

# DIABETES MANAGEMENT™

*The Complete Diabetes Disease State Management Resource*

## INSIDE

- **Progressive thinking:**  
Ralph Hall, MD, points to a paradigm shift in diabetes management . . . . . 63
- **Treatment by stages:**  
Adjusting medication keeps diabetes in control . . . . . 63
- **Patient privacy:**  
Will it hinder disease management? . . . . . 65
- **Youngest patients:** There are risks of hypoglycemic reactions in babies . . . . . 68
- **Complications:** Black patients at higher risk . . . 69
- **Triad troubles:**  
Diabetes, sleep apnea, obesity conspire on stroke risk . . . . . 71
- **Inserts:**  
— Proposed curriculum to train future doctors on diabetes treatment  
— Treatment algorithm

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## How prepared will future doctors be to treat diabetic patients?

*From training to continuing education, diabetes should be a priority*

**A**re medical students getting enough training to be able to treat their future diabetic patients successfully? Today's doctors have mixed opinions.

"As a group, we have dramatically lagged behind the research providing the tools to assist us in improving our patients' lives. Why?" asked **Irl B. Hirsch, MD**, editor of *Clinical Diabetes*, in an editorial in the April issue.

Hirsch, an endocrinologist, associate professor of medicine at the University of Washington, and medical director of the Diabetes Care Center at the University of Washington Medical Center in Seattle, answers his own question by placing the blame on what he calls woefully inadequate physician education in medical schools and in residency programs.

"It's a giant mess," he says. "Everybody has different thoughts on the issue. Nobody knows how to fix it, and some even say there's no problem."

He notes that medical students at the University of Washington, which is the state medical school for five northwest states, receive one afternoon of didactic diabetes education, which includes a two-hour lecture and small discussion groups that review various treatment issues relating to diabetes drugs, hypoglycemia, and complications. The university's six-session elective endocrine course attracted less than a quarter of the students last year, Hirsch says.

## KEY POINTS

- Some diabetes specialists criticize the quality and quantity of diabetes-related medical school training.
- Some medical schools spend as little as half a day directly addressing diabetes diagnosis and treatment.
- The Society of General Internal Medicine and Clerkship Directors in Internal Medicine recommend using their curriculum to ensure new doctors are adequately prepared to diagnose and treat diabetic patients.

During residency, he says, primary care doctors tend to focus largely on inpatient treatment and have little exposure to formulating treatment plans and working with diabetics as outpatients.

The problem of not getting enough training in diabetes care proliferates in practice, says Hirsch. "The reality is that once they get out of training, they tend to stay on the same track with medications and treatment programs."

While he recognizes how difficult it is for primary care physicians to stay current in the rapidly changing world of diabetes management, Hirsch says doctors are doing their patients a disservice.

He also takes aim at managed care for exerting time pressure on doctors. "Real diabetes management has almost become academic since they just don't have time," Hirsch says. "They barely have time to write scrips, much less look at feet, eyes and take blood pressure."

"I think I have it easy compared to the primary care people," he adds. "I only have to be on the cutting edge of one disease. I don't think I could do it if I had to do that with ten diseases."

However, Hirsch compliments some managed care organizations for "doing a better job than most of us in keeping current."

While many doctors agree the training can be improved, the problems may not be as severe as Hirsch says.

"I don't doubt we could do a better job training doctors," says **Stephen Spann**, MD, medical director for diabetes and professor and chairman of family and community medicine at Baylor University in Houston. But he defends curricula like Baylor's that focus on teaching basic science in medical school, holding off on specific diabetes care until residency programs. "A lot learning takes place in their medical rotation in the hospital," he says.

Spann notes residency programs are designed to train doctors in the day-to-day reality of managing chronic diseases like diabetes. "Our primary care residents follow diabetic patients for three years," he says.

As chairman of the American Academy of

Family Physicians' annual clinical focus training, Spann promoted a diabetes training program for family practitioners, designed to help them make their skills "state of the art" and to provide them with the latest patient education materials.

### ***Physicians need to be teachers***

"We also need to do a better job of teaching our patients," he says. "Family doctors can provide excellent care for the vast majority of diabetics," says Spann. "But we must be up-to-date and be aware of new drugs, the advantages of tight control, and the risks for minorities."

Medical schools are taking action, says **Eric Bass**, MD, associate professor of medicine at Johns Hopkins University School of Medicine. Bass participated in formulating a core medical clerkship curriculum guide for the Washington, DC-based Society of General Internal Medicine (SGIM) and Clerkship Directors in Internal Medicine (CDIM). (See information on curriculum components, inserted in this issue.)

