ABSTRACT

Historically, type 2 diabetes mellitus has been viewed primarily as a disease of older patients, but current prevalence data show dramatic increases in younger populations. Thus, the complications associated with diabetes—cardiovascular disease, stroke, diabetic retinopathy, peripheral neuropathy, and nephropathy—will increasingly begin to manifest in patients at an earlier age. With less than 50% of the diabetes population at the American Diabetes Association’s target goal for glucose control, there is an acute need for better medical intervention and more emphasis on diabetes education. As the most frequently visited providers across the healthcare spectrum, pharmacists are in a unique position to explain how daily glucose monitoring impacts hemoglobin A1c, and the relationship between A1c and diabetes complications such as heart disease. This article provides insights into the emerging epidemiology of diabetes, explains some of the basic pathophysiology of diabetes, and highlights the importance of the pharmacist’s role.

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Although media reports have alerted the public to the growing problem of the diabetes epidemic, few people are aware of the data and seriousness of this disease. As many as 20.8 million Americans (7% of the population) are living with diabetes and more than 6 million of them remain undiagnosed. Thirty-five million Americans are living with prediabetes, which will likely progress to established disease in the years ahead. Diabetes was the sixth leading cause of death listed on US death certificates in 2002.

Approximately 90% of all cases of diabetes mellitus are type 2 diabetes mellitus (T2DM). Historically, T2DM has been viewed primarily as a disease of older patients, but current prevalence data show dramatic increases in younger populations. In recent years, there has been a 76% increase in the number of people aged 30 to 39 years diagnosed with diabetes, and a 50% increase of T2DM in children aged 13 to 18 years (Table 1). This means that the macrovascular and microvascular complications associated with diabetes—cardiovascular disease, stroke, diabetic retinopathy, peripheral neuropathy, and nephropathy—will manifest in patients at an earlier age. It is not inconceivable that we will begin to treat myocardial infarctions in some patients as early as the teenage years.

The costs, both human and financial, are tremendous. Currently, the estimated cost of diabetes is $132 billion a year, $92 billion of which accounts for direct medical costs and $12 billion for medication costs. As the disease becomes more prevalent and manifests at younger ages, the financially strained American healthcare system may become overwhelmed with providing care to all those who need it. A profound ripple effect into the American workforce and the national economy at large is likely.
DIABETES MANAGEMENT

Appropriate management of diabetes, including self-management education, monitoring of blood glucose, achieving optimal glycemic control, regular foot care, and ophthalmic examinations, can help to reduce the incidence and progression of medical complications (Figure 1). However, it is estimated that fewer than 2% of American adults with diabetes attain optimal blood glucose levels. It is not uncommon for patients to average blood glucose values greater than or equal to 200 mg/dL (fasting) and 300 mg/dL (postprandial). Compared with established targets for glycemic control (Table 2), existing levels show an acute need for better medical intervention and more emphasis on self-management education. Less than 50% of the diabetes population is at goal for the American Diabetes Association’s (ADA) target for \( A_1c \) of less than 7% (Figure 2).

Self-monitoring of blood glucose (SMBG) is an important part of diabetes self-management by allowing patients to make informed decisions in the management of their diabetes with nutrition, activity, and, sometimes, medication. However, the \( A_1c \) is the clinical outcome most utilized by physicians in assessing a patient’s blood glucose control. Many patients do not understand the correlation between \( A_1c \) and SMBG. This provides an opportunity for pharmacists, who interact with patients daily, to explain how daily glucose monitoring impacts \( A_1c \), in addition to explaining the relationship between \( A_1c \) and diabetes complications such as heart disease. Figure 3 shows the \( A_1c \) level that can be expected for selected mean plasma glucose levels. Pharmacists can use this tool to counsel patients and provide them with a clearer understanding of the relationship between blood glucose monitoring and the overall goals of diabetes management.

