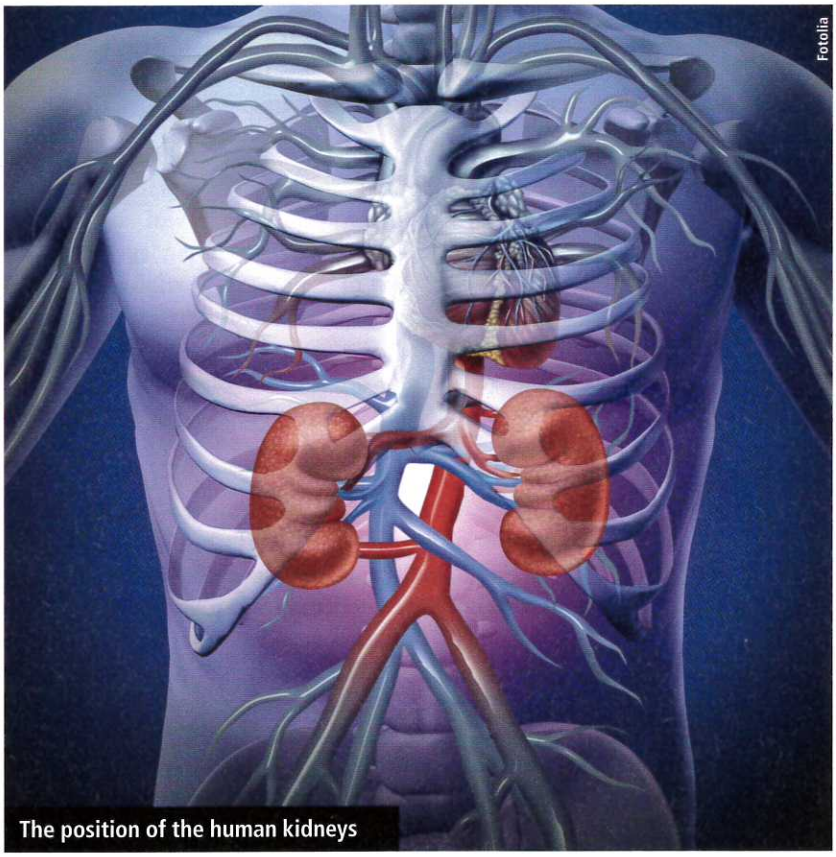
Kidneys

Rachel Lennon

Function, disease and treatment

Rachel Lennon, who researches kidney disease, describes how kidneys work, how their function is affected by disease and how kidney disorders can be treated



The position of the human kidneys

In addition to producing urine, which is the body's way of removing metabolic waste products, our kidneys help to control blood pressure, keep bones healthy and stimulate the production of red blood cells.

Cleaning the blood

Most humans have two kidneys (see Figure 1), which lie on either side of the spine, just below the rib cage. The main job of the kidneys is to clean the blood. This is done by millions of nephrons (see Figure 2), which are located in the outer cortex of the kidney. Each nephron contains a glomerulus (a bundle of capillaries) that allows water and small solutes to filter out but retains large molecules and cells in circulation.

