What causes hATTR amyloidosis?

hATTR amyloidosis is a genetic disease caused by a change (mutation) in the gene that makes a protein called transthyretin (TTR), which is primarily made in the liver. These mutations change the shape of TTR proteins – causing them to fold incorrectly and build up as abnormal protein structures (called amyloid fibrils) in various organs in the body.

What does hATTR amyloidosis lead to?

The buildup of amyloid fibrils damage the organs where they are found – especially in the nerves, heart, and digestive system. Because these buildups can occur in almost any part of the body, individuals with hATTR can have a range of symptoms that may seem unrelated.

If hereditary ATTR amyloidosis runs in my family, what are the chances that my children will have the condition?

hATTR amyloidosis is passed down through family members. Every individual inherits two copies of the TTR gene - one from each parent. As an autosomal dominant disease, to develop hATTR amyloidosis, an individual needs to inherit **only one copy of the mutated gene from one parent.** If one parent has hATTR amyloidosis, there is a **50% chance** their child will inherit the mutation.

Inheriting a mutated copy of the TTR gene does not always lead to the disease and having the disease does not always lead to symptoms. Even family members with the disease caused by the same mutated gene may not necessarily develop the same symptoms. However, even without symptoms, a parent with a mutated copy of the gene is a carrier and still has a 50% chance of passing on the mutation.

Resources & Support

Due to the progressive nature of hATTR amyloidosis, managing symptoms is an ongoing process. Physicians may prescribe you with medications to treat some of these symptoms and reduce the daily impact they may have on you.

For additional information and assistance:

Hereditary Amyloidosis Canada
www.madhattr.ca

The Canadian Amyloidosis Support Network
www.thecasn.org

Canadian Organization for Rare Disorders
www.raredisorders.ca

Orphanet (Canada Page)
http://www.orpha.net/national/CA-EN/index/homepage/

Regroupement québécois des maladies orphelines (RQMO)
https://rqmo.org

Hereditary Amyloidosis Canada
Amyloïdose Héréditaire Canada

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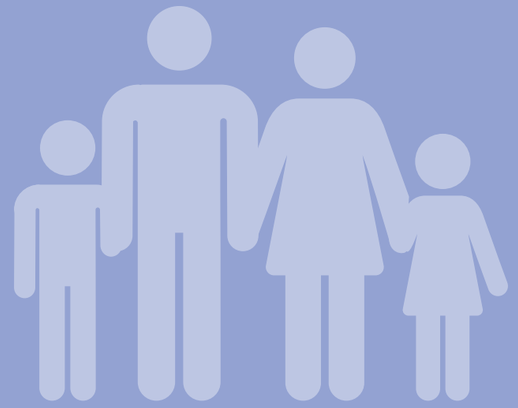


Hereditary ATTR (hATTR) amyloidosis

An introduction for patients, caregivers and families

Hereditary Amyloidosis Canada
Amyloïdose Héréditaire Canada

What is hATTR amyloidosis?

Hereditary ATTR (hATTR) amyloidosis is a progressive and rare inherited disease that affects multiple parts of the body, including the nervous system and the heart.

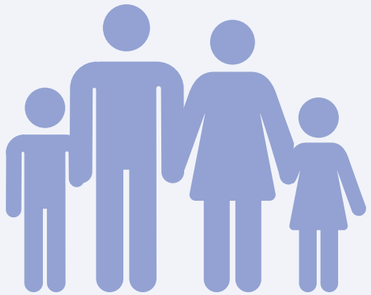
About
50,000
people worldwide
have hATTR amyloidosis

Patients often have to see
5+ doctors
across different specialties
before getting the right diagnosis

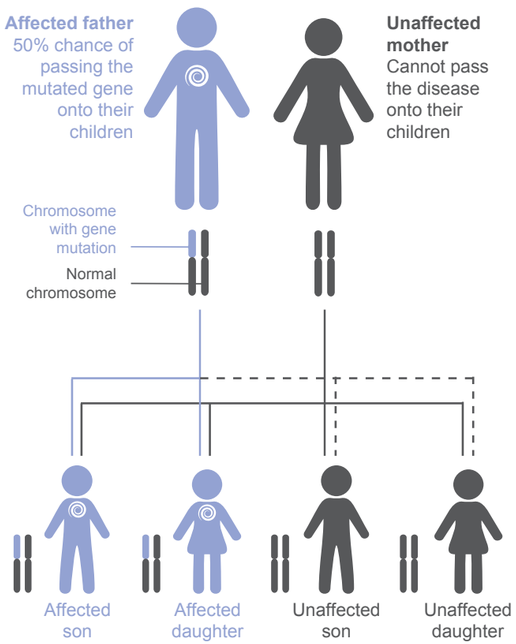
Often takes more than
4 years
from symptom onset
to a diagnosis

Genetics of hATTR amyloidosis

More than 120 different TTR gene mutations have been discovered – with individuals of Portuguese, Japanese, Swedish, Irish, and African American descent being more likely to have certain TTR gene mutations.



What does hATTR amyloidosis mean for you and your family?



