CONDITION

Indiana type amyloidosis

Indiana type amyloidosis is an inherited condition in which abnormal transthyretin protein builds up mainly in nerves and the heart.

WHAT IT IS
Inherited transthyretin amyloidosis linked to the Ile84Ser variant

BODY SYSTEM
Nerves, heart and circulation, eyes, and digestive system

MAIN SYMPTOMS
Numbness, weakness, standing dizziness, shortness of breath

WHAT CAUSES IT
Inherited TTR gene variant causing abnormal protein deposits

HOW IT IS DIAGNOSED
TTR genetic testing plus amyloid typing or characteristic imaging

MAIN TREATMENT
Transthyretin-targeted therapy and symptom management

CAN IT BE CURED?
No - current treatments slow further amyloid buildup

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

LONG-TERM OUTLOOK
Progressive, but treatment can slow decline and protect function

Overview

Indiana type amyloidosis is a historical name for a form of hereditary transthyretin amyloidosis, often shortened to hereditary ATTR or ATTRv amyloidosis. It has also been called familial amyloid polyneuropathy type II.

The name originally described families from Indiana with a specific change in the TTR gene. This change is usually written as Ile84Ser using older protein numbering, or p.Ile104Ser when the protein's signal sequence is included. Modern records may use either name.

The TTR gene provides instructions for making transthyretin, a protein produced mainly by the liver. The altered protein can become unstable, separate into smaller pieces, and form abnormal deposits called amyloid. These deposits build up gradually in tissues.

The peripheral nerves are commonly affected. These are the nerves outside the brain and spinal cord that control feeling, movement, and automatic functions such as blood pressure and digestion. Amyloid may also affect the heart, eyes, and other organs.

Indiana type amyloidosis matters because nerve and heart damage can progress over time. Treatments can reduce the production or instability of transthyretin, so recognizing the condition before advanced damage develops may help preserve function.

Symptoms

Symptoms often begin in adulthood, but the age of onset and pattern are not the same in every family. Some people who inherit the gene change may remain well for many years.

Nerve symptoms may start in the feet or hands and gradually spread. They can include:

Heart involvement is called ATTR cardiomyopathy. Cardiomyopathy means that the heart muscle has become abnormal. Amyloid can make the heart walls thicker and less flexible, so the heart has difficulty filling and pumping efficiently.

Possible heart-related symptoms include breathlessness, reduced stamina, ankle swelling, palpitations, dizziness, or fainting. An irregular heartbeat may occur. These symptoms have many possible causes and do not by themselves show that someone has amyloidosis.

Some people develop cloudy material in the eye's vitreous, the clear gel inside the eye. This can cause floaters, blurred vision, or reduced sight. Glaucoma, which damages the optic nerve through raised or poorly controlled eye pressure, may also occur.

- Tingling, burning pain, numbness, or reduced temperature sensation
- Weakness, poor balance, or difficulty walking
- Carpal tunnel syndrome, sometimes affecting both wrists
- Dizziness or faintness when standing because blood pressure falls
- Changes in sweating, bladder control, or sexual function
- Constipation, diarrhoea, nausea, early fullness, or unexplained weight loss

Causes and risk factors

Indiana type amyloidosis is caused by an altered copy of the TTR gene. It is inherited in an autosomal dominant pattern. This means that a person with the variant has a 1 in 2 chance of passing it to each biological child.

Inheriting the variant does not always mean that symptoms will appear. This is called reduced penetrance. Age, family background, and other biological factors can influence when or whether the condition becomes noticeable.

The condition is not caused by diet, exercise, alcohol, infection, or anything a parent did during pregnancy. It is also different from AL amyloidosis, which is caused by abnormal cells in the bone marrow producing parts of antibodies called light chains.

A known TTR variant in a parent, sibling, or child increases the chance that another biological relative carries it. A family history of unexplained neuropathy, heart failure, rhythm problems, bilateral carpal tunnel syndrome, or amyloidosis may also lead to testing.

Diagnosis

Diagnosis usually combines genetic testing with evidence that amyloid is affecting the body. A TTR gene test can identify the Ile84Ser variant. However, carrying a variant does not by itself prove that current symptoms are caused by amyloid.

Your assessment may include a neurological examination, nerve conduction studies, blood pressure measurements while lying and standing, and tests of automatic nerve functions. Heart assessment may include an electrocardiogram, echocardiogram, cardiac MRI, blood tests, or a heart rhythm monitor.

A nuclear medicine scan using a bone-seeking tracer can strongly support ATTR cardiac amyloidosis in the right setting. Blood and urine tests must also look for abnormal antibody proteins because AL amyloidosis requires different and often more urgent treatment.

Sometimes a biopsy is needed. A small tissue sample may be taken from fat, a salivary gland, nerve, heart, or another affected site. A Congo red stain can confirm amyloid. The amyloid should then be typed, often with mass spectrometry, to identify the protein forming the deposits. A negative fat-pad biopsy does not completely rule out ATTR amyloidosis.

Genetic counselling is useful before and after testing. It can help you understand what a result means for your own health, relatives, insurance or employment rules in your country, and family planning.

Treatment and management

Treatment aims to slow further amyloid formation, manage organ problems, and maintain independence. Existing amyloid damage may not fully reverse, so follow-up often continues even when disease-modifying treatment is working.

Transthyretin-targeted medicines work in two main ways. Gene-silencing medicines reduce how much transthyretin the liver produces. TTR stabilizers help keep the protein together so it is less likely to form amyloid. Which medicines are available depends on the country, whether nerves or the heart are affected, and local approval and funding arrangements.

