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Getting New Islet Cells

Facts about Clinical Islet Transplants

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Getting New Islet Cells

Facts about Clinical Islet Transplants

What is an islet cell transplant?

An islet cell transplant is a treatment for people with type 1 diabetes who have trouble controlling their glucose (blood sugar). There is a limited supply of islet transplants available, so transplant centers are careful to select only those patients who really need the procedure. Islet transplants are done alone or together with a kidney transplant (kidney and islet, or islet after kidney).

How does a person get an islet cell transplant?

Most centers require patients to enter a clinical trial, also called a study. A clinical trial is a research study where doctors try new drugs or medical treatments to learn more about diseases and their cures. During your clinical trial, transplant doctors will watch how your body reacts to different tests and treatments. It is a lot of work to be in a clinical trial. You have to visit the clinic a lot and have extra blood work done.

When you sign up for the clinical trial, you will be given an application package. The doctors will need to gather a great deal of information about your health, so you will fill out many forms.

Here is what you will find in the application package:

Inclusion/exclusion checklist
This checklist will help you and your doctors decide if an islet transplant is right for you. Complete the checklist before you fill out any other forms. (Each transplant center has its own checklist.)

Laboratory requisition
This is a list of the lab tests you will need for your medical evaluation.

Medical history form
This form asks questions about your medical history.

Diabetes questionnaire
This form asks questions about your diabetes history and treatments.

Physician referral form
The doctor who treats your diabetes will fill out this form.

Release of information
This form allows the transplant center to get copies of your medical records. They will review them to see if you qualify for the islet transplant.

When the center has all the information it needs, the local research team will review it. They will decide if your tests and health information match what the doctors are looking for in clinical trial patients.

- If you are a good match for the clinical trial, you will get an appointment at the assessment clinic. The purpose of this appointment is to see if islet transplant is right for you.
- If you are not a good match, the center will let you know. Your name can be added to a waiting list so you can try again in the future.

Many people apply for a transplant. Only a few get one. You may not hear from the center for a long time, so please be patient. It can take a while for some transplant centers to get back to you about your application.

The Assessment Process

What happens after my application is reviewed?

You will be scheduled for an assessment. You will meet with the transplant center's team so they can get to know you. You will meet with the transplant doctors and nurses. They will ask you questions about your health and do more tests. They will talk to you about the benefits and risks of islet cell transplantation. They will talk with you about the clinical trials at the center. You will then have some time to think about what you have learned and whether you want to join a clinical trial or not.

If you are a match for one of the clinical trials and you want to join, then you will get another appointment at the center for a full assessment.

What is a full assessment?

A full assessment is a more complete evaluation of your health. You will spend 4 to 8 days at a transplant center where you will have many tests done. You will also answer more questions about diabetes and other health conditions you have. The tests and exams are different at each center.

Blood tests

The blood tests are done on the first day of your assessment. The staff will take many tubes of blood. The total amount of blood that is taken is less than the amount given during a regular blood donation. It should not affect your health.

Other tests

The other tests take 2 to 3 days to complete. After you are done, you will go back home and wait while the doctors look at your test results. You might need to go back for more tests. Once all tests are done, the islet transplant team will look at the results and decide what to do next. In 3 or 4 days, the transplant coordinator will let you know your test results and what will happen next.

What happens if I am a good match for a clinical trial?

If you are a good match for a study, you will meet the doctors who are running that study. They will tell you all about the study, the risks involved, and what you can expect. If you still want to be part of the study, they will ask you to sign a consent form. Then you will meet with a coordinator to go over the plan for your transplant. They might give you a pager so they can reach you right away.

What happens while I am waiting for them to call or page me?

