What I tell my patients about polycystic kidney disease

Lukas Foggensteiner
BM BSc PhD FRCP
Consultant Nephrologist, Renal Unit, Queen Elizabeth Hospital, Birmingham

Polycystic kidney disease (PKD) is an inherited condition that is characterised by the development of cysts in the kidneys. It also may cause cysts to form elsewhere and often is associated with high blood pressure (hypertension) and other features. It is a common cause of kidney disease in the UK and may lead to kidney failure requiring treatment with dialysis or transplantation. In this article we will discuss the inherited nature of the condition, some common symptoms you may get and the treatment options that are available.

Your kidneys are a pair of organs that are about 12 cm (five inches) in length. They lie at the back of your abdominal cavity just below the edge of the ribcage. They are richly supplied with blood vessels. This allows your kidneys to function as filters, clearing your blood of unwanted waste substances, which are excreted in the urine.

Your kidneys also help regulate your blood pressure, the total amount of salt and water in your body, the balance of calcium in your blood and bones, and the level of haemoglobin in your blood. Your kidneys, therefore, have a wide range of important functions that are essential to maintaining good health. There are many diseases that can affect the kidneys, some of which are quite common and some of which are very rare. Among the more common conditions are diabetes, hypertension, inflammation of the kidneys and PKD.

PKD is a term used to describe a range of conditions in which cysts develop in the kidney. The most common form is called 'autosomal dominant polycystic kidney disease' and this is the type we will be talking about; it affects about one in every thousand people. Some of the other, rarer, conditions associated with cysts in the kidney include autosomal recessive polycystic kidney disease, medullary cystic kidney disease, and juvenile nephronophthisis.

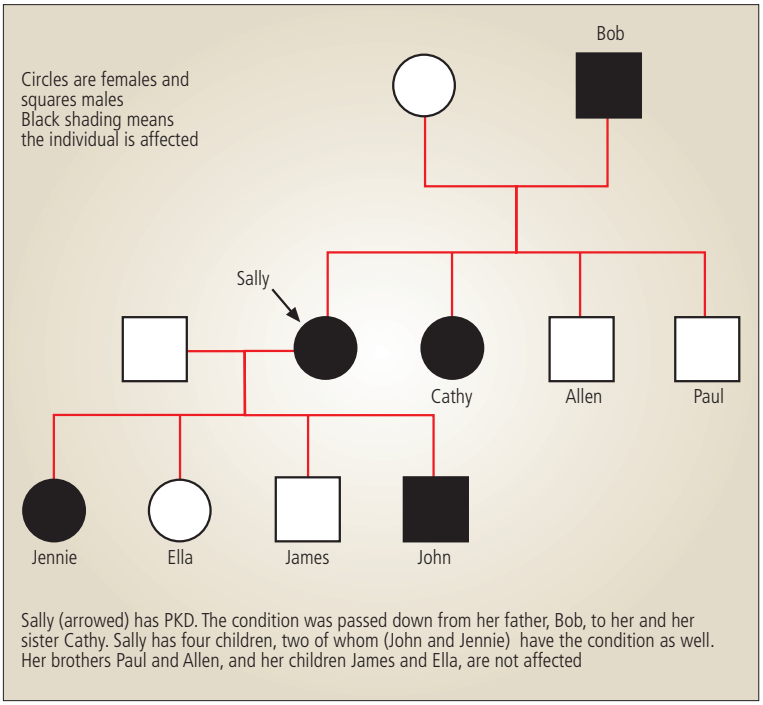
PKD is an inherited condition

Your body is made up of millions of cells and each of these cells has a nucleus that contains DNA. This DNA is the blueprint for your body. It can be divided into smaller units called genes and these genes are like plans for individual components of your cells. Different genes control different physical features of your body such as height, hair colour and skin pigmentation. As well as visible characteristics, genes control invisible factors such as the structure and function of all your cells.

Mostly, these genes work away without us really being aware of them, but if there is a mistake (usually called a mutation) in one of the genes, this can lead to disease. In PKD, there is a mutation in one of the genes involved in regulating the behaviour of certain cells in the kidney.

