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Abciximab could be a great equalizer for diabetic heart patients

When teamed with angioplasty, stenting, new drug gets good outcomes

Despite its "super-aspirin" nickname in the popular press, the anti-clotting agent abciximab isn't aspirin at all. Still, researchers say it may be responsible for some super feats anyway, such as acting like a great equalizer. They recently found that among diabetic heart patients who undergo balloon angioplasty and stenting, those who also received the new drug could expect nearly the same good outcomes as nondiabetic patients. That's good news, considering how notorious re-stenosis can be, especially when a patient has diabetes.

Abciximab, a potent anticoagulant sold under the brand name ReoPro, produced a marked reduction in mortality rates for diabetic patients who are predisposed to re-stenosis after balloon angioplasty and stenting.

Most surprising to one analyst was the long-term prevention of re-stenosis for stent patients who received a 12-hour bolus of abciximab after the procedure.

These results from the multicenter study EPISTENT (Evaluation of Platelet IIb/IIIa Inhibitor for Stenting Trial), which included 491 diabetics, were reported in the Dec. 21 issue of the journal *Circulation*.

Lead author **Steven Marso**, MD, interventional cardiology fellow

KEY POINTS

- Diabetic patients who get triple therapy (balloon angioplasty plus a stent and the anti-platelet drug abciximab) have a significantly lower rate of re-stenosis than those who do not receive the drug.
- A post-surgical bolus of abciximab breaks up clots that block blood flow.
- After six months, abciximab recipients had a re-stenosis rate that was half that of angioplasty and stent patients who did not receive the drug.

at MidAmerica Heart Institute of St. Luke's Hospital in Kansas City, MO, says the study "is an important step forward" in the effort to improve outcomes for diabetic patients with coronary heart disease, because balloon angioplasty, even with the addition of stenting, has produced outcomes that are "less than ideal," with a re-stenosis rate averaging 25% or more six months after the procedure.

Patients in the EPISTENT study were randomized to three groups:

1. stent and placebo;
2. stent and abciximab;
3. balloon angioplasty and abciximab.

The diabetic patients who received a single bolus of abciximab after stenting got these benefits:

• Their one-year death rate was just 1.2%; those who got the stent and a placebo had a rate of 4.1%.

• Their rate of myocardial infarction was 6.2%, compared to 12.7% in the stent-placebo groups.

• And the balloon-stent-abciximab group's six-month re-stenosis rate was 8.1%, compared to 16.6% for stent-placebo and 18.4% for balloon-abciximab. The re-stenosis rate with balloon angioplasty alone is (in general in the United States) estimated to be as high as 60%.

The death rate for the ballon-stent-abciximab group is approximately the same as what is found in nondiabetic patients undergoing balloon angioplasty and stenting, which Marso describes as helping to "level the playing field for patients with diabetes."

EPISTENT subjects had single-vessel disease. Balloon angioplasty and stenting were considered appropriate treatments for those patients.

"These results would suggest that the use of stents and abciximab should become a standard of treatment in the vast majority of patients," wrote Eric J. Topol, MD, chairman of the trial and chairman of cardiology at the Cleveland Clinic, in a formal statement.

Topol noted that, based on these results, the addition of abciximab to the standard balloon angioplasty and stent procedure could save 8,000 lives a year. "Approximately 600,000 people will undergo some type of percutaneous coronary revascularization in the U.S. in 1999. If all of these patients were treated with the combination of stents and abciximab, these data would indicate that as many as 8,000 lives could be saved per year."

Angioplasty vs. bypass

Other research has shown the benefit of surgery over ballooning in diabetic patients. In the Bypass Angioplasty Revascularization Investigation (BARI), investigators found their diabetic participants had better outcomes and five-year survival when they went the bypass route. The BARI patients were different from than those in the EPISTENT study, however, because the bypass recipients had multivessel disease.

The diabetics randomized to coronary bypass surgery had a higher five-year survival rate, but more importantly, only 8% of the diabetic patients randomized to surgery had re-stenosis as compared to more than half of the angioplasty group.

"The question of whether stenting plus abciximab might produce results equal to bypass is yet to be answered." says Marso. He cautions that clinicians need to pay particular attention to the contrast dye used in stenting and angioplasty because of the propensity for kidney toxicity in diabetic patients. "We need to be particularly vigilant for anyone with evidence of proteinuria or elevated creatinine levels."

Marso's EPISTENT findings were enthusiastically supported in an accompanying editorial by **Spencer B. King II**, MD, professor of medicine and cardiology and director of interventional cardiology at Emory University in Atlanta.