1. **Make sure you have a ride to the hospital before you get the call.**
   Make a list of 5 or 6 people you know who will be able to drive you to the hospital. The center might call on a weekend, late at night, or early in the morning. When you get the call, you will need to go to the hospital right away. So if one person on your list cannot drive you, call the next person on your list. Keep this list with you at all times.
2. **Make sure you know ahead of time what you need to pay for and have the money with you.** You might have to pay for tests, medicine, or a ride to the hospital. So make sure you always have enough money with you to pay for these things. If you have any questions about this, talk to your transplant nurse coordinator or the social worker at the program.

3. **Have a bag packed and ready to go at all times.** Transplants are often done on weekends or at night. Make sure you have everything you need for the hospital packed in your bag. Bring all your medicines with you. You will need to monitor your blood sugar regularly, even while in the hospital. So be sure to bring your glucose monitor with you. Check through your bag often to make sure you have packed everything you need.

Being on the list does not mean you will get an islet transplant. But if you do, it can happen any time day or night. So be ready. Know in advance who at home will take over your responsibilities. Some patients make a list of chores and who will do them while they are away. Know which friends and family members can help at any time.

If your health changes, see your regular doctor soon. Also tell the transplant team about any changes. Test your blood sugar at least four times every day. Your center might have a glucose meter with memory, which would allow them to download your readings and compare your glucose control before and after the islet transplant.

The Transplant Procedure

It is your responsibility to be ready when the center calls. If the center cannot reach you, you could lose your chance for a transplant. When the center calls, they might tell you the following things (it can be different with each center):

- Do not eat or drink anything after they call.
- Check your blood sugar level.
- Call friends and family and tell them that you might be having your transplant.
- Go to the transplant center. Take your pager and cell phone with you. This way, if the transplant is cancelled, you can be reached while you are on your way to the hospital.

Even if the center calls you, you may not get the transplant. This is because sometimes doctors cannot get enough cells from the pancreas to make the transplant work. If that happens, they will cancel the transplant. You may already be in the hospital when the transplant gets cancelled. There are many steps in getting the islet cells ready. The transplant might be cancelled at any step, and you will be sent home.

Where does the pancreas come from?

The pancreas comes from the same donors that give hearts, lungs, livers, and kidneys. These people tell their family and friends that they want to give their organs to someone else after they die. By donating, these people are giving the gift of life.

Transplant centers need one, two, or three pancreas organs for every transplant patient. The goal is for the patient to no longer need insulin. Because one transplant needs one whole pancreas, people cannot donate a section of their pancreas. This is different from a kidney transplant, where people can donate one kidney and still be healthy with the one they have left.

In the United States, we have a system for acquiring organs. It is called UNOS. This system makes sure that donated organs are sent to the patients who need them. These teams arrange for the removal, storage, and transport of all donated pancreases to the centers' islet preparation laboratory.

We need more donors.

Please sign your organ donation card, and make sure your family knows your wishes.

What happens when I get to the hospital?

When you arrive at the hospital, you will be registered and given a room. Your nurse will ask some questions about your medical history, then start an intravenous line (IV) for your medicines. You will usually sign consent forms for the transplant and the medicines. Your care team will draw blood and take a chest x-ray.

Islet cell transplant is done in the Radiology Department or in the Operating Room. While waiting to go in for the procedure, you will be given medicine. You will also be asked to monitor your glucose and tell the nurse what your level is each time.

In the Radiology Unit, you will get a local anesthetic. This is a drug that will be injected into the right side of your abdomen where the liver is located. The drug will numb the area. The radiologist will then place a needle and a tube into the main vein (portal vein) of the liver. Using a special x-ray machine (fluoroscopy) and dye, doctors will inject the solution containing the islet tissue. Then they will remove the tube and take you back to the Nursing Unit where you will remain for several hours. You will lie on your right side to lower the chance of bleeding.

Some centers do the islet transplant in the Operating Room. Your center may prefer this option, especially if you are having a kidney transplant at the same time. Doctors will make a small incision to directly enter the liver. In the operating room, the surgeon will inject the islets into a vein that flows into the liver.