Data from the National Health and Nutrition Examination Survey (NHANES) show that approaches to treating diabetes have changed significantly in recent years. Increasingly, patients with diabetes are using oral medications instead of diet and exercise to manage blood glucose (Figure 4). Notably, this increased reliance on drug therapy is accompanies showing higher levels of glycemic control, with the NHANES IV reporting only 35% of patients at the ADA \( A_1c \) goal of less than 7%, as compared with 44.5% reported at goal in NHANES III. These trends clearly show that diet and exercise are important for diabetes management and

Table 1. Estimated Number of New Cases of Diagnosed Diabetes in People Aged 20 Years or Older, by Age Group—United States, 2005

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Number</th>
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<tbody>
<tr>
<td>20-39</td>
<td>700,000</td>
</tr>
<tr>
<td>40-59</td>
<td>750,000</td>
</tr>
<tr>
<td>60+</td>
<td>800,000</td>
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Table 2. Targets for Glycemic Control

<table>
<thead>
<tr>
<th>ADA Clinical Guidelines</th>
<th>ACE Clinical Guidelines</th>
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</thead>
<tbody>
<tr>
<td>( FPG ) 90–130 mg/dL</td>
<td>( FPG ) &lt;100 mg/dL</td>
</tr>
<tr>
<td>( -2 ) h pp &lt;180 mg/dL</td>
<td>( -2 ) h pp &lt;140 mg/dL</td>
</tr>
<tr>
<td>( Bedtime ) 100–140 mg/dL</td>
<td>( Bedtime ) 100–140 mg/dL</td>
</tr>
<tr>
<td>( A_1c ) &lt;7%</td>
<td>( A_1c ) 6.5%</td>
</tr>
</tbody>
</table>

that pharmacological treatment is not a panacea, but only 1 component of a multifaceted approach to diabetes management. Lifestyle and behavioral changes are critical to successful treatment.

**PATHOPHYSIOLOGY AND RISK FACTORS**

Pharmacists can play an important role in patient self-management education by helping them better understand the pathophysiology of diabetes and its related conditions, the rationale for medication therapy management as adjunct treatment to diet and exercise, and the effects specific medications exert on fasting and postprandial blood glucose levels. T2DM usually begins as insulin resistance, a disorder characterized by increases in lipolysis and free fatty acid concentrations, which in turn triggers increased glucose production by the liver. Initially, this results in an increase in insulin production by the pancreas to maintain glucohomeostasis. However, as the disease progresses and the need for insulin continues to rise, insulin production declines, and the body cannot effectively use the insulin that is produced. Under normal metabolic conditions, insulin interacts with its receptors in the cell membrane, resulting in an intracellular insulin signaling cascade, signaling glucose 4 (GLUT-4) transporters inside the cell to move to the surface, and allowing the transport of glucose from the bloodstream into the cell (Figure 5). In people with impaired insulin production or utilization, the signals are inadequate, resulting in a minimal supply of GLUT-4 transporters bringing the excess glucose in from the bloodstream. The result is hyperglycemia.

A simple analogy to conceptualize the process by which glucose gains entry into the cell would be to think of insulin as being the key to a hotel room, where the hotel room is the body's cells. However, to gain access to the room, you need a bellboy to escort you, in addition to the keycard (insulin). The bellboy is a GLUT-4 transporter. In the case of diabetes, there are not enough bellboys to check people into their rooms. Therefore, even though the insulin is the keycard for entry into the room, there are no transporters to bring you there. When a multitude of glucose molecules attempt to check into the hotel at the same time, they are all left to wait in the lobby (the bloodstream). These

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**Figure 2. Aggressive Control of Type 2 Diabetes Is a Challenge**

![Chart showing percentage of patients with A1C levels](chart)


**Figure 3. Correlation Between A1C and Mean Plasma Glucose Levels**

![Graph showing correlation between A1C and mean plasma glucose levels](graph)

Adapted with permission from the American Diabetes Association. Standards of medical care in diabetes—2006. Diabetes Care. 2006;29(suppl 1):S4-S42.2

**Figure 4. Changes in Diabetes Treatment**

![Bar chart showing changes in diabetes treatment](chart)

Adapted with permission from Koro et al. Diabetes Care. 2004;27:17-19.6

NHANES = National Health and Nutrition Examination Surveys.
molecules attempt to find other places to go, typically the polyol pathway, which is not insulin dependent (no keycard necessary to gain access). There, molecules are broken down into sorbitol, which easily permeates cells, damages tissues, and initiates microvascular complications. At the same time, sorbitol reduces nitric oxide production, thereby increasing blood pressure, a common macrovascular comorbidity of T2DM.

