



Type 1 Diabetes Facts - Still A Serious Disease

- 1.4 million individuals in the US-40% before age 20, 1:100 adults
- 30,000 new cases are diagnosed each year
- Autoimmunity can precede diagnosis by 13 years
- Onset most common at these ages: 2, 4-6, and 10-14 years
- DKA present in 20-40%
- Mortality is between 3-6% within the first 20 years of life
- Lifespan shortened overall by 15-20 years
- 40% of patients survive over 40 years and 50% of these people have complications
- Mortality is primarily related to coronary artery disease
- Glycation, hypertension, inflammation and endothelial dysfunction affect microvascular circulation resulting in nephropathy and retinopathy
- Autonomic neuropathies and hypoglycemia unawareness can impact most organ systems



General Eligibility For Islet Transplantation

- Type 1 diabetes for 5 years
- Active management with an endocrinologist
- Close monitoring of glucose levels
- Require less than 50 units of insulin
- Hypoglycemia unawareness or labile glucose levels
- No smoking
- No infection



Islet Transplantation

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Exciting developments in islet transplantation are occurring almost daily. New protocols are being developed. Funding is improving. More accurate information is flowing to people with diabetes and the medical community. Despite these advances, challenges still remain to improve the efficiency of the processes involved in islet transplantation. Professionals delivering diabetes care to potential islet candidates must stay abreast of eligibility criteria and benefits for their patients if they want them to have access to all treatment options.

Conventional Treatment

The Diabetes Control and Complications, Finnish and Japanese Trials demonstrated the ability to reduce complications for many with type 1 diabetes. However, titrating multiple insulin doses, frequent self-monitoring of blood glucose, adjusting food intake and managing subsequent hypoglycemia requires more effort than some individuals can exert. Only 20% of individuals with diabetes see an endocrinologist and less than 50% have access to an interdisciplinary team.

Hypoglycemia Unawareness

Current medical treatment has little to offer people with hypoglycemia unawareness. In addition to lost productivity, function, and quality of life, severe hypoglycemia has been shown to result in cumulative neurological and psychological impairment. Mortality rates associated with current injected/pumped insulin treatment regimens are commonly estimated at 4%, a truly alarming rate. Successful pancreas transplantation has demonstrated restoration of epinephrine responses and symptom recognition during hypoglycemia in patients with autonomic neuropathy. For islet transplant recipients with hypoglycemia unawareness and defective hormonal counter-regulatory responses, improvements are seen one month following transplantation.

Restoring Beta Cell Function

Similar to pancreas transplants, islet transplants help the body regulate blood sugar by replacing beta cells. A donor pancreas containing approximately 1 million islets (more in obese patients) may yield 400,000-500,000 islets following removal, storage, transportation, and purification. Islets comprise 2-3% of the pancreas mass. An islet transplant is a minimally invasive procedure and can be performed in a radiology suite using local anesthesia and takes less than two hours. Currently, islet transplants are performed only as part of clinical trials and are monitored by the Food and Drug Administration (FDA) for safety and efficacy.

Goals of Islet Transplantation:

- Restored normoglycemia and insulin independence.
- Improved quality of life by eliminating exogenous insulin, many of the dietary restrictions, fear and uncertainty associated with hypoglycemia.
- Prevention, retardation, and/or reversal of the secondary complications of diabetes.
- Prolonged life expectancy.
- Reduction of health care dollars per quality adjusted life years saved.

Clinical Research

Islet transplants are only available to people who fit defined clinical trial criteria.

Edmonton Protocol- Additional effort was stimulated in 2000 when the University of Alberta reported a substantial increase in the success rate of islet transplants. For five out of seven patients, two sequential islet transplants reversed insulin dependence when a steroid-free drug regimen was used.

University of Minnesota- The U of M reported recent successes using approximately half of the islets previously employed in the pivotal Edmonton protocol. Other improvements in the new series addressed islet ischemia during pancreas storage, induction immune treatment in addition to limited doses of long-term immunosuppression. This breakthrough may allow one donated pancreas to be used more widely in the future.

Collaborative Islet Transplant Registry (CITR)- According to the CITR, multiple centers now have 19/36 recipients who are insulin free for at least one year. Additional and different trials will incorporate changes in drug regimens, procurement, storage, and cell requirements as well as measure multiple outcomes.



