# Better, Smaller: The Future of Continuous Monitors

BY BRUCE JANCIN
*Denver Bureau*

KEYSTONE, COLO. — Look for next-generation continuous glucose monitoring devices to be more accurate, less obtrusive, and easier for diabetic patients and their families to use, according to H. Peter Chase, M.D.

Among the numerous devices in development, he singled out two for purposes of illustration. Both are far along in the pipeline and provide a glimpse into a not-so-distant future in which continuous glucose monitoring is likely to transform diabetes management.

One of the devices, the TheraSense FreeStyle Navigator, is now under review by the Food and Drug Administration and likely will receive marketing approval in a year or so. The other, the DexCom G1, features a long-term implantable sensor half the size of a triple-A battery which is placed subcutaneously in the abdominal wall, where it measures glucose levels every 30 seconds and transmits the data wirelessly to a small receiver, Dr. Chase said at a conference on management of diabetes in youth.

Development of continuous glucose monitoring sensors is an extremely active area within the medical devices industry. Part of the impetus lies in a recognition that most patients really dislike self-monitoring blood glucose by fingerstick multiple times daily as part of intensive insulin therapy.

Indeed, studies show few patients do it as often as recommended. And even when they do, all they get are a series of snapshots of blood glucose levels at a few instants in time, hours apart, that tell nothing about how blood glucose fluctuates between tests.

In contrast, the DexCom G1 displays 1-, 3-, and 9-hour glucose trends and sounds an alert when real-time levels run low or high. Similarly, the FreeStyle Navigator's pocket-sized display monitor has a trend arrow that can point in five directions.

"This is ingenious. If the glucose is dropping fast, you want to know," said Dr. Chase, professor of pediatrics at the University of Colorado, Denver.

TheraSense has petitioned the FDA to approve the device as a replacement for blood glucose testing, an indication for which neither of the two continuous glucose monitoring systems now on the market is approved. The company believes the technology it uses makes the Navigator more accurate at low glucose levels than currently devices.

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But whether TheraSense receives its sought-after indication will depend in large part on the results of independent accuracy studies now being conducted by DirecNet, a National Institutes of Health–funded five-center consortium of which the university is a part.

Satish K. Garg, M.D., professor of medicine and pediatrics at the university, was the principal investigator in a recent clinical trial in which the DexCom device markedly improved glucose excursions compared with usual care in adults with type 1 diabetes.

For 30 days in the 90-day study, the 14 participating patients and their physicians were kept blinded to the sensor data. When they were unblinded and the sensor's alarm function was turned on—with alerts at glucose levels of 100 and 200 mg/dL and a continuous alarm at 55 mg/dL—their glucose profiles improved markedly.

Patients experienced a mean 37% increase in the number of hours per day spent with a glucose of 80-140 mg/dL, a 38% reduction in time spent at 40-55 mg/dL, and a 31% decrease in hours spent with a glucose level of 240-400 mg/dL compared with the blinded period.

Improved glucose profiles, over the long term, will substantially reduced rates of diabetic microvascular complications, Dr. Garg said at the conference, sponsored by the University of Colorado and the Children's Diabetes Foundation at Denver. ■

# For Type 1 Diabetes Patients, Islet Cell Transplants Are a Potential Therapy

BY BRUCE JANCIN
*Denver Bureau*

KEYSTONE, COLO. — Formidable obstacles continue to prevent pancreatic islet transplantation from having a major impact on type 1 diabetes despite the spectacular technical advances of the past 4 years, Ronald G. Gill, Ph.D., said at a conference on management of diabetes in youth.

The breakthrough in islet transplantation began in 2000 with the success of what since has come to be known as the Edmonton protocol.

**'It's probably the single most important advance in transplant biology.'**

**DR. GILL**

Previously, only about 10% of recipients of islet transplants ever achieved insulin independence. But investigators at the University of Alberta, Edmonton, discarded the standard islet-toxic immunosuppressive regimen routinely used in whole-organ transplants in favor of a gentler sirolimus- and tacrolimus-based, corticosteroid-free regimen utilizing daclizumab, a monoclonal antibody directed against the interleukin-2 receptor on activated lymphocytes. They also boosted the islet dose, infusing islets harvested from two donor pancreases per recipient.

