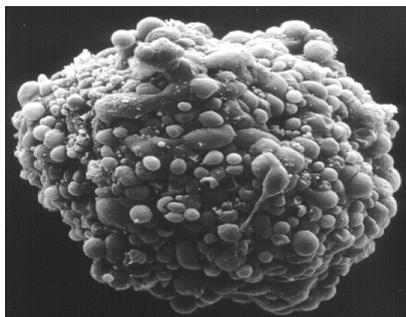


ISLET TRANSPLANTATION

What you need to know before you take part



Information for Canadian Residents

The following individuals are closely involved with the Clinical Islet Transplant Program in Edmonton:

Dr. James Shapiro (Director)
Dr. Peter Senior (Medical Director)
Dr. David Bigam (Transplant Surgeon)
Dr. Norman Kneteman (Transplant Surgeon)

And many others: interventional radiology doctors and staff, nurse coordinators, islet isolation staff, dietitian, social worker, metabolic coordinator, research staff and clerical staff.

Information for International Residents

US and international inquiries regarding islet transplant programs outside of Canada should be directed to:

Clinical Islet Transplantation Consortium www.citisetstudy.org/

or

Juvenile Diabetes Research Foundation International www.jdrf.org

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ARE YOU A CANDIDATE?

Shortage of applicants

Currently our wait list is not long, partly because we have successfully transplanted many people who formerly had Type 1 diabetes. In addition many people have been reluctant to apply, often because they think that islet transplant is for "other people". Our islet transplant recipients are regular people, just like you.

We are actively processing applications...so if you think that an islet transplant might be right for you, please complete and return the application package which is found online at www.islet.ca, or you can call the Islet Program Application line at 780-407-1501.

We will accept incomplete or partial applications, particularly if you are just exploring the possibility of islet transplant (see cover letter in application package). At this point things are at a very preliminary stage and no commitment is required.

Are you a candidate for a transplant?

You will benefit most from an islet transplant if you have Type 1 diabetes complicated by:

- frequent or severe episodes of hypoglycemia
- hypoglycemic episodes with minimal or no warning symptoms
- extremely variable blood glucose levels

Some common things that could disqualify you from an islet transplant:

- weight greater than 90 kg, or Body Mass Index above 30 kg/m²
- insulin use greater than 0.9 units/kg/day
- severe kidney dysfunction (creatinine above 200 µmol/L or other parameters)

If you have previously received a kidney transplant you may be eligible to take part in a research study of islet transplant.

The main benefits of an islet transplant are freedom from hypoglycemia, stable blood glucose levels and excellent glycemic control. We aim to achieve insulin independence and can usually achieve this goal, although usually more than one transplant may be required. However, patients have needed to go back on insulin eventually, but usually at much lower doses than before transplant. Currently, 15-20% of patients remain insulin independent for five years after transplant, although many more (80%) continue to enjoy islet function with stable blood sugars and protection from hypoglycemia at this time point. The longer term results are improving all the time, and some of our newer protocols seem to be effective in preserving full function longer.

ASSESSMENT FOR TRANSPLANT

Your application will be reviewed by the transplant team and your blood glucose records will help us judge the severity of your hypoglycemia and glucose fluctuations. If it looks as if your diabetes is causing significant problems, we will ask you to come to Edmonton to our assessment clinic.

Assessment clinic

The purpose of the visit to the assessment clinic is twofold - firstly to allow us to make an individualized assessment of the risks and benefits of islet transplantation for you: and secondly, to allow time to discuss this with you and allow you to ask questions about the procedure face to face. The appointment will take approximately two hours. We will take a medical history and do a physical assessment

If you are felt to be a suitable candidate and wish to proceed, we will arrange for further tests and appointments to help confirm that you are a suitable candidate and ensure you are healthy enough to undergo a transplant safely. Many of these tests are listed on Page 11.

You will also meet other members of our team, including our social worker and dietitian and attend an education session with a nurse coordinator. There will be many opportunities for you to ask questions. Once these tests and appointments are completed, the entire transplant team will discuss your case and come to a final decision as to whether you will be suitable for islet transplantation. If yes and you agree, you will be placed on our transplant waiting list. The entire process from the assessment clinic to when you are listed actively on the transplant waiting list can take several months.

Support person

It is mandatory that you have a support person who can accompany you to clinics and appointments and provide you with physical and emotional support before and after transplant. This person will also help to remind you to take your medications and keep appointments. After transplant we expect you and your support person to stay here in Edmonton for one month before returning home.

