Genetic counselling and genetic testing in ADPKD

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

Which genes are involved in ADPKD?

Autosomal Dominant Polycystic Kidney Disease (ADPKD) 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 most genes, 1 from each of our parents.

ADPKD is caused by an abnormality – often called a mutation – in 1 of 2 genes called *PKD1* and *PKD2* [2]. In about 8 out of every 10 people with ADPKD, the mutation is in the *PKD1* gene [1].

To have ADPKD, a person must have at least 1 copy of the faulty gene. This can be inherited from a parent with the condition. But, in about 10 to 15 out of every 100 people with ADPKD, there is no known family history [3]. This may be due to a new gene mutation occurring for the first time in the patient. It could be for other reasons, including mild disease in an affected parent or lack of information.

If you have a copy of a faulty *PKD* gene, there is a 1 in 2 chance (50% chance) of passing it on to **each** child you have [1]. See Figure 1.

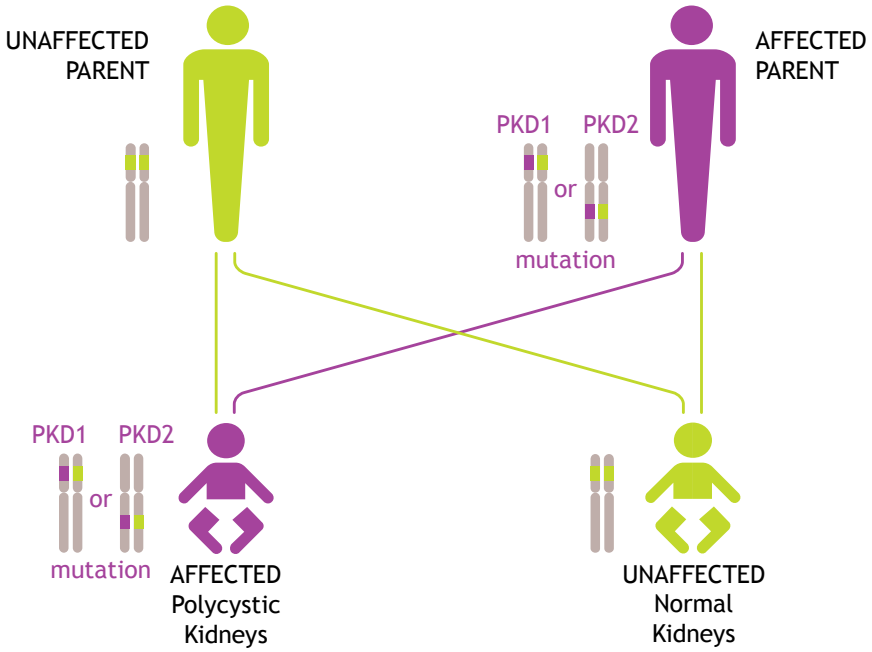

***Figure 1**: ADPKD inheritance diagram, for illustration only. The parent with ADPKD can be either a mother or a father, and ADPKD occurs in males and females, boys and girls, equally.*

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 can understand. It is not primarily psychological counselling, but aims to discuss options in a way that helps you or family members to understand and make the decisions that are right for you and them. Genetic testing is complicated in ADPKD, so an appointment may not always involve testing for the gene fault. Other tests such as ultrasound scans, tests of renal function, and blood pressure checks may be advised.

To have genetic counselling, you will need to be referred by your kidney specialist or your GP [a]. An appointment would normally be at your nearest NHS regional genetic centre [a]. As the centres cover large geographical areas, many centres may 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.

People with ADPKD tell us that they have different experiences of genetic counselling and testing, with some finding it easier to get the information than others. If you feel you're not getting the information you need, ask if you could be referred to a specialist.

Testing (particularly for alterations in *PKD1*) is technically challenging and understanding the results can be difficult. It's important that the doctor and the laboratory doing any testing are experts. Bear this in mind if you're considering private testing. Genetic testing may not be appropriate for everyone, but discussion with knowledgeable experts may help in your decision making.

