Cardiomyopathy UK
the heart muscle charity

Genetic Testing in Cardiomyopathy

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?

Humans are made from genetic material, called DNA. We all have lots of changes or 'variants' in our DNA. Most variants are harmless but some can be 'disease-causing'. Genetic testing is therefore used to look for disease-causing variants in our DNA. This is usually done by taking a blood or saliva sample. As part of this process, it is also helpful to draw a person's family tree, to see if other members of the family have the same or similar conditions.

Genetic testing can be offered for various purposes, such as:

- in someone who has been diagnosed with a medical condition, to try and identify a disease-causing variant;
- 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 have inherited the gene mutation that causes it);
- to see if an individual is likely to pass on a condition to their children.

Genetic testing and cardiomyopathy

If you have a definite diagnosis of cardiomyopathy you may be offered a genetic test. This is particularly likely if other members of your family have the condition as well. Scientists can check specific parts of our DNA, called our genes, to look for disease- causing variants in genes that can cause cardiomyopathy.

What are the results of genetic testing?

There are usually three possible outcomes in a genetic test:

- a disease-causing variant is identified. This is the case in around 25–60% of people who have genetic testing for cardiomyopathy. In this case, a test can be offered to that person's relatives to check if they have inherited the same variant.
- no disease-causing variant 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.
- there could be variant in other genes not currently known about. There may still be a chance that your relatives could develop the condition if a 'variant of uncertain significance' (VUS) is identified. This means that a variant in a gene has been found but that there is not currently enough evidence to be certain if the variant is harmless or disease-causing. This result could not be used to offer a genetic test to a person's relatives. Further work would be needed in the future to understand these variants.

What is the role of genetic testing for me?

Genetic testing has various benefits, including the following:

- It can identify 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 and Noonan syndrome.
- It can help an individual to understand the chance that their children or other relatives may develop the condition.

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 variant). 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 variant, they will be offered regular screening 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 variant has been found, your relatives will usually be offered genetic testing as well.

a: 75a Woodside Road, Amersham, Bucks, HP6 6AA
t: 01494 791224
helpline: 0800 018 1024
website & livechat: www.cardiomyopathy.org

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If no disease-causing variant is found in your test, your relatives would not be offered genetic testing, as there would be no known variant to test for in them.

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 usually have a degree in science and in genetic counselling, and work alongside geneticists within Clinical Genetics services.

If you are referred to Clinical Genetics, 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 next page). They will also talk to you about the possible emotional impact of genetic testing.

What is the impact of genetic testing?

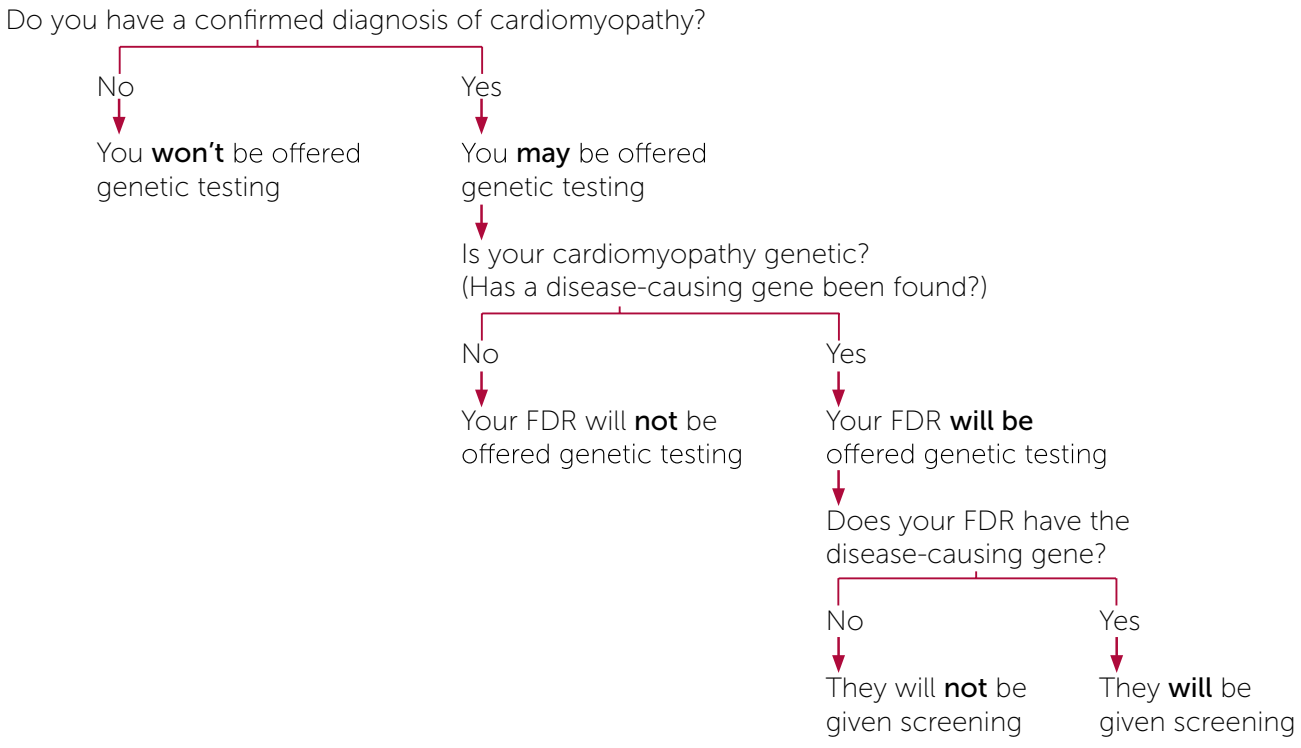
Having genetic testing can be a worrying time. You may have concerns and questions, or conflicting feelings about it. Some people feel scared or guilty that they might have passed on the variant to their children and worry about what this means. Genetic testing also looks at the family history and whether any family members have the condition and this can sometimes be upsetting. 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.