T2DM typically progresses from glucose intolerance, initially as elevated postprandial levels, to an increase in fasting blood glucose, and finally to diagnosed diabetes. Throughout this progression, beta cells, pancreatic cells that generate insulin, continue to decline, thereby worsening blood glucose control over time. The physiological sequelae of hyperglycemia are shown in Table 3.\(^6^{12}\)

Although older age is a known risk factor for T2DM, it is becoming clear that other factors are also highly significant. Abdominal obesity is an especially strong risk factor, and 90% of people newly diagnosed with diabetes are overweight.\(^{13}\) Additional risk factors include a family history of diabetes, history of gestational diabetes, impaired glucose metabolism, physical inactivity, and race/ethnicity. African Americans, Hispanic/Latino Americans, American Indians, and some Asian Americans, Native Hawaiians, and other Pacific Islanders are at particularly high risk for T2DM and its complications.\(^1\)

**Diagnostic Tests**

The classic symptoms of diabetes include polyuria, polydipsia, polyphagia, and unexplained weight loss.\(^14\) However, T2DM is often not diagnosed until after complications are already present. The ADA estimates that by the time patients are finally diagnosed with T2DM, they have actually had diabetes for approximately 9 years.\(^4\)

According to ADA guidelines, screening is reserved for patients aged 45 years or older. However, given the increased prevalence of T2DM in younger adults, the American College of Endocrinology recommends screening people aged 30 years and older with risk factors, specifically, a body mass index of 25 kg/m\(^2\) or higher.\(^15\) Criteria for testing children for T2DM include weight for height greater than 85th percentile combined with additional risk factors.\(^2\)

The recommended initial screening test for non-pregnant adults is fasting plasma glucose (FPG). This test is more convenient for patients, less costly, and easier to administer than the oral glucose tolerance test (OGTT).\(^2\) The use of hemoglobin A\(_1c\) for the diagnosis of diabetes is not recommended at this time.\(^14\) Criteria for diagnosis include FPG of at least 126

![Figure 5. How Glucose Gets Into the Cell](image)

**Table 3. Harmful Effects of Hyperglycemia Due to Oxidative Stress**

<table>
<thead>
<tr>
<th>Effect</th>
<th>Effect</th>
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<tbody>
<tr>
<td>Increased capillary basement membrane thickening causing microvascular problems</td>
<td>Increased blood pressure</td>
</tr>
<tr>
<td>Impairment of phagocytosis (ability to fight infections)</td>
<td>Increased platelet adhesiveness</td>
</tr>
<tr>
<td>High levels of (glycosylated) proteins: advanced glycosylation end products that interfere with the protein’s normal physiology</td>
<td>Increased serum fibrinogen</td>
</tr>
<tr>
<td>Glucose metabolized to sorbitol via the polyol pathway</td>
<td>Increased blood viscosity</td>
</tr>
<tr>
<td>Faulty lipid metabolism yields hypercholesterolemia and hypertriglyceridemia</td>
<td>Decreased red blood cell flexibility</td>
</tr>
<tr>
<td>Increased neonatal morbidity and mortality</td>
<td>Increased coagulation factors such as plasminogen activator inhibitor -I</td>
</tr>
<tr>
<td></td>
<td>Increased activation of some isoforms of protein kinase C causing reduced vascular contractility</td>
</tr>
<tr>
<td></td>
<td>Increased coronary artery disease</td>
</tr>
<tr>
<td></td>
<td>Increased dental cavities and gum disease</td>
</tr>
<tr>
<td></td>
<td>Increased incidence of cataracts</td>
</tr>
</tbody>
</table>

Data from Ceriello,\(^9\) Mehta et al,\(^10\) Monnier et al,\(^11\) Stump et al.\(^9\)
mg/dL, or symptoms of diabetes plus a random plasma glucose concentration of at least 200 mg/dL. OGTT criteria are postload glucose concentration of at least 200 mg/dL 2 hours after start. To confirm the diagnosis, repeat testing should be performed on a different day. More research is supporting the use of postprandial glucose for diagnosis, suggesting earlier detection of T2DM.\textsuperscript{15,16}

