

Sigrun Schwendinger—Islet Transplantation Holds Great Hope for Type 1 Diabetes Patients

Sigrun Schwendinger lived with type 1 diabetes for 50 years. Diagnosed at age 7, she took insulin daily to keep her blood sugar levels within normal range—and to stay alive. Today, at age 57, Sigrun is insulin free thanks to a revolutionary new treatment originally developed by researchers at the University of Alberta in Edmonton, Canada, and now reproduced by a team at the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) and National Institutes of Health (NIH) Clinical Center. Commonly referred to as the “Edmonton protocol,” insulin-producing beta cells found in clusters called “islets” are extracted from the pancreases of deceased donors and then transplanted into patients with type 1 diabetes, who then are treated with an experimental combination of immunosuppressive drugs. So far, only a few people worldwide have undergone this experimental yet promising new transplant technique. In fact, Sigrun, having undergone the procedure at the NIH Clinical Center in December 2000, is the first person in the United States to have been successfully transplanted using the new protocol. “I feel extremely fortunate that I qualified for this procedure, and that my prayers of years ago to be insulin free have been answered,” she says.

Islet transplantation using the new protocol, however, is still very much in its infancy. No one knows, for example, what the outcome will be five, ten, or twenty years from now for people who undergo the protocol today. But scientists both at the University of Alberta in Edmonton, Canada, and the NIDDK are hopeful that the new islet-cell research may eventually lead to treatment not only for type 1 diabetes patients, but for some type 2 patients, as well.

LIVING WITH DIABETES

Type 1 diabetes results when the body’s immune system destroys the pancreatic insulin-secreting beta cells that control blood sugar (glucose) levels. As a



Sigrun Schwendinger, 57, underwent pancreatic islet transplantation in Winter 2000-2001. As a result of this procedure, Sigrun says: “I’m very hopeful for not only my future, but for the future of the millions of others who suffer with type 1 or type 2 diabetes.”

FACT:

An estimated one million Americans suffer from type 1 diabetes; an additional 15 million have type 2.

result, people with type 1 diabetes fight a constant battle to keep their blood glucose levels from going too low or too high. People with type 1 diabetes must

“manage” the disease by taking daily injections of insulin—sometimes as often as four or five times a day, depending on their glucose levels—and by controlling their dietary intake.

FACT:

Even those who “manage” their diabetes well are at high risk for heart disease, stroke, and nerve damage.

Diabetes is also the leading cause of kidney failure, blindness (in adults), and non-traumatic amputations, and shortens average life expectancy by up to 15 years.

Unlike most with the disease, Sigrun, an admissions assistant at a private school, says diabetes did not hamper her lifestyle for many years. Until recently, she required only one shot of insulin a day. Even as a teenager, Sigrun says “I never had a craving for sweets, and when I did have something like pudding, I’d only take one spoonful, and no more.” Also, she was fortunate in that she never suffered any early complications as a result of her diabetes. She married, gave birth to and raised three healthy, non-diabetic sons, and, for the most part, led a normal life—until around the age of 50.

“Everything was going well,” Sigrun says. “After menopause, however, my blood sugar periodically would spike to 300 in a matter of hours (a non-diabetic normal range is between 80 and 120 after a meal).” Every couple of weeks she experienced rapid heart beat, excessive perspiration, and felt confused due to extremely low blood sugar levels. Although Sigrun never had serious kidney ailments, by her mid 40s she began manifesting symptoms of nerve and eye diseases associated with diabetes, and had cataracts removed from both of her eyes. After years of successfully living with diabetes, “I suddenly became more frightened of my situation,” she says, “and its terrible side effects.”

EDMONTON PROTOCOL

Islet-cell transplantation is not new. Over the past 25 years or so, more than 300 patients have undergone such transplants in medical centers around the world. But only a few were successful, and very few if any

proved effective long term (beyond one year). Most scientists believe that the poor long-term success rate has been due to the body’s rejection of the transplanted cells.

The scientists in Edmonton, Alberta, Canada, developed a clinical protocol that uses a novel, steroid-free combination of three drugs. The drug combination appears to prevent rejection as well as halt autoimmune destruction of the islets. In this technique, islets are isolated from the pancreas of organ donors. Following isolation, the islets are injected into the portal vein, which supplies blood to the liver. The islets then migrate to the liver, where they flourish and produce exactly the amount of insulin required to maintain almost perfect blood sugar control. A high percentage of patients who have been transplanted using this new protocol have remained insulin free. As a result, the approach taken in the Edmonton protocol is now being tested in a larger number of patients.

Research to Increase Supply of Islets

One of the limiting characteristics of the Edmonton protocol is that it usually requires two or more pancreases to yield sufficient islets for each patient. Should the protocol become more commonplace, the demand on an already short supply of donor organs will inevitably increase dramatically. Scientists at the NIDDK and elsewhere already are trying to induce islet cells to reproduce in laboratory cultures. They also are attempting to determine whether or not animal stem cells can be programmed to grow into islets.

BECOMING INSULIN-FREE

After going through an extremely rigorous screening process that included filling out a lengthy questionnaire and meeting with several physicians, Sigrun underwent a battery of tests, including EKGs, stress tests, and insulin tests. She was eventually placed among the NIDDK’s list of 60 candidates for the procedure. “I was

advised of all the risks involved,” says Sigrun, including blood clots, and side effects from a depleted immune system. Sigrun emphasized the fact that she was told repeatedly by her NIDDK research physician that she could leave the protocol at any time. But with the support of her husband and family, Sigrun decided to go through with the procedure, and as a result, played a part in the history of this new transplant technique.

Because the procedure is so new, researchers don’t know what complications might arise over time. “Therefore, the biggest risk is the unknown,” says David Harlan, MD, Chief of the Transplantation and Autoimmunity Branch of NIDDK, who attended to Sigrun during her transplant. He adds that, while Sigrun has benefited from her new-found and—hoped for—long-term independence from insulin, she also has contributed toward the development of a treatment that may one day legitimately be called a cure for type 1 diabetes. “Not only has she helped win a victory for humanity,” he says. “Sigrun also afforded me the privilege I have long sought. That is, she was the first patient I was able to look in the eye and say, ‘Congratulations, you no longer, at least for today, have diabetes.’”

As this document goes to press, it has been eleven months since Sigrun underwent the two-stage islet transplant procedure—and she remains insulin free. NIDDK physicians monitor her condition on a regular basis, and she continues to take immunosuppressant

Undergoing Islet Transplantation

A single donor pancreas provides about 250,000 to 500,000 islets. Each recipient patient, however, needs about 800,000 cells before he or she is insulin free. As a result, the patient normally needs two infusions of cells, from two donors.

In Sigrun’s case, after being called in for her first infusion, she was sent home because researchers were unable to isolate enough islets in the lab. A week later, another donor organ of her blood type was received and she was able to undergo the first infusion. It took a month and a half before a second suitable organ was found to complete her islet transplant. Between the first and second infusions her dosage of insulin was reduced by half. A day after the second infusion, she was insulin free.

drugs. She says the dosage of these drugs is being gradually reduced as time goes by.

Sigrun, who describes herself as an optimistic, confident, cheerful person, as well as a risk taker, admits that she had given up all hope years ago of being cured of diabetes. “As a result of this procedure, and the follow-up I am receiving at NIDDK, I’m very hopeful for not only my future, but for the future of the millions of others who suffer with type 1 or type 2 diabetes.”