Smoking, alcohol and drug use

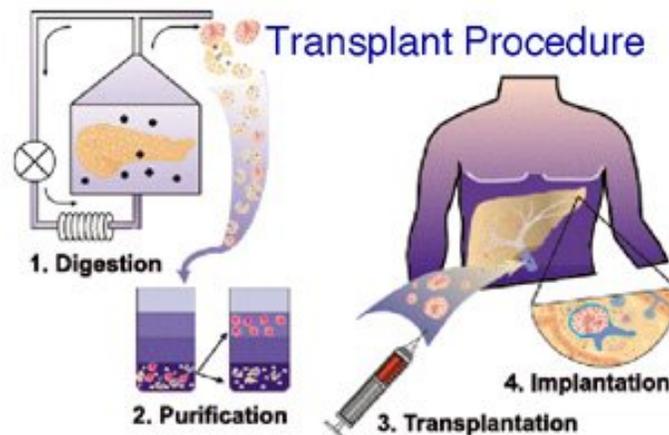
You must stop smoking before you can be placed on the waiting list for transplantation. Persons with a history of drug or alcohol abuse will be required to have an assessment by their provincial addictions counseling association such as AADAC in Alberta. You may be asked to sign a contract stating that you will not drink alcohol or use illegal street drugs. This contract allows the Islet Transplant Program to check for alcohol or drugs in your blood. If the test is ever positive you will be taken off the waiting list.

Some work while you wait to be called for a transplant

The waiting time for transplant varies greatly, from a few weeks to a year or more. During this time you should update all your vaccinations and get the vaccine for both hepatitis A and B. Your provincial medical coverage must be current and we strongly recommend that you have supplementary medical insurance that covers medication costs. During this waiting period we will not take over the responsibilities of your regular physician. You must notify the transplant team if your condition changes or if you start or stop any medications.

You need to have a cell phone or pager so that we can contact you when you are not at home. You must ensure that you have transportation to the University of Alberta Hospital in Edmonton at any time. You should make arrangements for your responsibilities at home to be taken over by friends and family members who can be activated with a phone call. It is important to have a bag packed and to review what is in the bag regularly.

ISLET ISOLATION AND TRANSPLANT PROCEDURE



What are islets and where do they come from?

The function of most of the pancreas gland is to make digestive juices. Only a tiny proportion of cells in the pancreas make hormones. The cells in the pancreas that make insulin and other hormones are organized into little clusters called islets and make up only 1% of the pancreas. The first step in islet transplantation is to separate the islets from the rest of the pancreas. The pancreas will have been donated by the family of a person who has died. Organ procurement teams across Canada make arrangements for the removal, storage and transportation of all acceptable donated pancreases to our isolation lab.

How are islets isolated from the pancreas?

The islet isolation team infuses enzymes into the pancreas to break down the tissue and free the islets from the rest of the pancreas. The islets are then purified, counted and checked to ensure that the number and quality of islets is satisfactory to proceed with the transplant. The isolation process takes six hours. The islets can be kept safely in culture for a few days until it is time for the transplant.

Preparation for the transplant



When you arrive at the hospital you will be admitted to the Transplant Unit. An intravenous line will be started for medications and blood sampling. You will also have a chest X-ray. You will be given medication (induction agent) to suppress your immune system before the transplant. Depending on the drug(s) given, the transplant may be scheduled for 1 or 2 days after admission.

On the day of transplant you will be transported to the x-ray department where you will receive a local anesthetic and a sedative. A radiologist will put a needle between your ribs on the right hand side into your liver, and through this thread a long, thin plastic tube into the portal vein, a large blood vessel through which blood flows into the liver. The bag containing the purified islets will then be connected to the plastic tube, and the islets allowed to flow into the blood vessel. The islets will float in the portal vein until they get lodged in the small branches of the portal vein within the liver. As the plastic tube is removed a paste is injected to prevent bleeding from the liver. Alternately (but rarely), the islets may be given through a simple surgical procedure in the operating room. If this is necessary, it will be discussed with you prior to transplant.



Back on the nursing unit you will stay in bed on your right side for four hours. You will be started on an insulin and heparin infusion to help the islets settle into the liver. The next day you will go for an ultrasound to ensure that there is no internal bleeding around the liver and that there are no blood clots in the liver. The average length of stay in hospital after transplant is two days.

AFTER THE TRANSPLANT – INSULIN AND MEDICATIONS

Insulin after transplant

You will continue to take some insulin although usually at much lower doses than before transplant. The islets will take several weeks to settle into their new home in your liver. We call this process engraftment. During this period we will need you to keep your blood glucoses within quite a tight range so the islets are not overworked. Initially we would like you to monitor your glucoses seven times daily and keep written records of your insulin use. The frequency of testing will be decreased over time as your glucose levels stabilize.

