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

This information sheet is about autosomal recessive polycystic kidney disease (ARPKD). It's for expectant parents who have been told that their unborn child has or may have ARPKD; parents of babies and children with ARPKD; and ARPKD carriers who are planning a family. It explains the causes of ARPKD, how it's diagnosed, its symptoms, treatment, and how the disease might progress.

We are sorry if you're upset by any of the information in this guide. ARPKD is often severe, and diagnosis is a worrying time for parents. Please call our helpline on 0300 111 1234 if you would like to talk to someone directly about ARPKD.

What is ARPKD?

ARPKD is a rare disease that affects the kidneys and liver [1]. It is usually diagnosed in babies and young children and occurs in roughly one in every 20,000 live births [1]. ARPKD causes cysts – sacs filled with fluid – to develop in the small tubes of the kidneys [1,2]. These tubes produce and transport urine. ARPKD also causes problems with the liver, including the formation of cysts, scar tissue (called fibrosis), and a swollen bile duct [1-3]. The bile duct is a tube involved in producing and transporting bile, a fluid that aids digestion.

Although ARPKD affects the kidneys and liver, the immediate risk to about a third of babies born with the disease is lung under-development [2]. This can make it difficult for your baby to breathe and mean they need emergency breathing support from a machine (ventilation) [4]. Over time, ARPKD causes damage to the kidneys, stopping them working properly, and eventually leading to kidney failure, often during childhood or young adulthood [5]. It can also cause complications in the liver and bile duct, such as infections [2].

ARPKD symptoms, severity of disease and the age that problems occur vary between different people. For example, some babies have serious lung and kidney problems, but others do not; and some children and adults have mainly kidney symptoms, while others have mainly liver problems [2,3,6-9].

Sometimes only the liver is affected; this condition is called congenital hepatic fibrosis (CHF) [1]. This information sheet, however, is about ARPKD when both the kidneys and liver are affected.

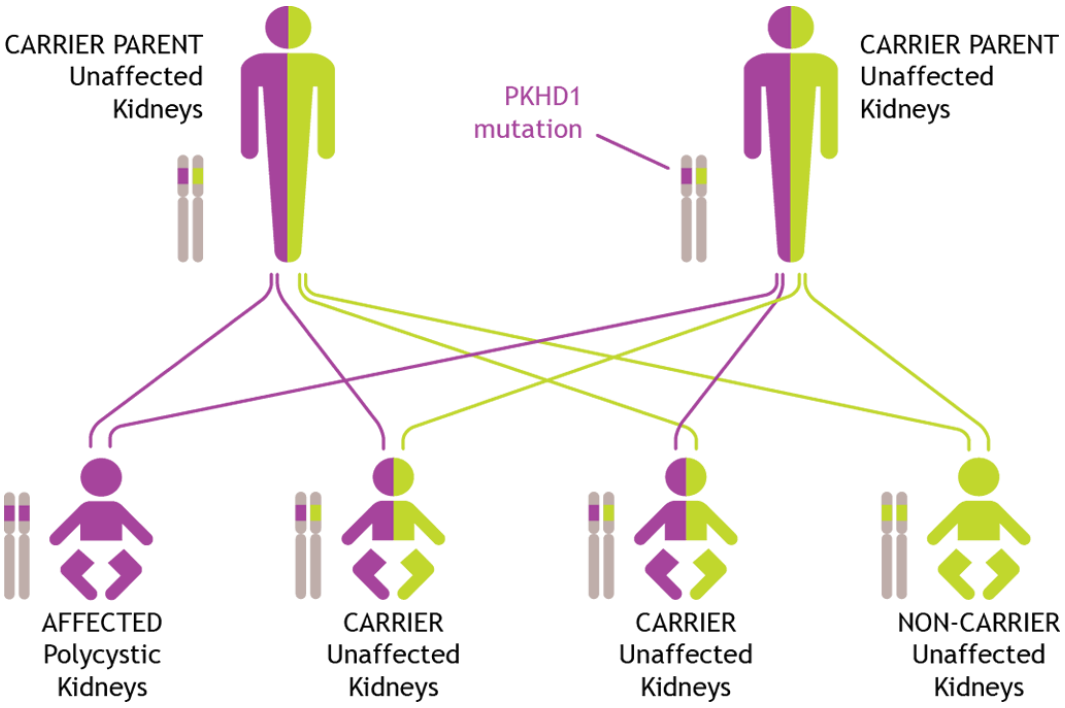
What causes ARPKD?

