

ISLET CELL TRANSPLANT

WHAT YOU NEED TO KNOW



Diabetes Research &
Wellness Foundation

UKITC

UK Islet Transplant Consortium

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WHO TO CONTACT

Referrals for islet cell transplant are being accepted by teams at seven centres across the UK. The doctors at each centre are very happy to discuss possible referrals and can be contacted directly, using the details given below.

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TRANSPLANT TEAM CONTACT DETAILS

(to be completed by your team):

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Lead doctor or/and surgeon:

Diabetes nurse:

Transplant ward:

Hospital pharmacy:

Hospital switchboard:

Patient support group:

Local web sites:

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1. SUMMARY INFORMATION

1.1 What are islet cells?

People develop Type 1 diabetes because they are unable to produce the hormone insulin. Typically, insulin is made by specialised cells found in clusters called the Islets of Langerhans (or simply 'islets').

Islet cells produce insulin when blood glucose levels in the body are high, bringing them down again, and stop producing insulin when blood glucose levels are low. A picture of an islet is shown in the pink area in the picture to the right (Figure 1).

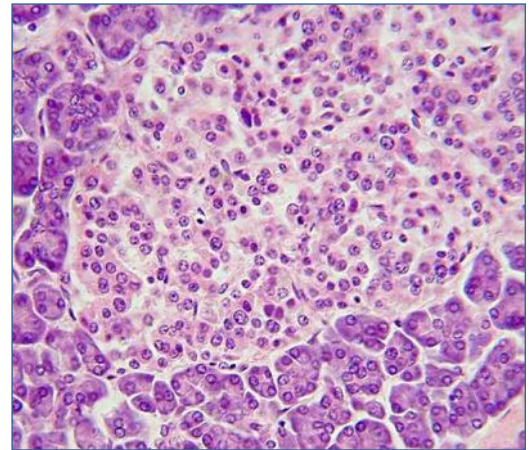


Figure 1: An islet (light pink) surrounded by normal pancreas

1.2 What is an islet cell transplant?

Islet cell transplantation involves extracting islet cells from the pancreas of a deceased donor and implanting them in the liver of someone with Type 1 diabetes (Figure 2). First islets are extracted from the pancreas of someone who has died and given consent for their organs to be used for transplantation. If this process produces a suitable number of good quality islets, they can be offered to someone in need of a transplant.

Donor islets are injected into a vein within the liver (the portal vein) and after a period of around two to six weeks, they start to produce insulin. At this time, the transplant patient will become aware that their blood glucose is easier to manage. **Most people require two transplants** (involving two hospital admissions) to get the maximum benefit from the procedure. Further details regarding the procedure and the hospital stay are given below.

At the time of the transplant, the transplant patient must take anti-rejection drugs to make sure that their immune system does not reject the newly transplanted islet cells. These drugs must be taken for the rest of the transplant patient's life and have known side-effects, which are discussed in detail in the appendix at the end of this guide.

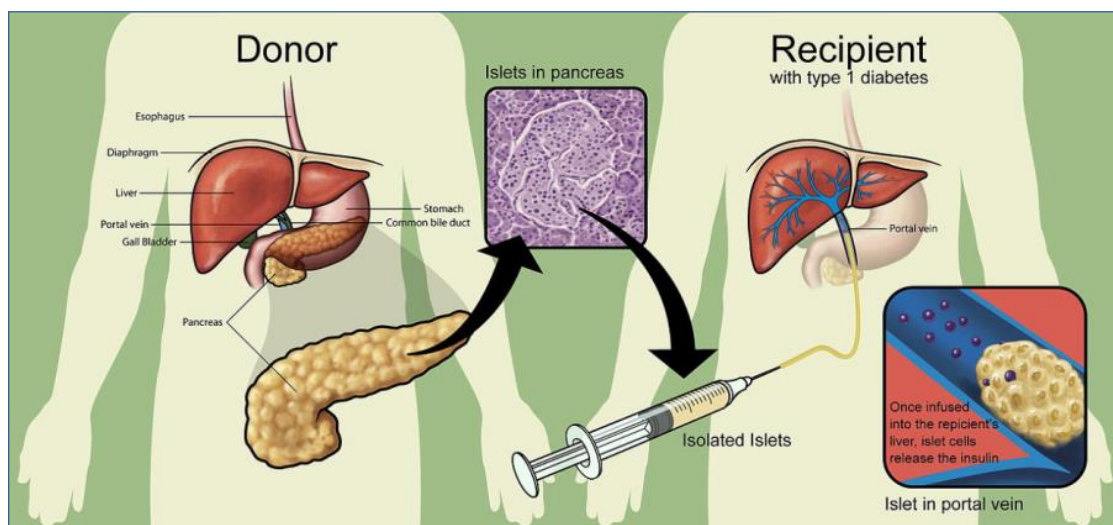


Figure 2: An islet cell transplant

1.3 Is an islet cell transplant suitable for me?

People who use insulin to control their blood glucose levels sometimes experience episodes of very low blood glucose or hypoglycaemia (hypos). Most people with Type 1 diabetes are able to manage these hypos because of characteristic symptoms that tell them when their blood glucose is low, such as feeling shaky, sweaty or anxious. These symptoms are vitally important because they prompt people to manage each hypo and so prevent their blood glucose levels from falling further, which could have potentially serious consequences.

About one third of people with Type 1 diabetes each year will experience a '**severe**' hypo – meaning that they need someone else to help them. These can be very dangerous because they could potentially lead to fitting, unconsciousness and, sometimes, even death. Severe hypos can occur in anyone taking insulin, but they are more likely to occur in people who have had diabetes for more than 15 years and those who are unable to recognise when their blood glucose is low (a problem known as **hypo unawareness**). People who have Type 1 diabetes and hypo unawareness are six times more likely to experience a severe hypo than people whose hypo awareness is intact.

If you think that the above is a good description of you, then an islet cell transplant might be a suitable option. The main reason to have an islet cell transplant is recurrent, severe, disabling hypoglycaemia **despite** the best medical therapy, which may include a trial of insulin pump therapy. The criteria used by doctors to guide them when selecting people for islet cell transplant are as follows.

1.3.1 Who might be suitable for an islet cell transplant?

- People with Type 1 diabetes who have experienced two or more severe hypos within the last two years, and have impaired awareness of hypoglycaemia.
- People with Type 1 diabetes and a **functioning kidney transplant** who experience severe hypos and impaired hypoglycaemia awareness **or** poor blood glucose control despite the best medical therapy.

1.3.2 Who might not be suitable for an islet cell transplant?

- People who need a lot of insulin (e.g. more than 50 units per day for a 70kg person).
- People who weigh over 85kg.
- People with poor kidney function. For example, those with an estimated glomerular filtration rate (eGFR, the rate at which fluid filters through the kidney) of less than 60ml per minute, which can be worsened by anti-rejection medication.
- Women who are planning a pregnancy (because the long term effects of some anti-rejection drugs on unborn children are uncertain).
- Other people with less common health issues - your medical team will discuss these with you.

1.4 What are the likely benefits of an islet cell transplant?

The goals and likely benefits of an islet cell transplant are to:

- Reduce the frequency of severe hypos
- Improve awareness of hypos
- Improve quality of life
- Reduce fear of hypos

- Reduce the risk of long-term complications of diabetes.

1.5 Will I still have to take insulin after an islet cell transplant?

For most people, the simple answer is 'yes'. The goal of an islet cell transplant is NOT to eliminate the need for insulin injections, although it can be a great bonus when this happens. In some cases, transplant patients will have freedom from insulin injections for up to one year and very occasionally for more than five years. Others will need to continue with some level of injected insulin from the start.

Results from the UK suggest that the majority of people who receive an islet cell transplant have to continue taking insulin, but their dose is usually around half of that required before their first transplant. Results from Edmonton, Canada show that, five years after an islet cell transplant, around nine out of ten transplant patients will need to resume treatment with insulin by pump or by injection. It is important to realise that islet cell transplantation is not an effective treatment for people whose aim is to stop insulin therapy.

1.6 Understanding your treatment options

It is important that you have sufficient information to help you make a decision about whether or not to undergo an islet cell transplant. Before you pursue a full clinical assessment to see if you are suitable for an islet cell transplant, you should be familiar with the risks and benefits of this therapy (please see Table 1 and section 4.3.3.) and of the other available therapies (see Table 1).

2. WHAT OTHER TREATMENT OPTIONS ARE AVAILABLE?

Several treatment options are available (see Table 1). These are listed here in order of increasing complexity:

- Revision of your insulin regimen and overall diabetes management
- An insulin pump and/or continuous glucose monitoring
- An islet cell transplant or a whole organ pancreas transplant

Your medical team will discuss the risks and benefits of these alternatives with you to help you to decide on your best option. The important differences between these treatment options are outlined below and compared to islet cell transplant in Table 1. Please study this carefully and discuss all of the treatment options with your healthcare team.

