

About GeneDx

GeneDx is a highly respected company that specializes in genetic testing for rare inherited disorders. Two scientists from the National Institutes of Health (NIH) founded the company in the year 2000 to address the needs of patients and clinicians concerned with rare inherited disorders. Currently, GeneDx offers testing for more than 350 rare Mendelian disorders, using DNA sequencing and deletion/duplication analysis of the associated gene(s). GeneDx also offers oligonucleotide microarray-based testing for detecting chromosomal abnormalities, testing for autism spectrum disorders, and testing for various inherited cardiac disorders. At GeneDx, our technical services are matched by our scientific expertise and customer support. Our growing staff includes more than 12 experts in molecular and clinical genetics as well as 12 genetic counselors who are just a phone call or email away. We invite you to visit our website www.genedx.com to learn more about us and the services we offer.

www.genedx.com



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Dilated Cardiomyopathy

A Guide for Patients

Dilated Cardiomyopathy

What is dilated cardiomyopathy?

Dilated cardiomyopathy (DCM) is a disease of the heart muscle. In DCM, one of the pumping chambers of the heart (i.e., the left ventricle) becomes enlarged (dilated). This dilation reduces the heart's ability to pump blood efficiently, which can lead to heart failure or cardiac arrest in severe cases. DCM affects individuals of both sexes and all ethnicities. It is more commonly diagnosed in middle-aged adults.

What are the symptoms of DCM?

Many patients with DCM are asymptomatic. However, for those who are symptomatic, the warning signs can include any of the following:

- Shortness of breath
- Dizziness
- Fainting
- Palpitations
- Chest pain
- Exercise intolerance or fatigue
- Swelling in legs, ankles, and feet
- Abdominal swelling
- Sudden weight gain

What causes DCM?

The causes of dilated cardiomyopathy are numerous, with the most common being ischemia (a lack of blood supply to the heart muscle, caused by coronary artery disease and heart attacks), valvular disease (heart valve problems), toxins (e.g., alcohol), substance abuse (e.g., cocaine), metabolic or infectious (e.g., viral) agents, pregnancy, and genetic causes. Many cases of dilated cardiomyopathy are described as idiopathic (with unknown cause), and among these idiopathic cases, 50 % are familial or genetic.

How is DCM diagnosed?

For patients who are asymptomatic, DCM may first be detected during a routine physical exam or by an electrocardiogram (ECG). However, physicians usually diagnose DCM using imaging techniques such as echocardiography

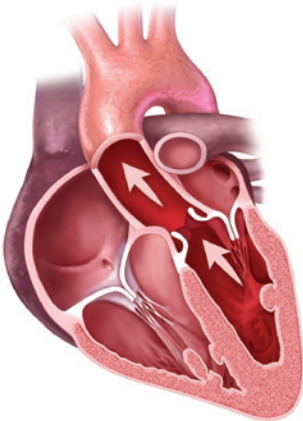
(a sonogram imaging of the heart with sound waves) or cardiac magnetic resonance imaging (MRI). A patient's medical and family histories are essential in evaluating genetic causes of DCM. Genetic testing can be used to confirm the clinical diagnosis.

How is DCM treated?

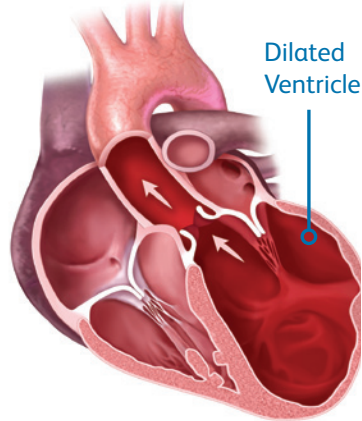
The clinical management of DCM depends on the severity of the disease and the patient's symptoms. Initially, therapy includes medications such as ACE inhibitors, angiotensin receptor antagonists, beta-blockers, aldosterone antagonists, digoxin, and diuretics. Some patients require surgery to have a pacemaker or defibrillator placed. For patients whose symptoms do not respond to these treatments, a heart transplant can be an option. Physicians usually recommend lifestyle adjustments such as alcohol avoidance, 2-g/day salt restriction, fluid restriction, endurance-type exercise for 30 minutes every day, and daily weight recordings. Family members at risk for DCM may be closely monitored using echocardiograms and ECGs.

● Dilated Cardiomyopathy

Normal Heart



Dilated Cardiomyopathy



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Genetic Testing for Dilated Cardiomyopathy

How is genetic testing for DCM performed?

The DCM genetic test is a blood test ordered by a physician. GeneDx will extract DNA and analyze it by specifically searching for mutations in the genes that are associated with DCM. After the test is complete (in about six to eight weeks), the results are sent to the physician who ordered the test. The physician will explain the test results to the patient.

What makes the GeneDx test different from others?

GeneDx offers a comprehensive genetic test for DCM. Enlargement of the heart, which is the key finding in DCM, can also be caused by certain multisystem disorders involving the heart muscle. Distinguishing the different genetic causes of enlargement of the heart is extremely important, as the treatment for DCM may differ depending on the cause. GeneDx also performs *free* testing for family members if it will help interpret a patient's result. For instance, if it is unclear if a genetic variation is actually causing DCM in the patient, another family member with DCM will be tested for free. In such circumstances, GeneDx will also evaluate a large panel of normal individuals to determine if the genetic variant is seen in normal individuals.

