No More Insulin Shots, Thanks to a New Type of Islet-Cell Transplant

Written by Sari Harrar

With commentary by Camillo Ricordi, M.D., director of the Diabetes Research Institute and a Stacy Joy Goodman Professor of Surgery, Distinguished Professor of Medicine, Professor of Biomedical Engineering, Microbiology and Immunology at the University of Miami Miller School

Left to right: Joshua Rednik, DRIF President and CEO; transplant recipient Wendy Peacock; transplant team: Dr. Camillo Ricordi and Dr. Rodolfo Alejandro

Decades after her own pancreas stopped producing insulin, a Texas woman with tough-to-control type 1 diabetes no longer needs daily insulin shots thanks to a new transplant procedure developed at the Diabetes Research Institute (DRI) at UHealth — University of Miami Health System. The process implants insulin-making islet cells onto a layer of fat in the recipient's abdomen, along with a sticky gel that helps hold the cells in place.

Wendy Peacock, 43, from San Antonio, underwent the transplant at Jackson Memorial Hospital in mid-August. In early September, a few short weeks after receiving the cells, researchers announced that the donated cells were working like a natural pancreas – sensing Peacock's blood sugar levels and pumping out enough blood-sugar controlling insulin, at the right times, so that she no longer needed insulin injections.

"The cells starting working right away," says Camillo Ricordi, M.D., director of the DRI and a Stacy Joy Goodman Professor of Surgery, Distinguished Professor of Medicine, Professor of Biomedical Engineering, Microbiology and Immunology at the University of Miami Miller School. Dr. Ricordi also serves as director of the DRI's Cell Transplant Program. "We continued

giving her insulin, in smaller and smaller doses, just to avoid stressing her new cells for several weeks. We've never seen this level of functioning from transplanted islet cells before. It's very exciting."

It's also early days for the innovative procedure, which Dr. Ricordi says could eventually replace islet-cell transplants into the liver— a procedure currently performed at transplant centers around the world for people with severe type 1 diabetes. (In the U.S., all islet-cell transplants are considered experimental.)

Long-term studies of the new procedure are needed, but Dr. Ricordi hopes it will have a better track record than islet-cell transplants to the liver. About 58% of islet-cell transplants to the liver are still functioning after 5 years – with some recipients no longer giving themselves insulin shots at all and others needing some extra insulin, but with better control of their diabetes.

"The liver is problematic," Dr. Ricordi explains. "In that procedure, islet cells are infused into the portal vein and travel to the liver, where they become trapped in tiny blood vessels. There, they sense blood-sugar levels and release insulin in response. It works, but the process triggers intense inflammation that can kill 50-60% of the cells. Many people need two or three infusions of donated cells."

In contrast, the new procedure developed by Dr. Ricordi and a large team at DRI bypasses the biggest source of inflammation: direct contact with blood. Working through tiny incisions in the recipient's abdomen, transplant surgeons spread tiny clumps of islet cells across an iPhone-sized stretch of the omentum – the apron of protective fat over internal organs in the abdomen. The gel — is a mix of plasma from the recipient's own blood along with a sticky substance called thrombin; future trials will also likely include anti-inflammatory agents, oxygen promoters, and growth factors along with the transplanted cells. A flap of the omentum is folded over the cells and held in place by the gel – creating a sort of sandwich.

"The islet cells begin sensing blood glucose levels in the body immediately," Dr. Ricordi says. "The omentum is highly vascularized, and so is able to provide nutrients and oxygen quickly. Insulin can pass into the bloodstream. Over time, blood vessels grow around the islet cells. And the DRI BioHub, a biological scaffold of sorts, is absorbed by the body."

"This minimizes the inflammatory reaction that happens when islet cells come in contact with blood during a transplant to the liver," Dr. Ricordi explains. "The other advantage of using the omentum is that it's in the same circulatory drainage system as the pancreas, so insulin enters the system and is carried to the liver where it begins regulating blood sugar – just as it does with a normal pancreas."

Brittle Diabetes and Anti-Rejection Drugs

Like liver-based islet cell transplants, the DRI BioHub approach requires recipients to take immune-suppressing medications for life. "There are two reasons for this," Ricordi notes. "First, we don't want the immune system to attack the foreign cells. And we don't want the same kind of auto-immune reaction that attacked a person's islet cells in the first place, causing type 1 diabetes, to happen again."

Anti-rejection drugs carry their own risks, including increased odds for infection especially in the first months after a transplant. For that reason, islet cell transplants are currently available only for individuals with type 1 diabetes who have frequent, severe episodes of hypoglycemia (low blood sugar) without warning symptoms. This hypoglycemic unawareness can be fatal; many become unconscious and require trips to the emergency room. "The risks outweigh the risks of anti-rejection drugs," Ricordi says.

He hopes the DRI BioHub approach will eventually do away with anti-rejection drugs. "We may be able to add anti-rejection agents to the gel scaffolding," he says. "And the location on the omentum may also mean less medication is needed. Once we have an islet cell transplant without anti-rejection drugs, we can call it a cure."

A Precious Resource: Islet Donor Cells

Other transplant experts were optimistic about the new transplant's promise. "Dr. Ricordi has created an omental sandwich that protects islet cells from at least one of the three types of rejection that threaten islet cells after transplantation – the immediate immune-system reaction that creates inflammation and kills so many cells," notes F. Charles Brunicardi, M.D., F.A.C.S., Professor and Vice Chair of Surgical Services at the David Geffen School of Medicine at UCLA and Chief of General Surgery at, Santa Monica Hospital. "It may protect against the other, later types of rejection as well. I was jumping for joy when I heard about the first recipient's success. Dr. Ricordi's brilliance and persistence have brought the field to where it is today. "

Brunicardi said the new technique also makes good use of a precious resource: donor islet cells. "You only need cells from one compatible pancreas, instead of from two or three with transplants to the liver," he notes. "Donor cells are in short supply in the U.S., which is why so many groups are trying to find new sources of islet cells."

Canadian islet cell transplant pioneer A.M. James Shapiro, M.D., Ph.D., Professor of Surgery, Medicine and Surgical Oncology and Director of the Clinical Islet Transplant Program at the University of Alberta, Canada, said he expects to work with Dr. Ricordi on the next stage of research. "We have approval to use the protocol here and expect to do about ten of the procedures here and ten in Miami and look at the outcomes," says Shapiro, who led development of a breakthrough technique in the late 1990s that's produced more successful transplants. "There are still many research questions to answer, but the biological scaffold opens up the possibility of co- transplanting other cells that would shield the islet cells from the immune system."

Dr. Ricordi hopes islet cell transplants will win U.S. Food & Drug Administration (FDA) approval in the next two years.