2.1 Enhanced standard therapy

People with Type 1 diabetes who are using a very simple, inflexible insulin regimen (such as twice daily injections) may benefit from learning how to use their insulin more effectively. If you have not been taught how to count the carbohydrates in different meals and to change your insulin doses in response to food intake, activity levels and glucose results (e.g. through a DAFNE-style education course) then the islet cell transplant team will discuss this with you.

If you are already using the best available insulin injection therapy, then the option of an insulin pump may be discussed with you (see Figure 3). This can be a safe and highly effective way of dealing with problematic hypos in people with Type 1 diabetes.

Most people with Type 1 diabetes who are referred to an islet cell transplant centre with problematic hypos are able to reduce the number of hypos they experience by working with their healthcare team to adjust their insulin regimen, and/or use an insulin pump. Ultimately these people can overcome problematic hypos without needing an islet cell transplant and therefore without the risks of undergoing an operation and taking anti-rejection medication.

2.2 Insulin pump therapy and continuous glucose monitoring

Insulin pumps are the size of a small mobile phone, and are usually worn under clothing on a belt around the waist. Pumps contain a battery, an electric motor and a syringe containing insulin. The insulin syringe is connected via a tube, to a plastic cannula which is inserted under the skin. The pump continuously provides a small amount of long-acting insulin, and gives extra, short-acting insulin at mealtimes when prompted by the pump user. A pump allows background insulin to be given continuously at different rates throughout the day and night, making it much easier for an individual to get the correct insulin dose than it would be if they were using multiple daily injections. An insulin pump also allows more flexibility when dealing with exercise, stress, alcohol and illness. In practice, people with Type 1 diabetes who use an insulin pump to manage their condition are four times less likely to experience severe hypos than those who use insulin injections.

Sometimes insulin pumps can be used with a monitor that records glucose levels continuously through a small plastic tube placed under the skin. Some continuous glucose monitors can 'talk to' the insulin pump and switch it off when blood glucose levels are low. This therapy can be a very effective way to reduce the risk of severe hypos. However, these devices are currently available in only a limited number of UK diabetes centres. Please discuss this option with your diabetes care team if you continue to have problematic hypos using standard insulin pump therapy.

Most people who might be suitable for an islet cell transplant are encouraged to trial an insulin pump and continuous glucose monitoring first. But these devices do not suit everyone, and, for some people, an islet cell or whole organ pancreas transplant might be better options.

2.3 Whole organ pancreas transplant

A whole organ pancreas transplant can be a very effective way of managing Type 1 diabetes and reducing the risk of severe hypoglycaemia. A successful whole organ pancreas transplant usually results in normal blood glucose levels, so that transplant patients can, for the most part, eat what they like, when they like and usually do not require insulin injections.

After five years, around 55 out of every 100 patients who receive a whole organ pancreas transplant are free from insulin injections, whereas after the same period only 10-20 out of every 100 islet cell transplant patients are free from insulin injections.

As yet, there have been no studies to compare the long-term effectiveness of whole organ pancreas transplant to that of islet cell transplant, but results are likely to be similar, with around two out of every three patients having a functioning transplant at five years.

The main drawbacks of a whole organ pancreas transplant are the risks of death or serious complications in the first few weeks after the transplant (see Table 1 below). A whole organ pancreas transplant is also a much bigger operation than an islet cell transplant, involving a one in three chance of needing another operation and a hospital stay of over 2 weeks.

Another drawback of having a whole organ pancreas transplant is the need to take anti-rejection medication for as long as the transplant continues to work (which could be for the rest of your life). Transplant patients may experience side-effects that range from inconvenient (such as stomach upset or diarrhoea), to more serious (including an increased risk of certain cancers, such as skin cancer). These risks are the same for all patients who receive a transplant of any type (including islet cell transplants) and are covered in further detail below. In this important respect, insulin pump therapy has a major advantage over both pancreas and islet cell transplantation: no anti-rejection medication is necessary and therefore risks of life-threatening infection and cancer are avoided.

Nevertheless, there are several benefits to whole organ pancreas transplant. For instance, it may be better suited to people requiring larger insulin doses. If you are interested in finding out more about having a whole organ pancreas transplant, then ask your diabetes care team or your GP to put you in contact with a transplant surgeon who can discuss this with you.

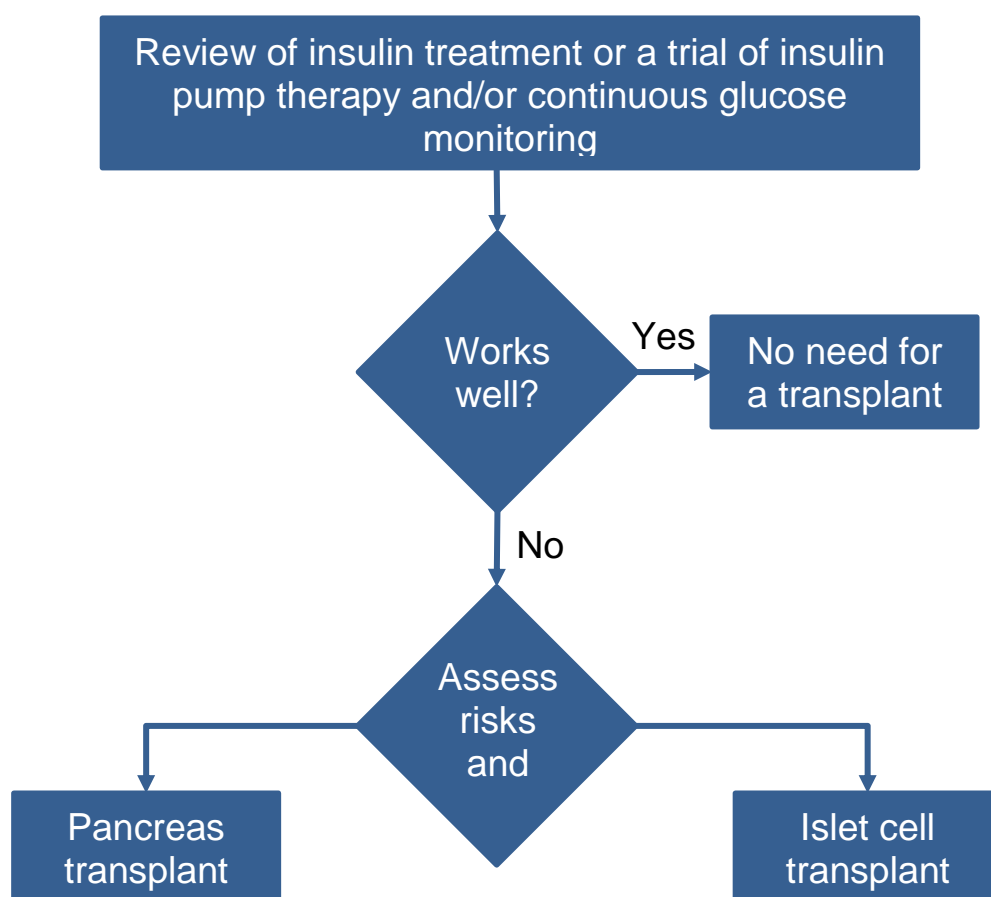


Figure 3: People interested in islet cell or a whole organ pancreas transplantation have a review of their insulin therapy and may be offered a trial of insulin pump therapy and/or continuous glucose monitoring

Table 1: Risks and benefits: islet cell vs. pancreas transplant vs. insulin pump therapy/continuous glucose monitoring

Risks and benefits	Islet cell transplant	Pancreas transplant	Pump/CGM
Death due to the operation or procedure	Less than one patient in 100	Three patients in 100	Close to zero
Operation to open the tummy	Two patients in 100	All patients	Zero
Recent operation on the tummy	Close to zero	30 patients in 100	Zero
Serious surgical complications including colostomy	Close to zero	30 patients in 100	Zero
When treatment starts to work	After 3-12 weeks	Straight away	Straight away
Any infection over six years	17 patients in 100	17 patients in 100	Not applicable
Life-threatening infection with long-term clinical effects over six years	Two patients in 100	Two patients in 100	Zero
Death due to infection over six years	One patient in 300	One patient in 300	Not applicable
Cancer, potentially life-threatening, over six years (except skin cancer)	Four patients in 100	Four patients in 100	Zero
Skin cancer including melanoma (often treatable) over six years	Eight patients in 100	Eight patients in 100	Zero
Severe reduction in kidney function due to anti-rejection medication	Sometimes	Sometimes	Not applicable
Freedom from insulin injections at one year	30-70 patients in 100*	80-90 patients in 100	Not applicable
Freedom from insulin injections at five years	10-30 patients in 100	50-60 patients in 100	Not applicable
Major reduction in severe hypos at 18 months	75-95 patients in 100	75-85 patients in 100	See below**
Reduced risk of severe hypos at five years	50-70 patients in 100	50-70 patients in 100	75 patients in 100
Improved HbA1c at five years	50-70 patients in 100	50-70 patients in 100	50 patients in 100
Improved diabetes complications	Likely	Proven	Likely

