Democracy Dies in Darkness

Diabetes took over her life, until a stem cell therapy freed her

Scientists are making progress replacing the critical insulin-producing cells that are destroyed by the disease.

By Carolyn Y. Johnson

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For years, Amanda Smith and her husband were jolted awake at night by a buzz-buzz-beep — an alarm warning that her blood sugar was too high or too low. She would reach for juice boxes stored in her nightstand or fiddle with her pump to release a bolus of insulin.

Smith, a 35-year-old nurse from London, Ontario, has Type 1 diabetes, which wipes out critical islet cells within the pancreas that produce insulin. Without them, Smith relied on vials of insulin from a pharmacy and constant vigilance to stay alive. “You have to pay attention to your diabetes, or you die.”

On Valentine’s Day 2023, doctors transplanted replacement islet cells, grown in a lab from embryonic stem cells, into a blood vessel that feeds Smith’s liver. By August, she no longer needed insulin. Her new cells were churning it out.

“I just feel normal again,” Smith said. “You didn’t realize how much of your life it took up — until it’s taking up none, now.”

Smith is at the forefront of a medical experiment that seeks to treat the root cause of diabetes by replacing the cells the disease destroys. It’s a key step forward in the long quest to develop a cure for diabetes and a front-runner to finally deliver the sci-fi promise that has enveloped the stem cell field for more than two decades.

Stem cells have the remarkable ability to develop into any cell or tissue in the body, and scientists have long dreamed of harnessing their regenerative power to repair the harm done by disease or injury.

Smith is one of a dozen patients who have received a full dose of islet cells generated in a laboratory from stem cells. Eleven of the patients in the clinical trial drastically reduced taking insulin or stopped altogether, according to data presented at an American Diabetes Association meeting in June.

Despite the promise, the therapy developed by Vertex Pharmaceuticals remains in early stages, and many experts consider it a major step forward, not the finish line.

No one knows how long these cells will keep churning out insulin or whether the therapy is safe long-term until it is tested and followed up in more patients, who must take immune-suppressing drugs to prevent their body from rejecting the foreign cells. One patient died of an infection caused by a complication of sinus surgery, highlighting the risk of immunosuppressive medications, which were among the factors contributing to the patient's death.

Scott Soleimanpour, director of the Michigan Diabetes Research Center, was diagnosed with Type 1 diabetes when he was 5 years old and recalled that throughout his youth, doctors told him there would be a cure within a decade. Soleimanpour, now in his 40s, made a pact with his childhood self not to promise specific timelines to his patients. Still, he remains hopeful.

"It's terrible to have diabetes, but this is the best time in the history of the planet to have diabetes, because we have these amazing technologies," Soleimanpour said. "We haven't reached the end of the road, but we're on the journey. It's okay to sit at this stage of the journey and say, 'This is good. Let's keep going.'"

An imperfect path forward

The quest to cure diabetes didn't start with stem cells. In 1966, doctors performed the first whole pancreas transplant in a diabetic patient. It was major surgery, not a practical treatment for the roughly 2 million people with Type 1 diabetes in the United States.

But as the biology of the pancreas was unraveled, scientists began imagining a stripped down version. Within the pancreas are islets, clusters of cells that produce insulin and other hormones. Instead of transplanting the whole organ, scientists wondered, what if they could use islets harvested from organ donors?

James Shapiro, a transplant surgeon at the University of Alberta in Edmonton, began working on the problem in the 1980s.

"None of the experiments I did worked," Shapiro recalled. "In the beginning, we could scarcely reverse diabetes in a rat."

Shapiro continued to chip away at the challenges, and in 2000, he and colleagues reported that seven patients had been transplanted with islets from organ donors — and were able to stop using insulin. The procedure, called the Edmonton Protocol, electrified diabetes researchers. It was proof that cells could be replaced and the disease could be reversed.

“Then, the warts started to become apparent,” Soleimanpour recalled.

Repeat transplants were often needed, and most patients eventually required some insulin again. The immune-suppressing drugs can increase the risk of infections, cancer or other side effects. And the supply of islets was extremely limited.

More than a thousand transplants in the years since showed the approach can work. Last year, U.S. regulators approved an islet cell therapy from organ donors. But use of the treatment is far from mainstream.

Body, heal thyself

Researchers looked to the field of stem cell research to solve the scarcity problem.

Unlike most of the body’s cells, embryonic stem cells — which are created from human embryos — can give rise to every tissue and organ in the body, from brain to muscle to insulin-producing islet cells found in the pancreas. In theory, scientists could create as many as needed, with far better control over quality and consistency.

