CONDITION

Illinois type amyloidosis

Illinois type amyloidosis is an inherited condition in which abnormal transthyretin protein can damage nerves and the heart.

WHAT IT IS
Inherited transthyretin amyloidosis caused by the Leu58His variant

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

MAIN SYMPTOMS
Numbness, carpal tunnel syndrome, weakness, shortness of breath

WHAT CAUSES IT
Inherited TTR gene variant

HOW IT IS DIAGNOSED
Genetic testing, amyloid typing, and heart or nerve tests

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

CAN IT BE CURED?
No - treatment can slow progression

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

LONG-TERM OUTLOOK
Usually progressive, though treatment may slow organ damage

Overview

Illinois type amyloidosis is a rare inherited form of transthyretin amyloidosis, also called hereditary ATTR or ATTRv amyloidosis. It is linked to a change in the TTR gene called Leu58His. In newer genetic naming systems, the same change may be written as p.Leu78His because the protein's signal sequence is counted.

The TTR gene provides instructions for making transthyretin, a protein that carries thyroid hormone and vitamin A through the blood. Most transthyretin is made in the liver.

In this condition, transthyretin can become unstable and separate into smaller pieces. These pieces form abnormal deposits called amyloid. Amyloid builds up between cells and can gradually interfere with how tissues work.

Illinois type amyloidosis most often affects peripheral nerves, which carry messages between the brain, spinal cord, and the rest of the body. It may also affect the heart, the automatic control of blood pressure and digestion, and other organs.

Symptoms usually develop in adulthood, but their timing and severity are not predictable from the gene result alone. Some people with the variant remain well for many years. Recognizing the condition matters because treatments can reduce the production or instability of transthyretin and may slow further damage.

Symptoms

Carpal tunnel syndrome may be an early feature. This happens when a nerve is compressed at the wrist, causing tingling, numbness, pain, or weakness in the hand. It may affect both hands and can appear before other signs of amyloidosis.

Damage to peripheral nerves is called peripheral neuropathy. Symptoms often begin in the feet or lower legs and may gradually move upward. Possible symptoms include:

Amyloid can also affect autonomic nerves. These nerves control body functions that usually happen without conscious effort. This may cause dizziness or faintness after standing, unusual sweating, erectile difficulties, or problems emptying the bladder.

Digestive symptoms can include early fullness after eating, nausea, alternating diarrhea and constipation, or unintended weight loss. These symptoms have many possible causes and are not specific to amyloidosis.

When the heart is involved, its walls can become thick and stiff because of amyloid deposits. The heart may then have difficulty filling and pumping efficiently. Symptoms can include shortness of breath, reduced stamina, ankle swelling, palpitations, or fainting.

Not everyone develops all these features. Some people mainly have nerve symptoms, while others have more noticeable heart involvement.

- Numbness, tingling, burning pain, or reduced temperature sensation
- Weakness, poor balance, or difficulty walking
- Loss of hand strength or trouble with fine movements
- Injuries to numb areas that are not noticed promptly

Causes and risk factors

Illinois type amyloidosis is caused by the Leu58His variant in the TTR gene. It is not caused by diet, infection, stress, or anything a person did.

The variant is inherited in an autosomal dominant pattern. This means a person with the variant has a 1 in 2 chance of passing it to each biological child. The chance is the same for every pregnancy.

Inheriting the variant does not show exactly when symptoms will begin or how severe they will become. This is called incomplete and age-related penetrance: not everyone with the variant develops recognizable symptoms, and the chance of symptoms may increase with age.

A family history of unexplained neuropathy, cardiomyopathy, heart failure, repeated carpal tunnel surgery, or amyloidosis can be an important clue. However, a family history may not be obvious because relatives were never tested, were given a different diagnosis, or remained symptom-free.

Diagnosis

Diagnosis usually combines genetic testing with tests that determine whether amyloid is present and which organs are affected. Genetic testing can confirm the Leu58His TTR variant, but a positive result alone does not prove that every symptom is caused by amyloidosis.

