What I tell my patients about pancreas transplantation

Murat Akyol MD FRCS MD Consultant Transplant Surgeon
Transplant Unit
Royal Infirmary of Edinburgh

In the past, pancreas transplantation did not enjoy the same success as other solid organ transplants. However, in the last five or six years, results have improved to match the success rate of other organ transplants, and the number of pancreas transplants performed worldwide has increased rapidly. A range of new procedures has also been introduced, so that diabetic patients now have a choice when considering transplantation.

Standard clinical procedures now include simultaneous pancreas/kidney transplantation; pancreas transplantation alone, early in the course of diabetes; pancreas transplantation after previous kidney transplantation; simultaneous pancreas/live-donor-kidney transplantation; and islet transplantation, with or without a kidney transplant.

What is the pancreas and why is it transplanted?

The pancreas is an organ inside the abdomen that consists of two different types of tissue with two separate functions. Most of the pancreas is a gland that produces a fluid rich in chemicals that help you to digest food. About 2–3% of the pancreas consists of clusters (tiny islands or 'islets') of cells that secrete small amounts of hormones into the bloodstream. The most important of these hormones is insulin. A lack of insulin causes diabetes. Pancreas transplants are performed to treat diabetes.

What is diabetes?

Both types of diabetes have one thing in common: a high level of sugar in the blood. The blood sugar level is normally controlled by insulin, and diabetes occurs when the body is either unable to produce insulin or is unable to respond to it.

Diabetes is a common condition. Nearly 1.5 million people in the UK today are known to be diabetic, and another estimated one million may have diabetes without knowing it.

Insulin-dependent diabetes mellitus (often referred to as IDDM, or type 1 diabetes) tends to occur in children and young adults, and arises because the insulin-producing cells in the pancreas gland are destroyed. Non-insulin-dependent diabetes mellitus (NIDDM, or type 2 diabetes) occurs in middle or old age and is much more common. It occurs because the body becomes resistant to the actions of insulin, and is unable to adequately compensate for this by increasing insulin production from the pancreas.

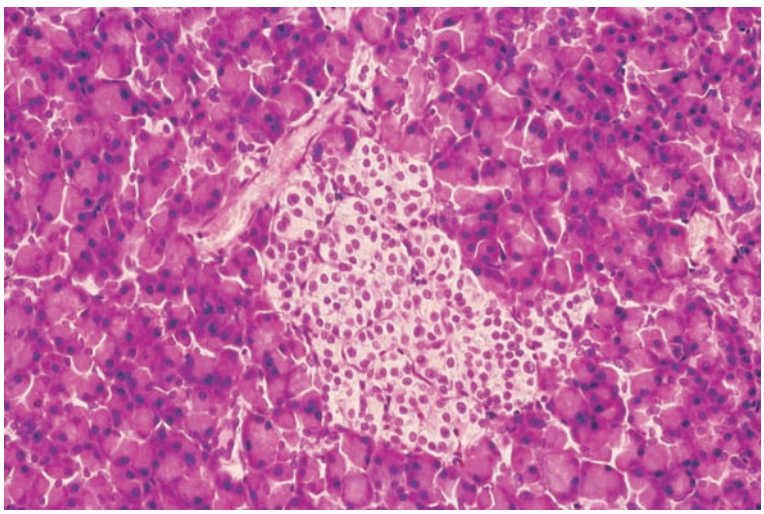
Can all diabetic patients be treated by pancreas transplantation?

No. Pancreas transplantation is only suitable for patients with type 1 diabetes, who lack insulin as a result of destruction of their insulin-producing islets. Such patients can be given new insulin-producing islets by pancreas transplantation.

What does pancreas transplantation offer to a diabetic individual?

Individuals with type 1 diabetes require lifelong treatment with regular injections of insulin (usually several times each day). Pancreas transplantation is the only treatment for diabetes that can restore complete insulin independence and normal blood sugar levels. After a successful pancreas transplantation, patients do not need insulin injections, have no special dietary requirements, do not need to prick themselves regularly to check their blood sugar levels, and are not at risk of developing low blood sugar levels (hypoglycaemia).

It is also known that most of the complications of diabetes – such as blindness due to retinopathy (see later); kidney failure due to nephropathy; and neuropathy, which may cause foot ulcers, digestive problems, abnormalities of heart