Douglas Melton was a biologist focused on frog development at Harvard University when, in 1991, his infant son, Sam, was diagnosed with Type 1 diabetes. His daughter, Emma, would also be diagnosed with the condition. Melton shifted his focus to study how insulin-producing cells normally develop, in hopes that scientists could imitate the process to help patients.

Melton quickly ran into a hard scientific truth about stem cells: Yes, they can become any kind of cell, but only if they’re coaxed through the right steps, akin to making an elaborate recipe. His laboratory spent two decades trying to devise the right steps, ingredients and timing, a trial-and-error process that resulted in a “six-step education process” that takes weeks.

Felicia Pagliuca had been working in cancer biology at the University of Cambridge when she met Melton at a seminar and was inspired to join his laboratory, drawn by the idea “that you could, instead of trying to kill cells to cure a disease, just use the cell itself as a building block of life — as a medicine,” Pagliuca said. “Especially the idea you could make these cells from scratch in the laboratory.”

To test their lab-grown cells, scientists put them in a dish with glucose and an indicator that changed color in the presence of insulin. After many experiments, they saw a flash of blue, a sign they had finally gotten the recipe right.

In 2014, they published those results and founded Semma Therapeutics, which was later acquired by Vertex Pharmaceuticals for $950 million. Semma was named after Melton’s now grown-up children, aimed at moving a laboratory breakthrough into the real world.

‘My life has changed’

For Amanda Smith, diabetes wasn’t a manageable illness. It haunted her days and clouded her future. A family member lost a limb to the disease.

Smith had a particularly difficult time anticipating “lows,” when her blood sugar would drop. Once she’d realize it was happening, it was too late — “You just feel like death, you’re so weak you can’t move, you feel nauseous. And then you know: It’s do or die.” In trying to reverse the low, she might eat too many carbs, causing her blood sugar to spike. “You feel like a slug.”

As a child, she would remind her mom, who also has Type 1 diabetes, to check her sugars. Then she began to hear her own family do the same to her. Smith’s daughter Draya, now 9, would borrow her mom’s cellphone to play games but be interrupted by the alerts. “Check your sugars,” Draya would remind her, vowing to become a doctor and develop a cure.

Smith looks back on the quiet of the past year — no buzzers, no alarms — with a bit of wonder. Her medical team feels much the same.

“It’s amazing to see what it’s like, living with diabetes and six months later, essentially not having it,” said Trevor Reichman, surgical director of the Pancreas Transplant Program at the University of Toronto. Andrea Norgate, a nurse who works with him, interjected: “It’s the most exciting thing that’s happened in the world, ever, is probably more accurate.”

Three times a day, Smith takes pills to stop her immune system from destroying the foreign cells. She has had some side effects — early on, she got canker sores, and she’s careful around sick people. But for Smith, that’s manageable compared with the roller coaster and health risks of diabetes.

For the treatment to become safer and accessible to more patients, including young children, the next step is to find ways to protect the cells from the immune system.

Irl Hirsch, an endocrinologist at the University of Washington who has diabetes and has consulted for Vertex, recalled that before he started medical school in 1980, he worked for a famous endocrinologist, Paul Lacy, who was pursuing transplants in rodents to cure diabetes.

“What he told everybody is: We’d be doing these cell transplants in humans in five years. Everybody believed it,” Hirsch said. “That didn’t happen, and the big problem has been the whole issue of [immune] rejection and the need for immunosuppression. It was the problem in 1980, and it’s the problem now.”

Scientists aren't waiting to tackle that problem. Vertex is testing a method of encapsulating the cells in a bioengineered device. The company is also using gene-editing techniques to make cells "hypoimmune," or invisible to the immune system. Other researchers are creating stem cells from individual patients and coaxing those to become islet cells. Because the immune system won't see those cells as foreign, it could reduce the amount of immunosuppression needed.

Trading one horrible disease for long-term immunosuppression gives many clinicians pause, but many patients and advocates are impatient. Today's diabetes technologies are lifesaving but imperfect. The risks of infection must be weighed, but so must the risk of "having a heart attack 15 years before your peers, going blind and losing your kidneys," said Aaron Kowalski, president of Breakthrough T1D, a research and advocacy organization.

Smith credits her insulin pump with keeping her alive but was elated to banish it to the back of a kitchen cabinet. She no longer has to plan her life around her illness.

"I pray this gets to everyone," Smith said. "My life has changed."