hATTR amyloidosis disease awareness

Alnylam PHARMACEUTICALS

Learn More About **hATTR Amyloidosis**

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You may or may not have heard of hereditary ATTR Amyloidosis (hATTR amyloidosis), a rare disease which has a unique , historic connection to the North-West and West of Ireland.

This leaflet is designed to give you information about the condition, the symptoms associated with it and what to do if you think you or a family member may be affected. Always talk to your doctor about any concerns you may have.

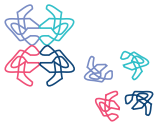
What is ATTRv amyloidosis?

ATTRv amyloidosis (v for variant) is an inherited condition where one of the proteins that is made by the body is not produced correctly. ATTRv amyloidosis is also commonly known as hereditary ATTR (hATTR) amyloidosis. The two terms are interchangeable.

The protein, which is called transthyretin (TTR), can become abnormal in ATTRv amyloidosis. In abnormal cases, it can break apart into smaller pieces of protein that bind together, forming clumps known as amyloid deposits.

These deposits can build up in different organs and tissues in the body, causing damage to them and creating health problems. ATTRv amyloidosis is a hereditary condition, meaning it may affect multiple people in the family.

TTR is a naturally occurring protein made in the liver, which is coded for by the TTR gene.



In ATTRv amyloidosis, an inherited variant or mutation occurs in the TTR gene, which can result in an abnormal TTR protein being produced – this protein is less stable and can misfold or break apart.

These abnormal pieces of protein bind together and form amyloid deposits.

Amyloid deposits build up in various parts of the body, including the nerves, heart and digestive system, causing symptoms.

How may ATTRv affect a family with the condition?

Would everyone in the family have ATTRv amyloidosis?

No, not all relatives inherit the mutated gene, and not all people who have the gene mutation develop symptoms.

Why is this?

A person only needs to inherit a copy of the gene mutation from one parent in order to develop the disease risk. This is known as an **autosomal dominant inheritance** pattern.

When one parent carries the gene mutation responsible for ATTRv amyloidosis, each child has a 50% chance of inheriting the gene.

> ***The first memories of amyloidosis was hearing that my grandfather has passed away with it. We thought it was a form of cancer. Basically we didn't know anything about the disease. They talk about it being a rare disease but it's not a rare disease when it's in your family.***

James Coyle

LIVING WITH HATTR AMYLOIDOSIS

Who can get ATTRv amyloidosis?

Does every family have the same risk of carrying the mutated gene?

ATTRv amyloidosis is a rare disease, but in some communities it is found more commonly than in others.

In some of these communities, the mutation that has caused the ATTRv amyloidosis is different. This is what is referred to as a **variant**.

There are over 150 variants of the TTR gene associated with ATTRv amyloidosis. Some of the more common variants are referred to as:

T80A

Also known as T60A, this mutation is thought to have originated in Ireland, and is the most common form seen in Ireland, the UK and in people with Irish ancestry. T80A is the 3rd most common hATTR mutation in the world.

V50M

Also known as V30M, this mutation is the most common worldwide.

V142I

Also known as V122I, this mutation is seen in around 3-4% of African Americans, and is commonly seen in people of Afro-Caribbean and African descent. It is the 2nd most common worldwide.

If you're experiencing any symptoms or if there's a family history, it's important that you talk to your doctor. Early diagnosis is key and can lead to better outcomes.

Rosaline Callaghan
LIVING WITH HATTR AMYLOIDOSIS

What are the symptoms?

Everyone's experience of ATTRv amyloidosis can be different and people may have a mixture of various symptoms. On this page, you will find information about some of the key symptoms to know about and what to look out for.

Which parts of the body can ATTRv amyloidosis affect?

Symptoms can appear in various parts of the body and can sometimes seem unrelated. These symptoms tend to fit into one of three main categories, which primarily relate to the peripheral nerves, autonomic nerves and the heart.

Are the symptoms always the same?

The symptoms of ATTRv amyloidosis may continue to get worse over time, so it's really important that Patients with the condition discuss all of their symptoms with their healthcare team, even if they think they might not be related to ATTRv (eg. erectile dysfunction). The more information the doctors have, the more they may be able to help.

Useful terms:

Neuropathy: disease that affects the nerves of the body.

Polyneuropathy: when more than one nerve system is affected.

Peripheral neuropathy: when the nerves responsible for movement are affected.

Autonomic neuropathy: when nerves controlling the internal organs are affected - this can lead to problems with digestion, sexual function and blood pressure.

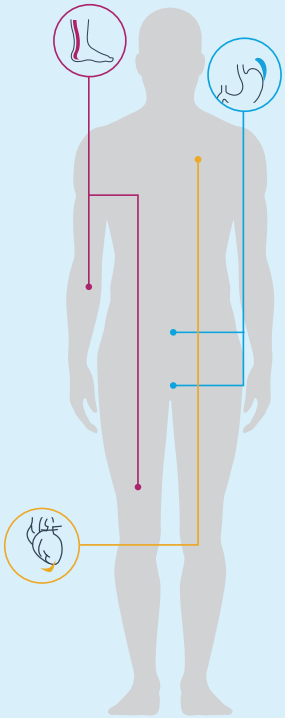
Cardiomyopathy: disease that affects the heart muscles.

