Title: Autosomal Recessive Polycystic Kidney Disease (ARPKD) - A Guide for Parents

Purpose – aims and who it is for:
This information sheet explains about autosomal recessive polycystic kidney disease (ARPKD). It is intended as general information for parents, about how ARPKD is diagnosed in children, how it might progress and how the disease can be treated.

What is ARPKD?
- ARPKD is a rare disease that affects the kidneys and liver. It is usually diagnosed in babies and small children.
- ARPKD causes bulges or cysts to develop in the small tubes of the liver and the kidneys. In the liver, these tubes are involved in producing and transporting bile (a fluid that helps in digestion) and 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]
- Sometimes only the liver is affected; this condition is called congenital hepatic fibrosis (CHF). This information sheet, however, focuses on ARPKD when it affects both organs.

What causes ARPKD?
- ARPKD is an inherited disease caused by a genetic alteration or 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.
- The parents of affected children do not themselves have the disease because they each have one normal copy of the gene without a mutation in addition to the mutated copy. They are often called ‘carriers’.
- This pattern of inheritance is called ‘autosomal recessive’. If both parents are carriers, then the chances of a child receiving the faulty gene from each parent is 1 in 4 (or 25%). (See Figure 1).
- If the child receives only one copy of the mutated gene, then they will be unaffected but will be a carrier of the disease.
How is ARPKD diagnosed?

- ARPKD is diagnosed by the presence of recognisable, typical ARPKD features and symptoms in the kidneys and liver. Genetic testing can be carried out, although this is not routine and is usually only carried out when a family already has an affected child. It can be especially helpful in supporting counselling before pregnancy (see later discussion). [1,3]

- The features and symptoms of ARPKD are very variable. They can appear before birth, later in childhood or, more rarely, in adulthood. [1-5]

Detection of ARPKD before birth

- The first sign of ARPKD is abnormal (called ‘echogenic’ or ‘bright’) and enlarged kidneys. These may be seen on a routine anomaly ultrasound scan, which is generally carried out at the 18 to 20th week of pregnancy to check for physical problems in the baby. However, kidney problems in babies with ARPKD are only seen later in pregnancy.

- The kidney function of some babies is severely affected before birth. Because the baby’s kidneys are needed to produce the amniotic fluid within the womb, ultrasound scans later in pregnancy may show that the volume of this fluid is low (this is called ‘oligohydramnios’). This can mean that the baby is born with serious problems because the fluid usually forms a water cushion to shield the baby from pressure and is needed to help his or her lungs grow and mature.
ARPKD in newborn babies

- Some babies with ARPKD have obvious symptoms when they are born:

**Kidneys**
- Babies often have very enlarged kidneys. These kidneys can be felt during a physical examination and may cause the baby’s tummy to appear swollen.
- On an ultrasound scan, the baby’s kidneys look very enlarged with an abnormal structure and visible cysts. Blood tests will often show that kidney function is affected. Babies with ARPKD commonly have high blood pressure (hypertension).

**Liver**
- The baby’s liver may also be enlarged and an ultrasound scan typically shows an abnormal structure and cysts. Blood tests may show that the baby’s liver function is abnormal.

**Lungs**
- Lung symptoms depend on the severity of the kidney problems. If oligohydramnios developed during pregnancy due to a lack of amniotic fluid, the baby’s lungs may be small and underdeveloped.
- This can result in breathing problems, which may mean that the baby needs help to breathe using a ventilator. In this case, the baby will need treatment in an intensive care unit.
- Sometimes the baby’s lungs are so underdeveloped that, sadly, the chance of the baby surviving is low.

**Feeding**
- If the enlarged organs cause the baby’s tummy to swell, he or she may only be able to have small amounts of feed at any one time. Vomiting of feeds (‘gastro-oesophageal reflux’) is common.

**Physical appearance**
- Because the amniotic fluid in the womb usually helps to protect the baby, oligohydramnios can cause the baby to be born with abnormalities of the face and limbs (called Potter sequence).

ARPKD in childhood

**Kidneys**
- Most children with ARPKD have some degree of kidney problem during childhood, but these can vary from mildly reduced function to complete kidney failure. Children with ARPKD also commonly have high blood pressure.
Liver

- The severity of liver problems can vary from mild impairment to complete failure. Children may develop a life-threatening infection called ascending cholangitis, when bacteria from the gut enter and infect the bile duct.

How is ARPKD treated?

- Unfortunately, there are as yet no proven treatments that can prevent the symptoms or slow the progression of ARPKD.
- Treatment is aimed at each child’s symptoms and should be managed by a specialist centre with expertise in this disease.
- It is important that the child is cared for by doctors who specialise in childhood kidney and liver diseases (paediatric nephrologists and paediatric hepatologists, respectively).

Kidneys

- Children with milder kidney problems may only need drug treatment and regular monitoring by kidney specialists.
- High blood pressure is common and can be difficult to treat, needing several different types of medication.
- Severe kidney failure can only be treated with dialysis or a transplant. If the child’s kidneys are very large, one or even both may need to be removed to give enough space in the child’s tummy to allow adequate feeding.
- Sometimes it is helpful to introduce artificial feeding via a nasogastric tube or gastric ‘button’.

Liver

- In milder cases of liver impairment, the child might need drug treatment and monitoring by liver specialists. Regular antibiotics may be needed to prevent cholangitis. Severe liver failure will require a liver transplant, which can be performed before, after, or at the same time as a kidney transplant.

What is the outlook for a child with ARPKD?

- The outlook for children with ARPKD depends on the severity of the individual 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 anomaly scan will thus usually have a poorer outlook than someone 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 in three affected babies die from breathing problems during the first four weeks after birth.

However, if the baby survives the first four weeks of life, then 80-90% of these surviving babies will still be alive when they are five years old.

A good number of children now survive into adulthood and are able to live 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 also under way into possible drug treatments for other similar diseases, called ciliopathies, and some of these treatments may prove to be of benefit to children with ARPKD.

What about antenatal counselling?

Antenatal counselling is available in specialised centres (see link below to UK Genetics Centres). It 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. Antenatal counselling provides an opportunity to discuss options about the future of the pregnancy.

Genetic testing can be very helpful when parents know that they are carriers of the mutated PKHD1 gene. However, at the present time, a mutation is not always identified due to the complexity of the PKHD1 gene, so the test results are not conclusive. However, testing is likely to become more reliable with improvements in genetic techniques.

When both parents are known carriers of a PKHD1 mutation, it is possible to discuss pre-natal and/or pre-implantation genetic diagnosis (PGD). In this technique, embryos are tested during a cycle of in vitro fertilisation (IVF) and only unaffected embryos are transferred into the mother’s womb to enable the birth of a child without ARPKD.

References


Useful sources of information

Human Fertilisation and Embryology Authority (HFEA)
[www.hfea.gov.uk](http://www.hfea.gov.uk)

Guy’s and St Thomas’ Centre for Preimplantation Genetic Diagnosis (PGD)
[http://www.pgd.org.uk/home.aspx](http://www.pgd.org.uk/home.aspx)

UK Genetics Centres
[http://www.bshg.org.uk/genetic_centres/uk Genetic_centres.htm](http://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. They support families, professionals and services, including children’s hospices.

NHS Choices - for general health information
[http://www.nhs.uk](http://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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