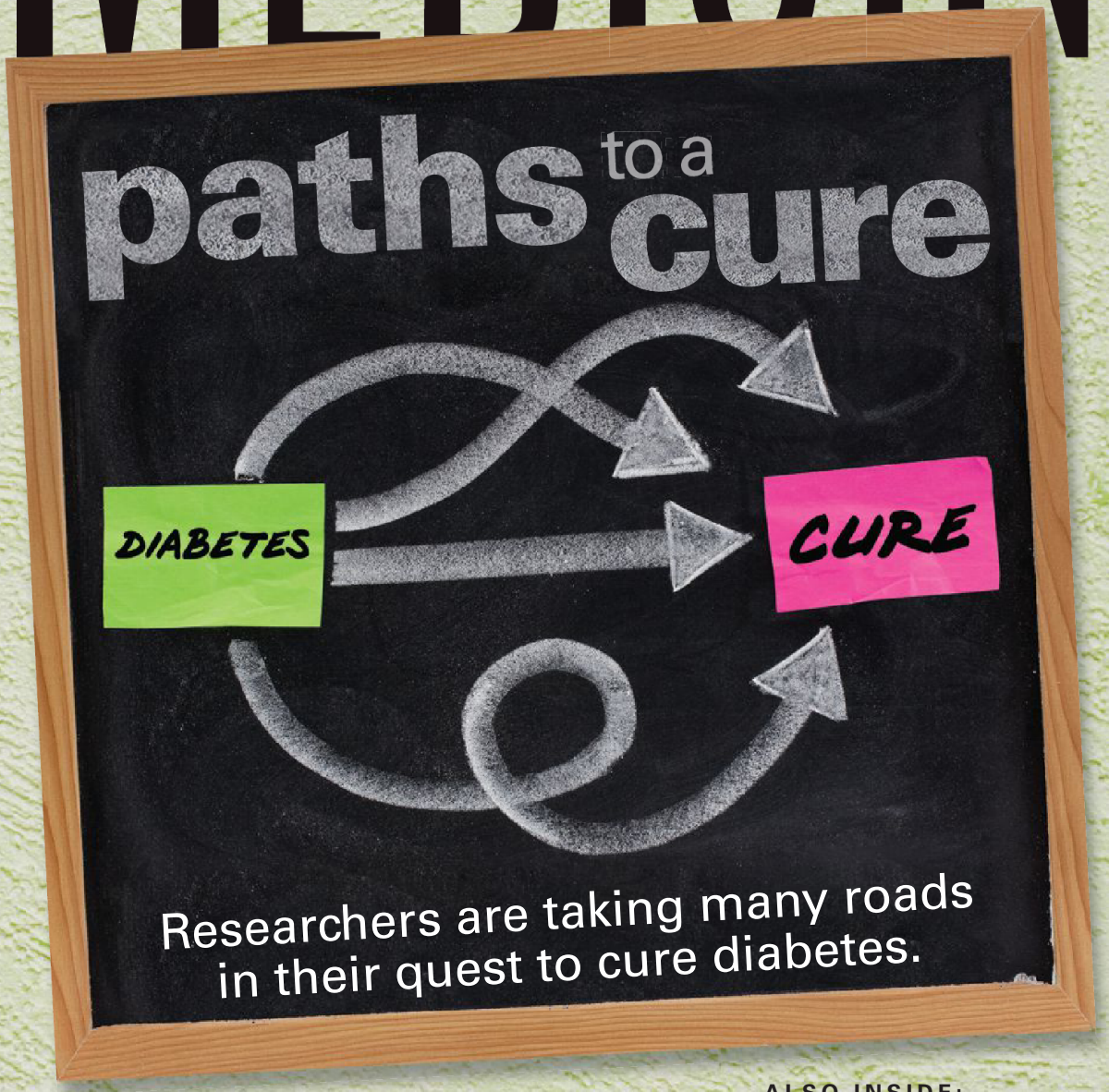
minnesota MEDICINE



Researchers are taking many roads in their quest to cure diabetes.

ALSO INSIDE:

Artificial Sweeteners and Obesity

Continuous Glucose Monitoring

Managing Children with Type 2 Diabetes

MINNESOTA MEDICAL ASSOCIATION | AUGUST 2011

minnesota MEDICINE
MINNESOTA MEDICAL ASSOCIATION
AUGUST 2011

TABLE OF CONTENTS

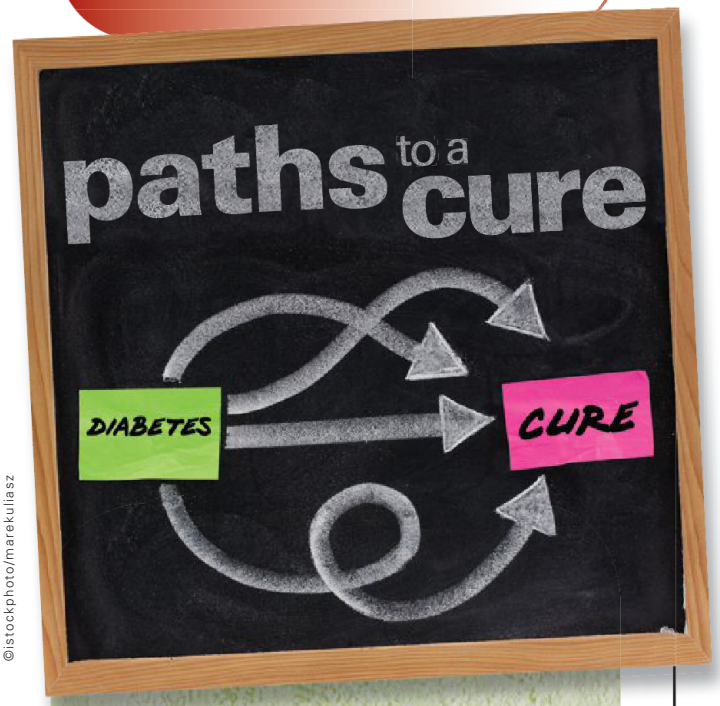
©istockphoto/craftvision

20 FEATURE

Sweet Debate

| By Trout Lowen

Do artificial sweeteners contribute to rather than combat obesity?



©istockphoto/marekuliasz

COVER STORY

Paths to a Cure

| By Jeanne Mettner

Researchers are going down many roads in their quest to cure diabetes.

p.24

MMA NEWS

ATTENTION PHYSICIANS

Complete your census. Go to mnmed.org/census (members), mnmed.org/censusnon-members (nonmembers).

ALSO INSIDE

Minnesota Medicine is intended to serve as a credible forum for presenting information and ideas affecting Minnesota physicians and their practices. The content of articles and the opinions expressed in *Minnesota Medicine* do not represent the official policy of the Minnesota Medical Association unless this is specified. The publication of an advertisement does not imply MMA endorsement or sponsorship.

To Submit an Article
Contact Carmen Peota at cpeota@mnmed.org.

The editors reserve the right to reject editorial, scientific, or advertising material submitted for publication in *Minnesota Medicine*. The views expressed in this journal do not necessarily represent those of the Minnesota Medical Association, its editors, or any of its constituents.

minnesota MEDICINE

Contact Us
Minnesota Medicine, 1300 Godward Street, Ste 2500, Minneapolis, MN 55413. Phone: 612/378-1875 or 800/DIAL MMA
Email: mm@mnmed.org
Web: minnesotamedicine.com

Owner and Publisher
Minnesota Medical Association
Editor in Chief
Charles R. Meyer, M.D.
Editors
Carmen Peota
Kim Kiser
MMA Communications Director
Terry Ruane
MMA News writer
Scott Smith
Graphic Designers
Janna Netland Lover
Michael Start
Kathryn Forss
Publications Assistant
Kristin Drews

Copyright & Post Office Entry
Minnesota Medicine (ISSN 0026-556X) is published each month by the Minnesota Medical Association, 1300 Godward Street NE, Suite 2500, Minneapolis, MN 55413.

Periodicals postage paid at Minneapolis, Minnesota, and at additional mailing offices. POSTMASTER, send address changes to *Minnesota Medicine*, 1300 Godward Street, Ste 2500, Minneapolis, MN 55413.

Subscriptions
Annual subscription - $45 (U.S.), $80 (all international)

Missing Issues and Back Issues
Missing issues will be replaced for paid subscribers at no additional charge if notification is received within six months of the publication date. Replacement of any issues more than six months old will be charged the appropriate single back issue price. Single back issues of Minnesota Medicine can be purchased for $25 (U.S.) and $30 (Canada, Mexico, and other international). Send a copy of your mailing label and orders to Kristin Drews, 1300 Godward Street, Ste 2500, Minneapolis, MN 55413 or fax it to 612/378-3875.

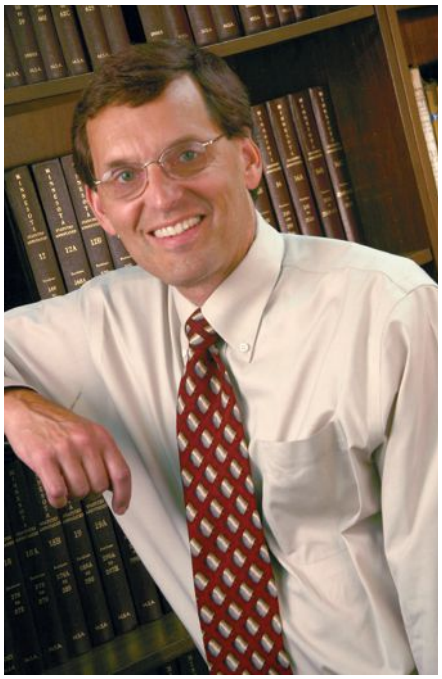


Photo by Scott Walker

Re-engineering Diabetes Care

For the time being, finger sticking and medication tweaking are with us.

I've often thought engineers make the best diabetes patients. They are precise. They like to measure and record things. And they usually take instruction well. I have patients who arrive for their follow-up visits with pages of blood sugars laid out in Excel spreadsheets, frequently with three-color graphs that show trends and even statistical significance calculations. With a precision bordering on the compulsive, they watch their diabetes and, as a result, they usually do well.

Diabetes needs watching. Few chronic diseases demand such hour-to-hour tending. Since studies in the early 1970s confirmed that tight control resulted in less end-organ damage, doctors have pushed their patients for fastidious blood sugar control. In the test-your-urine-sugar, nonglycosylated hemoglobin era, diabetes treatment was part guesswork, part art, with a touch of science. As a result, even the most obsessive patients could achieve only a modicum of control.

Now, with pocket glucometers, patients on oral medications can do regular blood sugar checks to catch any trend, low or high. Insulin-dependent patients can adjust their insulin doses three or four times a day. Constant blood sugar monitors the size of quarters with probes inserted subcutaneously can give doctors and patients a 24-hour snapshot of blood sugar values with enough data and graphs to keep any engineer happy.

But both patient and doctor would rather not do all this fussing. Ideally, a person with diabetes would be just like a person without the disease, not having to think about his pancreas or blood sugar during the course of a day. The technological answer to this is the insulin pump, delivering jolts of insulin with increasingly sophisticated algorithms to keep blood sugar as close to physiologic as possible. Yet it still requires the patient to measure blood sugar and adjust the pump. A totally hands-off feedback system of blood sugar driving insulin delivery hasn't been developed yet.

Another solution is to replace the pancreas with one that works. Yet even though pancreas transplants have taken giant strides forward since the first successful one in 1966, only a small fraction of people with diabetes still qualify for consideration and transplanted patients trade insulin hassles for immunosuppressive troubles.

The ultimate answer to the demands of diabetes is cure. Centuries after the first patients tasted their sugary urine and 90 years after insulin was isolated and used on patients, it somehow seems that we would be closer to finding the cure for a disease that afflicts millions. As Jeanne Mettner's article indicates, it's not for lack of trying. As with so many diseases, initial searches for a single etiology that can be zapped by a magic bullet have been stymied by the realization that diabetes is many diseases, and one cause will not likely be found and one cure will not likely suffice.

So, for the time being, finger sticking and medication tweaking are with us. And we'll have to teach patients with diabetes to be engineers.

Charles R. Meyer, M.D., editor in chief, can be reached at cmeyer1@fairview.org

More on In-Flight Emergencies

The article "Is There a Doctor on Board?" (June 2011, p. 25) reminded me of two experiences I had responding to emergency situations in the air. I got my first call to help on a flight from Minneapolis to Atlanta a little over a year ago that was already running almost two hours late. I was asked to evaluate a young man, whom I was told had had juice and a single cocktail (his companions were adamant he had not had more), who was drifting in and out of consciousness.

After fending off an inebriated passenger in the seat ahead of him who wanted to give advice, I attempted to examine him and get a history. Using my own stethoscope, which I had with me because I was on a mission trip to Guatemala, and my husband's glucometer (the flight attendant claimed there was no medical kit), I was able to determine that the man was not hypoglycemic and had a regular heart rhythm.

I eventually learned that the same thing had happened to him the previous year after he pulled an all-nighter without eating and then imbibed. That time, he made it to the beach at his destination before passing out. Thank goodness I didn't divert our already-late flight when I was thinking about PEs and cerebral aneurysms. Next time, I will push the flight attendants harder about checking for a medical kit, now that I know that planes are mandated to have one.

My next call came a year later on a flight from London to Bahrain. It was for a lethargic kid who had stomach pain. I never found out for sure what was in the plane's medical kit because a very nice paramedic accompanying a passenger had packets of oral rehydration salts in his kit that worked quite nicely for the child.

Because I've vacationed and volunteered in remote spots, I have thought a lot about what I need to take with me to care for people when backup is perhaps hours away. I was very pleased to see that the list of mandated items on planes included airway items and something for postpartum hemorrhage. As a family physician who does OB, one of my big fears is the possibility of miscarriage with severe bleeding or preterm delivery with or without maternal bleeding. Now I carry misoprostil.

I definitely agree with those physicians in your article who said it helps to have thought about how to approach such situations before they happen and to gather one's thoughts first. I also agree that we do have valuable knowledge and an obligation to use it for others in true emergency situations.

Thanks for the article.

Jennie Orr, M.D., AMC
Family physician, Hastings

Correction: The image of the pagoda on the cover of the July 2011 issue of *Minnesota Medicine* should have been credited to Rachel Steckelberg. We regret the error.

WHAT'S ON YOUR MIND?

Send your thoughts to Letters at *Minnesota Medicine,*
1300 Godward Street NE, Suite 2500, Minneapolis, MN 55413
or cpeota@mnmed.org.

WE WANT TO HEAR FROM YOU!

■ **Childhood Obesity**

Perfect Blend

In St. Cloud, physicians, hospitals and clinics, schools, community groups, and even a grocery chain are rallying to fight childhood obesity. | BY KIM KISER

When Jodi Rohe takes her 11-year-old daughter and 7-year-old son grocery shopping, she tells them they can pick out any cereal they want as long as it has a number of 30 or higher.

The number is the product's NuVal score. The scores, which are used in Coborn's grocery stores in St. Cloud where they live, indicate a food's overall nutritional value. The system was designed by David Katz, M.D., M.P.H., of the Yale-Griffin Prevention Research Center and introduced at Coborn's in October 2010. The higher the number, the better the nutritional content. (Post's Shredded Wheat' N Bran has a score of 91, for example, while Quaker's Life cereal has a score of 25.) "My kids can't read a nutritional panel, but they do know there's a difference between a 10 and a 50," Rohe says.

The use of NuVal scores is just one project being promoted by Better Living: Exercise and Nutrition Daily (BLEND), for which Rohe is the coordinator. The goal of BLEND, which is supported by the CentraCare Health Foundation, is to reduce obesity rates among children. "Physicians are frustrated by the issue of childhood obesity," says David Tilstra, M.D., a pediatrician and geneticist with the CentraCare Women and Children's Clinic in St. Cloud, who talked about BLEND at the Institute for Clinical Systems Improvement's annual colloquium in May. "Two minutes of counseling won't change their lifestyle."

Tilstra, who is also medical director for CentraCare Clinic and who helped initiate BLEND, was hearing from his colleagues about the number of overweight children they were seeing in their practices. "They were seeing the same trends as the rest of the country: an increased number of kids with obesity, and younger and younger kids with adult diabetes and other complications," he says.

According to the Centers for Disease Control and Prevention, childhood obesity has more than tripled in the last 30 years. The percentage of obese children ages 6 to 11 years of age increased from 6.5 in 1980 to 19.6 in 2008. The percentage of obese adolescents rose from 5 to 18.1 during the same period. "As medical director, people were coming to me saying we should be looking at doing a project around childhood obesity," he says.

In 2005, Tilstra brought together representatives from area clinics and schools to discuss ways to address the problem. But he knew the medical community couldn't tackle it alone, and neither could the schools.

The following year, he convened a group that included physical therapists, school nurses and dietitians, and representatives from area businesses and nonprofit organizations including the YMCA, Boy Scouts, United Way, and the Central Minnesota Initiative Foundation. They set a goal of reducing childhood obesity by 10 percent by 2016 and decided to focus on changing the environment as well as behaviors. "We really had no idea where we could go or what we could accomplish," Tilstra says.

In 2007, with $309,000 from the CentraCare Health Foundation to fund the initiative for three years, they hired Rohe, who previously had run the Smoke Free Communities coalition in St. Cloud, to work with other groups to promote BLEND's agenda. "We didn't want to compete," she says, "we wanted to build on what was working well."

Going it Together

One of BLEND's first partnerships was with St. Cloud State University on its Earth Day half-marathon, which included a kids' 1K run and expo in addition to the adult race. In the past, the expo had featured crafts and a petting zoo. BLEND wanted to change the focus to health and fitness. So they teamed up with Coborn's to set up an area where kids and their parents could taste healthful foods. "Jicama was one example of something people liked," Rohe says. They also set up stations where kids could try activities such as bouncing on BOSU balls and riding stationary bikes.

Photos courtesy of BLEND

During St. Cloud State University's Earth Day half-marathon, BLEND sponsored activities including a 1K kids' run (left) and an expo where children could taste-test healthful foods (above).

In addition, they used the 2010 half marathon events to kick off the BLEND Fit Kids Club. Kids who complete certain BLEND-endorsed activities can earn awards. The incentives seem to have worked. In 2010, 400 youngsters took part in the Earth Day 1K kids' run. In 2011, nearly 700 completed it.

BLEND also got involved with National Family Dinner Night, an effort to encourage families to share a meal. Working with Coborn's and their suppliers, BLEND offered recipes and coupons to families so they could make a healthful dinner for under $10. Rohe says sales of items such as yogurt went up more than 300 percent in response.

In 2007, Coborn's and BLEND did a 13-week study involving more than 300 children from five St. Cloud-area child-care centers. The children and their parents took part in educational activities around promoting good nutritional choices. Coborn's also delivered samples of healthful foods to the centers so that the children could try them. "All sites we evaluated were seeing slight or significant changes in terms of parents learning about healthy snack options and the importance of daily physical activity," Rohe says.

Since then, Coborn's and BLEND have partnered with Benton County to bring the program to 20 child-care centers. Rohe says they now target not only parents but also child-care providers and facility directors. "It has evolved to where there's talk about creating policies around physical activity and food: What's being served for breakfast? As snacks? What's acceptable for birthday celebrations? How many minutes of physical activity should kids get each day?"

BLEND staff also worked with the Benton County Public Health Department to promote a walk-at-school initiative. The idea is to encourage schools to replace fundraisers that involve selling pizza, candy, cookie dough, and other foods with walk-a-thons. South Junior High School began doing walk-a-thons several years ago. The first one raised $8,000 for the school; this past year's raised more than $33,000.

Rohe and others affiliated with BLEND worked with the staff from South to create a guide for other schools interested in doing a walk-a-thon. This past school year, eight schools from the St. Cloud, Sauk Rapids, and Avon-Albany school districts held walk-a-thons. "It's easier for schools," Rohe says. "And it promotes physical activity while reducing the sale of unhealthy foods."

Doctors Do Their Part

BLEND has also involved physicians. One initiative was getting clinics to measure children's body mass index (BMI). "In the past, we haven't done that," Tilstra says. "We need to make sure people are looking beyond height and weight when they are seeing kids." He says physicians often fail to identify kids with high BMIs—especially in the 5- to 8-year-old group. "It's surprising who is actually overweight," he says. "You can't just eyeball the patient."

In addition, Tilstra says a group of providers led by David Smith, M.D., a pediatrician with St. Cloud Medical Group, created "Rx 5210," which is based on work of the American Academy of Pediatrics and providers in Maine and is a way to help parents remember that kids should have five or more servings of fruit and vegetables a day, limit screen time to two hours a day or less, get at least one hour of physical activity a day, and consume zero calories from sugar-sweetened beverages. "We put this together on a prescription pad to distribute to parents like a prescription," Tilstra says. "It's an easy way to remind them of the basics of a healthy lifestyle."

Tilstra says they have been distributing the prescription pads with the 5210 message for about a year. "We've done small surveys just to see what uptake we had. About 75 percent of the physicians who got them are using them in one way or another," he says.

As for whether BLEND will meet its 2016 goal, Tilstra says it's hard to tell yet. (Last year, the CentraCare Health Foundation did provide $680,000 to fund the project for another three years.) From what his group has seen, however, the rate of childhood obesity isn't shooting up at the rate it was when they started BLEND. "It looks like the curve has somewhat flattened," he says. ■

■ Diabetes by the Numbers

Counting the Cost

$83 billion

the amount U.S. hospitals spent in 2008 caring for people with diabetes

1 in 5

hospitalizations in 2008 that involved a person with diabetes

25% more

the average additional cost of hospital stays for people with diabetes ($10,937 versus $8,746)

60%

the proportion of cost of hospital stays for people with diabetes paid by Medicare (private insurance, 23% and Medicaid, 10%)

Source: Agency for Healthcare Research and Quality data for 2008 (most recent year)

■ Driving and Diabetes

Driving While Low

Should people with diabetes be required to test before they drive? | BY LISA HARDEN

Minneapolis attorney Claire Topp doesn't remember much about the 11 car accidents she had while driving down Interstate 35E one day three-and-a-half years ago. Topp was driving from a friend's house in Eagan, where she had been playing her cello that afternoon, to her home in Eden Prairie when she crossed lanes of traffic and careened between construction barrels and the concrete median, overshot an exit ramp, and backed into a car before coming to a stop in Forest Lake, which is about 45 miles from Eden Prairie.

