



# My46 Trait Profile

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## Dilated cardiomyopathy

*Dilated cardiomyopathy is a condition in which the heart muscle becomes weakened and enlarged, and cannot pump blood effectively. It can be caused by mutations in any one of many different genes, by environmental factors, or a combination of these.*

### Characteristics of Dilated cardiomyopathy

Dilated cardiomyopathy (DCM) is a condition in which the heart muscle weakens, leading to enlargement of the heart's lower left chamber (left ventricle) and decreased blood pumping ability (low ejection fraction). DCM may be silent, that is, individuals may not have any symptoms for months or years. When the disease progresses develop symptoms, that include those associated with heart failure (such as fatigue, shortness of breath, fluid retention) and arrhythmias or irregular heart beats (such as palpitations, dizziness, or sudden onset of black out spells). The typical age of onset is between ages 40-60 years old, although childhood and late onset DCM has been (less frequently) observed. Some cases present during or soon after pregnancy, which is known as peripartum or pregnancy associated cardiomyopathy (PPCM/PACM).

DCM can have many causes. The most common cause is blocked coronary arteries (coronary artery disease). Other less frequent causes include infections, exposure to certain chemotherapy drugs (such as Adriamycin), as well as amphetamine and opiate use, among others. In about 40%-50% of cases, the cause cannot be identified. In these cases, the term idiopathic DCM (IDC) is used. (For the purpose of this Trait Profile, DCM is used when referring to IDC.)

Approximately 20% of DCM is familial (i.e., it is passed on from parents to their children). When DCM is inherited, the term familial dilated cardiomyopathy (FDC) is used.

### Diagnosis/Testing

DCM is diagnosed by echocardiogram (ultrasound of the heart) or cardiac magnetic resonance imaging (MRI). In affected individuals, results from these tests show an enlarged left ventricle and a low ejection fraction. These heart findings can be present in the absence of symptoms.

When DCM is diagnosed, the cause must be identified in order to establish a management plan. Additional testing such as a coronary angiogram should be performed to rule out coronary artery disease. Other test results and past medical history will also be evaluated to rule out other causes such as infections and drug exposures.

When coronary artery disease and other acquired causes are ruled out, a genetic cause is more likely. Identifying a DCM-causing gene change or mutation can help in the management of at-risk relatives. Gene mutations in over 30 different genes have been found to cause DCM/FDC. A limitation of the currently available genetic testing is that can identify a mutation in only 40% of cases. For this reason, we know that there must be yet-to-be identified genes. Ongoing research aims to find those genes.

Not all individuals who have a DCM-causing mutation show signs of DCM. This is known as reduced penetrance. Although more research is necessary, preliminary studies suggest that penetrance for autosomal dominant DCM may be almost 90% (9 of 10) by adulthood. This means that out of 10 people with a DCM-causing mutation, 9 will develop DCM and one will escape the condition. We also know that individuals with the same gene mutation, even if members of the same family, may not display the same age of onset or severity. Therefore, a positive genetic result in an unaffected person can only predict that he or she is at increased risk for DCM. In these cases, frequent follow up will be

indicated. It cannot, however, predict, if, when or how symptoms will occur.

## **Management/Surveillance**

Management of DCM includes medications (ACE inhibitors and beta blockers) and in some cases, intracardiac defibrillator/pacemaker (devices that regulate heart rhythm) for people at risk for serious arrhythmias. For severe DCM or DCM that is not responsive to therapy, placement of a left ventricular assist device (a mechanical blood pump) and heart transplantation are indicated. Pregnancy is not indicated in women with DCM or who have been diagnosed with PPCM/PACM.

Because DCM can be familial and genetic mutations have been identified in a proportion of cases, a genetic evaluation, including family history and genetic counseling/testing is indicated for people with DCM. Periodic cardiac evaluation (every 3-5 years beginning in childhood) by echocardiogram, electrocardiogram and physical examination is indicated for all first-degree relatives (parents, children, siblings) of people with DCM/PPCM/PACM. If genetic testing is performed in the family member with DCM and a DCM-causing mutation is identified, testing for the family mutation is offered to at-risk relatives to help predict who may develop DCM. Family members who are found to carry the family mutation should undergo more frequent periodic cardiac screening (yearly in childhood; every 1-3 years in adults). Periodic screening is normally not indicated for those in whom the family mutation is not found.

## **Mode of inheritance**

In each family in which DCM is known to be inherited, DCM may be inherited in one of four patterns of inheritance: autosomal dominant, autosomal recessive, X-linked recessive and maternal mitochondrial. They are explained below.

**Autosomal dominant inheritance:**

DCM is most often inherited in an autosomal dominant pattern. This means inheriting one mutation increases the chance to develop DCM. The mutation can be inherited from an affected parent or it can occur brand new (de novo) in an affected child.