"Diabetes is a high-priority area, and it needs to be a core part of the curriculum," Bass says. "It's important that students and house staff see diabetic patients in inpatient and outpatient settings." Several medical schools are using the guide to help them further develop their curricula, he adds.

But Hirsch contends much needs to be done to change the way people think about treating diabetic patients.

In his editorial, he concluded, "We currently tolerate poor diabetes care by our colleagues . . . As a group, we need to catch up with all of the new diabetes-related research. Diabetes also needs to be a greater priority in our training programs. Otherwise we lose the opportunity to translate research into clinical practice and progress cannot continue."

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## **COMING IN FUTURE MONTHS**

■ Highlights from the ADA's 59th Scientific Sessions

■ Hypertension education: A neglected part of diabetes management

■ Management strategies for primary care physicians

■ Prioritizing and managing comorbidities and complications

■ Age and diabetes: More on pediatric, teen, adult, and geriatric issues

# Changing attitudes: Diabetes is progressive

*The specifics are left to the individual physician*

*(Editor's Note: The following is a commentary from Diabetes Management's consulting editor, Ralph Hall, MD, emeritus professor of medicine, School of Medicine, University of Missouri-Kansas City. Hall will be presenting a session on this subject at the American Diabetes Association scientific sessions in San Diego in June.)*

The UKPDS (United Kingdom Prospective Diabetes Study) dramatically demonstrated the progressive nature of Type 2 diabetes. Patients in each arm of this 10-year-plus study had gradually increasing HbA<sub>1c</sub> determinations, and the vast majority of patients who started out on monotherapy eventually required another oral drug or insulin. Many patients had evidence of beta cell failure and required insulin.

In truth, diabetes is almost inevitably a progressive disease in those who are not managed vigorously.

The earliest phase of Type 2 diabetes in many patients who are obese is manifested by insulin resistance with blood glucose levels that don't quite reach levels that are considered diagnostic of diabetes.

The early phase of insulin release may be blunted, and the post-prandial blood glucose rises despite increased release of insulin by the beta cell. At this time, diet and exercise may suffice to bring glucose levels back into the normal range.

## ***Diet and exercise still important***

In fact, diet and vigorous exercise are still the best forms of treatment at every stage of the disease. However, most patients are not able to lose enough weight or exercise adequately and as a result, will eventually need oral therapy or insulin. Traditionally, monotherapy with a sulfonylurea has been started at this point.

Now, however, there are a number of alternative oral drugs that lower blood glucose by a variety of mechanisms other than stimulating the beta cells to secrete insulin.

There are many questions left for the individual physician to answer:

1. Is there a particular agent that will lower the blood glucose and prolong the life of the beta cell either by decreasing insulin resistance or preventing further weight gain in this patient?
2. Further, will this approach lower the number of cardiovascular complications?
3. Some investigators believe that metformin is the drug of choice in overweight patients when monotherapy is started. What then is the next choice if another agent is eventually needed?
4. Do we now have any data to support a choice or are we left with a decision based on what therapy is likely to lead to the best compliance, i.e. a pill that has to be taken once a day or several times per day. Or will we simply choose on the basis of cost?

There is preliminary evidence that the various stages can be prolonged based on whether patients maintain good control on metformin and tolazamide.

If clinicians control the blood lipids, hypertension and other risk factors, both macrovascular and microvascular disease can be markedly reduced. ■

## **New paradigm: Treat diabetes by stage**

*Programs target caregivers as much as patients*

Clinicians are beginning to think of Type 2 diabetes as a progressive or even degenerative disease. And they are discovering that by aggressively managing diabetes and acting quickly to adjust medications when necessary, they can slow the progression of the disease and delay the onset of complications.

The newest thinking is far from fatalistic, although all recent studies point to a grim prognosis for patients who fail to maintain tight glycemic control.

"In many patients, all strategies will fail over time," says **Mitchell Hamburg**, MD, FACE, associate clinical professor of medicine at the University of Missouri-Kansas City Medical School and consulting physician at St. Luke's

## KEY POINTS

- Diabetes is increasingly being seen as a progressive disease as beta cells “wear out.”
- Physicians need to regularly adjust medications to gain optimum glycemic control.
- Most diabetics will eventually need insulin to achieve control.

Hospital in Kansas City, MO.

Hamburg is an advocate of a metformin and sulfonylurea combination therapy, which “may be the best at all stages of the disease.”

“I wouldn’t call diabetes a degenerative disease,” he says. “It’s a disease with two facets — diminished beta cell function and insulin resistance. Over time, the beta cells will fail and insulin will become necessary.”