ARPKD is genetic condition caused by a fault – often called a mutation - in a gene called *PKHD1* [1,5]. We all have two copies of the *PKHD1* gene, one from each of our parents. ARPKD occurs when a child is conceived from parents who both pass on a faulty copy of the *PKHD1* gene [4,10]. Very uncommonly, it can happen when a new mutation occurs in the *PKHD1* gene [4], which means that at least of one parent hasn't passed on a faulty gene.

Parents of children with ARPKD don't have the disease themselves because they have one normal copy of the gene and one faulty copy [10]. They're often called 'carriers'. About one in every 70 people in the general public is an ARPKD carrier [11].

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

Figure 1: How ARPKD is inherited



How is ARPKD diagnosed?

ARPKD is diagnosed when typical features and symptoms of the disease are present in the kidneys and liver [1]. These features and symptoms are widely variable and can appear before birth, later in childhood or, more rarely, in adulthood [2,3,6-9,12].

If ARPKD is suspected, investigations and tests will be carried out – such as blood tests and scans – to confirm the diagnosis [3]. Genetic testing can be used to support a diagnosis, although it's not routine and is usually only carried out when parents already have a child with ARPKD [1]. There is more information about genetic testing further on in this information sheet.

ARPKD before birth

The first sign of ARPKD is enlarged kidneys [1,5]. They may be seen on the routine ultrasound scan that is generally carried out at around the 20th week of pregnancy (trimester 2) to check for physical problems in the baby [1,5]. The kidneys may be described as 'echogenic' or 'bright' – this means they're more visible on an ultrasound scan [5].

In the first four months or so of pregnancy, the amniotic fluid that surrounds the baby is produced by the mother's placenta [13]. When the baby's kidneys start to function, they take over this job [13]. In some babies with ARPKD, their kidneys are very badly affected before birth and don't function properly, so they do not produce very much amniotic fluid [13]. Reduced amniotic fluid is called 'oligohydramnios', and may show up in scans later on in pregnancy [5,13]. This can cause other problems that may not be apparent until the baby is born, which are discussed below.

If your baby is suspected to have ARPKD during your pregnancy, you'll have more regular scans and check-ups to check your baby's size and the amount of amniotic fluid [1]. Your obstetrician will discuss plans for the birth with you, such as being in a unit with specialist intensive care and, possibly, having a Caesarean birth [1].

ARPKD in newborn babies

Many babies with ARPKD have obvious symptoms when they are born [1,5]. The disease can affect the lungs, feeding and physical appearance, as well as the kidneys and liver [5].

Kidneys - when a newborn's kidneys are very large they take up more space, so his or her tummy may look swollen [5]. 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 cysts [5]. Blood tests will often show that the kidneys aren't working properly, but how much function is decreased varies

between babies [3]. Our kidneys help to control blood pressure, and many babies with ARPKD have high blood pressure, known as hypertension [2].

Liver – problems with the liver may show up on scans [3]. However, tests a likely to show that your baby's liver is functioning well, as ARPKD doesn't affect the way the liver tissue works.

Lungs – babies with badly affected kidneys in the womb might have underdeveloped lungs [1,5]. This is because kidney function is important to the production of amniotic fluid by the baby [13]. As well as protecting the baby, amniotic fluid helps to expand the lungs so they grow properly [10]. If there is not as much fluid as usual, this can stop the lungs growing fully [13]. This can cause breathing difficulties [1,5]. Also, very enlarged kidneys can push on the lungs and diaphragm, making breathing difficult [5,10].

Your baby may the help of a machine called a ventilator to take over his or her breathing. At least 4 in 10 babies suspected to have ARPKD before birth need a ventilator when they're born [2]. This will normally happen in a specialist intensive care unit for newborns.

Feeding – if your baby's kidneys and liver are enlarged and cause their tummy to swell, he or she may only be able to take small amounts of feed at any one time [5,11]. Problems can include vomiting, lack of appetite and problems with food moving through the gut [11]. If feeding is particularly difficult, or if your baby isn't getting enough nutrients, their feeds might need to be supplemented or replaced [11]. He or she may receive 'artificial feeding' through a small tube passed through the nose into the stomach (a nasogastric tube) or a tube that goes directly to the stomach through the abdomen (a gastronomy) [11].

Physical appearance - amniotic fluid provides a protective cushion around the baby in the womb to shield it from pressure [13]. When there is very little amniotic fluid, the baby may not have as much room as usual to grow [13]. This can cause abnormalities to the shape of the face and limbs, a condition known as Potter sequence [5,13].