Topp, who has type 1 diabetes, was just a mile into the drive when she went into a state of reduced consciousness because of low blood sugar. (She experienced none of the usual warning symptoms.) Miraculously, neither Topp nor anyone else was hurt; but the state revoked her driver's license for four months.

Although Topp agreed to test her blood sugar every time she gets behind the wheel in order to get her license back, she doesn't want testing before driving to be mandated through legislation. Yet she shares her story every chance she gets to raise awareness about the importance of testing.

"More people need to be

© Mark Poprocki - Fotolia.com

One study of adults with diabetes found that more than half had had a driving mishap caused by low blood sugar in the past year.

aware of how serious it could be that one time," Topp says. "I didn't have a history of problems with driving until that day, so I didn't test before I got in the car. Either I gave myself too much insulin at lunch or I didn't eat enough and that, combined with the cello practice, caused my blood sugar to drop."

Like Driving Drunk

Elizabeth Seaquist, M.D., Topp's physician and director of the Center for Diabetes Research at the University of Minnesota, says she sees about two or three cases of diabetes-related driving mishaps a year in her practice. Although the state does not keep data on such incidents, state troopers say they encounter drivers who are having problems managing their diabetes "quite regularly," according to Lt. Eric Roeske, public information officer for the Minnesota State Patrol.

A December 2009 University of Virginia Health Sciences Center study of adult drivers with diabetes in Minneapolis, central Virginia, and Boston found more than half of 452 participants reported at least one driving mishap such as zoning out, becoming disoriented, being stopped by police, or having someone else take over driving when their blood sugar was low in the past year. Of those, 35 percent had checked their blood sugar 30 minutes prior to driving and 78 percent had a reading of less than 90 mg/dL and 48 percent had a reading of less than 70 mg/dL.

According to Chris Kodl, M.D., head of endocrinology for HealthPartners Medical Group, driving simulation experiments show that blood sugar levels less than 70 mg/dL can affect the driver's ability to steer and control speed and braking. Blood sugars higher than 270 mg/dL slow cognitive function, cause inability to focus, and impair memory.

"Driving with hypoglycemia is as dangerous as driving drunk," says J. Michael Gonzalez-Campoy, M.D., Ph.D., F.A.C.E., medical director and CEO of the Minnesota Center for Obesity, Metabolism, and Endocrinology in Eagan. "The same holds true for very high glucose levels, especially if they are associated with diabetic ketoacidosis in type 1 diabetes, or hyperosmolar nonketotic state in type 2 diabetes."

The Test Question

Testing glucose levels every time they drive is recommended for people with insulin-dependent diabetes but is not legally required. The American Diabetes Association (ADA) advises people with diabetes to check their blood glucose before getting behind the wheel and at regular intervals, carry a snack, and wait 15 minutes if their glucose level is low and check it again before driving. People with diabetes who experience hypoglycemia unawareness should stop driving, talk with their health care provider, and not resume driving until it's no longer an issue, the ADA advises.

But Chris Schaefer, director of ADA-Minnesota and who has type 1 diabetes and tests every time she gets behind the wheel, notes that the ADA has been reluctant to issue a blanket statement about driving. "Every person has a different response when driving, and different factors can affect blood sugar, so it's important for patients and doctors to talk about driving when they are first diagnosed as well as when they are filling out the state driver's license evaluation form," she says.

The ADA will issue a position statement on driving with

Blood Check Reminders from Your Car

A few years from now, cars may remind drivers to check their blood sugar.

Fridley-based Medtronic and the Ford Motor Company announced last spring that they are working together to develop an application that would connect a car's Sync computer system to Medtronic's continuous glucose monitor and alert drivers with a dashboard message when their blood glucose level gets low.

The application is still years from becoming a reality and may only benefit those individuals who use continuous glucose monitors. Only about one-third of patients with type 1 diabetes currently use such monitors, according to Chris Kodl, M.D., head of endocrinology for HealthPartners Medical Group.—L.H.

Teaching Teens to √B4U DRIVE

As a parent, Troy VanDyke knows it can be hard to get teenagers to do things for their own good. So the mom of a 17-year-old with type 1 diabetes asks her daughter to text her her blood sugar levels prior to driving.

"Texting works because I don't feel like my mom is nagging me, and I know I have to test every time to keep myself and others safe," says Cameron VanDyke.

To address the unique issues teen drivers with diabetes face, the American Diabetes Association (ADA)-Minnesota is working with the Minnesota-based Juvenile Diabetes No Limits Foundation to offer a free day-long program called √B4U DRIVE this fall.

The national program, now in its second year, includes training on managing diabetes by a certified diabetes educator, a behind-the-wheel session on driving safety, and a pep talk by race car driver Scott Kuhne.

"Teenagers aren't always good at testing because they don't want to be different than others," says Chris Schaefer, director of ADA-Minnesota. "We want them to know they need to check every time they get in the car."

The √B4U DRIVE program will be offered in Minneapolis September 24 and 25. For more information, go to www.jdnolimits.org.—L.H.

diabetes later this year.

Minnesota law requires people who are diagnosed with insulin-treated diabetes or who have an episode where they lose consciousness or voluntary control to be evaluated by a physician to determine if they are medically qualified to drive. Patients should be re-evaluated for a period determined by their physician as long as they are episode-free.

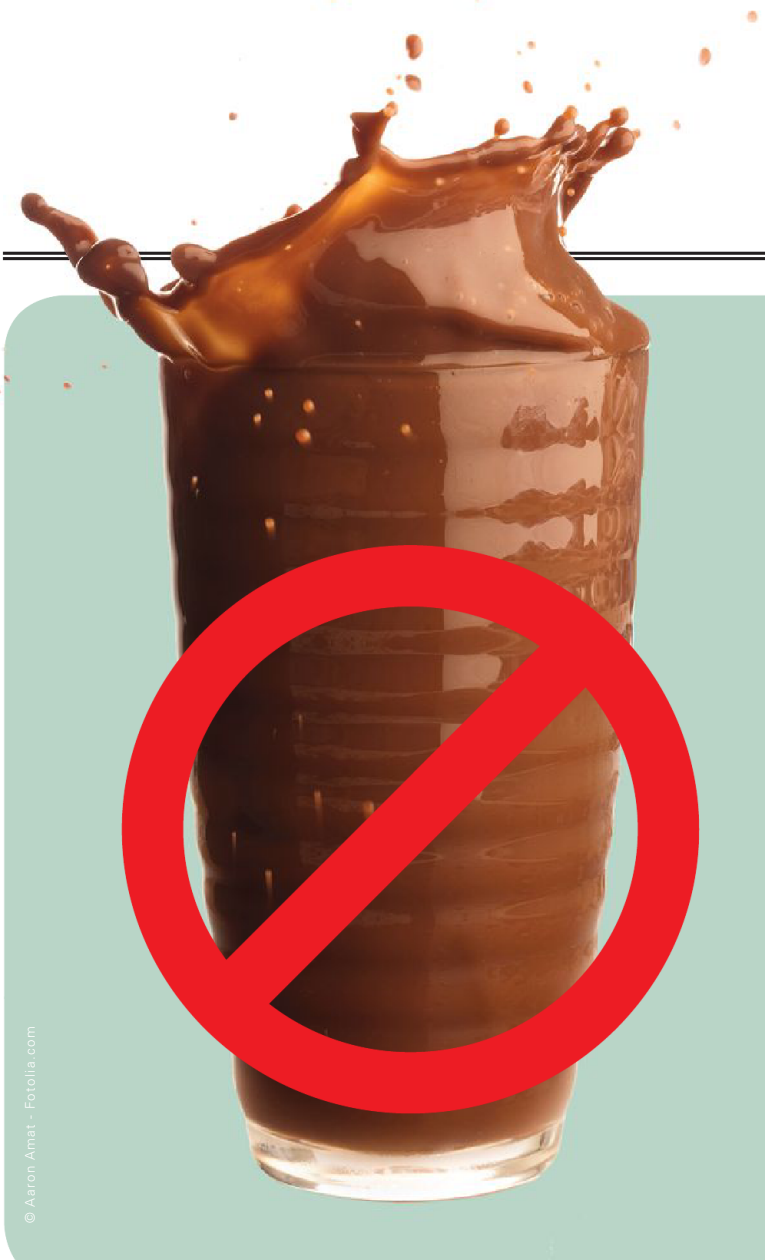
According to Joan Kopcinski, a driver's services director for the Minnesota Department of Public Safety, the state relies on the physicians' evaluations when it comes to issuing driver's licenses. "When you take away someone's driving privilege, it has a significant impact on an individual's life, so we evaluate very carefully," she says, adding that they receive about 35 medical forms a day related to diabetes. "But in the interest of public safety, we want to make sure they are getting medical treatment."

Talking with Patients

Richard Bergenstal, M.D., director of Park Nicollet's International Diabetes Center, only recommends testing every time before driving to patients who tend to have frequent low blood-sugar levels or those who do not feel their low blood-sugar levels until they become dangerously low. But when any patient comes in with the Minnesota driving evaluation form, he discusses the dangers of low blood sugar and reminds them to be safe before driving.

Steven Smith, M.D., medical director of patient education at Mayo Clinic, recommends testing every time to anyone taking insulin. In addition, he stresses to them that because reactions vary among individuals, each person needs to recognize his or her own symptoms and know that hypoglycemia may not present with the typical sweating, dizziness, and heart palpitations. "Everyone has their own set of symptoms, and patients can even stop having symptoms for a while and then not recognize them," he says. "That's why I tell patients, Training yourself to test every time you get behind the wheel is good practice. Just like you don't get behind the wheel after drinking, you don't get behind the wheel before testing your blood sugar."

The University of Minnesota's Elizabeth Seaquist says ultimately it's the patient's responsibility to ensure their own safety. "But it is my obligation as a physician to make sure they are aware of what they need to think about." ■



■ **School Lunch**

Milk Move

Chocolate milk won't be available in the lunch line in Minneapolis public schools this fall. In a move reflecting the growing concern about obesity among children, the school system banned chocolate milk from its offerings. The lunchroom favorite joined French fries on a growing list of foods the district has deemed unhealthy—a cup of chocolate milk contains more sugar (about three teaspoons more) than plain milk.

Not all health experts would recommend such a ban, however. In an article on childhood nutrition on its website, the American Academy of Pediatrics articulates its concern about kids' inadequate calcium intake: "Encouraging kids to have milk, milk products, or calcium-rich alternatives, even if it means they have to add chocolate syrup to their milk to make it more palatable, should help them get more calcium."

Sources: *Star Tribune* (May 24, 2011) and American Academy of Pediatrics (www.healthychildren.org/English/healthy-living/nutrition/pages/Childhood-Nutrition.aspx)

■ **Health IT**

A Beacon in the State

With the aid of a federal grant, southeastern Minnesota communities are connecting to improve diabetes and asthma care. | BY CARMEN PEOTA

Southeastern Minnesota is one of 17 regions in the nation now known as a Beacon community. Last May, a coalition that includes Olmsted Medical Center, Austin Medical Center, Mayo Clinic, Mayo Clinic Health System, and Winona Health as well as area schools, public health departments, and other organizations was awarded a $12.3 million grant from the Office of the National Coordinator for Health Information Technology (IT) to demonstrate how the IT infrastructure already in place in the region could improve health care. Nearly all primary care providers in the 11-county area have electronic health record systems (EHRs), and Winona County has years of experience with electronic exchange of information among health care and community partners. With the new funding, the southeastern Minnesota community will focus on using technology to improve the care of patients with two chronic conditions: asthma and diabetes.

Victor Montori, M.D., director of health care delivery research programs at Mayo Clinic, says the Beacon designation and funding is acknowledgment that Minnesota is already a national leader in health IT. He says the additional support makes national leadership in treatment of asthma and diabetes a possibility as well. "That Minnesota could lead the country in optimal health care delivery for a condition like diabetes is within grasp," he says. "Here is the federal government making an investment in making that happen."

Patient-Centered Diabetes Care

On the diabetes side are two projects aimed at incorporating the patient's perspective into their care.

Montori is leading a group that is trying to use technology to enable patients with type 2 diabetes to participate in decision making about their treatment. Several years ago, he and a team at Mayo created cards that physicians can use with patients to help them sort through their preferences and priorities with regard to taking various medications. "The card format is about discussing what issue is most important to you," Montori says, noting that the issues they cover are the treatment's effect on weight, its cost, how the medication is taken, whether and how often it requires a person to check his or her blood sugar level, and its effect on hemoglobin A1c values.

Through the Beacon project, Montori's group is trying to improve on the approach. Their plan is to use information available in the EHR to tailor the options presented to the patient so that only offered the most appropriate treatment choices are offered. In addition, information about the encounter, patient preferences, and outcomes will be recorded in the EHR to expedite future decision-making.

Jeff Sloan, Ph.D., a professor of oncology and biostatistics at Mayo Medical School, is leading a group that is working on the other diabetes-related project: a web-based survey to elicit diabetes patients' concerns related to their quality of life. Sloan's group is also developing algorithms to help clinicians know what to do about various issues that come up.

Sloan says the focus of a clinic visit for a patient with diabetes traditionally has been his or her lab values. If there's time left, the physician might ask about other indicators of the patient's well-being such as their mood, energy level, or stress level. "It's not that these things are not discussed in the clinical setting," Sloan says, "but it's been hit and miss."

Sloan, who has done similar work with oncology patients,

> "That Minnesota could lead the country in optimal health care delivery for a condition like diabetes is within grasp."
>
> —Victor Montori, M.D.

says the survey covers 10 domains. "We're not trying to find everything we might deal with in a clinic visit," he says. "We tried to target a small number of things. The idea is that the patient would take the survey at each encounter with a health care provider, whether in the clinic or another setting. Their scores would be accessible to all members of the Beacon community including social workers, home health nurses, and other professionals.

Montori says he has two hopes for the Beacon efforts: that the patient input ends up in the EHR and is used by clinicians and that patients themselves are rewarded for their efforts to participate in their health care. He hopes those rewards might take the form of experiencing care that is more patient-centered and fits better with people's goals and circumstances.

Sharing Information about Asthma Patients

Family physician Barbara Yawn, M.D., is part of the group that is focusing on improving communication around asthma. If their efforts come to fruition, a school nurse will be able to go to a computer, pull up a student's asthma action plan, administer the appropriate treatment, then type in a note that will find its way into the child's electronic medical record as well as to his or her parents' email.

Yawn, an expert in childhood asthma, says it's important for a physician to have information about what's really happening in their patients' lives. But she says they frequently don't learn what happens on a daily basis—what things might trigger problems, how often they occur, or how severe they are. "Patients are in our offices 1/100,000th of their lives," she says. "Frequently, when they're in our office, they're doing fine."

Yawn's group hopes to have the beginnings of a system in place by September when school starts. "We're working with schools, students, parents, and IT people. We're doing focus groups with students and parents and school people because they may have another dream that we haven't thought of yet that we ought to include. … We have our dreams, but we need to make sure that we're really making a system that's useful to everybody." ■

Photo by Steve Wewerka

David C. Thorson, M.D.
Chair, Board of Trustees

From Doubter to Believer

I know it's not very Minnesotan to highlight one's achievements, but I am simply amazed by the progress some of the clinics in our group—Family HealthServices Minnesota—have made to improve their vascular care scores, one of the measures used to rate clinics in the state. Seven years ago, I wouldn't have thought it was possible.

In July, MN Community Measurement released statewide results for optimal vascular care. Our White Bear Lake Clinic achieved optimal care for 70 percent of 125 of its patients with heart or vascular disease. Optimal care includes controlling patients' blood pressure and cholesterol, getting them to stop smoking, and having those who need it take an aspirin a day. Overall, the percentage of patients who received optimal vascular care in the state jumped from 37.1 percent in 2008-2009 to 39.7 percent last year. That means about 3,500 additional Minnesotans with heart disease or vascular disease are receiving better care than in the past.

It is heartening to see changes like these, and it makes me feel proud that the MMA, as one of the founders of MN Community Measurement, has led in the move to improve the quality of care in Minnesota.

As a practitioner, I know how much work it is for clinics to move the needle on these measures. So how did we do it? Our strategy is to have doctors work with each patient to create an action plan. Together, they set goals for losing weight, improving eating habits, and using medications to lower blood pressure and improve cholesterol levels. They also discuss aspirin and tobacco use.

We find that this up-front work is the key to our success. When patients share in decisions about their health care, they are more likely to achieve the goals they set. Also critical to engaging patients is convincing them that these changes will make a difference in their quality of life and decrease their risk of having a stroke or heart attack. Another thing we do is give the patient a report card with letter grades based on how well they've met the goals in their action plan. This allows patients to measure their progress in a way that is easy to understand. I understand why some even proudly display their report cards on their refrigerator.

To further support our patients, we've hired a case manager who follows up with them by phone after their office visit. In addition, we've implemented an electronic medical record and have a patient registry to help us keep track of each patient's progress. We've also tried different tactics to ensure the examining doctor always knows when a patient's blood pressure is out of control. We tried leaving the blood pressure cuff on the patient and putting a sticky note on the exam room door. Eventually, we came up with a color code in the electronic medical record to indicate that a blood pressure was out of range.

As I said, I am amazed at the success we've been able to achieve. I remember going to a MN Community Measurement meeting seven years ago and thinking the combined diabetes measure was a bad idea. I believed a 30 percent rate of optimal care using that measure was probably the maximum that could be achieved. But now my personal case load is at 60 percent. I never thought I could get there.

The experience of going from doubter to believer has convinced me that the MMA needs to continue being a champion of quality improvement. Just like patients need encouragement from their doctor to try one more time to eat right and exercise, we as physicians also need encouragement from our colleagues to help us believe we really can make a difference in these areas.

I am convinced that the MMA needs to continue being a champion of quality improvement.

© Henryk Sadura - Fotolia.com

Budget Includes Reimbursement Cuts, Provider Tax Repeal

After a government shutdown that lasted more than two weeks, lawmakers and Gov. Mark Dayton finally agreed to a budget solution in late July that included mixed news for Minnesota physicians.

On the positive side, the final Health and Human Services (HHS) budget bill included a provision repealing the 2 percent provider tax by 2019. A gradual phase-out would begin in 2014, the year the federal government will start providing subsidies for low-income individuals such as those enrolled in MinnesotaCare to purchase health insurance in the private market. Currently, MinnesotaCare is partially funded by the provider tax.

The MMA has long pushed for elimination of the tax. "Minnesota physicians have fought hard for the repeal of the provider tax, and we are relieved that lawmakers are finally acknowledging that a selective tax on the sick is the wrong way to fund health care programs," says MMA President Patricia Lindholm, M.D.

The budget deal would also keep in place the early expansion of Medicaid that the governor approved in March, allowing adults without children to receive Medical Assistance, the state's version of Medicaid. It does not include significant eligibility or benefit cuts.

However, the budget does cut Medical Assistance and MinnesotaCare fee-for-service payment rates for physicians and other providers of outpatient services by 3 percent. It also cuts payments to health plans that administer Medical Assistance and MinnesotaCare benefits on behalf of the state by 10 to 13 percent to reflect savings from efforts to decrease hospital admissions and contract negotiations with providers.

↳

Controversial Items Left Out of the Budget

- Changes to the state's newborn screening program or limitations on collection of that data
- Limits on the use of vaccines that include "fetal DNA"
- A proposal to reduce reimbursements to "high-cost providers"
- A proposal to create pregnancy health care homes and mental health care homes
- Limits on stem-cell research or abortion-related services

"We expected cuts, and it appears lawmakers attempted to minimize them," Lindholm says. "But the bottom line is that Medical Assistance is already underfunded and additional cuts will cause financial hardships for some clinics and result in either reduced access or cost shifting."

Budget Details

Overall, the new budget authorizes $35.4 billion in spending over the next two years including $12.4 billion for health and human services, an 11.6 percent increase over what was spent in the previous biennium. However, that figure is below the amount projected for costs during that period.

The HHS budget includes $11.3 billion in general fund money, which is nearly $500 million more than the Legislature proposed and $180 million less than the governor asked for.

It also includes a proposal to privatize MinnesotaCare for about 8,000 adults without children who earn between 200 and 250 percent of federal poverty guidelines. Enrollees would receive a subsidy to purchase private health insurance. The MMA is not opposed to such an approach, but is concerned that the money the state would provide may not be enough to allow those Minnesotans to afford adequate coverage.

Budget Pros

- Approximately $500 million more for health and human services programs than was approved by the House and Senate in May
- Continues the early enrollment of adults without children in Medical Assistance, allowing the continued elimination of the General Assistance Medical Care program and the ability to capture federal funds
- Does not completely cut off anyone from Medical Assistance or MinnesotaCare
- Allows the state to receive federal money from the Affordable Care Act
- Begins phasing out the 2 percent provider tax and repeals it altogether in 2019
- Provides $15 million to the State Health Improvement Program for fiscal year 2012

Budget Cons

- Cuts general fund spending in health and human services areas by nearly $1 billion
- Cuts physician and other outpatient provider reimbursements for state health insurance programs by 3 percent across the board
- Reduces payments to state health plans by 10 to 13 percent (those cuts will likely be passed on to physicians and other providers)
- Implements a voucher program for MinnesotaCare that may not allow enrollees to afford adequate coverage for outpatient services
- Cuts the Medical Education and Research Cost program by 50 percent in 2012 and 25 percent in 2013

MMA Argued for Tobacco Tax Increase

During the government shutdown, the MMA urged lawmakers to increase the fee on tobacco products in order to raise revenue to prevent cuts to state health care programs, help close the state's budget gap, and reduce smoking rates in Minnesota.

