

UMMS ISLET TRANSPLANTATION PROGRAM

PATIENT REFERRAL INFORMATION PACKAGE

Revision 1.3
7/2/01

**UMMS TRIAL OF THE EDMONTON PROTOCOL
FOR ISLET TRANSPLANTATION**

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www.umassmed.edu/diabetes/research/



UMMS ISLET TRANSPLANTATION PROGRAM

The UMMS Islet Transplantation Program is pleased to announce that we are seeking patients with Type 1 diabetes who wish to be considered for islet cell transplantation using the Edmonton Protocol. Islet transplantation is a way of treating diabetes by giving a person new insulin-secreting islets. The “Edmonton Protocol” received widespread media attention last summer when researchers from the University of Alberta reported that they had developed a new method for transplanting islets that was successful in seven patients with Type 1 diabetes [N.E.J.M., 343:230-8,2000]. Although it appears to be very effective at reversing the need for insulin shots the long-term effectiveness and side effects of islet transplantation using the Edmonton Protocol are not yet known.

Goals and objectives of the Trial

The UMMS trial of the Edmonton protocol for islet transplantation has been developed to verify that the procedures developed by the Edmonton team can be successfully and safely repeated at other clinical centers. UMMS will do this as an affiliate of the Immune Tolerance Network (ITN) multicenter-trial. Working together, the ITN researchers will be able to try the protocol on a large number of patients.

Enrollment in the trial is limited

Persons with diabetes who would like to participate in this experimental research and who believe that they qualify for enrollment should know that enrollment in the trial is very limited. Meeting all of the basic entry criteria does not guarantee that you will be selected for an islet transplant.

Risks involved in the Procedure

It is important to keep in mind that islet transplantation using the Edmonton Protocol is an experimental treatment for diabetes. Although it appears to be effective in reversing or at least reducing the need for insulin shots, the long-term effectiveness and side effects of this procedure are not yet known. Following islet transplantation, patients are required to take medications known as immunosuppressants – drugs that prevent the body from reacting to and destroying the transplanted islets that have been introduced into the liver. These drugs must be taken each and every day after the transplant, as long as the islet cells continue to work. These drugs decrease the activity of the immune system and therefore pose a number of potential risks, many of which are not yet well defined. These risks could include increased susceptibility to various infections and cancer. For this reason children (<18 years of age) will not be considered for participation.



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BACKGROUND ON ISLET TRANSPLANTATION USING THE EDMONTON PROTOCOL

How are Islet Transplants Performed?

Pancreatic islets contain insulin-producing beta cells that regulate how the body utilizes glucose (or sugar). In Type 1 (or "Juvenile") diabetes, the immune system mistakenly attacks these cells leaving sufferers unable to make insulin. Islet transplantation restores the body's ability to produce insulin by implanting new functioning islet cells. These islets are usually obtained from cadaver donors. Islets are separated from the surrounding tissue of the donor pancreas using a special machine. After the islets have been isolated, the rest of the transplant is done as quickly as possible. Under X-Ray guidance, the freshly isolated islets are injected into the portal vein of the diabetic recipient's liver. Once in the portal vein, blood flow carries the islets into the liver where they become lodged in capillaries. The islets in the liver do the job the islets in the pancreas once did.

What happens after the transplant?

After transplantation, the body's natural defenses recognize the transplanted islets as foreign cells and would destroy them if left unchecked. Because of this, transplant recipients must take "immunosuppressive" drugs to prevent the destruction of the islets by the immune system. In the Edmonton protocol, immunosuppression is achieved using a combination of three drugs – rapamycin (brand name Sirolimus), tacrolimus, (brand name Prograf), and daclizumab (brand name Zenapax). Steroid-type drugs are not used because they may be toxic to transplanted islets.

Is Islet Transplantation a Cure for Diabetes?

In principle, yes! The Edmonton protocol is a breakthrough and a sign that Type 1 diabetes can indeed be conquered. However, at present, the supply of cadaver pancreases severely limits the number of patients who can receive transplants. In addition, as with any experimental technique, it is important learn in detail what the good and bad effects of the treatment are. Immunosuppression is associated with a number of side effects, including increased risk of infection and certain cancers.

For islet transplantation to become a reliable and widely available cure for diabetes, we must:

- ❑ confirm that the Edmonton Protocol works in a large patient population,
- ❑ determine the long-term risks associated with immunosuppression,
- ❑ investigate the biological reasons behind both the rejection or acceptance of transplanted islet cells,
- ❑ develop new, improved methods of transplantation.