“Whatever it takes to control diabetes, you’ve got to do,” says **Phil Levy**, MD, a member of the board of directors of the American Association of Clinical Endocrinologists and a practicing endocrinologist in Phoenix.

### *Finding some answers*

Developing easy-to-follow treatment plans and signals for deteriorating conditions is key to helping busy primary care physicians manage their diabetic patients, Levy says.

For 11 years, the International Diabetes Center (IDC) in Minneapolis, has done just that, adjusting and re-adjusting algorithms for treatment plans as new research, new therapies, and new treatments become available.

The IDC’s most recent version of its Master DecisionPath for Type 2 diabetics was recently readjusted after troglitazone came on the market and conforms with the results of the United Kingdom Prospective Diabetes Study released last fall. It is one of several diabetes DecisionPaths aimed at primary care physicians and their care teams to make their jobs easier. **(See DecisionPath, inserted in this issue.)**

“It’s important for us to remember that the patient doesn’t fail; the therapy fails,” says **Renea Bradley**, RN, MSN, ARNP, CDE, manager of the IDC’s Staged Diabetes Management Training. Bradley helped develop most of the guidelines currently in place.

So, Bradley says, therapy needs to be ever-evolving. “Every time there is a new drug approved by the FDA, we change our DecisionPaths,” she says.

“Our mission is to translate research into practice.”

Bradley says it is now well-recognized that beta cells become exhausted as diabetes progresses, making glycemic control more difficult to achieve and requiring even more potent drug therapies to keep HbA1c results at acceptable levels and prevent or delay the onset of complications.

### *Six stages*

She defines these stages of Type 2 diabetes and their drug treatments:

☐ **Stage 1:** There are slight elevations in blood glucose — diet and exercise program recommended.

☐ **Stage 2:** The patient requires treatment with a single oral agent — usually sulfonylureas or metformin.

☐ **Stage 3:** The patient receives a combination therapy of oral agents — troglitazone and/or sulfonylureas and/or insulin.

☐ **Stage 4:** Insulin therapy is initiated.

☐ **Stage 5:** Additional insulin injections are added if patient experiences persistent midafternoon hyperglycemia.

☐ **Stage 6:** Additional insulin injections are added if patient continues to experience midafternoon hyperglycemia and begins nocturnal hypoglycemia.

Of course, Bradley says, some patients enter the chart at higher stages depending on their plasma glucose levels at diagnosis. She also notes some patients can move to lower stages as they achieve control, particularly if they had an extremely high blood glucose at diagnosis (greater than 300 mg/dL).

Bradley says patients don’t get “stuck” at a particular level for long periods of time.

In the staged diabetes management (SDM) program, if they don’t reach their target goals in a very short period of time — two to four weeks in the oral agent monotherapy stage — they are moved to the combination therapy stage. If they reach their target goals, their caregivers try to keep them there. They’re moved to progressively aggressive insulin therapy in equally short order if they don’t respond to combination therapy.

### *Physician- and patient-friendly*

“Our job is to take a complex disease and organize it in a way that is understandable and user-friendly for physicians and patients alike,” says Bradley.

The IDC's staged diabetes management training, based on American Diabetes Association guidelines, is offered all over the world. It has shown dramatic results in terms of lowering HbA<sub>1c</sub> and cholesterol levels, while lowering per-patient costs to the wide range of clinics, hospitals, managed care plans that use IDC's comprehensive education programs.

Each course includes all members of the care team and lasts between four and eight hours.

But the training is more involved than attending the sessions. Assessments precede and follow the training. Educational materials are provided, and there is considerable support for the team as it decides what strategy to follow, which "gets everybody on the same page in terms of treatment," Bradley.

"We now know these therapies and tight control make a difference," she says.

### **Data support SDM**

A wide variety of studies show the benefits of SDM. Many of these studies were conducted by Bradley's pioneering team. Over and over they show dramatically improved outcomes in a broad spectrum of settings:

□ In a rural primary care clinic, 660 patients with an average age of 62 dropped their average HbA<sub>1c</sub> from 8.7% to 7.5% over a one-year program.

□ In an Indian Health Service clinic, the number of lower-extremity amputations was reduced by 48% over an 11-year period with increasingly tight control, neuropathy screenings, and aggressive treatment of foot ulcers. Twenty-two people were able to avoid amputations.

□ In an SDM management program designed to change the practice behavior of health care providers in managed care, HbA<sub>1c</sub> levels of 130 patients dropped from 8.6% at baseline to 7.2% in three months and dropped another .4% in the following three months.

