CONDITION

Prealbumin tyr-77 amyloidosis

An inherited condition in which a Ser77Tyr transthyretin variant causes abnormal protein deposits that can damage nerves and the heart.

WHAT IT IS
Inherited transthyretin amyloidosis caused by the Ser77Tyr variant

BODY SYSTEM
Nervous system, heart and circulation, and digestive system

MAIN SYMPTOMS
Numbness, weakness, dizziness on standing, breathlessness

WHAT CAUSES IT
Inherited TTR gene change causing amyloid deposits

HOW IT IS DIAGNOSED
TTR genetic testing plus organ assessment or amyloid biopsy

MAIN TREATMENT
Transthyretin-targeting medicines and organ-specific supportive care

CAN IT BE CURED?
No - treatments slow progression but cannot remove the gene

IS IT AN EMERGENCY?
Sometimes - chest pain, fainting, or severe breathlessness

LONG-TERM OUTLOOK
Often progressive; treatment may slow nerve and heart damage

Overview

Prealbumin tyr-77 amyloidosis is a rare inherited form of transthyretin amyloidosis, also called hereditary ATTR amyloidosis. Transthyretin, or TTR, is a protein made mainly by the liver. Its older name was prealbumin.

In this condition, a change in the `TTR` gene makes the protein less stable. The change is commonly called Ser77Tyr because the usual amino acid serine is replaced by tyrosine at position 77 of the mature protein. A genetic report may instead call it p.Ser97Tyr because modern numbering includes the protein's 20-amino-acid signal sequence.

Unstable TTR can separate into smaller pieces that misfold and collect as amyloid. Amyloid is abnormal protein material that builds up between cells. Over time, deposits can interfere with nerves, the heart, and other organs.

Published information about this particular variant is limited because it is uncommon. Reports suggest that nerve problems are often important, although heart involvement can also occur. The genetic result alone cannot predict which organs will be affected or how quickly symptoms will change.

Symptoms

Symptoms usually develop gradually. Early problems may be mild and can resemble more common conditions.

Peripheral neuropathy means damage to nerves outside the brain and spinal cord. It can cause:

Amyloid can also affect autonomic nerves, which control automatic functions. This may cause dizziness when standing, faintness, changes in sweating, sexual difficulties, bladder problems, constipation, or diarrhoea. Unplanned weight loss or feeling full quickly may result from digestive involvement.

Heart deposits can make the heart muscle stiff. Possible symptoms include breathlessness during activity, ankle swelling, tiredness, palpitations, chest discomfort, or fainting. An abnormal heartbeat or conduction problem may sometimes be found before clear symptoms develop.

Not everyone has all these symptoms. A person who carries the variant may have no symptoms, especially earlier in life.

- Tingling, burning, pain, or reduced feeling in the feet and hands
- Poor balance, leg weakness, or difficulty with fine hand movements
- Carpal tunnel syndrome, which causes hand numbness or pain
- Injuries to numb areas that are not noticed promptly

Causes and risk factors

The condition is caused by an inherited change in one copy of the `TTR` gene. It follows an autosomal dominant inheritance pattern. This means each child of someone carrying the variant has a 1 in 2 chance of inheriting it.

Inheriting the variant does not always mean that active amyloidosis will develop. This is called reduced penetrance. Age at symptom onset and the organs affected can differ even within the same family.

The main risk factor is having the Ser77Tyr variant. A family history of unexplained neuropathy, heart thickening, heart failure, rhythm problems, carpal tunnel syndrome, or amyloidosis may provide a clue. However, an apparently negative family history does not rule it out. Relatives may have been mildly affected, misdiagnosed, or never developed symptoms.

This inherited condition is different from AL amyloidosis, which is caused by abnormal antibody-producing cells in the bone marrow. Distinguishing ATTR from AL amyloidosis is important because their treatments are different.

Diagnosis

Diagnosis usually combines genetic testing with evidence that amyloid is affecting an organ. A positive genetic test by itself shows that someone carries the variant; it does not prove that current symptoms are caused by amyloid.