UMMS ISLET TRANSPLANTATION PROGRAM

COMPLETING YOUR APPLICATION

Please read all the directions and documents before filling out the forms. Spend some time looking over the criteria for enrollment in the trial. After considering each point, if you still feel you may qualify (or if you are unsure how any of the criteria apply to you), you should make an appointment with your physician to investigate further if you are indeed a qualified candidate. Prior to your appointment with your physician, you should complete and sign the “Islet Transplant Patient Information Form”. This will provide the transplantation research team with some very basic information regarding your diabetes and overall health. You should also complete the letter that authorizes your physician to provide UMMS with additional medical information pertaining to your condition. Discuss with your physician how each of the enrollment criteria applies to you. If, after reviewing all the criteria, your physician agrees that you are a suitable candidate, he/she should complete and sign the “Referral for Islet Transplant” form provided in this package. Your physician must mail both this form and the Patient Information Form you completed to:

Patient Referrals

UMMS Islet Transplantation Program
University of Massachusetts Medical School
373 Plantation Street
Suite 218
Worcester, MA 01605

The applications of everyone who applies will be evaluated. As the applications are received, some individuals who appear to meet the basic criteria will be identified. These individuals will be asked to participate in a more detailed evaluation process consisting of a series of interviews and laboratory tests designed to identify those applicants who most closely meet the criteria for participating in the trial.

Note on Confidentiality: The information you provide to us will be kept in the strictest of confidence and will be used only for the purpose of evaluating your suitability for involvement in the clinical trial. The information you provide will not be shared with other individuals or organizations under any circumstances, without your express written consent.



UMMS ISLET TRANSPLANTATION PROGRAM

CRITERIA FOR ENROLLMENT

IMPORTANT:

Only persons with **Type 1 Diabetes between the ages of 18-65, diagnosed at least 5 years ago**, are eligible for participation in the trial. In addition, you must have conscientiously adhered to dietary and lifestyle modifications, and an optimal insulin regime. Candidates must have been in close contact with a physician during the 6 months preceding enrollment during which intensive management of diabetes was attempted. *Intensive management is defined as the administration of at least 3 insulin injections per day and self-monitoring of blood glucose at least 4 times per day.*

Despite your best efforts, **at least one of the following must apply:**

- ❑ Evidence of poor control of diabetes defined as a glycohemoglobin A_{1c} >8.0% on at least two occasions prior to enrollment. *Glycohemoglobin A_{1c} is a blood test that measures diabetes control over the preceding 3-4 months.*
- ❑ A history of recurring hypoglycemia and documented evidence of at least 3 episodes of hypoglycemia severe enough to be incapacitating.

You will be ineligible for participation for as long as the following apply:

- ❑ Being Overweight (body mass index >26 kg/m²).
Body Mass Index (BMI) = (Weight in Kilograms) / (Height in Meters Squared)
Step One: Divide your weight in pounds by 2.2. This is your weight in Kilograms.
Step Two: Divide your height in inches by 39.37. This is your height in meters.
Step Three: Square your result from step two.
Step Four: Divide your result from step one by the result from step three.
- ❑ Being pregnant
- ❑ Significant kidney disease (creatinine clearance rate <60 ml/min).
- ❑ Liver disease (ALT or AST greater than twice normal, or portal hypertension)
- ❑ Current or prior infection with hepatitis B, hepatitis C or HIV
- ❑ Presence of a bleeding problem (elevated PT or PTT)
- ❑ Cancer, or an abnormally elevated prostate-specific antigen (men), or abnormal mammogram or pap test (women)



UMMS ISLET TRANSPLANTATION PROGRAM

ISLET TRANSPLANT PATIENT INFORMATION FORM

This form must be completed and signed by the patient. After completing this form, take it to your physician and along with a copy of the release form, ask him/her to complete an Islet Transplant Referral Form.