It is the mutated version of the TTR gene that is passed down through family members, which can lead to disease. It is not always easy to determine whether a disease in a family is passed down from parent to child and genetic tests can help. Genetic testing uses laboratory methods to look for mutations or changes in your genes. Through genetic testing, you can learn if you carry one or more of TTR gene mutations known to be associated with hATTR amyloidosis.

If you have a family history of hATTR amyloidosis, ask your doctor about genetic testing.

Symptoms of hATTR amyloidosis

Initial symptoms of hATTR amyloidosis typically appear between 30 and 70 years of age. Symptoms can vary widely and can involve multiple tissues and organs - **especially the nervous system and the heart**. Because symptoms aren't always specific, often seemingly unrelated, and may be confused with other more common conditions, hATTR amyloidosis can be hard to diagnose.

Nerve damage

Because amyloid fibrils can build up in the nervous system, hATTR amyloidosis can cause symptoms of nerve damage such as tingling, numbness, pain in the arms and legs, and sexual dysfunction. As the disease progresses with more buildup of amyloid, nerve damage caused by hATTR amyloidosis can worsen over time – making daily tasks such as fastening buttons on a shirt and walking (without a cane or wheelchair) more and more difficult over time.

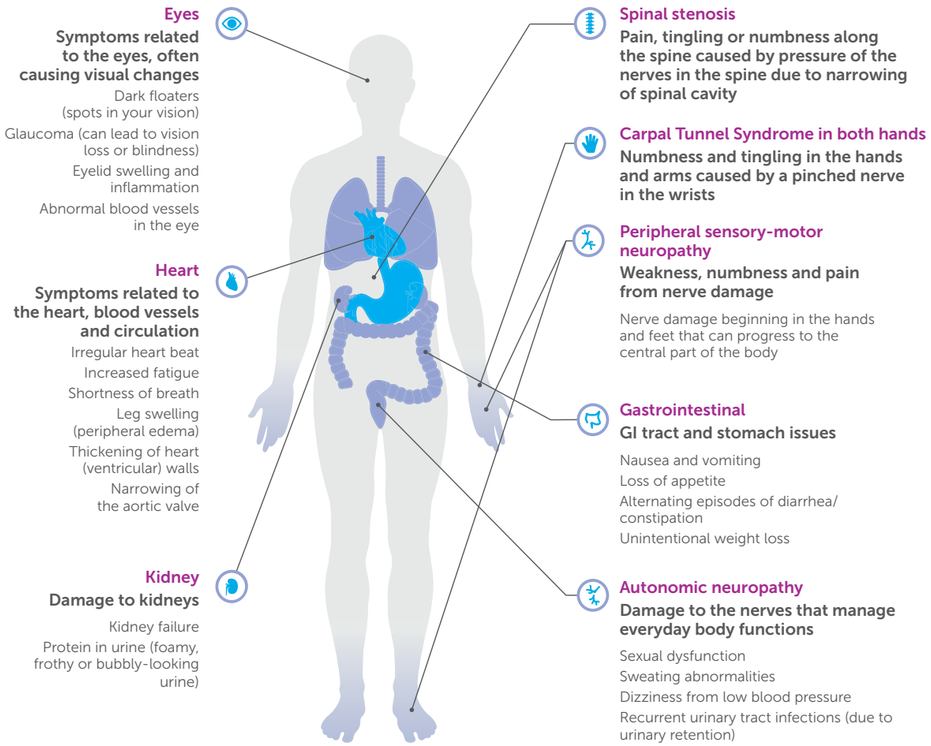
Damage to the heart

Buildup of amyloid fibrils in the heart can cause symptoms of cardiomyopathy – including irregular heart beat, fatigue, and shortness of breath. As the disease progresses, damage to the heart caused by hATTR amyloidosis can worsen over time potentially leading to heart failure.

Clusters of red-flag symptoms

On top of nerve and heart damage, patients with hATTR often present with a cluster of two or more seemingly unrelated symptoms that may be **red-flags** for hATTR.

If you are experiencing two or more symptoms related to hATTR amyloidosis, consider discussing genetic testing with your doctor



Talking with your family about genetic testing for hATTR amyloidosis

It can be hard to talk with loved ones about genetic testing for hATTR amyloidosis. For some people, genetic test results serve as a relief, removing some of the uncertainty surrounding their health. For others, learning that they or someone in their family has hATTR amyloidosis can be scary. Some people can also feel guilty, angry, anxious, or depressed when they find out their results.

As with any important family discussion, there are benefits and risks to discussing a serious topic, such as genetic testing.

Potential benefits of talking with your family about genetic testing include:

- Helping family members understand their risk for hATTR amyloidosis
- Helping family members watch out for signs of hATTR amyloidosis and start screening earlier

Potential risks to keep in mind when talking to your family about genetic testing:

- Learning that you or someone in your family has, or is at risk for a disease, can be scary
- Family members may find it upsetting to get genetic testing if other family members have already died of hATTR amyloidosis
- Having a mutated gene or passing this gene on to children can also lead to guilt or anger

There is support available. If you are concerned about your genetic status or that of your family member, be sure to discuss this with your doctor.