**Autosomal recessive inheritance:**

Autosomal recessive inheritance accounts for a small proportion of DCM. This inheritance pattern means that an individual has to inherit two mutations (i.e., one from each parent) to be affected. If both parents are carriers of a mutation they have a 1 in 4 (25%) chance with each pregnancy of having a child with the condition.

**X-linked recessive inheritance:**

While a proportion of DCM can be inherited in an X-linked recessive pattern of inheritance, actual figures for X-linked DCM are unknown. The gene mutations causing this type of inheritance are found on the X chromosome. An X-linked recessive pattern means that in females, both copies of a gene (i.e., one on each X chromosome) must have a change or mutation, whereas in males, only one copy of a gene must have a mutation to be affected. A female with a mutation in one copy of a gene on the X chromosome is said to be a “carrier” for an X-linked condition, and is typically not affected.

**Maternal mitochondrial inheritance:**

Mitochondria are structures inside the cells that are responsible for generating the energy that is needed to perform daily activities. Humans also carry DNA in mitochondria, and mutations in mitochondrial DNA can result in DCM. The proportion of DCM inherited in a maternal mitochondrial pattern is unknown, but it is thought to be more frequently associated with childhood-onset DCM along with other clinical issues outside the cardiovascular system.

Humans inherit mitochondria only from their mothers. Therefore, in maternal mitochondrial inheritance, the affected mitochondria are passed from mothers (who may or may not show symptoms) to children of either sex. Because males do not transmit mitochondria, a male with a maternal mitochondrial disorder generally cannot pass it to his children. Mitochondrial DNA mutations can also occur brand new (de novo) in an affected individual. When de novo, parents and siblings of an affected person are not at increased risk, but if the affected person is a female, her children are at increased risk.

Inside each cell, there is a mixture of mutated mitochondrial DNA and normal mitochondrial DNA. Symptoms are more likely when the mixture contains more mutated mitochondrial DNA. The number of mitochondria with mutated versus a normal mitochondrial DNA is variable across different body tissues (blood, brain, heart, skin, hair, etc.). Moreover, the number of mutated versus normal mitochondrial DNA can change dramatically when passed from mothers to their children.

## Risk to family members

The risk to family members depends on the pattern of inheritance.

### Autosomal dominant inheritance:

The risk to family members depends on whether or not the individual with DCM has a parent affected with DCM. If a parent also has the condition, the risk of having a child with DCM is 50% with each pregnancy. If a parent does not have DCM, the risk of other siblings being affected is very low.

### Autosomal recessive inheritance:

Parents of a child with DCM are carriers of DCM. If a sibling of a child with DCM is unaffected, he/she has a 66% (or 2/3) chance of being a carrier of DCM.

### X-linked recessive inheritance:

If a father is affected with DCM, his daughters will be carriers of DCM and his sons will be unaffected. If a mother is a carrier of DCM, each daughter has a 1 in 2 chance (i.e., 50%) of being a carrier and each son has a 1 in 2 chance (i.e., 50%) of being affected with DCM.

### Maternal mitochondrial inheritance:

Maternal mitochondrial inheritance is associated with a significant degree of variability. Because of this remarkable variability, it can be difficult to provide inheritance risk estimates for people with a maternal mitochondrial condition; however specific information may be available depending on the identified mitochondrial DNA mutation.

## Special considerations

None

## Resources

Familial Dilated Cardiomyopathy Research Project

<http://www.fdc.to/>

American Heart Association

[http://www.heart.org/HEARTORG/Conditions/More/Cardiomyopathy/Dilated-Cardiomyopathy\\_UCM\\_444187\\_Article.jsp](http://www.heart.org/HEARTORG/Conditions/More/Cardiomyopathy/Dilated-Cardiomyopathy_UCM_444187_Article.jsp)

The Cardiomyopathy Association

<http://www.cardiomyopathy.org>

Children's Cardiomyopathy Foundation

<http://www.childrenscardiomyopathy.org>

Cardiac Inherited Diseases Group

<http://www.cidg.org/webcontent/cidg/Home/tabid/53/Default.aspx>

Genetics Home Reference: Dilated Cardiomyopathy

<http://www.ncbi.nlm.nih.gov/books/NBK1309/>

## References

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Hershberger RE, Kushner JD, Parks SB. (Updated 29 March 2009). Dilated Cardiomyopathy Overview. In: GeneReviews at GeneTests Medical Genetics Information Resource (database online). Copyright, University of Washington, Seattle. 1997-2013. Available at <http://www.ncbi.nlm.nih.gov/books/NBK1309/>. [Accessed 04/15/2013].

[Posafalvi, A. et al. \(2012\).](#) "Clinical utility gene card for: dilated cardiomyopathy (CMD)." *European Journal of Human Genetics* e1-e5.

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