What is particularly surprising is that no earlier studies have shown abciximab to reduce restenotic events long after the procedure has been done, he says. So after six months, more patients are spared the pain, risk, and expense

COMING IN FUTURE MONTHS

- Help your patients stop smoking
- Elevated insulin levels associated with impaired blood clotting function
- Diabetes and uncontrolled blood pressure can cause mental deterioration
- Magnets lessen foot pain in diabetics
- Higher mortality rates reported in for-profit dialysis centers

of undergoing another procedure.

"The late events probably represent a very different mechanism from the early clotting events. We just didn't expect it." He adds that the BARI results were originally surprising, too, but eight years of ongoing Emory University research now affirms the improved long-term bypass survival rate for diabetics.

King pointed out in his editorial that Marso's study compares hypertensive, obese diabetic patients and nonhypertensive, nonobese, nondiabetic patients. "It will be interesting to compare diabetics with and without insulin resistance in a larger cohort in future trials," King wrote.

He notes that there are many aspects of heart disease in diabetics that are different from the manifestations of the disease in nondiabetics. "They clearly had a more aggressive re-stenosis rate, perhaps because of altered platelet function. It's a different manifestation of the disease, in my opinion."

King and Marso agree that abciximab may level the playing field as suggested by EPISTENT, giving diabetic patients a chance of survival at least comparable to their nondiabetic counterparts.

"Unless there is some reason not to, on diabetic patients, I use abciximab or some similar drug. I certainly use it on the ones I think have a possibility of an acute thrombotic events," King explains.

[For more information, contact Steven Marso at (816) 932-5742 and Spencer King at (404) 712-4677.] ■

Will insurers join the 4S club?

Costs drop when diabetics take simvastatin

The data from the Scandinavian Simvastatin Survival Study (4S) hold good news for diabetic patients who have high cholesterol. After analyzing the 4S results, a team of Michigan researchers report that diabetics who took the cholesterol-lowering therapy generated short-term cost savings and long-term heath benefits, both of which should help convince insurers to pick up the bill.

Simvastatin is costly, about $6,000 per patient over the five-year study. But the numbers show the results are worth the initial cost, says **William H. Herman**, MD, MPH, an endocrinologist and professor of medicine at the University of Michigan in Ann Arbor. "Most interventions are more cost-effective when applied in higher risk patients, so by being truly aggressive, you can prevent more events and save money, too," he says.

"This paper adds major financial reasons for putting patients on simvastatin in addition to the obvious medical benefits." In the short term, Herman explains, few drugs of any type have had these kind of impressive results in terms of health benefits and cost savings.

Earlier analysis of the 4S results showed diabetic patients with coronary heart disease treated with simvastatin had 36% lower low-density lipoprotein cholesterol levels than placebo-treated subjects and a 43% lower risk of all-cause mortality. The new numbers continue to look good. Here is what Herman's team found:

✔ 37% reduction in revascularizations;

✔ 40% reduction in cardiovascular disease-related hospitalizations;

✔ 26% reduction in the frequency of all-cause hospitalizations;

✔ 34% reduction in total length of hospital stays;

✔ reduction in direct costs over the duration of the five-year follow-up of $3,872 per patient, which offset approximately 60% of the cost of the drug.

Nondiabetic patients with impaired glucose tolerance also benefited in a big way. They reduced their hospitalization costs by $4,478, which offset 74% of the drug's cost. According to the study, the net savings to insurers when a diabetic takes simvastatin are $1,801.

Insurers should take notice of these results, according to **Paul Jellinger**, MD, an endocrinologist in private practice in Hollywood, FL, and president-elect of the American Academy of

KEY POINTS

- New analysis of 4S study data (Scandinavian Simvastatin Survival Study) shows diabetic patients who received simvastatin had shorter, less expensive hospitalizations than those who did not receive the drug.
- Short-term economic returns may encourage insurers and managed care to be more lenient with the use of the expensive cholesterol-lowering drugs.
- Results probably translate to other drugs in the statin class, researchers say.

Clinical Endocrinologists. "We can usually get an approval for a statin drug, but because of the cost, frequently managed care will only approve the weaker statins," says Jellinger.

That means patients have to go through a three- or four-month course of the weaker statin, only to have unsatisfactory results that finally lead to approval for the stronger drug, he explains. "It's terrible for the patient and wastes three or four months of his life."

Herman's conclusions are "very valid," Jellinger says. "We've been treating our patients very aggressively with the statins, and we know they result in fewer events and lower costs. This just puts it in black and white."

[For more information, contact William Herman at (734) 936-8279 and Paul Jellinger at (954) 963-7100.] ■

Depression linked to heart disease in diabetics

Study relates optimism to reduced complications

Connections between depression and diabetes have been big news in diabetes care in the past year.

