Assessment of Glycemia in Diabetes Mellitus - Self-Monitoring of Blood Glucose

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Abstract
Self-monitoring of blood glucose (SMBG) is an integral component of diabetes self-care and, if used optimally, essential to obtaining glycemic control. There are many methods currently available and the use of glucometers can provide readily available information on blood glucose patterns over time. However, some barriers to the use of SMBG, such as its cost, are significant. Other barriers, such as pain, patient denial or insufficient encouragement from the health care professional, should be overcome. While we find pre-prandial testing to be more informative, there are instances where post-prandial testing may be useful such as in pregnancy or in patients with early stages of glucose intolerance. In the future, continuous glucose monitoring will become available, and ultimately an insulin delivery device will be linked to continuous monitoring making the “closed loop” artificial pancreas a reality. At present, SMBG is an under-utilized but important part of modern diabetes care and should be recommended for all people with diabetes.

The data are now overwhelming that good control of blood glucose in diabetes can prevent or delay complications. This has been proven for both type 1 and type 2 diabetes, and at least according to the Diabetes Control and Complications Trial (DCCT), the benefits of intensive glycemic control are demonstrable whether the patients have no complications (primary prevention) or already have mild to moderate complications. The positive preventive effects of tight glycemic control are especially well demonstrated for microvascular complications including retinopathy and nephropathy, for neuropathy, and, while probably having less impact, also for macrovascular complications such as cardiovascular disease and stroke. The association of blood glucose levels with cardiovascular risk also extends to glucose levels below the diabetic threshold.

The DCCT also suggested a continuous, graded benefit on complication risk, seen whether the person is improved from poor to fair control, from fair to good control, or from good to excellent control. Indeed, the data indicate that the reduction of complication risk is proportionally the same for every percent improvement in hemoglobin A1c (HbA1c). Finally, important recent data from the long-term follow-up of DCCT subjects in the EDIC Study suggest that the benefit seen at the end of the DCCT, after a mean of 5.5 years of intensive glycemic control, persists for at least 9 years despite disappearance of the difference in HbA1c between the intensively and conventionally treated groups.

The challenge of modern diabetes management, then, has become not whether but how to achieve glycemic control. Many new treatment options have become available. The armamentarium of oral agents has expanded greatly, as has the spectrum of insulin formulations. Why is it, then, that the majority of people with diabetes remain sub-optimally controlled? Why is diabetes still the leading cause of adult blindness, of non-traumatic amputations and of end stage renal disease in the United States? There are many reasons, of course, including lack of patient education, self-care, and access to health care. But the thesis of this review is that one major reason people with diabetes do not achieve adequate glycemic control is that glycemia is not adequately assessed—in other words, people with diabetes along with their health care professionals do not adequately assess glycemic control.

In fact, blood glucose levels can be easily and well assessed. People with diabetes and their health care professionals can share information as to whether they are adequately controlled, and whether they are controlling the risk of complications. The tools are available and, as part of good health care for people with diabetes, the effort should be made.
is that in each case the standard, available approaches are not used nearly as regularly as they should. This discussion will focus on SMBG.

The relatively quick, rapid laboratory assessment of blood glucose, developed in the early part of the 20th Century, was a crucial step in the discovery of insulin.\textsuperscript{1,12} It was later developed into a glucose oxidase-based method for measuring urine glucose. This was the first home-test available to patients interested in controlling their diabetes, and was the only such test available for over 50 years. The serious deficiencies of urine glucose testing, however, have become well known. For instance, urine glucose is only a post-hoc assessment, indicating generally what blood glucose may have been hours before, not currently. Urine glucose concentration is extremely sensitive to hydration state and the amount of free water clearance varies enormously hour to hour. (For example, a 2% urine glucose measurement may well become 0.5% if the person simply drinks several glasses of water, diluting the urine). And perhaps most importantly, urine glucose gives no indication of hypoglycemia. It is positive only if blood glucose has been over roughly 180 mg/dl. A urine negative for glucose may indicate that blood glucose was anywhere from 40 to 180 mg/dl.

It was a significant physical chemical feat in the 1960’s to fix glucose oxidase on a strip capable of developing color in direct proportion to glucose concentration when exposed to a drop of blood, and to develop this into a practical approach to diabetic control in the 1970’s.\textsuperscript{13,14} The original colorimetric assays required comparing colors on the side of a vial, but these were relatively quickly replaced by small colorimeters that displayed a specific result; and these were replaced more recently by technology that measures current flow generated directly rather than requiring a color reaction.