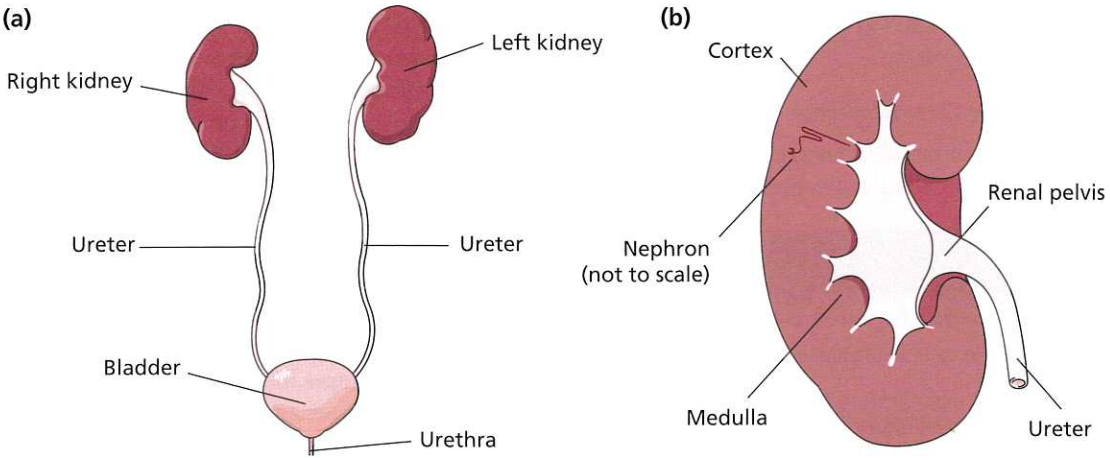


Figure 1 **(a)** Urine is produced by the kidneys and drains from the ureters to the bladder **(b)** Filtration of the blood occurs in the outer cortex of the kidney. The filtering unit of the kidney is the nephron

Key words

Kidney
Nephron
Glomerulus
Filtration
Dialysis
Transplantation

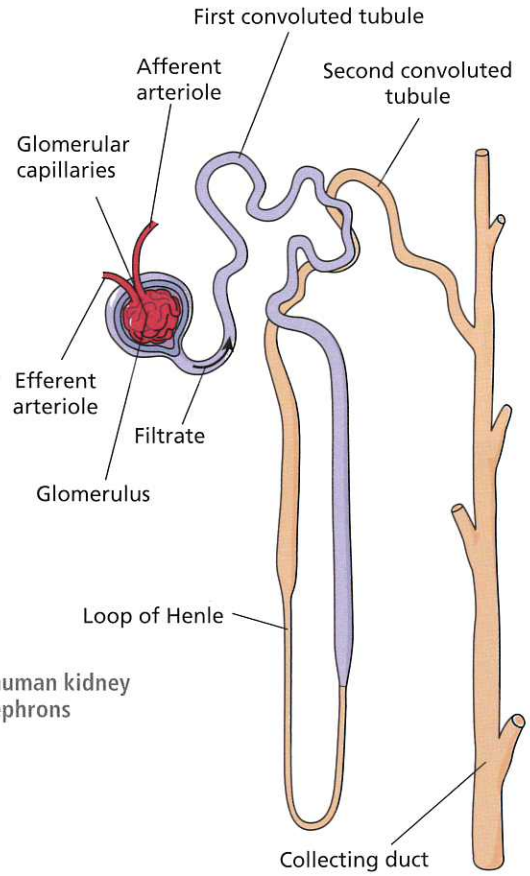


Figure 2 A nephron. Each human kidney contains around 1 million nephrons

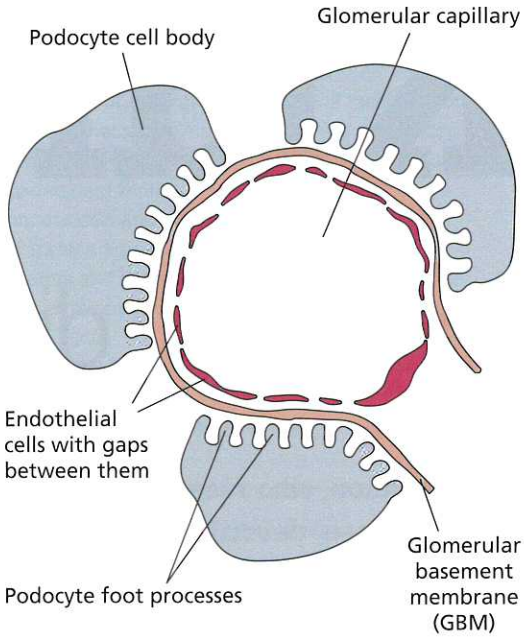


Figure 3 The glomerular filtration barrier

In the glomerulus

The glomerular filtration barrier (see Figure 3) is permeable to water and small solutes but it prevents cells and large molecules from leaving the circulation. It comprises endothelial cells, a basement membrane and podocytes (specialised epithelial cells). The endothelial cells line the inner surface of capillaries. There are gaps between these cells, which helps the process of filtration.