□ In a program at Tufts University, eight hours of SDM training for doctors in an internal medicine residency resulted in an increase in referrals to a diabetic educator from 17% to 83%. Referrals to a nutritionist increased from 26% to 74%; annual influenza vaccine rates increased from 52% to 74%; annual lab screenings for cholesterol and microalbumin increased from 30% to 70% and 52% to 82% respectively.

□ In another study, the training of nurse-dietitian teams was productive in lowering HbA<sub>1c</sub> levels from 9.6% to 7.6% in six months. Patients were

able to lower their cholesterol levels from a baseline average of 218.5 mg/dL to 203.7 mg/dL in the same period. HDL levels increased from 38.2 mg/dL to 42 mg/dL.

□ Significant cost savings were demonstrated with SDM programs as opposed to typical primary care. A group of 183 patients with Type 2 diabetes showed a cost savings of \$171,000 to one health plan over one year, which translated to a savings to the health system of \$2.57 for every dollar spent on staged diabetes management.

Bradley says she isn't daunted by the Herculean task of tackling diabetes and slowing its progression because treating the disease in stages means approaching it one step at a time.

[Contact Renea Bradley at (612) 993-2721.] ■

## **Proposed privacy bills could be detrimental**

*Advocate organizations not lobbying on the issue*

**B**ob Stone is concerned about how legislation pending before the U.S. Senate could adversely affect people with diabetes. The executive vice president of Diabetes Treatment Centers of America (DTCA) in Nashville, TN, has been to Washington lobbying missions several times in recent weeks.

"From our perspective, what's important is that we prevent the creation of artificial barriers to care," says Stone.

"Everybody's concern is that this is an easy political issue," he says. "Our concern is the unforeseen fallout."

### **Many patients need to be nudged**

He explains that people with diabetes need a very broad health care team to prevent complications. And that includes companies like DTCA, which contract diabetes care to hospitals and managed care companies around the country.

In addition, Stone says, many patients tend to deny they have the disease and need to take care of themselves, so they need little nudges from a health care team. Both of those could be curtailed under some of the currently pending bills.

Stone isn't getting much support from the

## KEY POINTS

- Patient privacy legislation, now under consideration by Congress, is designed to protect medical records from being indiscriminately distributed to those who might exploit or misuse them.
- Some providers are concerned that the legislation in its current form may hinder the free flow of information necessary among the extensive team of health care professionals who treat diabetics, including proprietary disease management companies.
- Previous legislation mandates Congress to pass its own patient privacy bill by August or the U.S. Department of Health and Human Services will implement its own guidelines.

American Diabetes Association (ADA) or the American Association of Clinical Endocrinologists (ACE), both deeply involved in the interests of diabetics.

An ADA spokeswoman says her organization's legislative affairs department is putting its energy into lobbying for increased funding for diabetes research.

ACE says simply that patient privacy legislation is expected to be discussed at a later date.

### *Time is running out*

There isn't much time, however. The Health Insurance and Accountability Act of 1996 created a system of health care information exchanges by computers. It joined previous laws that set a deadline of August 1999 for privacy protections to be established for medical records. If the Senate doesn't pass patient privacy legislation by then, the regulatory job will be left up to the U.S. Department of Health and Human Services (HHS).

Three bills have been introduced in the Senate, and a bipartisan compromise bill combining the common features of the three was being prepared at press time.

The House of Representatives is waiting to take its cue from the Senate.

"It's pretty clear there will be some legislation passed by Congress because they don't want to leave this in the hands of HHS," Stone says.

What Stone explains to any legislator who will listen is that diabetes is a unique disease with unique treatment modalities and a unique

psychology. Some of the legislation, Stone asserts, will reduce compliance at a time when the number of patients with diabetes is burgeoning.

"With the diabetic population, generally, it's a disease of denial," he says. "The horrible effects take time to develop, and most people don't want to think about it until they have to."

"With most program interventions, they will avoid treatment if given the option because it forces them to confront the disease," Stone says.

DTCAs have found that patients are unlikely to remember to make their own appointment for labs, eye and foot screenings, and for nutrition counseling, he says.

Stone argues if businesses like his can have

## Proposed Privacy Legislation

All three pending bills in the Senate have these common themes:

- ✓ Require one-time authorization for treatment, payment, and health-care-operations-related disclosures.
- ✓ Allow patient to self-pay to avoid payment-related disclosures. Other disclosures require authorization separate from treatment and payment authorization.
- ✓ Allow disclosure without consent for emergency circumstances, public health purposes, health oversight, coroners, medical examiners, and next of kin.
- ✓ Allow some access by law enforcement officials; all require a warrant or grand jury subpoena and a showing of probable cause before a warrant may be issued.