Personal Information (please print)			
Name (Last, First)		Sex: <input type="checkbox"/> Male <input type="checkbox"/> Female	Date of Birth (MM/DD/YY)
Street Address			
City	State	Zip/Postal Code	E-Mail Address
Home Telephone		Work Telephone	Fax Number

Race and Ethnicity
<p>In accordance with the National Institutes of Health regulations the UMMS ISLET TRANSPLANTATION PROGRAM must obtain information regarding the race and ethnicity of all trial participants. In the selection of patients UMMS will make every effort possible to ensure equal access to all, regardless of race or cultural origin.</p> <p>Race/ Ethnicity (select one or more):</p> <input type="checkbox"/> Hispanic or Latino <input type="checkbox"/> American Indian or Alaska Native <input type="checkbox"/> Asian <input type="checkbox"/> Black or African American <input type="checkbox"/> Native Hawaiian or other Pacific Islander <input type="checkbox"/> White

Supplementary Personal Information
<p>Your Marital Status: <input type="checkbox"/> Single <input type="checkbox"/> Married <input type="checkbox"/> Widowed Number of dependents: _____</p> <p>Your current weight: _____ lbs. Your height: _____ ft. _____ in.</p> <p>Occupation _____</p>

Patient's Signature

I, hereby certify that the information contained within this document is true, to the best of my ability.

Name (print) _____ Signed: _____

Date: _____

Continued on next page...



Patient Statement

Please briefly describe your health as it pertains to the enrollment criteria (described on page 5).

- Do you have poor diabetes control (Hemoglobin A1c >8.0%), despite attempts at intensive management?
- Do you have a history of recurring hypoglycemia (at least 3 episodes of severe hypoglycemia)?

Medications

In the table below, list any medications you are currently taking (attach additional page, if necessary).

Name of Drug	Amount Taken	When is your medication taken

List known allergies to medications: _____

Significant Medical History

In the table below, list your significant illnesses or major surgeries. Begin with the date of onset of your diabetes.

Major Illness or Surgery (attach additional page, if necessary).	Date (month/year)
Onset of Type 1 Diabetes	

Doctor's Name and Address	
Name	
Address	
Telephone	Fax Number

Authorization for Consideration in Future Trials
<p>In the future, UMMS may conduct other clinical trials of islet transplantation techniques that may or may not be specifically related to the Edmonton Protocol trial. If you wish to be considered for participation in any of these, please indicate this desire by checking the box below. (Note that your response to this question will not be used in any way to assess your eligibility for the Edmonton Protocol Trial, and does not serve as a commitment to participate in any subsequent research trial).</p> <p><input type="checkbox"/> Please keep my information on file for consideration in future islet transplantation trials conducted by the UMMS ISLET TRANSPLANTATION PROGRAM and/or its collaborating clinical centers.</p>

When complete and signed, take this form to you physician together with the attached "referral for Islet Transplant" form. Your physician must mail these forms directly to:

Patient Referrals
 UMMS Islet Transplantation Program
 University of Massachusetts Medical School
 373 Plantation Street
 Suite 218
 Worcester, MA 01605



UMMS ISLET TRANSPLANTATION PROGRAM

PERMISSION FOR RELEASE OF INFORMATION FORM

Date: _____

Dear Doctor _____,

I, _____ give you permission to release any information related to my diabetes and overall health to the UMMS ISLET TRANSPLANTATION PROGRAM for evaluation of my suitability to be included as a participant in a clinical trial of the "Edmonton Protocol" for islet transplantation.

Thank you

Signature

Name (please print)

[Complete, sign and present this letter to your physician to authorize him/her to release your confidential information to us.]



UMMS ISLET TRANSPLANTATION PROGRAM

REFERRAL FOR ISLET TRANSPLANT

To the Physician: Please complete and sign this form and return it, along with a copy of the "Patient Information Form", completed and signed by the patient, to: Patient Referrals, UMMS Islet Transplantation Program, University of Massachusetts Medical School, 373 Plantation Street, Suite 218, Worcester, MA 01605

Patient's Name and Address	
Name (Last, First)	Date of Birth (DD/MM/YY)
Address	
Home Telephone	Work Telephone

Indications		
Does this patient have any of the following indications for islet transplant?		
1) Frequent hypoglycemic comas	<input type="checkbox"/> YES	<input type="checkbox"/> NO
2) Hypoglycemia unawareness	<input type="checkbox"/> YES	<input type="checkbox"/> NO
3) Metabolic instability/lability	<input type="checkbox"/> YES	<input type="checkbox"/> NO

Please provide additional details on any of these indications in the space below:

Referring Physician's Name and Address	
Name	
Address, City, State	
Telephone	Fax Number
I certify that the above information is correct, to the best of my knowledge.	
Signed: _____	Date: _____