Now a University of Pittsburgh study shows that depressed Type 1 diabetic patients have nearly 50% greater risk of cardiovascular disease than diabetics with a more optimistic outlook. That increased risk goes well beyond the high rate of cardiovascular complications found in patients with diabetes.

Specifically, the study shows that diabetic patients who reported they were feeling down or experiencing sleep disturbances or appetite changes were much more likely to develop heart disease.

"We're not yet at a point where we can say that treating depressive symptoms early can prevent heart disease, but we need to find out more about these mechanisms," says **Trevor Orchard**, MD, professor of epidemiology, medicine, and pediatrics at the University of Pittsburgh School of Public Health. "We don't know the underlying cause. There are several possible mechanisms at work here."

Those possible mechanisms include:

❒ Individuals with excessive stress reactions and cortisone production are more prone to depression. Those same individuals tend to have more central adiposity and therefore more insulin resistance.

❒ There may be a link to autonomic neuropathy, but Orchard says that's a remote possibility.

❒ There may be a distinctive personality type from birth that is characterized by depression and a more obsessive nature.

Orchard points out that Beck Depression Inventory scores have been linked to increased instances of angina and myocardial infarctions. **(See sample of the Beck Depression Inventory, pp. 29-30.)**

"The depression came before the heart disease, since none of the subjects had heart disease at the beginning of the study." While the reason for the link may not be clear, there is a clear message to clinicians treating diabetics, says Orchard.

"The standard of practice says physicians must carefully monitor blood pressure. I would say a careful monitoring of depressive symptoms is just as important," he says.

He notes there is a difference between a person with depressive symptoms and someone who is clinically depressed. "Every diabetic patient should be carefully evaluated, and if depressive symptoms are found, that patient should be considered at high risk for heart disease."

Orchard recommends the Beck Depression Inventory as a valuable tool to look at depressive characteristics in a patient. "There are many types of symptoms in the index that should raise the flag that a patient may be depressed."

Orchard stops short of recommending universal depression screening for all diabetic patients. "It simply warrants our attention as health care professionals, since we know diabetics are two

(Continued on page 30)

KEY POINTS

- A University of Pittsburgh study shows diabetic patients who are depressed have nearly 50% more likelihood of developing heart disease than those who have a more optimistic outlook.
- A researcher recommends formal and informal screenings in an office setting for any patient a clinician suspects may have depressive symptoms.
- Getting a family member involved in the screening may elicit a more accurate report of feelings of pessimism and/or depression.

Beck Depression Inventory

The Beck Depression Inventory is the self-assessment tool used by the University of Pittsburgh study mentioned in this article. There are many such tools, and this one often is considered one of the most effective. The tool was developed by Aaron T. Beck, MD.

Record the number next to the answer which best reflects how you have been feeling during the past few days. Be sure to answer all 21 questions.

1. ___0 - I do not feel sad.
___1 - I feel sad.
___2 - I am sad all the time, and I can't snap out of it.
___3 - I am so sad or unhappy that I can't stand it.

2. ___0 - I am not particularly discouraged about the future.
___1 - I feel discouraged about the future.
___2 - I feel I have nothing to look forward to.
___3 - I feel that the future is hopeless and that things cannot improve.

3. ___0 - I do not feel like a failure.
___1 - I feel I have failed more than the average person.
___2 - As I look back on my life, all I can see is a lot of failures.
___3 - I feel I am a complete failure as a person.

4. ___0 - I get as much satisfaction out of things as I used to.
___1 - I don't enjoy things the way I used to.
___2 - I don't get real satisfaction out of anything anymore.
___3 - I am dissatisfied or bored with everything.

5. ___0 - I don't feel particularly guilty.
___1 - I feel guilty a good part of the time.
___2 - I feel guilty most of the time.
___3 - I feel guilty all of the time.

6. ___0 - I don't feel I am being punished.
___1 - I feel I may be punished.
___2 - I expect to be punished.
___3 - I feel I am being punished.

7. ___0 - I don't feel disappointed in myself.
___1 - I am disappointed in myself.
___2 - I am disgusted with myself.
___3 - I hate myself.

8. ___0 - I don't feel I am any worse than anyone else.
___1 - I am critical of myself for my weaknesses or mistakes.
___2 - I blame myself all the time for my faults.
___3 - I blame myself for everything bad that happens.

9. ___0 - I don't have any thoughts of killing myself.
___1 - I have thoughts of killing myself, but I would not carry them out.
___2 - I would like to kill myself.
___3 - I would kill myself if I had the chance.

10. ___0 - I don't cry any more than usual.
___1 - I cry more now than I used to.
___2 - I cry all the time now.
___3 - I used to be able to cry, but now I can't cry even though I want to.