When is genetic testing useful?

Genetic testing is not normally used to make a diagnosis of ADPKD if specialists are already sure you have ADPKD. If someone in your family has ADPKD and you or others are being checked to see if you may have it too, then an ultrasound of your abdomen (tummy) may be used. This is because cysts in the kidney can often be detected at an early stage by an ultrasound [2].

However, genetic testing to confirm whether you have a faulty *PKD* gene might be helpful in these situations [3]:

- to confirm whether or not you have ADPKD if you have no symptoms yet or specialists are uncertain of your diagnosis
- if you are considering donating a kidney to a family member with ADPKD (or if you have ADPKD and a family member is considering donating a kidney to you) [a]
- if you are considering having children, to help you make decisions

What are the pros and cons of genetic testing?

It can be difficult to decide whether you want to have genetic testing [3,4]. Talking to your genetic counsellor, friends and family may help. Below are some of the more common pros and cons to having genetic testing. However, your genetic counsellor will be able to help you explore the implications that are most relevant and important to you.

Possible pros of genetic testing include:	Possible cons of genetic testing include:
• You may get a definite answer as to the specific gene causing ADPKD in yourself or your family • Getting an answer on whether or not you have ADPKD genes can be a relief, whether the result is good or bad news • If you're found to carry a faulty gene, this might help to make decisions about your care or plans for starting a family • Identifying the gene responsible for ADPKD in your family may mean that other family members can be tested too. If they have the genetic fault they can be encouraged to have appropriate care. If they don't it may be a relief for them	• Waiting for test results can be a difficult and emotional time • Your test result might not be able to identify the specific fault in the ADPKD gene or may give an inconclusive result that cannot be interpreted (this happens for about 1 in 10 people) [5] • If you don't have any symptoms of ADPKD and a predictive test shows you have inherited the ADPKD gene, this may lead to a range of emotions (e.g. shock, anxiety about the future, anger) • Some family members might not want to have genetic testing, and feel uncomfortable about you having the test

Will having a genetic test affect my insurance premiums?

Some people have concerns about insurance and genetic testing. In the UK, there is currently an agreement between the Department of Health and the Association of British Insurers that they will not use predictive genetic test results to set premiums and cannot ask for the results of genetic tests [8]. If you have signs and symptoms of ADPKD, this may affect your insurance whether or not you have a genetic test.

Who can have genetic testing?

If there is reason to believe you may have ADPKD and the results could confirm your diagnosis or help you make choices about starting a family, testing is available on the NHS [3]. A specialist renal service or a specialist genetic service may request this test for you. However, testing is not available to the general population [3]. If someone in your family has ADPKD, you will only be able to have a predictive genetic test if a faulty gene has already been found in your family member with ADPKD [1a].

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, or cells from other tissues [a]. To test an unborn child, cells from the placenta or amniotic fluid can be tested [a]. If a special type of *in vitro* fertilisation (IVF) is being used, the embryo can be tested (see more on testing during pregnancy 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 2 ADPKD genes. Interpreting the information can take some time. The result of the initial test in a person with ADPKD could take a couple of months or longer to come [a].

If a faulty gene is found, then samples of DNA from family members can be checked too [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 2 genes that we know can cause ADPKD, and there are many different possible mutations that can occur in them [5]. If you have ADPKD and have genetic testing, there is about a 9 in 10 chance (90% chance) that it will find the fault in a *PKD* gene that has caused your condition [5]. But there is a 1 in 10 chance (10% chance) that the fault in your DNA is not detectable even though it is clear you have ADPKD [5].

If you have ADPKD, the possible results of a genetic test are:

- a gene fault is found in PKD1 or PKD2 that explains why you have ADPKD
- no faulty DNA code is found to explain your ADPKD
- an unusual piece of code is found in 1 of your PKD genes, but genetics specialists are not sure whether this is the cause of your ADPKD

Can the progression of my ADPKD be predicted by the specific gene fault I have?

