Alnylam®

ATTR AMYLOIDOSIS REVEALED™

DOCTOR DISCUSSION GUIDE

TALKING TO YOUR DOCTOR ABOUT ATTR AMYLOIDOSIS

If you think you may be experiencing symptoms of ATTR amyloidosis (ATTR), the first step is to speak with your doctor. **Bring this discussion guide to your next appointment with your general practitioner or specialist**–it covers everything you need to have an informed discussion about ATTR.

If you haven't already, complete the Symptoms Tracker & Checklist and bring the results with you. Having a record of your symptoms can help your doctor better understand what you are experiencing.

ABOUT ATTR

ATTR is an underdiagnosed, rapidly progressive, and often fatal disease.[1,2] It is caused by the breakdown and misfolding of transthyretin (TTR) proteins, which are primarily produced in the liver. Normally, TTR helps carry thyroid hormones and vitamin A (retinol) through the blood.[3]

There are two main types of ATTR. Knowing which type you have is crucial for understanding your treatment options–and in some cases, potential risks for your family:

wtATTR

Wild-type ATTR: This type is not inherited. It is usually related to ageing and most often affects the heart, impacting an estimated 200,000 – 300,000 people worldwide.[4]

hATTR

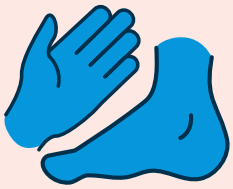
Hereditary ATTR: This affects approximately 50,000 people worldwide and is caused by an inherited variant in the *TTR* gene, which may mean other family members are also at risk.[5]

Diagnosing ATTR can be challenging because symptoms can vary widely from person to person and may affect multiple parts of the body. Your doctor might use terms like ATTR-CM (affecting the heart) or ATTR-PN (affecting the nerves). These are the two most common ways ATTR presents, though some people experience a combination of both.

- **ATTR with polyneuropathy (ATTR-PN):** Polyneuropathy refers to nerve damage that affects sensation, movement, strength, the digestive system and other bodily functions.[6,7,8]
- **ATTR with cardiomyopathy (ATTR-CM):** Cardiomyopathy is a disease of the heart muscle that makes it difficult for the heart to pump blood to other parts of the body, which can lead to heart failure.[9]

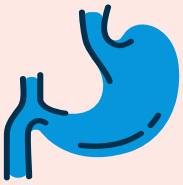
Common Signs of ATTR[2,10]

Some common symptoms of ATTR include:



Pain and numbness in the feet and hands

Shortness of breath



Digestive tract symptoms such as diarrhoea or constipation

Fatigue

Carpal tunnel syndrome

Erectile dysfunction

Heart related symptoms such as abnormal heart rhythms (arrhythmias), Irregular heartbeat, fainting or leg swelling (oedema)

Note: These are not the only symptoms. Because ATTR can affect many systems in the body, it's important to talk to your doctor about any unexplained health issues. Early diagnosis is important, as untreated ATTR can progress quickly.

5 Get Familiar with the Tests

If your doctor suspects ATTR, they may assess heart or nerve function through imaging, lab tests, or other evaluations.

Tests that measure how well your heart is working:

- ✓ **Electrocardiography (ECG/EKG)** can detect heart-related conditions. Electrodes are used to record electrical activity and the rhythm of the heart.
- ✓ **Echocardiography (Echo)** is a type of imaging that uses ultrasound to visualize the heart structure and measure heart valve function and cardiac muscle strength.
- ✓ **Cardiac magnetic resonance imaging (CMRI)** is a type of imaging that uses a magnetic field to visualize the heart structure and determine how well blood flows through the heart.

Tests that measure how well your nerves are working:

- ✓ **A nerve conduction study (NCS)** can detect nerve damage. It uses electrodes to test the speed at which electrical impulses move through the nerves.
- ✓ **Electromyography (EMG)** can detect abnormalities in the nerves and muscles by measuring the electrical activity of muscle in response to a nerve's stimulation.

Confirming A Diagnosis

6

If preliminary test results suggest the possibility of ATTR, your doctor may perform additional tests to help confirm the diagnosis, such as:

Technetium pyrophosphate scintigraphy (PYP scan), which is a type of imaging and a non-surgical way of detecting amyloid deposits in the heart

A tissue biopsy to identify amyloid deposits in the tissues

Genetic testing from DNA samples (blood, cheek swab, or saliva) to detect genetic variants in the TTR gene

Genetic testing is needed to determine if you have wild-type or hereditary ATTR. If hereditary, family members may also want to consider testing to understand their risk.

Note: This is not an exhaustive list. Your doctor may recommend other tests based on your specific symptoms.

QUESTIONS FOR YOUR DOCTOR

7

Asking the right questions can help you get the most out of your appointment. If there is a suspicion of ATTR, your GP may refer you to a specialist. Consider asking:

If you're experiencing symptoms:

- I've been having [insert symptom, e.g. numbness, shortness of breath, fatigue]. Could ATTR be a possible cause?
- Are there tests you can do to check whether my heart or nerves are affected?
- Could my symptoms be related to more than one condition? What are the next steps to narrow it down?

If you're concerned about risk:

- I've read that ATTR can be hereditary in some cases. Could my symptoms be related to a hereditary form?
- Does my family history, age, or ethnic background increase my risk for ATTR?
- Would genetic testing help clarify whether I have a hereditary form of the disease?

If a diagnosis is being considered:

- What kinds of tests will you use to evaluate my symptoms?
- What would the results mean, and how would they guide next steps?
- If ATTR is suspected, can you refer me to a specialist for further evaluation?

