Genetic testing in cardiomyopathy

Cardiomyopathy UK
the heart muscle charity

An introduction to the role of genetic testing

- Cardiomyopathy can be caused by changes in genetic material.
- Genetic assessments involve looking at someone's genes for changes (genetic testing), as well as looking at a family tree for a history of cardiomyopathy.
- Genetic testing can be important for both individuals with the condition, and their family.

What is genetic testing?

Genetic testing is looking at an individual's genetic material (DNA) to look for possible changes that can cause diseases. These 'changes' are referred to as 'variants' if they are different to the 'normal' genes, and as 'mutations' if these changes cause diseases or medical conditions (also known as 'disease-causing mutations' or 'disease-causing genes'). Testing also includes mapping a person's family tree, to see if genetic traits occur in other members of their family.

Genetic testing has various purposes. It can be used:

- in someone who has *been* diagnosed with a medical condition, to see if that condition is caused by a genetic mutation;
- in someone who has *not* developed or been diagnosed with a medical condition to see if they are *at risk* of developing the condition (if they carry the gene mutation that causes it);
- to see if an individual has *inherited* a condition from one of their parents (even if they currently have no symptoms); or
- to see if an individual is likely *to pass* on a condition to their children.

Genetic testing involves two parts:

- studying an individual's genetic material (DNA) by taking a blood test or a mouth swab, and looking for specific genes that are known to cause diseases or conditions; and
- looking at the individual's family history to see if other members of the family also have these diseases or conditions.

Genetic testing and cardiomyopathy

If you have a definite diagnosis of cardiomyopathy you may be offered genetic testing. This is particularly likely if other members of your family have the condition as well. Testing can be used to confirm whether your cardiomyopathy has a genetic cause (caused by a mutation in one of your genes).

First-degree relatives (FDR) are close blood relatives: parents, full siblings (sharing both parents) and children. (Grandparents, grandchildren, aunts and uncles, for example, are second-degree relatives).

What are the results of genetic testing?

Genetic testing will find either that:

- the disease-causing gene is identified. This is the case in around 25–60% of people who have genetic testing for cardiomyopathy. In this case, the test can be used to identify whether the person's first-degree relatives also have the same gene (as it is easy to check for this if you know which gene to look for); or
- no disease-causing gene is identified. However, this doesn't necessarily mean that the condition is not genetic, it could just be that the particular gene causing it was not found.

How are genetic variants and mutations found?

In genetic testing, an individual's genes are compared to a 'panel' of genes that are known to cause cardiomyopathy. This testing will show if there are variants, or mutations that may be disease-causing, in that individual's genes.

However, the gene panel only compares to variants and mutations that are currently known about: there are likely to be others that cause cardiomyopathy that we don't yet know about and cannot be tested for. Testing might also find a variant or mutation that isn't currently understood. Work to understand these variants and mutations will be needed in the future.

What is the role of genetic testing for me?

Genetic testing has various benefits, including the following.

- It can identify particular types of cardiomyopathy that require particular treatment or management. For these types of cardiomyopathy there may also be certain known risks that can be treated as soon as they are recognised. Examples of this include Fabry disease (a rare genetic condition carried on X chromosomes) and Noonan syndrome (an autosomal dominant condition).
- It can be useful if you are considering starting a family, as it can look at whether you may pass on the gene to your children.

Genetic testing can also be important for your family.

What is the role of genetic testing for my family?

Genetic testing can identify whether an individual's relatives have, or are at risk of having, the same condition (if they have the same gene mutation). This can be particularly important in relatives who currently don't have any symptoms of the condition, but who may develop symptoms in the future. If a relative is found to have the same gene mutation, they will be offered regular screening for symptoms so that symptoms can be detected, and treated, as soon as possible.

If your cardiomyopathy is confirmed to have a genetic cause, and the specific disease-causing gene has been found, your first-degree relatives will usually be offered genetic testing as well. Testing is offered only to first degree relatives in the first instance, because if they do not have the disease-causing gene, then other relatives will not need to be tested. If, however, they are found to also have the gene, other relatives may also be offered testing.