Assessment may include a neurological examination, nerve conduction tests, blood pressure measurements while lying and standing, and tests of heart rhythm and structure. An electrocardiogram records the heart's electrical activity. An echocardiogram uses ultrasound to examine its muscle and pumping function. Cardiac magnetic resonance imaging may provide more detail.

Blood and urine tests are used to look for other causes of neuropathy or heart problems. They also check for abnormal antibody proteins associated with AL amyloidosis.

A nuclear medicine heart scan can detect transthyretin deposits in certain circumstances. Before interpreting this scan as ATTR amyloidosis, clinicians generally need to exclude abnormal antibody proteins. A scan does not identify the specific inherited variant, so genetic testing remains important.

Sometimes a small tissue sample is needed. This is called a biopsy. Amyloid is confirmed using special staining, and the protein should be typed accurately, often by mass spectrometry. A negative biopsy from one site does not always exclude amyloidosis because deposits may be unevenly distributed.

Because genetic names can differ, a genetics or amyloidosis service can confirm whether Ser77Tyr and p.Ser97Tyr refer to the same variant on a particular report.

Treatment and management

There is no treatment that removes the inherited gene change. Treatment aims to reduce the production or instability of TTR, slow further organ damage, and manage symptoms.

TTR stabilisers attach to the protein and help prevent it from breaking apart. Medicines in this group are used mainly for ATTR cardiomyopathy, meaning heart muscle involvement.

TTR-silencing medicines reduce the liver's production of transthyretin. Several types are available for hereditary ATTR with polyneuropathy, and some may also be used for heart involvement. Access and approved uses differ by country and can change over time.

These treatments may slow progression, but they do not reliably reverse established nerve or heart damage. The choice depends on the organs involved, functional ability, other health conditions, local approval, and the possible benefits and burdens of treatment.

Liver transplantation greatly reduces the main source of variant TTR and was once a central treatment. It is now reserved for selected people because medicines are available and because transplantation does not remove existing deposits. Normal, or wild-type, TTR can sometimes continue collecting on deposits after surgery.

Supportive care is tailored to the problems present. It may include:

Regular follow-up usually involves both symptom review and repeat testing of the organs at risk. Care is often coordinated through an amyloidosis centre or a team familiar with inherited ATTR.

- Treatment for fluid retention, abnormal heart rhythms, or conduction problems
- Pain management and physical or occupational therapy for neuropathy
- Measures to reduce dizziness from low blood pressure on standing
- Nutrition and digestive support
- Foot care and mobility aids when sensation or balance is reduced
- Carpal tunnel treatment and eye assessment when needed

Complications

Progressive nerve damage can lead to weakness, falls, difficulty walking, loss of hand function, or unnoticed wounds. Autonomic nerve damage may cause marked blood pressure drops, digestive problems, poor nutrition, or bladder difficulties.

Heart involvement can lead to heart failure, in which the heart cannot fill or pump effectively. It can also cause slow, fast, or irregular rhythms, blood clots, and fainting.

The emotional effects can also be significant. Genetic results may affect decisions about family planning, work, insurance, and testing relatives. Genetic counselling can help people consider these issues without pressure.

Prevention

The inherited `TTR` variant cannot be prevented through diet, exercise, or lifestyle choices. A person who inherits it did not cause the condition.

Genetic counselling can explain inheritance and the choices available to relatives. Predictive genetic testing can show whether an adult relative carries the familial variant. Testing should be voluntary and accompanied by clear information about possible medical and personal effects.

Family-planning options may include testing during pregnancy or testing embryos created through in vitro fertilisation. These are personal choices, and availability differs by location.

Monitoring cannot prevent inheritance, but it may identify early nerve or heart changes in someone known to carry the variant. Earlier recognition may allow treatment to be considered before substantial organ damage develops.

Living with it and what to expect

Hereditary ATTR amyloidosis usually changes over years rather than days. Without effective treatment, amyloid can continue to collect and symptoms may gradually involve more functions or organs. The pace is not the same for everyone, and information about the Ser77Tyr variant is based on relatively small numbers of families.

Treatment may slow new damage. Some symptoms can improve with supportive care, but numbness, weakness, or heart stiffness that is already established may remain. Follow-up therefore continues even when symptoms feel stable.