Postprandial hyperglycemia is one of the earliest abnormalities of glucose homeostasis associated with T2DM and is often markedly exaggerated in diabetes patients with fasting hyperglycemia.\textsuperscript{17} Avignon et al demonstrated in 66 untreated T2DM patients that postprandial plasma glucose correlated significantly and independently with $A_1^c$, but that prebreakfast glucose levels did not. Moreover, postprandial glucose concentrations demonstrated better sensitivity and specificity in predicting poor glycemic control.\textsuperscript{18} However, other studies reported that preprandial plasma glucose concentrations were related to $A_1^c$ more strongly than postprandial concentrations,\textsuperscript{19} so this subject is a matter of ongoing debate.\textsuperscript{20,21} What is conclusive from the medical literature, however, is the finding that postprandial hyperglycemia is an important predictor of cardiovascular disease.\textsuperscript{22-27}

Postprandial blood glucose testing can be useful for assisting patients in identifying patterns with meals, oral medications, and insulin. By testing 2 hours after the first bite of food, patients can determine: (1) whether they ate the appropriate amount of food—too much or too little; (2) whether certain oral antidiabetic medications are working; and (3) whether their insulin dosage is appropriate.

**The Pharmacist’s Role**

The fact that 6 million patients with T2DM remain undiagnosed identifies a clear and profound need for screening, awareness, and education within the community. Pharmacists, who are in frequent contact with patients and are a trusted source of health information, are uniquely positioned to provide screenings or refer patients for particular screening services.

At Midwestern University Chicago College of Pharmacy (MWU-CCP), our chapter of the American Pharmacists Association Academy of Student Pharmacists (APhA-ASP) collaborates with local and state community pharmacies to participate in a program called Operation Diabetes. APhA offers students an instructional manual and encourages them, under faculty supervision and training, to perform diabetes screenings in the community. At MWU-CCP, students use advertisement flyers instructing patients to eat a meal prior to the screening test, which is typically scheduled between 11 AM and 2 PM or between 4 PM and 7 PM to capture postprandial glucose concentrations. Patients identified as potentially having diabetes or at high risk are asked to return to the pharmacy for a follow-up glucose testing appointment with the pharmacist. In community pharmacies where these services are not provided, we will schedule a follow-up student screening or refer patients to their primary care physicians for further evaluation.

This program offers community service learning for pharmacists and students, reinforces the role and enhances the image of the community pharmacy in patient care, and raises awareness among future pharmacists about the importance and seriousness of diabetes.

**DISCUSSION**

**Mr McAllister:** A recent article about the diabetes epidemic in New York City reported that the city now requires providers to report hemoglobin $A_1^c$ to the City Health Department. That really highlighted the seriousness of this issue, and yet, I think that many of my staff are unaware that diabetes has evolved into a major public health crisis. What can we do to educate those within our own profession, in addition to the healthcare community at large?

**Dr Cryder:** We begin by shifting the mindset of the students coming in to pharmacy practice. Many community pharmacists are unwilling to make that leap into diabetes education. We need to change that at the ground level to help pharmacists think of diabetes as a medical priority. We can begin to instill in students during pharmacy school the fact that diabetes is going to be “the” important epidemic in the not-too-distant future. They also should comprehend that the practice of pharmacy is shifting from medication and product-centered service to patient-centered care.

**Dr Holaway:** I am on the sports medicine faculty with the fellowship program at the University of Georgia College of Pharmacy. We provide free physicals to elementary school kids. Through this program, we have learned that approximately 30% of our children and adolescents are developing a high body mass index and elevated blood pressure. This leads me to
believe that the area we have the greatest ability to impact is this young age group. One of the prime places to reach this group is at summer youth programs, YMCAs, and mall screenings.

**Dr Cornell:** Working to raise awareness among people aged 30 to 39 years is also a good idea because they are the parents of children at risk or those already diagnosed with T2DM. Behavior change in this population, which is also the fastest growing diabetes population, can positively impact the health of the entire family and, hopefully, future generations.