If your cardiomyopathy is not genetic, or no disease-causing gene is found, your first degree relatives will not be offered genetic testing (as there has been no gene found in you to compare to).

The results of any genetic testing will only be shared with your family members if you have given specific permission to do this.

The role of geneticists and genetic counsellors

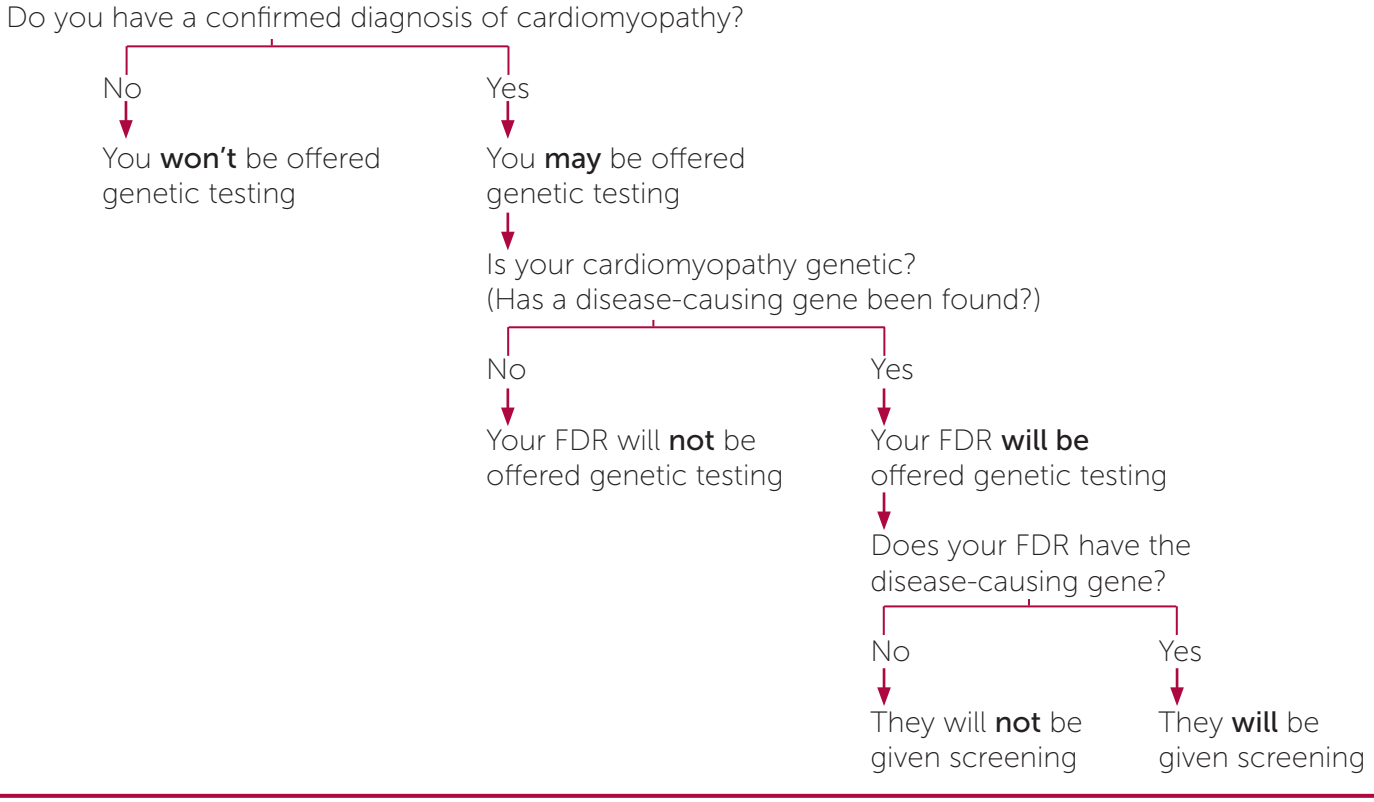
Geneticists are doctors who provide specialist services for people with genetic conditions. Some geneticists have a particular area of interest and expertise, for example in cardiology. Genetic counsellors have a degree in science and in genetic counselling, and work alongside geneticists within genetic services. If you are referred for genetic testing (also known as 'genetic counselling'), you will usually see a genetic counsellor. They will talk to you about the process of testing, how it works, what it might show, and what the results might mean. They will ask you about your condition and together you will create a family tree (see below). They will also talk to you about the possible emotional impact of genetic testing.

