Penn trial offers hope in insulin-cell transplants

By Paul Jablow
FOR THE INQUIRER

Andy Gordon was in his 50s when the symptoms of his Type 1 diabetes mysteriously started to fade.

He had lived with the disease since he was 12, injecting himself with insulin and then switching to an insulin pump that regularly infused him with the lifesaving substance that his pancreas could no longer make.

But now he no longer had the typical warning signs - the sweats, shaking, and dizziness - that used to tell him he needed insulin. He knew this was not a good thing. His early-warning system had stopped functioning, making him vulnerable to diabetic coma. "I'd wake up at night and think I'd been having bad dreams," he said. "Then I'd test my blood sugar and it was dangerously low."

That ominous development helped persuade the Silver Spring, Md., resident to bank on an experimental procedure being tested at the University of Pennsylvania that could add years to his life.

In March 2010, Gordon underwent an islet cell transplant at the Hospital of the University of Pennsylvania. The insulin-producing cells from a pancreas donor were surgically implanted in his liver.

The treatment has worked - so far. It raises the joyful prospect that he will no longer need the insulin pump he has used for decades. And he might avoid the many medical perils of low blood sugar.

Still, earlier patients who got the treatment have seen its healing effects wane. The Penn trial had some improvements, but Gordon will not know for several years how it will turn out.

Gordon, now 57, had heard about the trial by accident, from a friend who spotted it on a website. And the treatment is not without a significant downside. Patients must take immunosuppressants to prevent their liver from rejecting the donated cells. Used with organ transplants of any kind, immunosuppressants can expose patients to some increased risk of other diseases such as cancer.

But doing nothing had risks, too. Gordon's Type 1 diabetes is considerably less common than Type 2, which affects about 90 percent of diabetic patients, but it is also more dangerous. Poorly treated Type 1 can cause severe kidney damage, heart disease, and retinal damage.

Gordon pondered these facts awhile and talked to endocrinologist Michael Rickels and other Penn physicians. Gordon "decided that the risks of adverse effects from diabetes were worse."

He was accepted into the study in the summer of 2007 and waited about 21/2 years until an acceptable donor was found. On March 10, 2010, he had the operation. Surgeon Ali Naji, working with a radiologist, inserted a thin plastic catheter through the abdominal wall and into the portal vein leading to the liver, where the islet cells would attach themselves. The entire procedure, under local anesthetic, lasted a bit over an hour.

Within about two months, Rickels and Naji hoped, the cells would be producing a regular flow of insulin.
"It's a very attractive procedure because it doesn't involve big-time surgery," said Naji, principal investigator of the Penn study. Seven other medical centers are also participating.

Starting in the 1960s, he said, surgeons had sometimes transplanted an entire pancreas into diabetic patients, usually accompanied by a kidney transplant because the disease had also wiped out their kidney function.

"The results were very dismal," he said, partly because it was a grueling, seven-hour operation and the patients were a lot sicker than Gordon was.

But by the 1980s, led by Clyde Barker at Penn and Paul Lacy at Washington University in St. Louis, researchers began experimenting with transplanting cells rather than the entire organ. This was a tricky proposition because 98 percent of the cells in the pancreas are used in the overall digestive process and have nothing to do with insulin.

Insulin is made by cells called the Islets of Langerhans. Using the enzyme collagenase, and centrifuges, researchers perfected a way to isolate those cells.

Earlier attempts using live patients, pioneered in the late 1990s at the University of Alberta in Edmonton, Canada, were initially successful. But only about 10 percent of the patients were insulin-free after five years, although others had reduced dependence. Two physicians with the National Institutes of Health (NIH), writing in 2009, termed the procedure "not ready for prime time."

But Naji says that information gleaned from the earlier trials and recent advances in immunotherapy and the transplant procedure give him hope for significant gains.

The current study, funded by the NIH, is aimed mostly at finding immunotherapy "cocktails" that will reduce rejection of the islets.

Preliminary results from Penn are promising, Rickels said. Nine patients including Gordon have received the transplants, and in each case they are generating insulin with no serious side effects. "Andy is doing fabulous," he said.

In about three years, the researchers will apply to the Food and Drug Administration to have the method declared safe and effective, the gateway to American medicine.

At the same time, Naji said, the researchers at Penn and the other sites are continuing to experiment with ways to fool the body so long-term immunosuppressants are no longer needed. He describes this as "the holy grail of transplant surgery."

Within about two months of the surgery, Gordon no longer needed the insulin pump.

He said he'd had only minor side effects since the procedure, mostly slight skin problems and occasional tremors.

"I'm fairly optimistic," said Gordon, a lawyer now retired from the U.S. Environmental Protection Agency. He knows the islets can begin to fail at any time. But "I don't have to be as rigorous in testing," he said. "I used to prick my fingers 10 to 12 times a day. Now I do it 3 to 4 times a day. I used to walk around with candy in my pocket [for instant sugar]. Now I don't."

As for the peril he faces daily, he said, "I live with that, but I don't think about it."

For information about the clinical trials and eligibility requirements, visit http://clinicaltrials.gov and search for...
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"islet cell transplants."

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