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.

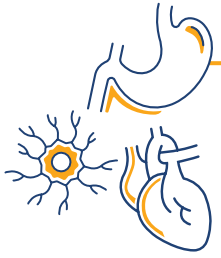
Different symptoms may appear at different times for each person with hATTR amyloidosis. Symptoms can affect several parts of the body, including the **nerves, heart, and digestive system**. See page 6 for more information.

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	Abnormal TTR	Amyloid deposits
TTR is a naturally occurring protein made primarily in the liver and carries substances such as vitamin A.	In hATTR amyloidosis, a variant, or change, in the TTR gene can cause the protein to misfold and take on an **abnormal shape**.	This change in shape causes the protein to **build up** in various parts of the body, including the nerves, heart, and digestive system. The buildup of abnormal proteins is called **amyloid deposits**.



Amyloid deposits cause symptoms of the disease.

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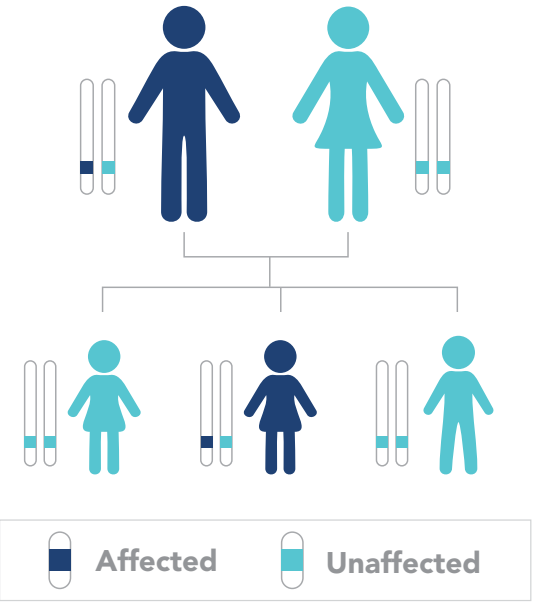
Although anyone can be at risk for this disease, it is more common for certain ethnicities, such as people of African, Brazilian, French, Irish, Japanese, Portuguese, or Swedish descent.

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*

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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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*

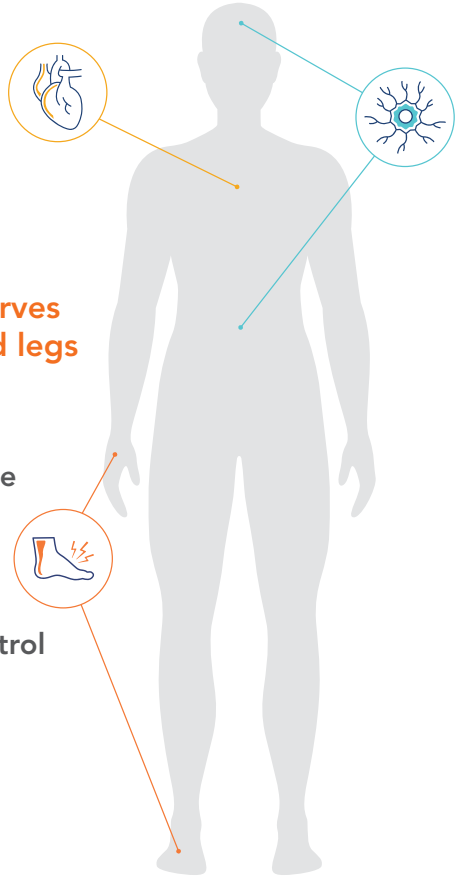
Symptoms of hATTR amyloidosis

Symptoms related to the heart

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

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 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**

Other symptoms

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

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.

This is not a complete list of symptoms that may be experienced by 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.

Talk to your doctor if you think you may be experiencing symptoms of hATTR amyloidosis, even if they seem unrelated.

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® Genetic Testing and Counseling Program

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

AlnylamAct®

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

If you are living with hATTR amyloidosis, starting treatment soon after diagnosis is key to managing your symptoms. There are treatment options available for patients with certain symptoms of hATTR amyloidosis that address the underlying cause of the disease. These work by:

- Decreasing the amount of TTR protein made in the body, which can help decrease the amount of amyloid deposits that form
- Preventing some TTR proteins from taking on an abnormal shape and forming amyloid deposits in the body

Since symptoms of hATTR amyloidosis can worsen quickly over time, managing symptoms is an ongoing process. Work with your doctor to ensure you are taking the right steps to manage your disease.

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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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

Caregiver Action Network
www.caregiveraction.org

The Foundation for Peripheral Neuropathy
www.foundationforpn.org

Global Genes
www.globalgenes.org

Mackenzie's Mission
www.mm713.org

National Alliance for Caregiving
www.caregiving.org

National Organization for Rare Disorders
www.rarediseases.org

oneAMYLOIDOSISvoice
www.oneamyloidosisvoice.com

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

Alnylam® PHARMACEUTICALS

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