The MMA sent a letter to Gov. Mark Dayton and legislative leaders July 1 urging them to come to a budget agreement that included a $1.50 per pack tax increase on cigarettes. "Not only would this increase raise nearly $400 million in revenue for the biennium, it would directly lead to lower health care costs by reducing the number of new smokers," MMA President Patricia Lindholm, M.D., said in the letter. "A tobacco tax increase is not only smart tax policy, but it is smart health policy."

The governor had previously said he preferred not to increase the tobacco fee, since it is a regressive form of raising revenue. However, on July 6, during final budget negotiations, Dayton offered a $1 per pack fee increase to GOP leaders hoping they would find it more palatable than an income tax increase. Increasing the tobacco fee is supported by nearly three in five Minnesotans, according to a poll released in June by the Raise It For Health Coalition. The MMA also sent an Action Alert to members asking them to urge their lawmakers to support the fee increase. GOP lawmakers rejected Dayton's offer to increase the fee as part of a budget solution the same day he proposed it.

MDH Warns of Additives in Temporary Tattoos

The Minnesota Department of Health issued a warning in June about use of henna products that contain additives to create "temporary tattoos."

Materials that are sometimes added to henna can cause allergic reactions when applied to the skin and can cause some people to develop lasting chemical sensitivities, according to health officials. One of the most commonly used additives—and one that is of particular concern—is a darkening agent called para-phenylenediamine. The Department of Health issued the warning after reports of allergic skin reactions in a group of 35 Twin Cities eighth-graders who had been given temporary tattoos using a dark-colored material. About half of the children had skin reactions, which included blistering and weeping lesions. In most cases, the lesions appeared within 20 days of getting the tattoo, and half occurred within seven days.

Medicare Physician Fee Schedule Includes 30 Percent Cut

The Centers for Medicare and Medicaid Services (CMS) has issued its proposed changes to the 2012 Medicare Physician Fee Schedule, including a plan to cut Medicare payments to physicians by 30 percent.

The agency is required to issue the fee schedule based on current payment rules. With the Sustainable Growth Rate (SGR) formula now in effect, physicians will see a nearly 30 percent decrease in reimbursement for services beginning in 2012.

CMS administrator Donald Berwick, M.D., expressed concern about the cut in physician payments in a statement: "We need a permanent SGR fix to solve this problem once and for all," he said. "That's why the president's budget and his fiscal framework call for averting these cuts, and we are determined to pass and implement a permanent and sustainable fix."

Although similar cuts have been averted almost every year by last-minute Congressional action, CMS cannot assume such a reprieve will occur and must issue its proposed fee schedule as if the payment cut were going to go into effect.

The proposed rule, issued July 1, also includes a significant expansion of the agency's misvalued code initiative, which CMS describes as an effort to ensure that Medicare is paying accurately for physician services.

It also includes adjustments for costs based on geographic area. In order to improve geographic variation adjustments under Medicare, the agency is replacing some of its data sources and making other changes based on public comments from prior years. The Patient Protection and Affordable Care Act required CMS and the Institute of Medicine (IOM) to study geographic variation, and the IOM issued its first of three reports on the subject on June 1.

The proposed rule also would begin to establish a new "value-based modifier" to reward doctors for providing higher quality, more efficient care. The modifier would debut in 2015 and be used only for certain physicians and physician groups, but it would be extended to all physicians by 2017. This year's rule includes proposed quality and cost measures that would be included in the modifier.

The MMA supported the creation of a value-based modifier as part of national health care reform. The assumption is that such a modifier will benefit Minnesota physicians, as they provide high-quality, low-cost care compared with national averages.

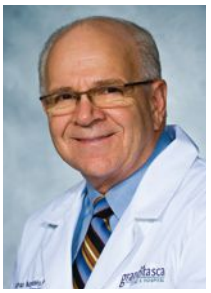
CMS will accept comments on the proposed rule until August 30 and will issue a final rule by November 1.

MMA *in Action*

Some of the recent ways MMA staff and members have worked for physicians in Minnesota.

■ Dave Renner, MMA director of state and federal legislation, went on a northern Minnesota road tour. On July 12, he participated in a District Dialogue with Rep. Carolyn McElfatrick (R-Deer River) hosted by the Grand Itasca Clinic and Hospital in Grand Rapids. A dozen physicians and hospital staff discussed the implications of health care reform as well as the new leadership at the Capitol. A freshman legislator, McElfatrick serves on the House Health and Human Services Finance Committee and the Health and Human Services Reform Committee. Nathan Noznesky, M.D., an MMA member and a surgeon at Grand Itasca Clinic and Hospital, attended the meeting and questioned McElfatrick about health care cuts and whether lawmakers intended to support Minnesota's medical infrastructure. Later that evening, Renner presented a legislative update to members of the Range Medical Society at the Timberlake Lodge in Grand Rapids. The next day, he met with physicians and staff at Sanford Health Bemidji and gave a similar update.

Dave Renner



Nathan Noznesky, M.D.

■ The MMA Foundation (MMAF) awarded scholarships to Crystal Bockoven from Milaca and Hannah Wangberg from Bemidji, both of whom will start medical school at the University of Minnesota Duluth in September. Eight other medical students are currently receiving MMAF scholarships. The scholarships are funded through physician and donor contributions. Learn more and donate at mmafoundation.org.

■ Eric Dick, MMA manager of state legislative affairs, joined the Twin Cities Medical Society's Senior Physicians Association for its monthly meeting on July 12. Dick provided the group of nearly 40 retired physicians with an update on the 2011 legislative session and discussed the government shutdown and its effect on physicians, hospitals, and the state's health care system.

Eric Dick

Complete Your Census

Each year, the MMA conducts a census of Minnesota physicians and their clinics. All physicians should have received a request for updated information by email or U.S. mail.

The MMA uses the information to describe the state of medicine to policymakers and to maintain the MMA's online Physician Finder—a directory of physicians in the state that gets about 1 million hits a year.

To ensure your information is accurate, please update it using either the paper or online form. MMA members can complete the form online at mnmed.org/census. Nonmembers, go to mnmed.org/censusnonmembers.

MMA Calls for Independent Payment Advisory Board Repeal

The MMA has joined other medical groups in calling for the repeal of a provision in the federal Patient Protection and Affordable Care Act that creates an Independent Payment Advisory Board (IPAB).

The 15-member commission would be tasked with cutting costs when Medicare's per capita growth rate exceeds a specified target. A U.S. House budget committee held hearings in July about the proposed board.

The MMA, the AMA, and other medical associations oppose the creation of the IPAB because it would be prohibited from cutting hospital payments until 2020 and from instituting other cost-cutting options such as rationing health care, raising premiums, or shifting costs to beneficiaries. This framework would put physicians and pharmaceutical companies at risk for bearing a disproportionate burden of any IPAB-initiated cuts.

When the proposal for the advisory board first surfaced, some physicians in Minnesota were open to the concept, says Dave Renner, MMA director of state and federal legislation. "Some of our physician members thought maybe there's some merit to this idea of depoliticizing decisions that are made on how we fund Medicare," Renner says. But that changed when doctors learned they did not get the same protections as hospitals or other organizations. That was particularly alarming for physicians, Renner says, because they already face annual payment cuts generated by the sustainable growth rate formula. A 30 percent cut is scheduled for 2012.

For now, the future of the IPAB appears to be in limbo. The Obama administration has yet to appoint members, who would ultimately need to be confirmed by the Senate.

Legislation that would repeal the IPAB provision was introduced in both the House and Senate earlier this year.

sweet debate

Do artificial sweeteners contribute to rather than combat **obesity**?

By Trout Lowen

Drink diet soda. Switch to low-fat or no-fat products. Cut down on or eliminate sugar. People who are overweight, have diabetes, or have metabolic syndrome hear advice like this all the time. But is it the right advice?

Some say it isn't. Results from several large-scale population studies suggest that regular consumption of artificial sweeteners such as aspartame and sucralose, particularly in diet soda, may actually contribute to rather than combat weight gain and type 2 diabetes.

No study so far has identified a direct causal link between artificial sweeteners and weight gain or diabetes, and proving one is difficult because there are so many confounding factors. But the positive association raises interesting questions: Do artificial sweeteners, most of which are hundreds of times sweeter than sugar, increase our desire for more and sweeter foods? Do diet soda drinkers overestimate the number of calories they're saving and then eat more? Do artificial sweeteners somehow disrupt or alter the body's processes in ways we don't yet understand? Or are those who are prone to weight gain or who have a family history of diabetes more likely than others to consume diet soda?

Of Mice and Man

In late June, epidemiologists and nutritional immunologists from the University of Texas Health Science Center at San Antonio presented the results

of two new studies at the annual meeting of the American Diabetes Association (ADA). One study found that artificially sweetened soft drink consumption was associated with increased waist circumference in elderly people. The second found aspartame raised glucose levels in diabetes-prone mice.

The human study tracked diet soda consumption and waist measurement in 474 participants in the San Antonio Longitudinal Study of Aging at enrollment and at three follow-up exams over 10 years. As a group, participants who consumed artificially sweetened soft drinks saw a 178 percent greater increase in waist circumference compared with those who did not, and those who consumed two or more beverages containing artificial sweeteners per day saw a 500 percent (or almost three times greater) increase. "That's quite a statistically significant trend," says Sharon P. Fowler, M.P.H., co-author of the study.

That study reinforced the results of Fowler and colleagues' earlier analysis of San Antonio Heart Study data published in *Epidemiology* in 2008 that looked at the relationship between consumption of beverages containing artificial sweeteners and weight gain. That analysis showed that subjects who were 25 to 64 years old at baseline who consumed more than 21 artificially sweetened beverages per week almost doubled their risk for obesity over the next seven to eight years, compared with nonconsumers, and that their adjusted body mass indices increased 47 percent more than those of nonusers.

Both of the San Antonio studies support the findings of an earlier analysis of data from the Baltimore Longitudinal Study of Aging presented at the annual meeting of the Endocrine Society in 2009. That analysis found artificial sweetener consumers were younger and heavier, and had a higher body mass index than nonconsumers, although the number of calories and the amount of fat, carbohydrates, and protein consumed was the same in both groups. Three other studies published in *Circulation* and *Obesity* in 2007 and 2008 also showed an association between consumption of artificially sweetened soda and the development of obesity and metabolic syndrome.

©istockphoto/Valentyn Volkov

"I feel fairly strongly this is not a causal relationship. It's about behavior patterns."

—Jennifer Nettleton, Ph.D.

In the mouse study presented at the ADA meeting, 40 diabetes-prone mice were divided into two groups. Both were fed a high-fat diet. Half of the mice were also fed high doses of aspartame. After three months, the mice that were given aspartame weighed the same or slightly less than the control mice, had better lipid and triglyceride levels, and their nonesterified fatty acids were much lower, Fowler says. But their fasting glucose values were 37 percent higher. In addition, 69 percent of the mice fed aspartame became hyperglycemic compared with 31 percent of the control group.

Fowler says having both lab and epidemiological studies strengthens the findings of each. "Having them together is so much more powerful to me than either separately." But she admits the results are preliminary. "How relevant these results would be for humans of different ages and diabetes risk levels is something that must be studied further."

Cause or Coincidence?

Fowler thinks there's compelling research suggesting a physiological explanation for why consuming artificial sweeteners might cause people to gain weight. As an example, she points to the work of Barbara Corkey, Ph.D., the most recent winner of the ADA's Banting Medal for Scientific Achievement, who was part of a team that looked at the effects of artifical sweeteners on the sweet taste receptor on the surface of pancreatic beta cells. Corkey and her colleagues found that in rats consumption of sucralose, aspartame, and saccharin increased insulin secretion.

But Jennifer Nettleton, Ph.D., a nutritional epidemiologist and faculty member at the University of Texas at Houston, thinks the data associating artificial sweeteners with weight gain says more about human behavior than human chemistry. "I feel fairly strongly this is not a causal relationship. It's about behavior patterns," says Nettleton, who did her doctoral and postdoctoral research at the University of Minnesota.

Nettleton's views may surprise some,


©istockphoto/migin

As a group, artificial sweeteners are much sweeter than sugar.

as she was the lead author on a paper published in *Diabetes Care* in 2009 that raised concern about artificial sweeteners and weight gain. The researchers examined data from the Multi-Ethnic Study of Atherosclerosis pertaining to diet soda consumption and the risk of metabolic syndrome and type 2 diabetes among 6,814 Caucasian, African-American, Hispanic, and Chinese adults (between the ages of 45 and 84 years) over six years. Nettleton and her colleagues found that people who consumed diet soda at least daily had a 36 percent greater relative risk of incident metabolic syndrome and a 67 percent greater relative risk of incident type 2 diabetes as compared with those who consumed no diet soda, after adjusting for demographic characteristics and energy intake. Those who consumed more than one daily serving of diet soda also were more likely to have a greater waistline circumference or higher fasting glucose levels than those who did not.

But in analyzing the data, Nettleton says she and the other researchers tried to rule out all of the other factors that could be responsible for the results. "We couldn't rule any of them out," she says. It isn't possible to conclude anything about the health effects of diet soda consumption from that research, Nettleton argues.

For that reason, she believes it is behavior, rather than diet soda consumption, that is the real culprit when it comes to weight gain. "When we focus on something like this, it really misses the bigger picture," she says, "which is people are overweight, people don't exercise, and people also eat an otherwise horrible diet.

"I just feel very strongly that it's just part of a larger behavior pattern," Nettleton adds. "But I do think, as it says in the paper, it is important to bring this up because a lot of studies have seen this association, and we need to figure out what is driving it. … If there is truly something, a biologically plausible mechanism by which those compounds increase your risk of diabetes or metabolic syndrome, or cause any kind of metabolic abnormality, we need to know about it."

Other Explanations

Isolating that mechanism, if there is one, will be difficult. A number of artificial sweeteners are on the market, and new ones are being developed all the time. Each has its own chemical signature and action when consumed. For example, saccharin, the first artificial sweetener used commercially, is not digested or absorbed into the body. Aspartame, one of the most widely used sweeteners under the trade names NutraSweet and Equal, is digested, and individuals who have the rare hereditary condition phenylketonuria are sensitive to phenylalanine, one of two amino acids that make up aspartame, must restrict their intake of aspartame. Sucralose, or Splenda, which is derived from sucrose, or sugar that has been chemically altered, is not digested. But a paper published in 2008 demonstrated that, in animal studies, it alters microflora in the gut.

One limitation of population-based studies is that they can't parse out which artificial sweetener participants are consuming, and most participants are likely ingesting several of them. "That to me makes it less likely that [artificial sweeteners] are the signal," Nettleton says. "It's a messy exposure. It's not just one artificial sweetener."

But could artificial sweeteners be changing human chemistry? Some researchers think they may increase consumers' desire for ever-sweeter tastes. As a group, artificial sweeteners are much sweeter than sugar—saccharine is 300 times sweeter than sugar, aspartame 180 times sweeter, and sucralose 600 times sweeter. Some experiments have shown that sweet taste, whether it's derived from sugar or artificial sweeteners, increases appetite. One study found drinking aspartame-sweetened water increased appetite in normal-weight adult males, but swallowing an aspartame capsule did not. In another study, aspartame, saccharine, and acesulfame potassium were all associated with an increased motivation to eat more.

Other research suggests that artificial sweeteners do not provide the same food reward that natural sweeteners do, and that may contribute to increased appetite and, as a result, weight gain.

There are also other variants on theories about behavior that may explain the study results. People may overestimate the calorie-saving benefits of artificially sweetened foods and eat more as a result. Study subjects may over-report their consumption of artificially sweetened soda when they are really drinking sugar-sweetened soda. Those mostly likely to drink diet soda may already have difficulty maintaining weight or have a family history of obesity or diabetes.

What about Sugar?

Although there is concern that artificial sweeteners may contribute to obesity and the diseases associated with it, there's clear evidence that sugar, particularly as it's consumed in sweetened beverages, is a major contributor to weight gain and the development of metabolic syndrome and type 2 diabetes. A recent meta-analysis of studies involving nearly 20,000 people in four countries published in *Diabetes Care* in 2010 found sugar consumption was associated with development of both metabolic syndrome and type 2 diabetes. In a lecture made popular on YouTube, Robert H. Lustig, M.D., professor of pediatrics in the division of endocrinology at the University of California, makes the case that sugar consumption is the main cause of obesity and diabetes and that it ought to be considered a toxin. Yet multiple studies

have shown consumption of sugar-sweetened beverages including soft drinks, fruit drinks, ice teas, and energy and vitamin water drinks is rising in the United States and around the world. Sugar-sweetened beverages are now the primary source of added sugars in this country.

Advice for Physicians

Whether consumption of sugar or artificial sweeteners is more likely to contribute to obesity and its byproducts—metabolic syndrome and diabetes—misses the bigger picture, according to Nettleton. She says the real issue in terms of preventing weight gain and development of metabolic syndrome and diabetes is simply overconsumption. From a public health perspective, preventing weight gain is more important than any single component of diet. "The elephant in the room is you're 250 pounds and you should weigh 160 pounds," she says. "So let's not worry about how many grams of sugar are in that candy bar. Let's worry about why you're eating a candy bar."

She says physicians would be better off counseling patients about diet, exercise, and maintaining a healthy weight, and connecting them with someone who can help them develop an eating plan that works for them, rather than discussing consumption of artificial sweeteners. "We try to make the message too complicated. Like 'you need to eat more of this and less of that,' and really it's just 'eat less and do more.'" **MM**

Trout Lowen is a Minneapolis freelance writer.

sweet choices

artificial sweeteners

First developed in the late 19th century, artificial sweeteners appear under a variety of trade names. The Food and Drug Administration (FDA) has approved five for general consumption:

- SACCHARIN (Sweet'N Low, Necta Sweet, and others) is the original artificial sweetener. It was discovered in 1879 by a chemist working on coal tar derivatives. It is 300 times sweeter than sugar, has no calories, and is not digested or absorbed by the body.
- ASPARTAME (Equal, NutraSweet, others) is made up of the amino acids phenylalanine and aspartate, plus methanol. It has been used in foods since 1981 and in diet sodas and other beverages since 1983. Unlike most other artificial sweeteners, it can be metabolized; but it has effectively no caloric impact because it is used in such small quantities. It is 180 times sweeter than sugar.
- ACESULFAME POTASSIUM OR ACESULFAME K (Sunett, Sweet One) was approved by the FDA in 1988. It is used in cooking and baking because it retains its sweetness when heated. It is 200 times sweeter than sugar and is not metabolized by the body.
- SUCRALOSE (Splenda) is a chlorinated hydrocarbon derived from sugar that is chemically altered by substituting chlorine for three of its hydroxyl groups. It was first approved by the FDA for limited use in 1999 and for general use in 2008. It's 600 times sweeter than sugar and has no caloric impact.
- NEOTAME is the most potent sweetener on the market. It is 7,000 to 13,000 times sweeter than sugar. Foodfacts.com lists neotame as an ingredient in 23 products including Tang breakfast drink. (In contrast, aspartame is listed in 1,396 products, sucralose in 2,015, acesulfame potassium in 1,752, and saccharin in 64.)

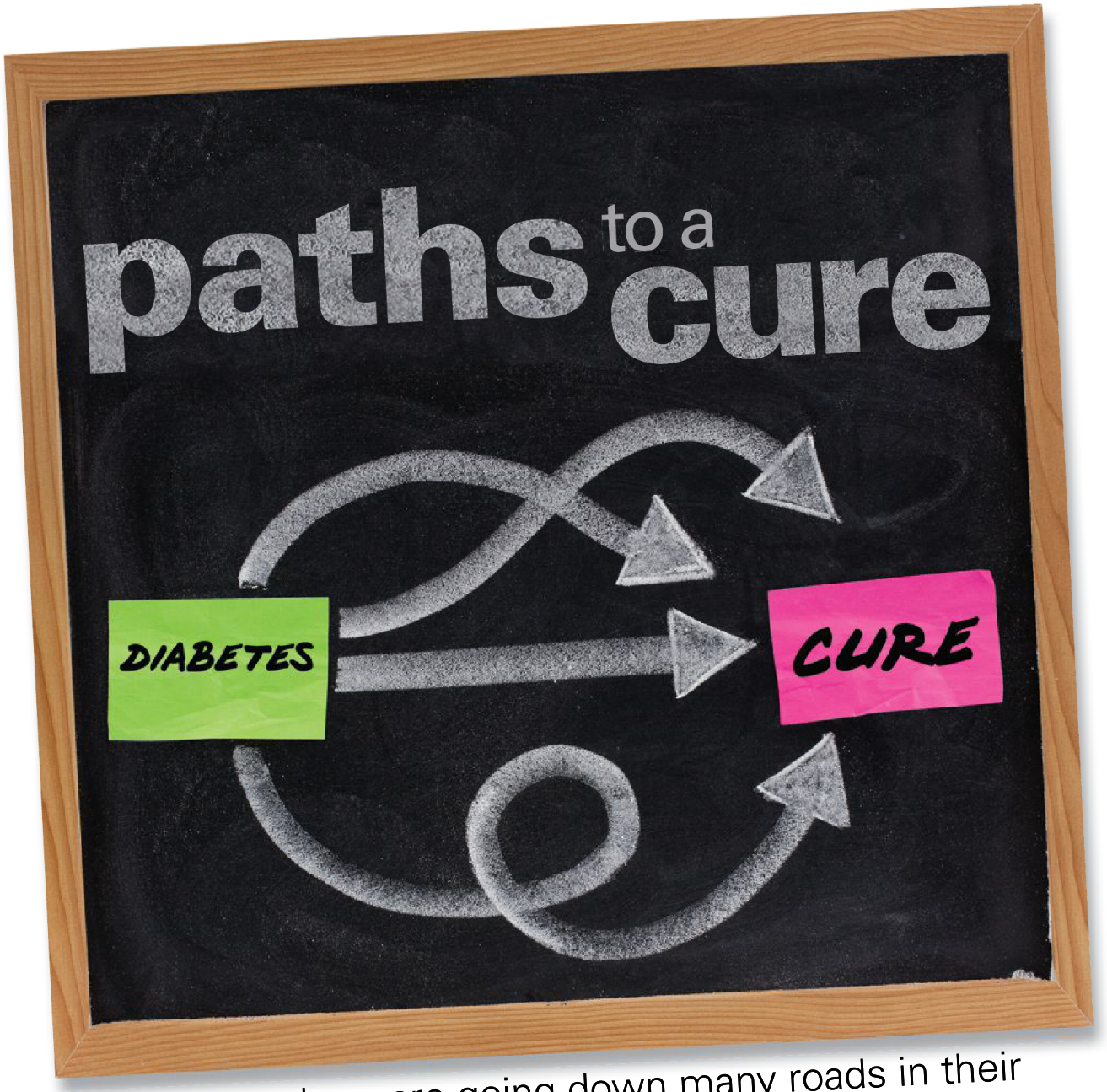
sugar alcohols

Sugar alcohols are used in a broad range of products including ice cream, chocolate, candy, cookies, desserts, chewing gum, toothpaste, and mouthwash. They occur naturally in certain fruits and vegetables and can be manufactured. Unlike artificial sweeteners, sugar alcohols are not sweeter than sugar; in fact, some are less sweet than sugar. Sugar alcohols usually replace sugar in equal measure. They contain about two calories per gram, less than regular sugar, which has four calories per gram. As with artificial sweeteners, the FDA regulates the use of sugar alcohols. Approved sugar alcohols include the following:

- Erythritol
- Hydrogenated starch hydrolysates
- Isomalt
- Lactitol
- Maltitol
- Mannitol
- Sorbitol
- Xylitol

"natural" options

- STEVIA, a South American plant, is one of the newest no-calorie sweeteners to enter the marketplace. The FDA has not permitted the use of whole-leaf stevia or crude stevia as a food additive, although it has approved highly refined forms of stevia (Truvia, Pur Via) for use in food products.
- JUST LIKE SUGAR. The marketers of this product claim it is the safest new sweetener on the market. Its promoters say it's an all-natural product that contains calcium, vitamin C, chicory root, and orange peel and has no calories.—T.L.