Medications to prevent rejection of the islets

Immunosuppressive (anti-rejection) drugs suppress your immune system just enough so that you do not reject your islets but still leave it active enough to deal with common infections. If you forget to take the drugs your body will likely destroy the islets over time by a process called rejection and the islets will no longer produce insulin. Unfortunately, by the time this happens it will probably be too late to reverse the rejection and the damage will be permanent.

Immediately before the transplant, and again shortly after transplant, you will be given induction medication to suppress your immune system. Some induction drugs that we may use include:

- basiliximab
- alemtuzumab (Campath®)
- Thymoglobulin®
- Etanercept

In the longer term you will also be required to take maintenance immunosuppression for as long as the islets are working. Two long term maintenance immunosuppressive drugs we frequently use are:

- tacrolimus (Prograf®)
- mycophenolate mofetil (CellCept®)

These drugs work together from several directions to stop the immune system from being activated and prevent rejection.

Medications to prevent and treat infection

Infection is common after transplantation because your suppressed immune system has less ability to fight the organisms that cause infection. This is particularly so in the first few months after transplantation because you would have received an induction agent that suppresses your immune system to a greater extent than the maintenance immunosuppressive drugs. Some medications we use to prevent or treat infections early on after transplant are:

- co-trimoxazole (Septra®, Bactrim®)
- Pentamidine®
- ganciclovir (Cytovene®)
- valganciclovir (Valcyte®)

AFTER THE TRANSPLANT – CLINICAL MONITORING

We will schedule you for a number of tests and appointments as part of our ongoing clinical monitoring following your transplant. Many of these tests are described on Page 11.

Laboratory blood work

Following your transplant you will have fasting blood drawn every Monday, Wednesday and Friday at the University of Alberta Hospital Outpatient Laboratory. The frequency of blood work will decrease over time as your islets begin to work and your drug levels are stabilized. Eventually, you can have your blood tests done in a lab closer to your home.

Follow-up clinic appointments

You will meet with a physician and nurse at the follow-up clinic every week until you return home. We need you to keep track of your daily blood glucose and insulin use and to bring those records with you to every clinic. Changes may be made to your medications and other appointments may be arranged.

Yearly tests and appointments

Some tests need to be repeated each year after transplant. We will work with you to schedule the appointments as conveniently as we can. Most are fasting appointments which have to be scheduled first thing in the morning. As a result, tests cannot be booked all on the same day and it may take one to two weeks to complete all the tests.

Here is a sample schedule:

WEEK 1

	MONDAY	TUESDAY	WEDNESDAY	THURSDAY	FRIDAY
AM	√ GFR: Nuclear Medicine Study	√ Blood Work √ Clinic	√ Ultrasound Abdomen/Pelvis √ Chest X-Ray	√ MIBI (Part 1)	√ MIBI (Part 2)
PM	√ Dietitian Consult	√ Social Worker Consult		√ MRI Abdomen	

WEEK 2

	MONDAY	TUESDAY	WEDNESDAY	THURSDAY	FRIDAY
AM	√ Metabolic Test: Ensure	√ Metabolic Test: Arginine √ Clinic	√ Metabolic Test: IVGTT		
PM					

We will also mail you a letter asking for additional testing and appointments. Please book these yourself. Make sure to take the letter with you to the appointment. Your physician will send us the results of that appointment:

- Fundal photography or Ophthalmologist (eye doctor)
- Family physician
- Dentist
- Electrocardiogram (ECG)

RISKS AND BENEFITS OF ISLET TRANSPLANT

Benefits of islet transplant

- on average, patients are insulin independent with good glycemic control for 2 ½ years; thereafter, they may need to go back on some insulin, but usually at much lower doses than before transplant
- long term freedom from hypoglycemia, stable blood glucose levels and excellent glucose control in the majority of patients
- improved quality of life
- diabetic eye disease and neuropathy generally remain stable after islet transplantation; however, people with advanced eye disease may continue to require treatment after islet transplantation

Risks of islet transplant

Risks of the transplant procedure:

- bleeding from the liver can result from the needle poke where the catheter is inserted. We now use a special paste to seal up the needle track as the catheter is removed and this has reduced the risk of bleeding substantially so the risk is small.
- blood clot in the portal vein may result from the infusion of islets. Small clots have been successfully treated with a 3-6 month course of blood thinning medication.
- allergic reaction to the dye used to locate the portal vein
- infection carried with the islets
- shoulder and abdominal pain - usually resolves within 2-3 days
- fat deposition around the islets in the liver in 20% of patients