Although PKD gene faults are thought to play a role in the development of ADPKD, other factors are involved too [2]. Even in the same family, those with ADPKD can get different symptoms, or experience problems at different ages [2,3]. So, it is not possible for specialists to predict exactly how your ADPKD is likely to progress from the gene fault you have.

However, in general, faults in the *PKD2* gene are associated with less severe ADPKD that is diagnosed at an older age and that progresses less quickly than faults in *PKD1* [2,3].

Should my children find out if they have ADPKD?

It is possible for children at risk of having ADPKD to have genetic testing at any age. In the past, children at risk of having inherited ADPKD were generally not tested for ADPKD, unless they showed symptoms (such as a urinary tract infection or blood in their urine).

The argument in favour of this approach is that making the diagnosis before symptoms show removes a child's right to choose and may cause them distress growing up. However, there is increasing evidence that some children with ADPKD develop high blood pressure – about one third have high blood pressure at night [6]. Because of this, many doctors now think it is useful to test children at risk of ADPKD for increased blood pressure and to look for signs of kidney problems using urine and blood tests [1].

Can I have a test during pregnancy?

If you or your partner has ADPKD, there is a 1 in 2 (50%) chance you will pass this on to each child that you have [1]. Very occasionally the routine ultrasound scan in a pregnancy will show the baby has cysts in their kidneys due to ADPKD [6,a]. Also, some families want the choice to test an unborn baby for ADPKD (prenatal diagnosis). This is only possible if a genetic mutation linked to ADPKD has already been found in a parent.

Testing in pregnancy involves testing small samples of amniotic fluid or tissue from the placenta, together with ultrasound scans [a]. Amniotic fluid is the liquid that

surrounds the baby in the womb. It is better to discuss options before becoming pregnant, because the genetic testing will need to be performed in specialised laboratories [a]. Referral to your local genetic centre may be helpful for further information and help with deciding which option is best for you.

What further help is available for people planning a family?

Parents might 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 ADPKD.

PGD is also specialised, and only offered in a few centres [7]. 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 about ADPKD in children on the PKD Charity website
- Read about How ADPKD is diagnosed on the PKD Charity website
- Read about Talking to children and young people about ADPKD 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. Simms R. Autosomal dominant polycystic kidney disease clinical review. BMJ 2016;352:i679 doi: 10.1136/bmj.i679
2. Harris PC, Torres VE. Polycystic kidney disease, autosomal dominant. GeneReviews® [Internet]. Last Updated 11 June 2015. http://www.ncbi.nlm.nih.gov/books/NBK1246/
3. KDIGO. Autosomal dominant polycystic kidney disease (ADPKD): Report from a Kidney Disease: Improving Global Outcomes (KDIGO) Controversies Conference 2015.
4. Genetic Alliance UK. Benefits and Risks of Genetic Testing. Last Reviewed 21 July 2016. http://www.geneticalliance.org.uk/information/services-and-testing/benefits-and-risks-of-genetic-testing/
5. GeneReviews. https://www.ncbi.nlm.nih.gov/books/NBK1246/#pkd-ad.Molecular_Genetics
6. Patil A, et al. Childhood Polycystic Kidney Disease. In: Polycystic Kidney Disease. Ed: Li X. Codon Publications, Brisbane, Australia https://www.ncbi.nlm.nih.gov/books/NBK373381/
7. Human Fertilisation and Embryology Authority. Preimplantation genetic diagnosis. Accessed May 2016 http://www.hfea.gov.uk/preimplantation-genetic-diagnosis.html
8. Department of Health. Agreement extended on predictive genetic tests and insurance. Updated 22 December 2014. https://www.gov.uk/government/publications/agreement-extended-on-predictive-genetic-tests-and-insurance

Published by the PKD Charity

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

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

First published February 2017
Due to be medically reviewed February 2020

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