MINNESOTA MEDICAL FOUNDATION
at the University of Minnesota

Dear friends,

Because you have supported diabetes research at the University of Minnesota, we are pleased to send you this inaugural issue of *Discoveries in Diabetes*, a publication that highlights our leading-edge work in this area.

You will get this newsletter twice a year and—if we have your e-mail address—e-updates in between. To make sure you're among the first to hear about diabetes breakthroughs at the University, please send an e-mail to Angela Lillie at a.lillie@mmf.umn.edu with "E-newsletter" in the subject line. If you'd like to receive a paper copy of these updates, call Angie at 612-625-9646 and she'll add your name to our list.

We look forward to sharing our exciting diabetes news with you. If you have ideas for upcoming newsletters or want to share your thoughts on the current issue, feel free to contact me directly at 612-625-0497 or j.gorell@mmf.umn.edu.

Thank you so much for your generous support of our mission.

Sincerely,

Jean C. Gorell, CFRE
Director of Development, Diabetes
Minnesota Medical Foundation

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Discoveries *in* Diabetes

A publication for those who support diabetes research at the University of Minnesota through the Minnesota Medical Foundation

University team continues to lead the charge toward a diabetes cure using islet transplants

Nearly a decade ago, Bernhard Hering, M.D., and his team were making strides for patients suffering from a dangerous complication of type 1 diabetes known as hypoglycemia unawareness.

Hering's group was among the first in the world to bring islet-cell transplantation to clinical trials, hoping to restore sensitivity to low blood sugar levels for the 12 percent of people with type 1 diabetes who no longer feel important warning signs like shakiness when their blood sugar plummets, which can result in a loss of consciousness or even brain damage.

The results of the first four islet-cell clinical trials at the University of Minnesota's Diabetes Institute for Immunology and Transplantation far surpassed expectations.

In nearly 90 percent of patients who received a transplant—consisting of a mere teaspoon-sized infusion of insulin-producing islet cells from a donor pancreas—the procedure not only cured hypoglycemia unawareness, but it also eliminated the need for daily shots of insulin, at least temporarily. Fifty percent of people in the trial were still insulin-independent after five years.

"The proof of concept has been shown," says Hering, who holds the Eunice L. Dwan Diabetes Research Chair and serves as scientific director of the Diabetes Institute. "We can reverse diabetes with a cell-based therapy."

Now Hering's group has initiated a critical round of studies to refine the course of treatment and improve long-term outcomes.

The goal is to improve the immunosuppression that's required to keep recipients from rejecting the donated cells. The agents they're investigating include antibodies given at the time of the transplant that may enhance islet-cell longevity as well as new drugs that may replace the potent immunosuppressive medication typically used in transplant surgery, which can be damaging to the kidneys.

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Photo by Tim Rummelhoff

Surgeon Bernhard Hering, M.D., is leading part of a national clinical trial aimed at improving long-term outcomes of islet-cell transplants.

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Sugar on the brain

Elizabeth Seaquist, M.D.

Key to diabetes care is managing how the body handles sugar. Glucose is stored as glycogen in tissues throughout the body until it's called on to provide energy. But little is known about what happens to glycogen stored in the brain.

"What glycogen is doing there and whether it's metabolically active hasn't been defined, particularly in humans," explains Elizabeth Seaquist, M.D., a professor of endocrinology and diabetes at the University of Minnesota. "We haven't had a way to measure it."

Seaquist, who holds the Pennock Family Land-Grant Chair in Diabetes Research, has long suspected that glycogen content in brain tissue may change dramatically in people with type 1 diabetes who suffer from hypoglycemia unawareness. These patients, who've lost the ability to sense when their blood sugar is low, might develop large concentrations of brain glycogen, a compensatory response to prolonged periods of low blood sugar. Moreover, that glycogen might be metabolized in a unique way.

Two years ago, Seaquist and an interdisciplinary team of investigators at the University's Center for Magnetic Resonance Research—one of the world's top imaging labs—began to test whether it's possible to see changes in brain glycogen using high-field magnetic spectroscopy.

They gave healthy subjects a non-radioactive isotope that gets incorporated into glycogen in the brain and then slowly lowered subjects' blood sugar. As the research participants lay in the hull of the magnet, investigators monitored the tagged molecules to see whether brain glycogen changed over time.

The results were clear. Researchers were able to quantify brain glycogen and see marked decreases after hypoglycemia. They were even able to determine how long it took for healthy brains to put the glycogen to use.

"Using spectroscopy, we're able to measure brain glycogen content as we've never been able to before," Seaquist says.

Now her team is beginning to study patients with type 1 diabetes who have hypoglycemia unawareness, comparing their brain glycogen metabolism with the measurements from healthy subjects. The results may reveal more about the conditions necessary for the complication to occur.

"As we know more about how hypoglycemia unawareness happens," Seaquist says, "we'll have a leg up on developing therapies to prevent it."

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Leading the charge continued from cover

For more information about the studies and requirements for participating, visit www.diabetesinstitute.org or call 612-626-3016.

But there's no doubt that successful islet transplants can be life-changing for patients.

Forty-four-year-old Stephanie Arneson grew up vigilant about monitoring her blood sugar. "You never get a day off from diabetes," she says.

Then, in 1999, she stopped sensing the signals of hypoglycemia and started passing out unexpectedly. For the energetic mother of two young girls, frequent finger pricks and strategic eating weren't maintenance enough. When she blacked out while driving, knocking into a cement wall on an exit ramp, she knew something had to change.