* Limited information due to small numbers of patients treated in UK at present

** No data for direct comparison, but on average approximately 50% reduced (some more, some less) compared to using subcutaneous insulin

Information from the [Collaborative Islet Transplant Registry](#), [Ryan EA et al.](#), [NICE technology appraisal guidance 151](#), [Engels EA et al.](#), [Kasiske BL et al.](#)

Caution: comparisons are provided as a guide only. No randomised controlled trials have been performed to compare these therapies and baseline risk

3. HOW DO I GET REFERRED FOR ISLET CELL TRANSPLANTATION?

In order to receive an islet cell transplant you will require a referral to a transplant team by your GP or diabetes care team. Your team will need to confirm that all possible alternative options have been explored to help you achieve stable blood glucose levels and avoid severe hypos.

3.1 What happens next?

Once the islet cell transplant team receive the referral, they will contact you and provide you with information about what is involved. They may also send you some questionnaires about your hypos to complete and return. These will allow them to assess whether or not you are suitable for an islet cell transplant. They will then contact you and arrange an outpatient appointment where you will meet the medical and nursing staff so that they can assess the severity of your diabetes in more detail, and give you further information about the procedure. They may also perform some blood tests, which will also help them to assess whether or not you might be suitable.

4. WHAT HAPPENS IF I DECIDE TO GO AHEAD WITH ISLET CELL TRANSPLANTATION?

If you are keen to proceed with an islet cell transplant, and initial blood tests confirm your suitability, further check-ups will then be arranged. Your islet cell transplant team will try to minimise the number of hospital visits you will need, but you must be prepared for at least five additional visits to the hospital during this phase of preparation. Your hospital visits will include the following:

- a) **General tests:** including a chest x-ray, an electrical recording of your heart (ECG), and blood tests to assess your tissue type and blood group. The islet cell transplant team will also test whether you have had viral infections in the past (such as HIV/AIDS, chickenpox or hepatitis) that could flare up if you were to receive anti-rejection medications. They may also perform a 24-hour collection of your urine to test the function of your kidneys, and will test one urine sample for signs of infection. Some women will be asked to have cervical screening (a 'smear'), a mammogram and a pregnancy test.
- b) **Scans:** the islet cell transplant team will arrange for you to have a kidney scan to assess how well your kidneys are working. The anti-rejection drugs given after an islet cell transplant can reduce kidney function and that is why people who already have poor kidney function are generally not given islet cell transplants, due to the risk that these drugs could lead to kidney failure. This test takes about four hours and involves having a radioactive dye injected into your arm so that it can be taken up by your kidneys. You will receive only a low dose of radiation as a result of the test and the care team at the nuclear medicine department will explain exactly what is involved.

The islet cell transplant team will also arrange a heart scan to see whether or not you have any important narrowing of the arteries that supply blood to your heart (the coronary arteries). If they do find that you have coronary artery disease then this may

influence some aspects of your treatment but is unlikely to prevent you from going ahead with an islet cell transplant. This test can take up to five hours to perform, and you may have to visit the hospital on two separate days. As with the kidney test, this procedure will involve having a radioactive dye injected into your arm, but you will receive only a low dose of radiation. During the test you may be asked to exercise, or your medical team may decide to simulate exercise using drugs that speed up your heart for a few minutes. This is a safe procedure and the care team at the nuclear medicine department will explain exactly what is involved.

The islet cell transplant team will also arrange for you to have an ultrasound scan of your liver, which will help to identify any problems that you might have with the islet cell transplant procedure itself.

- c) **Psychological assessment:** the islet cell transplant team will arrange for you to have a meeting with a clinical psychologist to help them find out if you might need extra psychological support during or after the procedure. It is unlikely that the psychological assessment will influence whether or not you can undergo a transplant.
- d) **Continuous glucose monitoring:** the islet cell transplant team will need to know how your blood glucose changes over time. Therefore they will arrange for you to be fitted with a small monitor that will record your blood glucose every five minutes over six or seven days. The monitor involves having a small plastic tube placed under the skin of your tummy (lower abdomen) using a needle. The monitor can be fitted in around 20 minutes and then you will be able to go home with it for a week or so. You will be asked to check your blood glucose frequently while you are wearing the monitor (up to seven times daily). You will then be asked to return to the hospital after one week so that the monitor can be removed (which takes about 20 minutes), after which you'll be able to go home again. Your medical team will discuss the results with you.
- e) **Dental and eye records:** the islet cell transplant team will also obtain information about your retinal screening results and your dental history.

If the results of all the above tests suggest that you would be suitable for an islet cell transplant, then your name will be added to the transplant waiting list.

4.1 What happens when I am on the waiting list for an islet cell transplant?

It is difficult to predict how long each individual will have to wait for an islet cell transplant but the average waiting time is currently about 18 months.

While on the waiting list, it is important that you contact the transplant team if:

- there is any change in your general health
- you are admitted to hospital for any reason
- there is any change in your telephone number(s) or address
- you decide to go abroad (for holiday or work)

It is important that you do this so that the transplant team know how and where they can contact you and so that your name can be temporarily removed from the waiting list if you are abroad or in hospital. If you are temporarily removed from the list, do not worry – you will

re-join it at the place where you left and your suspension will not affect your chances of getting a transplant.

While on the waiting list, you will be required to provide a monthly blood sample so that you can be matched with an islet donor. These blood samples can be taken at your diabetes clinic or at your GP's surgery.

4.2 What happens when I'm called in for a transplant?

The islet cell transplant team will telephone you to let you know that a suitable donor pancreas has become available. They will ask about your general health and if you still wish to go ahead. For example, if you have an infection when they call you, then you may not be able to receive a transplant because of the risk of causing a more severe infection with the anti-rejection drugs.

If all is well, you will be admitted to hospital for three to six days. When admitted, you will be seen and examined by your medical team and you will have a series of blood tests.

For a few hours before the transplant, you will be asked to stop all short-acting insulin injections (such as *NovoRapid*) and to stop eating and drinking. At this time, a small plastic tube (intravenous drip) will be inserted into a vein in your arm (though in rare situations, it may be inserted in your neck – just above your collar bone). Insulin and fluids containing glucose will be given to you through this tube in carefully adjusted doses to keep your blood glucose as close to normal as possible.

If your glucose level goes low, you will be given more glucose and your insulin drip will stop until your level goes back up. Hypos are unlikely to happen because your blood glucose and the insulin dose you receive will be checked and adjusted at least every hour. You will be able to take glucose tablets or Lucozade in an emergency situation, but this is unlikely to happen.

This drip will usually be kept running for the first 48 hours after the transplant to help you achieve near-normal glucose levels while the islets settle into their new environment.

Anti-rejection drugs will be given once the medical team has final confirmation that the transplant will be going ahead. These drugs are given through a vein or sometimes by an injection under the skin.

4.3 What does the transplant procedure involve?

The transplant procedure will usually take place in your hospital's x-ray department. Before the procedure begins you will be given drugs to relieve pain and a sedative to help you relax via the drip in your arm. When the procedure starts, you are likely to feel sleepy, but awake, and will be aware of what is happening during the procedure. However, you may find later that your memory of the procedure is limited because of the sedative given to you.

You will be given a local anaesthetic injection to numb a small area of skin on the right side of your chest. The radiologist will use ultrasound and x-rays to identify your portal vein, which is located within the liver. Using a needle, the radiologist will insert a plastic tube (a catheter) through your liver and into the portal vein. The islets are then injected slowly into the portal vein over a period of 15 to 30 minutes.

4.3.1 Can I have a general anaesthetic routinely?

One of the advantages of islet cell transplantation is that it is a fairly minor surgical procedure with small risks associated with it. A general anaesthetic involves additional risks, which are best avoided. Some patients may prefer to have a general anaesthetic (and be put to sleep) for the duration of the transplant, and sometimes this may be recommended to you by your medical team. This will be discussed with you before you are placed on the transplant waiting list.