Each gene is present in two copies, one inherited from your mother and one from your father. In some genetic conditions both copies have to be abnormal and these conditions are called 'autosomal recessive'. In other conditions, including PKD, only one copy needs to be abnormal. These are called dominant conditions. The important feature of dominant conditions is that they are passed down through the generations from parent to child. A child of someone with PKD has a 50% chance of having the condition themselves and a brother or sister of

Figure 1. Family tree of a typical family with polycystic kidney disease (PKD)



Sally (arrowed) has PKD. The condition was passed down from her father, Bob, to her and her sister Cathy. Sally has four children, two of whom (John and Jennie) have the condition as well. Her brothers Paul and Allen, and her children James and Ella, are not affected

someone who is affected is also at 50% risk of being affected. This is sometimes called a 'dominant mode of inheritance'. This is very important to remember if a family member is diagnosed with PKD. Doctors will often draw a family tree for families affected by the condition. Figure 1, on page 15, shows a typical pattern of inheritance.

The situation with PKD is further complicated by the fact that there are actually two pairs of genes that can be abnormal, giving rise to the condition. These are called the PKD1 and the PKD2 genes. About 85% of people with PKD have mutations in the PKD1 gene and the remaining 15% have mutations in the PKD2 gene. The disease in each case is the same but the PKD2 form does seem to be slightly milder, with less chance of developing kidney failure and needing dialysis.

How does the abnormal gene cause kidney cysts in PKD?

To understand how kidney diseases can cause your kidneys to fail, it is important to understand a little about how your kidneys work. Each kidney is made up of about one million tiny filters and tubes called nephrons. These consist of a 'tuft' of small blood vessels called capillaries, which sit in a capsule called Bowman's capsule. This makes up the filter part of the nephrons, called the glomerulus. Bowman's capsule is connected to a tube (called a tubule), which is connected, via a network of larger tubules, to the ureters and then to the bladder. In practice, your blood is passed through the glomerulus, where waste products, salts and water pass through tiny holes in the capillaries but blood cells and proteins are retained. The mixture of salts, water and waste products ultimately becomes urine but before it does, it has to pass through the network of tubules, which further processes the fluid. Finally, the urine passes from your kidneys into your bladder and then out when you pass urine.

PKD mainly affects the tubules of your kidney. Each tubule is about the width of a human hair and made up of a lining of cells called tubular epithelial cells, each of which contains two copies of the PKD genes, which we think regulate the growth of cells to maintain the normal structure of the tubule. If one of these copies carries a mutation, then the cells start to grow abnormally and the tubule starts to balloon out, forming a cyst (see Figure 2). In PKD there are hundreds of these cysts in each kidney. As they slowly grow, they start to compress the surrounding kidney and eventually impair the flow of blood and urine within the kidney, causing kidney failure.

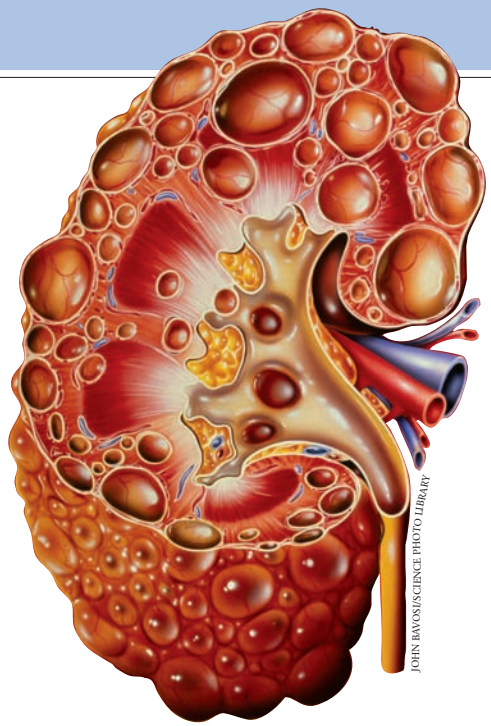


Figure 2. A polycystic kidney. Normal cells lining the tubule start to grow abnormally. The tubule balloons out, forming a cyst which eventually detaches from the tubule. Cysts may form to be many centimetres in size. Eventually the whole kidney becomes enlarged and replaced with cysts

PKD does not just affect the kidneys

PKD is often described as a systemic condition, meaning it can affect a wide range of systems within the body. Although kidney cysts are the most common problem, cysts in the liver may occur and cause the liver to enlarge. Cysts can develop in other organs and PKD can also have an effect on the heart and blood vessels. The most common problem is hypertension. This is easily treated with medication and is one of the major aspects of managing the disease.