Researchers are going down many roads in their quest to cure diabetes.

BY JEANNE METTNER

Each day, patients with diabetes painstakingly choreograph decisions about issues that people without diabetes take for granted—what and when to eat, when and how much to exercise, how to ensure that hypoglycemia doesn't debilitate them, especially when they sleep. Type 1 diabetes, in particular, demands a vigilance that tries even the most conscientious, compliant patient. The body's immune system turns on its own tissues, destroying the precious beta cells housed within pancreatic islets that the body needs to produce life-saving insulin. The disease takes a huge physical and emotional toll.

The good news for people in Minnesota is that they are surrounded by researchers who are dogged in their determination to find better treatments and even a cure for the disease. The University of Minnesota's Schulze Diabetes Institute, which was launched in 2008 with a $40 million gift from the Richard M. Schulze Family Foundation, is unabashed about its goal of finding a cure. And last October, the Minnesota Partnership for Biotechnology and Medical Genomics launched an ambitious Mayo Clinic-University of Minnesota partnership to "prevent, optimally treat, and ultimately conquer diabetes." "If the passion

to find a cure were directly related to how quickly we could discover it, we would have found it 10 years ago—right here in Minnesota," says Elizabeth Seaquist, M.D., an endocrinologist and director of the University of Minnesota's Center for Diabetes Research. "I am very optimistic that something very good will come out of that kind of relentless dedication."

Here are some of the paths that Minnesota researchers are taking on their quest to minimize the impact of type 1 diabetes in patients' lives—or eliminate the disease altogether.

> "If the passion to find a cure were directly related to how quickly we could discover it, we would have found it 10 years ago—right here in Minnesota."
>
> —Elizabeth Seaquist, M.D.

Innovations in Islet Cell Transplantation

For more than 40 years, pancreas transplantation has been a treatment option for patients with type 1 diabetes. University of Minnesota surgeons performed the first pancreas transplant in 1966 and have been world leaders in the field since. Numerous clinical trials have demonstrated the procedure's effectiveness in restoring normal glucose levels and freeing patients from insulin injections. But while the procedure generally makes recipients diabetes-free, the risk for surgical complications is relatively high, so researchers have continued looking for alternatives.

In 1974, David Sutherland, M.D., Ph.D., led a team that performed the world's first human islet cell transplant on a patient with diabetes, using cells from a deceased donor. Although the patient was not able to stop taking insulin, the team was undeterred.

Since then, investigators in Minnesota have been working to perfect the procedure to increase the length of time that patients remain free of insulin injections and further define protocols for bringing islet cells to patients with type 1 diabetes. University of Minnesota transplant diabetologist Bernhard Hering, M.D., scientific director of the University of Minnesota's Schulze Diabetes Institute, has led eight clinical trials of islet transplantation. The protocol changes he implemented have markedly improved short-term and long-term outcomes in such patients. Ninety percent of the patients who undergo a transplant no longer require insulin injections and can enjoy a life no longer restricted by constant fear and worry. The procedure has stood the test of time; five years after transplant, more than 50 percent of patients remain insulin-independent—and 80 percent remain protected from severe hypoglycemia. Three of the first six patients who participated in Hering's first clinical trial at the University of Minnesota between 2000 and 2002 have remained insulin-free and diabetes-free for 10 years (and counting). The protocol he published in 2005 has been adopted by the NIH's Clinical Islet Transplant Consortium for the ongoing Phase III licensure trial of human islet medical products.

Hering says seeing the transformed lives of patients who've undergone successful human islet transplants has inspired him and others to seek ways to make islet transplant a possibility for more people. "Human-to-human islet transplantation has shown proof in concept, but even if we maxed it out, really only one or two thousand patients can benefit from it annually in the United States," he explains. "To amplify access to islet cell transplant and make it accessible to many more populations, we need to develop an unlimited supply of insulin-producing cells for transplantation."

Hering's solution: using islet cells from pigs, the animals that supplied us with therapeutic insulin for six decades, before human recombinant insulin could be readily manufactured. Toward the end of the 1990s, Hering demonstrated that islet cells harvested from pig pancreases could reverse type 1 diabetes in mice. By February 2006, Hering showed that the therapy could yield long-term success in monkeys. "At that point, we realized that pig islets could most likely offer a new therapy with very profound implications for humans," he says. "We started to build momentum." Soon after, Hering helped create the Spring Point Project, a nonprofit that operates a 21,000-square-foot biosecure facility in western Wisconsin, where it is raising a population of medical-grade pigs.

Hering says University of Minnesota researchers are "getting close" to doing human clinical trials using transplanted pig islet cells. But he doesn't want to speculate when those might begin. "We don't want to rush. Every single time my team and I have done a clinical trial, the first person who has participated has shown a substantial benefit, so we are not going to do this without the utmost regard for our patients." ↳

Another potential way to create an unlimited supply of islet cells for transplantation is with stem cells. In the past few years, University of Minnesota researcher Meri Firpo, Ph.D., has been exploring how skin and other cells can be reprogrammed into a pluripotent state. Until recently, the only stem cells that were pluripotent—that is, able to evolve into different cell types, including islet cells—were embryonic stem cells. In her lab, Firpo has discovered that these reprogrammed cells, called induced pluripotent stem (iPS) cells, can be differentiated into insulin-producing cells.

"The reason that iPS cells are so exciting is because they allow us to transplant patients' own cells back into their bodies, versus what is done now, which is to take the islets or pancreas from cadavers," she explains. "The major drawback is that iPS cells may not be as safe as embryonic stem cells because we are genetically modifying the cells to make them pluripotent, and that may increase the risk of these iPS cells causing cancer."

Currently, Firpo is putting iPS cells to the test in animal models. After collecting skin-cell samples from patients with and without type 1 diabetes, she reprograms them, first turning them into iPS cells and then differentiating those cells into pancreatic precursor cells, which are transplanted into diabetic mice. Although Firpo won't disclose the results of the research because she has not yet published her data, she is confident that the strategy will be clinically useful.

> "Our strategy is to re-educate the T cells, so they no longer attack and destroy the islet cells."
>
> —Brian Fife, Ph.D.

Gauging when and if iPS cells might be used in the clinical setting is difficult. The current challenges, Firpo says, are twofold: 1) determining which iPS cells are better—those from the patient's own body (autologous) or those from another donor (allogeneic) and 2) ensuring the safety of introducing genetically re-engineered cells into the body. Among others is the concern about cancer risk. "The reason it is so hard to predict whether we will be able to use iPS cell therapy is because it is a completely new field, and given the fact that these cells are genetically modified, we don't know what safety standards we need to meet in order for the FDA to approve them," she says. "The limiting factor is not the proof of concept but what needs to be done to ensure safety. Once we have that answer, we may have a slightly better idea of how long it will take before this therapy gets to the clinic."

Managing the Immune Response

Regardless of how effective a transplant or cell therapy is in reducing the burden of diabetes, the key to ensuring the success of those therapies in humans will be managing the body's immune response. At the University of Minnesota, researchers are working on immunoreactivity from two angles: 1) stifling the autoimmune response in people with type 1 diabetes and 2) suppressing the body's immune response to a friendly foreign body such as transplanted islet cells or a pancreas.

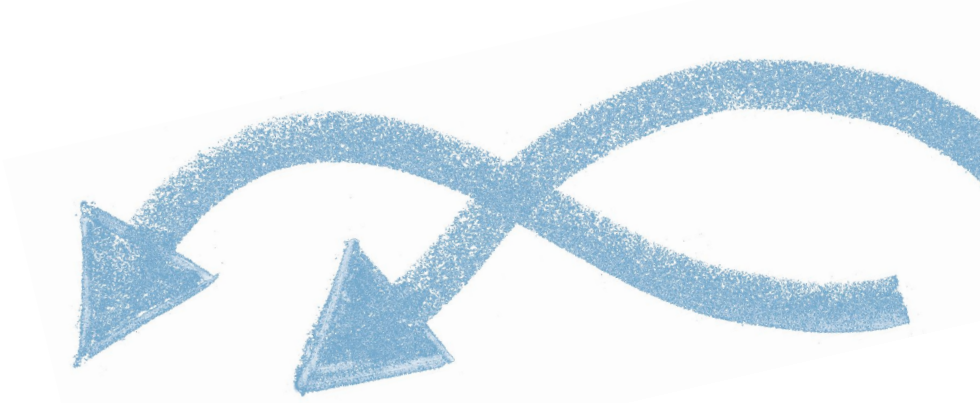
The fact that type 1 diabetes is an autoimmune disease that kills patients' own insulin-producing cells presents a critical challenge to those attempting to find a cure. A therapy won't be considered successful unless that autoimmune attack can be stifled. For researcher Brian Fife, Ph.D., a professor in the university's department of medicine and a member of the Center for Immunology, the definition of a cure for type 1 diabetes is two-pronged: "It essentially involves 1) restoring the body's supply of insulin-producing cells (beta cells) and 2) deactivating the part of the immune system that causes the body to attack its own beta cells. … The fundamental purpose of my research is to understand why the immune system is attacking itself and then develop ways to counteract that process."

In the case of type 1 diabetes, the immune system views its own insulin-producing cells as a threat, and in doing so, signals T cells to attack the islet cells, which eventually destroys the body's ability to produce insulin. Since 2001, Fife has been fine-tuning a way to turn off only the diabetes-causing T cells—effectively training them to be tolerant of islet cells—without turning off the T cells that protect the body from real threats such as viruses.

"Each T cell is like a specific lock and key for a particular protein; it only targets the cells that it recognizes," Fife says. "Our strategy is to re-educate the T cells, so they no longer attack and destroy the islet cells; thus in effect, you turn off that process of self-destruction." Fife has proven the concept in mice. After turning off T cells in mice with new-onset type 1 diabetes, half were cured and returned to normal glycemic levels. The remaining 50 percent had improved glycemic function but did not return to normal presumably, Fife speculates, because they needed to replenish their stores of insulin-producing cells that were destroyed in the original attack. "The advantage of our treatment approach is that you could use the patient's own (autologous) blood cells

to induce the immune system's tolerance to the islet cells. The injected cells are decorated with islet targets and inactivated, rather than genetically altered, thus eliminating any risk of the cells releasing viruses or developing tumors," he says.

Like Firpo, Fife hesitates to say when his research results could be applied in a clinical setting, but he and his group are currently working with samples from patients with type 1 diabetes. His technique for inducing tolerance could ultimately be used with the introduction of cell-based treatments such as Firpo's iPS cell therapy. "I believe the research we are doing is certainly on the path to finding a cure," Fife says. "If you can effectively silence the immune system and then replace the lost beta cells, that would constitute a cure in my mind."



> "By literal definition, a cure has to be when you develop a therapy that prevents the patient from worrying about the disease at all."
>
> Yogish Kudva, M.B.B.S.

As Fife works to prevent the immune system from attacking itself, Pratima Pakala, Ph.D., another University of Minnesota diabetes researcher, is focusing on therapies that can suppress the body's rejection of a transplanted islet cell or pancreas, thus minimizing a transplant patient's need to take anti-rejection medications. "Even though they continue to improve, today's immunosuppressive drugs definitely affect quality of life; they increase patients' susceptibility to infection, to cancer, to reactivation of viruses; and overall, those risks affect a patient's ability to take the medication, which increases the risk of rejection of transplanted organs," Pakala says. "The aim of our research is to better control the body's immune response to organ transplant by increasing the body's regulatory T cells, which help suppress transplant rejection." Regulatory T cells are sparse in the average human, comprising only about 1 to 2 percent of total lymphocytes.

Pakala and her group have shown that they can extract regulatory T cells from the blood of monkeys, grow them in culture for 21 days to increase their quantity, and then reinfuse them into the blood. "In a very recent study we just concluded, we found that this expansion of regulatory T cells could protect the islet cell graft from rejection," Pakala says. "Interestingly, we also found that we could remove all the chemical immunosuppressive drugs that would be used in the clinical setting." In addition to extending the survival of the islet cell grafts, the animals maintained normal glucose levels for more than 180 days—and in one case, almost a full year.

Currently, Pakala and her team are running a protocol in which monkeys are kept on a low dose of the immunosuppressive drug rapamycin. At the end of one year, they will review the data and approach the Food and Drug Administration to get an opinion regarding whether to apply for investigational new drug status, which would move the therapy into clinical trials.

Pakala hesitates to call regulatory T-cell therapy a cure for type 1 diabetes. "It is primarily meant to replace immunosuppressive drugs and support an islet cell replacement product," she says. "The islet cell replacement source becomes the cure, and regulatory T-cell expansion will be the supplemental therapy that supports the ability of the islet cell replacement to work for a long period of time."

Closing the Loop

Mayo Clinic endocrinologist Yogish Kudva, M.B.B.S., knows that finding a cure for diabetes is the ultimate goal. But he says the significant advances that arise before the monumental discoveries are made are also valuable. "By literal definition, a cure has to be when you develop a therapy that prevents the patient from worrying about the disease at all," Kudva says. "But there are levels below 'cure' that can limit self-management such that a patient experiences a vast improvement in quality of life."

Kudva sees the closed-loop system, or artificial pancreas, technology he is working on with fellow Mayo endocrinologist Ananda Basu, M.B.B.S., M.D., as a significant advancement. Although there are different versions of the artificial pancreas, the main components of any closed-loop system are a continuous glucose monitor, a central processing unit that reads glucose measurements, and an automatic insulin pump that delivers doses of insulin according to the blood glucose reading generated.

After their research revealed that physical activity after meals lowers glucose levels in people with type 1 diabetes, Kudva and Basu decided to add ancillary tools such as a physical activity monitor to the artificial pancreas system in hope of fine-tuning precisely how much insulin each patient needs. Clinical trials of this modified artificial pancreas will likely begin in November. In an inpatient setting, a handful of participants will use an artifi-

> "Moving toward an artificial pancreas, which some consider a mechanical cure for diabetes, is a stepwise process."
>
> —Richard M. Bergenstal, M.D.

cial pancreas system that combines a continuous glucose monitor, insulin delivery system, activity monitor, and a computerized algorithm that mimics the body's natural process of monitoring and responding to glucose levels in the bloodstream. "We believe detection of physical activity—and modeling of its effect on glucose dynamics—is vital to designing an automatic insulin delivery system because we know now that physical activity enhances insulin action," Kudva says. "Ultimately, the computerized algorithm makes the decision-making process simpler for the patient—not a cure, as I mentioned, but a reduction in the self-management activities that often create so much disruption in the lives of patients with diabetes."

Meanwhile, the artificial pancreas is currently being evaluated in clinical trials throughout the country. In these trials, which are generally conducted in inpatient settings, the patient wears the device for three to seven days and all the while is monitored to determine the effectiveness of the therapy. Some studies have also been done outside of the hospital setting. In Minnesota, researchers at Park Nicollet's International Diabetes Center (IDC) have shown that after one year, insulin-pump therapy augmented with a continuous glucose monitoring device more effectively lowered hemoglobin A1c levels than multiple daily insulin injections in patients 7 to 70 years of age who had poorly controlled type 1 diabetes. A report on that study was published in the July 22, 2010, *New England Journal of Medicine.* "Moving toward an artificial pancreas, which some consider a mechanical cure for diabetes, is a stepwise process," says Richard M. Bergenstal, M.D., endocrinologist and executive director of the IDC. "Combining a glucose sensor and an insulin pump is step one; soon we will start a study with an insulin pump that can shut off the delivery of insulin if the glucose is dangerously low; and eventually the hope is the pump will be programmed to increase the insulin if the glucose is definitely high."

The Cure Conundrum

Although diabetes researchers are taking different approaches to finding a cure and even define the term somewhat differently, all seem to understand that what matters most is improving the lives of patients. The university's Meri Firpo says she has talked with dozens of people with type 1 diabetes. "Of course, there is a range of what 'cure' means to them; but for most of these patients, cure means not having limitations on life because of their disease, even if that means they may have to take anti-rejection medication the rest of their lives," she says, adding that she hopes that if iPS cell therapy is found to be safe and effective, patients could regard it as a cure.

Fellow researcher Bernhard Hering notes that recipients of islet cell and pancreas transplants speak of their disease in the past tense. "They say, 'When I had diabetes, I had to endure this; I had to do this.' They no longer refer to themselves as a patient with diabetes." And, he says, before a transplant, patients say they spent a huge amount of time making plans for getting through the day with their diabetes. "Now, they are making plans for the next 20 years." **MM**

Jeanne Mettner is a frequent contributor to *Minnesota Medicine.*

Diabetes in Tanzania

A summer project offers a glimpse at the problems that plague the Tanzanian health care system.

By Lilian Msambichaka

Help me! Someone help me please! My child is dying, please someone help me!

A woman holds her convulsing son outside a café a few steps from the Muhimbili University of Health and Allied Sciences (MUHAS) hospital in Dar es Salaam, Tanzania. The café is frequented by patients and their family members and MUHAS staff. I am there on an August afternoon to meet a family friend after my orientation at the Tanzania Diabetes Association (TDA), where I am doing a five-week project. I stand, look in the direction of the crying voice, and notice that a nurse sitting a few tables away continues to eat her lunch as if unaware of what is happening. People gather around the crying woman and her seizing son as his body jerks, his eyes roll upward, and blood-tinged foam covers his mouth. I vainly try to recall what I've learned about first aid for seizures. Then, people around her begin praying. When the seizure stops, the mother thanks them and explains that her son has recently sustained a head injury in a car accident and that he is going to MUHAS to be examined.

That was not how I had envisioned health care in Tanzania. I hadn't expected to see such apathy. I had thought health care providers would rise to the call of duty and offer their services despite whatever strains they might be feeling. I was shocked and angry at the indifference of the nurse. How could she not offer to help?

To begin to understand her, to begin to understand the health care system in Tanzania, I had to look beyond this incident.

I had come to Tanzania in the summer of 2010 to do research on the prevalence and management of diabetes mellitus. As it turned out, that focus provided me with a lens through which I could see the bigger picture of this country.

My parents lived in Tanzania, so I was familiar with the country. I got interested in metabolic diseases in developing countries after hearing Antoinette Moran, M.D., an endocrinologist at the University of Minnesota, where I am a medical student, give a talk on diabetes in Uganda. Before Dr. Moran's talk, I had no idea how prevalent diabetes was in Tanzania nor that the disease is on the rise and poses a serious problem for the future because neither society nor the health-care system is equipped to handle the management of people with chronic diseases. Like most people who consider studying or working in Africa, I was initially thinking of pursuing a project on infectious diseases such as HIV or malaria.

Dr. Moran put me in touch with the TDA. The association was formed in 1985 with the assistance of Dr. Donald McClarty, a British physician who taught medicine at

Photos courtesy of Lilian Msambichaka

Patients wait in front of Amana District Hospital, one of Tanzania's government-owned hospitals that provides diabetes care and education.

Muhimbili Medical Centre and who noticed that many patients with diabetes were unaware of their condition. He also noticed many Tanzanian doctors were treating symptoms but missing the diagnosis. And many Tanzanians regarded diabetes as a disease of developed countries, rather than one that could affect them.

The TDA provides education about diabetes to the public, health care professionals, and newly diagnosed patients, and gives free insulin and glucometers to people younger than 22 years of age. During my stay, I attended diabetes education sessions at the Temeke and Amana district hospitals, and at the MUHAS diabetes clinic, all of which are government-run facilities. At the district hospitals, a dozen people gathered in small rooms for the two-hour sessions, during which educators dispelled myths about diabetes being a communicable disease or a curse. Many patients believed that people with diabetes should only eat millet with a few vegetables three times each day. Those who followed this regime got both constipated and hyperglycemic. It was refreshing to see these patients' relief as this folklore was discounted.

The diabetes doctors who I worked with were as dedicated and hard-working as their colleagues in the United States. But they are stretched thin and paid less than most professionals in the private sector. The doctor-patient ratio in Tanzania is 1:26,000. (World Health Organization guidelines are 1:7,500. In the United States, the ratio is about 1:400.) The Tanzanian physicians see as many as 50 patients during a three- to four-hour clinic. At Amana District Hospital, a 350-bed facility, the one trained diabetes doctor is occasionally assisted by other doctors who have attended only a few seminars on working with patients who have diabetes.