4.3.2 When is a larger operation and a general anaesthetic necessary?

There are two situations when you may be offered a general anaesthetic routinely:

- In about 5 out of every 100 people who receive an islet cell transplant, it is impossible for the radiologist to insert a tube into the portal vein. If this happens, then you will be offered an operation on the tummy. Your surgeons will aim to locate a vein on the surface of your bowel, and inject the islets into this vein, which is connected to the portal vein. The consent that you will give before you are sedated will cover this possibility, just in case it is necessary to go ahead with this larger procedure. If you find that it is very uncomfortable for you to have the islets given under a local anaesthetic, then a general anaesthetic will be offered if this can be arranged immediately.

4.3.3 Are there additional risks not listed in Table 1?

Islet cell transplantation is generally considered to be a low-risk medical procedure, but there are several additional complications not listed in Table 1, as follows:

- a) **Pain:** Tummy pain is common, and some pain should be expected. It is usually mild, but it can be severe and require strong painkillers, such as morphine. This pain would be expected to resolve a few hours after the islet cell transplant.
- b) **Bleeding:** You will be given a medication called heparin to thin your blood. This is given to protect you from developing a clot in the portal vein where the islets are given. The heparin is given with the islets and later as a drip or by subcutaneous injections. Bleeding inside the tummy, and sometimes from the skin where the islet infusion needle goes in, occurs in approximately 1 in 10 people. Bleeding or bruising is usually minor and stops without treatment. However, it can be more severe, and occasionally requires an operation on the tummy to stop it.
- c) **Clots (thrombosis):** Clots in the portal vein occur in approximately 1 in 20 people. These have not been known to cause any important problems, and they are usually prevented and treated with a blood thinning medicine (heparin, as described above). A clot affecting the whole of the portal vein is a potentially life-threatening complication but this has not been seen in any patient treated worldwide (more than 1,000 people).
- d) **Damage to other organs:** A small number of people (less than 1 in 50) have experienced damage to the gall bladder, liver or other parts of the tummy as a result of an islet cell transplant and this may require a surgical operation under general anaesthetic to fix.
- e) **Infection:** This can occur as a result of the islet cell transplant procedure, but is usually mild and can be treated easily with antibiotics.
- f) **Abnormal changes in liver blood tests:** These develop in nearly half the people treated with an islet cell transplant, but this does not usually cause important symptoms or any long-term harm.

4.3.4 What are the other risks?

The main risks associated with an islet cell transplant relate to rejection of the islet cells by your body's immune system, and the potential risks of anti-rejection therapy:

- a) **Rejection:** This means that your new islets stop producing insulin. Although this can occur at any time after your transplant, complete failure of the islets is uncommon. For example, five years after an islet cell transplant, about 7 out of every 10 transplant patients will continue to benefit from their transplant, with fewer severe hypos, better control of blood glucose and better quality of life.
- b) **Side-effects of anti-rejection drugs:** This medication can cause a range of side-effects, which include worsening of your kidney function (occasionally severe), mouth ulcers, nausea, diarrhoea, constipation, acne, joint aches, hand shaking and ankle swelling. Some of these side-effects can be severe enough to warrant a change in therapy, but this occurs in less than 1 in 20 people treated. These drugs can also cause elevation in blood fats (cholesterol) and blood pressure, but these changes can usually be addressed by prescribing additional medication. Further details are given at the end of this document.
- c) **Infection:** The anti-rejection medication increases the risk of infection. It is difficult to put figures on the risk of infection. However, severe infections such as pneumonia occur in approximately 3 out of every 100 people treated. Most infections can be treated and the risk of dying or having serious long-term complications because of infection is probably less than 2 people in every 100 treated over six years with immunosuppressant medication. Some of these are discussed in the next section.
- d) **Cancer:** The anti-rejection drugs used in islet cell transplantation increase the risk of some cancers. The likelihood of developing a serious cancer with anti-rejection drugs is difficult to work out from the small number of people around the world who have received an islet cell transplant. Therefore, we have to work out the risk of developing cancer from the large number of kidney transplant patients who have received the same type of medication. We assume that the risk of cancer in people receiving islet cell transplants and kidney transplants will be similar.
- i) **Overall risk of cancer (except skin cancer):** Over six years, approximately 4 out of every 100 people receiving anti-rejection drugs for islet cell transplantation are likely to develop cancer **as a direct result of the therapy**. A larger number of people would be expected to develop cancer even if they had not received this medication. Most of these cancers are likely to be treatable, but sadly, some of these will be fatal. These figures exclude skin cancer, which is more common (see below). The fact that you will be monitored closely after your transplant will mean that most cancers, if they develop, will be picked up at an early and potentially treatable stage.
 - ii) **Skin cancer:** Over six years, approximately 8 out of every 100 islet cell transplant patients treated are likely to develop skin cancer. Almost all of these cancers will be treatable and they are unlikely to be fatal. Less than 2 out of every 1000 people treated with anti-rejection drugs will develop the most serious skin cancer - melanoma. The risk of skin cancer can be reduced by having regular skin examinations (arranged routinely for all patients), by using the highest factor sun-block and by covering up in the sun. You will be encouraged to examine your skin on a monthly basis and let your medical team know about any changes, or unusual lumps or bumps.
 - iii) **Please note:** Women are advised to have cervical screening (a 'smear') once a year, as the risk of cervical cancer is higher after a transplant. Cervical

cancers may not be serious if they are picked up early. Women are also advised to have ultrasound scans of their ovaries after a transplant, as they may also be at higher risk of developing ovarian cysts if taking the anti-rejection drug *Sirolimus*.

- iv) If you would like to know more about cancer and anti-rejection medication, you may like to read the following medical articles which are available on the internet or through your medical team:

[Engels EA et al.](#) (2011) Journal of the American Medical Association. 306(17): 1891-1901

[Kasiske BL et al.](#) (2004) American Journal of Transplantation. 4(6): 905-913

4.3.5 How can I prevent infection, and how might I know that I have an infection?

In general, the risk of infection as a result of anti-rejection medication can be reduced by taking simple precautions, such as washing your hands, avoiding people with infections, avoiding eating out in places with poor kitchen hygiene, and practising safe sex.

The islet cell transplant team will encourage you to remain as fit and healthy as possible, take light to moderate exercise, eat healthily, have regular dental check-ups and take good care of your teeth. They will also recommend an annual flu jab and encourage people who smoke to quit. These precautions will help to minimise the risk of infection and help your body to fight any infections that do occur.

Transplant patients who develop the symptoms of infection should contact their transplant team at an early stage. These symptoms include:

- High temperature, chills and shivering
- Pain, swelling, redness or heat in any area of the body
- Excessive tiredness with aching muscles or joints
- Vomiting or diarrhoea
- Pain when passing urine or passing urine frequently
- Coughing up green phlegm
- Cold sores

If you develop an infection that causes you to be unable to take or absorb your anti-rejection drugs (e.g. if you develop vomiting or diarrhoea), you should contact your transplant team immediately.

4.3.6 What specific types of infections are common?

There are several infections that are commonly seen in people who have had a transplant:

- a) **Thrush:** This is caused by a fungal infection, and commonly affects the mouth, and less often the chest or urinary system. In the mouth, thrush can cause discomfort or difficulty swallowing and a white film may be seen on the tongue and in the throat. In women, thrush can cause vaginal discharge and itching. It is important that you let your medical team know if you think you might have this infection. Thrush can be treated with medication.

- b) **Cytomegalovirus (CMV):** Most adults have been exposed to this virus when they were younger, but when people receive drugs that suppress the immune system the virus can sometimes become active. Symptoms of CMV infection are tiredness, fever, sweating (especially at night), aching joints and headaches. If you develop these symptoms, particularly in the first few weeks after an islet cell transplant, you should inform your medical team because you may need to be admitted to hospital for treatment.
- c) **Cold sores (herpes virus):** Like cytomegalovirus, most adults have been exposed to the herpes virus, and it can become active when people have a transplant. If you develop painful blisters in the mouth or in the genital area then you should inform your medical team. The virus can be treated (but not cured) by medical therapy.
- d) **Shingles (herpes zoster):** If you develop a rash or small water blisters on the side of your face, chest or tummy, please call your medical team so that you can receive treatment as soon as possible.
- e) **Chickenpox:** If you have not previously had this infection in childhood, and you are exposed to someone with chickenpox or shingles, you need to contact your medical team immediately. You may require treatment to prevent you from becoming unwell.
- f) **Pneumocystis:** This infection can cause a chest infection or pneumonia. Please contact your medical team if you have a cold or flu like symptoms that do not go away, or if you become breathless for no obvious reason. This infection can be treated with antibiotics.