Risks of lifelong immunosuppression

- decreased ability to fight infection, especially viral and fungal infections; serious infections have been experienced by approximately 2% of recipients.
- slightly higher risk of certain skin cancer and other kinds of cancer; the estimated risk of post transplant lymphoproliferative disorder (PTLD) is less than 1%. Over 10 years, in 119 patients, we have not seen any cases of PTLD or deaths from cancer.
- sensitization to foreign tissues which could make finding a match for other transplants more difficult in the future
- decreased kidney function
- women should not get pregnant and men should not impregnate someone while taking these medications
- common side effects are tremor, headache, nausea, fatigue, diarrhea, constipation, acne, and painful joints

COST

The cost for the assessment and the procedure will be covered by your provincial medical plan. The cost for transportation to Edmonton for assessment, transplant, and follow-up visits, and for accommodation and medications when you leave the hospital is your responsibility. Our social worker can help you explore issues related to drug coverage and financial assistance before you decide to proceed with a transplant.

Parking

The University of Alberta Hospital has parking available provided you have a signed letter validating your transplant patient status. This letter can be obtained from us and taken to the parking office at WMC 0H1.01 (407-8890). Page 12 has a map of the where the Islet Office is located with some information of parking for that area.

Accommodation

There is an Outpatient Residence attached to the University of Alberta Hospital. To arrange residence you must inform the nurse coordinator of the days you require and we will book them for you.

Hotels, motels, hostels, bed and breakfasts, vacation home rentals, campgrounds and apartments are listed on the web site – www.discoveredmonton.com

Travel

Some airlines offer discounts if the travel is for medical purposes. A good website to check out is www.hopeair.org for they may be able to offer assistance to those who can demonstrate a financial need.

Blood glucose testing

A blood glucose meter will be provided to you by the program. However, the strips are not supplied and will be at your own expense.

FREQUENTLY ASKED QUESTIONS

Do I need to be a Canadian resident or citizen?

Yes, you must be a Canadian **resident or** citizen to be eligible for our program. Patients from outside of Canada cannot buy their way onto any transplant list in Canada.

Information about islet transplant programs outside of Canada is available from the Juvenile Diabetes Research Foundation International, www.jdrf.org

What if I do not meet the criteria now?

If you do not meet the current criteria we will keep your name on file, if you wish, so that we may offer you the opportunity to participate in the future.

Do I need to come to Edmonton?

Our program treats patients from across Canada. You will need to come to Edmonton to be assessed in clinic but you can return home while you are waiting to be called for a transplant. After your transplant you will need to stay in Edmonton for an average of one to two months.

Can I do some tests at home or will all tests have to be done in Edmonton?

Some tests need to be done in Edmonton. Others can sometimes be arranged closer to home.

PRE AND POST TRANSPLANT TESTING AND APPOINTMENTS

Blood tests

- CBC & Diff: complete blood count and differential; measure the levels of various blood cells and level of hemoglobin which carries oxygen throughout your body
- Electrolytes, creatinine and BUN: information about kidney function
- PT INR & PTT: assess blood clotting time
- Magnesium: affected by immunosuppressive drugs
- Phosphorus: indicates kidney and bone health
- Calcium and vitamin D: bone health
- TSH: thyroid stimulating hormone; indirect measure of thyroid hormone which affects metabolism
- Immunosuppression levels
- Blood type, tissue typing and antibody screen: for matching organ donors and recipients and assessing risk of rejection