The other effect on blood vessels is, fortunately, much less common. Sometimes, small weaknesses in the blood vessels develop, leading to ballooning of the vessel. This is called an aneurysm. Rarely, an aneurysm may leak and, if it is in your brain, it can cause a type of stroke. This does not happen very often, though, and if there is a history of leaking aneurysms in your family, it is common practice to scan your brain regularly to guard against this.

PKD seems to weaken some of the connective tissues in the body. These are involved in holding and connecting parts of the body together. For example, in PKD the wall of the abdomen is slightly weakened, leading to an increased risk of a hernia forming (when internal organs bulge between the muscles surrounding them).

Diagnosis of PKD

Symptoms of PKD

The symptoms you may experience with PKD all relate to the abnormalities described above. It is

important to remember that each individual is different. Not everybody will have the same experience with the disease. Some people are unaware that they are affected, while others have troublesome symptoms. The age at which different people run into these problems varies. Sometimes children are affected, more commonly it is middle-aged adults, and sometimes the condition becomes apparent only in old age. You may think the severity of the disease would be consistent within families. However, sometimes two affected brothers or sisters have very different diseases, with one needing dialysis at a young age and the other much later in life. Fortunately, few have all the problems described below.

Symptoms relating to kidney cysts

The hallmark of PKD is the development of round, fluid-filled cavities in the kidney called cysts, which start out as very tiny structures but grow over the years and may become as large as 15 cm (6 inches) in diameter. As they develop and grow, they may cause a number of problems.

The cysts can get quite big and you may become aware of a lump in your belly on one or both sides. The enlarged kidneys may also press on the stomach and cause indigestion or a feeling of fullness. As the cysts continue to grow they become more fragile and may leak or burst. Although this is not dangerous in any way, it can be painful and you may notice blood in your urine. This is best treated with simple painkillers. Cysts can also get infected if bacteria get into the kidney. This can cause pain, blood in the urine and make you feel generally unwell and feverish. This usually requires antibiotic treatment.

Symptoms relating to kidney failure

As your cysts continue to grow, they will eventually start to impair the function of the kidneys themselves. This is called kidney failure. Kidney failure is diagnosed by blood tests, which measure the level of waste products in the blood. It is the abnormal accumulation of waste products that cause the symptoms of kidney failure. When the function of your kidneys becomes so impaired that you become unwell, this is called end-stage renal disease (ESRD). This will cause you to become tired and lethargic, lose your appetite, become pale and anaemic and generally feel unwell. ESRD requires treatment in the form of dialysis or a kidney transplant. The development of ESRD is perhaps the most important part of PKD because of its implications for your life and health. The age at which ESRD develops varies between individuals and ranges from childhood to old age. About 50% of people with the condition will need dialysis or a transplant by the age of 50 but a small number may never need it.

Symptoms relating to abnormalities of the blood vessels

Hypertension affects most people with PKD. Mostly, this does not cause any symptoms at all and is detected by your doctor or nurse when your blood pressure is measured. Hypertension makes your kidney disease worse and can lead to strokes and heart attacks. For these reasons your doctor will almost certainly wish to treat it with medication. Hypertension also increases the risk of aneurysms, which is another reason for treating the blood pressure carefully.

Symptoms relating to abnormalities of connective tissue

The most common problem you may encounter is the development of hernias affecting the wall of the abdomen. These are common in the general population as well, but they are somewhat more common in people suffering from PKD. They are

Box 1. Some frequently asked questions

Q. I have polycystic kidney disease (PKD) but my parents seem to be unaffected – is this possible?

A. Yes – in 10% of cases the disease appears spontaneously.

Q. I have PKD. Should my young children be checked?

A. If your children are completely well, then no. If they have tummy pain or blood in the urine, they should have an ultrasound scan of their kidneys.