4.4 What happens after the procedure?

After the transplant, you will be transferred back to the transplant ward where you will be closely monitored. This will include hourly checks of your blood glucose, and checks for signs of bleeding. Your blood glucose will be controlled via the drip in your arm that will provide insulin and glucose and aim to keep your blood glucose levels as close to normal as possible. You will be treated with medicine to thin the blood, and this will require blood tests to be done approximately every four hours until this medication is stopped (usually within 48 hours of the transplant procedure). You will be able to eat and drink after about four hours, which will be covered by doses of short-acting insulin as usual.

The day after your transplant, you will have an ultrasound scan of your liver to check for any signs of bleeding or clots within the portal vein. You will have additional blood tests on a daily basis to monitor your kidney, liver, blood and the levels of anti-rejection drugs in your system.

After your transplant you will stay in hospital for about three days, but may need to stay longer if you experience any of the problems described above.

During your hospital stay, you will be seen frequently by members of the islet cell transplant team, and by the pharmacist, who will help to explain the details of your medication including the important anti-rejection drugs.

4.4.1 Will I continue taking insulin?

It may take 6 to 12 weeks before the transplanted islets work properly, and it is likely that you will make no major changes to your usual insulin doses when you leave hospital after an

islet cell transplant. However, some transplant patients start to see a reduction in their insulin requirement 2-3 weeks after the procedure. You will be asked to monitor your blood glucose seven times a day, and to keep in close contact with your medical team. We would expect your insulin requirement to come down by **one quarter** or **one half** during the first three months after the first transplant.

After your first islet cell transplant we would **not** expect you to stop taking insulin. However, after your second transplant it is possible that you may be able to stop taking insulin and stay off it for a few months. However, most islet cell transplant patients continue to take a small amount of insulin - usually about half the dose that they were taking before their first transplant. After five years, we would expect no more than one in every ten transplant patients to remain off insulin. Taking a small dose of insulin after an islet cell transplant may be beneficial to the transplant and extend the length of time that it continues to work.

4.5 What medications will I need?

4.5.1 Tips for managing your medications

People who receive islet cell transplants are required to take many different tablets and this may seem very confusing. Your transplant team and the transplant pharmacist will be ready to help you, and the information provided here should help too. When you leave hospital, you should aim to have a good understanding of your medication. The following are some general suggestions that may help you.

- You should get to know:
 - the **name** of each medication and **the reason you are taking it**
 - **what time of the day** to take each medication
 - **how long** to take each medication
 - the **main side-effects** of each medication
 - what to do if you forget to take a dose
- Make sure that you **never run out** of your medications, because missing doses of your anti-rejection therapy could cause you to lose your transplant through rejection. Make sure that you always have at least a **two week supply** of medication prescribed by your transplant team or by your family doctor.
- Keep an **up-to-date list** of your medication and bring this with you to every clinic appointment.
- **Store your medicines safely.** Most medicines are packaged to protect them from moisture and light. So keep your medicines in the original container, and only remove them when you are about to take them. Medicines should be stored in a cool dry place and out of direct sunlight. Keep them out of the reach of children, in a locked cupboard if necessary.
- Develop a good relationship with your pharmacist and let them know when you have had a transplant. They will be able to advise you on what **over-the-counter medications** are safe for you. In general, simple painkillers such as paracetamol and simple cough mixtures are safe. Before you start any new medication you need to discuss how safe this will be for you with your pharmacist or transplant team. Some

medication cannot be taken safely with your anti-rejection therapy. This also applies to herbal, flower or Chinese remedies. Please discuss this with your pharmacist if necessary.

4.5.2 What drugs will I take when I leave hospital?

The medications given to individual patients will vary according to the transplant centre, and therefore only the commonly used medications are discussed here. If you are prescribed drugs that are not listed here, please ask your transplant team for further information.

The medications that you will take after an islet cell transplant can be split into three main types:

- **Anti-rejection medications (or immunosuppressants):** These will be the most important of your new medications and will help your body to accept the transplanted islet cells. They will have to be taken **for as long as your transplant is working** (which could be for the rest of your life). It is vital that you take your medication exactly as recommended, or you could put your transplant at risk.
- **Preventative medications:** These help to prevent the side-effects of anti-rejection medication. These are generally prescribed to prevent infection and are usually taken for 3 to 6 months after your transplant.
- **Other medicines:** These are likely to include insulin, blood pressure and cholesterol-lowering medication.

4.5.3 Anti-rejection drugs - general information

The immune system is your body's natural defence mechanism. It is there to find and destroy anything that is 'foreign' in your body, including the germs that cause infection. Your transplant will be seen as 'foreign' by your immune system, and to prevent it from attacking your transplant, you will be prescribed anti-rejection medications (also known as immunosuppressants). These **dampen down** your immune system just enough to prevent your body from rejecting the transplanted islet cells, but keep it active enough to fight infections.

It is important that you know **which brand** of anti-rejection medications you are taking. If your medications look different from your previous prescription, always check with your transplant team before taking them.

The doses of these medications will need to be finely tuned. Too little may lead to rejection, and too much may lead to side-effects. In the first few weeks after your transplant, the risk of rejection is higher, so the doses of anti-rejection therapy need to be higher than in later months. The results of regular blood tests will guide your medical team regarding your ideal doses of these medications.

Some people experience side-effects as a result of these medications. If you think you may be experiencing side-effects **do not stop taking any of these medications** and contact your transplant team immediately, as there may be a simple solution. Side-effects should improve over time as the dose of your tablets is reduced after the first few months.

For women only: if you become pregnant, treatment with some of these drugs may increase the risk of your baby having a **birth defect**. If you are thinking about having children, then you are strongly advised to discuss the risks with your medical team.

For men only: there is a small risk that your medication could cause a birth defect in any children that you father. If you are thinking about having children, then you are strongly advised to discuss the risks with your medical team.

4.5.4 Which anti-rejection drugs will I be given?

Immediately before your transplant you will be given an anti-rejection drug that works quickly. The drugs in this class (**induction agents**) include *Alemtuzumab*, *ATG* and *Basiliximab*. It is usual for only one or two doses of one of these drugs to be given to each patient undergoing a transplant.

In the first few days after your transplant, you will start taking long-term (**or maintenance**) anti-rejection medication. It is usual to take two of these drugs together and the most commonly used combination is *Tacrolimus* and *Mycophenolate*. Another drug in this class is *Sirolimus*, which is sometimes used in combination with one of the others.

The appendix **at the end of this guide** gives detailed information about the commonly used drugs. You should read all of this information so that you are aware of the potential side-effects of taking these drugs. If you have questions or require further information, please speak to your transplant team.

4.6 After your transplant

4.6.1 What information can I expect when I leave hospital?

When you leave hospital your medical team will inform your GP by phone and letter, and provide you with written information about:

- Your insulin regimen
- Your medication card, including your anti-rejection drugs
- Your clinic appointments
- Food safety
- Advice about vaccination and travel
- Contact numbers and follow up visits

4.6.2 How often will I need to attend the clinic?

Your medical team will need to see you very often for the first few weeks after your transplant, which can be very demanding for some people. These visits are needed because your medication doses, including your insulin doses, will need to be changed frequently in the early stages. The following timetable should give you an idea of how often you will need to be seen, but this will vary depending on individual circumstances.

- Weeks 1 – 2: three times a week
- Weeks 3 – 6: twice a week
- Weeks 7 – 18: once every two weeks
- Weeks 19 – 52: once a month
- After the first year: once every three months

Visits are likely to take between 30-90 minutes, including blood testing. Please talk with your team about local parking arrangements and help towards travelling expenses and the cost of parking.

On days when you are scheduled to attend the transplant clinic, do not take your *Tacrolimus* or *Sirolimus* tablets until after your blood tests have been taken in the clinic. It will be helpful to take your tablets with you to the clinic, so that you can take them as soon as your blood has been tested.

4.6.3 How often will I need to check my blood glucose?

High blood glucose levels could harm the transplanted islet cells, and so your transplant team will work with you to keep your glucose levels as close to normal as possible after your transplant. To help you achieve this, they will ask you to check your blood glucose levels seven times a day (before every meal, two hours after your meals and also at bedtime) for the first few weeks after your transplant. After several weeks, the number of blood glucose checks per day can be reduced as your glucose levels improve, and your insulin dose is reduced. The islet cell transplant team will also ask you to keep a written record of your blood glucose levels and your insulin doses, and you should take this record with you to every clinic visit.

4.6.4 How will I know if my transplant is working?

One to two months after your transplant, the islet cells should start to produce insulin, your blood glucose levels should improve and you should be able to reduce your insulin doses. Until this happens, it can be difficult to be sure that your transplant is working.

Your medical team will check your blood and possibly your urine to find out how much insulin your transplant is producing. Another way that they can find this out is by giving you a test meal (like a milk shake) and then measuring the amount of insulin produced in your blood. This so-called 'meal tolerance test' is performed routinely after one month, and again every three months after your transplant. However, it is unusual to get the results of these tests immediately, so it might be a few weeks before the transplant team can be sure that your transplant is working.