**Dr Malone:** Historically, the pharmacist has been the great communicator in the healthcare system between providers and patients. We are in the best position to promote prevention. You do not have to access clinical records to prevent diabetes, you simply have to look at the patient. You can review medications and, if you are a community pharmacist, become familiar with their families and dietary habits. Also, you can make your interventions right at the pharmacy. What I have learned, however, is that many students and even providers do not know what the therapeutic goals of diabetes are. If you do not know where to start, you cannot be effective. Not only must we know the goals, we must also understand that we must set goals with patients so that they are able to take care of themselves. Pharmacists, in particular, must become thoroughly familiar with target goals.

We dispense many diabetes monitors, but we rarely connect the monitor to the goal and necessary interventions. We may tell patients how to use the monitors but we fail to connect the dots. Lastly, you must understand the basics of disease progression to know how to treat it effectively.

**Dr Triplitt:** I have educated many pharmacists about diabetes and, in my experience, although most pharmacists are interested in learning about diabetes, many do not apply their diabetes knowledge to their practice. It is crucial that we support and promote pharmacists’ application of diabetes knowledge, and continue to strive to find new avenues for pharmacists to obtain this information.

**Mr McAllister:** Let’s talk more about connecting the dots in the context of inpatient practice. That means pharmacists need to be paying attention to monitors in relation to therapeutic goals and bringing that information home to patients. For the pharmacists who do not wish to actively intervene, what is the next step? Do they refer the patient to a diabetes educator?

**Dr Malone:** Yes, but they must be able to identify where those resources are. In my experience, it is confusing in the hospital setting to determine what to do with monitors and glucose strips because of payment scales and payor restrictions. Perhaps patient education before discharge is key; however, not every institution has those resources. I receive phone calls regularly asking how to send a patient home, but connecting them with follow-up on the outpatient side is key, and the pharmacist can play an important role in this.

**Dr Holaway:** In my hospital practice, we identify an abnormality in blood glucose values in a patient, I ask the patient to measure blood glucose values with a monitor preprandially and postprandially for 2 days prior to discharge. Not only will I ask a nurse to observe this, I will also appoint a nursing student and a pharmacy student to be with the patient during monitoring. The students serve as educators and explain to the patient the importance of the monitoring and the relationship between the monitoring and A1C levels. Once we provide a patient with a meter, my approach is to look at the “ABCDE”: A being A1C, B being blood pressure at goal, C being cholesterol at goal, and D being depression. In some older men, I add E for erectile dysfunction. I am an advocate of treating not just the blood sugar but the entire patient.

**Dr Cornell:** My practice has had success with a 2-step process. At the first appointment, the pharmacist instructs the patient how to use their SMBG meter correctly and when to test their blood glucose. At the 2-week follow-up appointment, the pharmacist can evaluate the patient’s testing technique and explain the relevance of the numbers to overall health goals.

**Dr Johnson:** In some hospitals, a diabetes educator is assigned to provide this instruction and the pharmacist stays in the pharmacy. Also in some settings, satellite pharmacies involve the pharmacists in discharge planning, but in the majority of hospitals this is the responsibility of the nursing staff. The pharmacist in the hospital setting must make a commitment to be part of the education of patients prior to discharge, and to work with social services to create a postdischarge plan that includes diabetes education and outpatient care.

**Dr Triplitt:** That plan should involve giving patients a list of community pharmacies that provide diabetes resources. In much of rural America, often-times there are not many resources available to patients for diabetes beyond the primary care physician, although the Internet is beginning to change this.
**Mr McAllister:** The Asheville Project, sponsored by a large North Carolina employer, was a prime example of involvement of community pharmacists in the care of patients with diabetes. Although reimbursement for such care is a continuing problem for pharmacy, these pharmacists—largely uneducated in the field of diabetes—agreed to pursue that knowledge to provide care to employees of a large employer, and to do so without reimbursement. Before they were even halfway through the project, the reductions in employee absenteeism and healthcare costs were large enough for the employer to offer payment for pharmacy services. This project clearly demonstrates the significance of the disease, its associated expenses, and the important role pharmacists can play in diabetes care once they make the commitment.

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