

**Diabetes: A Worldwide Epidemic**  
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# DIABETES: A Worldwide Epidemic



As all forms of diabetes continue to increase in incidence, testing options also expand.

By Shannon Rose

**A**pproximately 23.6 million children and adults in the United States—almost 8% of the population—suffer from diabetes, according to the 2007 National Diabetes Fact Sheet.

Of these, approximately 5.7 million go undiagnosed, and 57 million people are estimated to be prediabetic. In addition, 1.6 million new cases are diagnosed every year in individuals 20 years and older, according to the fact sheet compiled by the Centers for Disease Control (CDC), National Institutes of Health (NIH), and the American Diabetes Association (ADA), among others. The World Health Organization (WHO) estimates that approximately 300 million individuals worldwide will be living with diabetes by the year 2025.

In all three forms of the metabolic disorder—type 1 and 2 diabetes, and gestational diabetes—the body is unable to effectively control its glucose levels. More than 90% of diabetics suffer from type 2 diabetes, in which either the pancreas does not produce enough insulin, or the body does not utilize the insulin it has to effectively control glucose levels. In individuals with type 1 diabetes, the body attacks the pancreas to such a degree that it does not produce insulin at all.

The high prevalence of the condition and its complications make diabetes a significant public health issue. The consequences caused by uncontrolled blood sugar in persons with diabetes are severe, and they include heart disease and stroke,

high blood pressure, blindness, diseases of the nervous system, amputations, and dental disease.

According to the fact sheet, costs of the disease in the United States are estimated at \$218 billion, including \$18 billion for those with undiagnosed diabetes and \$623 each for the 180,000 pregnant women with gestational diabetes. In 2006, the condition was the seventh leading cause of death in the nation.

"It's not that diabetes is difficult to diagnose," says Randy Byrd, vice president and chief technical officer at Bionostics Inc, Devens, Mass. "The problem is that many people are undiagnosed. The challenge for labs is the ability to access patients to perform the testing which provides diagnosis."

### Changing the Gold Standard

Until recently, the gold standard for diagnosis of diabetes was the measurement of glucose levels, with increased glucose concentration in urine or blood indicating diabetes.

The two main tests are the direct measurement of glucose levels in the blood during an overnight fast—the fasting plasma glucose test (FPG)—and a test that measures blood glucose levels four to five times over a 3-hour period—the oral glucose tolerance test (OGTT). While the WHO advocates the OGTT, the ADA advocates the FPG.

However, at the ADA's annual meeting in June, a committee of international experts recommended the A1C assay test as a new diagnostic tool, except for gestational diabetes. The A1C test,

also known as glycated hemoglobin or HbA1c, is a blood test that measures a person's average blood glucose control over the preceding 2 to 3 months. The excess glucose produced by diabetics glycosylates with—or sticks to—hemoglobin, which carries oxygen from the lungs to the body's cells.

The A1C test measures the percentage of this glycated hemoglobin in the blood, which is a reflection of average blood glucose control. The test is not new, but has been used for the past 30 years to determine how well a patient controls diabetes, rather than as a diagnostic tool.

The report could instigate a change in the way diabetes is diagnosed, the ADA said. The international committee concluded that an A1C level of 6.5% indicates that a person has diabetes, while values between 6% and 6.5% are likely to be at highest risk for developing diabetes.

"The A1C test is a more stable, reliable diagnostic tool than the OGTT or the FPG," says Ranka Milojkovic, HPLC product manager at Tosoh Bioscience Inc, San Francisco. "There are problems with reproducibility and accuracy with the tests that measure glucose."

### Advances in Instrumentation—the Next Generation

According to Milojkovic, lack of standardization kept the A1C test from being recommended as a diagnostic tool. Advances in instrumentation and standardization have eliminated the major roadblocks to the use of the test for diagnosis. Currently,

it is mainly performed in hospital and reference laboratories, using either high-performance liquid chromatography (HPLC), often considered the gold standard, or immunoassay methods.

Launched in December 2008, Tosoh's G8 HPLC Analyzer is the next generation of Tosoh's industry-leading HPLC testing systems. Designed from a user perspective and using ion-exchange technology, the G8 HPLC Analyzer enhances overall safety and convenience of operation.

The system, which is certified by the National Glycohemoglobin Standardization Program, features stable A1C results in 1.6 minutes through in vitro diagnostic measurement of HbA1c in blood specimens. It has a compact footprint of 21 x 20 x 19 inches and automated daily maintenance.

"We are always thinking of our customer," Milojkovic says. "Labs are under pressure as there is greater demand to run more samples in less time, and we wanted to address that and design a high-speed analyzer with high resolution. There is no faster HbA1c assay out there."

Forty flags, or machine parameters, allow the system to print out only those results that the user needs to analyze.

"This reduces review time for patient results," Milojkovic says.

The throughput for 50 tests takes 1 hour and 20 minutes, while 100 tests can be performed in 2 hours and 40 minutes. There are two loaders available: the standard 90-sample loader, which has a walkaway time of 2 hours and 24 minutes, and the 290-sample loader, which has a walkaway time of 7 hours and 44 minutes (basically one shift for a lab technician).

"The technician can load it in the morning and leave it for the whole day," Milojkovic says.

### Diabetes Testing at the Point of Care

Bio-Rad Laboratories Inc, Hercules, Calif, offers a point-of-care A1C analyzer, the in2it. The fully automated system is designed for simplicity, convenience, and speed in near-patient testing, providing results while the patient waits. Requiring only 10 µL of capillary or venous blood, the system uses boronate affinity chromatography for results that are largely free from hemoglobin variant interference.

