FAMILIAL CARDIOMYOPATHY

GENETIC TESTING

Cardiomyopathy is an abnormal change in heart muscle. Cardiomyopathies may cause heart muscle to become thick and stiff or stretched out (dilated) and weak. These changes may cause the heart to be less effective at pumping blood, or they may disrupt the electrical signals that control the heartbeat. There are a number of cardiomyopathies that can run in families, including the following[1,2]:

- **Dilated cardiomyopathy (DCM)**
- **Hypertrophic cardiomyopathy (HCM)**
- **Arrhythmogenic right ventricular dysplasia/ cardiomyopathy (ARVD/C)**
- **Restrictive cardiomyopathy (RCM)**

People with cardiomyopathy are at increased risk for the following health conditions[1-3]:

- Irregular heart rhythms (arrhythmias)
- The formation of abnormal blood clots that could travel to the lungs or brain, where they may block the flow of blood
- Heart failure (reduced ability of the heart to pump blood)
- Sudden cardiac arrest (a condition in which the heart stops beating)

Familial cardiomyopathies can affect people of all ages. Some people will have no symptoms at all or only mild symptoms and will not need treatment. Others may have a disease that starts at a young age, quickly worsens, and causes severe symptoms and complications.[1-6]

Familial cardiopathies may be managed with[1,4-6]:

- Medications.
- Surgical placement of a device called an implantable cardioverter defibrillator (ICD) that can send an electric current to the heart to bring it back into a normal rhythm.
- Lifestyle changes.

What causes familial cardiomyopathies?

Familial cardiomyopathies are caused by abnormal changes in certain genes. Genes are found in every cell in your body. They carry the instructions for making proteins that control how each of your cells work. Genes can undergo abnormal changes (called mutations) that may cause cells to stop working the way they should. Gene mutations may result in health conditions, and they may be passed from parent to child (inherited).

Mutations in many different genes have been linked with familial cardiomyopathies. Not all of the gene mutations that cause these disorders have been identified.

How are familial cardiomyopathies inherited?

Normally, each of your cells carries 2 copies of all your genes. You inherit 1 copy of a gene from each of your parents. The gene mutations that cause familial cardiomyopathies are passed from parent to child in different ways, including the followng[1,3-6]:

- Autosomal dominant inheritance, the most common way in which familial cardiomyopathies are passed from parent to child. This means a child only needs to inherit 1 copy of a gene mutation in order to be affected with a familial cardiomyopathy.
- Autosomal recessive inheritance, which means a child must to inherit 2 copies of a gene mutation (1 copy from each parent) in order to be affected with a familial cardiomyopathy.
- X-linked inheritance. In these cases, the gene mutation is located on the X chromosome, which is one of the 2 chromosomes responsible for determining whether a person is male or female. (Females have two X chromosomes, and males have one X and one Y chromosome.) A female who inherits 1 copy of a gene mutation may have a mild form of cardiomyopathy. A male who has a mutation in his only X chromosome will generally have a more severe form of cardiomyopathy.

How are familial cardiomyopathies diagnosed?

Cardiomyopathies have specific signs that can be observed by a doctor during a routine physical exam, such as abnormal heart sounds, an abnormal heart rate and rhythm, abnormal sounds in your lungs, or swelling in your legs, ankles, feet, or abdomen.

A heart specialist (cardiologist) may perform exams and tests that will provide information about your heart, such its size and shape and how well it is working, the electrical activity in your heart, the regularity of your heart rhythm, and how well blood is able to flow through the vessels in your heart.

Information about your family medical history will be an important part of your medical workup. If other members of your family have cardiomyopathy, heart disease, or high blood pressure, strokes or clotting disorders, or died of sudden cardiac arrest, your doctor may recommend a genetic test called gene sequencing to find out if you have a familial cardiomyopathy.

What is gene sequencing for familial cardiomopathy?

Gene sequencing for familial cardiomyopathy is a procedure that reads the instructions (DNA) that make up certain genes known to cause the disorder. This test, which is performed on a sample of blood, is a way to identify the presence of altered genes in a person's cells, which can help a doctor[3-6]:

- Confirm a diagnosis of a familial cardiomyopathy.
- Determine which type of cardiomyopathy is present.
- Identify close relatives of an affected person who also carry a familial cardiomyopathy gene mutation and could benefit from regular monitoring of their heart health or treatment to reduce their risk for stroke, heart failure, and sudden cardiac arrest.

What possible results of gene sequencing can be reported, and what might they mean?

- **Negative:** No mutations were found in the genes tested. A negative result may reduce the chance that you have a familial cardiomyopathy but cannot completely rule it out.
- **Positive:** A mutation was found in 1 or more f the genes tested, confirming the diagnosis of a familial cardiomyopathy.
- **Variant of unknown significance:** A mutation was found in the genes tested that either has not been reported before, or previous reports about the mutation are conflicting. Therefore, it is unclear if the mutation is the cause of your signs and symptoms. Genetic testing of your family members may provide more information. If all affected family members have the same mutation, then it is likely to be linked to the inherited disorder. If some affected family members do not have the mutation, it is less likely to be linked to the disorder.

Gene sequencing test results should be combined with clinical findings and reviewed by a heath professional who specializes in medical genetics.

Where can I find more information?

If you have questions or want more information about genetic testing for familial cardiomyopathy, ask your doctor or genetic counselor. You may search for a genetic counselor in your area using an online address book provided by the National Society of Genetic Counselors at **www.nsgc.org**.

Other information resources include:

- American Heart Association
  Telephone: 800-242-8721
  Home page: **www.heart.org**
- Genetics Home Reference
  Home page: **http://ghr.nlm.nih.gov**
- National Heart Lung and Blood Institute
  Telephone: 301-592-8573
  Home page: **www.nhlbi.nih.gov**

Note: This material is provided for general information purposes only. It is not intended as a substitute for medical advice and/or consultation with a physician or technical expert.

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