When you are back in your hospital room, the nurses will monitor your vital signs and blood glucose levels. After about 6 hours, you will have a blood test. You will also have an ultrasound to make sure there is no bleeding around the liver and that the blood is flowing well in your liver. If the test results are good, you may be able to go home. Or you may need to stay in the hospital longer. Your stay could be as long as 4 days. It depends on your center's treatment plan and how well you are doing.

Care after Your Procedure

What do I need to do when I get home?

Once you are back at home, your care is your job. You will be on strong anti-rejection drugs for as long as the islet cells are working. Your body will always know that the new islet cells came from someone else. If you do not take the anti-rejection drugs, your body will destroy the islet cells.

You need to monitor your blood sugar levels very carefully. At first you will need to take insulin. Your insulin needs will change with each islet cell transplant. The transplant team will help you adjust the amount of insulin you need.

Remember that the islet cells will take some time to settle into their new home in your liver. We do not want to put stress on the islet cells, so it is important to keep your glucose at a good level. You do not want to make the new islets work too hard in the beginning.

Taking care of your islet cells is like planting seeds in your garden. Not every seed you put in the ground grows into a plant. If you prepare the soil, and feed and water the seeds, they have a better chance of growing into a plant. This is how it is with the islet cells. If you take good care of the cells right after your transplant, you have a better chance of good islet cell function. You can do this by sticking to your diet and living a healthy, balanced life.

What is rejection?

Rejection is the body's natural defense against foreign cells or particles like bacteria and viruses. Your immune system knows that your new islet cells are not part of your own body, so it may reject and destroy them.

What can be done to keep my body from destroying my new islet cells?

The doctors will use medicines that slow down your immune system enough to keep it from rejecting your islet cells. These medicines are called immunosuppressants. Some examples of these medicines are tacrolimus (Prograf®), sirolimus (Rapamune®), and daclizumab (Zenapax®). They work to stop the rejection. Doctors may also try other medicines or antibodies to prevent rejection.

The center will monitor your blood levels closely to make sure you do not reject your islet cells, or have too much of these drugs in your system. Over time, you will need less monitoring.

What can I do to prevent infections?

You need to be careful about infections. Here are some things you should do to prevent them:

- Wash your hands well and often.
- Do not visit friends who are sick.
- Get a flu shot every year.
- Practice safe sex (use condoms). Have yourself and your partner tested for sexually transmitted diseases.
- Tell the transplant center right away about any symptoms of infection such as fever, chills, aches, pains, vomiting, or diarrhea.

Your chances of getting cancer are greater than a person who has not had a transplant. Therefore, you need to do what you can to lower your chances of getting cancer. Here are some things you should do:

- Use sunscreen (SPF 15). Wear a hat every time you are in the sun. Do not lay or sit out in the sun. Also, do not stay outside very long during the hottest time of the day (between 10:00 AM and 2:00 PM).
- If you have any unusual skin growths, have them checked by your skin doctor right away.
- Get mammograms or prostate exams every year if you are over 40. Do a breast or testicular exam often.

What about medicines?

You will be given several drugs to take. Not every center gives the same drugs, so ask your center to tell you which ones they prefer to use. Make sure you know when to take them and how much to take.

<u>Here are some common drugs used to prevent infection after transplant:</u>

Septra®, Bactrim®: These are "sulfa drugs." They are used to prevent pneumonia.
Pentamidine: This drug is used to treat infections. It is used when **cotrimoxazole** is not a good choice.
Ganciclovir (Cytovene®): This drug is used to prevent infections from your donor organ. If you get an infection, you will be given larger doses through an IV.
Nystatin (Nilstat®): This drug helps prevent yeast infection in your mouth.

What about vitamins?

Do not take vitamins until you have been off insulin for 3 months. After 3 months, you might need high doses of vitamins. This is because when the islet cells are transplanted, they get injured and make oxygen-free radicals that hurt the cells. Vitamins may help lower the amount of these toxic radicals in your body, and they have almost no side effects.

