



Discoveries in Diabetes

A publication for those who support diabetes research, education, and care at the University of Minnesota

Study yields surprising results

U researchers explore benefits of gastric bypass, lifestyle changes

Which is better at controlling type 2 diabetes, gastric bypass surgery or lifestyle management?

That was the question University of Minnesota researcher Sayeed Ikramuddin, M.D.—along with scientists at Columbia University and in Taiwan—aimed to answer when they began a three-year study in 2011.

“This had never been tested in this way before,” says Ikramuddin.

They fully expected that the two test groups—60 patients having gastric bypass surgery and 60 patients making drastic lifestyle changes—would experience roughly similar results. After all, both groups would lose weight—typically the best way to reverse type 2 diabetes.

But the results weren’t even close: After one year, 19 percent of the lifestyle-management group had met the health standards set by the study’s sponsor, the American Diabetes Association, and a whopping 49 percent of the gastric bypass participants had reached the goal.

Even more astonishing, the gastric-bypass patients’ type 2 diabetes was controlled in days, sometimes hours, postsurgery—long before they had actually lost weight.

To find out why, Ikramuddin teamed up with U researcher David Bernlohr, Ph.D., who specializes in adipose biology.

“We thought that the group on the low-cal diet would, in essence, perform the same as the surgery group,” says Bernlohr, “but there were molecular changes [in surgery patients] that happened because of the surgery.”

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Photo by Scott Strebbe

Sayeed Ikramuddin, M.D.

Study yields surprising results *(continued from cover)*

One patient's story

Take 65-year-old LaVonne A. Swenson. A type 2 diabetic for approximately 15 years, Swenson applied to the study. "Family members have died from complications of diabetes," she says, explaining her motivation. She especially wanted to participate in memory of her son, who died after struggling with a kidney disorder.

After reviewing the potential risks, Swenson underwent surgery in September 2011. Immediately afterward, her type 2 diabetes was reversed, and her blood pressure dropped below 130. Nearly two years later, her blood sugar is at 4.9, down from 10.1; her cholesterol numbers are in the healthy range; and she weighs 155 pounds—down from 240—thanks to the surgery and her determination to eat a healthy diet and exercise.

"Fantastic numbers—I still can't believe that's really me," says Swenson, who adds that she's healthier and more active now than she's been in 30 years.

A nonsurgical approach

Swenson's all-around positive results make sense. Recent University of Minnesota studies have pointed to the efficacy of healthy lifestyle choices—like eating breakfast and walking after meals—for people with type 2 diabetes. But

Bernlohr and Ikramuddin don't yet know why the surgery sparked such decisive results.

Regardless of the surgery's clear results, gastric bypass is not a likely long-term future treatment for diabetics, because not all patients can benefit, given the risks of surgery.

"What we need to find are inroads—nonsurgical ways—to accomplish this result," says Bernlohr, who is busy studying the biology of the patients' adipose, or fat, tissue and why its inflammation is reversed.

Bernlohr notes that funds donated by a U diabetes research supporter paid for some of his equipment. "It's very important to have access to philanthropic dollars, so that we can move quickly," he says.

So while their one-year data collection in December 2012 provided the early findings they needed for publication in June 2013, Ikramuddin and Bernlohr are now collecting two-year data and determining how gastric bypass surgery affects mitochondrial function, or energy production, in adipose tissue.

"What is it about that tissue that can drive improvements in diabetes?" Ikramuddin asks. He's hopeful that studies like theirs will reenergize the National Institutes of Health and other major funders to invest in large-scale trials. He and Bernlohr will complete their current study in July 2014, with the hope of developing a nonsurgical intervention.

Meanwhile, Swenson loves her new life: her husband has taken up cooking nutritional meals; she walks about 7,000 steps a day; and now she's able to play with her grandchildren. "I used to be the cheerleader on the sidelines," she says.

Diabetes is a growing problem in the Lower Sioux Community, of which Swenson is a member. She says she is determined to spread the news of healthful living. "I want to go to all of the reservations in the state, tell my story, and show before-and-after pictures."



Can submarine technology transform islet transplantation?



Photo by Scott Strebler



Photo by Tim Rummelhoff

Research collaborators working with the University of Minnesota and University of Arizona embarked on a unique experiment in August. A donor pancreas, chaperoned by a graduate student, was flown by commercial jet from Minneapolis to Tucson, Arizona. The goal: to see if a new organ preservation technique could extend the life of the donor pancreas. It did.