What are family trees and why they are helpful?

Family trees – also known as 'pedigrees' – are a way of drawing 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

How genetic testing works



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grandchildren, nieces, nephews and cousins) and whether they have cardiomyopathy. Note; the further away you are from a relative, the fewer variants you share with them. For example, you are more similar to a brother or sister than to a cousin.

If my relatives have the variant, will they develop cardiomyopathy?

Having a disease-causing variant increases the chance of developing cardiomyopathy at some point in that person's future, but this does not mean that everyone who inherits the disease-causing variant will definitely develop it. 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 variant, they can be screened for symptoms and any symptoms found can be treated early.

Can gene variants 'skip' generations?

No, gene variants can't skip generations. Gene variants 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 that parent must have the disease- causing gene variant in order to have passed it on to their child. This makes it appear as though the condition has skipped a generation but the gene variant has not and that parent may still develop cardiomyopathy in the future.

In some cases, a gene variant causing cardiomyopathy will not have been inherited from either parent and the variant will have started in that individual for the first time in their family. This means that the older generations in that family would not have the gene variant, but it could still be passed on to the next generation.

What is pre-implantation genetic diagnosis?

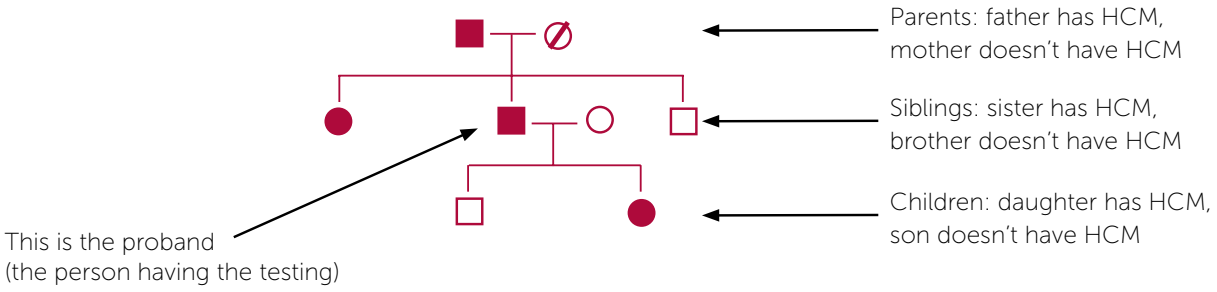
Pre-implantation genetic diagnosis (PGD) is a type of IVF (in vitro fertilisation) that tests the fertilised eggs for certain medical conditions before they are implanted into the mother's womb.

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 variant are then implanted.

PGD is very technical and highly regulated and it may not be possible to offer this to all individuals with, or at risk of cardiomyopathy. Funding may be available if couples meet certain strict criteria. If this is something you wish to explore, your Clinical Genetics service will be able to advise further.

An example of a family tree

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



Key:
- Man without the condition
- Woman without the condition
- Man with the condition
- Woman with the condition
- Deceased

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

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 variant, they will usually be offered screening to check whether they are having symptoms of the condition. If they don't have the disease-causing variant, 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

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