SMBG has come a long way. The new meters are small, between the size of a deck of cards and a credit card. They are more accurate, with analytic errors in the 10% range.\textsuperscript{15} They are quick, giving results in approximately 5 to 15 seconds. They require only tiny amounts of blood, in the 1 µL range. And the spring-loaded lancet devices are considerably less painful than the old hand-held lancets. Many meters and lancet-holding devices are now available for SMBG.\textsuperscript{16}

SMBG meters have other capabilities made possible by advances in electronics. The display is large and clear. They memorize results, usually including the time and date of the assay. This allows patients to scroll backwards and see their more recent blood glucose results. They generally calculate readily visible 14- and 30-day averages. The most useful, though vastly under-used feature, in our view, is the capability of meters to download data. An inexpensive cable to any small computer, and free software, allows the health care professional or even the patient to see at a glance smartly arranged displays of previously stored blood glucose results.

Figure 1 shows some representative results of a glucose meter download. For the health care provider, these results make poring over a patient diary obsolete. At a glance, summary statistics are available including the average blood glucose and the variance (standard deviation) expressed as percent falling above or below patient-specific targets. Various displays are also possible, such as a display (Fig. 1a) of all blood glucose values by time of day, and (Fig. 1b) by date over several weeks or months. With relative ease, the provider can see whether there are certain periods during which glycemia changed (such as with concurrent illness or holidays or after a treatment change). Diurnal patterns are readily apparent (such as going high after supper). And results at one visit can be compared with those of the prior visit.

**WHY ENCOURAGE SMBG?**

Blood glucose, unlike serum cholesterol, thyroid hormone concentration or body weight, is not a static number. Rather, it changes continuously. In non-diabetics, blood glucose often varies about two-fold in the course of a normal day, e.g. from 60 to 120 mg/dl. In people with diabetes, it may vary ten-fold. SMBG is therefore the only practical way a person with diabetes can know their blood glucose at any given moment. SMBG is therefore the only practical way a person with diabetes can know their blood glucose at any given moment. This has many advantages, such as those listed in Table 1. Specific evidence is hard to cite that assessment of blood glucose alone will better control diabetes, as this relationship is contingent upon the response that both the patient and the physician have to abnormal blood glucose readings. However, this does not diminish the importance of glycemia
assessments, as SMBG provides potentially key information that if optimally used, can be the basis for management decisions and serves as the first step towards attaining glycemic control.

In our experience, SMBG is usually accepted into the lifestyle of the person with diabetes. More often than not, patients take to it and appreciate the ability to “know where they stand”. Properly used, it gives them a level of independence in self-care as well as an ability to communicate effectively with the health care professional.

**Factors That Limit The Use Of SMBG**

In the United States, SMBG was used daily by 56.5% of people with diagnosed diabetes— not terrific, but increased from 35.7% in 1994 ([http://www.cdc.gov/diabetes/statistics/preventive/FigXData.htm](http://www.cdc.gov/diabetes/statistics/preventive/FigXData.htm)). In India, the frequency of self-monitoring among patients with diabetes is probably much lower. While one study suggests that 46.7% of patients monitored blood sugar in a resettlement colony in Chandigarh, a far more detailed survey suggests otherwise. Bjork, Kapur, et al. surveyed 5,516 patients in 187 towns of India, found that only 6.5% “monitor disease status” more than once monthly. By monitoring, they mean any assessment: SMBG, laboratory or urine glucose testing. Self-testing as such was used exclusively by 2% of patients. 72% of respondents rated their disease as “under control” and “felt well”, but mean glucose levels were more than 180 mg/dl. In sum, this survey suggested a significant degree of self-deception; people thought they were in good control when they were not.

Despite recommendations for the use of SMBG ([http://www.diabetesindia.com/diabetes/monitoring_glycemic_control.htm](http://www.diabetesindia.com/diabetes/monitoring_glycemic_control.htm)), there is little doubt in our opinion that SMBG is under-used throughout the world. While circumstances vary from place to place, our experience with diabetes in America suggests that at least six important barriers come up repeatedly. They are offered not as justifications or excuses but as observations that may explain this underutilization of an important assessment approach. With each, we provide brief comments and in some cases “action plans” since we strongly believe that SMBG should be more widely utilized.