Only a small proportion of people (less than 1 in 20) find that their transplant does not work at all after three months. If this happens to you, your medical team will discuss with you whether or not you should continue taking your anti-rejection medication.

If it becomes clear that your transplant has failed, this may be because your body has rejected it. Fortunately, this does not happen very often, but you need to be aware that this can happen at any time, even if you take your anti-rejection tablets regularly.

4.6.5 What can I do to prevent rejection?

The best way to prevent your body from rejecting the transplanted islet cells is to:

- Take your anti-rejection medication as prescribed
- Attend all of your follow-up visits at the hospital so that your medical team can give you the best possible care.
- You can also look after the transplanted islets by keeping your blood glucose levels as close to normal as possible by eating sensibly and by taking insulin as advised by your medical team.

It is important that you do what you can to prevent transplant rejection, but you should not be overly concerned if your body does reject the transplanted islets, or if your transplant fails for other reasons. Transplant rejection is unlikely to be the result of anything you did or did not do.

4.6.6 How long will I be off work?

In the weeks after your transplant, you will need to attend the outpatient clinic very frequently (see section 4.6.2). Therefore, even if all goes very well, it will not be practical for you to return to work until two months after your transplant. Most transplant patients will be off work for about two to three months. You will be given a medical certificate to pass on to your employer if you need one.

4.6.8 When will I be called in for my second transplant?

The timing of a second islet cell transplant will vary quite a bit between individuals. Some people are offered a second transplant within three months of the first, while others may have to wait for more than a year. This is because of the limited number of organs donated for transplant in the UK.

If your first transplant is very successful, you may be advised to delay having a second transplant until there are signs that this is required. These include whether you are able to control your blood glucose levels (and avoid hypos), your insulin requirement and the results of your blood and urine tests. A small number of transplant patients never need a second transplant.

4.6.9 How long will my transplants work?

Currently, at least half of islet cell transplants work for six years or longer. Some transplant patients continue to benefit from transplants given more than 10 years ago. The long-term results of islet cell transplantation continue to improve as anti-rejection medications and the ways that donated islets are prepared get better.

4.6.10 What happens if my transplant fails?

Five years after receiving an islet cell transplant three out of ten transplant patients will no longer benefit from their transplant. If your islet cell transplant does fail, your blood glucose levels and insulin requirements will return to pre-transplant levels, as will your risk of severe hypos. Transplant loss will be confirmed by your medical team using blood and urine tests and your anti-rejection medication will be stopped unless another transplant is planned. Unfortunately, it is not possible to work out in advance which transplant patients will gain long-term benefit from their transplant, and which will lose their transplant soon after it is given.

4.6.11 If my transplant fails, can I have another?

Most islet cell transplant patients in the UK will have two transplants, but if these fail they will not normally be offered another because third and fourth transplants do not tend to work well for reasons that are still unclear.

4.7 Will I be involved in research?

The islet cell transplant procedure has been researched thoroughly, is safe and is now part of routine NHS care. However, there are several ongoing research projects that you may be invited to take part in. The main purpose of these projects is to improve the care that you and future islet cell transplant patients will receive. Although your islet cell transplant team would be interested to involve you in these projects, you should not feel obliged to take part and not taking part will not affect the care you receive or the speed with which you receive a transplant.

5. FURTHER INFORMATION

If you would like additional information, the following websites may be of some interest:

- [Information on islet cell transplantation from the U.K.'s National Institute for Health and Clinical Excellence \(NICE\)](#)
- [Information on islet cell transplantation from Edmonton in Canada where the current procedure was developed](#)
- [Information on islet cell transplantation from the American National Institutes of Health](#)
- [Information on the outcome after islet cell transplantation from the International Collaborative Islet Transplant Registry](#)
- [Information on insulin pumps from Diabetes UK](#)
- [Information on insulin pumps from INPUT \(with other useful links\)](#)
- [NHS information on insulin pumps](#)
- [Information and free advice on legal matters relating to chronic health problems](#) (or phone 0845 3454345)
- [Facts and figures on transplantation in the UK](#)
- [Information on finding a local NHS dentist](#) or contact NHS Direct on 0845 4647

APPENDIX 1: DETAILS OF MEDICATION USUALLY TAKEN BY ISLET CELL TRANSPLANT PATIENTS

First immunosuppressant drugs given

Only one of the three drugs listed here will be offered to you

1. Alemtuzumab (Campath®)

What is Alemtuzumab?

Alemtuzumab is an antibody that will help prevent your body rejecting your islet cell transplant by reducing the number of white blood cells in your blood.

Why is it used, and how is it given?

Alemtuzumab works quickly to suppress your immune system. It is given a few hours before you receive your islet cell transplant, usually as a single injection under your skin. Your medical team may decide to give you a second dose approximately 24 hours after your islet cell transplant.

What are the side-effects of Alemtuzumab?

Alemtuzumab does not normally cause side-effects when it is first given. However, in less than 1 in 100 people treated, allergic reactions can occur. This can be a serious side effect, causing skin swelling (hives); difficulty breathing; swelling of the face, lips, tongue, or throat; and (very rarely) serious heart problems including death.

Less severe side-effects at the time of the injection include feeling dizzy, hot or cold, nauseated, light-headed, sweaty, itchy, or having a fast heartbeat, or chest tightness.

Approximately 12 hours after receiving Alemtuzumab, it is quite common to experience flu-like symptoms, such as feeling generally unwell, fever, chills, body aches and light-headedness. These symptoms usually settle after a few hours and can be relieved with paracetamol.

More serious side-effects of Alemtuzumab that occur later include developing viral illnesses such as cytomegalovirus (CMV), and an increased chance of conditions such as anaemia or an overactive thyroid gland. You will be monitored for these conditions. In general, they are treatable but very occasionally they can be severe and life-threatening. Like other drugs used to suppress the immune system, Alemtuzumab may also increase your risk of cancer and other severe infections (as explained in section 4.3.4).

Is there anything else I should know?

Alemtuzumab is not currently licensed in the UK for people receiving an islet cell transplant; though it is licensed for other conditions, and it is commonly used in most transplant centres (in the UK, USA and Europe). Your transplant centre has approved its use through its official committees having carefully reviewed evidence in the medical literature. Your medical team will be required to secure your agreement to receive Alemtuzumab and document this in your medical notes.

2. Antithymocyte Globulin (ATG)

What is Antithymocyte Globulin (ATG)?

This is an antibody-based drug that helps prevent rejection by reducing the number of white cells in the blood.

Why is it used, and how has it given?

ATG is given intravenously through a drip put in your upper chest or neck. One or two doses are given each day over several hours for five days.

What are the risks of Antithymocyte Globulin?

When the drug is first given it often causes flu-like symptoms, such as feeling generally unwell, fever, chills, headache and muscle aches. Occasionally it can cause severe allergic reactions that can be life-threatening.

Like other drugs that are used to prevent rejection, it can increase the risk of severe infections and cancer. It can also increase the risk of bleeding and anaemia.

3. Basiliximab (Simulect®)

What is Basiliximab?

This is an anti-rejection drug.

How is Basiliximab given?

The drug is given intravenously as a drip immediately before your transplant and then usually repeated a few days after.

What are the risks of Basiliximab?

This is generally a safe drug, but it can cause constipation, stomach upset, headache or swelling of the feet and hands.

Second immunosuppressant drugs given

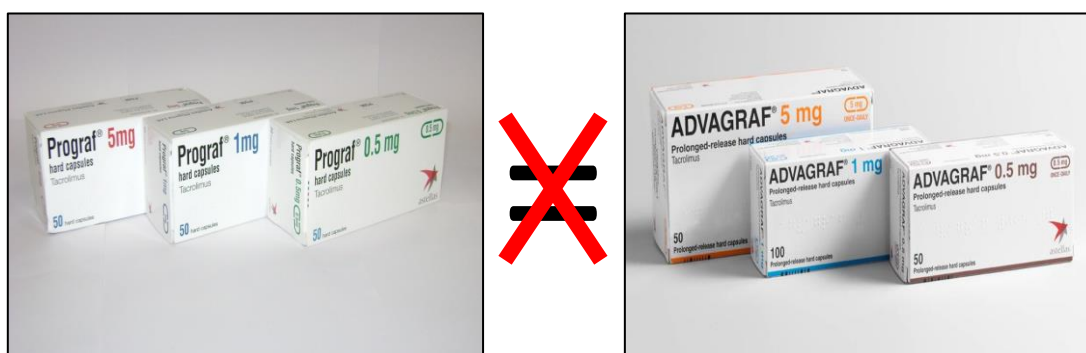
Usually two of the drugs listed here will be offered to you

1. Tacrolimus (Prograf® or Advagraf®)

Prograf® (also called **standard release tacrolimus**) is the most commonly used brand. It is available in three different strengths: 0.5mg capsule (yellow), 1mg capsule (white), 5mg capsule (greyish-red).