Regulations offered by the U.S. Department of Health and Human Services:

- ✓ Presume consent for treatment and payment-related disclosures. Other disclosures require authorization separate from treatment and payment authorization.
- ✓ Allow disclosure without consent in emergency circumstance, for public health purposes, for state health data systems, next of kin.
- ✓ No warrants required for law enforcement; allow unrestricted access to individual records for legal purposes. Law enforcement officers are not subject to prohibitions on disclosure, except as provided by other laws.

access to patient files, they can supervise diabetes care and alert patients to what they need to do to stay in control.

So the nationwide diabetes management provider has created a “negative option.” This means appointments are made for a patient, but he or she can cancel them with a phone call.

“We found that we get an 85% return on this type of program, as opposed to a maximum 25% return on cards reminding people to make appointments,” Stone explains.

At the same time, he says, “We also believe people are entitled to decline health care services. To do so is as simple as a phone call.”

His point regarding patient privacy is that this type of treatment plan would not be possible under at least one of the bills now pending that prohibits private companies from soliciting patients.

“There are proven benefits for comprehensive management programs for diabetics,” says Stone, differentiating them from some pharmaceutical companies’ disease management programs that he says are actually ways to approach patients to sell them their products.

“Legislation shouldn’t create any barriers to access to these legitimate programs,” he says.

Legislation might also impede the flow of information between a wide range of health care providers who treat diabetic patients.

Depending on which version of the bill passes, movement of a patient’s records between primary care physicians, endocrinologists, ophthalmologists, urologists, cardiologists, podiatrists, nurse practitioners, educators, dietitians, and a host of other professionals who care for diabetic patients could be hindered or even prohibited without separate authorizations.

### ***Pending bills***

Three versions of patient privacy legislation are now pending in the Senate. The least acceptable, says Stone, is the Kennedy-Leahy bill sponsored by Sens. Edward Kennedy (D-MA) and Patrick Leahy (D-VT) because it provides the most stringent protection for patients and the strictest regulation on information sharing.

“The tougher bill like that would significantly reduce the number of patients we could take care of without additional time and expense,” Stone says.

“The requirement for a patient to give written consent for every exchange of information

## **Other Privacy Bills**

- In mid-May, Democratic members of the House Ways and Means Committee introduced a bill providing full Medicare drug coverage for five major conditions, including diabetes.
- House sponsors say 6.3 million Medicare beneficiaries suffer from diabetes. Beneficiaries would have to pay a \$250 annual deductible and copayments of 20% for brand-name medications. There would be no copayments for generics.
- Lead sponsor of the bill, Rep. Ben Cardin (D-MD) told Reuters-Health that the measure could save Medicare money by preventing hospitalizations and other costly complications.
- Also covered under the Medicare Chronic Disease Drug Benefit Act are hypertension, major depression, rheumatoid arthritis and congestive and ischemic heart disease.

among members of the health care team will make it impossible for the team to function,” Stone says. “All the literature says the team needs to communicate.”

A spokesman for Kennedy says the goal of the legislation is not to limit care, but to put an end to “too much access to medical records without written consent.”

### ***What are the drawbacks?***

The bills sponsored by Sens. James Jeffords (R-VT) and Christopher Dodd (D-CT) and another by Robert Bennett (R-VT) are “more acceptable” in terms of comprehensive diabetes management, Stone says, because they allow more freedom of information exchange.

Spokesmen for Jeffords and Bennett told *Diabetes Management* they are not aware of any drawbacks.

That’s why Stone says he is traveling from office to office, presenting his case over and over. Many legislators don’t realize the importance of disease management or even really understand what it means, since it is a very new field, Stone says.

“The evidence in diabetes and other chronic

disease is that privacy is a good thing, particularly when it pertains to keeping employers from having access to medical records and discriminating against patients with diabetes and other diseases.

That's illegal now, and this legislation should and will make that stronger," Stone says. But he cautions that legislators and health care professionals must work together to ensure adequate communications within the health care team, something Stone equates to throwing out the baby with the bath water.

[Contact Bob Stone at (615) 665-2760.] ■

## Tight glycemic control may be harmful to babies

### *Hypoglycemic incidents more frequent*

Contrary to the dictums of the Diabetes Control and Complications Trial (DCCT), tight glycemic control may be harmful to infants and toddlers with Type 1 diabetes, as confirmed by findings in a recent Mayo Clinic study.

When all signs are pointing toward the benefits of tight control, researchers at Mayo Clinic in Rochester, MN, found that tight blood glucose control in infants and toddlers younger than 2 increases the risk of severe hypoglycemic reactions.