They electrified the diabetes and transplant communities, reporting that their novel protocol had rendered seven consecutive type 1 diabetic patients insulin independent.

"The Edmonton protocol was something drastically different. It's probably the single most important advance in transplant biology in all of the transplant literature," said Dr. Gill, an immunologist at the university.

The Edmonton experience has been replicated in an as yet unpublished 10-center study, conducted by the National Institutes of Health–sponsored Immune Tolerance Network, that underscored the importance of extensive experience in isolating and handling pancreatic islets as the key to transplant success.

The experience at the universities of Alberta, Minnesota, Miami, Pennsylvania, and other highly experienced centers is that roughly 80% of islet recipients remain insulin independent at 1 year, and 65%-70% at 2 years. Those results are as good as for whole-organ pancreatic transplantation, a mature procedure reimbursed by Medicare. There now are more than 100 islet transplant recipients off of exogenous insulin, with complete reversal of hypoglycemia and normal glycosylated hemoglobin values. However, the grafts do not counter regulate.

The islet graft is placed in the liver via intraportal infusion. Acute complications have included moderate to severe portal vein bleeding. Long-term complications have consisted of fatty liver, hypertension, hypertriglyceridemia, and mouth ulcers secondary to immunosuppressive therapy, he said at the conference, sponsored by the University of Colorado and the Children's Diabetes Foundation at Denver.

Medicare soon will begin reimbursing for islet transplants in kidney transplant recipients. The federal National Center for Research Resources has funded 10 U.S. centers to serve as regional islet resource centers in anticipation of a ramping-up of islet transplants.

Dr. Gill noted an ethical distinction between islet and other forms of transplantation.

"We know for sure there's tremendous long-term collateral damage and toxicities from immunosuppressive drugs. In conventional organ transplantation, you endanger the host with toxic drugs in order to preserve the graft because the graft is important to their life. In islet transplantation, we must be willing to endanger the graft in order to preserve the host because diabetes is not an immediately life-threatening disease."

Only about 2,000 cadaveric pancreases per year are available for islet harvesting and two pancreases are typically required per transplant. The procedure in its current form will remain beyond the reach of most of the nation's 1.4 million type 1 diabetic patients. ■

# *Mother's Pediatric Type 2 Diabetes Affects Offspring*

BY KATE JOHNSON
*Montreal Bureau*

QUEBEC CITY — The long-term complications of childhood type 2 diabetes can stretch beyond the patient and into the next generation, according to new data from the University of Manitoba, Winnipeg.

In a cohort of almost 90 children born to mothers diagnosed with childhood type 2 diabetes, 3 of the 9 children who are older than 7 years have already developed the disease themselves, Elizabeth Sellers, M.D., reported at the joint annual meeting of the Canadian Diabetes Association and the Canadian Society of Endocrinology and Metabolism.

The results are part of an ongoing study led by Heather Dean, M.D., a colleague of Dr. Sellers. The study is looking into the high rate of youth-onset type 2 diabetes in northern Manitoba, where the majority of the population is First Nations Ojee-Cree.

A previous study by Dr. Sellers found that this population has a 14-fold increased risk of youth-onset type 2 diabetes. "We do not yet know how generalizable our findings our to other populations," Dr. Sellers said.

An earlier study of 76 "graduates" of the first childhood type 2 diabetes cohort, who have now reached early adulthood (ages 18-30), documented 7 deaths, with 5 patients on dialysis for end-stage renal disease, 2 patients with blindness, and 1 who had had an amputation, she said.

That study has also documented a high rate of obstetrical complications among 56 young women in this cohort, with 13 first-trimester miscarriages, 3 second-trimester losses, and 2 stillbirths, Dr. Sellers said.

The latest study, called the Next Generation project, is following the offspring of young adults with type 2 diabetes, who were diagnosed when they themselves were children. These offspring are thought to be at high risk for developing youth-onset type 2 diabetes, and the preliminary findings back that up, she said.

The project will follow the offspring through childhood with annual screening for diabetes and will describe the evolution and natural history of the problem, she said. ■

Pages 26a—26b