ARPKD in childhood

Kidney-related problems – Most children with ARPKD have some problems with their kidneys [5]. Our kidneys filter waste products from the blood and convert them into urine [14]. They also boost the production of red blood cells, which carry oxygen around the body [14-17]. They help control blood pressure and balance chemicals in the body, and keep our bones healthy [14-17].

Because the kidneys perform so many functions, a child's symptoms and the effect the disease has on their lives can vary quite widely [5]. Your child may only have slightly reduced kidney function with no or very few symptoms, or they might have reduced kidney function making them unwell [5]. In very severe cases, the kidneys stop working altogether [5]. This is known as kidney failure and means your child will need a kidney transplant or dialysis [5].

Children with ARPKD also commonly have high blood pressure, which will need to be treated [5].

Up to half of children with ADPKD get urinary tract infections [9,10]. These are more common in girls [9,10].

Liver-related problems – The severity of a child's liver problems can vary from mild impairment to serious complications that can be life-threatening [2]. The liver has many roles, including processing digested food and turning it into energy, controlling levels of fat, acids and sugar in the blood, and storing essential chemicals such as iron and vitamins [18].

For most children with ARPKD, their liver continues to function well. But cysts, infections, fibrosis and other complications can cause a range of symptoms.

Serious complications that can occur in the liver due to ARPKD include:

- An increase in blood pressure in the vein going to the liver (the portal vein), which in turn can enlarge the spleen and affect liver function [1,2]

- An infection of the bile duct with bacteria from the stomach (called cholangitis), which can cause blood poisoning (sepsis) [1]
- Less commonly, enlarged blood vessels (varices) in the oesophagus (gullet) and stomach, which can bleed [2,3]

Developmental problems – About a third of children with ARPKD have growth impairment, meaning they are shorter and weigh less than usual for their age [5]. Growth hormones usually work well to boost children's growth, if needed [5].

Some children with ARPKD have behavioural problems or cognitive difficulties [5]. This might mean, for example, that your child doesn't perform so well at school, and has difficulties with concentration, memory, decision making or control [5].

How is ARPKD treated?

Treatment is aimed at each child's symptoms and should be managed by a specialist centre with expertise in ARPKD. Different treatments carry different potential risks, and doctors should always explain clearly to you the benefits and possible drawbacks of each option. Specialists will also monitor your child's health carefully [10]. You may need to travel to specialist units for some appointments, for example for dialysis.

Unfortunately, there are, no proven treatments that can slow the progression of ARPKD. It's possible that controlling blood pressure carefully might help to delay damage to the kidneys, but experts are not yet sure. This has been shown for patients with chronic kidney disease in general, but not for children with ARPKD in particular [1,5].

Your child's treatment team

Your child's care team should include [1]:

- a **paediatric nephrologist**, who'll monitor your child's kidney health and can provide treatment

- a **paediatric hepatologist**, who'll monitor your child's liver health and can provide treatment

Depending on your child's needs, additional specialists involved in his or her care could include [1,5,10]:

- a **perinatalogist and neonatalogist**, who provide monitoring, care and advice before and after birth
- a **paediatric gastroenterologist**, who can help to treat any problems with your child's gut or digestion
- a **geneticist or genetics counsellor**, who can provide information, advice and counselling on inherited diseases
- a **feeding specialist or dietitian**, who can help to ensure your child gets the nutrients they need
- a **psychologist or psychiatrist**, who can help with behavioural or psychological problems your child may develop

Monitoring health

Your child will have regular check-ups of their health – the frequency of these and the tests included will depend on your child's symptoms and needs [11]. Commonly, monitoring includes [11]:

- Blood pressure checks
- Scans of the kidneys and liver
- Blood and urine tests to check kidney and liver function and levels of electrolytes (salts) and minerals
- Checks for hydration and nutrition

Treating kidney-related problems

Children with mild kidney problems may not need any treatment, or may only require medication for specific symptoms.

High blood pressure is common in children with ARPKD. It's important that it is treated, because high blood pressure can increase the risk of later cardiovascular

problems including stroke and heart failure [2]. High blood pressure can be difficult to treat. But with several different types of medication, it can be successfully controlled [4,5,10].

If your child's kidneys are very large, one or even both may need to be removed to make enough space in his or her tummy to feed [1,5]. He or she may receive 'artificial feeding' though a small tube passed through the nose into the stomach (a nasogastric tube) or a tube that goes directly into the stomach through the abdomen (a gastronomy) [11].