Even at reasonably well-controlled HbA<sub>1c</sub> levels of 8 or below, they found 55% of the children under 2 experienced severe and unpredictable hypoglycemic reactions, compared to 45% of the children ages 2 to 5 and only 13% of the

children ages 5 to 9.

Parents and patients of appropriate age were taught to determine plasma glucose concentrations and to adjust doses of insulin accordingly.

"Many clinicians responsible for the care of infants and young children with Type 1 diabetes mellitus think that less aggressive plasma glucose control is needed in these patients," wrote Aida N. Lteif, MD, and W. Frederick Schwenk II, MD, authors of the study of 59 children published in *Mayo Clinic Proceedings*.

While tight control can be achieved, researchers concluded, it may not be advisable because of possibility of errors in administering the correct amount of insulin, especially when small doses must be administered.

Although Type 1 diabetes is relatively rare in infants and toddlers, incidents of hypoglycemia in apparently well-controlled young patients are not uncommon, says **Robert Goldstein**, MD, PhD, vice president of research of the Juvenile Diabetes Foundation in New York City.

While about 40% of children with newly diagnosed Type 1 diabetes are younger than 10, that number is increasing each year, says Goldstein.

### *Changing environmental factors*

"The main recurring theme is that somehow the environment has changed, and environmental factors are triggering the autoimmune response," he says.

While the Lteif-Schwenk study recommends a relaxed pre-meal blood glucose range for young children, it does not designate a specific level.

But Goldstein recommends that the goal for children under 2 should be 100 to 150 mg/dL. "Clinicians need to loosen up their criteria in taking care of young kids," he says.

The problem of infant hypoglycemia is well-known and well-defined, Goldstein says.

While the Mayo study is very small, he agrees that incorrect measurement of insulin may be the cause of the hypoglycemic reactions and should serve as an alert to physicians treating very young children.

"They are more susceptible to hypoglycemia because they're not like little adults. They need smaller amounts of insulin, and it has to be measured very carefully because it is easy to make a mistake," he says.

Goldstein advises clinicians to be certain parents are measuring correctly and re-check their skills if there are repeated hypoglycemic

### KEY POINTS

- Tight glycemic control in infants and toddlers with Type 1 diabetes may lead to more frequent hypoglycemic reactions.
- Some clinicians say less aggressive plasma glucose control is needed for the youngest patients.
- A study suggests children under age 5 should have a higher goal for pre-meal plasma glucose levels.

incidents. "Tight glycemic control is achievable in young patients, therefore you should change the guidelines you're aiming for," he says.

[Robert Goldstein can be reached at (800) 533-2873.] ■

## Researchers find fungus helps lower blood glucose

*Preliminary studies show dramatic reduction*

A promising oral alternative to insulin is on the lab bench at Merck Research Laboratory in Rahway, NJ.

And what is even more exciting, one expert says, is the screening technique Merck researchers used to screen more than 50,000 compounds to determine if any of them had glucose-lowering properties.

Compound L-783,281 is derived from a fungus found growing on another plant near Kinshasa in the Democratic Republic of the Congo.

"It is exciting," says **Bei Zhang**, PhD, senior research fellow at Merck. "We are really working very hard to come up with new diabetes drugs that are different from the ones that are currently available. It's too early to project when, and even if, this medication will become available."

The research article published in the May issue of *Science* magazine says Zhang and her team identified *pseudomassaria* as the first small molecule with a capability of functioning as an insulin sensitizer.

It was selected as an insulin receptor rather than for insulin-like growth factor properties.

In vitro and in vivo studies confirmed the fungus' anti-diabetic properties as an oral agent, which makes it a promising alternative to injected insulin somewhere several years from now.

Studies with L-783,281 in diabetic mice showed single oral doses produced a 50% correction of hyperglycemia, Zhang says. Longer term treatment of up to 15 days in mice did not affect food intake, organ weights, blood chemistry, or liver function.

Beyond the potential for L-783,281 as an oral diabetic agent in itself, Zhang says, the discovery "shows it is possible to selectively activate insulin receptors, so it will help us find other

### KEY POINTS

- Merck researchers find fungus that shows promise as an anti-diabetes agent.
- Animal studies show 50% blood glucose reduction with use of *pseudomassaria* found growing on a plant in the Congo (formerly Zaire).
- Human trials are still several years away.

possible anti-diabetic compounds."

Zhang declined to say if Merck researchers have identified other promising compounds.

In a targeted approach to drug development, researchers used a cell-based assay to screen the compounds for actions that mimic insulin.