The basement membrane is a collection of extracellular matrix molecules that form a dense protein network between cells. Podocytes are on the outer surface of the capillary. They have large cell bodies and foot processes that form a lattice to cover the capillary wall. Blood is filtered between the gaps in the foot processes.

Glomerular filtration rate

The selective filtration is based on size and electrical charge of circulating molecules. Blood cells and many proteins are too big to pass through the filter, and proteins have a negative charge, which also prevents them from escaping.

Filtration across this barrier occurs at a rate known as the glomerular filtration rate (GFR). We can measure this rate in humans by tracking a molecule (e.g. chromium^{51}EDTA). In a typical adult, the GFR is normally 90–120 ml min^{-1}. This value can be used to calculate the volume of fluid crossing the filtration barrier (see Box 1). In patients with kidney disease, the GFR decreases and blood tests are performed to monitor kidney function.

Round the loop

Blood enters the glomerulus through a small blood vessel — the afferent arteriole. After passing through the capillaries, blood leaves via the efferent arteriole. Fluid that has crossed the filter is called filtrate and this flows into the first convoluted tubule, where ions, water and other small molecules are reabsorbed into the body. Levels of solutes, such as sodium and potassium, are regulated by reabsorption or secretion across specialised ion channels. The loop of Henle, second convoluted tubule and collecting duct help to concentrate the filtrate to produce urine for excretion.

Other functions

In addition to selective filtration and regulated excretion, kidneys have other important functions:

- By sensing changes in blood volume, cells close to the glomerulus release a hormone called renin, which helps to control blood pressure in the body.
- Kidneys help to keep the balance of calcium and phosphate in the blood by modifying vitamin D so

Terms explained

Immunosuppressant A medicine used to reduce the effects of the immune system

Polycystic kidney The presence of multiple cysts in the kidney, usually associated with genetic mutation.

Proteinuria The presence of an abnormal amount of protein in the urine.

Recombinant erythropoietin A synthetic preparation of the hormone which stimulates red blood cell production.

Box 1 Calculating the GFR

If the glomerular filtration rate in an adult is 100 ml min^{-1}, in each hour the kidneys will filter 6 litres of blood. In 24 hours a remarkable 144 litres of fluid will cross the filtration barrier. Most of this fluid will be reabsorbed in the kidney tubules, leaving 1–2 litres of urine for excretion.

it becomes active. Activated vitamin D is needed to maintain healthy bones.

- Kidneys stimulate the production of red blood cells by producing the hormone erythropoietin, which acts on the bone marrow to produce red blood cells.

Kidney disease

There is a wide spectrum of kidney disease. The earliest problems result from abnormalities in kidney development, where babies are born with absent or poorly formed kidneys. This can be due to mutant genes but often the cause is not known.

Kidneys can be injured by infections and inflammation. They are also vulnerable to the effects of toxins, including medicines used to treat other medical conditions. Later in life, kidneys can be affected by metabolic disorders such as diabetes — diabetic kidney disease is now the most common cause of kidney failure in the world.

The signs and symptoms of kidney disease can be hidden for some time and can vary depending on whether there is a defect in glomerular barrier function or in the tubular activity.

Urine testing sticks are a simple means of screening urine for molecules that may be connected with disease. The stick is briefly dipped into a fresh sample of urine and the different reagent squares detect the presence of blood cells, protein, glucose and other components. The presence of glucose in urine can indicate diabetes, while white blood cells and nitrates can indicate urine infection. The persistent presence of protein in the urine can be an early indicator of glomerular or tubular kidney disease.