If your child's kidneys begin to fail or need to be removed to create space for other organs, your child will need a kidney transplant or dialysis [1]. Dialysis is a way of artificially replacing some of the kidneys' functions. We explain more about dialysis later in this information sheet.

If your child develops a urinary tract infection, they'll need a course of antibiotics to treat this [19].

Treating liver-related problems

If your child's liver is only mildly affected, they might only need medication aimed at treating specific symptoms. He or she will need to be monitored by specialist liver doctors. If your child develops complications, they'll need additional monitoring and treatment. For example, if your child develops a bile duct infection (cholangitis), he or she need antibiotics to treat this [1]. If your child is suffering from severe complications, their liver specialist might discuss the option of a liver transplant with you [11].

Transplants

If your child has kidney failure, they will need a kidney transplant to survive, unless they are receiving dialysis. A liver transplant is the only treatment for liver failure. If your child needs both procedures, they might be performed at the same time [11].

By age 10, about 6 in every 10 children with ARPKD needs dialysis or a kidney transplant, and 1 in 10 needs a liver transplant (or joint kidney and liver transplant) [9]. These procedures come with some risks - make sure that your child's treatment team explains these to you fully.

People who have organ transplants need to take a lot of medication to stop their bodies attacking the new tissue [20,21]. This is called immunosuppression. They will be carefully monitored by specialist teams. Children can live relatively normal, active lives after a transplant, and can usually eat a normal healthy diet [20,21].

Dialysis

Dialysis can be done using a machine to filter the blood (haemodialysis) or by adding fluid to the abdominal space for a few hours at a time to absorb waste products (peritoneal dialysis). If your child has dialysis, they'll need regular check-ups and you'll need to watch what they eat and drink [22]. But it is possible for them to live a relatively normal and healthy life while on dialysis [22].

What is the outlook for a child with ARPKD?

The outlook for each child with ARPKD depends on the severity of their disease [10]. As a general guide, the earlier the disease is diagnosed, the more severe it is [9,10]. For example, a baby with obvious kidney problems at the routine scan will usually have a poorer outlook than a child who is diagnosed later in childhood. Children who are diagnosed later tend to have more symptoms associated with the liver than kidneys [2,10]. However, this is not always the case, as the disease is so variable [3,4,7-9,12].

In general, ARPKD is a very severe disease: about 1 in every 3 babies with suspected or confirmed ARPKD dies from breathing problems during the first 4 weeks after birth [5]. But, about 9 in ten 10 (89%) who survive the first 4 weeks of life are still alive at 5 years old [5]. Encouragingly, most children now survive into adulthood and can live full and productive lives [23].

There's 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.

Antenatal counselling

If your baby is diagnosed with ARPKD during your pregnancy, antenatal counselling will be available for you and your partner. This counselling takes place at specialised centres. It provides you with an opportunity to get more information on what to expect, and to discuss options about the future for your baby.

Genetic testing

Genetic testing can be used to look for the faulty gene – *PKHD1* – that causes ARPKD. These tests can be used when:

- There is reason to believe that an unborn baby, newborn or child might have ARPKD
- If a child has been diagnosed with ARPKD, their siblings can have the test to see whether they also have ARPKD, or are carriers of the disease
- If both parents are carriers of the *PKDH1* gene fault, testing can be used as part of *in vitro* fertilisation (IVF) to select an embryo without the gene fault

You can find out more in our information sheet Genetic counselling and genetic testing in ARPKD.

Transitioning to adult services

As your child approaches adulthood, they'll need to transition from child to adult health services. This can be an unclear time, but can also give your child more ownership of their care. For more information on transition, see *Transition from children's to adults' services – what you should expect*, from the National Institute for Health and care Excellence.

More from the PKD Charity

- Genetic counselling and genetic testing in ARPKD

Information and support from others

- The British Kidney Patient Association provides information and support to kidney patients and their families, including a scheme to give patients holidays (01420 541424; info@britishkidney-pa.co.uk)
- InfoKID provides information to parents and carers of children with kidney diseases (they can be contacted using an online form: http://www.infokid.org.uk/contact-us)
- The Children's Liver Disease Foundation provides information and support for children with liver disease and their families (0121 212 3839; info@childliverdisease.org)
- 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 (0808 8088 100)
- Kidney Kids Scotland provides support for children with kidney disease and their families (01324 555843; office@kidneykids.org.uk)
- Kidney Wales provides support for children with kidney disease and their families (029 20 343 940; team@kidneywales.cymru)

- NHS Choices provides general health information, including on kidney and liver transplants, www.nhs.uk

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