Hereditary ATTR (hATTR) amyloidosis

A closer look at an inherited condition
What is hATTR amyloidosis (ama-loy-doh-sis)?

hATTR amyloidosis is a rare condition that affects an estimated 50,000 people worldwide. It is caused by a gene change, or mutation, that affects the function of a protein called transthyretin (TTR).

Individuals with hATTR amyloidosis can have a range of symptoms that may not seem connected. Symptoms can affect several parts of the body, including the nerve (nervous), heart (cardiac), and digestive (gastrointestinal) systems. See page 7 for more information.

When I was diagnosed with hATTR amyloidosis, I worked hard to understand the disease through research and conversations with my doctor. Giving up was not an option.

CECE, living with hATTR amyloidosis
How hATTR amyloidosis develops

TTR, a naturally occurring protein made primarily in the liver, helps carry substances such as vitamin A.

In hATTR amyloidosis, a change or mutation in the TTR gene causes the protein to take on an abnormal shape and misfold.

This change in shape causes the protein to build up in various parts of the body, including the nerves, heart, and digestive system. The collection of abnormal proteins is called amyloid deposits.

These amyloid deposits cause symptoms of the disease.
How is hATTR amyloidosis inherited?

hATTR amyloidosis is passed down through family members.

If one parent has hATTR amyloidosis, each child will have a 50% chance of inheriting the genetic mutation that causes this condition. A family member may inherit the TTR gene with a mutation, but that does not necessarily mean he or she will develop hATTR amyloidosis.

Although anyone can be at risk for this disease, it is more common for certain ethnicities, such as people of African, Portuguese, and Irish descent.

hATTR amyloidosis can be passed down to children, so it’s important to understand how it is inherited in families.
RON SR, living with hATTR amyloidosis
I began to notice some changes in my body. My hands and feet were getting numb and I had some digestive issues. When the numbness started to creep up my legs and arms, I knew it was time to get tested.

RICK, living with hATTR amyloidosis
hATTR amyloidosis can cause a range of symptoms

Symptoms of hATTR amyloidosis can be very different from patient to patient, even within families. The age that symptoms appear can range from the mid-20s to the mid-60s. Since symptoms of hATTR amyloidosis can worsen over time, it’s important to talk to your doctor as soon as possible.

hATTR amyloidosis can affect several parts of the body, including:

The peripheral nervous system, which is made up of nerves that branch out from the brain and spinal cord
  - Nerve damage in the peripheral nervous system results in communication problems between the brain and the rest of the body, including your arms and legs

The cardiac system, which includes the heart and blood vessels, transports blood through veins and delivers oxygen to cells
  - Damage to the heart muscle can lead to heart failure

The autonomic nervous system, which is made up of nerves that connect the brain and spinal cord to organs such as the heart, stomach, and intestines
  - When the autonomic nervous system is not working correctly, it may affect involuntary bodily functions such as breathing, digestion, and heart rate
Possible symptoms of hATTR amyloidosis

Symptoms related to nerves in hands, feet, arms, and legs

- Tingling
- Numbness
- Carpal tunnel syndrome
- Burning pain
- Loss of sensitivity to temperature
- Loss of movement control
- Weakness

Symptoms related to the heart

- Fatigue
- Dizziness
- Shortness of breath
- Leg swelling (edema)

Symptoms related to control over bodily functions

- Recurrent urinary tract infections (UTIs)
- Abnormal sweating
- Dizziness upon standing
- Sexual dysfunction
- Nausea and vomiting
- Diarrhea
- Severe constipation
- Unintentional weight loss

The bold symptoms may be caused by polyneuropathy, which is damage to nerves that affect sensation, movement, strength, and bodily functions such as digestion, urination, and sexual function.
Other symptoms

- Glaucoma
- Blurred or spotty vision
- Floaters in the eye
- Worsening dementia
- Stroke-like episodes
- Kidney dysfunction

This is not a complete list of symptoms that may be experienced in patients with hATTR amyloidosis. Each patient has a different experience and you may not experience all of these symptoms, or you may not experience them at the same time. Symptoms of hATTR amyloidosis may worsen over time.
Getting the right diagnosis is key

Misdiagnosis is common with hATTR amyloidosis because the symptoms are similar to those of other conditions. Learning about the symptoms of hATTR amyloidosis can help you identify them if they occur.

Take the next step

If you experience symptoms or become aware of a family history of the disease, speak to your doctor to find out the right action plan. Your doctor may refer you to a physician experienced in managing the disease or to a genetic counselor.