Barrier breakdown

In glomerular disease the filtration barrier becomes leaky and protein is lost from the blood into the urine. The loss of small amounts of protein, known as **proteinuria**, does not cause symptoms but it can be an early sign of disease. It is possible to detect proteinuria by testing a sample of urine with a urine testing stick (see Figure 4).

When proteinuria is severe, the levels of circulating blood proteins drop. This greatly affects the ability of the blood to retain water. As a consequence, water collects in spaces outside of the circulation, resulting in body swelling or oedema (see Figure 5). The combination of massive proteinuria, low circulating proteins and oedema is known as nephrotic syndrome. This disorder can affect adults and children. In most cases it will respond to treatment with corticosteroids, which are anti-inflammatory medicines. This improves the barrier function, but it is not always effective and patients may progress to kidney failure.

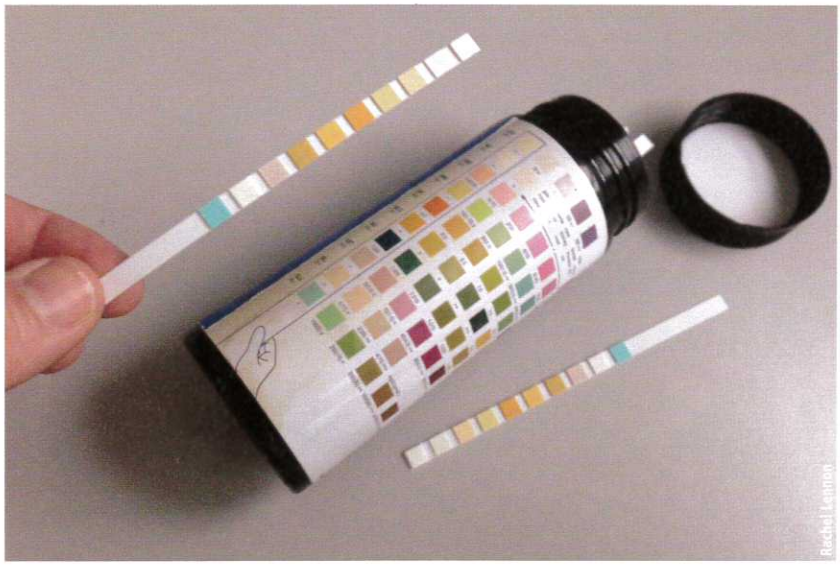


Figure 4
Urine testing stick

Tubular trouble

In disorders affecting the kidney tubules, the regulated reabsorption and secretion of solutes or water is disrupted. Depending on which tubule segment is affected, different signs and symptoms will be present.

One example is a rare condition known as cystinosis, which affects approximately one in 100 000 individuals. In this disorder, the body has an enzyme deficiency. This leads to the toxic

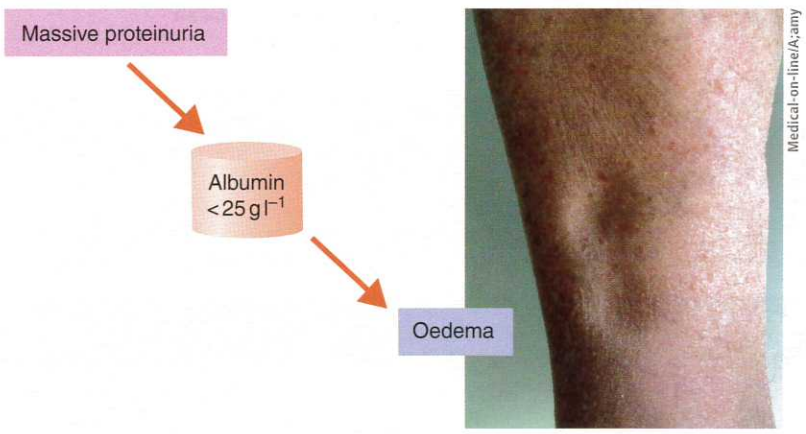


Figure 5 Massive loss of protein from the blood into the urine leads to low levels of circulating proteins such as albumin. When albumin levels fall below 25 g $litre^{-1}$, the osmotic pressure exerted by proteins is not sufficient to hold water and this leaks into spaces outside the circulation, causing oedema to develop. The photo shows lower leg oedema in an elderly man