11. ___0 - I am no more irritated by things than I ever am.
___1 - I am slightly more irritated now than usual.
___2 - I am quite annoyed or irritated a good deal of the time.
___3 - I feel irritated all the time now.

12. ___0 - I have not lost interest in other people.
___1 - I am less interested in other people than I used to be.
___2 - I have lost most of my interest in other people.
___3 - I have lost all of my interest in other people.

13. ___0 - I make decisions about as well as I ever could.
___1 - I put off making decisions more than I used to.
___2 - I have greater difficulty in making decisions than before.
___3 - I can't make decisions at all anymore.

14. ___0 - I don't feel that I look any worse than I used to.
___1 - I am worried that I am looking old or unattractive.
___2 - I feel that there are permanent changes in my appearance that make me look unattractive.
___3 - I believe that I look ugly.

15. ___0 - I can work about as well as before.
___1 - It takes an extra effort to get started at doing something.
___2 - I have to push myself very hard to do anything.
___3 - I can't do any work at all.

16. ___0 - I can sleep as well as usual.
___1 - I don't sleep as well as I used to.
___2 - I wake up 1-2 hours earlier than usual and find it hard to get back to sleep.
___3 - I wake up several hours earlier than I used to and cannot get back to sleep.

17. ___0 - I don't get more tired than usual.
___1 - I get tired more easily than I used to.
___2 - I get tired from doing almost anything.
___3 - I am too tired to do anything.

18. ___0 - My appetite is no worse than usual.
___1 - My appetite is not as good as it used to be.
___2 - My appetite is much worse now.
___3 - I have no appetite at all anymore.

19. ___0 - I haven't lost much weight, if any, lately.
___1 - I have lost more than 5 pounds [2 kg].
___2 - I have lost more than 10 pounds [4 kg].
___3 - I have lost more than 15 pounds [6 kg].

20. ___0 - I am no more worried about my health than usual.
___1 - I am worried about physical problems such as aches and pains, upset stomach, or constipation.
___2 - I am very worried about physical problems, and it's hard to think of much else.
___3 - I am so worried about my physical problems that I cannot think about anything else.

21. ___0 - I have not noticed any recent change in my interest in sex.
___1 - I am less interested in sex than I used to be.
___2 - I am much less interested in sex now.
___3 - I have lost interest in sex completely.

Total the score for each of the above items. Interpret according to the scale below.

Total score _____

Levels of depression

1-10: These ups and downs are considered normal.

11-16: Mild mood disturbance

17-20: Borderline clinical depression

21-30: Moderate depression

31-40: Severe depression

40 or higher: Extreme depression

A score of 17 or more requires professional treatment.

to 10 times more likely to have heart disease than nondiabetics," he says. "This opens an avenue to explain the enormous risk of heart disease in diabetes."

Depressive disorders are more common in Type 1 diabetics than in Type 2, says **Alan M. Jacobson**, MD, director of the mental health unit at Joslin Diabetes Center and a professor of psychiatry at Harvard Medical School in Boston. "Depression is a risk factor for any illness, and it changes adherence to any regimen." Furthermore, depression is associated with worse glycemic control, says Jacobson, and with higher risk of retinopathy, probably because of that association.

While there has been no firm link established between poor control and heart disease, many experts think the leap wouldn't be that difficult to make, considering the other evidence in existence.

"Temperament is a predictor of health outcomes. Pessimistic people do worse in the long term than optimistic people," he says.

Any type of depression can be hard to discover, considering the patient may not be showing signs to the physician, he says. "A patient can be sitting there smiling at you and still be severely depressed. You have to get to know the patient and spend a little time."

He recommends simple screenings during office visits that can be both efficient and effective in finding patients at risk. "Ask questions quickly. It can be done in just a couple of minutes if you just ask a few questions. Are they feeling a loss of interest in things that once interested them — experiencing . . . feelings of pessimism, mood swings, loss of energy, sleep disturbances, or a decrease in appetite? That should give you a good idea of whether they are depressed."

If the clinician suspects that a patient is severely

depressed, matters of medication and counseling should be handed over to a specialist. There has been a great deal of criticism about physicians who routinely prescribe antidepressants without any other type of attention, and the antidepressants alone may not best serve the patient's interest. The time to refer, Jacobson notes is "anytime you have the slightest feeling you are getting out of your element."

"It's not hard to do this simple screening, if you practice it," he adds. "But if it is out of the ordinary, it should become ordinary."

Talking with family members also can be helpful, says **Mary Amanda Dew**, PhD, a professor of psychiatry and member of the cardiothoracic team at the University of Pittsburgh Medical Center.