Diabetes and islet function tests

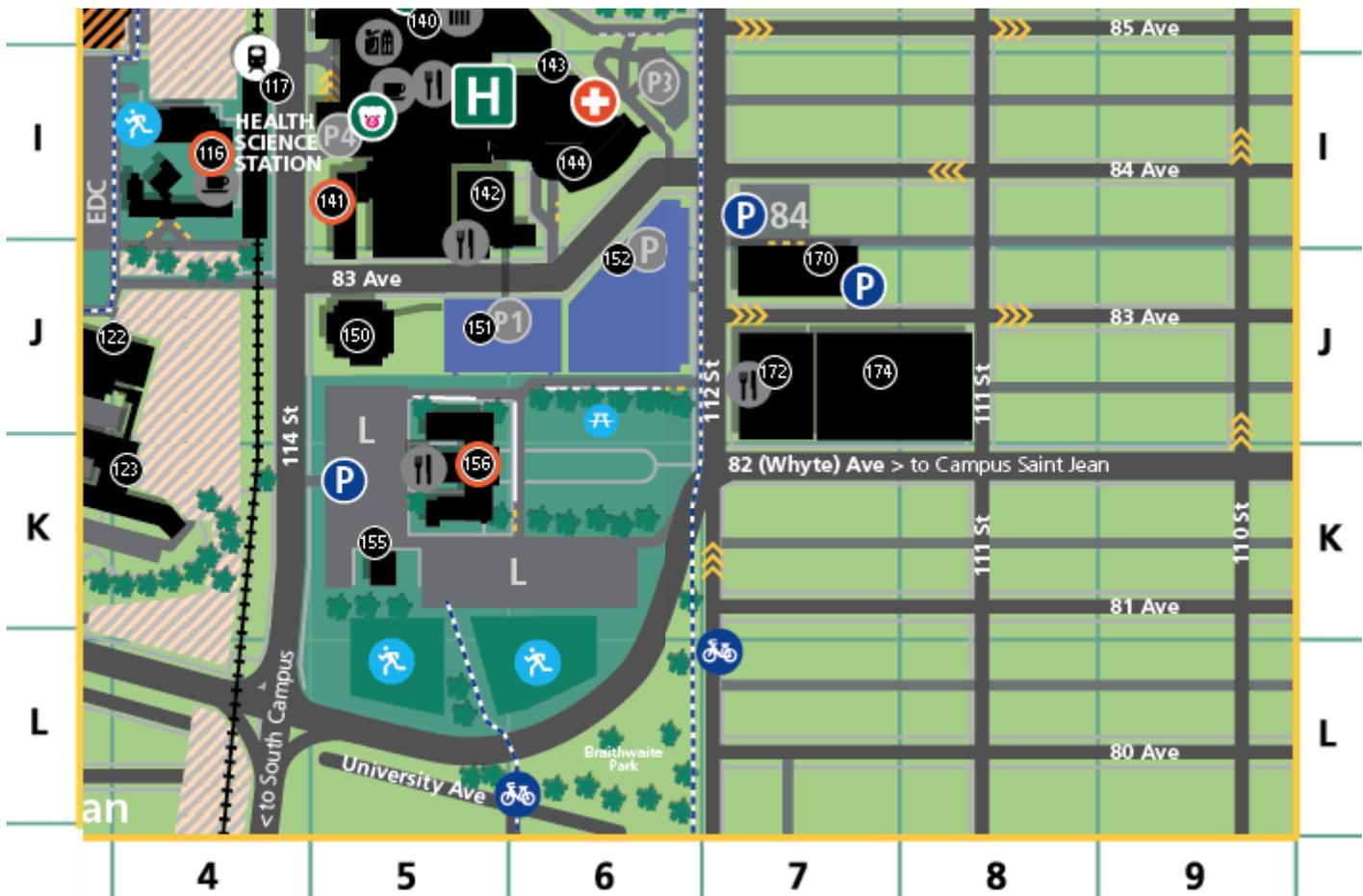
- HbA1c: indicates average blood glucose level over time
- C-peptide: a protein that is attached to insulin when it is produced in the body; tells us how much insulin the transplanted islets are producing
- Self-monitoring of blood glucose for assessing problems with hypoglycemia and glucose control
- Islet function tests: you will be given a meal replacement drink or an intravenous infusion of arginine or glucose to stimulate the islets

Tests for diabetes complications and general health

- Heart function
 - blood lipids measure cholesterol, triglycerides and other types of fats
 - ECG measures electrical conductivity in your heart to detect underlying heart disease
 - MIBI exercise stress test measures blood supply to the heart
- Liver function
 - abdominal ultrasound and Doppler flow studies assess blood flow to the liver
- Kidney function
 - 24 hour urine samples
 - glomerular filtration rate (GFR)
- Eye exam and fundal photography
- Dental exam

Other important tests

- Chest X-ray screens for lung or heart disease
- Serology profile tells us what infectious diseases you may have had
- Mantoux tests for exposure to tuberculosis
- Mammography assesses the breast for tumors
- Peripheral sensory assessment measures nerve function
- Appointments with the dietitian and social worker



***CLINICAL ISLET TRANSPLANT PROGRAM
COLLEGE PLAZA (J7 #172 ON MAP)***

Suite 2000
8215 – 112 Street
Edmonton, Alberta T6G 2C8
780-407-3571
www.islet.ca

**PARKING
COLLEGE PLAZA (J7 #172 ON MAP)**

8215 – 112 Street
Edmonton, Alberta T6G 2C8

- Underground heated parking.
- Meter parking is available on 82 Avenue on the south side of the building.

UNIVERSITY TERRACE (J7 #170 ON MAP)

8303 – 112 Street
Edmonton, Alberta T6G 2T4

- Must enter into the parkade off of 83 Ave. Keep in mind that 83 Ave is a one way and can only be entered off of 112 Street.