Autosomal recessive polycystic kidney disease (ARPKD) - A guide for parents

This information sheet is about autosomal recessive polycystic kidney disease (ARPKD). It is intended as a general guide for:

- Expectant parents who have been told that their unborn child has or may have ARPKD
- Parents of young babies and children who have been diagnosed with the disease
- Couples who are thinking about having a baby and have been told any children they have could have ARPKD.

It explains the causes of ARPKD, how it is diagnosed, its symptoms and how they are treated, and how the disease might progress.

What is ARPKD?

ARPKD is a rare disease that affects the kidneys and liver. It is usually diagnosed in babies and young children and occurs in about one in every 20,000 live births in the UK. Sometimes only the liver is affected; this condition is called congenital hepatic fibrosis (CHF). This information sheet, however, is about ARPKD when both the kidneys and liver are affected.

ARPKD causes cysts – sacs filled with fluid – to develop in the small tubes of the liver and both kidneys. In the liver, these tubes are involved in producing and transporting bile (a fluid that helps in digestion); in the kidneys the tubes produce and transport urine.

ARPKD eventually causes scarring (called fibrosis), which destroys the healthy tissues in the kidney and liver. If it is severe, ARPKD can lead to kidney and liver failure. However, the disease doesn't affect the liver and kidneys equally and the severity of the disease can vary between these two organs. [1,2,4,5]

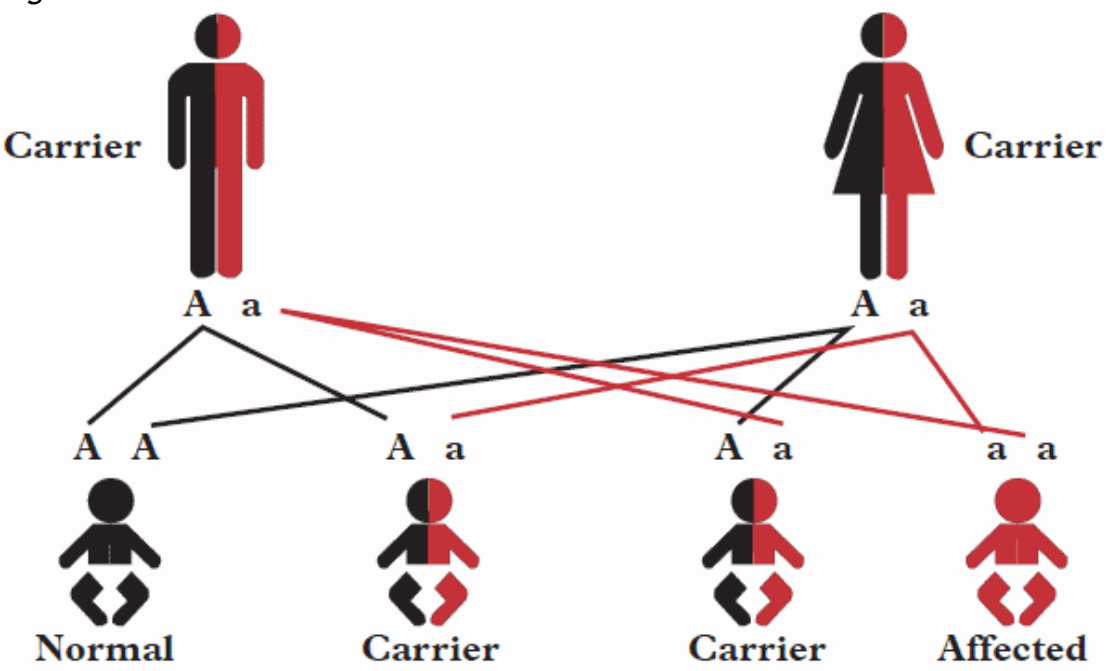
What causes ARPKD?

ARPKD is an inherited disease, meaning it is passed on from parents to their children. It is caused by an abnormality – often called a mutation - in a gene called PKHD1. We all have two copies of the PKHD1 gene, one from each of our parents. ARPKD only occurs when a child is conceived from parents who each pass on a copy of the PKHD1 gene with a mutation.

Parents of children with ARPKD do not have the disease themselves because they each have one normal copy of the gene in addition to the mutated copy. They are often called 'carriers'. The number of carriers in the general public is 1 in 70.

If both parents are carriers, the chance of a child inheriting the faulty gene from both parents is one in four (25 per cent). If the child receives only one copy of the mutated gene, they will not have ARPKD but will be a carrier of the disease. This pattern of inheritance is called 'autosomal recessive', and is shown in figure 1.

Figure 1: How ARPKD is inherited



Red (a) = copy of ARPKD gene with mutation
Black (A) = copy of normal ARPKD gene

How is ARPKD diagnosed?