Advagraf® (also called **Tacrolimus MR**) is occasionally used and is available in three different strengths: 0.5mg capsule (yellow), 1mg capsule (white), 5mg capsule (greyish-red).

These brands are not the same, and you should not change brand unless you have detailed advice to do this from your transplant team.



It is important that you check your prescriptions and supplies carefully to make sure you have the correct product. If in doubt contact your transplant team.

Tacrolimus may be used alone or in combination with azathioprine, mycophenolate or prednisolone. Tacrolimus is never used with ciclosporin.

When do I take Tacrolimus?

Prograf® is taken twice daily allowing around 12 hours between each dose.

Advagraf® is taken once daily half an hour before your breakfast in the morning.

Both Prograf® and Advagraf® are taken on an empty stomach (one hour before or two hours after food). If you forget to take a dose or take an extra one by mistake, tell your medical team when you come to clinic as this may affect how your blood tests are interpreted.

How is the dose of Tacrolimus decided?

The amount of Tacrolimus in your blood is important because too little Tacrolimus can lead to rejection and too much Tacrolimus can also be harmful to your islet cell transplant and to your kidneys. Blood levels need to be checked on a regular basis so your medical team can decide what dose of Tacrolimus is right for you. On the day you attend the transplant clinic, do not take a dose of Tacrolimus at home **but bring it with you**. Once you have had your blood test taken you can take your usual dose of Tacrolimus.

What are the side-effects of Tacrolimus?

Tacrolimus is an effective drug but can cause side-effects in some people, for example: trembling, 'pins and needles' in the arms or legs, blurred vision, headache, indigestion and feeling sick. You need to inform your medical team if you experience any of these symptoms. Tacrolimus may also cause high blood pressure or high blood glucose but these can usually be managed by reducing the dose or by using other medication (though only on the advice of your medical team).

What do I do if I forget a dose or take too much?

If you forget to take a dose, take it as soon as you remember. If it is almost time for your next dose, miss out the forgotten dose and continue as normal and inform your transplant team. If you accidentally take a larger dose than recommended, inform your medical team straight away.

Can I take other medicines with Tacrolimus?

Some other medicines can affect the amount of Tacrolimus in the blood. Examples of some medicines that do this include: Aspirin and products containing Aspirin for pain relief (low-dose aspirin for the blood is safe), Ibuprofen (also known as ibuprofen) and products containing this drug such as Advil and Nurofen, anti-migraine preparations such as Migril and Cafergot, Cimetidine (also called Tagamet), Erythromycin, Clarithromycin, Fluconazole and Rifampicin. This is not a full list so be sure to check with your medical team or pharmacist before taking other medicines alongside Tacrolimus, including herbal remedies.

Can I drink grapefruit juice with Tacrolimus?

Grapefruit juice can affect the level of Tacrolimus in your blood and therefore this is best avoided especially within three hours of taking your Tacrolimus medication.

2. Mycophenolate

Mycophenolate is an immunosuppressant and is available as two different brands, so it is important that you know which brand you are taking:

1. **Mycophenolate Mofetil (Cellcept®)** is available in two strengths: 250mg capsules (blue/brown) and 500mg tablets (lavender). Cellcept is the brand of choice in most transplant units.
2. **Mycophenolate sodium (Myfortic®)** is available in two strengths: 180mg tablets (lime-green) and 360mg tablets (pale-orange). Myfortic is usually prescribed for people who experience side-effects with Cellcept.

Both of the brands above are as effective as each other so **do not worry** if your medical team suggests switching brands. Mycophenolate is usually used together with tacrolimus or ciclosporin with or without prednisolone. Mycophenolate is never used with azathioprine. Mycophenolate should not be taken at the same time of day as indigestion remedies as these may reduce the effectiveness of mycophenolate.

When do I take mycophenolate?

Mycophenolate is taken twice daily allowing around 12 hours between each dose. If you suffer side-effects such as stomach upset or diarrhoea your medical team may advise you to

split the dose so you take it three or four times daily. If this is the case, you should take each dose evenly spaced throughout the day, for example: morning, midday, evening (tea-time) and night-time. Tablets and capsules should be swallowed whole with a glass of water.

How is the dose of mycophenolate decided?

You will usually start mycophenolate with the brand Cellcept at a dose of 1g twice daily though this may be reduced if you experience side-effects. If you are started on the similar drug called Myfortic, your starting dose will be 720mg twice daily.

What are the side-effects of mycophenolate?

Mycophenolate may cause side-effects in some people including bloating, heartburn, diarrhoea, and feeling sick. Less commonly mycophenolate can cause a low white blood cell count which can increase your risk of infection. Your medical team will monitor your blood tests closely and if your white blood cell count drops your medical team will reduce your dose or stop the drug.

What should I do if I miss a dose?

If you forget a dose, take it as soon as you remember. If it is almost time for your next dose, miss out the forgotten dose and continue as normal. Please inform your medical team at your next clinic appointment if you miss a dose or accidentally take a larger dose than prescribed.

Can I take other medicines with mycophenolate?

You should not take antacids for heartburn or indigestion (such as Milk of Magnesia) at the same time of day as mycophenolate, as this may reduce its effectiveness.

3. Sirolimus (Rapamune®)

Sirolimus is available in two strengths: 1mg tablets (white triangle) and 2mg tablets (white/beige triangle). Sirolimus can be used in combination with Tacrolimus or Mycophenolate.

When do I take Sirolimus?

Sirolimus is taken once daily in 30 to 60 minutes before food with a glass of water.

How is the dose of Sirolimus decided?

The dose of sirolimus is adjusted according to the amount in your blood. On the day that you attend the transplant clinic do not take a dose of sirolimus at home, but **bring a dose with you**. Once you've had your blood test taken, you can take your usual dose of sirolimus.

What are the side-effects of Sirolimus?

Sirolimus can cause diarrhoea, stomach cramps, feeling sick, sore mouth, mouth ulcers and increased cholesterol levels. If you experience any side-effects, please contact your transplant team before you make any change to your medication.

Can I take other medicines with Sirolimus?

Some other medicines can affect the amount of sirolimus in the blood. For example: rifampicin, erythromycin and fluconazole. You should also avoid ibuprofen, some antihistamines and some medicines used for heart problems, including diltiazem. Always check with your medical team or pharmacist before taking other medicines, including those that can be bought over the counter and herbal remedies.

Can I drink grapefruit juice with Sirolimus?

Grapefruit juice can affect the level of Sirolimus in your blood and therefore this is best avoided especially within three hours of taking your Sirolimus medication.

Preventative medication

Usually all of these will be offered to you:

Anti-rejection tablets are essential in protecting your new transplant from rejection, but they do have side-effects, some of which can be prevented by other medication. Following your transplant, you are likely to be prescribed the following:

1. Co-trimoxazole (Septrin® or Bactrim®)

This antibiotic is given for six months to prevent urine and chest infections, and in particular, a chest infection known as Pneumocystis (see 4.3.6 above). The usual dose is 480mg (one tablet) taken once daily (sometimes just three times per week) and preferably before bedtime.

What are the side-effects of co-trimoxazole?

This drug can cause nausea, diarrhoea and sensitivity (rash) to sunlight. Very rarely, it can cause a drop in the white blood cell levels, and if this happens, your medical team may reduce or stop this medicine. Some people are allergic to this drug and are prescribed an alternative called dapsone.

What should I do if I miss a dose?

Take it as soon as you remember. However, if it is almost time for your next dose, miss out the forgotten dose and continue as normal. There will be no need to inform your medical team.

2. Valganciclovir (also called Valcyte®)

This drug may be given to prevent infection by cytomegalovirus (CMV). The drug is given for three months if either you or your islet cell donor has had this infection in the past. Many people carry this virus without it ever causing problems. However, in people who receive anti-rejection therapy, the virus can become active. This infection can be serious and can affect your lungs, your tummy and your eyes.

Valganciclovir comes in oval pink tablets, and should be swallowed with a glass of water after food. The dose varies between two tablets daily to as little as one tablet twice per week depending on how well your kidneys are working.

What are the side-effects of Valganciclovir?

This drug can cause stomach upset, diarrhoea, headaches and confusion. Occasionally it can cause a drop in some blood cell levels leading to tiredness, signs of infection or bruising. If this occurs, tell your medical team, who will most likely reduce or stop this medicine.

What are the side-effects of Valganciclovir in relation to pregnancy?

