EDUCATIONAL BROCHURE

A family living with hATTR amyloidosis

Hereditary ATTR amyloidosis

A closer look at an inherited condition

the BRIDGE® hATTR amyloidosis

What is hereditary ATTR (hATTR) amyloidosis?

hATTR amyloidosis is a rare condition that affects an estimated **50,000 patients worldwide**.

It is caused by a gene change (mutation) that affects the function of a protein called transthyretin (TTR), made primarily in the liver.

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*

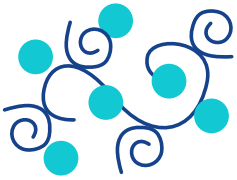
How hATTR amyloidosis develops

TTR

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

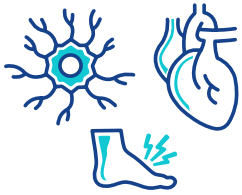
Abnormal TTR

In hATTR amyloidosis, a mutation in the TTR gene can cause the protein to take on an abnormal shape (misfold).



Amyloid deposits

This change in shape causes the protein to gather and build up in various parts of the body such as the nerves, heart, and digestive system. These gathered proteins are called amyloid deposits.



Symptoms of hATTR amyloidosis

These amyloid deposits cause symptoms of the disease.

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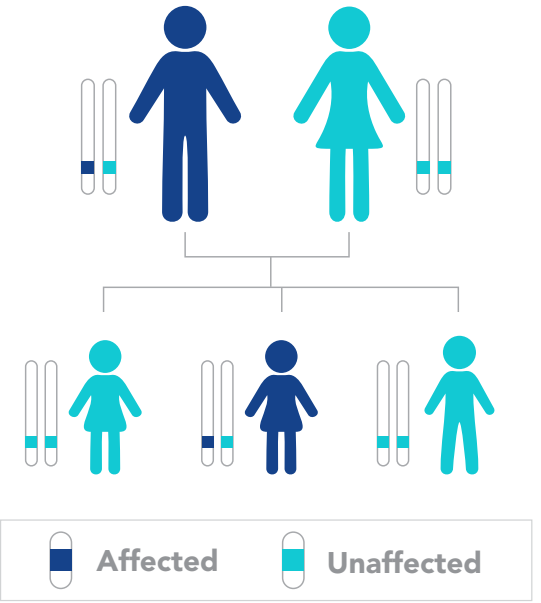
How is hATTR amyloidosis inherited?

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 American, 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*

Receiving the diagnosis was empowering for me and my family. We could now focus on getting appropriate care.

CECE, *living with hATTR amyloidosis*

hATTR amyloidosis can cause a range of symptoms

These symptoms can be **very different** from patient to patient, and even within families, although some see a pattern develop. The age that symptoms appear can range from the **mid-20s to the mid-60s**. Since symptoms of hATTR amyloidosis can become more severe over time, it's important to talk to your doctor about them 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 and communicate with the rest of the body, including your arms and legs

- **Nerve damage** in the peripheral nervous system results in improper function

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**

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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)
- Chest pain

Symptoms related to control over bodily functions

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

ANGEL, *family is living with hATTR amyloidosis*

Other symptoms

- Glaucoma
- Blurred or spotty vision
- Floaters in the eye
- Detached retina
- 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 become more severe over time.

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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.

Getting started with genetic counseling

Genetic counselors can help you and your family learn more about the condition as well as your chances of inheriting it and what may happen after a diagnosis. Genetic counselors can help you understand the issues related to genetic testing—from personal risk to possible insurance impact—and can help you determine if a genetic test is right for you.

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 clusters.

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 may reduce the daily impact on patients.

Additional treatment options 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.

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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 Support Groups
www.amyloidosissupport.org

Amyloidosis Research Consortium
www.arci.org

Amyloidosis Foundation
www.amyloidosis.org

National Organization for Rare Disorders
www.rarediseases.org

Global Genes
www.globalgenes.org

The Foundation for Peripheral Neuropathy
www.foundationforpn.org

Alnylam Act®

Alnylam Pharmaceuticals is sponsoring no-charge, third-party **genetic testing and counseling** for individuals who may carry gene mutations known to be associated with hATTR amyloidosis.

AlnylamAct®

www.AlnylamAct.com

Genetic testing and counseling may help to:

- Identify risk of disease for patients and their family members
- Shorten the time to diagnosis and prevent misdiagnoses
- Help patients consider clinical trials
- Provide information about support resources such as patient advocacy organizations

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 receives contact information for healthcare professionals who use this program. Genetic testing is available in the U.S. and Canada. Genetic counseling is only available in the U.S. Healthcare professionals who use this program have no obligation to recommend, purchase, order, prescribe, promote, administer, use or support any Alnylam product.

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Notes

We must still advocate for ourselves and our entire families to help doctors understand what we have and how to manage this condition.

SUE, *family is living with hATTR amyloidosis*

Learn more about hATTR amyloidosis at **www.hATTRbridge.com.**

Alnylam® PHARMACEUTICALS

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