Generally, a donor pancreas must get from its origination city to its destination—sometimes across the country—in just eight hours to be suitable for transplantation. After that, the organ has spent too much time without oxygen to be used. But a new oxygen preservation technology developed by U adjunct professor Klearchos Papas, Ph.D., in collaboration with Giner Inc., would extend the life of this organ up to 24 hours.

With this technology, Papas estimates that the percentage of usable pancreas organs could jump from 42 percent to 60 or 70 percent. The better-preserved pancreases will result in higher quality islet cells as well, he says, increasing the number of people who could become insulin independent with a first pancreas transplant.

But because the donor organ supply is inadequate to meet current demands, Papas and U imaging expert Mike Garwood, Ph.D., are working towards the goal of creating an artificial, implantable pancreas, where human, pig, or stem cell islets could be implanted and protected, meeting the needs of people with type 1 diabetes. This work is championed by the Schott Foundation, which made a recent gift of \$100,000 to fund it—bringing its historic U diabetes research support to more than \$385,000.

“We are a small foundation, so we tend to work with startup projects that aren’t yet eligible for national grants,” says foundation principal Owen

Schott, adding the gift is in part personal—several members of his wife’s family have diabetes. Also, he appreciates Papas’s creative approach.

Papas began this work by teaming up with Giner Inc. and tapping oxygenation technology designed for nuclear submarines—converting water into oxygen. By miniaturizing that process, he was able to extend the viability of a donor pancreas. Now, Papas and Garwood plan to adapt this technology and further miniaturize it, so that it can preserve islets inside an implantable, artificial pancreas.

Garwood says putting the islets into the device solves two problems: “We can monitor the oxygen”—helping islets remain optimal post-transplant—“and we can use human islets without immunosuppression, because the artificial device separates the islets from the body,” which would otherwise reject them.

This approach with human islets could alleviate the need for immunosuppressive drugs, which can cause serious health issues, and could have applications for use in treating children.

“This is an extremely promising approach for eliminating type 1 diabetes and getting people back to normal lives,” says Garwood, who calls the Schott Foundation’s gift “critical.”

Owen Schott and his brother, Dell Schott, believe that their family foundation’s continued support for U diabetes research is just one part of the puzzle. “We can’t all be 3M Foundation or the McKnight Foundation, but we can all do our part and help,” says Owen Schott.

Papas says that he and Garwood couldn’t achieve their goals without this kind of seed-funding. “These gifts are invaluable. Without them, our work would in no way be doable.”

Klearchos Papas, Ph.D., (left) and Mike Garwood, Ph.D.

A family foundation backs research extending the life of donor pancreases

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U celebrates 50th anniversary of solid organ transplantation with gala, patient conference

October 18 & 19

The University of Minnesota recently performed its 8,000th kidney transplant—which coincided with the 50-year anniversary of Minnesota’s first-ever kidney transplant, also performed at the U of M. In the past half century, the University has established its place as a world leader in solid organ transplant.

“As the field has evolved, so has our program,” says Timothy Pruett, M.D., chief of the Medical School’s Division of Transplantation. “We have pushed and refined transplant treatment.”

He cites cell-based therapy, steroid-avoidance therapy, and allo-islet cell transplants (in which islet cells from a donor pancreas are infused into a patient with severe diabetes) as just a few of Minnesota’s pioneering advances.

U physicians and patients are gearing up to celebrate the anniversary with a gala on Oct. 18 and a patient education conference Oct. 19 on the University of Minnesota campus. To register or learn more about the event, visit <http://bit.ly/UMN50SOT>.

U, Park Nicollet seek volunteers for diabetes drug study

Learn more about the study at

<https://grade.bsc.gwu.edu>

The University of Minnesota and Park Nicollet International Diabetes Center are seeking volunteers to take part in a study comparing the long-term benefits and risks of four widely used diabetes drugs in combination with metformin, the most common first-line medication for treating type 2 diabetes.

The Glycemia Reduction Approaches in Diabetes: A Comparative Effectiveness (GRADE) Study will manage participants’ diabetes medications and provide at least four medical visits per year free of charge throughout the study, but participants will receive other health care through their own providers.

“Type 2 diabetes is a progressive disease, and over time effective therapy usually requires the use of more than one medication,” says Elizabeth Seaquist, M.D., principal investigator of the U’s clinical site. “Patients and their caregivers have many options for treatment but have no evidence to tell them which combinations work best together. GRADE will provide this evidence and simplify the choices.”

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