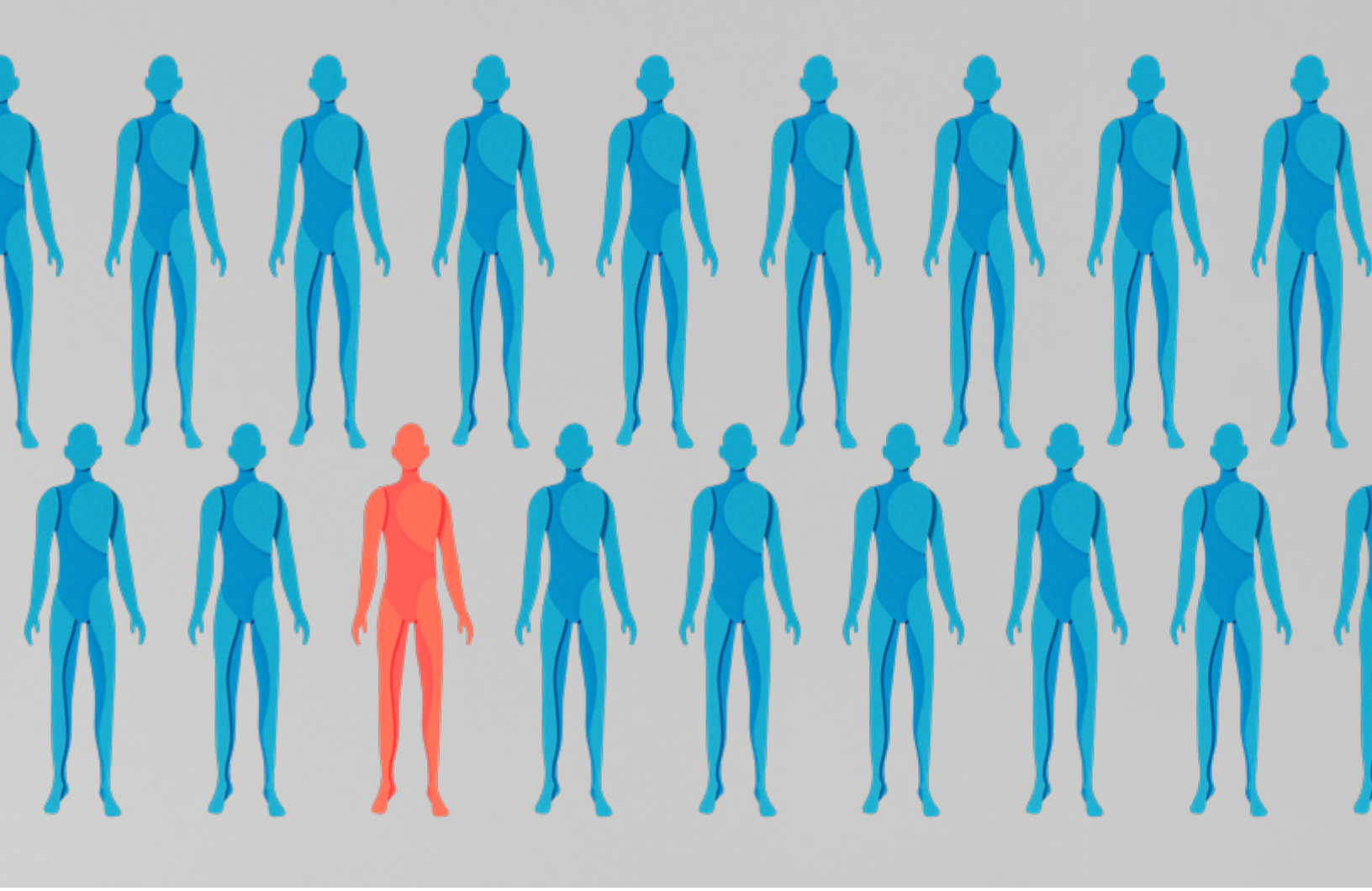
If referral is needed:

- If my symptoms are heart-related, could you refer me to a cardiologist familiar with ATTR?
- If my symptoms are nerve-related, could you refer me to a neurologist experienced in rare diseases?

If ATTR is confirmed or strongly suspected:

- What treatment options are available?
- How quickly does ATTR progress if left untreated?
- Will other family members need to be tested?

This guide is intended to provide general information and should not be considered a substitute for professional medical advice. Always talk to your doctor about any health concerns you may have.



Visit www.ATTRrevealed.co.uk to receive more educational resources and learn about ATTR.

References

[1] Hawkins PN., Ando Y., Dispenzeri A., et al. Ann Med. 2015;47(8):625-638.
[2] Ando Y., Coelho T., et al. Orphanet J Rare Dis. 2013;8:31.
[3] Liz MA., Coelho T., et al. Neurology and therapy, 9(2), 395-402.
[4] Data on file.
[5] Gertz MA. Am J Manag Care. 2017;23(7):S107-S112.
[6] Conceição I., et al. Journal of the Peripheral Nervous system, 21.1 (2016): 5-9.
[7] Sekijima Y. The Lancet Neurology. 2021;0;17
[8] Maurer MS., Hanna M., et al. J Am Coll Cardiol. 2016;68(2):161-172
[9] Maron, BJ., Towbin JA., et al. Circulation. 2006;113(14):1807-1816
[10] Kittleson MM, et al. J Am Coll Cardiol. 2023;81(11):1076-1126;

Alnylam®

ATTR AMYLOIDOSIS REVEALED™