BIOPHOTO ASSOCIATES/SCIENCE PHOTO LIBRARY

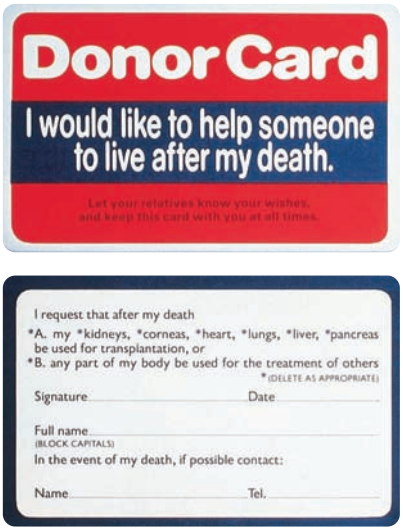
A cross-section through a healthy pancreas showing an islet (centre, pale pink) which secretes insulin into the bloodstream

rhythm, hypoglycaemic unawareness or angiopathy and accelerated atherosclerosis (see later) – are related to blood sugar control. Strict and effective blood sugar control in diabetic patients is associated with a delay in the onset of complications and a reduction in their severity – perhaps even prevention of some complications. There is no better means of blood sugar control than a successful pancreas transplantation. Therefore, pancreas transplantation should also benefit diabetic patients by preventing or alleviating some of the long-term disabling complications of diabetes.

Is a pancreas transplantation guaranteed to prevent diabetic complications?

There is still a degree of uncertainty about this. There has been no controlled clinical trial directly comparing pancreas transplantation with insulin treatment in two similar groups of diabetic patients. We, therefore, rely on indirect evidence rather than scientific proof that the presumed long-term benefits of pancreas transplantation do genuinely exist.

However, there is a large amount of indirect evidence for the influence of successful pancreas transplantation on the long-term complications of diabetes. We can say with a reasonable degree of confidence that a successful pancreas transplantation will prevent, or even reverse, early changes in diabetic kidney disease, so that diabetic patients will not go on to develop end-stage kidney failure and need dialysis.

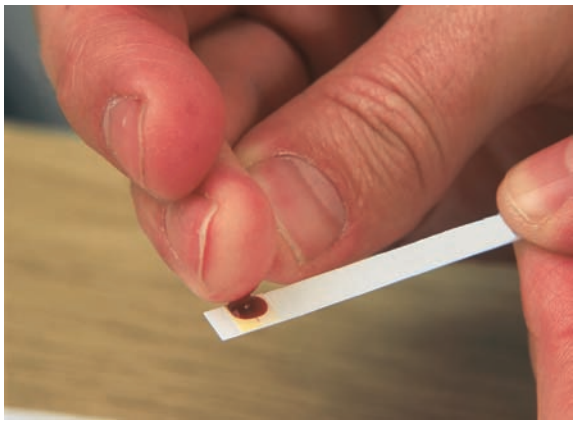


CHRIS PRIEST/SCIENCE PHOTO LIBRARY

If islet transplantations become a reality, there will be a major donor shortage of islets

There is also reasonably strong evidence that a successful pancreas transplantation can prevent or partially reverse diabetic neuropathy. The symptoms of neuropathy – which are multiple and varied and include vomiting, diarrhoea or constipation, tingling and numbness of hands and feet, neuropathic ulcers of the feet, some abnormalities of the heart rhythm and hypoglycaemic unawareness – can be prevented by pancreas transplantation, or, if they already exist, they may be improved.

Retinopathy is also a common complication of diabetes and is a major concern for patients since it can progress to blindness if untreated. The influence of a successful pancreas transplantation on the course of retinopathy is unclear. It is unlikely that pancreas transplantation will change the clinical course of retinopathy during the first two years after transplant. There is even some concern that during this period retinopathy might progress more rapidly. In the longer term, the available evidence suggests that retinopathy does stabilise in patients with pancreas transplants compared with those who remain on insulin. It is likely that five years after transplantation, patients with retinopathy will be better off compared with those who remain on insulin.



SATURN STILLS/SCIENCE PHOTO LIBRARY

After a successful pancreas transplantation, patients no longer need to prick themselves regularly to check their blood sugar levels

Clearly, the amount of benefit that we can expect from a pancreas transplant depends on exactly when the transplant is performed in the course of the disease. For example, retinopathy with blindness, or significant neuropathy and vascular disease (which may have necessitated amputation) are both very advanced and irreversible complications and would not be influenced by pancreas transplantation.

Do diabetic patients receiving pancreas transplants live longer?

They probably do. Almost all studies have shown better long-term survival in diabetic patients who have undergone a pancreas transplantation compared with those who have been treated with insulin. It may be that younger and fitter diabetic patients receive pancreas transplants, whereas older diabetics with other health problems are those who remain on insulin. Better long-term survival rates with pancreas transplantation could, therefore, simply be a reflection of patient selection.

However, more recent studies have suggested that pancreas transplantation does confer a genuine survival advantage to diabetic patients. This is probably due to the influence of pancreas transplantation on long-term diabetic complications. Five years (and certainly ten years) after transplantation, the difference in the survival prospects for patients with transplants is considerably different from those who remain on insulin.

Why don't we offer pancreas transplantation to all patients with type 1 diabetes?

Mainly because it has risks. Lifelong treatment with insulin injections is still safer for most patients with type 1 diabetes. Even if pancreas transplantation could be made much safer, there would be the problem of a shortage of organ donors to provide the number of pancreas transplants needed to meet the demand.