Things to Expect after Transplant

Blood tests

You might need to go to the center often for blood tests. You need to fast before having a blood test, so ask your center what time you should stop eating. Do not take your morning insulin until after the tests have been completed. You might also need to wait until after the blood tests to take your other drugs.

As your islet cells begin to work and your drug levels stabilize, you will need fewer blood tests. After a while, you will be able to get your blood work done in a lab closer to your home.

You will also have your lipids (fat levels) tested. You will need to fast for 12 hours before the test, so do not eat or drink anything other than water.

Clinic appointments

You will go to the transplant clinic often for follow-up visits. Your doctors will talk to you about changes to your medicines. They will also tell you how often you have to come for blood work and appointments.

Medicine supply

Always keep 2 weeks worth of your medicines at home.

Blood sugar levels

Right after your transplant, you must check your blood sugar 7 times a day. As time goes by, you can check your levels less often. On the first and second day of each month, be sure to test your blood sugar before and after meals and before bed.

Rejection

Doctors will know if your body is rejecting your new islet cells when the cells no longer make insulin. By the time this happens, it will probably be too late to prevent the rejection. You can prevent rejection by taking your anti-rejection drugs correctly and by doing your best to not get an infection.

Infections

The drugs you are taking to prevent rejection suppress your immune system. This means your body can get infections easier. So try not to get infections, but if you do, see your doctor right away. Also tell your transplant team. You might have an infection if you have a fever, diarrhea, pain, or are vomiting.

Additional tests

You will need to have other tests done for 5 years after your transplant.

Some risks from islet transplantation:

- Lots of bleeding. You may need a blood transfusion or surgery.
- A large blood clot in the portal vein. Doctors may give you blood thinners.
- Liver failures.
- A hole in the bowel or gallbladder. You may need surgery to repair this.

- Low blood sugar levels after islet cell injection.
- Allergic reaction to the dye used to locate the portal vein.
- Infection in the new islet cells.
- Slow bowel movements.
- Shoulder and stomach pain.

Immunosuppressive drugs

You will be on these drugs for as long as your islet cells are working. The drugs keep your body from rejecting the new cells. There are some risks, though, from taking these drugs.

1. You are more open to getting infections and cancer due to suppression of your immune system. It is very important to have regular exams to look for cancer. It is also important to avoid exposure to infections.

2. Mouth sores. These are common and usually can be treated. Some patients may need minor surgery for cleaning mouth sores.

3. Upset stomach and diarrhea are common.

4. Thin nails.

5. A rise in your cholesterol levels.

6. Your kidneys may not work as well.

7. Women undergoing islet transplantation should not get pregnant while on these drugs. There is no information on how the medicines daclizumab and rapamycin can affect a pregnancy.

Some health complications

Vision problems

You will have a lot of insulin therapy during the first year after transplant. You have an 8% chance of developing eye injury or loss of vision. Because of this, doctors will check the backs of your eyes often during the first year and every year thereafter to identify any problems early on. If the doctors see any changes in your eyes, they will refer you to an eye specialist for treatment.

Immune problems from the islet transplant

Antibodies fight infections and foreign objects in the body. Transplant can cause antibodies to form against the proteins on the islet tissue. These proteins are called antigens. The antibodies will remember these antigens and mark them for destruction. This can make it harder for you to get another transplant because the immune system will respond much quicker the next time your immune system sees these antigens. This can affect the success rate of a kidney or other organ transplant.

Questions about Islet Cell Transplantation

If I am not a match now, how can I become a match later?

Keep checking your center's Web site for new studies and the kind of match the center is looking for.

When will more people with diabetes be able to have this procedure?

Islet transplant studies are happening at many centers in the United States, Canada, and Europe. Researchers need to collect more safety data before these transplants are considered standard care in the United States.