Q. I have PKD and I am pregnant. Can my baby be tested?

A. It may be possible to test your baby but this is rarely done. You should talk to your specialist about this.

Q. I sometimes have pain and bleeding from my polycystic kidneys. Can I have an operation?

A. Operations to remove cysts are rarely helpful in the long run but in extreme cases the kidneys can be removed.

Q. I want to have a transplant. Do my polycystic kidneys need to be removed?

A. Sometimes polycystic kidneys are so large that there is no room in the tummy for a transplant unless they are removed. Fortunately, this is rare.

Q. I have had a kidney transplant. Can the PKD affect my transplant?

A. No, your transplanted kidney will not have the abnormal gene, so it will not be affected.

treated in the conventional manner with a minor operation and rarely give rise to serious problems.

Another association with PKD is an increase in the risk of diverticular disease of the bowel. This is caused by weakness of the bowel wall allowing small sections of the bowel to bulge out, causing pain and diarrhoea or constipation. This rarely causes serious problems and is easily treated.

Treatment of PKD

Usually, people affected by PKD will be seen regularly at a specialist kidney clinic, often called a renal or nephrology clinic, where specialists keep a close eye on how your disease is progressing and offer treatment as appropriate. Sadly, at the present time there are no proven treatments that specifically slow down or stop the features of PKD developing. The management of PKD, therefore, focuses on maintaining general health, treating blood pressure, monitoring for the development of kidney failure and offering dialysis or transplantation if necessary.

Maintaining general health

This will help greatly if you do end up needing dialysis. Things you can do include not smoking, avoiding being overweight, getting plenty of exercise, eating a healthy diet and getting your blood pressure and cholesterol checked regularly.

Blood pressure

Hypertension is very common in PKD and should be treated. The main reason for treating it is that the hypertension itself can further damage the kidneys and accelerate the decline in kidney function. It is mainly treated with medications and, frequently, more than one drug is needed. Limiting salt and alcohol intake can also help.

Pain and discomfort in the kidneys

As your kidneys enlarge, they can become painful, especially if a cyst bursts, bleeds or becomes infected. These episodes are best treated with painkillers and antibiotics if necessary. Usually, the pain settles but sometimes the pain or discomfort becomes persistent and disabling. In some people these symptoms become so severe that an operation on the kidneys is suggested. Options include removing cysts or parts of a kidney, or removing both kidneys completely. Removing individual cysts can sometimes offer temporary relief but as they soon grow back this is not helpful in the long run. Removal of both kidneys is sometimes performed and will relieve the symptoms caused by the enlarged kidneys but, of course, you would need dialysis treatment or a transplant afterwards.

Dialysis and transplantation

If your kidneys fail, you will need dialysis or a kidney transplant. Dialysis is a technique for removing the waste products from your body that are normally removed by your kidneys.

Some people with kidney failure benefit from a kidney transplant. These may come from an anonymous donor or from a living friend or relative. Your clinic will have plenty of information about dialysis and transplantation.

New treatments for PKD

Over the last 20 years there has been an enormous amount of research on PKD. We now know of some drugs that slow down or even stop the progression of the disease in laboratory animals. There is great interest in trying these drugs out in humans and early studies have begun, although it is too early to say if the drugs will be effective.

Screening family members for PKD

If you have PKD, then your siblings and children have a 50% chance of being affected. Furthermore, one of your parents is likely to have the condition. The question then arises of whether family members who are at risk should be screened for the condition. Screening is done by simply doing an ultrasound scan of the kidneys. If this is done at the age of 20 or older then it is very accurate at determining whether the person is affected.

Screening tells you whether you are affected and allows you to be seen by a specialist clinic. As no specific treatments for the condition exist, however, some people feel that screening is not helpful. There is also a potential problem with getting life insurance if you know you are affected by the condition. For these reasons, if you are feeling completely well, it may be sensible to defer screening to later life.

Box 1 contains some more common questions you may have about PKD. Talk to a healthcare professional if you have any other concerns ■

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Key points

- **Polycystic kidney disease (PKD) is an inherited condition causing cysts in the kidney and elsewhere.**
- **There are no specific treatments for PKD at the moment but a healthy lifestyle and good blood pressure control are important.**