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Understanding Transthyretin Amyloid Cardiomyopathy (ATTR-CM)

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Transthyretin amyloid cardiomyopathy (ATTR-CM) is a rare and serious type of amyloidosis (am-uh-loy-doh-sis) that affects your heart (called cardiac amyloidosis). Amyloidosis is a group of diseases in which certain proteins become unstable, change shape (misfold), and build up in the body's organs and tissues. This may affect how the organs function.[1]

ATTR-CM is a progressive disease, which means it gets worse over time. Getting a diagnosis as early as possible is very important. The more you know about ATTR-CM, the more prepared you'll be to make decisions about your care.[1]

What is transthyretin (TTR)?

There are thousands of proteins inside our cells. Each plays an important role in keeping us healthy. Our DNA (genes) contains instructions that control the shape of these proteins. Normal proteins fold into a specific shape, do their tasks, and are then removed from the body.[1]

One of these proteins is called transthyretin (trans-thy-re-tin) or TTR. Its job is to carry substances through the bloodstream. TTR works well when it's neatly folded. In some people, TTR can become unstable, misfold and tangle together, forming amyloid fibrils which can build up in your body's organs and tissues. When these misfolded proteins build up in your heart, it may lead to ATTR-CM.[1,3]

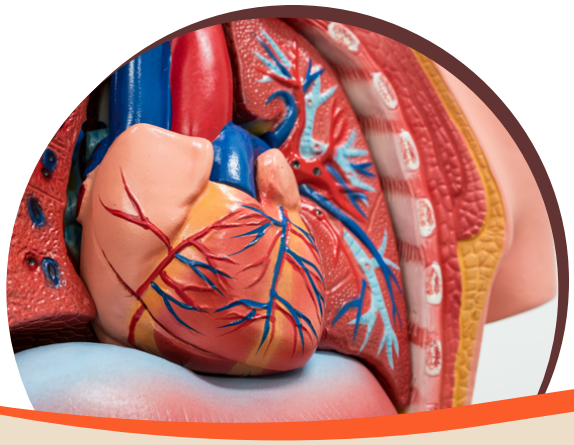
Amyloid	A starch-like substance caused by proteins that misfold (change shape).[2]
Fibrils	Clusters of amyloid that build up in tissues and organs.[2]
Cardiomyopathy	A condition where the heart is unable to relax and fill with blood properly, preventing the heart muscle from pumping blood to the rest of the body like it should.[3]

What happens with ATTR-CM?

With ATTR-CM, the build-up of amyloid fibrils causes the heart muscle to thicken and stiffen. Over time this makes it harder for your heart to pump blood and eventually leads to heart failure. There are two types of ATTR-CM – wild type and hereditary.[3]

Wild type ATTR-CM (wtATTR)[2,3]

- It's the most common form of ATTR-CM
- It usually affects White men over age 60
- It's linked with aging
- It doesn't run in families and is not caused by a genetic mutation



Hereditary ATTR-CM (hATTR)[1,3]

- It's caused by a change (mutation) in the TTR gene that's passed down from a parent
- There are more than 120 mutations that cause hATTR. The most common mutation in the U.S. is V1221. V1221 is found almost exclusively in African Americans
- It can affect both men and women
- It affects mainly people of African American, African, or Afro-Caribbean descent
- It most often affects people 50 years and older
- Some people with this type may never develop symptoms

What are the signs and symptoms of ATTR-CM?

Heart-Related Symptoms[1,3]

Because ATTR-CM affects the heart, the symptoms are often like those of heart failure. These may include:

- Shortness of breath
- Tiredness (fatigue)
- Swelling in the feet and legs (edema)
- Irregular heartbeat (arrhythmia)

Symptoms in Other Organs and Tissues[1,3]

If amyloid fibrils build up in other organs and tissues, you may also have symptoms in other parts of your body. These may include:

- Bicep tendon rupture (not related to an injury)
- Digestive problems such as diarrhea, constipation, nausea, feeling full quickly
- Eye problems such as glaucoma
- Numbness or tingling in the hands and feet
- Carpal tunnel syndrome in both hands; a weak grip
- Pain or numbness in the lower back or legs

Having one or more of these symptoms doesn't mean you have ATTR-CM. But if you have heart failure and you're experiencing any of these symptoms, it's important that you talk with your doctor.