Arneson signed on for one of the early clinical trials at the Diabetes Institute. Despite initial setbacks, which are now rare, the islet-cell transplant that took prompted an instant turnaround. Arneson was able to feel signs of low blood sugar again.

Now she's gone five years without needing a single insulin shot, taking only daily immunosuppressive medication to keep her body from rejecting the transplanted tissue.

The hardest part today, she says, "is explaining to people, 'Well, I *used* to have diabetes.'"

Hering's group hopes that more people will have to offer that explanation in the near future. The Diabetes Institute is one of three principal sites in the United States conducting phase III trials, the final round of study before applying for licensure from the Food and Drug Administration, to determine whether human islets can be used as a standard therapy for diabetes.

"This will be a landmark achievement," says Hering. "It will really open the door to more opportunities for patients."

Lauren, Julia, Stephanie, and Rob Arneson

Creating a new supply of islet cells

For people who have diabetes, the use of islet-cell transplantation to eliminate the need for insulin injections holds great promise.

But the supply of islet cells available for those transplants is limited. The cells typically come from the pancreases of deceased donors, and it sometimes takes cells from two or three donor pancreases to reverse diabetes in one person.

moving beyond diabetes
spring point PROJECT

In 2006, research led by University of Minnesota innovator Bernhard Hering, M.D., showed that islet cells from pigs could be used to reverse diabetes in monkeys. He thinks that pig islet cells could be used to reverse diabetes in humans as well.

But first Hering would need a safe source of high-quality pigs from which to harvest the cells.

Enter Spring Point Project, a nonprofit organization founded by entrepreneur Thomas Cartier that aims to expedite the widespread availability of islet cells for transplantation by creating a source of disease-free pig islet cells at a secure, sterile facility.

Cartier's son Cory was diagnosed with type 1 diabetes at age 10. Doctors told the family that there was no cure—Cory would just have to deal with it.

"When I realized that dealing with it means watching him take shots and prick his fingers, like millions of people do, my wife and I said it's just not acceptable," Cartier says.

Today the Spring Point Project facility houses pigs whose islet cells will someday be used to try to cure diabetes in humans. Clinical trials at the University to test this idea are scheduled to begin in late 2009 or early 2010.

"We're going to find the answer to this," Cartier says. "We're not going to accept it the way it is."

Giving research a sporting chance

Jeff Dobbs had been enthralled by golf since his childhood days, when he would hit balls with his dad in the backyard of their New Hope, Minnesota, home. An avid sportsman, the robust and enterprising father of four also loved helicopter skiing, fishing, coaching his children's soccer teams, and driving race cars.

When he was diagnosed at age 35 with type 1 diabetes, he battled its effects but still tried to keep the disease from interfering with the activities he loved. "He would tell people he was with on the trip [about his diabetes], in case he needed help," says his wife, Kay, "but it was something he didn't share with everyone."

And Jeff Dobbs was captivated by the idea of advancing diabetes research. "He was really passionate about trying to find a cure," says his 19-year-old daughter, Jennifer, "not for himself, but for us, his kids, and for people in the future."

In the mid-1990s, as friends batted around the idea of creating an annual diabetes fund-raising golf tournament, Dobbs stepped in with characteristic vigor. Through ProStaff, the Minneapolis-based temporary staffing company he had started from scratch, he helped underwrite the expenses of the University of Minnesota's first Golf Classic "fore" Diabetes Research in 1996. His quiet gesture ensured that all money raised could go directly to studies focused on eliminating the disease.

The annual tournament he started has become a mainstay and a critical source of funding for the University's Diabetes Institute for Immunology and Transplantation. In its 13 years, the tournament has raised more than $4 million for studies at the Diabetes Institute.

At this year's event, which took place on June 16, the early-bird round of the Golf Classic "fore" Diabetes Research had a special meaning for the golfers. Dubbed "Jeff's Derby," the round was reserved for more than 120 family members and friends of Jeff Dobbs, who died in October 2007 at age 51.

The institute that Dobbs supported with such enthusiasm recently honored his commitment to raising money for diabetes research by renaming the endowed chair held by pioneering physician-scientist David E. R. Sutherland, M.D., Ph.D., head of the Transplant Division in the University's Department of Surgery and director of the Diabetes Institute. Historically called the Golf Classic "fore" Diabetes Research Chair, it's now called the Jeffrey Dobbs and David E. R. Sutherland, M.D., Ph.D., Diabetes Research Chair.

Kay Dobbs is certain that her husband would have been astounded by the personal recognition. "He was just very excited by the possibilities he saw happening at the institute and was impressed with the dedication of the doctors," she says. "He was motivated to do everything he could to bring about a cure."

Jeff Dobbs and family

To make a gift to the Dobbs-Sutherland Diabetes Research Chair, visit www.mmf.umn.edu/goto/dschair or contact Jean Gorell at 612-625-0497 or j.gorell@mmf.umn.edu.

Revving up for diabetes at the Lightning Run bike rally

Hundreds of bikers hit the streets of St. Paul July 25 and 26 for the ninth annual Lightning Run rally to support diabetes research at the University of Minnesota.

More than 1,500 people attended this year's weekend of events—which included a kick-off party with live music, auctions, and an awe-inspiring motorcycle parade—to benefit the University's Diabetes Institute for Immunology and Transplantation.

This year's events raised more than $135,000, including a record-breaking amount from Saturday evening's live auction.

Since its inception in 2000, the Lightning Run has raised more than $1.5 million for the Diabetes Institute.

Save the date for next year's event: July 17-18, 2009