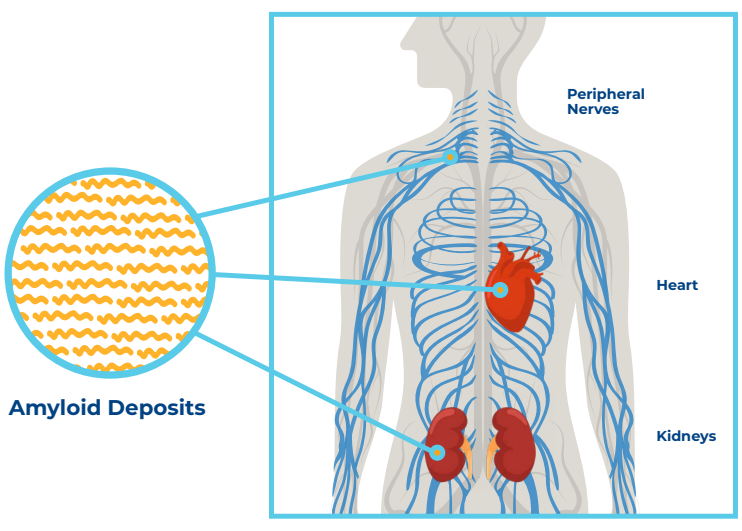
Transthyretin Amyloidosis Cardiomyopathy (ATTR-CM)

ALEXION
AstraZeneca Rare Disease

WHAT IS AMYLOIDOSIS?

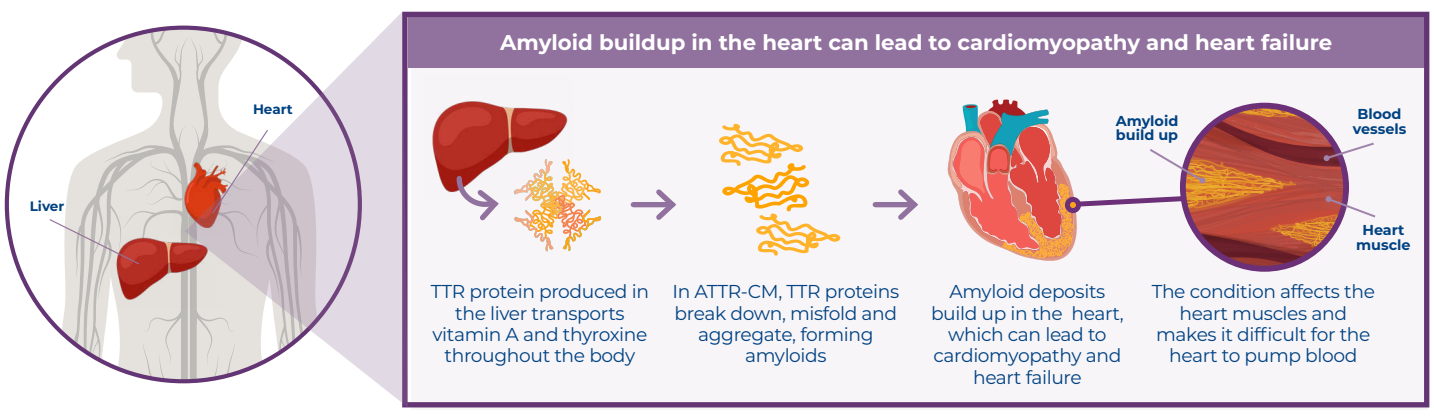
Amyloidosis is a **group of complex rare diseases** caused by abnormal proteins that **misfold and clump together to form amyloid deposits** in tissues or organs, including the heart, kidney and peripheral nerves.[1-3]

This build up can result in **significant organ damage and organ failure** that can severely impact quality of life and can ultimately be fatal.[1-3]



WHAT IS ATTR-CM?

ATTR-Cardiomyopathy (ATTR-CM) is a **systemic and progressive type of amyloidosis** caused by the breakdown, misfolding, aggregation and deposition of a protein called transthyretin (TTR) in the heart. TTR is a protein primarily produced in the liver that mainly serves to transport vitamin A and a thyroid hormone called thyroxine. The buildup of these misfolded proteins in the heart can lead to cardiomyopathy, a condition of the heart muscle that **makes it hard for the heart to pump blood** and can **lead to heart failure.**[3-7]



ATTR-CM can be **hereditary,** which occurs when mutations in the TTR gene are passed down from parents, or **non-hereditary** (wild-type), which does not have a known cause.[7]

The hereditary form of the disease **affects people as young as 20 years old**, while the non-hereditary form predominantly **affects people over the age of 60.**[8,9]

Worldwide, there are an estimated **300,000 - 500,000 people** living with ATTR-CM.[10,11]

People with ATTR-CM may experience a range of signs and/or symptoms, including:[6,12-14]

- **Fatigue**
- **Difficulty breathing (dyspnoea)**
- **Dizziness**
- **Weakness**
- **Loss of consciousness**
- **Swelling of the lower legs or ankles (oedema)**
- **Irregular heartbeat or heart rate (arrhythmia)**
- **Carpal tunnel syndrome**
- **Spinal stenosis (narrowing of the spinal canal)**

and many other vague symptoms that mimic other diseases that often complicate diagnosis.

HOW IS ATTR-CM DIAGNOSED?

ATTR-CM may be suspected when there are cardiac symptoms and/or there is a family history of amyloidosis. Most frequently, it is recognised when people experience cardiac symptoms of heart failure or worsening of heart failure.[15,16]

A diagnosis of ATTR-CM can be confirmed with **nuclear imaging**, **magnetic resonance imaging (MRI)** or a **heart biopsy.**[15,16]

It is important to confirm the type of amyloidosis, which can be done through a specialised blood test.[17]

The hereditary form of the disease can be confirmed through a **genetic test.**[17]

The journey to diagnosis can be long, with the disease sometimes initially misdiagnosed due to non-specific signs and symptoms that are common with heart failure. **Initial diagnosis of ATTR-CM can be complex** and may involve visits to several types of healthcare specialists, delaying diagnosis and treatment.[3,12,14]

On average, **diagnosis of ATTR-CM can take 6-8 years.** People often progress to a moderate or severe stage of the disease by the time an accurate diagnosis is received.[14,18,19]

WHAT ARE CURRENT TREATMENT NEEDS?

There are no approved treatments that are designed to directly remove ATTR-amyloid deposits from the heart and other tissues and organs.[20]

Current treatment approaches include therapies that prevent or suppress the formation of amyloid deposits as well as manage symptoms. However, **organ damage may continue to progress** due to the existing amyloid deposits and ultimately **lead to organ failure and death.** In some cases, liver or heart transplant is performed.[6,15,21]

Given the progressive nature of ATTR-CM and its significant impact on quality of life, **there remains a need for increased awareness of the disease and continued innovation to improve outcomes for people living with ATTR-CM.**[3]

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