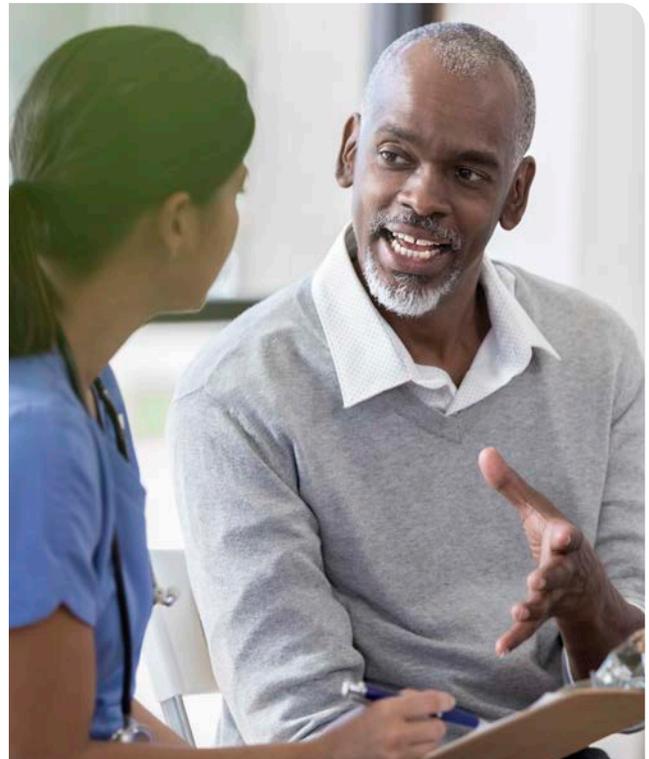


What is Transthyretin Amyloid Cardiomyopathy (ATTR-CM)?

Transthyretin (trans-thy-re-tin) Amyloid Cardiomyopathy (ATTR-CM) is an underdiagnosed and potentially fatal disease. It's characterized by deposits of amyloid protein fibrils in the walls of the left ventricle, the main pumping chamber of the heart. In ATTR-CM, the amyloid protein is made of transthyretin. The amyloid protein deposits cause the heart walls to become stiff, resulting in the inability of the left ventricle to:

1. Properly relax and fill with blood
2. Adequately squeeze to pump blood out of the heart



Is There More than One Type?

There are two types of ATTR-CM. With the first type, **hereditary ATTR-CM**, there's a mutation in the transthyretin gene, which results in amyloid deposits in the heart, nerves and sometimes the kidneys and other organs. Hereditary ATTR-CM can run in families. Symptoms may start as early as age 20 or as late as age 80.

Hereditary ATTR-CM is more common in localized parts of Portugal, Sweden and Japan. There are a number of mutations which are found in different parts of the world. Some mutations are more common in people of Irish ancestry while others are more common in people of African descent.

In the United States, the most common mutation occurs in African Americans (prevalent in approximately 1 in 25) and in older patients who may be misdiagnosed with high blood pressure-related heart disease. Different mutations have different patterns of disease progression and involve different organs.

The second type is **wild-type ATTR-CM**. With this form of the disease, there's no mutation in the transthyretin gene.

Wild-type ATTR-CM doesn't run in families. It most commonly affects the heart and can also cause carpal tunnel syndrome and peripheral neuropathy (pain and numbness in the hands and feet). The symptoms usually start after age 65.

The clinical course isn't well understood because the condition is likely underdiagnosed and more common than previously recognized. Some patients may have no symptoms and others may progress to end-stage heart failure. The symptoms of wild-type ATTR-CM may be mild and remain undiagnosed. In its early stages, ATTR-CM may mimic the symptoms of other conditions, such as heart failure related to hypertension (high blood pressure) and hypertrophic cardiomyopathy (enlargement and thickening of the heart).

What is transthyretin?

Within our cells, proteins have many different jobs. Transthyretin is a transport protein. It's created in the liver. Its job is to carry thyroxine (a thyroid hormone) and retinol (vitamin A) to the places in the body where they're needed.

(continued)

What is Transthyretin Amyloid Cardiomyopathy (ATTR-CM)?



What is cardiomyopathy?