"That's just a part of good clinical care. Sometimes the patient may not be very forthcoming or may not even recognize the symptoms of depression, but a family member may be able to shed a little more light on it." The stress of living with diabetes can lead to depression, anxiety, and other mental health problems, she says.

Dew suggests using the simplest possible depression screening techniques — "just a few simple questions. If you established rapport, you'll get the full story, and then you might go a long way toward preventing further problems, both mental and physical."

[For more information, contact Trevor Orchard at (412) 383-1032, Alan Jacobson at (617) 732-2657, and Mary Amanda Dew at (412) 624-3373.] ■

Patients need education about underlying causes

Lack of information equals poor control

A survey showing 62% of patients with Type 2 diabetes are unable to identify insulin resistance as the underlying cause of their disease, astonishing leaders of the American Association of Diabetes Educators (AADE), who commissioned the survey.

Not surprisingly, those who cannot define the cause of their disease have much poorer control, according to AADE president **Christine Tobin**, RN, MBA, CDE, an Atlanta-based health care consultant.

A telephone poll was conducted by Yankelovich Partners of Norwalk, CT. The research firm called 1,000 Type 2 diabetics over the age of 45. The results include:

• 88% reported diet and exercise were part of their diabetes regimen.

• 84% said they were using oral agents to help control their diabetes.

• 72% wanted more information about their disease.

• 75% did not seek support in coping with their diabetes.

• 92% knew their blood sugar level, and 88% knew their blood sugar level target.

• 75% did not know their HbA_{1c} level, and 77% did not know the target HbA_{1c} for control.

• 97% were being treated by a physician, but only 28% had discussed insulin resistance with a physician or other health care professional.

"These findings are alarming and demonstrate the critical need for greater education about insulin resistance to help patients keep their diabetes in check," says Tobin.

Since most diagnoses were made by primary care providers, and most physicians do not employ a diabetes educator, the education needs to be done outside the doctor-patient office visit, says Tobin. "With less than 10 minutes to examine, diagnose, and prescribe, how much diabetes education do you think occurred?" she asks. "This survey underscores the need for increasing access to educational efforts to let patients know where to go to get help."

Tobin's advice to diabetes educators: "This survey tells you to make contacts and market yourself and your program. Ask for referrals. Make sure physicians and other health care providers know what you can do for them and their office as well as for their patients."

Diabetes education is expensive and currently is not covered by many insurance plans. Medicare does not cover education, but Tobin says new

KEY POINTS

- An American Association of Diabetes Educators' survey shows 62% of Type 2 diabetics cannot correctly define insulin resistance.
- Most Type 2 diabetics surveyed also did not know their HbA_{1c} levels or what their target level should be.
- Those with poor knowledge of the disease have higher HbA_{1c} levels.

Health Care Financing Administration (HCFA) regulations — now mired in bureaucratic red tape — eventually may change that and bring most insurers into the diabetes education arena as well.

"That puts a lot of lot of education programs out on a limb and on hold." She adds it likely will be several more months before HCFA sifts through more than 1,000 comments received on regulations drafted in response to the August 1997 legislation that includes coverage for diabetes education.

Until then, diabetes education is out of reach for many patients, says **Betsy Bohannon**, MD RD, CDE, educator at the diabetes clinic at the University of Tennessee at Knoxville. She says it is "mind boggling" how few patients have an opportunity to get information about the best way to manage a very complex disease.

She notes that the University of Tennessee's basic half-day program for newly diagnosed diabetics costs $350 and the four-day intensive program "for people in trouble" costs $2,000. "That's just not in reach for most people unless insurance helps out."

"Diabetes education is a lifelong process, so someone who was diagnosed a few years ago may need a refresher. The amount of information they receive when they are newly diagnosed cannot possibly be completely absorbed," she says.

The state of diabetes self-management is rapidly evolving, says Tobin, which means re-education and constant reinforcement are essential to help patients achieve good control.

She says that researchers have demonstrated the benefits of tight glycemic control for Type 1 and Type 2 diabetics alike. New drugs like the thiazolidinediones or "glitazones" being developed can make a major difference in helping patients achieve glycemic control. But there's more to diabetes education than hammering home the idea of glycemic control. Diabetes educators need to be talking with their patients about more than just diabetes.

"Don't forget to talk to them about the comorbid diseases such as hyperlipidemia, hypertension, and heart disease," she says. "And when those complications arise, it is crucial that they get the information they need at that time."

So many patients don't get the concepts behind their diabetes because there is frequently little physical manifestation of the disease in the newly diagnosed, says **Anne Whittington**, MBA, MSN, RN, CDE, a diabetes educator at the Medical College of Georgia in Augusta.