Transplantation of the pancreas involves a major operation. Like all surgical procedures, this puts the patient at risk of complications and even a small chance of death. Recent advances in surgical techniques and medications have greatly improved the safety of the pancreas transplant operation, so that around 97–98% of patients undergoing pancreas transplants will survive. Other complications, such as bleeding and infection, can occur and about one in four patients undergoing a pancreas transplant will require at least one more operation to deal with complications.

Other risks relate to the medication that patients need to use after transplantation. All organ transplants, including pancreas transplants, involve the transfer of foreign tissue to individuals, which is normally rejected by the immune system. It is, therefore, necessary to use medication to suppress the immune system and prevent the rejection of the transplanted organs. These medicines (immunosuppressants) have many potentially serious side-effects, such as an increased risk of infection and even a small increase in the probability of developing cancer.

How successful are pancreas transplants?

The success rate – expressed as the probability of being cured of diabetes (not needing any insulin) one year after the transplant – is around 85%. This is similar to the success rate of other organ transplants such as kidney, liver or heart transplants. In the longer term (beyond one year) patients with pancreas transplants are likely to do at least as well as those with other types of organ transplants.

Recent advances have greatly improved the safety of transplants

Diabetes can also cause kidney failure. Can such patients receive kidney transplants?

Yes. In fact, if a diabetic patient requires a kidney transplant to treat kidney failure, they can also be given a kidney transplant at the same time as a pancreas transplant. This type of double transplant (simultaneous pancreas and

SCIENCE PHOTO LIBRARY

Type 1 diabetes tends to occur in children and young adults and standard treatment requires regular insulin injections for life

kidney transplant) is particularly attractive since patients have already been selected for one transplant and subsequent immunosuppression, and with only minimal additional risk it is possible to treat diabetes as well as treating kidney failure.

Can diabetic patients who do not have kidney failure receive pancreas transplants?

Yes they can, but this will only be appropriate in a small proportion of selected diabetic patients. As discussed above, for most diabetic patients without kidney failure, lifelong treatment with insulin, despite its problems and inconvenience, is still safer than a pancreas transplant. However, a small number of diabetic patients have life-threatening complications of diabetes (for example, hypoglycaemic unawareness). In such patients the benefits of a pancreas transplant outweigh the risks; indeed, a pancreas transplant can be lifesaving.

A small number of patients have received successful islet transplants

Why is the whole pancreas transplanted, when only the insulin-producing islets are needed?

Insulin-producing cells comprise only about 2% of the pancreas gland. If these islets could be separated from the remainder of the pancreas gland they could be transplanted with a very simple procedure like a blood transfusion. This has been attempted for many years without much success for various technical reasons. We are making progress, and only in the past year or so a small number of patients have received successful islet transplants. This avoids the surgical risks of a major operation. However, even then, patients receiving islet transplants require lifelong immunosuppressive medication which has potentially serious side-effects.

Are islet transplants going to replace pancreas transplants in the future?

It is difficult to know. Problems with islet transplantation are complex and have not yet been solved. We are making some progress but, at least for the next decade, the only realistic option to make diabetic patients independent of insulin will still be an organ transplant.

When we eventually overcome the difficulties preventing successful islet transplantation, we will still face a major shortage of islets from organ donors to meet the need of diabetic patients. Genetic manipulation of islet tissue from animal sources may provide the solution to the donor shortage. Advances in genetic engineering and our understanding of the genetic basis of diabetes will also make it possible to develop better treatment, and even prevention, for diabetes in the future ■

Key points

- Diabetes occurs when the body is either unable to produce insulin or is unable to respond to it.
- Diabetes is a common condition. Nearly 1.5 million people in the UK are known to be diabetic, and another one million may have diabetes without knowing it.
- Pancreas transplantation is the only treatment for diabetes that can restore complete insulin independence and normal blood sugar levels.
- If a diabetic patient requires a kidney transplant to treat kidney failure, they can be given a kidney transplant at the same time as a pancreas transplant.
- In the past year or so, a small number of patients have received successful islet transplants, which avoids the surgical risks of a major operation.
- Advances in our understanding of the genetic basis of diabetes will make it possible to develop better treatment, and even prevention, for diabetes.

For further advice about diabetes and membership details for Diabetes UK, contact:

Diabetes UK
10 Parkway
London, NW1M 7AA.
Tel: 020 7424 1000.
Fax: 020 7424 1001.
website: www.diabetes.org.uk

The National Kidney Research Fund
Kings Chambers
Priestgate
Peterborough
PE1 1FG
Telephone helpline: 0845 300 1499.
website: www.nkrf.org.uk

If you would like to receive additional copies of the *What I tell my patients about...* features from this issue, please send your request and mailing address by post to Suzanne Wigley at Hayward Medical Communications, Rosemary House, Lanwades Park, Kentford, Newmarket CB8 7PW.