Using Chinese hamster ovary cells that overexpress the human insulin receptors, the researchers incubated intact cells and assayed them. L-783,281 showed it was reproductively active in the test. By comparison, a closely related natural product analog, L-767,827 (hinulliquinone) was 100 times less active in the assay, Zhang wrote in *Science*.

"This is very, very, very preliminary, but it is also very promising," says **Robert Ratner**, MD, medical director of Medlantic Clinical Research Center in Washington, DC.

"Is it safe? We don't know. Is it ready for human trial? Not for many, many years — five years or more," he says.

Ratner says what he finds most exciting about the find is the assay method by which the 50,000 compounds were screened. "The promise is really in the technique for screening new compounds."

[Contact Bei Zhang at (908) 423-6492.] ■

## Black youths more at risk for diabetic deaths

*Late diagnosis, lack of access to health care blamed*

Young African-Americans with Type 1 diabetes are nine times more likely to die of complications of the disease than whites, say University of Illinois researchers.

In addition, the death rate of black diabetics under 25 was three times higher than the general

## KEY POINTS

- Young African-Americans with Type 1 diabetes are nine times more likely to die from complications before the age of 25 than white youths.
- A researcher says lack of access to health care is the primary cause of elevated death rate.
- Clinicians are advised not to neglect the possibility of Type 1 diabetes in minority youth despite its relative rarity.

black population, while white youngsters were no more likely to die than their non-diabetic peers.

Young blacks may be diagnosed later than whites because physicians dismiss the likelihood of Type 1 diabetes in blacks.

The disease is somewhat less common than in whites, says **Rebecca Lipton**, BSN, MPH, PhD, a research fellow at the University of Illinois at

Chicago School of Public Health and lead author of the study published in the May 5 issue of *Pediatrics*.

“They think of blacks as having Type 2 diabetes, so they don’t look closely enough at the youngsters and consider the possibility of Type 1,” Lipton explains. “But what many of us may not realize is that diabetes is the second-most common chronic disease among black youngsters after asthma.”

Lipton says the number of cases is small, with an overall mortality rate for Type 1 diabetes in Chicago at 247.2 deaths per 100,000 cases. But the numbers are telling when they are separated by race. The death rates were 447.8 per 100,000 in blacks, 175.6 in Hispanics, and only 48.2 in whites.

Late diagnosis most likely costs young black patients a great deal in terms of preventing mortality and complications, Lipton says, noting that of 23 black patients who died, seven occurred at or near the time of diagnosis.

*“Unless they’re girls and get pregnant or they are alcoholics or drug abusers and can get in federal programs, they’re out of luck.”*

At the same time, of those who died, the average time between diagnosis and death was 7.1 years.

She adds that end stage renal disease, which was the primary cause of death in four of the total 30 deaths in all races, was found by searching death certificates, medical records, and U.S. Census data in Chicago from 1987 through 1994. All four patients who died of renal failure were black.

“It may be argued that virtually all the deaths recorded in this study could have been prevented by adequate preventive care or by proper emergency interventions,” Lipton wrote. “Since metabolic decompensation is relatively easy to recognize in young people, and appropriate treatment for IDDM usually can be delivered in a clinic or hospital emergency department setting . . . inadequacies in clinical care are suspected generally when death occurs from acute IDDM complications.”

Economic deprivation common in racial minorities seems to contribute to the death rate among young black diabetics, says Lipton, because they lack access to the kind of health care that will result in an early diagnosis and prevent complications.

“Socioeconomic deprivation is the most obvious answer to me,” she says. “Blacks have no genetic predisposition to dying more frequently than whites.”

### ***Lack of insurance fuels noncompliance***

Lack of insurance is certainly a major factor in the death rate among young blacks, Lipton says.

“All kids with diabetes who don’t have other insurance should be eligible for Medicaid, but even that’s not enough,” she says. “In Chicago, many kids get excellent care at clinics, but they are kicked off Medicaid when they are 18 and can’t pay for their medications. Unless they’re girls and get pregnant or they are alcoholics or drug abusers and can get in federal programs, they’re out of luck.”

There are few, if any, insurance plans, including Medicaid that pay for test strips, for example, Lipton says, and the cost of test strips for a diabetic testing three or four times a day is about \$75 a month.

Worse yet, young diabetics who reach the age of 18 without insurance are likely to fall into non-compliance because of the high cost of supplies. At \$22 a 1,000-unit vial for insulin and \$22 per 100 syringes, in addition to the cost of test strips

— plus medical office visits and quarterly labs at a cost of about \$200 per quarter — the cost of compliance is beyond the means of many. At a minimum total cost approaching \$200 a month, it's a given that many young people cannot afford the medical care and medicines they need to survive, Lipton says.