Mark Your Calendar!

Upcoming Meetings

American Diabetes Association

◆ 53rd Annual Advanced Postgraduate Course
February 10-12, 2006
San Francisco, CA
www.diabetes.org



In The Loop... Resources

Transplant Centers

There are 57 islet transplant centers in the world; 31 in the US
(<http://www.isletservice.com>)

NIH recently awarded \$75 million dollars to a five center network located in Minneapolis, Miami, Philadelphia, Edmonton (Canada) and Uppsala (Sweden).

Islet Cell Resource Centers (ICRs)

Ten newly funded centers will model best practices for isolating, purifying, and distributing while perfecting storage and shipping.

JDRF website www.jdrf.org

To learn about funding research for a cure.

Diabetes Portal www.diabetesportal.com

For your patients with Type 1 diabetes

To be considered for participation in the Minnesota Diabetes Institute for Immunology and Transplantation's clinical islet transplant trials, candidates may complete the **Clinical Trials Registration form** at the Center's website, www.DiabetesInstitute.org.



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The Procedure

Candidates are entered into a waitlist after screening. When candidates are selected to participate, they are admitted to clinical research centers for final tests. The patient is mildly sedated for the islet transplant procedure. The portal vein is viewed with ultrasound and islets are infused either directly through a PIC line or a mini-laparotomy over 15-30 minutes. Recipients are given exogenous insulin via injection or pump which is withdrawn as the islets function on their own. One to two days post procedure, patients return home.

Immunosuppression and Other Medications

Immunosuppressants are needed to tolerate foreign tissue, but they have multiple side effects including insulin resistance, and require close monitoring. Newer products and induction treatment offer advantages. The long-term immunosuppressants are titrated over time by research centers using recipient laboratory samples sent to their own labs. Patients initially monitor blood glucose frequently as it remains the best means of detecting islet function. Medications are administered to recipients for several additional purposes: anticoagulation, infection prophylaxis, and inflammation. Most of these drugs are discontinued over time. Activity is rarely restricted and meals are ad lib post procedure. Healthy lifetime habits are encouraged including weight management, good nutrition, vitamin supplementation, smoking avoidance, etc.

Overcoming Barriers to Progress

As with most medical innovations, the struggle to perform sufficient numbers of islet transplants to perfect technique is limited by financial, human, and other resources. To this point, barriers have included:

- Need for multiple organs
- Unresolved logistics of organ allocation
- Lack of third party reimbursement
- Unknown risks of new drug regimens
- Risks of the transplant procedures
- Lack of integration with usual diabetes care
- Longevity of islet functions
- Inadequate organ donation

Costs

Research grants cover many islet transplants and follow-up expenses. Costs borne by the recipients include some transportation costs, glucose monitoring, and some long-term drug costs. Medicare (CMS) has recently agreed to pay for routine costs and appropriate items and services for beneficiaries with type 1 diabetes having islet transplants and participating in an NIH sponsored clinical trial. This is likely to mean that islet/kidney transplants will be supported.

Outcomes of Successful Islet Transplants

Rapidly improving success rates can be traced to decreasing known barriers. Clinicians are encouraged that even partial success among those who still require insulin may still have substantial benefit. You can find inspiring individual case reports to share with your patients at several transplant center websites. Patients describe restoration of social and family functions, improved quality of life, loss of fear, more flexible lifestyles and elimination of severe hypoglycemia.

Tracking Results

The Collaborative Islet Transplant Registry, sponsored by the NIDDK, is charged to expedite progress and promote safety in islet/beta-cell transplants performed in North America. Analysis of this data is hoped to accelerate the identification of critical risk factors and determinants of success to guide future research protocols. Their first 2004 annual report stated that of the 86 recipients from 1999-2003, 28 received one, 44 received two, and 14 received three infusions of islets. At 1 year post transplant, 58% were insulin independent. The report is available at:

<http://spitfire.emmes.com/study/isl/index.html>

Informing your Patients

Current trials enrolling volunteers can be found at research center websites. Investigators and their staffs' welcome the opportunity of discussing eligibility with clinicians. Alliances between adults with type 1 diabetes, their caregivers and research centers may expedite utilization of the best care available to those in need.

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