Autonomic nerve-related ('autonomic dysfunction')

- Urinary tract infections
- Excessive sweating
- Dizziness upon standing
- Sexual dysfunction
- Nausea and vomiting
- Diarrhoea
- Severe constipation
- Unintentional weight loss

Peripheral nerve-related ('polyneuropathy')

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



Heart-related ('cardiomyopathy')

This is one of the most common signs of ATTRv amyloidosis; symptoms typically affect the heart:

- Increased fatigue
- Dizziness
- Shortness of breath
- Leg swelling (oedema)
- Palpitations and abnormal heart rhythms (atrial fibrillation)
- Chest pain

Gastrointestinal Symptoms

- Nausea and vomiting
- Excessive diarrhoea
- Severe constipation
- Unexplained weight loss

Getting a diagnosis

How do you test for ATTRv amyloidosis?

Healthcare professionals will use a combination of tests to diagnose ATTRv amyloidosis. These may include:

• Genetic testing

This test will determine if you carry a mutation in the TTR gene associated with ATTRv amyloidosis.

It involves taking a sample of blood and analysing it to see if the DNA inside the cells contain any mutations.

Genetic counsellors may be available to help you understand the issues related to genetic testing – including consequences of a positive result and what this might mean for your family. They will also be able to help you decide if the test is right for you.

• Tissue biopsy

This test allows your doctor to confirm the presence of amyloid deposits.

A small sample of tissue is removed from the body with a needle and examined in the lab. Most biopsies are painless and some use anaesthetic treatments to numb the area beforehand. After having a biopsy, you usually won't feel any pain.

• Other tests

Some tests can determine the impact of amyloid deposits on the heart, nerves and other organs.

These can include nerve conduction studies, muscle test and other types of scans like an echocardiogram (ECG) or magnetic resonance imaging (MRI) of the heart.

Who is the Patient likely to see?

The GP will most likely refer a Patient they suspect may have ATTRv amyloidosis to one or more Specialists - this might include a neurologist, a cardiologist or a gastroenterologist. This is because ATTRv amyloidosis is a multi-system disease, meaning it can affect multiple organs that need to be checked by different people.

Why is it so important to get an early diagnosis?

Without treatment, the symptoms of ATTRv amyloidosis are likely to continue to progress over time, so catching and treating them early is important. Your doctor can only treat you for ATTRv amyloidosis once you have a diagnosis.

Once this happens, your doctor can find you the most appropriate treatment(s). These treatments might delay worsening of the disease, manage your symptoms and/or help you to maintain your daily activities.

> ***"It's not as rare as people think, and it's not rare to us. It's not rare to John who has to go through it."***

Rosemary
WIFE TO JOHN WHO IS LIVING WITH AMYLOIDOSIS

Where can I go to get more information?

hATTR Amyloidosis Ireland Disease Awareness

- https://www.hattr-amyloidosis.org/
- This website is developed and produced by Alnylam Pharmaceuticals. Inc. It is designed to help raise awareness of hATTR amyloidosis and promote education on the condition of patients and their families.

Amyloidosis Ireland

- https://amy.ie
- info@amy.ie
- Amyloidosis Ireland offers support to patients affected by ATTRv amyloidosis and ATTRwt amyloidosis (wt for wildtype). They are committed to raising awareness to ensure people are diagnosed and have access to available treatments at the earliest opportunity.

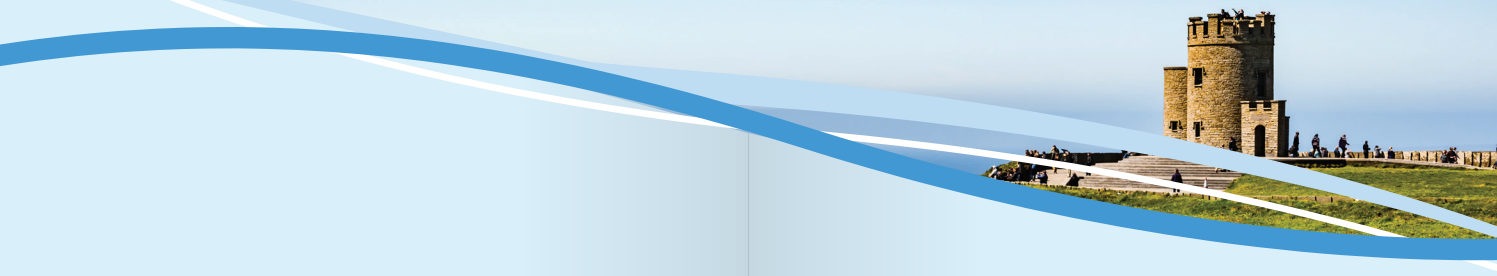
Amyloidosis Alliance

- https://www.amyloidosisalliance.org
- contact@amyloidosisalliance.org
- Amyloidosis Alliance is an international umbrella patient advocacy organisation, aiming to raise awareness and improve the quality of care of amyloidosis patients.

Suggested Next Steps

1. Speak with your **healthcare professional.**
2. Talk to **your family** members.
3. Learn and understand your family's **medical history.**
4. Do consider getting a **genetic test** if you have reason to suspect you may have hereditary **ATTR amyloidosis.**

KNOWLEDGE IS **POWER.**
STAY **INFORMED.**



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