

Genetic counselling and genetic testing in ARPKD

Find out how genetic counselling and genetic testing may help you learn more about ARPKD in your family.

Which genes are involved in ARPKD?

Autosomal Recessive Polycystic Kidney Disease (ARPKD) is an inherited disease, meaning it is passed on from parents to their children through their genes [1]. Genes are the instructions our cells need to make our body parts and organs. We all have 2 copies of each gene, 1 from each of our parents.

ARPKD is caused by an abnormality - often called a mutation - in the PKHD1 gene [1]. This is the only gene that is known to be involved in ARPKD [1]. This gene provides instructions for making a protein whose exact function is unknown. It is thought to be involved in transporting chemical signals across the cell membranes [1]. It is not known how alterations in the gene cause multiple cysts to form in the kidneys.

To have ARPKD a person has to have 2 copies of the faulty gene, normally 1 inherited from their mother and 1 from their father [1]. Carriers of the altered gene (having 1 normal copy and 1 faulty copy) are usually healthy [1]. However, when 2 carrier parents have children they have a 1 in 4 chance (25% chance) of each child they have inheriting both copies of the faulty gene and developing the disease. See Figure 1.

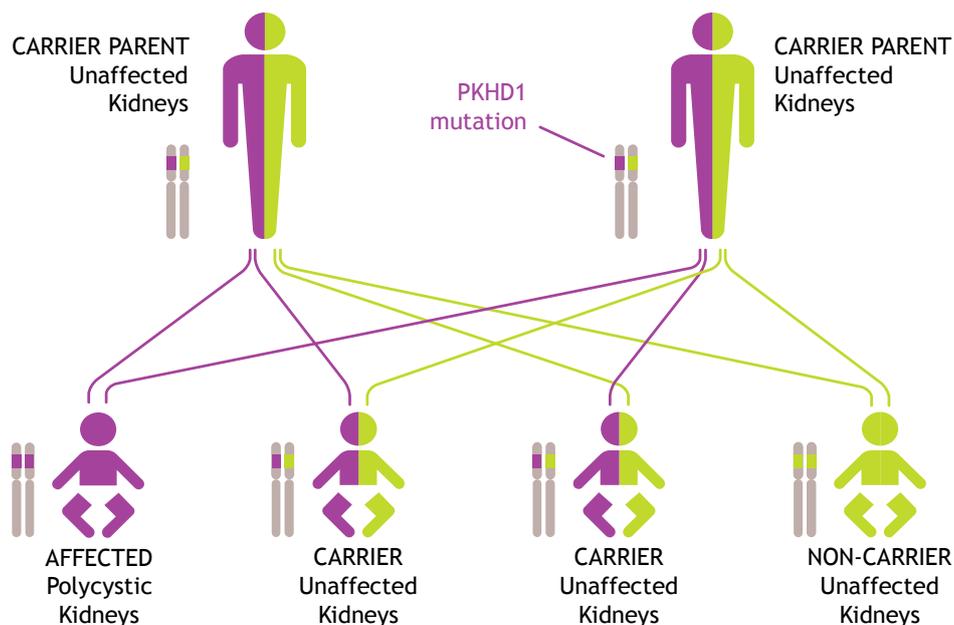


Figure 1: ARPKD inheritance diagram, for illustration only. ARPKD occurs in males and females, boys and girls, equally.

What is genetic counselling?

Genetic counselling aims to give you or your family accurate information about the genetic condition you have, and help in understanding the condition and any options that may be available. It can often be very difficult to talk about genetic issues in families, and discussing this with a specialist in genetics may be helpful.

The facts of the condition will be explained as accurately as possible, in a way that you understand. It is not primarily psychological counselling, but aims to discuss options in a way that helps you or your family members to understand and make decisions that are right for you and them. Very often, but not always, it may involve genetic testing.

To have genetic counselling, you'll need to be referred by your **kidney specialist or your GP [a]**. The appointment would normally be at your nearest NHS regional genetic centre [a]. As the centres cover large geographical areas, many centres have outreach clinics at local hospitals or health centres. You may see a genetic counsellor, a clinical geneticist or a **specialist genetic nurse [a]**.

How you manage the genetic information and talking about genetic testing is a very individual experience. It can be influenced, for example, by your own perspectives on risk, your relationships with family members, their reactions and views, and the results of any tests you have.

When is genetic testing useful?

Genetic testing is not normally used to make a diagnosis of ARPKD before or after birth if specialists are already sure of your child's diagnosis.

However, it can be useful in these situations:

- If specialists are unsure whether your child has ARPKD, ADPKD (autosomal dominant polycystic kidney disease) or another condition, genetic testing can confirm the correct diagnosis [3].
- If you and your partner both carry a faulty PKHD1 gene and are expecting a baby, genetic testing can be used to test your unborn baby in the womb, to check whether they have inherited ARPKD [a].
- If you and your partner both carry a faulty PKHD1 gene and are planning a family, genetic testing can be used alongside a special type of in vitro fertilisation (IVF) called pre-implantation genetic diagnosis to select an embryo that has not inherited ARPKD [3].

Who can have genetic testing?

If it helps to confirm a diagnosis of ARPKD or to help you plan a family if there is a risk that your children will inherit ARPKD, testing is available on the NHS [3]. A

specialist renal service or a specialist genetic service can request this test for you. However, testing is not available to the general population [3].

How is genetic testing performed?