Many people remain independent and continue working and taking part in family life, particularly during earlier stages. Others need changes in footwear, mobility support, work duties, diet, or daily routines as nerve or heart problems progress.

Keeping an up-to-date medicine list, family genetic report, and summary of organ assessments can make care easier when several specialists are involved. New symptoms should be discussed rather than assumed to be part of amyloidosis, because common and treatable conditions can occur as well.

When to get medical help

Arrange routine medical follow-up if you have a known `TTR` variant, even if you feel well. Seek

a prompt appointment for new or worsening numbness, weakness, balance problems, diarrhoea, constipation, weight loss, ankle swelling, reduced exercise tolerance, or dizziness when standing.

Contact your care team promptly if symptoms are progressing between planned visits or treatment side effects are interfering with eating, walking, sleep, or daily activities.

Call emergency services for:

These symptoms can have several causes. Emergency assessment is needed rather than waiting for a routine amyloidosis appointment.

- Severe or sudden breathlessness
- Chest pain that is new, severe, or persistent
- Fainting, especially during activity
- A sustained rapid or very slow heartbeat with weakness or dizziness
- Sudden facial drooping, arm weakness, speech difficulty, or other stroke signs

Common questions

Is prealbumin the same thing as transthyretin?

Yes. Prealbumin is an older name for transthyretin. This condition is not diagnosed by the routine blood test sometimes called a prealbumin level. That test mainly reflects nutrition, inflammation, and liver protein production.

Does a positive Ser77Tyr genetic test mean I already have amyloidosis?

No. It confirms that you carry the variant, but active amyloidosis requires evidence of amyloid-related organ involvement. Some carriers remain free of symptoms for many years, and some may never develop clear illness.

Can prealbumin tyr-77 amyloidosis be cured?

There is currently no complete cure that removes the gene change and all existing deposits. TTR-targeting treatment can reduce the formation of new amyloid and may slow progression. Supportive treatment can improve particular symptoms.

Will my children inherit it?

Each child of a carrier has a 1 in 2 chance of inheriting the variant. Each pregnancy has the same chance, regardless of whether another child inherited it. A child who inherits the variant will not necessarily develop the same symptoms or follow the same course.

Is this the same as AL amyloidosis?

No. Hereditary ATTR amyloidosis comes from transthyretin made mainly by the liver. AL amyloidosis comes from abnormal antibody proteins made by cells in the bone marrow. Testing to distinguish them is essential because treatment is different.

Can amyloid deposits be removed?

Current treatments mainly prevent TTR from becoming unstable or reduce the amount produced. The body may clear some material slowly, but established deposits and organ damage may persist. Improvement is possible in some areas, but it cannot be guaranteed.

Sources

- Sekijima Y. Hereditary Transthyretin Amyloidosis . GeneReviews, University of Washington, Seattle. Updated January 7, 2021.
- Ando Y, Coelho T, Berk JL, and colleagues. "Guideline of transthyretin-related hereditary amyloidosis for clinicians." Orphanet Journal of Rare Diseases . 2013;8:31.
- Rowczenio DM, Noor I, Gillmore JD, and colleagues. "Online registry for mutations in hereditary amyloidosis including nomenclature recommendations." Human Mutation . 2014;35(9):E2403-E2412.
- Gillmore JD, Maurer MS, Falk RH, and colleagues. "Nonbiopsy Diagnosis of Cardiac Transthyretin Amyloidosis." Circulation . 2016;133(24):2404-2412.
- Garcia-Pavia P, Rapezzi C, Adler Y, and colleagues. "Diagnosis and treatment of cardiac amyloidosis: a position statement of the European Society of Cardiology Working Group on Myocardial and Pericardial Diseases." European Heart Journal . 2021;42(16):1554-1568.
- Kittleson MM, Ruberg FL, Ambardekar AV, and colleagues. "2023 ACC Expert Consensus Decision Pathway on Comprehensive Multidisciplinary Care for the Patient With Cardiac Amyloidosis." Journal of the American College of Cardiology . 2023;81(11):1076-1126.