

# GENETIC TESTING

## *A Guide for Patients with Transthyretin Amyloidosis*

Being diagnosed with hereditary transthyretin, or hATTR, amyloidosis can leave patients with many questions. But through conversations with trusted health care providers and thorough educational materials provided by patient organisation, patients can develop a clearer understanding of the disease. One powerful source for information is genetic testing.

### What is transthyretin amyloidosis?

Transthyretin amyloidosis is a rare condition caused by abnormal proteins, called amyloid, building up in the body. As protein deposits develop in organs or tissues, they can cause disruptions in the nerves, heart or digestive system, as well as in the kidneys and eyes.

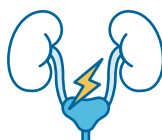
Depending on where abnormal proteins build up, patients may experience:



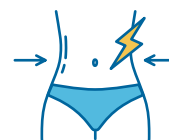
Weakness, numbness, or pain in limbs



Shortness of breath

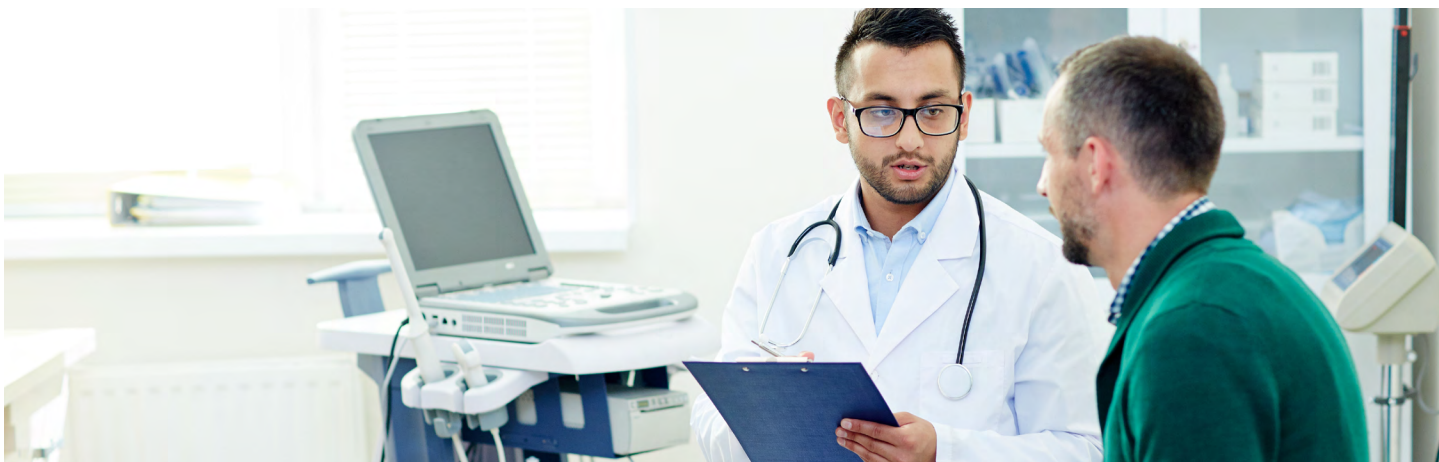


Bladder problems, bowel problems or sexual dysfunction



Decreased appetite, stomach pain or weight loss

Because symptoms are complex and often resemble signs of other conditions, reaching a diagnosis for amyloidosis may be difficult. One option for people who know that a direct family member has hATTR amyloidosis is genetic testing.



## What is genetic testing?

Genetic testing takes a closer look at a patient's genetic makeup. A sample of DNA is collected — from blood, hair, skin, bodily fluid or tissue — then inspected for genetic variants that can trigger the disease. Genetic testing can confirm that a patient has a genetic variant that can cause the inherited form of transthyretin amyloidosis. Results can also aid family members in understanding whether they too carry the genetic variant for the disease. Indiscriminate testing is to be discouraged, however, especially among very young people. All genetic testing should be undertaken only after discussions with an appropriately trained genetic counselor or patient consultant with expertise in amyloidosis.