1. **Denial—Patient does not want to know**

   In one form or another, and to one degree or another, it may be human nature to ignore, or deny unpleasant facts of life. With diabetes, this is only too easy, since symptoms are often mild until long-term complications develop, at which time they can be irreversible. Denial is also promoted if people with diabetes have a fatalistic attitude or belief system, feeling that their fate is inevitable, and not in their hands.

   The first antidote to denial may be to recognize it. A frank, encouraging discussion may help, addressing the issue head-on. Patients must believe deeply that they can work with their health care professional to effect positive change; they must believe that complications and early death are not inevitable, that their fate is in their hands.

   One way or another, the barrier of denial must be overcome if people with diabetes are to take part in successful self-care.

2. **Doctor doesn’t recommend or promote SMBG**

   As with most elements of health care, the doctor’s recommendation holds the most weight. At least in the U.S., and more commonly with primary care physicians than with endocrinologists, SMBG is not as emphatically recommended as it could be. There may be over-concern about whether the patient will reject the procedure, or too little office time to teach it. There may be an even deeper barrier, perhaps subliminal: SMBG gives the patient a degree of independence, and an ability to see for themselves the efficacy of their own treatment. We believe that this independence and empowerment is a distinct advantage; but it may take some adjustment on the part of the health care professional.

   We think that all people with diabetes should be strongly encouraged by their physician to self-monitor regularly, as do both the American Diabetes Association ([http://www.diabetesindia.com/diabetes/site_consensus.htm](http://www.diabetesindia.com/diabetes/site_consensus.htm)) and an India Consensus Statement ([http://www.diabetesindia.com/diabetes/site_consensus.htm](http://www.diabetesindia.com/diabetes/site_consensus.htm)).

3. **Results are not acted upon**

   If the patient has, at the request of the physician, regularly self-monitored blood glucose then it is incumbent upon the doctor to review the results and discuss them with the patient. Patients otherwise quickly learn that SMBG has no purpose—the results are not considered important to the physician. As
described and illustrated in Figure 1, downloading the meter and printing the data-managed results is an easy, quick way to have figures, graphs and comparisons that can be easily visualized and discussed. But even simply recalling the 14- and 30-day averages on the monitor screen can form the basis of useful feedback to patients.

When physicians totally ignore patients’ hard-earned SMBG results, it is extraordinarily discouraging to patients. But there are two patterns of SMBG that also prove discouraging. One is when results are “always the same”, and the other is when the results seem totally random. In the former case, if patterns of highs and lows are established, or if the results are always high, this is exactly what should provide a useful doctor-patient interaction. If results are always in a good range, e.g. < 140 mg/dl, then the frequency of SMBG can be reduced, for instance to once every few days. In the latter case, if the results are seemingly random without known reason, then basic aspects of self-care need to be addressed: consistency of diet, adherence to medication, and so forth.

4. Expense

Cost is without question a significant barrier, all the more so in countries such as India where health care resources can be extremely limited in certain settings. Payment for the SMBG strips is usually more expensive than for the meter itself, but both are significant costs. When insurance coverage is available or patients are in a position to pay out-of-pocket, it is a very justifiable component of diabetes care. There is also an obligation, we believe, for professionals to educate the payers-government officials, insurance carriers, etc.-about the importance of SMBG as integral to good diabetes care. Ultimately, it must be understood that the personal and financial cost of diabetes is due to the long-term complications (especially coronary heart disease and end-stage renal disease) much more than to day-to-day treatment. Any intervention that can prevent diabetic complications saves money and personal suffering.

5. Convenience

SMBG takes some time to perform, but the new meters generally give results in less than 15 seconds once the drop of blood is on the strip and in less than one minute from start to finish. We find that patients who say they reject the technique because of the inconvenience are often those confronting the number one obstacle, denial. Realistically, most people can find a few minutes to monitor each day, no matter how busy they are.

6. Pain

The finger prick can hurt, but several points should be made. First, patients are well advised never to use the old, dagger-shaped lancets that prick far deeper than needed. Spring-loaded lancet holders can be adjusted for depth of injection. While the lancets can be re-used, they eventually become dull. The sides of the fingers are less sensitive than fingertips, and “alternate site testing” (such as on the forearm) has proven useful for some patients. The amount of blood required now is very small, usually under 1 μL. And it may be that patients develop calluses or denervation at regularly used sites. But for whatever reason, people who do SMBG regularly report very little actual pain or discomfort.