As in the United States, the children with diabetes who do the best have parents who are actively involved in the management of their disease. The adults who can afford to buy medication or have some education also do better than others. Adolescents and young adults who don't have jobs struggle the most. When they turn 22, their access to the TDA's free supplies ends. A month's supply of insulin costs $10 to $20; glucose strips and syringes bring the monthly treatment cost to $65, far beyond the reach of many. Unless they come from families that can afford to pay for the medications, patients frequently end up in hyperglycemic crisis and return to the pediatric clinic at MUHAS seeking free medication. One kid begged the doctor to let him stay at the clinic forever.

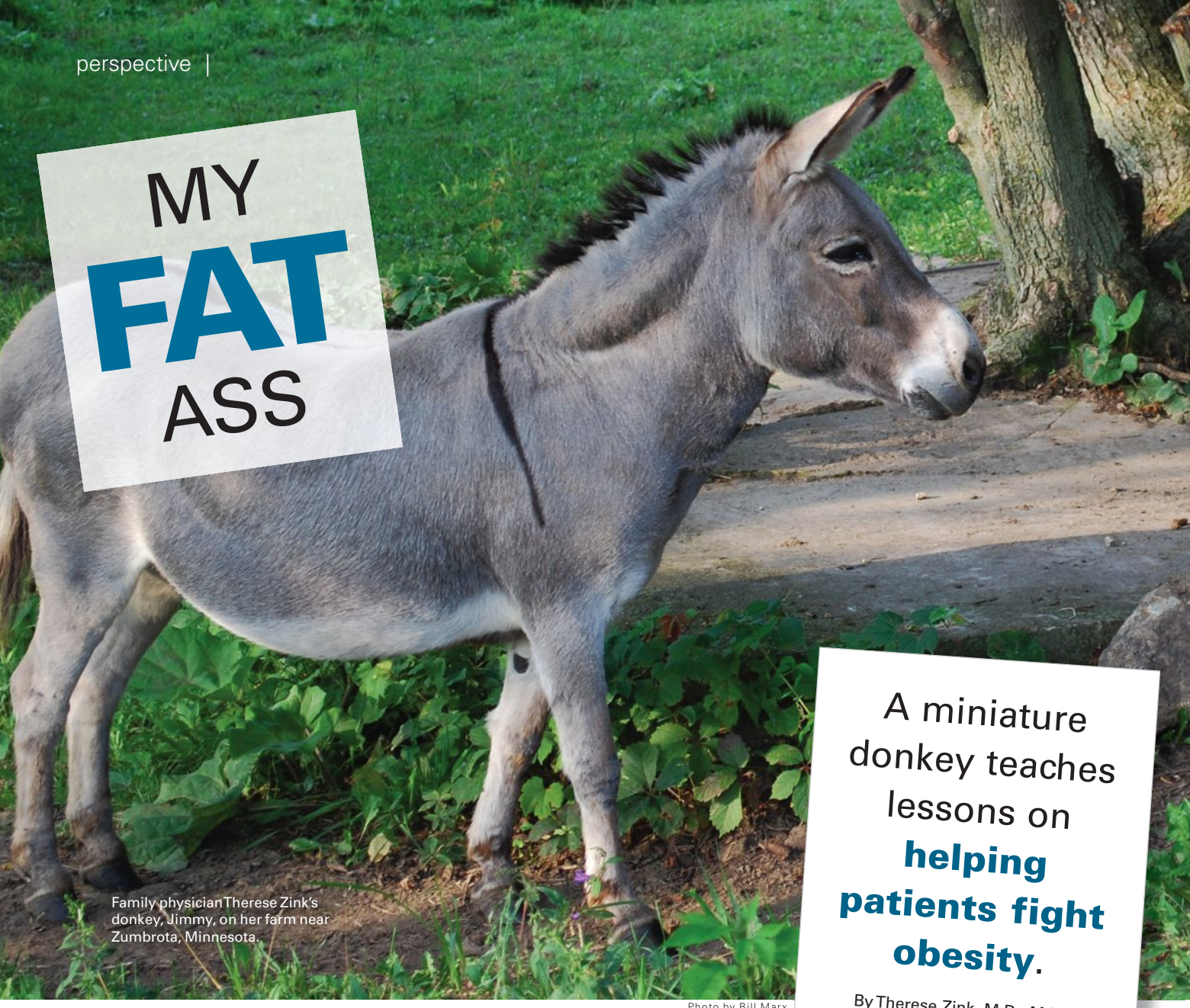
Half of Tanzania's 33 million residents live below an unimaginably low poverty level. The cost of living is high, and people struggle to make ends meet. The gap between the poor and the middle class keeps growing wider. Those who have means can afford to go to a "good" hospital and get good health care; those who don't rely on under-resourced government hospitals.

A few weeks after my encounter at the café, I was no longer angry at the nurse who stood by while the young man had the seizure, nor was I surprised that people resorted to prayer to solve their problems. I was beginning to understand what scarcity and need could do to a society. I saw that the public health care system in the country was burdened, under-resourced, and understaffed. The medical personnel were overwhelmed, which led them sometimes to the point of not caring. Prayer gave people hope and a sense of peace. It made them feel empowered when they felt the health care system and society had failed them. **MM**

Lilian Msambichaka is a third-year medical student at the University of Minnesota and a junior scientist in the department of medicine's hematology office.

The Tanzania Diabetes Association's diabetes center at Muhimbili University of Health and Allied Sciences is the main diabetes clinic in Tanzania and provides free supplies to young patients.

MY FAT ASS



Family physician Therese Zink's donkey, Jimmy, on her farm near Zumbrota, Minnesota.

Photo by Bill Marx

A miniature donkey teaches lessons on **helping patients fight obesity.**

By Therese Zink, M.D., M.P.H.

My ass has an obesity problem. I am not speaking of my derriere, although over the years my own weight challenges have given me empathy for the trials of my patients. Rather, I am talking about my miniature donkey, Jimmy.

Jimmy's back reaches my waist. (I'm 5 feet 2 inches tall.) Twig-like legs support his big-bellied body, like a pregnant woman wearing high heels. His tan, fuzzy ears edged in black are about four times the size of a horse's. When I talk to him, they stand at attention and turn in my direction. When he's angry, they lay flat against his head. His spiky mane, as black and upright as a punk rocker's hair, marches down his neck. Liquid brown eyes outlined in black, like Charlie Chaplin's Little Tramp's, track my movements.

Jimmy's lot in life is eating and hanging out with his pal Indy, a quarter horse. Food gives both of them pleasure; they graze in their three-acre grassy pasture all day. Each morning, they receive a measure of oats. Jimmy nibbles a mouthful, then meanders to the stable door and chews as he gazes out at the bucolic Midwestern scene. The morning sunrise bathes the pasture with its stand of maple and poplar trees in a rosy light. Beyond the three-strand electric fence, a patchwork of soybean and corn fields stretch to the hem of the sky.

In other countries, Jimmy's relatives enjoy the same vibrant sky, but their pastures are less ample, and they expend more calories pulling carts and lugging packs. As a result, they are much thinner than Jimmy. Clearly, like many Americans, Jimmy's obesity problem is attributable to his lifestyle—too much food and too little exercise. Because he is unable to restrain himself or increase his activity on his own, I muzzle him. A muzzle ensures portion control: A two-inch hole at the bottom of a rubber basket that attaches to his halter limits the size of a bite of grass to nibbles only, no super-size servings.

If I happen to leave the gate open, he

bounds out of his pasture like a racehorse, bucking and kicking his hooves in glee. The escape artist gallops into the yard with unusual speed and makes a bee-line for the farthest corner. There, he settles in for a good chew; as the saying goes—the grass is always greener. If I approach, he skirts away. Herding him back into the barn is impossible, even with the help of my dog. However, if I leave the door open and ignore him, he eventually wanders inside the barn to be near to Indy.

Encouraging behavior change is one of the toughest challenges we face as physicians.

Of course, as physicians, we can't muzzle our overweight patients. So we try to encourage them to change their behavior. Research tells us that mentioning concerns about weight does make a difference, and sometimes it does.

Joanne came to see me for a follow-up visit regarding her blood pressure. "Did you see how much weight I've lost?" she asked, looking for my approval. I pulled up a chart on the computer that mapped her weight and oooed and aahhed at her 50-pound success. She'd even stopped by the clinic a month earlier for a weight check to document her progress. The line angled sharply downward; she was now under the 200-pound mark.

"What motivated you?" I asked.

"Well, you told me that it would help my blood pressure if I lost some weight."

That's all? I thought, how uninspiring.

"I went home and thought and prayed about it. I decided to join TOPS (Take Off Pounds Sensibly). Now I run the group."

Adam, a 20-year-old patient, came to see me after his father was diagnosed with diabetes. "I don't want to be like Dad," he told me, his stomach concealing his belt. We talked about healthful foods and exercise. When he returned a month later, he'd lost almost 20 pounds. He had stopped eating fast food and started going to the local gym after work. For the next year, he checked in with me monthly, and we watched the line of the weight graph in the electronic health record trend downward. He dropped 100 pounds. I cheered him on and even asked the hospital to tell his story in the quarterly newsletter. In both cases, I only mentioned the issue of weight.

Despite me mentioning my concerns, more of my overweight patients retain their obese status than change it. I often feel I am fighting an uphill battle and lose steam when talking about it. I wish I could simply muzzle those patients. There is a fine line between inspiring and shaming patients. If I push too hard, they won't return. Some patients refuse to stand on the scale in my office; some avoid the clinic altogether because they don't want to face the scale.

Encouraging behavior change is one of the toughest challenges we face as physicians. Exploring the barriers to change takes time, which is a precious commodity when you're on today's health care treadmill.

Jimmy has taught me lessons about doing this that translate to patient care. A moody fellow, some days I approach to pat him, offer him a treat, and he darts away, turning his rear end toward me. Other times, he can't wait for the carrot or apple I have to offer. At those times, he approaches with caution, sticks out his muzzled nose, and nudges my arm.

Like Jimmy, my patients are receptive to me only some of the time. Persistence and leading by example are crucial. When patients see me running during my lunch hour, they know that I am serious about my suggestion that they exercise. It's hard for me to talk about healthful eating and exercise if I am not doing those things myself. Although it took a number of years, I've figured out how to manage stress without food and how to incorporate exercise into my daily routine. An overweight colleague who eventually lost 50 pounds told me that patients used to laugh at him when he brought up the issue of weight. Doctor heal thyself. Attend to your own ass.

As leaders in our communities, we physicians need to be strong voices for environmental change. We can support community efforts that address the obesity epidemic. We can raise questions about what is served in our school cafeterias and work to ensure that gym class is part of the school day and is fun for all kids, even those with little athletic talent. We can work to ensure that children have options after school besides watching television and playing video games and encourage parents to limit children's access to sugary beverages and fast food. We can ask important environmental questions: Can urban areas support gardens to grow fresh produce? Is affordable, healthful food available in grocery stores in poor parts of town? How can we make our neighborhoods safer for exercise?

But on the individual level, we need to meet our patients where they are and gently encourage them to make healthier choices. Jimmy knows that I care for him because I meet him where he is each day. My patients are not so different. **MM**

Therese Zink is a family physician in Zumbrota, Minnesota, and a professor in the department of family medicine and community health at the University of Minnesota.

Recognizing and Managing Type 2 Diabetes Mellitus in Children

An Algorithm for Primary Care Providers

By Muna Sunni, M.B.B.Ch., Rita Mays, M.S., R.D., L.N., Tara Kaup, R.N., C.D.E., Brandon Nathan, M.D., and members of the Minnesota Department of Health Diabetes Steering Committee

During the last two decades, type 2 diabetes mellitus increasingly has been seen in children. Although still not as common as type 1 diabetes among children, it has become the leading form of diabetes among adolescents of certain ethnicities. It is imperative that primary care providers recognize the risk factors, perform appropriate screening tests, and initiate therapy for children who have type 2 diabetes or prediabetes. This article discusses the epidemiology and pathogenesis of the disease, complications, and treatments, and includes a concise, easy-to-follow algorithm to assist providers in diagnosing and treating young patients.

Type 2 diabetes and features of the metabolic syndrome (obesity, insulin resistance, dyslipidemia, and hypertension) almost exclusively have been observed in adults. However, over the past two decades, the prevalence of pediatric type 2 diabetes mellitus has been increasing steadily in the United States, particularly among children of certain ethnic backgrounds.[1,2] Although the absolute number of new pediatric cases remains relatively small, type 2 diabetes mellitus accounts for the majority (or near majority) of diabetes cases among Native American, Asian/Pacific Islander, African-American, and Latino adolescents in the United States. A dramatic rise in the rate of pediatric obesity among children has undoubtedly been a factor in the increase in cases of pediatric type 2 diabetes, as obesity is a well-established primary risk factor for developing the disease.[3-5]

The rise in the pediatric obesity and type 2 diabetes rates affects not only health outcomes but also resource planning. Since obese children are also more likely to become obese adults,[6,7] a generation of young adults facing obesity-derived metabolic complications and a shorter life expectancy is likely to emerge. Moreover, the same complications occurring alongside or independent of type 2 diabetes in adults are now being seen in the pediatric population,[8] placing this generation of obese children at greater risk for early cardiovascular disease and related health problems. Children with type 2 diabetes mellitus are also at an increased risk for early development and accelerated progression of microvascular complications such as nephropathy.[9]

Estimated costs related to diabetes in the United States in 2007 were $174 billion,[10] a figure that is likely to increase in the years ahead as rates of diabetes continue to rise.[11] Those trends have mandated the need for developing effective screening and treatment plans to prevent, diagnose, and manage pediatric patients with type 2 diabetes.

In this article, we briefly review current epidemiologic data regarding pediatric type 2 diabetes mellitus in the United States and population-based estimates in Minnesota, the pathophysiologic mechanisms of the disease, and basic therapeutic approaches. We also

provide an algorithm written by members of the Minnesota Department of Health's Diabetes Steering Committee that offers primary care providers a simplified strategy for identifying, testing, and intervening with peripubertal youths who have or are at risk for type 2 diabetes.

Epidemiology

In the past, type 2 diabetes mellitus comprised a very small percentage of all childhood diabetes cases; however, recent data indicate that that percentage is growing.[12] The SEARCH study, an ongoing, observational, population-based study analyzing rates of diabetes in different geographic areas of the United States including Washington, Colorado, California, Hawaii, Ohio, South Carolina, and American Indian reservations, has provided valuable information about the trends in pediatric diabetes, especially type 2 diabetes.[1]

Not surprising, age is a highly influential factor in determining rates and type of disease. Cases of type 2 diabetes among 5- to 9-year-olds are exceedingly rare, with an incidence rate of only 0.8 per 100,000 person-years. However, rates increase sharply during adolescence to an incidence of 8.1 per 100,000 person-years in 10- to 14-year-olds and 11.8 per 100,000 person-years in 15- to 19-year-olds.

Incidence rates are also strongly influenced by ethnic background. The incidence of type 2 diabetes mellitus is highest among older American Indian adolescents (49.4 per 100,000), followed by Asian/Pacific Islander (22.7 per 100,000), African-American (19.4 per 100,000), Hispanic (17 per 100,000) and finally non-Hispanic white youths (5.6 per 100,000).[1]

Overall, the prevalence estimate for type 2 diabetes in the United States ranges from about 1 in 5,000 white children to close to 1 in 500 American Indian children. This is equivalent to approximately 3,700 new cases of type 2 diabetes in children in the United States each year.[13] Nearly 90% of children diagnosed with type 2 diabetes are obese or overweight,[5] magnifying the positive relationship between obesity and type 2 diabetes. In addition, females are 1.7 times as likely as males to develop the disease, regardless of race.[14] This difference is most dramatic among American Indian children, where a ratio of 4 to 6:1 females to males with type 2 diabetes has been reported.[14]

Pediatric Type 2 Diabetes in Minnesota

Based on 2009 state census data, more than 705,000 children ages 10 to 19 years of age reside in Minnesota.[15] According to the 2010 Minnesota Student Survey, approximately 20% of children in grades 6 through 12 are of African-American, Latino, American Indian, or Asian heritage.[16] Based on current national incidence rates among people with these racial and ethnic backgrounds, it can therefore be reasonably deduced that approximately 35 to 45 new cases of type 2 diabetes will occur among this group each year in addition to 15 to 25 new cases among Caucasian adolescents. Perhaps much more alarming, an estimated 92,000 adolescents between the ages of 12 and 19 years may have prediabetes[17] and be at risk for progression to full-blown disease.

Because of the slow-but-steady increase in cases of pediatric type 2 diabetes and its associated comorbidities and complications, it is imperative that effective strategies be used to prevent, identify, and treat type 2 diabetes among youths. Given the declining supply of pediatric endocrinologists in the country,[18] especially in rural areas, this task will increasingly fall to primary care providers. To aid them, a subcommittee from the Minnesota Department of Health's Diabetes Steering Committee created a diagnostic and therapeutic algorithm (Figure) to increase awareness of pediatric type 2 diabetes among providers; guide clinicians in regard to diagnostic evaluations and therapeutic interventions; and provide practitioners with a concise tool that can be easily referenced in clinic.

Pathogenesis of Type 2 Diabetes in Children

Insulin resistance refers to a decrease in hepatic and peripheral cellular glucose uptake.[19] It is the core metabolic derangement that predisposes to type 2 diabetes. However, for diabetes to occur, it must be accompanied by a decline or defect in pancreatic beta cell function. A continuum of insulin resistance leading to variable beta cell failure exists, accounting for the progression from insulin resistance to prediabetes and eventually to type 2 diabetes. Obesity, particularly central or visceral adiposity, is strongly associated with the development of insulin resistance in both children and adults.[20] Increased visceral adiposity promotes a cascade of metabolic derangements and inflammation that negatively affect insulin signaling and increase the strain on the already-stressed beta cells to overcome inherent insulin resistance in order to maintain euglycemia. When an individual's beta cells can no longer compensate, glycemic decompensation occurs, leading to frank type 2 diabetes mellitus. Because puberty is a period of physiologic increased insulin resistance,[21,14] most cases of type 2 diabetes in children present around this time.

Although few specific genes have been linked to pediatric type 2 diabetes, strong familial tendencies and increased prevalence among children of certain ethnic backgrounds point to the importance of genetic variation on disease risk. As an example, a case control study in Germany demonstrated that polymorphisms in TCF7L2 are associated with an increased risk of impaired glucose tolerance in obese youths,[22] similar to the association observed in adults. Several other loci have been identified as imparting risk for development of type 2 diabetes in the adult population (although not always consistently), but additional pediatric associations have not yet been identified. Nevertheless, a family history of type 2 diabetes is extremely common among pediatric patients who have prediabetes or type 2 diabetes mellitus.[23] Indeed, compared with those who are overweight and have no family history of type 2 diabetes, an overweight child with a sibling who has type 2 diabetes, carries a four-fold increased risk of having impaired glucose tolerance.[24]

Intrauterine and perinatal factors have also emerged as important risk factors for

the development of type 2 diabetes. Maternal gestational diabetes is a risk factor for a child becoming insulin resistant and obese later in life.[25] Alternatively, infants who are born small for their gestational age or who have a history of intrauterine growth retardation and rapid weight gain during the first few months of life have also been found to be at increased risk for later development of the disease.[26] "Malprogramming" of the hypothalamic center, which is responsible for controlling metabolism, food intake, and subsequent weight gain, has been proposed as a possible mechanism for this phenomenon.[25]

Comorbidities and Complications

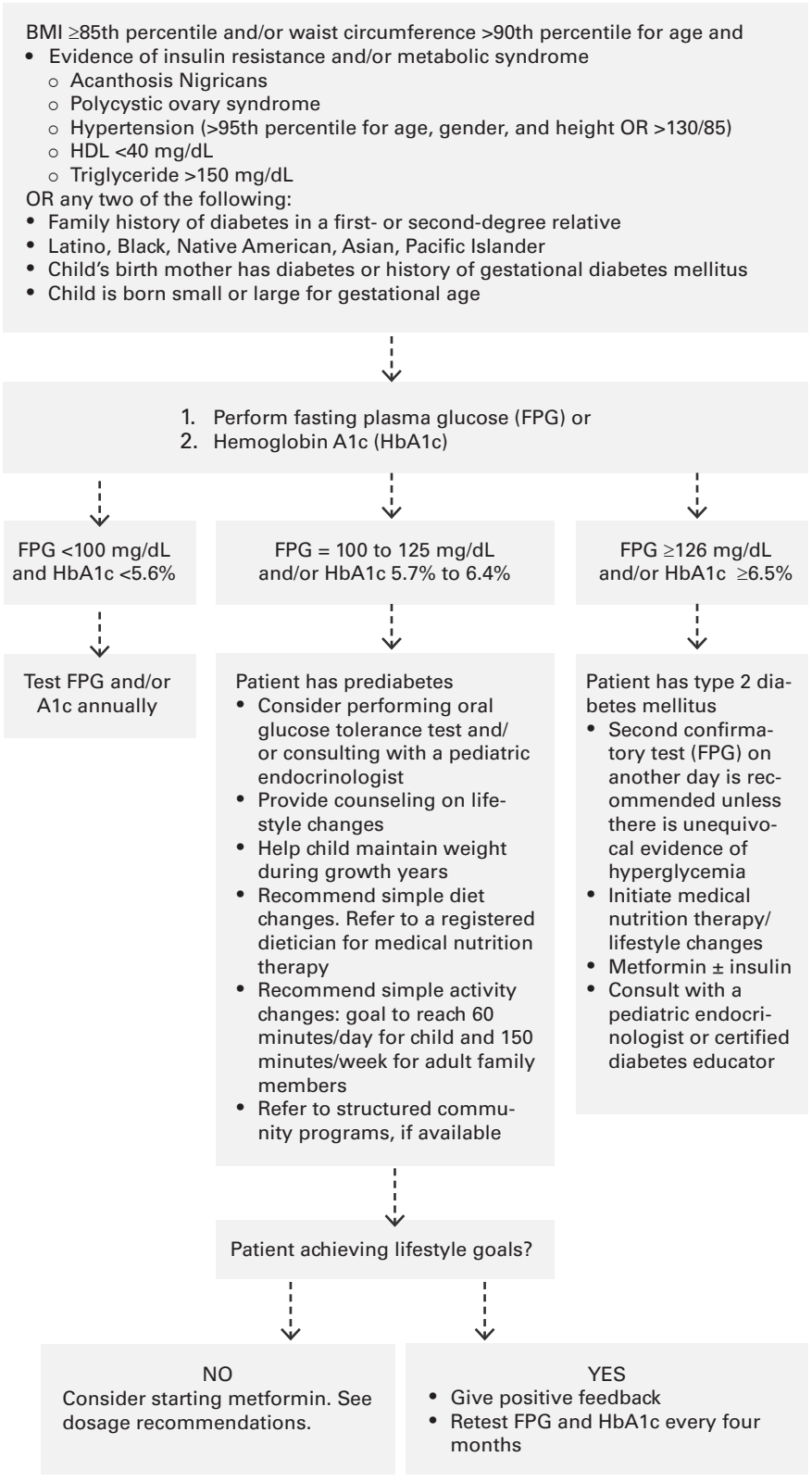
The micro- and macrovascular complications associated with poorly controlled diabetes in adults are well-documented. For example, individuals with diabetes are two to four times as likely to experience cardiovascular disease as others; in addition, diabetes mellitus is now the leading cause of blindness, lower leg amputation, and chronic kidney disease among adults in the United States.[27] Children with type 2 diabetes may have their own set of comorbid metabolic abnormalities. For example, those presenting in diabetic ketoacidosis have a more rapid decline in their beta-cell function compared with adults.[28] Microvascular disease in the form of microalbuminuria is often present at the time of diagnosis.[29] Dyslipidemia is more common among youths with type 2 diabetes compared with those with type 1 diabetes.[30] Hypertension is present in 14% to 32% of cases of pediatric type 2 diabetes at the time of diagnosis.[29] Twenty-five percent to 40% of children with the disease will present in a state of diabetic ketoacidosis, and the hyperglycemic hyperosmolar state may also occur, carrying with it a very high mortality rate.[31]