Until complications arise, there is little impetus to take preventive measures in the usual health care setting, she explains. "It's not human nature to do anything about something that doesn't exist yet."

Obviously, she does not advocate waiting until complications arise to educate patients about the need for good glycemic control. "We need to find methods for the patients to connect the causes and effects of insulin resistance to their daily lives so we can help facilitate changes in behavior."

The ongoing challenge, says Whittington, involves tailored, individualized attention to each patient, finding that patient's "hot buttons."

Bohannon adds it is important to prepare patients emotionally to hear the message an educator is sending. "A person is usually in shock and overwhelmed at the time of diagnosis. That doesn't set a good stage for much learning at all, yet that's when people are referred to an education program if they are going to be referred at all."

Whittington offers a suggestion: "We need to work with the patients to find out where they are coming from and what they are willing to do to accomplish short-term goals. When [the situation] is seen with crystal clarity by the patient, the patient will make the changes."

[For more information, contact Christine Tobin at (404) 636-0213, Betsy Bohannon at (423) 544-9858, and Anne Whittington at (706) 721-6895.] ■

Preventive insulin therapy could help at-risk kids

Daily injection may tip autoimmune balance

For the past five years, 21-year-old Neil Gilbert of Acton, MA, has injected himself with a tiny dose of insulin each day. Gilbert doesn't have diabetes. He and his doctors are hoping the daily regimen will keep him from ever getting it, since he has the antibodies that could make him predisposed to diabetes.

The young man is one of hundreds of at-risk individuals participating in the Diabetes Prevention Trial, Part 1 (DPT-1) aimed at discovering ways to keep young people like Gilbert from getting the disease, or at least delaying its onset.

Researchers are working under the guidance of **Jay Skyler**, MD, chairman of the DPT-1 study and professor of medicine and pediatrics at the

DPT-1 Clinical Centers

More than 350 screening centers in the United States and Canada are linked with the following clinical centers. Information on the study can be obtained by calling: (800) HALT DM1.

Children's Hospital of Los Angeles
Box 61/ 4650 Sunset Blvd.
Los Angeles, CA 90027
Telephone: (888) 835-3761
Fax: (323) 953-1349
E-mail: jvalenzuela@chla.usc.edu

University of Southern California
Los Angeles County Medical Center
Endocrine & Diabetes Service, Room 19629B
Los Angeles, CA 90033
Telephone: (323) 226-7626
Fax: (323) 226-5709
E-mail: azeidler@hsc.usc.edu

Stanford University
S-302 Medical Center
Stanford, CA 94305-5119
Telephone: (650) 725-0497
Fax: (650) 725-8375
E-mail: darrell@forsythe.stanford.edu

Barbara Davis Center for Childhood Diabetes
Box B140/ 4200 E. 9th Ave.
University of Colorado
Denver, CO 80262
Telephone: (800) 572-3992
Fax: (303) 315-4124
E-mail: sherrie.harris@uchsc.edu

University of Florida
Box 100275
Gainesville, FL 32610-0275
Telephone: (800) 749-7424, ext. 2-7836 or (800) 552-0219
Fax: (352) 392-3053
E-mail: Dennis.pathology@mail.health.ufl.edu

University of Miami
P.O. Box 016960 (D-110)
Miami, FL 33101
Telephone: (305) 243-DPT-1 [(305) 243-3781]
Fax: (305) 243-3313
E-mail: dmatheso@med.miami.edu

Joslin Diabetes Center/Children's Hospital Beth Israel Hospital
1 Joslin Place
Boston, MA 02215
Telephone: (800) 2-HALT-DM (242-5836)
Fax: (617) 732-2432
E-mail: dconboy@joslin.harvard.edu

University of Minnesota
424 Harvard St. S.E., Box 101
Masonic Bldg. Room 203
Minneapolis, MN 55455
Telephone: (800) 688-5252, ext. 58944
Fax: (612) 626-3133
E-mail: schmi094@maroon.tc.umn.edu

University of Washington
1660 S. Columbian Way #358285
Seattle, WA 98108
Telephone: (206) 543-4561
Fax: (206) 764-2615
E-mail: diabetes@u.washington.edu

University of Miami. They have sifted through tens of thousands of medical records looking for the right subjects — family members of patients with Type 1 diabetes who test positive for the antibodies that destroy insulin-producing pancreatic cells.

Skyler's team is still recruiting at nine centers nationwide in hopes of finding as many as 300 more patients to add to the 500 already enrolled. **(See list of centers, above.)**

Close relatives of Type 1 patients are 10 to 20 times more likely to develop the disease than the general population, but 96.5% of those who are tested do not have the antibodies, so recruiting study participants is a process of searching for "needles in haystacks," says Skyler.