We also need to increase our supply of islet cells. Right now, this treatment is available to only a few patients. We need more organ donors. We must also look for other sources of islet tissue. We need to improve how well the transplanted islet cells function. We also need to do more research.

Lifelong immunosuppressive drugs have side effects. We need to do more research so we can learn more about these medicines. We also need to do more research to develop medicines with fewer side effects. We hope to learn how to prevent diabetes. More funding is needed to continue research on diabetes and transplants.

Is islet cell transplantation a cure?

No. It is still being developed, and long-term outcomes are still not known. What an islet cell transplant patient gets to do is exchange insulin shots for immunosuppressive drugs and glucose monitoring. It is a tradeoff. Patients who used to have irregular glucose levels now take immunosuppressive drugs so they have stable glucose levels. This is a possible long-term treatment for people who suffer from type 1 diabetes.

Who can donate?

A pancreas comes from the same donors that give hearts, lungs, livers, and kidneys after they die. The donor or the donor's family decides that, in the event of brain death, they wanted to donate their organs and give the gift of life. There is a critical need for more donors. Please sign your organ donation card, and discuss your wishes with your family. More than one donor pancreas is often needed for every patient who receives an islet transplant. Because we need a full pancreas for the transplant, a living person cannot donate their pancreas.

How do I get on the list for an islet transplant?

Talk to your doctor about the criteria for a good transplant candidate. If you decide to join a center's study, you will have some blood work done, and you will need to fill out some forms. These forms can be found on the center's Web site or at the center. The center will review your paperwork and blood work. If you meet the criteria, they will ask you to come to the center for a clinic appointment. Afterwards, you will have a more complete assessment and then be placed on a waiting list. If you do not meet the current criteria, they will keep your name on file in case you match the criteria of another study.

Can I buy an islet transplant?

No. Patients cannot buy a transplant or pay to have their name put on a transplant list.

Are there risks involved?

Yes. See the list of risks in the above section. Islet transplantation is still being studied by research doctors. As more patients are having transplants, more risks are being observed. Some common problems have been painful mouth sores, but they seem to go away after being treated with medicines. Two other problems patients have also had are thinner nails and diarrhea.

Some of the more severe problems have been bleeding after the procedure; clots in the blood vessels that go to the liver; liver failure; and kidney disease.

The drugs we use to fight rejection make your body less able to fight infections and cancer. These drugs also have side effects that can lead to kidney problems, ulcers in the mouth, high blood pressure, and diarrhea. These drugs are new, so we are still learning about them.

How much time does it take to be in a study?

The first assessment takes about 10 days. After the transplant, you will have a lot of checkups at the clinic. Once you are stable and your risks are lower, you will go less often. At first, you will have blood work done three or more times a week. After a while, you will need blood work only once a month.

The center will monitor you closely for many years after the transplant and for as long as the islets are working.

Can I have an islet cell transplant if I have had a kidney or other organ transplant?

Yes. Some centers have patients who have combined kidney and islet transplants, either at the same time or one after the other. The islets may sometimes be ready at the same time as the kidney. They can also be made ready at a later time, from a different donor, once the new kidney is stable.

What does an islet cell transplant cost?

The costs for a transplant are different at each center. Most costs are paid for by research programs. The patient usually pays for transportation, housing, and medicines after leaving the hospital. If you need financial help, ask your transplant team if there are other programs that can help you pay for some of your costs. Sometimes the drug companies or clinical trial sponsors pay for the drugs, at least for a while. It is a good idea to know ahead of time what you will owe at the end of the study.

You might need to pay for:

Capillary glucose strips

Glucose meters and strips may be given to you by your program, but ask ahead of time so you know for sure.

Medicines

The cost of your drugs will depend on your treatment. In the beginning, it will cost more because you will have more drugs to take. But after 6 months, the drugs will cost less because the dosages will decrease. Make sure you have health insurance to help pay these costs. If you have any concerns, please discuss them with your transplant coordinator.

For more information about islet cell transplants, go to your center's Web site.