FAMILIAL ARRHYTHMIA

GENETIC TESTING

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What are familial arrhythmias?

An arrhythmia is an irregular heart rhythm. Arrhythmia may increase your risk for stroke and sudden death due to cardiac arrest (a condition in which the heart stops beating). Symptoms of arrhythmia may include[1-3]:

- **Fainting**
- **Rapid heartbeat (palpitations)**
- **Dizziness**
- **Shortness of breath**

There are a number of arrhythmia disorders that tend to run in families. These include the following[1-4]:

- Familial atrial fibrillation
- Long QT syndrome (LQTS)
- Catecholaminergic polymorphic ventricular tachycardia (CPVT)
- Aarrhythmogenic right ventricular dysplasia/ cardiomyopathy (ARVD/C)
- Brugada syndrome (BrS)

In each of these conditions, the cause of arrhythmic events is different, and the long-term outlook for the health of a person affected by one of these conditions depends on the type and severity of the arrhythmia.[1,4,5] The age at which heart rhythm problems start varies by condition. In some cases, arrhythmias occur during early childhood or adolescence.[1-3,4,6]

Familial arrhythmias may be managed with[1,4]:

- 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 arrhythmias?

Familial arrhythmias 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 several different genes have been linked with familial conditions that cause arrhythmias.

- The gene defects that cause familial atrial fibrillation, long QT syndrome, CPVT, and Brugada syndrome affect the production of proteins that play a role in the heart's ability to maintain a normal rhythm. When those proteins don't work the way they should, heart rhythm irregularities and symptoms of arrhythmia result.
- The gene defect that causes ARVC/D affects the production of proteins found in heart muscle cells. When these proteins don't work the way they should, structures that connect heart muscle cells to one another don't do their job, and the cells separate from each other and die. Scar tissue and fat build up in the damaged areas of the heart, preventing the heart from pumping blood effectively. The scar tissue and fat buildup also disrupts electrical signals that control the heartbeat, which can result in arrhythmias.

How are familial arrhythmias 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. Familial arrhythmias are typically inherited in an autosomal dominant manner.[1-4,6] That means a child only needs to inherit 1 copy of a gene mutation (from 1 parent) to be affected with one of these conditions.

In rare cases, mutations that cause familial arrhythmias are inherited in an autosomal recessive manner. This means a child needs to inherit 2 copies of the mutation (1 from each parent) to be affected.[1,2,4,6]

How are familial arrhythmias diagnosed?

Arrhythmias have specific signs that can be observed by a doctor during a routine physical exam, such as abnormal heart sounds and/or an abnormal heart rate and rhythm. A heart specialist (cardiologist) may perform exams and tests that will provide information about the electrical

activity in your heart, the regularity of your heart rhythm, and events that cause that rhythm to become irregular.

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

What is gene sequencing for familial arrhythmias?

Gene sequencing for familial arrhythmias is a procedure that reads the instructions (DNA) that make up the genes known to play a role in the development of these disorders. This tes, 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[1,4-6]:

- Confirm a diagnosis of familial atrial fibrillation, long QT syndrome, CPVT, ARVC/D, or Brugada syndrome.
- Identify events that are likely to cause arrhythmias, which may be specific to the underlying genetic cause of the disorder.
- Identify close relatives of an affected person who have a familial arrhythmia gene mutation and could benefit from regular monitoring of their heart health or treatment to reduce the risk of stroke and sudden cardiac arrest.
- Determine the best way to manage arrhythmia.

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 a person is affected with a familial arrhythmia but cannot completely rule it out.
- **Positive:** A mutation was found in 1 or more of the genes tested, confirming the diagnosis of a familial arrhythmia.
- **Variant of unknown significance:** A mutation was found in the genes tested that either has not been reported before or previous reports are conflicting. Therefore, it is unclear if the mutation is the cause of the person's signs and symptoms. Genetic testing of 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 arrhythmias, 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.

References

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