Consider genetic counseling and testing

If your doctor thinks you may be at risk for hATTR amyloidosis, he or she may recommend you work with a genetic counselor. Genetic counselors are trained healthcare professionals who can:

- Work with people who are considering a genetic test and provide guidance after a test
- Help people understand genetics, inheritance, and disease risk
- Discuss the benefits, limitations, and potential implications of genetic testing
- Provide information about support and resources

Genetic testing can help determine whether a person carries a genetic mutation associated with hATTR amyloidosis, which may help shorten the time to diagnosis and prevent potential misdiagnoses.
I’ve learned a lot about this disease, and I’m less fearful about it. I’m also more hopeful knowing that there are a lot of healthcare providers out there for families like ours.

**SUE, member of a family living with hATTR amyloidosis**
Alnylam Act®

Through the Alnylam Act® program, Alnylam Pharmaceuticals sponsors no-charge, third-party counseling and genetic testing for individuals who may carry one of the 120 or more gene mutations known to be associated with hATTR amyloidosis.

The Alnylam Act® program was created to provide access to genetic testing and counseling to patients as a way to help people make more informed decisions about their health.

- While Alnylam provides financial support for this program, tests and services are performed by independent third parties
- Healthcare professionals must confirm that patients meet certain criteria to use the program
- Alnylam receives de-identified patient data from this program, but at no time does Alnylam receive patient-identifiable information. Alnylam uses healthcare professional contact information for research and commercial purposes
- Genetic testing is available in the US and Canada. Genetic counseling is only available in the US
- Healthcare professionals or patients who use this program have no obligation to recommend, purchase, order, prescribe, promote, administer, use, or support any Alnylam product
- No payers, including government payers, are billed for this program
Consumer genetic services

In addition to genetic tests ordered by your doctor, direct-to-consumer genetic services, like 23andMe, are available for purchase to help you learn more about how genetics may influence your risk for certain hereditary conditions.

Alnylam has teamed up with 23andMe to offer consumer genetic services for the 3 most common genetic mutations associated with hATTR amyloidosis. The home-based saliva collection kit is quick and simple—no needles or blood required. This report does not identify all TTR variants that can cause hATTR amyloidosis, nor does it diagnose hATTR amyloidosis or any other health conditions. Please talk to your doctor if this condition runs in your family, you think you might have this condition, or you have concerns about your results.

If you have a TTR variant detected by the 23andMe test, the Alnylam +myFamily program will provide 23andMe Health + Ancestry Service Kits to your first-degree family members (parents, full siblings, and biological adult children)—at no charge.²

²23andMe services provide information on a person’s risk for certain diseases, but cannot provide a diagnosis. The Hereditary Amyloidosis (TTR-related) Genetic Health Risk Report provides information on the 3 most common TTR mutations in the United States. There are over 120 mutations associated with hATTR amyloidosis. If you have symptoms of hATTR amyloidosis or other symptoms you are concerned about, regardless of results reported by a 23andMe Health Risk Report, it is important to talk to your doctor as soon as possible. Only a doctor can confirm a diagnosis of hATTR amyloidosis.
Managing the condition

There are therapies available for the treatment of hATTR amyloidosis that address the underlying cause of the disease by decreasing the amount of TTR protein that’s made in the body. There are also treatments that bind to TTR proteins and help prevent them from forming deposits.

Liver and/or heart transplant is also an option for some patients who meet certain eligibility criteria.

Doctors may prescribe medication to help manage some of the symptoms that patients experience. Since symptoms of hATTR amyloidosis can worsen over time, managing symptoms is an ongoing process.

Additional therapies for hATTR amyloidosis are currently being researched.

Living with hATTR amyloidosis

When you or your loved ones receive a diagnosis of this inherited condition, it can have a significant impact on your daily life. As a patient, relative, or caregiver, building a solid support network with your family and doctors can relieve some of the potential burden.

Talk to your doctor if you begin to experience symptoms or to learn about treatment options for hATTR amyloidosis.
Get the facts about hATTR amyloidosis

The Bridge® is a program designed to help raise awareness, promote education, and provide valuable tools for patients, their families, and caregivers.

Sources for additional information and assistance

Amyloidosis Foundation
www.amyloidosis.org

Amyloidosis Research Consortium
www.arci.org

Amyloidosis Support Groups
www.amyloidosissupport.org

The Foundation for Peripheral Neuropathy
www.foundationforpn.org

Global Genes
www.globalgenes.org

National Organization for Rare Disorders
www.rarediseases.org

CECE, living with hATTR amyloidosis
Learn more about hATTR amyloidosis at www.hATTRbridge.com.