Treatment may also address individual effects of the condition. This can include support for nerve pain, mobility, nutrition, bowel problems, low blood pressure, fluid retention, heart rhythm problems, and vision changes. Physiotherapy, occupational therapy, walking aids, and adjustments at work or home can help protect mobility and safety.

Some usual treatments for heart failure or high blood pressure may be difficult to tolerate when amyloidosis causes low blood pressure. Medicines therefore need careful review rather than being started, stopped, or changed without medical advice.

Liver transplantation was used more often before transthyretin-targeted medicines became available. It replaces the main source of variant transthyretin but does not remove existing deposits, and normal transthyretin can continue accumulating on old amyloid. It is now considered only in selected circumstances. Heart transplantation may be an option for a small number of people with severe cardiac involvement.

Eye amyloid may need separate treatment because some transthyretin is made within the eye. Procedures may be used for severe vitreous clouding, while glaucoma requires regular monitoring and treatment.

Complications

Progressive nerve damage can lead to loss of sensation, muscle weakness, falls, foot injuries, and reduced ability to walk. Reduced pain sensation means that cuts, pressure areas, or burns may go unnoticed, so routine foot care is important.

Damage to automatic nerves can cause persistent low blood pressure, fainting, digestive difficulties, bladder problems, and sexual dysfunction. Poor appetite, diarrhoea, or early fullness may contribute to weight loss and malnutrition.

Heart complications include heart failure, rhythm disturbances, and electrical conduction problems. Some people need a pacemaker or other rhythm treatment. Fluid can collect in the legs, abdomen, or lungs when the heart cannot manage circulation effectively.

Vision may decline because of vitreous amyloid or glaucoma. These problems need specialist eye follow-up and may progress separately from nerve or heart symptoms.

Prevention

The inherited TTR variant cannot be prevented through lifestyle changes. Exercise, supplements, and special diets cannot remove it or guarantee that amyloid will not develop.

If you carry the variant but have no symptoms, planned monitoring may identify early nerve, heart, or eye changes. The timing and type of monitoring are usually based on your age, family history, and the organs affected in relatives.

Genetic counselling can explain reproductive options. Depending on local services and personal values, these may include natural conception with or without prenatal testing, in vitro fertilisation with preimplantation genetic testing, donor eggs or sperm, or adoption. These are personal choices, not requirements.

Living with it and what to expect

Indiana type amyloidosis is usually a long-term, progressive condition. Without effective treatment, amyloid deposits can increase and organ function may decline over months or years. The pace cannot be predicted accurately from the gene result alone.

Treatment may slow progression or stabilize some measurements, particularly when started before severe nerve or heart damage. Symptoms caused by established nerve loss or heart scarring may continue even after amyloid production has been reduced.

Regular follow-up commonly tracks strength, sensation, walking ability, weight, blood pressure, heart function, rhythm, and vision. Report changes between planned appointments rather than waiting if they affect eating, walking, breathing, or consciousness.

Many people continue working, travelling, and managing daily activities, especially during earlier stages. Some later need mobility aids, help with personal care, dietary support, or treatment for heart failure. Rehabilitation and practical adjustments can help you remain active without assuming that every symptom is unavoidable.

The inherited nature of the condition can also affect family relationships and emotional well-being. It is reasonable to seek genetic counselling, psychological support, or contact with an amyloidosis patient organisation. You can decide when and how to discuss genetic risk with relatives, supported by a genetics service if needed.

When to get medical help

Arrange a routine medical review if you develop new or gradually worsening numbness,

weakness, balance problems, digestive symptoms, weight loss, ankle swelling, breathlessness, palpitations, or changes in vision. People already under follow-up should also report repeated falls, foot wounds, or treatment side effects.

Seek urgent same-day assessment for a new fainting episode, rapidly increasing swelling, a sustained fast or irregular heartbeat, severe dizziness, or breathlessness that is clearly worse than usual.

Call emergency services for:

These symptoms can have causes other than amyloidosis, but they need prompt assessment.

- Severe or sudden breathlessness, especially at rest
- Chest pain, collapse, or loss of consciousness
- New facial drooping, speech difficulty, or one-sided weakness
- A very fast or irregular heartbeat with faintness or chest pain

Common questions

Is Indiana type amyloidosis the same as ATTR amyloidosis?

It is a specific inherited form of ATTR amyloidosis associated with the Ile84Ser TTR variant. "Indiana type" and "type II" are older names. Modern services are more likely to use hereditary ATTR amyloidosis and record the exact genetic variant.

Is type II amyloidosis related to type 2 diabetes?

No. The "type II" label came from an older classification of familial amyloid neuropathies. It has no connection with type 2 diabetes, although a person could have both conditions.

Will I get symptoms if I carry the gene variant?

Not necessarily. Some carriers develop symptoms earlier than others, and some may remain without clear illness for a long time. Your family history may offer clues, but it cannot provide a definite timetable.

Can amyloid deposits be removed?

Current transthyretin treatments mainly reduce new amyloid formation or stabilize the protein. The body may clear some deposits slowly, but established nerve or heart damage may not disappear. Treatment goals are usually to slow decline and preserve function.

Should my family be tested?

Adult biological relatives may choose predictive genetic testing after counselling if a disease-causing TTR variant has been confirmed in the family. Testing should be voluntary and

should use the known family variant. Testing children who have no symptoms requires specialist genetic advice because this condition usually begins in adulthood.

Can I exercise with Indiana type amyloidosis?

Many people can remain active, but the safest level depends on heart function, blood pressure, balance, and nerve damage. A tailored plan may include low-impact aerobic activity, strength work, or supervised rehabilitation. Stop and seek advice if activity causes chest pain, faintness, unusual palpitations, or marked breathlessness.

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