Who should undergo genetic testing for DCM?

- A patient with a clinical diagnosis of DCM
- Family members of a patient who has a disease-causing mutation (although these individuals need only targeted testing for the mutation that the patient has)

How is genetic testing for DCM helpful?

- Can confirm the clinical diagnosis of DCM, especially when the diagnosis is clinically uncertain
- Can identify family members who are at risk of developing DCM
- Can aid in the making of informed family-planning decisions

How long does it take to complete the genetic test?

It usually takes six to eight weeks to complete the test (from the time the lab receives the blood sample to the time your physician receives the results). It can take longer if GeneDx has to study clinically normal individuals or test family members to interpret results.

What type of test results can I expect?

Three types of results are possible:

- A **positive result** indicates that we identified a disease-causing mutation in one of the genes associated with DCM. This finding confirms the diagnosis of DCM and provides valuable information to family members. All first-degree relatives (i.e., children, siblings, parents) of the patient can then be offered diagnostic or predictive genetic testing to determine their individual risks of developing DCM. If a family member has the mutation but is asymptomatic, he or she is at risk for DCM and should be monitored closely. If a family member does not have the mutation, he or she is not considered to be at increased risk for DCM based on genetic causes.
- A **negative result** indicates that we did not identify a disease-causing mutation in one of the genes associated with DCM. However, this does not rule out DCM or a genetic cause of DCM, and the patient should be managed according to his or her clinical symptoms. A possible reason for a negative result is that the patient has a mutation in a gene or part of a gene that is not included in the panel of genes that we test. When a result for a patient with DCM is negative, predictive genetic testing of family members will not be informative and is therefore not warranted. Careful review of the patient's family history may help determine if his or her disease is hereditary, so that family members can have their hearts monitored by their doctors.
- A **variant of unknown significance (VOUS) result** indicates an inconclusive finding. This happens when we find a new DNA abnormality (i.e., one that has never been seen before) but it is unclear if that change causes DCM. A VOUS report is sent only after GeneDx has confirmed that no individual in a large panel of normal controls carries the variant. To further clarify the clinical significance of the VOUS, it may be helpful to test the patient's family members. If an affected relative also has the variant, it is more likely that the variant causes disease. The more affected family members who carry the VOUS, the greater the likelihood that the VOUS is responsible for DCM in that family.

How will I learn my test results?

Your physician will share your results with you and discuss them in the context of your health care.

Will my insurance cover this test?

GeneDx accepts all commercial insurance. GeneDx will bill your insurance company and appeal for payment. Currently, GeneDx does not accept Medicare or Medicaid. For more information, please visit our website at:

www.genedx.com/cardiology or call us at 301-519-2100, x 6727.

What if I do not have insurance?

For patients who do not have health insurance or cannot afford to pay the full cost of testing, GeneDx provides a generous financial assistance program that includes a significantly discounted price. For more information, call us at 301-519-2100, x 6106.

Do my family members need to be tested?

If you have a disease-causing mutation in one of the DCM genes, your family members can be tested for that specific mutation. If you have a VOUS, GeneDx may ask to test your family members at no additional cost if it is necessary to interpret your test results.

Does GeneDx test family members?

Yes, GeneDx offers mutation-specific testing (for an identified familial mutation) for family members of any patient who has been shown by GeneDx to have a genetic mutation. For more information, please call one of our genetic counselors at 301-519-2100.

How does testing of family members differ from full DCM panel testing of a patient?

The first DCM patient in a family to be tested typically requires analysis of all 27 genes in the DCM panel. Once a disease-causing mutation(s) is identified in a specific gene(s), family members are tested only for that specific mutation. The cost and turnaround time are significantly reduced when family members get tested only for specific mutation instead of the full gene panel.

Does GeneDx perform prenatal testing?

Yes, GeneDx can provide prenatal testing for families that have had previous testing at GeneDx for a known familial mutation in any gene. For more information, please call one of our genetic counselors at 301-519-2100.

Can my health insurer or employer discriminate against me based on my test results?

No, The Genetic Information Nondiscrimination Act of 2008, also referred to as GINA, is a federal law that protects Americans from discrimination by health insurance companies and employers based on their genetic information. The President signed the act into federal law on May 21, 2008. The parts of the law relating to health insurers took effect on May 2009, and those relating to employers took effect on November 2009. **However, this law does not cover life insurance, disability insurance, or long-term care insurance.** For more information, please visit <http://www.genome.gov/10002328>.

Where can I find more information?

You can find more information at the following websites:

- GeneDx cardiology page:
www.genedx.com/cardiology
- Cardiomyopathy Association, a patient organization focusing on a variety of cardiomyopathies, including DCM:
www.cardiomyopathy.org
- Hypertrophic Cardiomyopathy Association, a patient organization:
www.4hcm.org
- Children's Cardiomyopathy Foundation, a patient organization for children with cardiomyopathy:
www.childrenscardiomyopathy.org
- Gene Reviews, a database of genetic diseases:
www.geneclinics.org
- National Society of Genetic Counselors, an organization that can help you find a counselor near you:
www.nsgc.org