ARPKD is diagnosed when typical features and symptoms of the disease are present in the kidneys and liver. These features and symptoms are widely variable and can appear before birth, later in childhood or, more rarely, in adulthood. [1-5]

If ARPKD is suspected, a number of investigations and tests will be carried out – such as blood tests and scans – to confirm the diagnosis. Genetic testing can be can be used to support a diagnosis, although this is not routine and is usually only carried out when parents already have a child who has ARPKD. There is more information about genetic testing further on in this information sheet.

ARPKD before birth

The first sign of ARPKD is enlarged kidneys, which may be seen on the routine ultrasound scan that is generally carried out at around the 20th week of pregnancy to check for physical problems in the baby. The kidneys may be described as 'echogenic' or 'bright' – this means they are more visible on an ultrasound scan.

In the first four months or so of pregnancy, the amniotic fluid that surrounds the baby is produced by the mother's placenta. When the baby's kidneys start to function, they take over this job. In some babies with ARPKD, their kidneys are very badly affected before birth and do not function properly, so they do not produce very much amniotic fluid. Very low levels of amniotic fluid is called 'oligohydramnios', and may show up in scans later on in pregnancy. This can cause other problems that may not be apparent until the baby is born, and which are discussed below.

ARPKD in newborn babies

Some babies with ARPKD have obvious symptoms when they are born. The disease can affect the lungs, feeding and physical appearance, as well as the kidneys and liver.

Kidneys - when a newborn's kidneys are very large they take up more space and as a result, his or her tummy may appear to be swollen. A doctor or midwife may be able to feel the kidneys when they examine the baby. An ultrasound scan will

reveal enlarged kidneys with an abnormal structure and visible cysts. Blood tests will often show that the kidneys aren't working properly, but the extent to which function is affected varies. Our kidneys help to control blood pressure, and about two in three babies with ARPKD will have high blood pressure, known as hypertension. [2]

Liver - cysts inside the liver may mean it, too, is larger than normal. As with the kidneys, an enlarged liver that has an abnormal structure is typically detected on an ultrasound scan. The scan will often show cysts as well, and blood tests may show that the baby's liver function is abnormal.

Lungs - if the kidneys are very badly affected before birth, the baby may develop lung problems. Amniotic fluid plays an important role in helping babies' lungs to grow properly. When the baby's kidneys do not produce enough amniotic fluid and oligohydramnios develops, his or her lungs may be small and underdeveloped.

This can result in breathing difficulties and may mean that the baby needs the help of a machine called a ventilator to take over his or her breathing. This will normally happen in a specialist intensive care unit for newborns.

Feeding - when the baby's kidneys and liver are enlarged and cause the tummy to swell, he or she may only be able to take small amounts of feed at any one time. Vomiting of feeds, known as 'gastro-oesophageal reflux', may occur. If feeding is particularly difficult, or if a baby is not getting enough nutrients, their feeds might need to be supplemented or replaced. He or she may receive 'artificial feeding' by way of a small tube that is passed through the nose into the stomach, called a nasogastric or NG tube, or a tube that goes directly into the stomach through the abdomen, called a gastronomy or G-tube.

Physical appearance - amniotic fluid provides a protective cushion around the baby in the womb to shield it from pressure. When there is very little amniotic fluid the baby does not have enough space around it. This can cause abnormalities of the face and limbs, a condition known as Potter sequence.

ARPKD in childhood

Most children with ARPKD have some degree of problem with their kidneys. As well as filtering waste products from the blood and converting them into urine, our kidneys boost the production of red blood cells, which carry oxygen around the body. They help control blood pressure and balance chemicals in the body, which helps the heart and muscles to function properly and keep bones healthy. Because the kidneys perform so many functions, a child's symptoms and the effect the disease has on their lives can vary widely.

A child with ARPKD may only have slightly reduced function with no or very few symptoms. In very severe cases, however, the usual functions of the kidneys stop working altogether. This is known as kidney failure. It is estimated that between 65 and 76 per cent of children with ARPKD also have high blood pressure [1, 2].

The severity of a child's liver problems can vary from mild impairment to complete failure. Like the kidneys, the liver has many roles, including processing digested food and turning it into energy, controlling levels of fat, acids and sugar in the blood, fighting infections, and storing essential chemicals such as iron and vitamins. Reduced liver function, therefore, can cause a wide range of symptoms and other problems.

In children with ARPKD, bacteria from the stomach can enter and infect the bile duct (the tube that transports bile from the liver). This is called ascending cholangitis and can be life threatening.

How is ARPKD treated?

Unfortunately, there are as yet no proven treatments that can slow the progression of ARPKD. Treatment is aimed at each child's symptoms and should be managed by a specialist centre with expertise in the disease. It is important that doctors who specialise in children's kidney and liver diseases – known as paediatric nephrologists and paediatric hepatologists respectively – are involved in the care of a child with ARPKD.

Different treatments carry different potential risks, and doctors should always be clear about the benefits and possible drawbacks of treatment options.

