Understanding Hereditary ATTR (hATTR) Amyloidosis

Hereditary ATTR (hATTR) amyloidosis is one of the two main types of ATTR amyloidosis – the other being wild-type (wtATTR) amyloidosis.

Unlike the wild-type form, hATTR amyloidosis is known to be linked with certain gene variants (gene mutations) that can be passed down to family members.

However, people with a specific gene variant linked to hATTR amyloidosis will not necessarily develop any symptoms.

What is hATTR amyloidosis?[i]

Transthyretin (TTR) protein is made naturally in the liver

In hATTR amyloidosis, an inherited gene variant can result in an abnormal TTR protein being produced which is less stable and can break apart

The pieces of protein clump together to form amyloid fibrils

These amyloid fibrils build up in the tissues and organs of the body, which can cause health problems

Gene variants

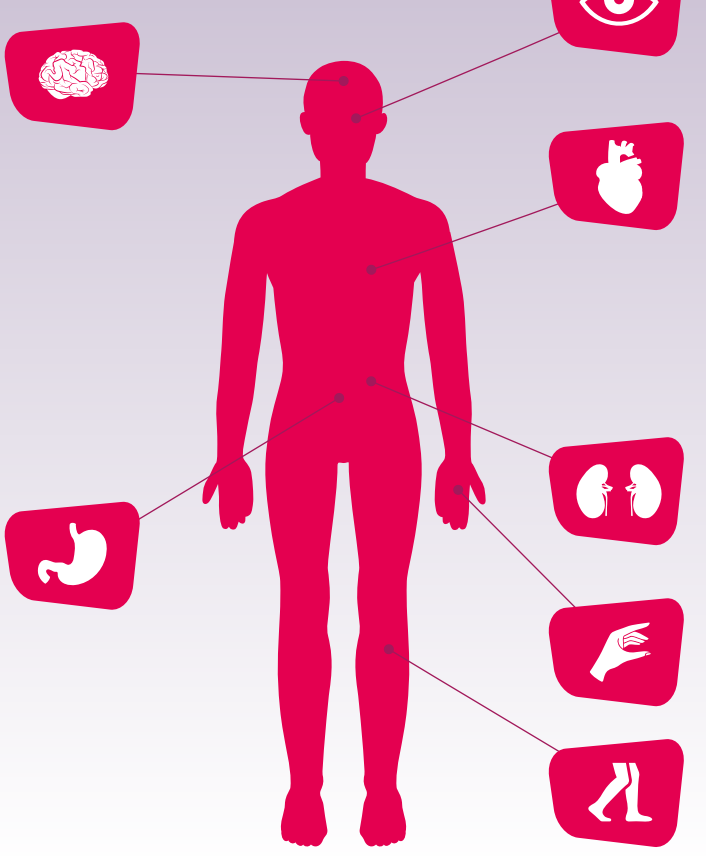
There are lots of gene variants known to be linked to this disease. Some are more prevalent in certain parts of the world or in certain groups of people than others. For example:

- **V30M** is the most common genetic variant associated with hATTR amyloidosis and is linked to certain parts of Portugal, where around 1 in 500 people carry this variant
- **V122i** is commonly linked to people of Black African or Afro-Caribbean descent
- **T60A** is the most common variant in the UK and is frequently linked to people with Irish ancestry

Can I pass it on to my children?

Although not all people with a genetic variant that is linked to hATTR amyloidosis will develop symptoms, the genes associated with this disease can be passed down through families. For each pregnancy, there is a 50% (1 in 2) risk that a child will have the gene variant.

Key symptoms[ii]



Nervous system

Peripheral neuropathy (damage to nerves in the body)
- Loss of sensation
- Limb weakness and pain

Autonomic neuropathy (damage to nerves that control your internal organs)
- Changes in heart rate and blood pressure
- Poor digestion
- Sexual dysfunction

Digestive system

- Nausea
- Weight loss
- Loss of appetite
- Wasting of muscles/tissues
- Diarrhoea/constipation

Eyes

- Glaucoma
- Abnormal eye vessels
- Eyelid swelling

Heart

- Heart palpitations and irregular heart rhythms
- Chest pain
- Fatigue
- Shortness of breath
- Disrupted sleep
- Congestive heart failure

Kidney

- Foamy or bubbly-looking urine
- Renal failure

Hands

- Carpal tunnel syndrome

Legs

- Leg swelling

Diagnosis

- Because patients often present with symptoms that resemble other, more common conditions it can be difficult to diagnose hATTR amyloidosis. Common diagnostic tests include:

Genetic tests

Blood or urine tests

Testing a sample of body tissue (biopsy)

Treatment

- While positive advances have been made and new treatment options are emerging, there is not currently a cure for hATTR amyloidosis.
- Treatment plans generally follow two principles:

Supportive treatment
using medication to treat symptoms and associated organ damage

Source treatment
preventing or slowing production of amyloid at the source, either through a liver transplant or using relatively new medicines that aim to disable production of the TTR protein

The National Amyloidosis Centre (NAC)

Patients with suspected or diagnosed ATTR amyloidosis should be assessed by a specialist unit. In the UK, the **NHS National Amyloidosis Centre (NAC)** at the Royal Free Hospital, London, will be where most people are referred to for specialist help.

References

i Amyloidosis: ATTR (transthyretin). Cleveland Clinic. Available at: https://my.clevelandclinic.org/health/diseases/17855-amyloidosis-attr. Last accessed: June 2021.

ii Hereditary Amyloidosis. Amyloidosis Foundation. Available at: https://amyloidosis.org/facts/familial/#symptoms. Last accessed: June 2021.