The in2it analyzer is cleared by the FDA for prescription home use, CLIA waived, and qualifies for CPT code 83037, offering the maximum US reimbursement limit of \$13.56. The analyzer supports multilingual screen displays and offers computer connectivity for complete data management.

Bionostics' RNA1c delivers a quality control solution for use with Siemens' point-of-care DCA2000 and Vantage Analyzers to confirm correct operation and measurement of HbA1c in patient samples.

According to Byrd, at the time of RNA1c's development in 2007, other quality control products were stored frozen, or were freeze-dried, so that reconstitution was required prior to use and

refrigerated storage.

"Because point-of-care HbA1c testing is often done in a physician's office or a clinic where access to refrigerated storage is limited, or where the additional handling required for thawing or reconstitution is difficult, we designed our product to be liquid," Byrd says. "It is stable for 30 days at room temperature after opening, or 90 days if refrigerated between uses."

According to Byrd, it is important to have a quality control solution with this type of long in-use dating because testing may only be done monthly on the Siemens system.

### New Levels of Performance for Glucose Testing

While HbA1c testing may be the touted diabetic diagnostic, companies such as Nova Biomedical are bringing glucose testing to a new level of analytical performance with the point-of-care blood glucose monitoring system, the StatStrip. Launched in 2006, the strip is an advanced system that elevates bedside analysis to a level that approaches the quality of central lab testing, according to Rick Rollins, who is part of Nova's marketing department.

"Our strip is the only one that measures and corrects hematocrit interferences, as well as interferences from acetaminophen, uric acid, ascorbic acid, maltose, galactose, xylose and lactose," Rollins says.

Hematocrit-related errors of 20% to nearly 50% were reported on every glucose meter system

easy sample acquisition and minimal pain for the patient. In addition, it requires no calibration codes, thereby eliminating a step and preventing a potential input error.

The CLIA-waived StatStrip is also approved by the FDA for use in neonatal testing because severe hematocrit abnormalities are routinely found in newborns.

Comprehensive Instrument Manager software provides management, control, and regulatory compliance, and allows the StatStrip system to be completely customized to the needs of each department within the hospital.

Thermo Fisher Scientific offers an OGTT that is particularly well-suited to test for gestational diabetes.

"The Trutol Glucose Tolerance Beverages are great for diagnosing pregnant women who are predisposed to gestational diabetes," says Patricia Rogler, marketing communications specialist. "The test provides information to the physician on how well the patient can process glucose while pregnant. Depending on the results, the physician will work with the patient to control the potential to develop gestational diabetes, or manage diabetes if the results are positive."

The beverage can be administered in the physician's office, reference lab draw station, or at a hospital laboratory draw station after a patient has fasted for a minimum of 12 hours. Then the patient will have blood drawn to see how well they process the glucose, with samples sent to a lab to be processed.

"Trutol comes in noncarbonated and carbonated formulas," Rogler says. "There are three different concentrations and flavors available in each formulation. The products are caffeine-free, certified kosher, and have a longer shelf life than most soft drinks."

In the approval stage is BioMedical Products' I-Chroma HbA1c test, expected to be available in mid-2010. The portable, compact analyzer had an easy-to-use immunoassay test disposable device, according to its general manager, John Geppert.

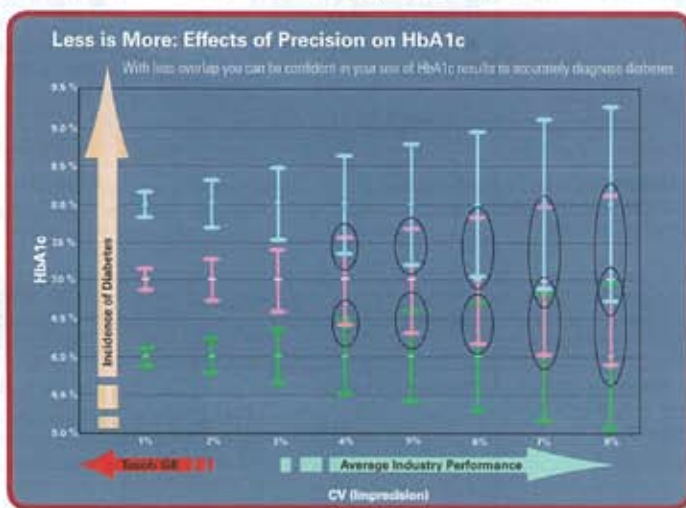
The I-Chroma fluorometer calculates HbA1c test results automatically within 5 minutes and displays a percentage of glycohemoglobin in blood on the LCD of the analyzer. An

optional printer is available, and there is an RS232 interface on the back of the analyzer.

"The market was our impetus for development," Geppert says. "The A1C gives a better indication of diabetes than glucose measurement, and we wanted to develop a smaller point-of-care product that is portable and allows for multisite testing."

As systems for measuring A1C continue to evolve in 2010, the test indeed may find its way into more labs and shoulder out the more common glucose measurement tests. ■

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tested except for Nova's StatStrip, according to a 2008 study by the Mayo Clinic. While other glucose monitoring systems may report an error if the hematocrit value is abnormal, StatStrip is the only glucose monitor that measures hematocrit on the strip, automatically correcting glucose values for hematocrit values.

"Accuracy is one of the biggest challenges for point-of-care testing," Rollins says.

The monitor incorporates a patented strip technology that uses four measuring wells, instead of the usual one. It has 6-second analysis time and color touch screen operation, with normal results displayed in green, and abnormal and critical results in pink. Its 1.2-µL sample size results in