**RECOMMENDATIONS**

* Consistent with modern recommendations in place throughout the world, SMBG should be used regularly by all people with diabetes. Accurate use of the technique requires one-on-one teaching and proper calibration of the devices.

* The frequency of glucose monitoring is highly individualized according to the needs and resources of the particular patient. The following guidelines may be used:
  - People with type 1 diabetes are generally metabolically unstable (labile), and should be in the habit of self-monitoring several times daily.
  - People with type 2 diabetes are usually more stable, and if so their self-monitoring may be anywhere from 1-2 times per day to once every few days. If done less than daily, we recommend that they check at various times of day, not only in the morning fasting condition. This way, they will be aware if their sugars are much higher or lower, for example, at bedtime.
  - Treatment changes should be accompanied by instructions to monitor more often, in order to gauge the effectiveness of a new regimen.

* The timing of SMBG, particularly whether it should be pre-prandial or post-prandial, is a matter of considerable discussion. We find pre-prandial testing to be more representative and stable, and this is our customary recommendation to patients. Testing after meals is highly variable, dependent on exactly the time after the meal, what was eaten, etc. There are three circumstances, however, in which post-prandial testing may be useful:
  - Pregnancy: Pregnancy is an indication for extremely tight glycemic control, and even high 1-hour post-prandial hyperglycemia women with diabetes in the third trimester can increase risk of fetal macrosomia. Good evidence suggests that in pregnant women with gestational diabetes, insulin adjustments based on post-prandial testing are more effective in preventing macrosomia and neonatal hypoglycemia than if based on pre-prandial testing. In pregnant women with pre-gestational type 1 diabetes, post-prandial monitoring has also been shown to significantly reduce the incidence of preeclampsia and neonatal triceps skin-fold thickness when compared with pre-prandial monitoring.
  - Discrepancy between SMBG results and HbA1c: Some patients will have HbA1c that is higher than expected given their SMBG results. In these cases, it may be that they have unusually high and prolonged post-prandial hyperglycemia so post-
The variability of blood glucose levels has important long-term consequences. For example, long-term variability of fasting plasma glucose may be an independent predictor of mortality in patients with type 2 diabetes, although this is a controversial issue to be addressed in our subsequent review of hemoglobin A1c.

Until recently, there has been no means to assess variability of blood glucose levels on a continuous basis and its impact on long-term complications. After decades of work, this could change. Continuous glucose monitoring is finally becoming possible, and could be a clinical reality before long.

Continuous glucose monitoring will change our way of thinking about diabetes. To begin with, any accurate, continuous monitor could provide an alarm as patients approach hypoglycemia, potentially reducing or eliminating near-catastrophic insulin reactions. Hypoglycemia is always the rate-limiting feature of diabetic control. Hyperglycemic alarms could also be set, allowing patients to know when they are going to be high and promoting better control. Patterns of highs and lows throughout the day could be easily recognized, even at times when SMBG is not practical. And trends from day-to-day, for example with illness or changes in lifestyle, would be evident.

The research potential of continuous glucose monitoring is virtually endless. Already, we have begun the evaluation of mild levels of glucose intolerance, comparing formal oral glucose tolerance testing results with continuous glucose monitoring in the free-living state. Extending our preliminary work, we suggest that diabetes will and should be ultimately defined on the basis of glucose excursions in free-living rather than only in the fasted state or after an oral glucose load.

Continuous glucose monitoring also provides the chance to observe glycemia in the everyday living of a person with diabetes. Considering nocturnal hypoglycemia alone, preliminary reports presented at the American Diabetes Association in June 2004, addressed its frequency in children, the lack of a true “Somogyi effect”, and the effect of caffeine intake. The abundant data available through continuous monitoring could also be used to evaluate new treatments, response to various foods, exercise, stress, and any number of other variables.