Treating kidney-related problems

Children with mild kidney problems may not need any treatment, or may only require medication for specific symptoms. They will need to be monitored regularly by specialist kidney doctors to check if their kidney function is stable. High blood pressure is common in children with ARPKD and can be difficult to treat, sometimes needing several different types of medication, although it can be successfully controlled.

If the child's kidneys are very large, one or even both may need to be removed to make enough space in his or her tummy so they can feed adequately. Sometimes it is helpful to introduce artificial feeding via an NG or G-tube.

Kidney failure can only be treated with a kidney transplant (see below), or dialysis – a means of artificially replacing some of the kidney's functions. This involves very close monitoring, long-term follow-up and a careful diet but it is possible to live a relatively normal and healthy life while on dialysis.

Treating liver-related problems

If the liver is only mildly affected and function is only slightly reduced, a child might need medication aimed at treating specific symptoms. He or she will need to be monitored by specialist liver doctors. Some children with ARPKD require regular antibiotics to prevent cholangitis.

Transplants

If dialysis does not work or is not an option for some reason, then a child with kidney failure will require a kidney transplant. The only treatment for liver failure is a liver transplant. Children with ARPKD may need both a liver and a kidney transplant, and the two can be performed at the same time or separately.

People who have organ transplants need to take a lot of medication to stop their bodies attacking the new tissue, and they will need to be carefully monitored by specialist teams. But children can live relatively normal, active lives after a transplant.

What is the outlook for a child with ARPKD?

The outlook for children with ARPKD depends on the severity of the child's disease. As a rule of thumb, the earlier the disease is diagnosed, the more severe it is. A baby with obvious kidney problems at the routine scan will therefore usually have a poorer outlook than a child who is diagnosed later in childhood. However, this is not always the case as the disease is so variable.

In general, however, ARPKD is a severe disease: about one baby in three with ARPKD dies from breathing problems during the first four weeks after birth. Eight to nine in 10 babies (80-90 per cent) who survive the first four weeks of life are still alive at five years old.

There has been very little scientific investigation around the world into how many children survive into adulthood, so it is very hard to predict the long-term prognosis for children with ARPKD [6]. Encouragingly, however, more and more specialists are reporting seeing adults with the disease in their clinics, suggesting that children are increasingly living into adulthood and are able to lead full and productive lives.

There is hope that specific treatments will be available in the future as we begin to understand more about ARPKD. Studies are underway into possible treatments for a group of genetic diseases similar to ARPKD. Some of these treatments may prove to be of benefit to children with ARPKD.

Genetic testing and antenatal counselling

Genetic testing can be used when there is reason to believe that an unborn baby, newborn or child might have ARPKD. Tests can be carried out on the parents, to check whether they are carriers and therefore whether it is possible that their child has ARPKD. Tests can also be carried out on the child to confirm the diagnosis of ARPKD, or if the parents already have a child with ARPKD and are concerned that their new baby is also affected. Genetic testing usually involves having a sample of blood or tissue taken.

When both parents are known carriers of a PKHD1 mutation, it is possible to carry out prenatal genetic testing. This means testing the unborn baby to see if he or she has the mutated gene and therefore, has the disease. It involves testing small samples of amniotic fluid and tissue from the placenta, together with ultrasound scans.

Parents who are both known carriers may also want to think about pre-implantation genetic diagnosis (PGD). This involves genetically testing embryos that are created through in vitro fertilisation (IVF) for the mutated gene. Only embryos that do not have the mutated gene are implanted into the mother, guaranteeing that a child born from that cycle of IVF will not have ARPKD.

Genetic testing can be especially helpful in supporting counselling before pregnancy. [1, 3] Antenatal counselling is available in specialised centres and is typically offered when an ultrasound scan during pregnancy raises a suspicion of ARPKD or if a couple already has a child with the disease. It provides an opportunity to discuss options about the future of the pregnancy.

At the present time, a mutation in the PKHD1 gene is not always identified due to the gene's complexity, so the results of genetic tests are not conclusive. However, testing is likely to become more reliable with improvements in genetic techniques.

Useful sources of information

- Human Fertilisation and Embryology Authority (HFEA)
  www.hfea.gov.uk
- Guy's and St Thomas' Centre for Preimplantation Genetic Diagnosis (PGD)
  www.pgd.org.uk/home.aspx
- UK Genetics Centres
  www.bshg.org.uk/genetic_centres/uk_genetic_centres.htm
- Together for Short Lives is a UK charity for all children with life-threatening and life-limiting conditions and all those who support, love and care for them.
  www.togetherforshortlives.org.uk/
- NHS Choices – for general health information
  www.nhs.uk

Authors and contributors

Written by Dr Detlef Bockenhauer, Dr Larissa Kerecuk and Dr Anand Saggar.

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The PKD Charity Helpline offers confidential support and information to anyone affected by PKD, including family, friends, carers, newly diagnosed or those who have lived with the condition for many years.

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We welcome feedback on all of health information. If you would like to give feedback about this information please email info@pkdcharity.org.uk.

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