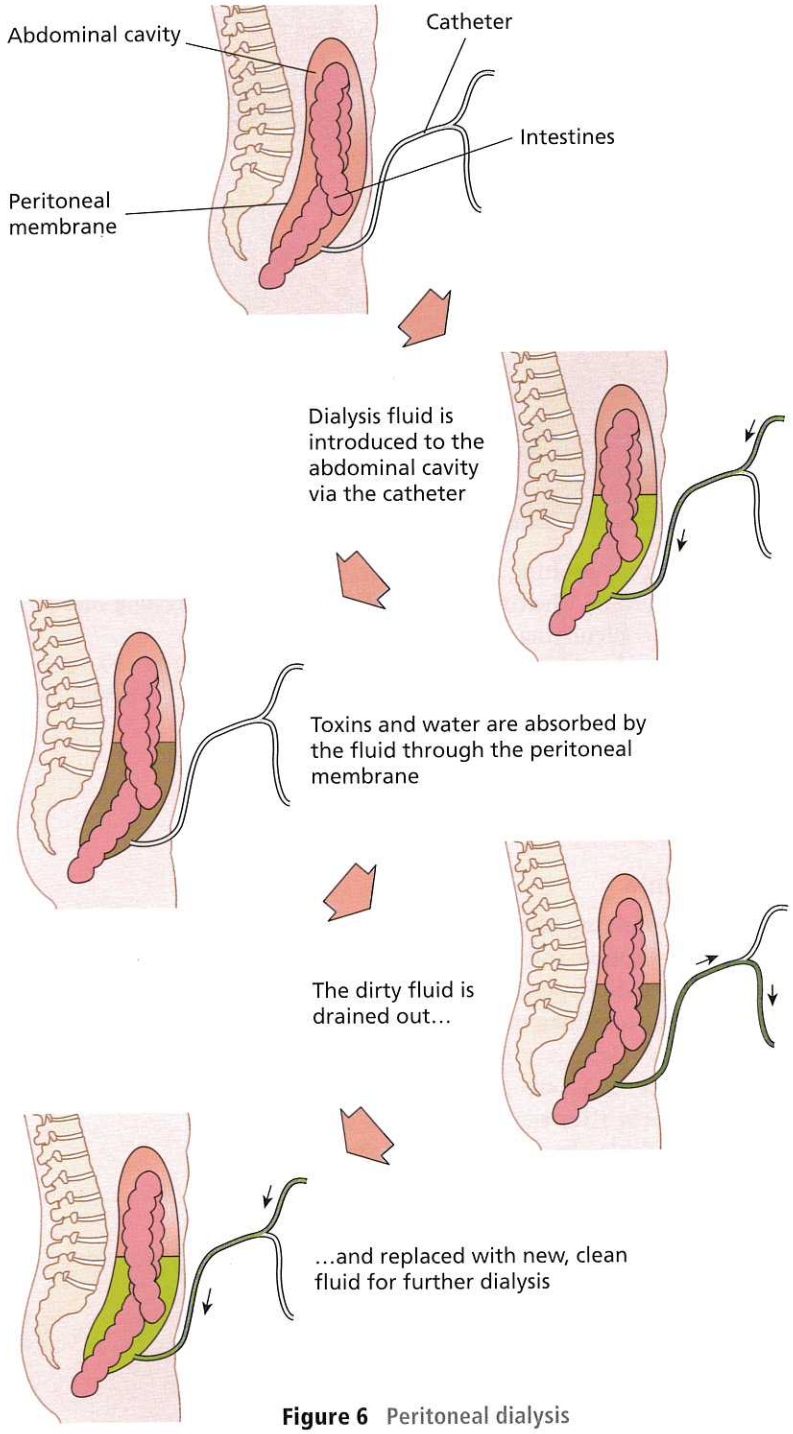


Figure 6 Peritoneal dialysis

build-up of the amino acid cystine, which forms crystals in cells. As a result, patients cannot regulate the reabsorption of solutes such as potassium, phosphate and bicarbonate, and so children with this condition may not grow or develop properly.