There are now two continuous glucose monitors that we know to be commercially available, Medtronic MiniMed’s Continuous Glucose Monitoring System (CGMS®) and Cygnus’ GlucoWatch®. The pros and cons of each are listed in Table 2. Each has significant limitations as presently marketed, but it is also important to realize that they are first generation devices that portend enormous possibilities; and these possibilities are quickly becoming realities. The CGMS, for example, has already developed a telemetered signal that communicates with a small alarm system warn on the belt, the so-called Guardian® system. It should not be long before real-time displays of glycemia are provided by the CGMS, and not long before significant improvements are made in the GlucoWatch system. It is less clear exactly how long it will be before they or other devices are, practically, easy enough to use and financially reasonable enough to allow constant continuous monitoring in many people with diabetes.

### Table 2: Comparisons of two available continuous glucose monitors

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Medtronic MiniMed CGMS®</th>
<th>Cygnus GlucoWatch®</th>
</tr>
</thead>
<tbody>
<tr>
<td>Size</td>
<td>Pager size, worn on belt</td>
<td>Large wrist watch</td>
</tr>
<tr>
<td>Alarms</td>
<td>Via “Guardian”</td>
<td>Yes</td>
</tr>
<tr>
<td>Longevity</td>
<td>3 days</td>
<td>13 hours</td>
</tr>
<tr>
<td>Output</td>
<td>Down-loaded after use</td>
<td>Real-time Display</td>
</tr>
<tr>
<td>Calibration</td>
<td>SMBG 4 times daily</td>
<td>Once at start</td>
</tr>
<tr>
<td>Fluid Sampled</td>
<td>Interstitial, via inserted sensor</td>
<td>Interstitial, via “reverse iontophoresis” which draws fluid through skin</td>
</tr>
<tr>
<td>Sampling Weaknesses</td>
<td>Averaged every 5 min</td>
<td>Reading every 10 min.</td>
</tr>
<tr>
<td></td>
<td>Sensor filament can cease to function</td>
<td>Stops if sweat present on skin; patient may feel current, have skin irritation</td>
</tr>
<tr>
<td>Accuracy</td>
<td>Generally good</td>
<td>Generally good</td>
</tr>
</tbody>
</table>

Medtronic MiniMed, Inc., also has, in quite advanced stages of development, a long-term intravenous continuous glucose monitor that could telemeter results to an external unit or link up directly with an implanted insulin delivery system such as the ones we have been using for some time. Also, a company called DexCom, Inc. is in trials using a long-term, implanted glucose sensor that will measure interstitial glucose concentration with relatively simple subcutaneous implantation.
would be to link the sensor to a delivery system, making the “closed loop” artificial pancreas. It is too early to tell when this will be a clinical reality, but it is very much under development. In fact, since both the delivery pump and the sensors can be external or implanted, simple factorial logic suggests that it should be possible for closed loop delivery to be developed by either linking an external sensor to an external pump, an external sensor to an implanted pump, an implanted sensor to an external pump or an implanted sensor to an implanted pump.

**CONCLUSION**

Self-monitoring of blood glucose is a cornerstone of diabetes self-care and should be recommended for all people with diabetes. The rationales for its use, the methods available, and practical clinical recommendations have been discussed. Other barriers, such as pain, patient denial or insufficient encouragement from the health care professional, should be overcome. In the future, continuous glucose monitoring will become available, and ultimately an insulin delivery device will be linked to continuous monitoring. At present, SMBG is an under-utilized but important part of modern diabetes care.

**REFERENCES**


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**Obituary**

**Harbans S Wasir (5.3.1937 - 23.8.2004)**

I am sad to inform you about the sudden and unfortunate demise of Dr. (Prof.) Harbans S Wasir, M.D., D.M., FAMS, FNASc., D.Sc (Hon Causa), Former Professor and Head of Cardiology, All India Institute of Medical Sciences, Chief Cardiologist and Medical Advisor, Batra Hospital and Medical Research Centre on 23.8.2004. Prof. HS Wasir was an eminent cardiologist of National and International fame. He was awarded Padma Shree in 1987 and Padma Bhushan in 2000. He had unique distinction of serving four Presidents of India as Honorary Physician (Cardiology).

He was recipient of the prestigious Dr. BC Roy award. He was Ex-President Cardiological Society of India (Delhi Branch) and Honorary Consultant Cardiology to Armed Forces of India.

He had published 10 books and contributed chapter in another 10 books. He has about 400 publications in National and International Journals.

Recently, he has been conferred the status of Emeritus Professor, Department of Cardiology, All India Institute of Medical Sciences (24.8.2004).

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