However, the rejection itself is very mild, unlike acute rejection. What does seem to happen is that the kidney gradually gets scarred, and this is caused by factors such as high blood pressure just as much as by any rejection. For this reason, many transplant doctors do not use the term ‘chronic rejection’ any more, but talk of ‘chronic allograft nephropathy’.

If it happens, it will usually be more than a year after the transplant operation. Doctors may suspect chronic rejection if a patient’s blood creatinine starts to rise slowly after it has been stable for some time. As with acute rejection (see above), the only sure way to diagnose the condition is to do a biopsy.

There is no treatment for chronic rejection that can be guaranteed to be successful, but some patients get an improvement if the anti-rejection drugs are changed. One particular concern is that the anti-rejection drugs cyclosporin and tacrolimus are slightly toxic to the kidney. They are normally so good at preventing rejection that this does not matter, but in chronic rejection they may worsen kidney damage. Therefore, if someone is on one of these drugs and has chronic rejection, either the dose will be markedly reduced, or they will be stopped and an alternative anti-rejection drug started, such as mycophenolate or sirolimus. They may not be as ‘strong’ as cyclosporin or tacrolimus, but are not directly toxic to the kidney.

The level of blood pressure is also thought to be very important in chronic rejection, as high blood pressure can also worsen kidney damage. A blood pressure of 130/80 or below is the ideal target, and may require the use of several different blood pressure drugs.

The severity of chronic rejection varies. Mild chronic rejection is not usually a problem. However, more severe chronic rejection will eventually lead to failure of the kidney (and therefore to restarting dialysis or having another transplant). Chronic rejection may take years to happen but it is much the most common cause of transplant failure after the first year.

Key Points:
- The normal function of the immune system (natural defence)
- Investigation of acute rejection
- Treatment of acute rejection
- Chronic rejection

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The normal function of the immune system (natural defence)

The usual job of the immune system is to fight invaders into the body. These might be germs or bugs, or foreign objects such as splinters. The body recognises these invaders and tries to eliminate them from the body. The blood not only carries oxygen and nutrients to all parts of the body, but also carries the natural defences to where they are needed in the body. The blood contains two main types of defence system. One is white blood cells which stick to germs and kill them. The other type of defence is antibodies which are smaller than the white blood cells and, by sticking onto germs, either make them burst apart or help the white blood cells to stick to them.

The immune system is very powerful, and is very good at recognising what is part of the body and what is not, and leaving alone those normal parts of the body which have a ‘friendly face’. Although blood transfusions can be given without rejection, this is an exception and organs such as kidneys, the liver, the heart and so on are recognised as invaders. Even though these organs may come from the same species (human), everyone (apart from identical twins) is slightly different, and the body can recognise these differences. The damage the immune system does to a kidney transplanted from one person to another is called rejection.

The rejection process

‘Rejection’ means that someone’s body recognises that the transplanted kidney is not ‘its own’ and tries to ‘reject’ it from the body. Even when someone is ‘well matched’ with their transplant kidney (in terms of blood group and tissue type), some degree of rejection is common (approximate risk is 15 out of 100 transplants). The severity of rejection varies from patient to patient. Rejection may be either acute (see below) or chronic (see later). Luckily, there are drugs - called immuno-suppressant drugs - that can help prevent and treat the rejection process.

Acute rejection

‘Acute’ means short-term and of rapid onset, requiring immediate action. Acute rejection can occur in the first few months (particularly the first few weeks) after a transplant. It is common - about 15% of people experience acute rejection in the first three months after a transplant. If acute rejection has not occurred within one year of the operation, then it is unlikely to happen, so long as the anti-rejection drugs are taken regularly. Acute rejection may sometimes cause pain and fever, but usually there are no symptoms. Doctors will suspect that someone has acute rejection if the blood creatinine is either not coming down after a transplant, or if it has started to fall and then remains stable or increases again. However, acute rejection is not the only reason why there may be problems with blood creatinine levels after a transplant and these other possibilities are usually looked for first.

Acute rejection can be caused by white blood cells attacking the kidney (‘cellular’ or ‘T cell mediated rejection’), or it may be caused by antibodies against the kidney. Antibody mediated rejection often requires stronger treatment.

It is not common to loose a kidney from acute rejection it can be treated. If you do not take your anti-rejection medications your risk is 100% and this invariably leads to the loss of the transplant.

Investigation of acute rejection

Tests that might be performed include an ultrasound scan (a sound-wave picture). This will show if the ureter (the tube that takes urine from the kidney to the bladder) is blocked and there is dilation of the kidney. Other tests use specialist scanning techniques called a radio-isotope scan and a Doppler scan. Either of these will show if there are any problems with the blood supply to the new kidney.

The only way to be sure whether a transplant kidney is being rejected is to do a test called a biopsy. For this test, a hollow needle called a biopsy needle is used to remove a very small piece of the new kidney. This piece of kidney is then looked at under a microscope for any signs of rejection. It is common to have two or more biopsies in the weeks after the operation.

Treatment of acute rejection

If the biopsy shows signs of rejection then a high-dose steroid drug called methylprednisolone will be given. This drug is usually given by intravenous injection, once a day for three days. These are called ‘pulses’ of methylprednisolone. Very often, this treatment will suppress the rejection process and the creatinine will start to decrease. Occasionally, someone may need two courses of this drug.

If pulse methylprednisolone does not work, the anti-rejection drugs will be changed to something stronger. The exact changes depend on the severity of rejection and the protocols in different transplant units. If cyclosporin is being used to prevent rejection, it may be changed to tacrolimus (‘Prograf/Adoprt’) and rejection may subside. If someone is already on tacrolimus, but is also taking azathioprine, the azathioprine may be switched to mycophenolate.

Sometimes a five-to-ten-day course of a stronger intravenous drug may be given, such as antithymocyte globulin (ATG). This powerful course of injections has a 90% success rate. There can be a reaction after the first dose with fever, diarrhoea, joint and muscle pain, wheeze, and shortness of breath due to fluid on the lungs (pulmonary oedema). There is a higher risk of infections for several months after a course.

Chronic rejection

‘Chronic’ means long-term and it starts slowly. The immune system may attack and reject the transplant kidney, but in a different way than in acute rejection. Chronic rejection looks like a slow ageing of the new kidney. It is probably started by a very low level of rejection on the kidney, perhaps caused by antibodies against the kidney.