Recognizing and Treating Children with Prediabetes and Type 2 Diabetes

Children identified as having prediabetes (impaired fasting glucose or impaired glucose tolerance on an oral glucose toler-

Figure

Algorithm for Prediabetes and Type 2 Diabetes Mellitus Identification and Intervention for Youths (Ages 10 to 17 Years or Peripubertal)



METFORMIN: Start dosage at 500 mg QD with food. Increase dose every one to two weeks to achieve clinically effective dose of 1,000-2,000 mg/day, based on tolerability. Consider use of extended-release formulation if patient is experiencing significant side effects. Follow-up: Every one to three months. Do not use in patients with underlying kidney disease. *Metformin use in overweight adolescents not meeting criteria for type 2 diabetes mellitus is off-label and based on limited published data and consensus of Minnesota Diabetes Steering Committee.*

Prediabetes and Diabetes: Screening and Diagnosis

The current recommended diagnostic test to identify children with prediabetes in order to begin lifestyle interventions is either HbA1c or FPG. HbA1c is a measure of long-term blood glucose control and is used to monitor the effectiveness of therapy and risk for complications in persons with diagnosed diabetes. However, an HbA1c of ≥5.7% may help identify an additional group of at-risk children. An HbA1c ≥6.5% performed in a laboratory using standardized methods is now considered a criterion for a diagnosis of diabetes. An oral glucose tolerance test may define impaired glucose tolerance or diabetes and should be considered in children with impaired fasting glucose or an HbA1c in the prediabetes range. To calculate BMI and blood pressure, refer to:

- www.cdc.gov/growthcharts/ (BMI)
- www.nhlbi.nih.gov/guidelines/hypertension/child_tbl.htm (blood pressure)

Prediabetes and Diabetes: Recommended Lifestyle Changes for Entire Family

Simple Dietary Changes

- Become a label reader and limit portion sizes; observe serving size and calories per serving
- Limit snacks to one serving size; try fresh fruits and vegetables for snacks two to three days per week
- Eat fewer processed and high-fat foods; limit fast-food and restaurant meals to fewer than one to two per month
- Switch to 1% or skim milk
- Encourage water consumption; eliminate carbohydrate-containing beverages (pop, sweetened tea, energy drinks, juice)
- Eat breakfast and try not to skip meals

Simple Activity Changes

- Be active together as a family; eat meals together whenever possible
- Walk and take the stairs; park in distant spots and walk farther when shopping
- Try new sports or activities that increase physical activity
- Limit screen time (TV, computer, video games) to two hours per day
- Participate in community programs (eg, YMCA, YWCA, park and recreation centers)

Resources

- NDEP - Tips for Teens: Lower Your Risk for Type 2 Diabetes at http://ndep.nih.gov/teens/index.aspx and http://ndep.nih.gov/media/kids-tips-lower-risk.pdf
- DHHS - Small Step Kids: www.smallstep.gov/ (also in Spanish)
- ADA - Nutrition Tips: www.eatright.org (for additional help with label reading)
- AAP - Pediatric Obesity Management: www.aap.org/obesity/practice_management_resources.html

References

Srinivasan S, et al. J Clin Endocrinol Metab. 2006; 91:2074-80. Freemark M, et al. Pediatrics. 2001;107(4):e55; Kay JP, et al. Metabolism. 2001;50:1457-61; Love-Osborne K, et al. J Pediatr. 2008;152:817-22; American Diabetes Association. Executive Summary: Standards of Medical Care in Diabetes - 2010 Diabetes Care. 2010;33:S11-69; Fernández JR, et al. J Pediatr. 2004;145:439-44 (waist circumference tables); Nathan DM, et al. Diabetes Care. 2009;32:1327-34.

Common ICD-9 Codes for Diabetes Screening

V77.1	Diabetes screening
790.21	Impaired fasting glucose
790.22	Impaired glucose tolerance test (oral)
790.29	Prediabetes NOS/abnormal glucose value

Codes Describing Risk Factors

277.7	Dysmetabolic syndrome
278.00	Obesity
278.02	Overweight
701.2	Acanthosis nigricans
V18.0	Family history diabetes

ance test, or an intermediate hemoglobin A1c [HbA1c] in the 5.7% to 6.4% range) should be counseled about lifestyle modifications (improving diet and increasing physical activity) that can lead to weight stabilization or loss. Instituting an exercise program has been shown to improve insulin sensitivity.[32] Use of metformin to prevent type 2 diabetes in such children remains controversial. However, there is growing evidence, including results of a recent randomized controlled trial,[33] that metformin may be a useful adjunct to stabilize weight in obese youth with evidence of insulin resistance or prediabetes who are at risk for progression to type 2 diabetes.

Treatment strategies for those who have type 2 diabetes should be aimed at reducing insulin resistance and enhancing insulin secretion. Goals of therapy need to include not only achieving glycemic control but also management of associated metabolic comorbidities (eg, dyslipidemia, hypertension, and nonalcoholic fatty liver disease).[34,35] The core therapeutic approach is to maintain a healthy weight and limit weight gain.

Addressing lifestyle issues is central to any diabetes-management plan. Eating healthful foods can be challenging for both practical and financial reasons: Unhealthy food is cheaper, easier to obtain, and can be more appealing to children than healthful food. Successfully overcoming such challenges requires the entire family to make a commitment to eating more healthfully.[35,36] Making simple changes is the first step in this process. These should include eliminating high-calorie beverages such as juices, soft drinks, and energy drinks, focusing on portion control, and eating smaller meals more often rather than one large meal per day. Physicians can advise limiting screen time to no more than two hours a day. In addition, young people should be encouraged to increase the amount of physical activity they engage in. They should be encouraged to explore different forms of exercise in order to find ones they enjoy.[37,38]

Although an essential part of managing patients with type 2 diabetes, lifestyle modifications are often not sufficient

to achieve adequate glycemic control.[39] Pharmaceutical agents may be required to maximize control of the disease. Several oral hypoglycemic agents that have different mechanisms of action are approved for use in adults. In the pediatric population, however, the only oral hypoglycemic agent approved for use for treating type 2 diabetes is metformin.[40] Metformin reduces hepatic gluconeogenesis while promoting insulin uptake by muscle and fat.[41] In addition to its effect on glycemic control, several studies have demonstrated a modest neutral or negative effect on weight.[40]

Insulin is also approved for use in treatment of pediatric patients with type 2 diabetes. Insulin should be considered if significant beta-cell failure, diabetic ketoacidosis, or nonketotic hyperosmolar state are present at diagnosis. Gradual transition to monotherapy with metformin along with continued lifestyle modifications may be possible once a patient achieves adequate glycemic control. With such patients, it is important to check for diabetes autoantibodies that may impose a more rapid deterioration of beta-cell function and require long-term insulin therapy.[42]

There are several other classes of oral hypoglycemic pharmaceuticals including sulfonylureas, maglitinides, glucosidase inhibitors, thiazolidinediones, and incretin-based therapies. At this point, none of those agents are approved for use in the pediatric population. The TODAY (Treatment Options for Type 2 Diabetes in Youth) study should provide important data on the relative effectiveness and safety of thiazolidenediones compared with metformin and/or lifestyle modifications.[43]

Conclusion

Type 2 diabetes mellitus is slowly becoming more prominent and troublesome among adolescents. We have new knowledge about risk factors for the disease and the proposed pathophysiologic mechanisms that lead to it. Thus, we are now aware of risk factors that need to be considered in children. Although there are few therapies for children and adolescents with type 2 diabetes,[39] strategies such as making lifestyle changes should be encouraged in this population. Reliable screening tools for type 2 diabetes in children and adolescents are needed, given the importance of early identification and intervention. The algorithm presented represents a step toward assisting primary care providers in diagnosing and treating pediatric patients. **MM**

Muna Sunni is a fellow in pediatric endocrinology at the University of Minnesota. Rita Mays is the diabetes prevention planner at the Minnesota Department of Health. Tara Kaup is a school nurse and diabetes educator with the St. Paul Public Schools. Brandon Nathan is an assistant professor of pediatrics at the University of Minnesota.

REFERENCES

1. Writing Group for the SEARCH for Diabetes in Youth Study Group, et al. Incidence of diabetes in youth in the United States. JAMA. 2007;297(24); 2716-24.
2. Fagot-Campagna A, Pettitt DJ, Engelgau MM, et al. Type 2 diabetes among North American children and adolescents: an epidemiologic review and a public health perspective. J Pediatr. 2000;136(5); 664-72.
3. Pinhas-Hamiel O, Dolan LM, Daniels SR, Standiford D, Khoury PR, Zeitler P. Increased incidence of non-insulin-dependent diabetes mellitus among adolescents. J Pediatr. 1996;128 (5 Pt 1); 608-15.
4. Dabelea D, Pettitt DJ, Jones KL, Arslanian SA. Type 2 diabetes mellitus in minority children and adolescents. An emerging problem. Endocrinol Metab. Clin North Am. 1999;28(4);709-29, viii.
5. Liu LL, Lawrence JM, Davis C, et al. Prevalence of overweight and obesity in youth with diabetes in USA: the SEARCH for Diabetes in Youth study. Pediatr Diabetes. 2010;11(1);4-11.
6. DeFronzo RA, Barzilai N, Simonson DC. Mechanism of metformin action in obese and lean noninsulin-dependent diabetic subjects. J Clin Endocrinol Metab. 1991;73:1294-1301.
7. Serdula MK, Ivery D, Coates RJ, Freedman DS, Williamson DF, Byers T. Do obese children become obese adults? A review of the literature. Prev Med. 1993;22(2):167-77.
8. Ode KL, Frohnert BI, Nathan BM. Identification and treatment of metabolic complications in pediatric obesity. Rev Endocr Metab Disord. 2009;10(3): 167-88.
9. Pinhas-Hamiel O, Zeitler P. Acute and chronic complications of type 2 diabetes mellitus in children and adolescents. Lancet. 2007;369(9575):1823-31.
10. American Diabetes Association. Economic costs of diabetes in the U.S. in 2007. Diabetes Care. 2008;31(3):596-615.
11. The day of diabetes: coming soon to a person near you. Lancet. 2010;376(9752):1513.
12. De Ferranti SD, Osganian SK. Epidemiology of paediatric metabolic syndrome and type 2 diabetes mellitus. Diab Vasc Dis Res. 2007;4(4):285-96.
13. SEARCH for Diabetes in Youth Study Group, et al. The burden of diabetes mellitus among US youth: prevalence estimates from the SEARCH for Diabetes in Youth Study. Pediatrics. 2006;118(4):1510-8.
14. Pinhas-Hamiel O, Zeitler P. Clinical presentation and treatment of type 2 diabetes in children. Pediatr Diabetes. 2007;8 Suppl 9, 16-27.
15. 2010 Minnesota County Health Tables. Available at: www.health.state.mn.us/divs/chs/countytables/profiles2010/ademog09.pdf. Accessed July 18, 2011.
16. 2010 Minnesota Student Survey. Statewide Tables Fall 2010. Available at: www.health.state.mn.us/divs/chs/mss/statewidetables/mss10statetablesfinal.pdf. Accessed July 18, 2011.
17. Minnesota Department of Health, Diabetes in Minnesota Fact Sheet, 2010. Available at: www.health.state.mn.us/diabetes/diabetes/pdf/FactSheet2010.pdf. Accessed July 13, 2011.
18. Mayer ML, Skinner AC. Influence of changes in supply on the distribution of pediatric subspecialty care. Arch Pediatr Adolesc Med. 2009; 163(12):1087-91.
19. Levy-Marchal C, Arslanian S, Cutfield W, Sinaiko A, et al. Insulin resistance in children: consensus, perspective, and future directions. J Clin Endocrinol Metab. 2010;95(12):5189-98.
20. Kanaya AM, Harris T, Goodpaster BH, Tylavsky F, et al. Adipocytokines attenuate the association between visceral adiposity and diabetes in older adults. Diabetes Care. 2004;27(6):1375-80.
21. Moran A, Jacobs DR Jr, Steinberger J, Steffen LM, et al. Changes in insulin resistance and cardiovascular risk during adolescence: establishment of differential risk in males and females. Circulation. 2008;117(18):2361-8.
22. Korner A, Berndt J, Stumvoll M, Kiess W, Kovacs P. TCF7L2 gene polymorphisms confer an increased risk for early impairment of glucose metabolism and increased height in obese children. J Clin Endocrinol Metab. 2007; 92(5):1956-60.
23. Arslanian SA, Bacha F, Saad R, Gungor N. Family history of type 2 diabetes is associated with decreased insulin sensitivity and an impaired balance between insulin sensitivity and insulin secretion in white youth. Diabetes Care. 2005;28(1):115-9.
24. Magge SN, Stettler N, Jawad AF, Levitt Katz LE. Increased prevalence of abnormal glucose tolerance among obese siblings of children with type 2 diabetes. J Pediatr. 2009;154(4):562-6.e1.
25. Plagemann A. A matter of insulin: developmental programming of body weight regulation. J Matern Fetal Neonatal Med. 2008; 21(3):143-8.
26. Fabricius-Bjerre S, Jensen RB, Faerch K, Larsen T, et al. Impact of birth weight and early infant weight gain on insulin resistance and associated cardiovascular risk factors in adolescence. PLoS One. 2011;6(6):e20595.
27. Centers for Disease Control and Prevention Complications of diabetes in the United States. Available at: www.cdc.gov/diabetes/pubs/estimates05.htm#complications. Accessed July 13, 2011.
28. Levitt Katz LE, Magge SN, Hernandez ML, Murphy KM, McKnight HM, Lipman T. Glycemic control in youth with type 2 diabetes declines as early as two years after diagnosis. J Pediatr. 2011;158(1):106-11.
29. Copeland KC, Zeitler P, Geffner M, Guandalini C, et al. Characteristics of adolescents and youth with recent-onset type 2 diabetes: the TODAY cohort at baseline. J Clin Endocrinol Metab. 2011;96(1):159-67.
30. Petitti DB, Imperatore G, Palla SL, Daniels SR, et al. Serum lipids and glucose control: the SEARCH for Diabetes in Youth study. Arch Pediatr Adolesc Med. 2007;161(2):159-65.
31. Rosenbloom AL. Hyperglycemic hyperosmolar state: an emerging pediatric problem. J Pediatr. 2010;156(2):180-4.
32. Bell LM, Watts K, Siafarikas A, et al. Exercise alone reduces insulin resistance in obese children independently of changes in body composition. J Clin Endocrinol Metab. 2007;92(11):4230-5.
33. Yanovski JA, Krakoff J, Salaita CG, et al. Effects of metformin on body weight and body composition in obese insulin-resistant children: a randomized clinical trial. Diabetes. 2011;60(2):477-85.
34. Flint A. Arslanian S. Treatment of type 2 diabetes

in youth. Diabetes Care. 2011;34 Suppl 2: S177-83.
35. Katz LL, Abraham M. Dominant Western health care: type 2 diabetes mellitus. J Transcult Nurs. 2006;17(3):230-3.
36. McGovern L, Johnson JN, Paulo R, Hettinger A, Singhal V, Kamath C, Erwin PJ, Montori VM. Treatment of pediatric obesity. A systematic review and meta-analysis of randomized trials. J Clin Endocrinol Metab. 2008;93:4600-5.
37. Giannini C, de Giorgis T, Mohn A, Chiarelli F. Role of physical exercise in children and adolescents with diabetes mellitus. J Pediatr Endocrinol Metab. 2007;20(2):173-84.
38. Amed S, Daneman D, Mahmud FH, Hamilton J. Type 2 diabetes in children and adolescents. Expert Rev Cardiovasc Ther. 2010;8(3):393-406.
39. Kaufman FR. Type 2 diabetes mellitus in children and youth: a new epidemic. J Pediatr Endocrinol Metab. 2002;15 Suppl 2:737-44.
40. Rosenbloom AL, Silverstein JH, Amemiya S, Zeitler P, Klingensmith GJ. Type 2 diabetes in children and adolescents. Pediatr Diabetes. 2009;10 Suppl 12:17-32.
41. Steinberger J, Moran A, Hong CP, Jacobs DR Jr, Sinaiko AR. Adiposity in childhood predicts obesity and insulin resistance in young adulthood. J Pediatr. 2001;138(4):469-73.
42. Klingensmith GJ, Pyle L, Arslanian S, et al. The presence of GAD and IA-2 antibodies in youth with a type 2 diabetes phenotype: results from the TODAY study. Diabetes Care. 2010;33(9):1970-5.
43. TODAY Study Group, et al. Treatment options for type 2 diabetes in adolescents and youth: a study of the comparative efficacy of metformin alone or in combination with rosiglitazone or lifestyle intervention in adolescents with type 2 diabetes. Pediatr Diabetes. 2007;8(2):74-87.

Call for Papers

Minnesota Medicine invites contributions (essays, poetry, commentaries, clinical updates, reviews, and original research) on these topics:

Drugs
Articles due August 20

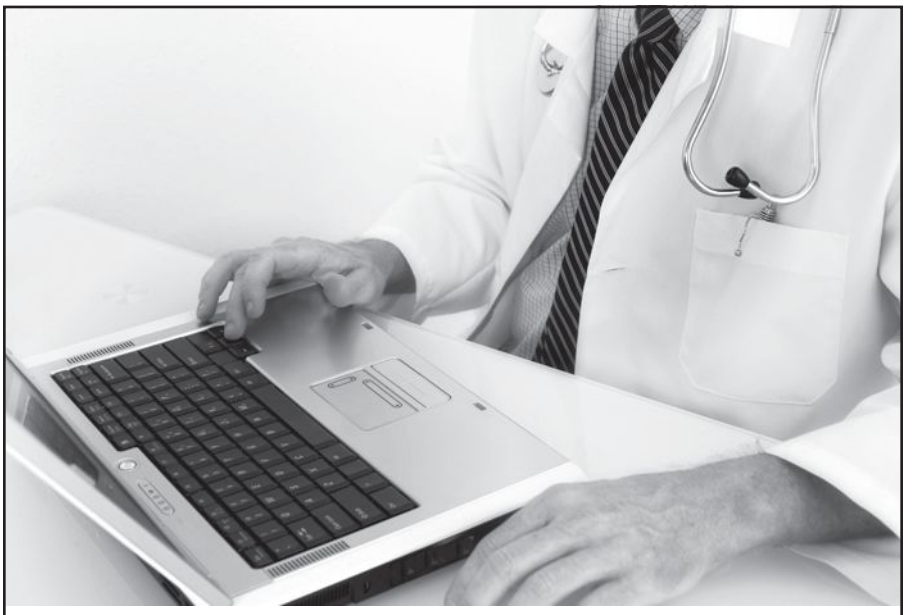
Ears, Noses, and Throats
Articles due September 20

Communication
Articles due October 20

We are also seeking articles on health care delivery and economics, professionalism, and other topics.

Manuscripts and a cover letter can be sent to cpeota@mnmed.org.

For more information, go to www.minnesotamedicine.com or call Carmen Peota at 612/362-3724.



Products and Services

The Minnesota Medical Association and Twin Cities Medical Society offer products and services tailored to the needs of physicians, their clinics, their staff, and their families. For more information on endorsed companies, call George Lohmer at 612/362-3746 or 800/342-5662, ext. 746, or visit the MMA website at www.mnmned.org.

Services and Products for Clinics

- Office Products
- Professional Liability Coverage
- Group Insurance Products
- Group Property and Casualty Insurance
- Identity Theft Protection/Legal Services
- Credentialing Services
- Physician Career Center

Services and Products for Physicians, Their Families, and Clinic Employees

- Medical Software
- Credit Card
- Individual Insurance Products
- Physician Career Center

MMA Minnesota Medical Association

Twin Cities Medical Society

An Overview of Continuous Glucose Monitoring and the Ambulatory Glucose Profile

By Roger Mazze, Ph.D., Bryan Akkerman, and Jeanne Mettner, M.A., B.E.L.S.