A medical assessment may include a neurological examination, heart examination, electrocardiogram, echocardiogram, and blood tests. Nerve conduction studies can measure how well electrical signals travel through the nerves.

Heart imaging may include cardiac magnetic resonance imaging or a nuclear medicine scan using a tracer that can attach to transthyretin amyloid. In the right setting, this type of scan can support a diagnosis of ATTR heart involvement without a heart biopsy.

Blood and urine tests are also used to look for abnormal antibody proteins. This is important because light-chain, or AL, amyloidosis is a different condition requiring different treatment. A positive nuclear scan should not be assumed to show ATTR amyloidosis until AL amyloidosis has been appropriately excluded.

Sometimes a tissue sample, called a biopsy, is needed. It may be taken from abdominal fat, a salivary gland, a nerve, the heart, or another affected tissue. Congo red staining identifies amyloid. Further laboratory analysis, preferably protein typing by mass spectrometry where available, determines the amyloid type.

Additional tests may assess walking, strength, blood pressure while lying and standing, nutrition, kidney function, heart rhythm, or digestive symptoms. These create a baseline for future follow-up.

Treatment and management

Treatment aims to slow the formation of new amyloid, manage symptoms, and protect affected organs. Existing nerve or heart damage may not fully reverse, so timely assessment is important.

TTR-targeting medicines work in two main ways. Stabilizers help keep the transthyretin protein together, making it less likely to form amyloid. Gene-silencing treatments reduce how much transthyretin the liver produces. The approved options differ according to whether nerve or heart involvement is present and according to the country or health system.

Treatment selection also takes account of the condition's stage, other health problems, monitoring needs, and practical access to therapy. These medicines are not interchangeable in every situation.

Supportive care is tailored to the affected organs. It may include treatment for fluid buildup or abnormal heart rhythms, measures to reduce dizziness on standing, and medicines for nerve pain or digestive symptoms. Physical therapy, occupational therapy, walking aids, hand splints, or foot care can help maintain safety and independence.

Carpal tunnel syndrome may need splinting, injections, or surgery. Surgery can relieve pressure on the nerve but does not treat amyloid elsewhere in the body.

Liver transplantation was used more often before TTR-targeting medicines became available because the liver makes most circulating transthyretin. It may still be considered in selected circumstances, but it does not remove existing deposits and may not stop all heart or nerve progression. Heart transplantation or combined organ transplantation is considered only for carefully selected people with advanced organ damage.

Regular follow-up may involve cardiology, neurology, genetics, and an amyloidosis specialist. Monitoring helps show whether symptoms are changing and whether treatment is having the intended effect.

Complications

Progressive neuropathy can lead to reduced sensation, muscle weakness, falls, foot injuries, or loss of mobility. Autonomic nerve damage may cause repeated faintness, bowel problems, bladder difficulties, or poor nutrition.

Heart complications can include heart failure, in which the heart cannot meet the body's needs efficiently. Amyloid may also affect the heart's electrical system, causing an unusually slow, fast, or irregular rhythm. Some people need a pacemaker or other rhythm treatment.

Reduced appetite, early fullness, diarrhea, or swallowing problems can contribute to weight loss and muscle wasting. Ongoing numbness can allow small wounds, burns, or pressure injuries to go unnoticed.

The emotional effect can also be significant. Symptoms may affect work, driving, family roles, and confidence about the future. Genetic results can create concerns for relatives as well as for the person tested.

Prevention

Illinois type amyloidosis cannot be prevented through lifestyle changes because it is caused by an inherited gene variant. Exercise, diet, or supplements cannot remove the variant.

Genetic counselling can help families understand inheritance, testing, and reproductive options. Predictive testing may be available to adult relatives who do not have symptoms. Testing is a personal decision because a positive result can have emotional, family, insurance, and employment implications that differ by location.

