emotion-focused interventions are featured in *Table 1*.[1] In addition, it is clear that interventions to stimulate the initiation of self-care must be augmented by attention to maintenance of initial intervention-induced gains: "The assumptions that once learned, major lifestyle changes can be easily maintained and that new challenges posed by diabetes over time do not require new knowledge and new techniques for problem resolution are contradicted by a long line of behavioral research."[1,27,28] It is suggested that maintenance of intervention gains may be facilitated by continuous monitoring and reinforcement of patient health status gains, and by periodic review, revision, and reinforcement of clinician behavioral management strategies.

We close this article on SMBG behaviors and barriers by asserting that we need to follow through with the implementation of already well-validated self-management interventions—not breakthroughs *per se*—in SMBG adherence promotion in diabetes care. A wide range of empirically supported self-management interventions that promote SMBG and are effective in achieving improved glycemic control currently exist in the literature. Implementation of self-management interventions remains to be accomplished, however, via relatively seamless and relatively low-cost integration into the ecology of clinical care and via alignment of intervention efforts with current clinical care approaches and priorities.

In addition, maintenance of intervention gains must be a planned-for focus in any intervention implementation program. We concur strongly with the view that "… all members of the diabetes care team need to be behavioral experts … The use of well-documented behavioral practices can improve clinical outcomes when they are applied systematically, conscientiously, and uniformly; when they are applied by all diabetes health professionals; and when they are considered part of each clinical team member's skill set."[1] ■

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