What is the impact of genetic testing?

Having genetic testing can be a worrying time. You may have concerns and questions, or conflicting feelings about it. Some people feel scared or guilty that they might have passed on the gene to their children, and worry about what this means. Genetic testing also looks at the family history and whether any family members have the condition, and this can sometimes be upsetting. But genetic testing can also be reassuring if it is found that someone hasn't passed on the condition, or that screening can be put in place to treat any symptoms early.

You can talk to your genetic counsellors about information and support for the emotional impact of preparing for and having genetic testing.

How genetic testing works



What are family trees and why they are helpful?

Family trees – also known as 'pedigrees' – are a way of mapping an individual's family and relatives.

The tree starts with the individual with the diagnosis of cardiomyopathy (called the 'proband'). The person's first degree relatives are added: parents, any siblings, and any children. On the tree it is noted whether any of the relatives are known to have cardiomyopathy as well. The tree might then be expanded to include other relatives (such as aunts and uncles, grandparents and grandchildren, and nieces, nephews and cousins) and whether they have cardiomyopathy.

Note: the further away you are from a relative, the fewer genes you share with them. For example, you are more similar to a brother or sister than to a cousin.

If my first-degree relatives have the gene, will they develop cardiomyopathy?

Because the genetics of cardiomyopathy is complex, having the disease-causing gene does not *necessarily* mean that someone will develop the condition, but it will determine the likelihood of them developing it (as they are more likely to develop the condition than if they don't have the disease-causing gene).

If they *do* develop cardiomyopathy, it may not affect them in the same way as it affects you. Different people can have different symptoms, and to different degrees (even if they are related). Symptoms often start in adulthood (rather than childhood) so it may depend on their age whether they have symptoms or not. If they are found to have the disease-causing gene, they can be screened for symptoms, and any symptoms found can be treated early.

Are 'genetic' and 'inherited' the same thing?

- 'Genetic' means that a condition is caused by a variant or mutation in an individual's genetic material.
- 'Inherited' means that a condition is passed from parent to child through their genes.

However, some genetic variants and mutations happen within an individual (while they are a developing embryo, or at some point during their life) and so they are not inherited on from their parent although they are still genetic. This is referred to as a 'de novo' or 'acquired' change in the person's genes.

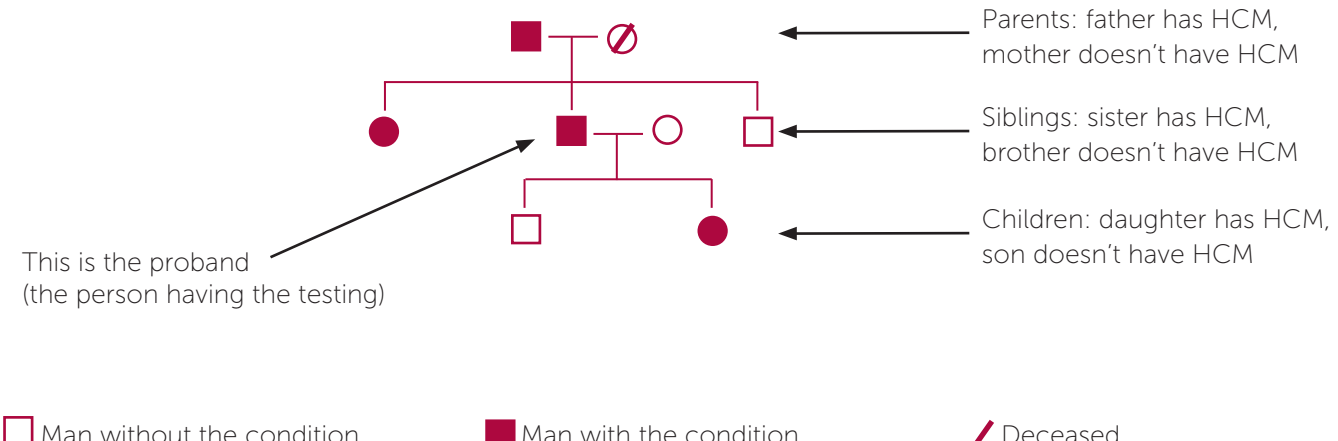
Can genes 'skip' generations?

