EDUCATIONAL BROCHURE

A family living with hATTR amyloidosis

Hereditary ATTR (hATTR) amyloidosis

A closer look at an inherited condition

the BRIDGE® hATTR amyloidosis

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 an inherited gene variant, or change, in the transthyretin (TTR) gene. This change in the TTR gene may also be referred to as a mutation.

Different symptoms may appear at different times for each person with hATTR amyloidosis. Symptoms can affect several parts of the body, including the nerves, heart, and digestive system. 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*

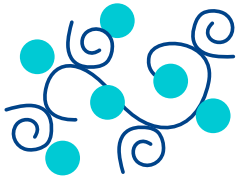
How hATTR amyloidosis develops

TTR

TTR is a naturally occurring protein made primarily in the liver and carries substances such as vitamin A.

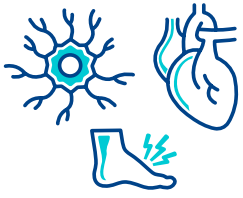
Abnormal TTR

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



Amyloid deposits

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.



Symptoms of hATTR amyloidosis

These amyloid deposits cause symptoms of the disease.

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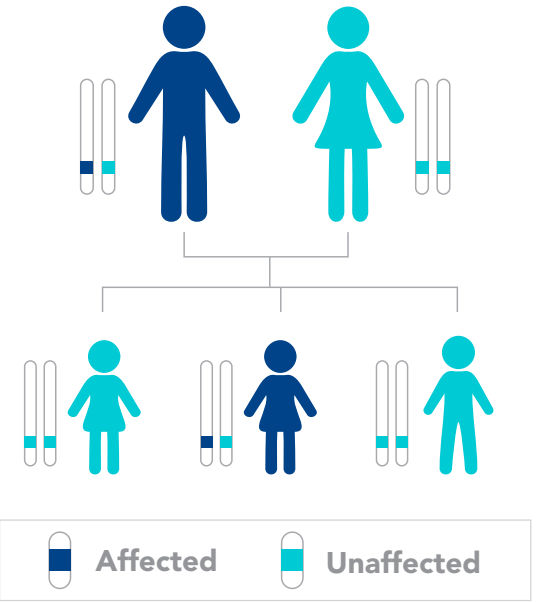
Although anyone can be at risk for this disease, it is more common for certain ethnicities, such as people of African, Brazilian, French, Irish, Japanese, Portuguese, and Swedish descent.

How is hATTR amyloidosis inherited?

hATTR amyloidosis is passed down through family members.

If one parent has hATTR amyloidosis, each child has a **50% chance of inheriting the genetic variant** that may cause this condition. A family member may inherit the TTR variant, but having the variant does not necessarily mean that they will develop hATTR amyloidosis.



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

The symptoms of hATTR amyloidosis can **vary widely** among people with the condition, even within families. The age that symptoms typically appear ranges from the **mid-20s to the mid-60s**. Because symptoms of hATTR amyloidosis can worsen 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 **somatic nervous system**, which is made up of nerves that connect the brain and spinal cord to the skin and muscles, controls sensation and voluntary movements.

- **Nerve damage** in this system can lead to a range of symptoms, including loss of voluntary movement of the hands and feet, and loss of sensitivity to temperature

The **cardiovascular system**, which is made up of the heart and blood vessels, transports blood through arteries and veins to deliver oxygen to cells and helps to remove metabolic wastes from 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 parts of the body, including the heart, stomach, and intestines.

- When this 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)

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 referred to as 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.

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Getting the right diagnosis is key

Misdiagnosis or delays in diagnosis are common with hATTR amyloidosis because the symptoms are similar to those of other conditions. Knowing what to look for can help you recognize the symptoms sooner and work with your doctors to determine an accurate diagnosis.

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 an hATTR amyloidosis specialist who can order further tests to make a diagnosis, or to a genetic counselor.

Consider genetic counseling and testing

If your doctor thinks you may be at risk for hATTR amyloidosis, they 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

A genetic test will determine whether a person carries a variant in the TTR gene associated with hATTR amyloidosis. If a gene variant is identified, family members of an affected individual can use this information to help determine their own risk.

My family's experiences with hATTR amyloidosis have taught me the importance of acquiring educational tools, empowering us all to advocate for one another's health and life.

SUE, *living with hATTR amyloidosis*

Alnylam Act®

Alnylam Pharmaceuticals sponsors no-charge, third-party **genetic counseling and testing** for individuals who may carry one of the **120 or more gene variants** 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 may use healthcare professional contact information for research purposes
- Both genetic testing and genetic counseling are available in the US and Canada
- 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 patients, healthcare professionals, or payers, including government payers, are billed for this program

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 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 are also options for some patients who meet certain eligibility criteria.

Doctors may prescribe medication to help manage some of the symptoms that may reduce daily impact on patients. 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 what treatment options for hATTR amyloidosis may be right for you.

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CECE, *living with hATTR amyloidosis*

Get the facts about hATTR amyloidosis

The Bridge is a program designed to help raise awareness and provide education and helpful 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

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

Alnylam® PHARMACEUTICALS

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