Patients can be treated with oral salt supplements to keep their levels within normal ranges. In addition, a medicine called cysteamine can help to remove the build-up of cystine in cells. However, this treatment is not a cure and most patients with cystinosis will need dialysis or a kidney transplant.

Chronic kidney disease

Some glomerular and tubular diseases do not respond well to treatment and patients develop chronic kidney disease (CKD). There are approximately 2 million people with CKD in the UK. In addition to the problems detailed above, these patients often develop high blood pressure. This can be due to abnormal renin production or because the kidneys are not able to excrete enough water.

The kidneys also lose their ability to produce activated vitamin D. This reduction affects bone growth and strength, and patients can develop rickets (where the bones are so soft they may fracture or become deformed) if left untreated. The problem can be helped by reducing phosphate in the diet and by taking vitamin D supplements.

Erythropoietin production also falls and patients often develop anaemia, where the red blood cell count drops. This can be treated by regular injections of **recombinant erythropoietin**. To avoid complications, children and adults with CKD often need to take a combination of medicines to control blood pressure and maintain healthy bones. These are all functions that healthy kidneys manage without us realising.

Replacing kidney function

When kidney function fails, a patient will need either dialysis or a kidney transplant.

Dialysis

Dialysis removes solutes, water and waste products from the body and therefore replaces the excretion function performed by healthy kidneys. In haemodialysis, patients are connected to a dialysis machine and their blood flows in and out of the machine over 4–6 hours to allow exchange or removal of solutes and water. This treatment is usually needed three or four times a week and generally takes place in a hospital dialysis unit, although some adults can receive dialysis at home.

Another mode of dialysis is called peritoneal dialysis (see Figure 6). Instead of the blood being cleaned by an artificial membrane outside the body, it is cleaned inside the body through the peritoneum. The peritoneum is a thin membrane that surrounds the organs in the abdomen and contains an abundance of capillaries. A specialised plastic tube — a catheter — is inserted through the patient's abdominal wall into the peritoneal cavity (the space between the two layers of the peritoneum). This cavity is then filled with dialysis fluid, which remains there for several hours. Excess waste products and water pass through the peritoneum into the dialysis fluid, which is removed from the abdomen through the same catheter.

This type of dialysis is performed at home and is repeated three or four times during the day or by

Further reading

This short video describes the anatomy and physiology of the kidney: **www.tinyurl.com/7ujhfbt**

This website is run by patients and has helpful information about kidney disease: **www.kidney.org.uk**

An animation showing how peritoneal dialysis works: **www.kidneypatientguide.org.uk/pdanim.php**

More information about dialysis: **www.nhs.uk/conditions/Dialysis**

More detail about kidney transplantation: **www.nhs.uk/conditions/Kidney-transplant**

a machine overnight. It is the preferred method of dialysis for children in the UK, because it causes the least disruption to their schooling.

Dialysis only replaces the excretion function of the kidneys and patients need medicines to maintain healthy bones and normal red cell numbers. In most patients, dialysis is a short-term treatment while they are being prepared for a kidney transplant.