They've tested more than 80,000 relatives of people with Type 1 diabetes thus far. Initially, researchers restricted the testing to first-degree relatives, but they have recently expanded the study to cover second-degree relatives as well in hopes of obtaining a sample of adequate size.

Those who do have the antibodies are tested for pancreatic function and given gene tests to determine if they have a gene that seems to protect against the disease.

Those who are assessed at high risk (50% or more likelihood of developing the disease within five years) are randomized, half to a control group and half to a group given a single dose of insulin a day. They are asked to monitor blood glucose sporadically. Skyler and his team are hoping that a single small dose of insulin each day might spare young people like Gilbert the pain and inconvenience of multiple daily insulin

injections and fingersticks, not to mention the complications that almost inevitably develop from the disease.

Participants also are admitted to a DPT-1 center once a year for four days of insulin therapy.

A lower-risk group assessed at a 25% to 50% likelihood of developing diabetes within five years is being randomized to daily doses of oral insulin.

Type 1 diabetes is caused by an autoimmune response to the body's own insulin-production system. "We are hoping that the insulin in small doses will tip the autoimmune balance in favor of these patients and keep them from getting the disease," says Skyler. Aside from a few sporadic incidents of shakiness, there have been no hypoglycemic incidents among study participants because the dosage is so low, he says.

Looking at close relatives of Type 1 patients is a good research tool. But it will certainly not catch those most at risk: the 90% who will be diagnosed with Type 1 diabetes who have no relatives with the disease, notes **Richard Furlanetto**, MD, PhD, science director of the Juvenile Diabetes Foundation International in New York City, a sponsor of the DPT-1.

However, relatives are a good starting point because their risk is 10 times that of the general population, he adds. "What we're trying to do here is almost like the process of desensitizing someone to an allergen by giving them small amounts of the irritant and building up their immunity over a period of time."

Results are not yet available, because the study population has not been closed, but Furlanetto says this part of the DPT-1 is a "good starting point, even though it is a shot in the dark."

"It's worth it if we an do something like this safely that might prevent the onset of diabetes," he says, although there are still several questions to be answered. "The general feeling is that this may help, but it's not the answer to the big question of how to prevent the onset of diabetes."

In mid-January, Skyler convened an international meeting in Miami, gathering 126 experts in the field. Some of the information collected may be published in the near future. The progress of the preventive insulin therapy study was on the agenda as well as a number of other topics related to DPT-1's mission to find out if Type 1 diabetes can be prevented.

[For more details, contact Jay Skyler at (305) 243-6018 and Richard Furlanetto at (800) JDF CURE.] ■

Ocular disease may predict all-cause mortality

Eye disease also a predictor of disease's progress

Patients with retinopathy should be treated for heart disease. That's the take-home message from a University of Wisconsin study that shows a strong correlation between retinopathy and all-cause mortality.

"Presence of ocular conditions associated with diabetes may identify individuals who should be under care for cardiovascular disease," says **Ronald Klein**, MD, a professor of ophthalmology at the University of Wisconsin Medical School at Madison.

Investigators examined 996 Type 1 diabetics and 1,370 Type 2s for retinopathy, macular edema, visual acuity, and cataracts in a study that began in 1980. In 1996, the Type 1 patients with the most severe retinopathy, macular edema, and cataracts were at the greatest risk of all-cause mortality and from ischemic heart disease.

Implications of eye disease

Those with proliferating retinopathy were 5.53 times more likely to die of all causes, and 11.02 times more likely to die of ischemic heart disease. Type 1s with severe visual impairment were 4.55 times more at risk for all-cause mortality and 4.66 times more likely to die of ischemic heart disease.

Even after controlling for systemic risk factors for mortality, visual impairment remained a significant predictor of all-cause and ischemic heart disease mortality in the Type 1s.

The severity of retinopathy was associated with all-cause, stroke, and ischemic heart disease mortality in Type 2s. For example, Type 2 diabetics with proliferating retinopathy had 2.27 times the mortality from all causes and 2.07 times the mortality from ischemic heart disease and 2.3 times the death rate than the control group.

The figures for Type 2s with severe visual impairment were striking as well — 2.35 for all cause mortality, 1.32 for ischemic heart disease, and 3.0 for stroke.

"Because vascular disease is involved in most deaths in people with diabetes, there should be a public health benefit accrued from identifying such individuals and monitoring them for heart disease," Klein wrote in the study published in

the *Archives of Ophthalmology* in November.