Cardiomyopathy is a heart condition that prevents the heart muscle from functioning normally. Some forms of cardiomyopathy are associated with an enlargement and weakening of the heart muscle. Other forms are associated with a stiffening of the heart muscle so that it can't relax and fill with blood effectively. In both cases, the blood isn't pumped adequately to the body and backs up into the lungs. This causes fatigue, shortness of breath, leg swelling and abdominal bloating, a condition known as heart failure.

There are many different causes of heart failure that might be underdiagnosed and treatable. ATTR-CM is one such condition. ATTR-CM can cause both weakening and stiffening of the heart muscle.

What causes ATTR-CM?

Due to genetic mutation or aging, the transthyretin doesn't assemble normally. These abnormal proteins then clump together and shape themselves into amyloid fibrils. The fibrils travel through the bloodstream and are deposited in many organs, including the heart. As fibrils accumulate in the tissue, they thicken and stiffen the myocardium or wall of the heart. This causes a cardiomyopathy and, ultimately, heart failure.

What are the risk factors?

For Hereditary Transthyretin Amyloid Cardiomyopathy:

- A family member with ATTR-CM or heart failure
- Age 50+ (although symptoms begin anywhere from age 20 to age 80)
- Gender - primarily male
- Race - African American

For Wild-Type Transthyretin Amyloid Cardiomyopathy:

- Age 65+
- Gender - primarily male

What are the symptoms of ATTR-CM?

Symptoms are like those associated with heart failure:

- Shortness of breath is the most common, especially with minimal exertion and when lying down; the other symptoms usually occur after the shortness of breath is already there
- Coughing or wheezing, especially when lying down
- Swelling in the feet, ankles and legs
- Bloating in the abdomen
- Confusion or trouble thinking
- Increased heart rate
- Palpitations or abnormal heart rhythms

Additional symptoms:

- Numbness or tingling in the hands and feet
- Carpal Tunnel Syndrome

How is ATTR-CM diagnosed?

The diagnosis may be suspected because of typical symptoms and the results of a routine cardiac test—an electrocardiogram or echocardiogram. Once suspected, more specialized tests are needed to confirm the diagnosis. These could include:

- Imaging studies of the heart, most commonly a cardiac MRI and/or a nuclear medicine scan of the heart
- A tissue biopsy of an affected organ
- Genetic testing



What is Transthyretin Amyloid Cardiomyopathy (ATTR-CM)?

How is ATTR-CM treated?

Although treatment options are currently limited, there are some promising new therapies on the horizon. Medications were recently approved to treat the neuropathy caused by hereditary transthyretin amyloidosis. Patients who have substantial neuropathy symptoms may need to see a neurologist.

Clinicians focus on easing the heart failure symptoms and slowing or stopping the formation and depositing of fibrils. In cases of advanced heart failure, a heart transplant may be an option. With some patients, both heart and liver transplants are required.

Clinical trials for medications to treat ATTR-CM continue and give great hope for breakthroughs in the near future.

Talk with your Primary Care Provider

Know that awareness of the disease among clinicians is low. In fact, it's often misdiagnosed as hypertensive heart failure or hypertrophic cardiomyopathy. Because of the many different and subtle ways it may present, ATTR-CM may already be advanced by the time the patient receives a diagnosis. It's important that you talk with your primary care provider if you have any questions or concerns. Starting that conversation could be a lifesaver.

Ask your primary care provider about your shortness of breath and ask for a diagnostic testing and treatment plan.



If the diagnostic tests don't provide an answer, or if the treatment fails to improve your symptoms, it's important to go back to the primary care provider and ask about next steps. It's important not to give up until the tests reveal a diagnosis and the treatment relieves your symptoms.

HOW CAN I LEARN MORE?

- 1** Call 1-800-AHA-USA1 (1-800-242-8721), or visit heart.org to learn more about heart disease and stroke.
- 2** Sign up to get *Heart Insight*, a free magazine for heart patients and their families, at heartinsight.org.
- 3** Connect with others sharing similar journeys with heart disease and stroke by joining our Support Network at heart.org/supportnetwork.

Do you have questions for the doctor or nurse?

Take a few minutes to write your questions for the next time you see your healthcare provider.

For example:

Why am I feeling short of breath?

Why are weight control and physical activity important?

How long will it be before I feel better?

MY QUESTIONS:

We have many other fact sheets to help you make healthier choices to reduce your risk, manage disease or care for a loved one. Visit heart.org/answersbyheart to learn more.