"These deaths shouldn't happen at all," she concludes.

**Robert Goldstein**, MD, PhD, vice president for research at the Juvenile Diabetes Foundation in New York City, agrees.

Yet, he says, "If there was perfect equivalent care, we could probably make [this discrepancy] go away. If I looked at 50 people in the ghetto and 50 people in the suburbs, I'd probably find the same thing — so it's not necessarily racial, but it is socioeconomic."

Goldstein criticizes the methodology of Lipton's study because it is retrospective and relies on notoriously inaccurate medical records and death certificates.

But, he says, the take-home message to health care professionals is clear: "Let's get on the stick here and pay attention to the possibility that young black kids can have Type 1 diabetes, too."

[Contact Rebecca Lipton at 312-996-0064.] ■

## Diabetes, sleep apnea, obesity form lethal combo

*Patients with all three at high risk of stroke*

**T**ype 2 diabetes, sleep apnea, and obesity may be tied into a deadly knot that increases the risk of stroke, say recent research from the University of California at Los Angeles.

While this idea comes as no real surprise

### KEY POINTS

- Type 2 diabetes, obesity, and sleep apnea combined mean a higher risk of stroke, finds a University of California at Los Angeles study.
- Health care professionals should look for linkages and examine patients for sleep apnea.

to most practitioners, this is the first time the three elements have been linked to the risk of stroke, according to the study's lead author, **Arthur Friedlander**, DMD, DDS. Friedlander is chair of dentistry at the U.S. Department of Veteran's Affairs of Greater Los Angeles Health Care System and a professor of oral and maxillofacial surgery at the UCLA School of Dentistry.

Given the well-documented link between Type 2 diabetes and obesity and the also well-documented link between obesity and sleep apnea — apparently caused by fat deposits on the neck which place an added burden on the throat — it's a small leap of logic to combine diabetes, sleep apnea, and obesity to come up with a lethal risk of stroke.

In Friedlander's study of 100 patients, published in the May issue of the *Journal of Oral and*

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### Editorial Questions

For questions or comments, call **David Flegel** at (404) 262-5537.

**Maxillofacial Surgery**, 58% of the 17 diabetic patients who had sleep apnea also had carotid blockages, signaling a risk of stroke.

Those numbers are small, says **Jeff Susman, MD**, a family practitioner in Omaha, NE, and professor of family medicine at the University of Nebraska Medical Center, but there's a message for doctors anyway: Pay attention to the potentially lethal combination of diabetes, obesity, and sleep apnea.

Friedlander and his colleagues speculate that nighttime oxygen depletion caused by sleep apnea and a history of diabetes may contribute to the buildup of plaque on the artery walls.

Sleep apnea, formally known as obstructive sleep apnea syndrome (OSAS), is rare, occurring in 2% of middle-aged women and 4% of middle-aged men. But Friedlander wrote that people with OSAS suffer strokes three to six times more frequently than those without it.

### **Patients and risks**

Patients in Friedlander's study were generally obese, with Type 2 diabetes that was diagnosed after the age of 40. Not surprisingly, 70% required antilipidemic medications to control elevated cholesterol levels.

And, Friedlander wrote, excessive low-density lipoprotein (LDL) production and excessive rates of LDL oxidation due to the hyperglycemic environment, places such patients at high risk of atherosclerosis because lesions calcify and protrude into the vessel lumen, inhibiting the flow of blood.

This condition promotes the formation of ulcers that act as sites for mural thrombus formation, says Friedlander, thereby increasing the risk for emboli which can plug an intercranial artery, causing a stroke.

Health care professionals should be aware of this linkage, says Friedlander, "So someone who goes to a doctor for a sleep apnea exam should have a screening for diabetes, especially if the patient is obese."

Susman says physicians should ask their diabetic patients about sleep apnea and take it as another signal of impending vascular disease.

"This is probably a reminder for physicians to be alert for sleep apnea, particularly in those individuals who are overweight, with or without diabetes," Susman says. "We can be more vigilant."

[Contact Arthur Friedlander at (310) 268-3196.] ■

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After reading each issue of *Diabetes Management*, the continuing education participant will be able to do the following:

1. identify particular clinical administrative, pharmacological, or patient education issues related to the disease state management of diabetes;
2. describe how those issues affect patients, health professionals, diabetes management efforts and diabetes-related medical costs;
3. cite practical solutions to problems associated with diabetes management, based on overall expert guidelines from the federal Centers for Disease Control and Prevention, the National Institute of Diabetes and Digestive and Kidney Diseases, the American Diabetes Association, or other authorities, or based on independent recommendations from clinicians at individual institutions. ■