## What do genetic tests for hATTR amyloidosis reveal?

Genetic tests can identify which genetic variant is causing a patient's hATTR amyloidosis. There are more than 120 genetic variants that can trigger hATTR amyloidosis. Each produces a different pattern of disease onset, symptoms and outlook. The three most common genes involved are:



**V30M**

Predominantly  
**Neuropathic  
Symptoms**

Most Prevalent In  
**Portugal, Spain,  
France & Sweden**



**V122I**

Predominantly  
**Cardiac  
Symptoms**

Most Prevalent In  
**People of  
African Descent**



**T60A**

Both  
**Cardiac &  
Neuropathic  
Symptoms**

Most Prevalent In  
**Ireland**



## How can genetic testing help family members?

Mothers, fathers, siblings or children of a person diagnosed with hATTR amyloidosis have a 50% chance of inheriting the disease-causing genetic variant. Simply having the genetic variant, however, does not necessarily mean the relative will develop the disease. Hence, genetic testing should be undertaken only after discussions with a trained genetics counselor or consultant with expertise in amyloidosis.

Genetic testing can help a patient's immediate family members understand their risk. If they are non-carriers, they can be reassured. If they are carriers, they can seek appropriate screening programmes. By seeking care early, affected family members can manage symptoms and slow disease progression.

## What roles do genetic counselling and genetic counselors play?

Genetic testing should go hand in hand with comprehensive genetic counselling. This can be provided by a genetic counselor or a doctor or nurse who has had specialized training. Genetic counseling helps patients assess their risk for hereditary diseases.

Prior to testing, genetic counselling will help patients understand what genetic testing for hATTR amyloidosis involves. This will also help patients understand how the results of genetic tests might impact important resources, including life and health insurance.

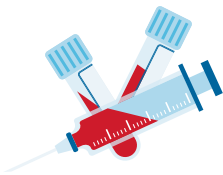
After testing, genetic counselling is also a key aspect to help explain genetic testing results and what they may mean for patients and family members. Patients also receive advice on best practices for communicating news about genetic testing results to family members.

## What steps are involved?



### Decision

Patients and members of their families who are interested in receiving a genetic test for hATTR amyloidosis can communicate with their specialists. Specialists can then refer patients and interested family to a genetic counselor or other trained health care professional, who will assess their risk level, inform them about the process and its implications, and work with the specialist to order a genetic test if appropriate.



### Sample Collection

A DNA specimen will be collected from the patient, then sent to a genetic testing lab. Testing generally requires a blood sample.



### Analysis

DNA will be sequenced, revealing any genetic variants associated with hATTR amyloidosis. Findings will be returned to the specialist who ordered the test. A genetic counselor or other trained health care professional will review the test results and discuss them with the patient.



### Treatment Decision

Together, patients and their specialist will assess and make treatment decisions based on test results.

## What are the limitations?

Genetic testing can be expensive, especially for people whose health insurance plans do not provide coverage.

Test results also do not give patients a conclusive “yes” or “no” on whether they will develop amyloidosis. Testing informs patients if they have inherited the disease-causing genetic variant.





## What treatments are available for hATTR amyloidosis?

For years, liver transplants were the only treatment option for hATTR amyloidosis. Thanks to research and innovation, there are now different medications available to:



Decrease the amount of abnormal protein production in the body. This can decrease deposition of the amyloid proteins, which may slow or stop the buildup of deposits.



Prevent the protein from taking abnormal shape and forming deposits in the body. This can delay or stop disease progression.

Clinicians may also prescribe supportive treatments that alleviate symptoms. Although they do not address the underlying cause of hATTR amyloidosis, they can improve quality of life.

There are several emerging treatments being studied in clinical trials that aim to:



Remove amyloid deposits in affected organs



Permanently 'knock out' the transthyretin gene, a process known as gene editing

Patients interested in accessing new treatments can speak to their specialist about how to enrol in ongoing clinical trials.

# Conclusions

As a rare disease, hATTR amyloidosis can be difficult at first for patients to fully comprehend. Empowered with information from genetic testing, however, patients can better understand the disease and the risk it poses to both them and their families. Most importantly, they can begin treatment early.



## Amyloidosis Working Group



*Amyloidosis Ireland  
Support Group*  
AWARENESS ADVOCACY SUPPORT





### **About the European Alliance for Patient Access**

The European Alliance for Patient Access is a division of the Global Alliance for Patient Access, an international platform for health care providers and patient advocates to inform policy dialogue about patient-centred care.

**GAfPA.org**



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