People known to carry the variant may be offered planned monitoring for early nerve, heart, or autonomic changes. Monitoring does not prevent amyloid formation, but it may identify organ involvement before symptoms become advanced.

General measures such as avoiding tobacco, staying physically active within personal limits, and managing blood pressure or diabetes support overall nerve and heart health. They are not specific prevention for this condition.

Living with it and what to expect

Illinois type amyloidosis is generally a progressive condition, meaning its effects can increase over time. The pace is different from person to person. Symptoms may remain mild for a period or become more limiting over several years.

Carpal tunnel symptoms can occur before broader neuropathy or heart problems. Numbness may gradually spread, while weakness and balance problems can make walking more difficult. If the heart is affected, stamina and fluid balance may change over time.

Treatment may slow new damage, but it does not reliably restore nerves or heart tissue that have already been seriously affected. Rehabilitation, mobility support, symptom treatment, and home adjustments can still improve daily function.

Follow-up is usually ongoing even when symptoms are stable. Visits may track strength,

walking, sensation, weight, blood pressure, heart rhythm, cardiac imaging, and laboratory markers. New symptoms should be discussed rather than saved automatically for the next scheduled review.

Many people continue working, travelling, exercising, and taking part in family life, although activities may need to be adjusted. Pacing, planned rest, suitable footwear, fall prevention, and checking numb skin for injuries can make daily life safer.

The inherited nature of the condition can affect the whole family. A genetics professional can help relatives receive accurate information without assuming that every family member wants testing.

When to get medical help

Arrange a routine medical review if you develop persistent numbness, burning pain, hand weakness, repeated carpal tunnel symptoms, dizziness on standing, unexplained bowel changes, ankle swelling, or a decline in exercise tolerance. These symptoms have many possible causes, but they deserve assessment if they are new or worsening.

If you already have Illinois type amyloidosis, contact your care team promptly about rapid weight gain, increasing swelling, worsening breathlessness, repeated palpitations, new falls, skin wounds on numb feet, or a clear decline in strength or walking.

Seek urgent or emergency help for:

These symptoms do not always mean amyloidosis has worsened, but they need prompt assessment.

- Severe or sudden shortness of breath
- Chest pain or pressure
- Fainting, especially during activity
- A sustained very fast or very slow heartbeat with weakness or dizziness
- Sudden facial drooping, arm weakness, speech difficulty, or other stroke signs
- New inability to walk or rapidly progressing weakness

Common questions

Is Illinois type amyloidosis the same as ATTR amyloidosis?

It is a specific inherited form of ATTR amyloidosis. "Illinois type" refers to amyloidosis

associated with the TTR Leu58His variant. ATTR also includes other inherited TTR variants and a non-inherited form associated with aging.

Why is the variant called both Leu58His and Leu78His?

Both names refer to the same change. Leu58His uses the numbering of the mature transthyretin protein. Leu78His counts an additional 20-amino-acid signal sequence and follows newer genetic naming conventions.

Does a positive genetic test mean I will become ill?

Not necessarily. The test shows that you carry the variant, but it cannot predict exactly whether symptoms will develop, when they will begin, or how severe they will be. Planned monitoring can look for early organ changes.

Can Illinois type amyloidosis be cured?

There is no established cure that removes the gene variant and all existing amyloid deposits. Current treatments can stabilize transthyretin or reduce its production, which may slow progression. Supportive treatments address nerve, heart, and digestive symptoms.

Can I pass it to my children?

A person with the variant has a 1 in 2 chance of passing it to each biological child. Whether a child who inherits it will later develop symptoms cannot be predicted with certainty.

Is carpal tunnel syndrome a sign that amyloidosis is getting worse?

Carpal tunnel syndrome can be an early feature, but it is also common in people without amyloidosis. In someone with the TTR variant, new or repeated symptoms in both hands may justify assessment for other nerve or heart involvement.

Sources

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