■ Managing diabetes is essentially a balancing act, as patients and physicians work together to control blood glucose levels to avoid the symptoms of and long-term organ damage caused by glucose variability—the often unpredictable fluctuations between levels that are too high (hyperglycemia) and too low (hypoglycemia). For years, self-monitoring of blood glucose levels has been the treatment standard. With newer technology, however, continuous blood glucose monitoring (CGM) is now possible. This article describes CGM, presents evidence about its efficacy, and outlines how visual displays of CGM data can improve clinicians' decisions about therapies.

The goal of treating patients with diabetes is helping them achieve good glycemic control. Landmark trials such as the Diabetes Control and Complications Trial and United Kingdom Prospective Diabetes Study have demonstrated that achieving good glycemic control reduces the risk of comorbidities of diabetes, particularly organ-related complications (eg, heart disease).[1,2] The definition of "good glycemic control," however, is still being debated. Also, research has shown that efforts to maintain an optimal level of control can result in increases in the rate and severity of glucose variability and hypoglycemia.[1] Recent evidence suggests that using such summary measures as hemoglobin A1c (HbA1c) and mean blood glucose may be insufficient for characterizing "good" glycemic control, as they do not take into account glucose variability, which many consider to be an important contributor to the development and progression of vascular diseases in people with diabetes.[3,4]

The association between glucose variability and microvascular/macrovascular disease appears to be that variability leads to overproduction of reactive oxygen species, which damage mitochondria and genomic DNA.[2] Furthermore, when hyperglycemia is characterized by oscillations (rapid changes in glucose level), especially during exercise, after meals, and when under stress, oxidative stress and endothelial dysfunction worsen.[4-6] Concern that abnormal glucose metabolism increases the risk of irreparable cellular damage that can lead to vascular complications has led some to suggest that glucose variability needs to be a focus of treatment.

Despite the best efforts of both patients and clinicians, glucose variability and hypoglycemia are still frequent complications of diabetes therapy. For decades, clinicians have relied on self-monitoring of blood glucose (SMBG) in order to help prevent hypoglycemic episodes. Research has demonstrated, however, that SMBG has significant flaws. In several studies, investigators compared data from blood glucose monitors that had onboard memory capability with patients' self-reported data and found underreporting (omission of undesirable values), overreporting (addition of values within target), and imprecise reporting (errors in reporting) in patients' reports.[7-10] In addition, overnight glucose values are generally not measured and thus not represented in an overall glucose profile. Moreover, the fact that each individual chooses when to mea-

sure his or her glucose level throughout the day could mean that a measurement may not always include the most useful information.

Technological innovations that have taken place during the last decade now allow for continuous glucose monitoring (CGM), which offers clinicians and patients a more comprehensive view of an individual's glucose levels. With CGM, an electrochemical sensor smaller than 5 mm in diameter is inserted into interstitial tissue, usually in the abdomen. (In most cases, the sensor can remain in place for three to seven days.[11,12])

Readings from the sensor are transmitted wirelessly to a pager-sized receiver worn by the patient. That data, when transferred to a computer for analysis, can show an individual's glucose patterns throughout the day, including at night and after meals, thereby providing information that is unbiased, complete, and verifiable.

Most CGM systems require that patients disconnect from the monitor and upload results before they can be analyzed. Newer ones allow real-time downloading of data, thus enabling clinicians to immediately intervene in response to the readings.

Advantages

The primary advantage of CGM is that it allows many patients to reduce their HbA1c level without significantly increasing the frequency or severity of hypoglycemic episodes.[13] Of the trials[14-24] that have been conducted comparing the efficacy of CGM with that of SMBG, all but one[24] demonstrated reductions in average HbA1c levels with CGM (ranging from -1.2% to -0.2%). Highlights of these studies include the following:

- In the Juvenile Diabetes Research Foundation CGM study completed in 2008,[14] which randomized 322 adults, adolescents, and children with type 1 diabetes to CGM or SMBG, CGM use reduced HbA1c levels 0.5 percentage points in the adult group. Children 8 to 14 years of age in the CGM group were more likely to lower their HbA1c level by at least 10% and achieve an HbA1c level below 7% compared with the control group. Participants in the 15- to 24-year-old CGM group experienced no significant improvements; however, only 30% of patients in this group used CGM at least six days per week, compared with 83% of the patients age 25 and older and 30% of those 8 to 14 years of age.
- Deiss and colleagues[15] randomized patients with type 1 diabetes to three months of continuous CGM, biweekly CGM, or intensive insulin treatment with SMBG. The group using CGM for three months experienced a 0.6 percentage point reduction in their average HbA1c levels compared with those doing SMBG; the group doing biweekly CGM experienced no significant improvement in their HbA1c levels.
- In the Sensor-Augmented Pump Therapy for A1c Reduction 3 (STAR-3) trial, Bergenstal and colleagues[16] randomized 156 children and 329 adults with type 1 diabetes to either initiate use of a continuous subcutaneous insulin infusion (CSII) pump with CGM or to maintain insulin injections with SMBG. After one year, the adults and children using the pump and CGM decreased their average HbA1c levels by 0.6 percentage points and 0.5 percentage points, respectively, compared with the group doing SMBG and insulin injections.
- In a study of 132 adults and children with type 1 diabetes, Raccah and team found combined use of CSII and CGM to be superior to CSII alone in reducing average HbA1c levels.[17]

Patients who use CGM have reported improved quality of life. In the late 2000s, Peyrot and colleagues[18] published results of a survey administered to 162 patients who used CGM with CSII and to 149 patients who used CSII alone. The group using CGM and CSII responded more positively than the other group to questions about convenience, acceptability of blood glucose monitoring requirements, control efficacy, diabetes worries, and overall satisfaction.[18]

Disadvantages

Despite studies that show the benefits of CGM, a number of concerns remain:

Questionable accuracy. When compared with actual glucose values measured in plasma, CGM devices can be inaccurate up to 21% of the time,[13] particularly during hypoglycemic episodes and during rapid rise and fall of plasma glucose.[25] This might be because CGM units measure glucose in the interstitial fluid, not the plasma, and glucose levels in interstitial fluid fluctuate more slowly than those in plasma. The fact that the electrochemical sensor records the glucose level at set time intervals (three minutes to five minutes) may exacerbate the difference. Keenan and team[26] reviewed commercially available, minimally invasive CGM units and found that the time lag between blood and plasma glucose levels ranged from three minutes to 12 minutes, while the processing lag with the electrochemical sensor was one minute to two minutes.

Questionable effect on severe hypoglycemia. Although recently published data have shown that CGM is associated with reduced time spent in hypoglycemia,[23] the majority of studies have failed to demonstrate that CGM is protective against hypoglycemia.[14-22] Specifically—and contrary to what was initially hypothesized—CGM does not seem to prevent severe hypoglycemic episodes; at this point, most studies have not demonstrated that hypoglycemia rates decrease significantly enough with CGM for it to be regarded as superior in lowering hypoglycemia. The inaccuracy of the devices may account for this.

Restricted use. Currently, CGM is used primarily in people with type 1 diabetes. Its application is limited in patients with type 2 diabetes, who account for 90 percent of all individuals with the disease. Research has demonstrated that use of CGM can lead to reductions in HbA1c levels among patients with type 2 diabe-

Figure 1

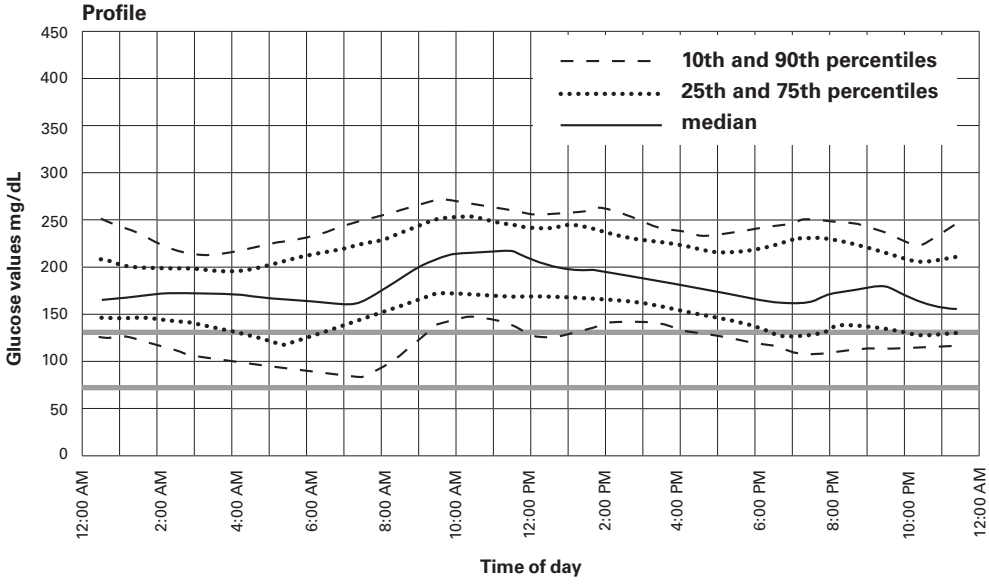
The Ambulatory Glucose Profile of a Male with Type 2 Diabetes

Study	Age	Diagnosis	Age Onset	HbA1c	Gender	Wt (lbs)	Ht (in)	BMI	SBP	DBP
All Studies	57	Type 2 diabetes	49	9.2%	M	303.40	70.40	43.0	126	67

N	Targets		Above	Within	Below		Mean	SD	Max	Min
3226	70	140	79.2%	19.9%	0.9%		186.0	54.7	323.0	24.0
Percentile	10th	25th	Median	75th	90th		Variability IQR	Stability Change Med Curve (mg/dL/hr)		
Curves	119.5	147.4	183.6	228.0	251.1		80.6	7.7		

Glucose Exposure - Area Under the Median Curve				
	Wake	Sleep	Total	
Time	7:00 AM	11:00 PM		
AUC	319.3	1214.6	4405.9	mg-24 hr/dL
Normalized	199.5	151.8	183.6	mg-hr/dL

Episode Statistics (CGM Only)	< 70	70-100	> 140
Mean Episodes per Day	0.1	1.2	1.2
Mean Duration of Episodes (Hours)	1.6	3.8	16.4
Proportion of Measured Time	0.9%	19.9%	79.2%
Total Hours of Continuous Data	537.7		
Total Days of Continuous Data	22.4		



This is the AGP of a man with type 2 diabetes who wore a CGM device for 30 days. The numeric report on the top part of the figure includes information about the patient's vitals and hemoglobin A1c values. Below this is a statistical breakdown of the patient's CGM data. The patient's glucose variability, glucose exposure, and above/within/below-target episodes were calculated. The graph reveals the patient's trends over the time period. The black line represents the median values, the dotted lines the 25th and 75th percentiles, and the dashed lines the 10th and 90th percentiles. The grey horizontal lines show the target glucose values for this patient (70 and 140 mg/dL).

tes,[27,28] but additional trials are needed to establish reliability and validity of CGM in this population.

Cost. The cost of treatment with CGM has been estimated at $4,380 per person per year compared with $550 to $2,740 when using SMBG (depending on frequency of monitoring),[29] and it is not typically covered by insurance. In the United States, the only likelihood for reimbursement is in cases where a patient with type 1 diabetes is experiencing severe, frequent hypoglycemia and is not achieving desired HbA1c values with SMBG.

Some data, however, indicate the technology can be cost-effective over the long term. In an analysis of people who significantly lowered their HbA1c level through CGM, researchers found that those patients' quality of life improved both immediately and over the long run, which translated into an "incremental cost-effectiveness ratio" of $98,679 per quality-adjusted life year in those whose HbA1c level remained at 7% or greater and $78,943 per quality-adjusted life year in those whose HbA1c level was less than 7%.[30]

The Ambulatory Glucose Profile

Although CGM technology may have flaws, it is an improvement over SMBG in that it reveals glucose variability and provides a more accurate view of glucose patterns during a given time period. Recent advances make it even easier to detect underlying glycemic patterns. The International Diabetes Center (IDC) in Minneapolis is conducting multiple ongoing clinical trials of CGM devices using newer data-analysis software. After collecting the data on glucose levels using CGM, IDC researchers connect the CGM device to a computer, download the data, and use software developed by the IDC team that can read data from any device regardless of the manufacturer to perform a statistical analysis of the data and generate a visual report for the clinician, called an ambulatory glucose profile (AGP). Rather than capturing a few isolated glucose readings, the AGP provides a comprehensive view of the patient's changing glucose levels over the period during which the device was worn, thus allowing the clinician to see patterns and adjust therapy accordingly.

Currently, the AGP software is being used to evaluate the effect of new medications and new combinations of medications and whether achieving normalized glucose patterns can lead to improved health outcomes (primarily the prevention of complications associated with diabetes). The IDC is licensing the use of its AGP software for research purposes. The hope is that by using CGM with the analysis software, researchers can more accurately observe the effects of diabetes medications on HbA1c levels and on the frequency and severity of hypoglycemia.

Figure 1 shows the AGP of a male with type 2 diabetes who wore a CGM device for 30 days. Using the AGP, we can easily interpret that this patient has poor glyce-

Figure 2

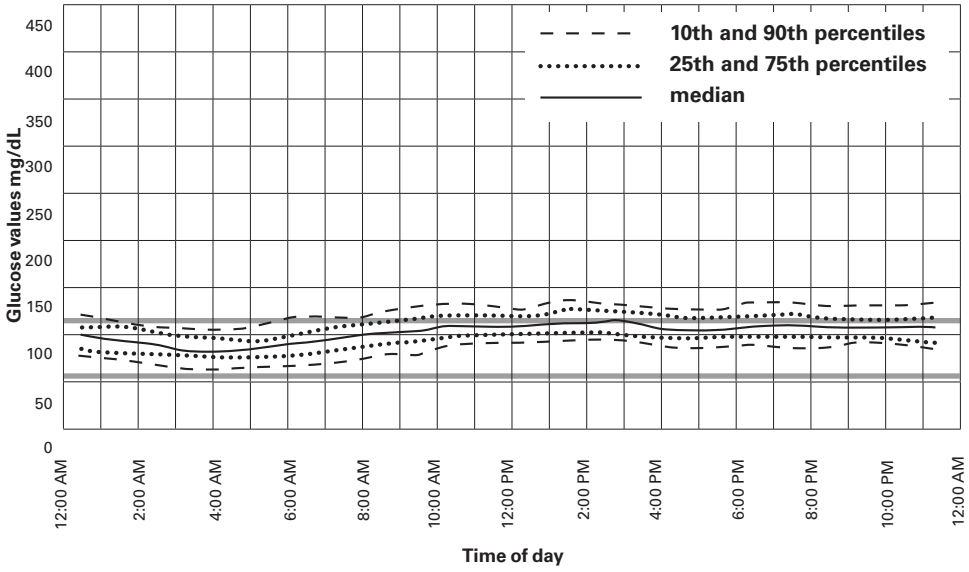
Ambulatory Glucose Profile of a Patient without Diabetes

Study	Age	Diagnosis	Age Onset	HbA1c	Gender	Wt (lbs)	Ht (in)	BMI	SBP	DBP
All Studies	58	Undefined	0	5.6%	F	166.60	65.20	27.6	104	66

N	Targets		Above	Within	Below		Mean	SD	Max	Min
3416	70	140	12.5%	86.1%	1.4%		117.3	21.6	200.0	19.0
Percentile	10th	25th	Median	75th	90th		Variability IQR	Stability Change Med Curve (mg/dL/hr)		
Curves	95.8	104.4	116.5	128.5	141.3		24.1	2.9		

Glucose Exposure - Area Under the Median Curve					Episode Statistics (CGM Only)			
	Wake	Sleep	Total			< 70	70-100	> 140
Time	7:00 AM	11:00 PM			Mean Episodes per Day	0.6	4.5	3.8
AUC	2060.3	734.8	2795.1	mg-24 hr/dL	Mean Duration of Episodes (Hours)	0.5	4.6	0.8
Normalized	128.8	91.9	116.5	mg-hr/dL	Proportion of Measured Time	1.4%	86.1%	12.5%
					Total Hours of Continuous Data	569.3		
					Total Days of Continuous Data	23.7		

Profile



This AGP shows the glucose profile of a patient without diabetes during a 30-day period of CGM wear. During this period, 3,400 data points were collected, and 86% of the values fell within the target range. The median is well within the specified glucose targets (70 and 140 mg/dL).

mic control both throughout the day and overnight despite his use of medications. The diurnal glucose patterns show that both basal and bolus insulin require adjustments. Interestingly, the patient does have periodic episodes of hypoglycemia lasting up to 100 minutes. Additionally, the AGP shows significant variability especially in the mid-morning hours. A clinician using this report could more accurately determine the proper course of treatment for this patient.

Figure 2 shows the AGP of a woman without diabetes who did CGM for 30 days. The lines are smooth compared with those of the patient with type 2 diabetes, indicating relatively greater stability throughout the day.

Interestingly, with CGM we see that even patients without diabetes can have higher and lower glucose levels. The AGP of the person without diabetes provides a good illustration of postprandial rises and overnight dips in blood glucose. The AGP can even be used by providers caring for patients without diabetes so that they can offer advice about diet based on the data gathered.

Conclusion

Treatment decisions are best made using accurate and comprehensive data. Many researchers now believe that CGM can provide such data on patients with diabetes, as CGM provides a more comprehensive view of glucose levels than does self-monitoring. Research has demonstrated that use of the technology can help reduce HbA1c levels without increasing the severity or frequency of hypoglycemic episodes. However, at this point, CGM has not yet consistently been shown to mitigate severe hypoglycemia. Innovations such as the AGP software and computerized treatment algorithms show promise for advancing the therapeutic benefits of CGM while protecting patients from unpredictable, severe hypoglycemia. **MM**

Roger Mazze is head of the World Health Organization Collaborating Center at the International Diabetes Center and Mayo Clinic and chief academic officer at the International Diabetes Center in St. Louis Park. Bryan Akkerman is a health informatics specialist at the International Diabetes Center's World Health Organization Technology Lab. Jeanne Mettner is a medical writer and the principal of Minneapolis-based Planetary Ink Editorial Consulting.

REFERENCES

1. The Diabetes Control and Complications Trial Research Group. The effect of intensive treatment of diabetes on the development and progression of long-term complications in insulin-dependent diabetes mellitus. N Engl J Med. 1993;329(14):977-86.
2. UK Prospective Diabetes Study (UKPDS) Group. Intensive blood-glucose control with sulphonylureas or insulin compared with conventional treatment and risk of complications in patients with type 2 diabetes (UKPDS 33). Lancet. 1998;352(9131):837-53.
3. Zaccardi F, Pitocco D, Ghirlanda G. Glycemic risk factors of diabetic vascular complications: the role of glycemic variability. Diabetes Metab Res Rev. 2009;25(3):199-207.
4. Brownlee M, Hirsch IB. Glycemic variability: a hemoglobin A1c-independent risk factor for diabetic complications. JAMA. 2006;295(14):1681-7.
5. Humpert PM. Oxidative stress and glucose metabolism—is there a need to revisit effects of insulin treatment? Diabetologia. 2010;53(3):403-5.
6. Ceriello A, Esposito K, Piconi L, et al. Oscillating glucose is more deleterious to endothelial function and oxidative stress than mean glucose in normal and type 2 diabetic patients. Diabetes. 2008;57(5):1349-54.
7. Shamoon H, Mazze R, Pasmantier R, Lucido D, Murphy JA. Assessment of long-term glycemia in type 1 diabetes using multiple blood glucose values

stored in a memory-containing reflectometer. Am J Med. 1986;80(6):1086-92.
8. Langer O, Mazze R. The relationship between glycosylated hemoglobin and verified self-monitored blood glucose among pregnant and non-pregnant women with diabetes. Pract Diabetes. 1987; 4(1):32-3.
9. Langer O, Mazze R. The relationship between large-for-gestational-age infants and glycemic control in women with gestational diabetes. Am J Obstet Gynecol. 1988;159(6):1478-83.
10. Zimmet P, Lang A, Mazze R, Endersbee R. Computer-based patient monitoring systems: use in research and clinical practice. Diabetes Care. 1988;11(Suppl 1):62-6.
11. Mazze RS, Strock E, Wesley D, Borgman S, Morgan B, Bergenstal R, Cuddihy R. Characterizing glucose exposure for individuals with normal glucose tolerance using continuous glucose monitoring and ambulatory glucose profile analysis. Diabetes Technol Ther. 2008;10(3):149-59.
12. Goldstein DE, Little RR, Lorenz RA, et al. Tests of glycemia in diabetes. Diabetes Care. 2004;27(7):1761-73.
13. Hermanides J, Phillip M, DeVries JH. Current application of continuous glucose monitoring in the treatment of diabetes: pros and cons. Diabetes Care. 2011;34(Suppl 2):S197-201.
14. Juvenile Diabetes Research Foundation Continuous Glucose Monitoring Study Group, Tamborlane WV, Beck RW, Bode BW, et al. Continous glucose monitoring and intensive treament of type 1 diabetes. N Engl J Med. 2008;359(14):1464-76.
15. Deiss D, Bolinder J, Riveline JP, et al. Improved glycemic control in poorly controlled patients with type 1 diabetes using real-time continuous glucose monitoring. Diabetes Care. 2006;29(12):2730-2.
16. Bergenstal RM, Tamborlane WV, Ahmann A, et al. Effectiveness of sensor-augmented insulin-pump therapy in type 1 diabetes. N Engl J Med. 2010;363(4):311-20.
17. Raccah D, Sulmont V, Reznik Y, et al. Incremental value of continuous glucose monitoring when starting pump therapy in patients with poorly controlled type 1 diabetes: the RealTrend study. Diabetes Care. 2009;32(12):2245-50.
18. Peyrot M, Rubin RR. Patient-reported outcomes for an integrated real-time continous glucose monitoring/insulin pump system. Diabetes Technol Ther. 2009;11(1):57-62.
19. Hirsch IB, Abelseth J, Bode BW, et al. Sensor-augmented insulin pump therapy: results of the first randomized treat-to-target study. Diabetes Technol Ther. 2008;10(5):377-83.
20. Juvenile Diabetes Research Foundation Continuous Glucose Monitoring Study Group. Effectiveness of continuous glucose monitoring in a clinical care environment: evidence from the Juvenile Diabetes Research Foundation continous glucose monitoring trial. Diabetes Care. 2010;33(1):17-22.
21. O'Connell MA, Donath S, O'Neal DN, et al. Glycaemic impact of patient-led use of sensor-guided pump therapy in type 1 diabetes: a randomized controlled trial. Diabetologia. 2009;52(7):1250-7.
22. Hermanides J, Norgaard K, Bruttomesso D, et al. Sensor-augmented pump therapy lowers HbA1c in suboptimally controlled Type 1 diabetes; a randomized controlled trial. Diabet Med. 4 February 2011. [Epub ahead of print]
23. Battelino T, Phillip M, Bratina N, et al. Effect of continuous glucose monitoring on hypoglycemia in type 1 diabetes. Diabetes Care. 2011;34(4):795-800.
24. Cooke D, Hurel SJ, Casbard A, et al. Randomized controlled trial to assess the impact of continuous glucose monitoring of HbA(1c) in insulin-treated diabetes (MITRE Study). Diabet Med. 2009;26(5):540-7.
25. Wentholt IM, Hoekstra JB, DeVries JH. Continuous glucose monitors: the long-awaited watch dogs? Diabetes Technol Ther. 2007; 9(5):399-409.
26. Keenan DB, Mastrototaro JJ, Voskanyan G, Steil GM. Delays in minimally invasive continuous glucose monitoring devices: a review of current technology. J Diabetes Sci Technol. 2009;3(5):1207-14.
27. Yoo HJ, An HG, Park SY, et al. Use of a real time continuous glucose monitoring system as a motivational device for poorly controlled type 2 diabetes. Diabetes Res Clin Pract. 2008;82(1):73-9.
28. Cosson E, Hamo-Tchatchouang E, Dufaitre-Patouraux L, et al. Multicentre, randomised, controlled study of the impact of continuous sub-cutaneous glucose monitoring (GlucoDay) on glycaemic control in type 1 and type 2 diabetes patients. Diabetes Metab. 2009;35(4):312-8.
29. Pham M. Medtronic. Diabetes: sizing the market for real-time, continuous blood glucose monitors from MDT, DXCM, and ABT. 2006. Available at www.research.hsbc.com/midas/Res/RDV?p=pdf&key=ate2b8rygn&name=127057.PDF. Accessed July 13, 2011.
30. Huang ES, O'Grady M, Basu A, et al. The cost-effectiveness of continuous glucose monitoring in type 1 diabetes. Diabetes Care. 2010;33(6):1269-74.