The test can be done on any source of DNA - normally white blood cells from a blood sample are used. To test an unborn child, cells from the placenta or amniotic fluid can be tested [a]. Amniotic fluid is the liquid that surrounds the baby in the womb. If a special type of in vitro fertilisation (IVF) is being used, the embryo can be tested (see more on planning a family below) [a].

Genes are essentially codes of letters. Once the DNA has been extracted from the cells, the laboratory staff can check for possible faults in the ARPKD gene. Interpreting the information can take some time - the result of the initial test in a baby or person with ARPKD could take a couple of months or longer [a].

If faults in both copies of the faulty genes are found, then samples of DNA from future children can be checked too during pregnancy or during IVF [a]. This is much quicker, as the laboratory staff already know exactly what faulty DNA code they are looking for. This round of testing usually takes about 2 weeks [a].

What could the results of my genetic test be?

There are many different possible mutations in the PKHD1 gene that can cause ARPKD [1]. If a baby has ARPKD, there is about a 75 in 100 chance (75% chance) that genetic testing will find the gene faults that have caused the condition [1]. However, there is a chance that the faults responsible won't be found [1].

If your baby has ARPKD, the possible results of a genetic test are:

- gene faults are found in both copies of the PKHD1 gene, explaining why your baby has ARPKD
- 1 faulty copy is found but the other 1 is not
- no faulty code is found in the DNA that explains your baby's ARPKD
- a fault or unusual piece of code is found in 1 or both PKHD1 genes, but genetic specialists are not sure whether this is the cause of your baby's ARPKD

If you have a child with ARPKD but no faulty code is found in their or your PKHD1 genes, it might still be possible for you to have future testing of embryos or during pregnancy. In that case, the laboratory will compare your DNA sample with those taken from the embryo/unborn baby.

It would not be usual to offer testing to the wider family e.g. brothers and sisters to see if they were carriers, even if a mutation is known. A baby with ARPKD must inherit a faulty copy of the PKHD1 gene from both parents. It's not possible to test

someone from the general population to see if they are a carrier, or to prove they are not a carrier. The chance of someone without a family history being a carrier is very low.

What if I want to start a family?

When both parents are known carriers of a PKHD1 mutation, it is possible to carry out prenatal genetic testing [1]. This means testing the unborn baby to see if he or she has the mutated gene and therefore, has ARPKD.

It involves testing small samples of amniotic fluid or tissue from the placenta, together with ultrasound scans. It is better to discuss options before becoming pregnant because the genetic test will need to be performed in specialised laboratories.

You may find it helpful to request a referral to your local genetic centre for further information and help with deciding how to plan your family.

Is there more that people planning a family can consider?

Parents might also want to think about pre-implantation genetic diagnosis (PGD) [1]. This involves genetically testing embryos that are created through in vitro fertilisation (IVF) for the 2 PKHD1 mutations. Only embryos that do not have 2 copies of the mutated gene are implanted into the mother, meaning that a child born from that cycle of IVF will not have ARPKD.

PGD is specialised, and only offered in a few centres [2]. Funding may be available through the NHS under certain conditions and you can seek referral for a discussion from your local genetics centre. For more information see the [Human Fertilisation and Embryology Authority website](#).

Getting more information and support

- Read [ARPKD - a guide for parents](#) on the PKD Charity website
- NHS Choices has information on [genetic testing and counselling](#)
- PatientPlus has a [general overview of genetic testing](#)
- The Genetic Alliance has a lot of information on genetic testing, including a list of [NHS genetic services](#)
- The Human Fertilisation and Embryology Association has more information on [pre-implantation genetic diagnosis](#) (Tel: 020 7291 8200; email: enquiriesteam@hfea.gov.uk; Opening 9:00-17:00 Monday to Friday)

References

- a) Expert opinion of Dr Christine Patch
1. Sweeney WE, Avner ED. Polycystic kidney disease, autosomal recessive. Updated 6 March 2014. In: Pagon RA, Adam MP, Ardinger HH, et al., editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2016. <http://www.ncbi.nlm.nih.gov/books/NBK1326/>
 2. Bergmann C. ARPKD and early manifestations of ADPKD: the original polycystic kidney disease and phenocopies. *Pediatr Nephrol*. 2015;30:15-30. <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4240914/>
 3. Human Fertilisation and Embryology Authority. Preimplantation genetic diagnosis. Accessed May 2016. <http://www.hfea.gov.uk/preimplantation-genetic-diagnosis.html>

Published by the PKD Charity

Authors and contributors

Written by Christine Patch, PhD RN, Reader in Genomic Healthcare, King's College London.

With thanks to all those affected by ARPKD who contributed to this publication.

Disclaimer: We have made every effort to ensure that the information in this publication is correct. We do not accept liability for any errors or omissions. The law and government regulations may change. Be sure to seek local advice from the sources listed.



This information has been produced under the terms of The Information Standard. References used to produce and review the information are available on request.

IS Ref No: ARPKD.GCT.2017.V1.0

© PKD Charity 2017

Registered charity in England and Wales (1160970) and Scotland (SC038279)

First published February 2017

Due to be medically reviewed February 2020

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

For further copies of this information sheet or other PKD Charity information visit www.pkdcharity.org.uk

If you don't have access to a printer and would like a printed version of this information sheet, or any other PKD Charity information, call the PKD Charity Helpline on 0300 111 1234 (weekdays, 10.00am-4.30pm) or email info@pkdcharity.org.uk

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.