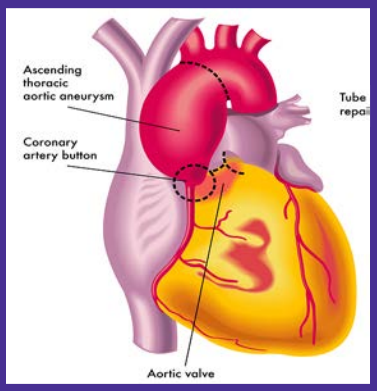
Genetic testing for Heritable Thoracic Aortic Disease (HTAD)



Heritable thoracic aortic diseases (HTAD) are conditions that run in the family and affect the aorta, the largest blood vessel in the body. The aorta goes from your heart to your lower abdomen and carries oxygen-rich blood to all parts of your body. The thoracic aorta is the upper part of the aorta located in your chest. The lower part of the aorta is called the abdominal aorta.

Weakened tissue in the aortic wall can make the aorta bulge and widen. This is called an **aneurysm**. The pressure from constant blood flow can stretch an aneurysm slowly over time. HTAD and aortic aneurysms make people more likely to have **aortic dissection**. This is a rare but life-threatening event when the layers of the aortic wall separate from each other, and emergency surgery is needed. Aortic aneurysms can sometimes lead to dissection, but aortic dissections can also happen without aneurysms.

What causes aortic aneurysms and dissections?

There are many common things that can lead to an aortic aneurysm or dissection, including high blood pressure, age, smoking, hardening of the arteries, trauma (like a car accident), and infection and inflammation of the blood vessels (vasculitis). There are also genetic causes. Changes in genes can cause weak aortic walls that are prone to stretching. Thoracic aortic disease (TAD) is more often due to genetic causes than abdominal aortic disease. A genetic cause is even more likely when there is a family history of TAD.

How is a thoracic aortic aneurysm diagnosed?

Thoracic aortic aneurysms can get larger over time. As the aneurysm grows, most people have no symptoms, but rarely a person may have chest pain, back pain, hoarseness, cough, and/or shortness of breath. A thoracic aortic aneurysm can be found by measuring the size of the aorta with an echocardiogram, CT (computerized tomography), or MRI (magnetic resonance imaging). Normal aortic size varies by age, sex, and body size. Doctors can estimate the expected size of the aorta for each person. An aneurysm is diagnosed when any area of the aorta measures larger than expected.

How is an aortic dissection diagnosed?

Aortic dissection usually causes sudden, intense chest pain, which can radiate to the back, shoulders, neck, or arm, similar to signs of a heart attack. It is often described as if something is “ripping” or “tearing” in the chest. These symptoms should prompt immediate medical care. The diagnosis is made using medical imaging, such as an echocardiogram, CT, or MRI.

When is HTAD suspected?

Your doctor may suspect a heritable thoracic aortic disease (HTAD) based on your personal and family history. However, it is not always easy to recognize this condition. There may be no one else in the family who has had their aorta measured. Some forms of HTAD only affect the aorta and have no other symptoms. Other forms of HTAD can include other features, like tall stature, eye problems, or fragile skin. A person with mild symptoms may not come to medical attention.

GATHERING YOUR FAMILY HISTORY

When you gather family history, it is helpful to ask about medical problems that might be related to HTAD.

Ask about:

- Known aortic aneurysms or dissections
- Which part of the aorta was involved (aortic root, ascending aorta, aortic arch, descending aorta, or abdominal aorta)
- Bicuspid aortic valve
- Dislocated lens in one or both eyes
- Heart surgery
- Sudden cardiac death

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How is HTAD inherited?

When a person has a change in a gene that can cause HTAD, others in the family may inherit the same change. These changes are called pathogenic variants. HTAD is usually an autosomal dominant condition. This means that both men and women can have the condition and there is a 50% (1 in 2) chance to pass the pathogenic variant to any child. Sometimes HTAD is caused by a new genetic change that is not present in either parent. This is called a de novo variant. A de novo variant happens randomly when an egg or sperm is formed. A person with a de novo variant can pass it to their offspring, but other family members are not at risk for the condition. Rarely, HTAD may be caused by a pathogenic variant in a gene with a different pattern of inheritance.

How is genetic testing done?

A blood or saliva sample is taken to look for pathogenic variants in HTAD genes. Genetic testing works best when your medical history and family history have a clear pattern of HTAD, and testing starts with a family member who has TAD. You can learn more about genetic testing by talking with a genetic counselor.

What are the benefits of genetic testing?

There are two main benefits of genetic testing: **better medical care** and **family screening**. Medical guidelines have been developed for certain forms of HTAD. By knowing the gene involved, you can get more personalized medical care. In addition, when a pathogenic variant is found in a person with TAD, other people in the family can be offered genetic testing. Testing can identify family members at-risk for aortic disease before they have serious symptoms. Aneurysms and dissections often have no warning signs. A person with a pathogenic variant in an HTAD gene can lower their risk with regular cardiac screening, medication, and risk-reducing heart surgery (when needed). A family member who did not inherit the variant can be reassured.

SCREENING FOR TAD IN RELATIVES

Aortic screening is recommended every 5 years for close relatives (children; brothers; sisters; parents) to identify aortic disease before there are serious symptoms.

Echocardiogram is a heart ultrasound. This is the most common test used to diagnose aortic aneurysms. It uses sound waves to create images of the heart and blood vessels. Your doctor measures parts of the aorta and looks for enlarged areas. The report should include the diameter of the aorta at the sinus of Valsalva (also called "aortic root"), the ascending aorta, and sometimes the aortic arch. The measurements can be adjusted based on a person's size, and a "Z score" is calculated for the aortic diameter.

An echocardiogram is the usual screening for TAD, but other types of medical imaging may be used in some cases:

CT or CAT scan is short for computed tomography. This test uses x-rays to take multiple pictures of the chest. A computer puts all the images together for a more detailed look at the internal organs and blood vessels.

MRI is short for magnetic resonance imaging. This test uses magnetic waves (similar to sound waves) to create images of the aorta. A special type of MRI called MRA (magnetic resonance angiogram) provides pictures of the blood vessels. There is no exposure to radiation with an MRI or MRA.

What if testing does not find a pathogenic variant?

Current testing finds a pathogenic variant in fewer than 1 in 10 people tested. Even in families with a strong TAD history, most testing is negative (no pathogenic variant). While there are many different genes known to cause HTAD, some HTAD genes have not been discovered yet. So, there could be a genetic cause for TAD even when test results are negative. Cardiac screening may still be recommended for close relatives.

What happens if I inherit a pathogenic variant in an HTAD gene?

A person who inherits a pathogenic variant is more likely to have an aortic aneurysm or dissection during their lifetime. However, some people with a pathogenic variant never develop any aortic problems. Regular cardiac screening is recommended for anyone with a genetic change that can cause HTAD.

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