No, genes can't skip generations. Genes, and the conditions they cause, have to be passed on from parent to child – they cannot appear in a grandparent and grandchild without at least one parent having it. However, genes are not always *expressed*. So, for example, a genetic condition might *appear* to affect a grandparent and a grandchild but not the parent. But at least one parent must *have* the disease-causing gene (in order to pass it on to their child) but they may not *express* that gene. In this way it appears to have missed a generation, but hasn't.

When a gene is present but not expressed, this is referred to as 'nonpenetrance'. This might happen due to different genetics backgrounds in different family members.

An example of a family tree

Using the example of a man with hypertrophic cardiomyopathy (HCM)



What is pre-implantation genetic diagnosis?

Pre-implantation genetic diagnosis (PGD) is a type of IVF (in vitro fertilisation) that tests the fertilised eggs for certain medical conditions before they are implanted into the mother's womb.

For people with certain types of cardiomyopathy with a genetic cause, this means that their fertilised eggs can be tested for the condition before they are implanted. Only eggs without the cardiomyopathy -causing gene (sometimes called 'non-carrier embryos') are then implanted.

PGD is still relatively new and is only available for some cardiomyopathies caused by specific genetic mutations. It is not yet widely available for all types of cardiomyopathy. If this is something that you are interested in, you can talk to your cardiologist about whether this is an option for you.

For more information visit the Human Fertilisation and Embryology Authority at www.hfea.gov.uk and search for 'PGD'.

Is 'genetic testing' the same as 'screening'?

'Genetic testing' and 'screening' are two different things. 'Genetic testing' is explained above.

'Screening' refers to a number of medical tests that are used to see whether someone is experiencing any symptoms that may indicate that they have cardiomyopathy. Screening usually includes:

- a physical exam – to check for any symptoms;
- an ECG (electrocardiogram) – to look at the electrical signalling in the heart; and
- an echo (echocardiogram) – to see the structure of the heart and how it is working.

If a family member has had genetic testing and is found to have the disease-causing gene, they will usually be offered screening to check whether they are having symptoms of the condition. If they don't have the disease-causing gene, they are no more likely to have cardiomyopathy than anyone in the general population and so there is no need for them to have routine screening.

What next?

You may be reading this factsheet because you, or someone you know, have been told that you may have cardiomyopathy. Or perhaps you have been recently diagnosed, and have been told that your condition might be genetic. This can be a difficult time and you may feel overwhelmed. You may have read information about the condition that has worried you. It is natural to have lots of questions, and you may want to talk to someone who understands.

We are here for you

At Cardiomyopathy UK we offer help and support for you and your family. We have information about each type of cardiomyopathy as well as diagnosis, treatment and lifestyle issues. Look on our website or call us for more information. Call our helpline to talk to our cardiomyopathy support nurses. We can put you in contact with other people affected by cardiomyopathy through our support groups, support volunteers and social media. Contact us for more about our services, or look online at www.cardiomyopathy.org

We are grateful to Professor Ruth Newbury-Ecob, Consultant Clinical Geneticist at University Hospitals Bristol NHS Foundation Trust for advising on and approving this factsheet.

Cardiomyopathy UK
the heart muscle charity

a: Unit 10, Chiltern Court, Asheridge Road, Chesham, Bucks HP5 2PX
t: 01494 791 224
helpline: 0800 018 1024
w: cardiomyopathy.org
facebook.com/cardiomyopathyuk
@cardiomyopathy