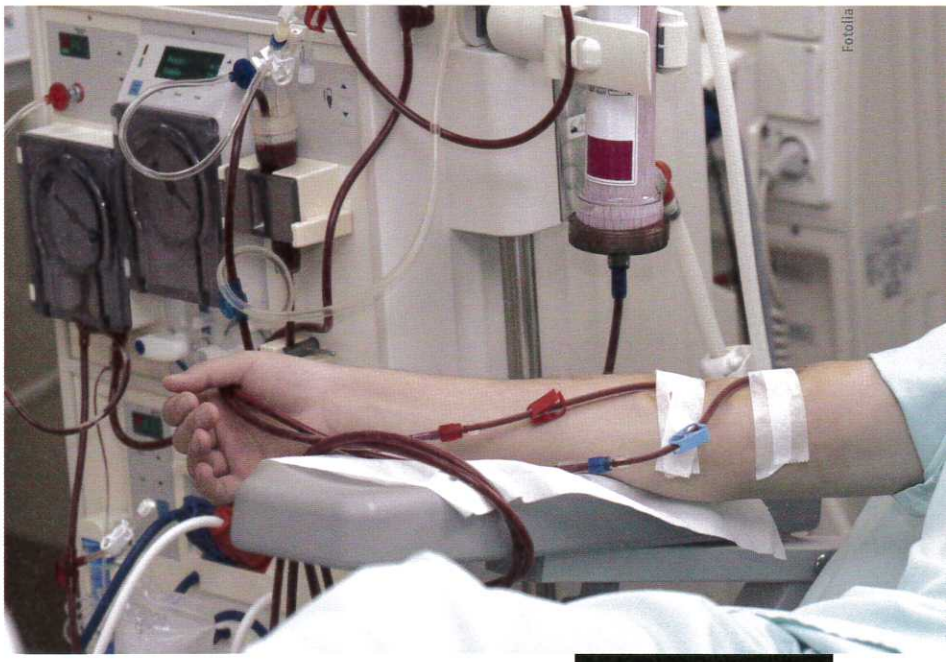
Transplantation

The first kidney transplant was performed in 1950 in Illinois, USA. The patient had kidney failure owing to an inherited tubular disorder known as **polycystic kidney** disease. The new kidney was from a deceased donor and although it worked for some time, it was eventually rejected by the recipient's immune system. The first successful kidney transplant came a few years later, when identical twins were donor and recipient. One brother had kidney failure and his twin brother donated a kidney. Since the twins were genetically identical, the recipient's immune system tolerated the new kidney and it was successful.

Since the 1950s there have been huge developments in transplantation, including the use of **immunosuppressant** medicines to prevent transplant rejection. Today, patients preparing for transplantation have blood tests to determine their compatibility. Once this analysis is complete, the search for a donor can begin. The donor may be living or deceased but will need to be a good match for the recipient. With a living donor, it is possible to schedule the transplant surgery; in the case of a deceased donor, the recipient is placed on a national waiting list until a kidney match is available (see Biological Sciences Review, Vol. 25, No. 1, pp. 32–37).

Ethical issues

Kidney transplantation raises ethical questions. One consideration in the case of living donation is the removal of a kidney from a healthy individual. Today, this is carefully evaluated by a team who assess the donor and decide whether or not it is safe to proceed. Other ethical issues relate to the use of kidneys from deceased donors. In the UK, kidneys from deceased donors may only be used if the donor previously agreed to kidney donation. Since the demand for kidneys far outstrips supply, kidney campaigners have proposed an 'opt out' scheme, where there is presumed consent to donation unless an individual has declared otherwise.



A patient receiving dialysis treatment

Kidney dialysis and transplantation are expensive procedures — the estimated worldwide cost for dialysis alone is over £50 billion. This is why such treatments are seldom available in developing countries. Research is now focused on developing new ways to improve the detection of kidney disease and to prevent progression. It is hoped that new discoveries will improve the lives of people across the world living with kidney disease.

Points for discussion

- Should the UK have an opt in or opt out system for organ donation?
- Would you donate a kidney to a stranger, or only to a relative?

Dr Rachel Lennon is a Wellcome Trust intermediate clinical fellow and consultant paediatric nephrologist. Her research is based at the University of Manchester, where she is investigating glomerular cell adhesion in health and disease.

Key points

- Kidneys have many important functions: excretion of waste products, solutes and water; production of hormones that control blood pressure and stimulate red blood cell production; and activation of vitamin D to help keep bones healthy.
- In kidney disease these functions are lost, although this may remain hidden for some time.
- When kidneys fail, their functions can be replaced with medicines, dialysis or a kidney transplant.