The Minnesota Partnership to Conquer Diabetes

By Elizabeth R. Seaquist, M.D., and Victor Montori, M.D.

■ The University of Minnesota and Mayo Clinic have launched a 10-year effort called the Decade of Discovery: A Minnesota Partnership to Conquer Diabetes. The partnership harnesses the extensive research expertise at the two institutions in an effort to make discoveries that will transform prevention, management, and treatment of diabetes—a disease that affects one in three people in the state. The ultimate goal is to find a cure. This article describes the vision for this undertaking as well as research that might one day lead to a cure.

According to the Minnesota Department of Health, one in three adults in the state has diabetes or prediabetes (impaired glucose tolerance that has a high likelihood of turning into diabetes in the future). Diabetes is the sixth leading cause of death in Minnesota, accounting for 17,485 years of potential life lost. It also has a tremendous impact on the quality of life of those who have the disease, as nearly one in two Minnesotans with diabetes report being limited in terms of their activity. Overall, diabetes costs the state $2.68 billion annually; about $1 billion of that is the result of lost productivity.

To reduce the burden of diabetes in our state, implementation of proven strategies for managing the disease as well as discovery of new methods to prevent, treat, and cure it are needed. During the past year, the University of Minnesota and Mayo Clinic have made a commitment to do just that. Through an effort called the Decade of Discovery: A Minnesota Partnership to Conquer Diabetes, the two institutions have set a goal of preventing, optimally treating, and ultimately curing type 1 and type 2 diabetes by 2020. Led by Aaron Friedman, M.D., senior vice president of health sciences and dean of the Medical School at the University of Minnesota, and Robert Rizza, M.D., executive dean for research at Mayo Clinic, the partnership is an attempt to harness expertise at the two institutions and elsewhere in the state in order to achieve this ambitious goal.

How the Partnership Came to Be

This collaborative is an offshoot of the Minnesota Partnership for Biotechnology and Medical Genomics, a partnership between Mayo and the university that was formed in 2003 with support from the state of Minnesota. The purpose was to position Minnesota as a world leader in biotechnology and biomedical research. The partnership has become a globally recognized model of innovation in the biomedical field. Since its inception, Minnesota has invested more than $90 million in the partnership. Those funds have been used to recruit new researchers and fund 45 research grants and 14 infrastructure improvement projects. As a result of that investment, more than $100 million have returned to the state in the form of grants from the National Institutes of Health, philanthropic contributions, and private industry investment. Projects supported by partnership grants have focused on understanding, treating, and preventing cancer, diabetes, heart disease,

multiple sclerosis, epilepsy, and other conditions.

In 2007, Gov. Tim Pawlenty challenged the two institutions to raise the bar on what they could do through the partnership by tackling a disease of importance to Minnesotans. After assessing their past work, their research strengths, and the work being done by other potential partners in the state, leaders from both the university and Mayo identified diabetes as the disease for which they collectively had the best chance of producing a major medical breakthrough in the next decade. The institutions were leaders in islet transplantation, regenerative medicine and stem cell biology, the pathogenesis of insulin resistance and obesity, diabetes prevention, diabetes care quality improvement, and the effect of diabetes on the brain, kidney, and cardiovascular system. In addition, together they had received more than $55 million in research funding from the National Institutes of Health to study diabetes, and the university had received a $40 million gift from the Schulze Family Foundation to cure type 1 diabetes.

Preventing and Curing the Disease

In October 2010, the university and Mayo launched the Decade of Discovery. The initiative will involve more than 150 researchers at the two institutions as well as other researchers and health care providers from around the state. Their work will focus on two core areas: 1) prevention and care delivery and 2) treatment and cure. Although both the university and Mayo have resources in place to support ongoing diabetes research in the form of philanthropic gifts, industry contracts, and grants from the National Institutes of Health and other governmental agencies and private foundations, expanding their efforts will require additional resources. Plans are underway to seek new funding from the state as well as from private donors and industry partners.

Prevention and care delivery. The prevention and care delivery portion of the initiative will focus on public health and health services delivery research led by Robert Jeffery, Ph.D., professor of epidemiology and community health and director of the Obesity Prevention Center at the University of Minnesota, and Nilay Shah, Ph.D., an assistant professor in the department of health sciences research at Mayo Clinic. As an expert in obesity and diabetes prevention, Jeffery has started taking a census of existing prevention programs in the state to identify potential partners and their areas of interest. Shah, an expert in population health, is compiling data on health status, disease control, health care usage, investments, and programs by county to create a map that can be used to help others make informed decisions when planning and executing interventions related to diabetes. In addition, this information will provide the necessary baseline data on the effectiveness of projects designed by Decade of Discovery researchers and their partners related to preventing and treating diabetes. Over time, the intent is to involve all stakeholders in preventing diabetes and providing optimal care to people who have the disease in Minnesota.

Treatment and cure. As for treating and/or curing diabetes, one emphasis will be exploring new approaches to replacing insulin-producing beta cells that can build upon the already successful islet transplantation program at the university. This work will be led by David Bernlohr, Ph.D., chair of the department of biochemistry, molecular biology, and biophysics at the University of Minnesota, and Stephen Russell, M.D., Ph.D., professor of molecular medicine at Mayo Clinic. They are now working with cell biologists, developmental and stem cell biologists, immunologists, clinical researchers, and experts in islet transplantation from both institutions to identify areas where there is synergy and potential for growth. As resources become available, new projects will grow out of these collaborative efforts, and new researchers will be attracted to the state.

Another aim of the treatment/cure effort is to build new relationships between the researchers investigating the pathogenesis of diabetes and obesity and their complications and the scientists with expertise in drug development. For example, Bernlohr is internationally known for his work on the relationship between obesity and insulin resistance, two major risk factors for the development of type 2 diabetes. He has identified new molecules that perturb cellular pathways involved in insulin resistance. With the support of the Decade of Discovery partnership, he can work with medicinal chemists in the College of Pharmacy's Institute for Therapeutics Discovery and Development to develop a new therapeutic approach.

Achieving the Goal

During this first year, our aim is to develop the relationships necessary to complete the prevention and care delivery census and diabetes map project, and to develop the infrastructure necessary to support new research in islet cell biology and novel drug development. The time it takes to achieve our ultimate goal of defeating diabetes will depend on the resources we receive and the creativity and hard work of researchers.

We estimate that an investment of $250 million to $350 million over 10 years will be necessary to build more robust research capabilities, advance the IT infrastructure, implement populationwide changes, and fully integrate recognized best practices into clinical practice. These funds will be sought from the state, the federal government, industry, and private donors. Minnesota researchers are already world leaders in diabetes research. With the additional investment, focus, and collaboration brought by the Decade of Discovery, we believe we can conquer diabetes in the coming decade. **MM**

Elizabeth Seaquist is the Pennock Family Chair in Diabetes Research at the University of Minnesota. Victor Montori is a professor of medicine at Mayo Clinic. Both serve as operation leads for the Decade of Discovery initiative.

The Minnesota Diabetes Plan 2015

Stemming the Tide on an Epidemic and Improving Patient Care

By Audrey Weymiller, Ph.D., C.N.P., Gregg Simonson, Ph.D., Mark Liebow, M.D., Kim Goodwin, M.P.A., and Gretchen Taylor, M.P.H., R.D.

■ The Minnesota Diabetes Steering Committee, a group of experts in diabetes care and prevention from around the state, in collaboration with the Minnesota Department of Health, is working to slow the incidence of diabetes and improve the care of Minnesotans who have the disease. The steering committee has developed a new five-year diabetes plan for the state that identifies nine areas around which stakeholders will focus energy and take action. This article describes that plan.

The news about the prevalence of diabetes in this country is sobering. One in three Americans born in the year 2000 will develop some form of the disease during their lifetime if current trends continue. For black and Hispanic children, the risk of developing diabetes is nearly one in two.[1] The prevalence of diabetes in the adult population in the United States is expected to increase 165% by 2050 (it rose 49% between 1990 and 2000). Already, 1.5 million adults (more than one in three) in Minnesota have diabetes or prediabetes, according to Minnesota Department of Health estimates.[2] Every year, 20,000 Minnesotans are diagnosed with the disease.

The impact of diabetes is tremendous. It is the sixth leading cause of death in Minnesota, and those living with the disease have a lower quality of life. Because diabetes can affect nearly every organ system, people with diabetes have higher rates of heart disease and stroke, depression, arthritis, blindness, kidney disease, and even infectious diseases. It is the leading cause of blindness, renal failure, and nontraumatic amputation in Minnesota.[2]

In addition to its toll on individual health, diabetes has an economic impact. People with the disease can expect to earn one-third less in their lifetime as a result of having it.[3] Because of often-preventable sick days and medical complications associated with diabetes, society as a whole also feels the effect, as it pays the cost of lost productivity and of treatment for a large number of people who have the disease. The American Diabetes Association estimates the total cost of diabetes in 2007 was $174 billion.[4] In Minnesota, diabetes costs an estimated $2.68 billion per year; about $1 billion of that is the result of lost productivity.[2]

We've known for some time that the impact of diabetes is distributed unevenly across ethnic, socioeconomic, and age groups. Those most affected by premature onset of diabetes and its complications include certain ethnic minorities, people with lower socioeconomic status, and older adults.[5]

Various social determinants of health have an effect on both the prevalence and treatment of the disease. A recent study showed the disparity in diabetes-related mortality across education levels grew from the late 1980s to 2005 overall and among men, women, blacks, whites, and Hispanics.[6] MN Community Measurement data show that Minnesotans who have government-sponsored health insurance do not receive the same quality of diabetes care as patients with private insurance when treated by the same health care providers.[7]

Diabetes does not have to exact this great a toll. We know type 2 diabetes can be delayed or prevented if individuals make modest lifestyle changes. In the Diabetes Prevention Program, a major multicenter clinical research study, conversion to diabetes was reduced by 58% over a three-year period among

people with prediabetes who achieved modest weight loss (7% of body weight) and increased their physical activity to 150 minutes a week. Study participants 60 years of age and older reduced their risk by 71%.[8] That study also showed that taking oral metformin can delay the onset of type 2 diabetes, although it is not as effective as making lifestyle changes. Participants in the group that received metformin reduced their risk of developing diabetes by 31% as compared with the group that received a placebo.[8]

In addition to studies showing that type 2 diabetes can be prevented, evidence about how best to help patients manage their disease is growing. Yet, although many aspects of optimal diabetes care have been defined, consistent high-quality diabetes care is not always delivered. In Minnesota, for example, only 25% of patients on average achieve the five goals that have the greatest impact on decreasing cardiovascular complications associated with diabetes.[7] These include having blood pressure less than 140/90 mmHg, a low-density lipoprotein level of less than 100 mg/dL, a hemoglobin A1c less than 8, not smoking, and taking a low dose of aspirin, if appropriate.[9] Indeed, the potential to make improvements in both the prevention and management of the disease is great.[10]

Minnesota Diabetes Plan 2015

Preventing diabetes as well as improving treatment for people who have the disease are the goals of the Minnesota Department of Health's diabetes program. In 1981, the Department of Health convened the Minnesota Diabetes Steering Committee to advise the diabetes program. Its members represented medical, professional, and volunteer groups with a strong interest in diabetes. Since then, the committee has provided the vision and direction for reducing the impact of diabetes in the state and has used its influence to advocate for action and policy change to make that happen.

One mechanism the steering committee has used to accomplish its mission has been the Minnesota Diabetes Plan. It updates the plan every five to 10 years. Among the accomplishments that can be attributed to the state plan are the standardization of diabetes care and related quality measures used in the state, the development of a diabetes guide for long-term care settings, institution of an annual health disparities conference for safety-net providers, reversal of the loss of MinnesotaCare coverage for people with diabetes, and dramatic reductions in the rates of certain complications such as lower-extremity amputations. The state's 2000 plan identified the need for adequate insurance coverage for people with diabetes. Subsequent advocacy efforts resulted in passage of the Diabetes Cost Reduction Act in Minnesota. This legislation standardized coverage for people with diabetes and was later replicated in 46 states.

Generally, the state's diabetes plan has articulated a high-level vision and a blueprint for achieving it. This year, the Minnesota Diabetes Steering Committee sought to address the epidemic of diabetes in a more concrete and comprehensive way. Committee members first identified a long list of potential areas where the diabetes community in Minnesota could expend dollars and effort, then winnowed that list down to the nine they felt might be the most realistic and effective (see "2015 Focus Areas"). Teams are now being formed to work on each of these.

A Role for Physicians

Physicians have always played a leadership role on the Minnesota Diabetes Steering Committee and in designing and implementing the state's diabetes plan. Physicians again participated in the development of the Minnesota Diabetes Plan 2015. The committee's physician members brought their unique perspective to the table as they discussed areas of need and set priorities. Among the concerns they raised were the need to identify the components of diabetes care that are best done in medical homes, improve hospital discharge summaries for people with diabetes, improve communication between primary care providers and subspecial-

2015 Focus Areas

The Minnesota Diabetes Plan 2015 identifies the following areas around which coordinated action will be needed in the coming years:

1. Increasing access to clinic and hospital care, especially among people with low incomes and populations of color;
2. Increasing accountability among providers and health systems for identifying and referring patients to community-based health resources;
3. Increasing care coordination between clinics and hospitals, between primary care providers and specialists, and between primary care and community-based health resources;
4. Developing and/or increasing the availability of community health resources for diabetes prevention and management for adults older than 60, new immigrants, and people of color;
5. Developing messages and methods to increase patients' knowledge and skills in diabetes self-management;
6. Increasing the number of organizations offering lifestyle-related diabetes prevention programs statewide, specifically to underserved populations;
7. Improving healthy behaviors and achieving diabetes self-management goals for women with or at risk for gestational diabetes;
8. Incorporating healthful eating and nutrition education into school curricula and establishing policies in child-care and school settings; and
9. Increasing access to affordable and healthful food in underserved communities.

ists when they share the care of a patient with diabetes, and develop comprehensive up-to-date lists of community resources for people with prediabetes and diabetes. Those issues were incorporated into the plan. Physicians' voices are now needed as groups are forming to determine how to best make progress in each of the nine areas.

The Minnesota Diabetes Plan 2015 urges everyone in the state to play a part in reducing the burden of diabetes, as achieving this goal will require a unified effort on many fronts. Physicians, as practitioners, researchers, community leaders, and educators, are encouraged to get involved in one of the nine action groups. To do so, contact Minnesota Diabetes Steering Committee Chair Audrey Weymiller, Ph.D., at weymiller.audrey@mayo.edu or Gretchen Taylor, diabetes program supervisor for the Minnesota Department of Health at gretchen.taylor@state.mn.us or 651/201-5390. **MM**

Audrey Weymiller is chair of the Minnesota Diabetes Steering Committee and a clinical nurse researcher and nurse practitioner at Mayo Clinic. Gregg Simonson is immediate past-chair of the steering committee and leads professional and industry educational programs at the International Diabetes Center. Mark Liebow is a consultant in internal medicine at Mayo Clinic. Kim Goodwin is plan coordinator and Gretchen Taylor is supervisor for the diabetes program at the Minnesota Department of Health.

REFERENCES

1. Narayan KM, Boyle JP, Thompson TJ, Sorensen SW, Williamson DF. Lifetime Risk for Diabetes Mellitus in the United States. JAMA. 2003;290(14):1884-90.
2. Minnesota Department of Health. The Diabetes in Minnesota Fact Sheet. Diabetes and Prediabetes in Minnesota, 2010. Available at: http://www.health.state.mn.us/diabetes/diabetesinminnesota/factsheet.html. Accessed July 18, 2011.
3. NG YC,Jacobs P, Johnson JA. Productivity losses associated with diabetes in the US. Diabetes Care. 2001;24(2):257-61.
4. American Diabetes Association. Economic costs of diabetes in the U.S. in 2007. Diabetes Care. 2008;31(3), 596-615.
5. Centers for Disease Control and prevention, Diabetes Data and Trends. Available at: http://apps.nccd.cdc.gov/ddtstrs/. Accessed July 18, 2011.
6. Miech RA, Kim J, McConnell C, Hamman RF. A growing disparity in diabetes-related mortality U.S. trends, 1989-2005. Am J Prev Med. 2009 Feb;36(2):126-32.
7. MN Community Measurement. 2009_Health_Care_Disparities_Report. Available at: http://mncm.org/site/upload/files/FINAL_2009_Health_Care_Disparities_Report_4.16.pdf. Accessed July 18, 2011.
8. Knowler WC, Barrett-Connor E, Fowler SE, et al. Diabetes Prevention Program Research Group. Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. N Engl J Med. 2002;346(6):393-403.
9. The D5: The Five Goals for Living Well with Diabetes. Available at: http://www.thed5.org/. Accessed July 18, 2011.
10. Agency for Healthcare Research and Quality. Making the Case for Diabetes Quality Improvement. Available at: www.ahrq.gov/qual/diabqual/diabqguide-mod1.htm. Accessed July 18, 2011.

Minnesota Diabetes Steering Committee Leadership Team

Audrey Weymiller, Ph.D., CNP, Mayo Clinic, chair

Gregg Simonson, Ph.D., International Diabetes Center, immediate past chair

Pat Adams, M.P.H., R.N., Office of Statewide Health Improvement Initiatives, Minnesota Department of Health

Robert Albee, A Partnership of Diabetics

Macaran A. Baird, M.D., Department of Family Medicine and Community Health, University of Minnesota

Carol Lange, M.P.H., Department of Family Medicine and Community Health, University of Minnesota

Don Bishop, Ph.D., Center for Health Promotion, Minnesota Department of Health

Marit Hansen, Novo Nordisk, Inc.

Sheila Kiscaden, Decade of Discovery: A Minnesota Partnership to Conquer Diabetes

Carol Manchester, M.S.N., A.P.R.N., A.C.N.S., University of Minnesota Medical Center

Jim McGowan, American Diabetes Association

Connie Norman, Native American Community Clinic

Teresa L. Pearson, M.S., R.N., Halleland Habicht Health Care Consulting, LLC

Rosemarie Rodriguez-Hager, Office of Minority and Multicultural Health, Minnesota Department of Health

Chris Schaeffer, American Diabetes Association–Minnesota

Bill Tendle, Southside Community Health Services

Sarah M. Westberg, Pharm.D., Pharmaceutical Care and Health Systems, University of Minnesota College of Pharmacy

Staff support provided by Gretchen Taylor, Kim Goodwin, Rita Mays, and Laurel Reger of the Minnesota Diabetes Program, Minnesota Department of Health.

The Unknown Suffering

By Zubin Agarwal

To remain strong
Is the challenge of our profession
Every day we walk through a valley of suffering
The addiction psychiatrist,
The radiation oncologist,
The cardiothoracic surgeon.

How does one overcome
Daily challenges to morale, esteem, integrity?
Uncertainty in the face of death
And certainty in death
How does one retain the strength to care
For patients, their families and loved ones?

We
The relievers of human suffering
Magicians of death and dying
Who heals the healers?
Who licks our wounds?
We have become so entranced by the Oath
That the saviors of health have become martyrs.

Finding relief from the daily turmoil of our profession
Is to achieve peace with failure
To discover reward in success
Some may find relief in writing, artistic expression
To remain strong
Is the challenge of our profession.

Zubin Agarwal is a student at Mayo Medical School.