"These results aren't really surprising given what we think is a connection between microvascular and macrovascular disease in diabetics," says **Andrew Vine**, MD, a retinal specialist at the Kellogg Eye Center of the University of Michigan at Ann Arbor. Because diabetics are at huge risk for either type of vascular disease, careful evaluation and close monitoring are an essential part of clinical care, says Vine.

"We know diabetes causes heart disease. It's just large vessels vs. small vessels that cause the eye disease," he adds. "Nevertheless, this is significant news for diabetics and those who treat them. As clinicians, it's something we need to think about. When you're seeing a patient with retinopathy, look for heart disease as well."

Clinicians should be particularly vigilant with patients who smoke, says Vine. "Smoking for a diabetic is close to suicidal because of its effects on the vascular system."

[For more information, contact Ronald Klein at (608) 262-4032 and Andrew Vine at (734) 763-0482.] ■

NEWS BRIEFS

New line of electrotherapy products to treat ulcers

A line of products containing neuromuscular stimulators is now available for the treatment of diabetic foot ulcers.

The Electro-Mesh stocking electrode and a complete line of soft braces and socks are manufactured by Prizm Medical of Duluth, GA.

The products contain electrodes that cover the extremity and, with electrical energy provided by a pulsed galvanic neuromuscular stimulator, deliver the charge deep into the tissue, increasing blood circulation to the injured area.

Clinical studies showed a gradual reduction in diabetic neuropathic pain and a marked rise in tissue oxygenation during stimulation with the products used over a four-week period. ▼

CE objectives

After reading this month's issue of *Diabetes Management*, the continuing education participant should be able to:

• Identify particular clinical, administrative, educational or managerial issues related to the disease management of diabetes patients.

• Describe how those issues affect diabetes patients, diabetes management programs, and diabetes costs.

• Cite practical solutions to disease management problems associated with diabetes, based on overall expert guidelines from the National Institutes of Health, the American Diabetes Association, the American Association of Diabetes Educators, or other authorities, or based on independent recommendations from clinicians at individual institutions. ■

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Editor: **Kathleen Barnes**, (828) 883-5695, (wolfeagle@citcom.net).
Group Publisher: **Brenda Mooney**, (404) 262-5403, (brenda.mooney@medec.com).
Executive Editor: **Leslie Coplin,** (404) 262-5534, (leslie.coplin@medec.com).
Managing Editor: **David Flegel**, (404) 262-5537, (david.flegel@medec.com).
Production Editor: **Ann Duncan**.

Editorial Questions

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

One Health announces self-management program

The affiliated One Health plans have initiated a new program to help people with chronic disease better manage their conditions. The program, CareResults, became available to One Health Plan PPO, POS, and HMO members with diabetes, heart conditions, and diabetes beginning Feb. 1.

The 3.5 million patient insurer developed the chronic disease program in conjunction with ProMedex,which currently offers health management programs for patients with chronic diseases that cover 20 million Americans.

Potential CareResults patients are asked to complete a detailed confidential health profile by using the One Health Plan Web site or the company's automated phone system.

Based on the profile, the patient's risk level and ability to manage his condition is determined by the medical team; a personalized health improvement plan is created for each individual. ▼

Internet retinopathy service available

The first Inoveon Advanced Diabetic Evaluation Retinopathy Service has been installed at the Veterans Administration Medical Center in Oklahoma City, making it possible for diabetic patients to get retinal exams at the same time they get other checkups, avoiding an additional trip to specialty clinics.

The system places a digital retinal camera in a doctor's office, where technicians take a series of retinal images of every diabetic patient they see. The images are sent over the Internet to the Inoveon reading center at Vanderbilt University in Nashville, TN, where diagnosticians analyze the images. Retinal scores for each eye are returned to the doctor's office within 48 hours, along with recommendations for follow-up.

In about 5% of the cases, retinal disease is sufficiently advanced to warrant a referral for possible laser surgical treatment. Current statistics show that fewer than 40% of all diabetics go to an ophthalmologist for an annual retinal exam, a failure that progresses into unnecessary blindness for 40,000 diabetic patients every year. ▼

FDA approval sought for ulcer healing treatment

A bilayered viable treatment for diabetic leg ulcers has been submitted to the FDA for supplemental product marketing approval. Apligraf, manufactured by Organogenesis, Inc. of Canton, MA, and marketed by Novartis, is currently approved to treat venous leg ulcers.

Clinical studies showed 57% of venous leg ulcers treated with Apligraf and compression were completely closed by week 24, compared to 40% of those treated with compression therapy alone.

Apligraf has an upper epidermal layer containing living human dermal cells but does not contain blood vessels, hair follicles, or sweat glands.

Apligraf is contraindicated for use on clinically infected wounds and in patients with known allergies to bovine collagen or hypersensitivity to the components of the shipping medium. ■