How is ATTR-CM diagnosed?

Awareness of ATTR-CM among patients and some doctors is low, which may lead to a slow or incorrect diagnosis. This can lead to a delay in managing the condition. Sometimes the journey to an accurate diagnosis can be long and complex.[1,3]

Here's what you might expect:

- **Initial tests.** If your doctor thinks ATTR-CM may be the cause of your symptoms, he or she may order some tests to see how well your heart is working and to help decide if more tests are needed. These tests may include:[1,2]
  - Electrocardiogram (EKG) – A test that reads the electrical signals from your heart to help identify conditions that may be related to ATTR-CM
  - Echocardiogram (ECHO) – A test that uses sound waves to create images of your heart and help determine the speed and direction of blood flow
  - Cardiac magnetic resonance imaging (Cardiac MRI) – A test that scans your heart using radio waves, magnets, and a computer to get detailed images of your heart
- **Rule out another type of amyloidosis.** Your doctor must also rule out another form of cardiac amyloidosis called light-chain amyloidosis (AL). AL can be ruled out using blood and urine tests. This is an important step because ATTR-CM and AL are managed in different ways[2]
- **Diagnostic tests.** If your doctor suspects ATTR-CM, special tests can be performed to confirm a diagnosis. These may include:[2]
  - Nuclear scintigraphy – A type of imaging test where a substance called a tracer is injected into your body to help your doctor see if there are amyloid fibrils in your heart
  - Cardiac biopsy – A procedure in which a sample of tissue is taken from your heart muscle and examined
- **Genetic testing and counseling.** If you're diagnosed with ATTR-CM, it's important to consider genetic testing and counseling to check if you have hATTR-CM. If you do, your family members are at higher risk of having the same kind of mutation. Genetic counseling before and after testing can help you and your family understand the test results and what steps to take next[1]

Working with Your Doctor

Because ATTR-CM is rare, many doctors are unaware of the disease, and it's often misdiagnosed. It's also common for ATTR-CM to mimic symptoms of other more common heart-related conditions. In some cases, this can result in patients having a more advanced stage of the disease when they do get diagnosed.[3]

If you have any questions or concerns let your doctor know. Talk about all of your symptoms, even those that seem unrelated to your heart. Think of each symptom as a clue that when put together, can help your doctor make a diagnosis.[3]

Here are some things you can do:[1,4]

- Keep a list of the symptoms you are having.
- To the best of your ability, make note of any heart-related issues that affect your relatives on either side of your family.
- You may have seen several doctors to understand why you're feeling discomfort. Be sure to share your medical history, medical records, and all test results with your cardiologist.
- Write down your questions and concerns to discuss with your doctor.
- Consider asking for a referral to a treatment center that specializes in amyloidosis.

For More Information and Support

Living with and managing ATTR-CM can be a challenge for patients, their families, and their caregivers. But you don't have to go it alone. These organizations offer education and support:

Amyloidosis Foundation (amyloidosis.org)

- Provides a range of services and resources for patients and caregivers through support groups, webinars, videos, and brochures
- Aims to educate health care professionals so patients can be diagnosed earlier
- Supports research for amyloidosis

Amyloidosis Research Consortium (arci.org)

- Offers support and resources to educate patients and caregivers and help ensure patients have access to the best care possible
- Supports research aimed at speeding up the development of and access to new treatments for amyloidosis
- Provides education and tools to help doctors diagnose patients earlier

Amyloidosis Support Groups (amyloidosissupport.org)

- Provides peer group support and education to patients and those affected by their disease including family, friends, and caregivers

References:

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