It is important that you **do not become pregnant while taking this drug** because it may damage an unborn baby. Women should use contraception, and men should use a condom while taking the drug and for three months after they stop it.

What should I do if I miss a dose?

If you forget to take a dose, this probably will not cause any problems but please inform your transplant team at your next clinic appointment.

3. Isoniazid and Pyridoxine

If you have had tuberculosis (TB), or have had contact with people that have had TB, then you will be advised to take isoniazid alongside the vitamin, pyridoxine, for six months after your transplant. This will reduce the risk of you developing TB, while taking anti-rejection therapy. Isoniazid is taken in a dose of 300mg once daily. Pyridoxine is taken in a dose of 10mg once daily.

What are the side-effects of Isoniazid and Pyridoxine?

Isoniazid can sometimes cause liver problems, but your medical team will monitor your blood test to detect this early and stop the drug if necessary. Isoniazid can cause numbness or tingling in the hands and feet, which is why you will be given pyridoxine to reduce the likelihood of this occurring.

4. Lansoprazole (Zoton®) and omeprazole (Losec®)

These medicines reduce the production of acid by your stomach. They may be prescribed to prevent or to treat heartburn or stomach ulcers. They are given either once or twice daily and you should preferably take them at around the same time each day.

What are the side-effects of lansoprazole?

These tablets can occasionally cause feelings of sickness, diarrhoea and headaches.

5. Aspirin

Aspirin works by making blood less 'sticky' which helps prevent blood clots. It can help reduce the risk of heart attacks and strokes in people who are at risk.

How should I take aspirin?

Aspirin is taken in a low dose of 75mg once daily. It is best to take this after food, such as after breakfast.

What are the side-effects of aspirin?

Aspirin can cause stomach irritation. Occasionally people can be allergic to it and may develop rashes or wheezing if they have asthma. If you are allergic to aspirin you may be prescribed medicine called clopidogrel instead, which works in a similar way as aspirin.

Other medicines

Medicines for conditions not related to your transplant, such as medicines for epilepsy, gout and high cholesterol, will almost certainly be continued.

Holiday/travel vaccinations

The immunosuppressant drugs you are taking to protect your transplant make it unsafe for you to have some vaccinations. The vaccines you can and cannot have are listed below:

Vaccines which you CAN have include:	Vaccines which you must NOT have are the 'LIVE' vaccines and these include:
<ul style="list-style-type: none"> ▪ Diphtheria ▪ Hepatitis A ▪ Hepatitis B ▪ Immunoglobulins ▪ Influenza ▪ Meningococcus ▪ Pertussis (whooping cough) ▪ Inactivated polio injection ('special order only') ▪ Pneumococcal ▪ Rabies ▪ Tetanus ▪ Typhoid injection ▪ Swine flu 	<ul style="list-style-type: none"> ▪ BCG ▪ Measles, mumps and rubella ▪ Oral polio ▪ Oral typhoid ▪ Yellow fever ▪ Rubella

Frequently asked questions about medication

Why are there lots of names for the same medicine?

Each medication has an approved name and this name will appear on the box it comes in. You may hear other names or abbreviations used for the same medicine, for example, Tacrolimus is sometimes called Prograf (the brand name) or 'tac' (an abbreviation often used by hospital staff). If you are unsure or confused by different names always ask. We encourage all our staff to use the approved names of medicines to avoid confusion.

Will I have to take tablets forever?

Some medicines you take after transplant are needed for only a short time and can be stopped after a few months. Others, including the immunosuppressant medication, must be taken as long as the transplant continues to work (which could be for the rest of your life).

What happens if I forget to take my tablets?

As mentioned above, if you accidentally miss a dose of your medicines, do not worry. For medicines **taken three or four times a day**, miss the dose and take the next dose at the

correct time. For medicines taken **once or twice daily**, if you remember within a few hours, take the dose as usual and take the next dose at the correct time. If, however, it is closer to when the next dose is due, miss the dose and take the next dose at the correct time.

Missing doses of anti-rejection tablets on a regular basis increases the risk that your body will reject the transplanted islet cells. Taking the tablets an hour or two later than normal occasionally will not cause any harm, but it is advisable to stick to a regular routine.

Will I experience all of the listed side-effects?

No. You may experience one or two, but most people experience none of them. Most medicines you receive will come with a detailed information leaflet, including a long list of possible side-effects. Though the list can be concerning for some people, the intention is to inform you, not to discourage you from taking your medicines. Do not alter the dose or stop taking any of your medicines without discussing it with your medical team first, even if you are feeling well. If you have any concerns about side-effects, please discuss them with your medical team or pharmacist.

Can I drink alcohol with my medication?

Alcohol can increase the side-effects of some medications. In general, small amounts of alcohol are okay. The safe limits for alcohol intake are:

- 21 units* per week for men
- 14 units* per week for women

* One unit is the same as half a pint of beer, one small glass of wine or one pub measure of spirits.

It is important that you avoid binge drinking as this may reduce the levels of immunosuppressants in your body and increase the risk of transplant rejection. We suggest that you alternate alcoholic drinks with soft drinks or water to reduce the risk of dehydration.

If I become pregnant, will my medicines affect my baby?

It is not advisable to become pregnant within a year of having a transplant, so it is important to take extra precautions during this time. Some immunosuppressants and other drugs used at the time of a transplant cannot be used during pregnancy, so if you are planning a pregnancy, or you think you may be pregnant, you must let your medical team know so they can ensure that you are on the safest medicines for you and your baby.

APPENDIX 2: PRE-LISTING CONSENT FORM (FOR PATIENTS TO COMPLETE)

This form summarises the risks and benefits of islet cell transplant. **If you choose to be listed**, we will ask you to sign below to confirm that you have understood this summary and the detailed guide.

Risks and benefits of islet cell transplantation

Death due to the operation or procedure	Less than one patient in 100
Operation to open the tummy	Two patients in 100
Recent operation on the tummy	Close to zero
Serious surgical complications including colostomy	Close to zero
When treatment starts to work	After 3-12 weeks
Any infection over six years	17 patients in 100
Life-threatening infection with long-term clinical effects over six years	Two patients in 100
Death due to infection over six years	One patient in 300
Cancer, potentially life-threatening, over six years (except skin cancer)	Four patients in 100
Skin cancer including melanoma (often treatable) over six years	Eight patients in 100
Severe reduction in kidney function due to anti-rejection medication	Sometimes
Freedom from insulin injections at one year	30-70 patients in 100*
Freedom from insulin injections at five years	10-30 patients in 100
Major reduction in severe hypos at 18 months	75-95 patients in 100
Reduced risk of severe hypos at five years	50-70 patients in 100
Improved HbA1c at five years	50-70 patients in 100
Improved diabetes complications	Likely

* Limited information due to small numbers of patients treated in UK at present

Caution: comparisons are provided as a guide only. No randomised controlled trials have been performed to compare these therapies and baseline risk factors may be different and influence outcome.

I have understood this summary and guide, and I have had the opportunity to ask questions and discuss them fully with my medical team:

Name (PRINT) _____ Hospital No. _____

Signed (patient) _____ Date _____

Signed (doctor) _____

Date _____

APPENDIX 3: NEW MEDICATION WARNING (FOR PATIENTS)

Please ask for specialist advice before starting these medicines as they may affect my drug levels and/or put my transplant at risk:

- Clarithromycin, Rifampicin, Erythromycin
- Allopurinol, if I also take Azathioprine
- Rosuvastatin, if I also take Ciclosporin
- More than 10mg daily of Simvastatin or Atorvastatin, if I also take Ciclosporin
- Fluconazole, Amiloride, ACE inhibitors
- Nitrofurantoin, Spironolactone, Trimethoprim
- Verapamil, Oral Contraception, Phenytoin
- Diltiazem, NSAIDs, Carbamazepine

This is not an exhaustive list. Consult the British National Formulary for more drug interactions.

For further advice contact my Transplant Team on:

Or contact Medicines Information on: _____

APPENDIX 4: CURRENT MEDICATION INFORMATION (FOR PATIENTS)

I have had an islet cell transplant

Name: _____ Hospital Number:

- I take the following immunosuppressants [Please tick]:
 - Mycophenolate mofetil (Cellcept)
 - Prograf [Tacrolimus standard release]
 - Advagraf [Tacrolimus modified release]
 - Mycophenolate sodium (Myfortic)
 - Sirolimus
- I must stay on the same brand of immunosuppressants
- I may have kidney impairment so please check my eGFR before prescribing any medicines.

For problems with supply please contact:

Prograf/ Advagraf	Astellas	01784 419 615
Sirolimus	Wyeth	0845 850 5544
Myfortic	Novartis	0845 741 9442
Cellcept	Roche	0800 731 5711