Scientists report transplant advance for type 1 diabetes

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Used in single patient, special chamber may allow implantation of insulin-producing cells without rejection.

(HealthDay)—Using a specially designed chamber, an international research team has transplanted islet cells into a patient with type 1 diabetes.

The new technique avoided having to use immune-suppressing medications, while still allowing the islet cells to function and make insulin. In theory, the chamber "hid" the transplanted islet cells from the patient's immune system, the researchers explained.

Islet cells are normally found in the human pancreas. One critical function of these cells is producing insulin—a hormone crucial for metabolizing the carbohydrates in food. In people with type 1 diabetes,

an autoimmune disease, the islet cells have been destroyed by the body's own immune system.

"In order to transplant replacement cells, heretofore, the immune response to the foreign cells has had to be controlled with immunosuppression," explained study co-author Dr. Norman Block.

Now, he said, senior study author Dr. Stefan Bornstein "has found a way to implant foreign cells and protect them without using immunosuppression"—drugs to dampen the immune system.

Medications used to suppress the immune system can come with significant risks and side effects.

The study was released online Oct. 28 in the *Proceedings of the National Academy of Sciences*.

Because their bodies lack working islet cells, people with type 1 diabetes no longer produce enough insulin to survive. They must take daily insulin injections or receive their insulin through a small catheter underneath the skin that's attached to an insulin pump.

Maintaining the proper levels is a difficult task. Too much insulin, and blood sugar levels can drop to dangerously low levels that at their worst can cause seizures and even death. Too little insulin, and blood sugar levels run high. Over time, these high levels can put someone with diabetes at risk of complications, such as vision problems and kidney disease.

Needed levels of insulin vary from person to person, and according to the types of food someone eats, how much they eat, how much they exercise and what type of stress they face.

Because islet cells can currently only be transplanted with the use of immune-suppressing drugs, the implant procedure is limited to patients who have difficult-to-control diabetes and experience repeated episodes of life-threatening low blood sugar levels. Immune-suppressing drugs have potential side effects, including the risk of infection and certain cancers.

To try to make the implant procedure available to more people, the researchers designed a semi-permeable chamber to house the islet cells, with the hope that the immune system wouldn't be able to "see" the new foreign cells.

However, when islet cells are first transplanted, they haven't established their own blood supply and aren't able to get oxygen when they're hiding in the chamber. For that reason, the current version of the device had an oxygen port on the outside of the body attached via tubing that had to be refilled daily by the patient for as long as a month or two, Block explained.

The device was implanted into a 63-year-old man, who'd had type 1 diabetes for 54 years. He was of average weight, and didn't have any serious complications from his diabetes.

Blood tests for a substance called C-peptide showed he wasn't producing any of his own insulin. C-peptide is a byproduct of insulin production, and is often used to measure the success of diabetes treatments in research settings. If C-peptide levels rise, it means insulin production has risen.

The transplant recipient had modest increases in his C-peptide levels, and the levels of C-peptide and insulin rose rapidly in response to an injection of glucose (a form of sugar). Over time, his long-term blood sugar control improved slightly, and his need for insulin decreased,

though not to the point where he didn't need insulin injections.

What was remarkable, however, was that after 10 months, there were no signs that the immune system was aware of the new cells. There were no signs of possible rejection of the new cells, and no signs that the immune system initiated an attack on the new islet cells.

The transplant only contained about half the amount of islet cells normally transplanted. "We only had a limited number of beta cells available from this one pancreas," explained Block, a distinguished professor of urologic research and clinical director of the Endocrine Polypeptide and Cancer Institute at the Veterans Affairs Medical Center Research Service, in Miami.

The limited availability of islet cells for transplant has been another barrier to more widespread use of islet cell transplantation. Block said that the device used in this study could help with that problem as well.

"The reality of this device, since the device protects the incorporated islet cells from immune attack, is that it doesn't really matter if you use human or porcine (pig) islets. Going to xenotransplantation could be a future step that would enable an unlimited number of islet cells that produce human-like insulin," he said.

Xenotransplantation is any procedure that transplants cells, tissues or organs from an animal into a human, according to the U.S. Food and Drug Administration.

A diabetes expert not connected with the study called the finding "exciting."

"They've clearly shown the ability to maintain some function without immunosuppression," said Julia Greenstein, vice president for cure

therapies at JDRF (formerly the Juvenile Diabetes Research Foundation).

But, she added, "It's a study of one patient, and the level of C-peptide wasn't enough to significantly impact the clinical situation of the recipient. The goal of transplantation is normal [blood sugar levels] or insulin independence." Neither of those goals was met in this study."

"This study is one early step on the way to developing a practical approach to providing islet function for a person with type 1 diabetes," Greenstein said.

More information: Transplantation of human islets without immunosuppression, www.pnas.org/cgi/doi/10.1073/pnas.1317561110

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