CONDITION

Hereditary amyloidosis

Hereditary amyloidosis is an inherited condition in which abnormal proteins build up and damage organs or nerves.

WHAT IT IS
Inherited protein-folding condition causing amyloid deposits in organs

BODY SYSTEM
Nervous system, heart, kidneys, eyes, and digestive system

MAIN SYMPTOMS
Numbness, weakness, breathlessness, swelling

WHAT CAUSES IT
Inherited gene change affecting an amyloid-forming protein

HOW IT IS DIAGNOSED
Amyloid typing and genetic testing; sometimes cardiac nuclear scanning

MAIN TREATMENT
Protein-targeted therapy and support for affected organs

CAN IT BE CURED?
No - treatment can slow further amyloid formation

IS IT AN EMERGENCY?
Sometimes - fainting, severe breathlessness, or stroke signs

LONG-TERM OUTLOOK
Often progressive, but treatment may slow organ damage

Overview

Hereditary amyloidosis is a group of inherited conditions in which a protein changes shape, clumps together, and forms deposits called amyloid. These deposits can build up in nerves and organs, making it harder for them to work normally.

The most common inherited form is hereditary transthyretin amyloidosis, often shortened to hereditary ATTR or ATTRv amyloidosis. It is caused by a change in the TTR gene. Transthyretin is a protein made mainly by the liver.

Less common forms involve other proteins, including fibrinogen, apolipoproteins, gelsolin, and lysozyme. The protein involved helps determine which parts of the body are affected.

Hereditary amyloidosis is different from AL amyloidosis, which begins in abnormal bone

marrow cells and is not usually inherited. It also differs from wild-type ATTR amyloidosis, which is related to ageing rather than an inherited TTR change.

Symptoms may begin in early adulthood or much later. Even relatives with the same gene change may develop different symptoms or become affected at different ages. An inherited gene change does not always mean that symptoms will develop.

Early and accurate identification matters because treatments are specific to the amyloid protein involved. Some treatments can slow the production or buildup of amyloid, but they may not reverse damage that has already happened.

Symptoms

Symptoms usually develop gradually. They depend on which nerves or organs contain amyloid.

Nerve symptoms may include:

Amyloid can also affect the nerves that control automatic body functions. This may cause dizziness when standing, fainting, sweating changes, sexual difficulties, or problems controlling the bladder.

Digestive symptoms can include nausea, vomiting, constipation, diarrhoea, feeling full after a small meal, or unintended weight loss.

When the heart is affected, its walls can become stiff. Possible symptoms include breathlessness, ankle or leg swelling, tiredness, palpitations, chest discomfort, or reduced ability to exercise. Abnormal heart rhythms and electrical conduction problems can also occur.

Some rarer inherited forms mainly affect the kidneys, causing protein to leak into the urine and sometimes reducing kidney function. Certain gene changes can affect the eyes, skin, or blood vessels around the brain.

These symptoms have many possible causes. Having one or more of them does not by itself mean that you have hereditary amyloidosis.

- Tingling, burning, numbness, or pain in the feet and hands
- Weakness or difficulty walking
- Reduced ability to feel heat, cold, or injury
- Carpal tunnel syndrome, sometimes affecting both hands

Causes and risk factors

Hereditary amyloidosis is caused by a harmful change, also called a pathogenic variant, in a gene that provides instructions for making a particular protein. The altered protein is less stable and more likely to form amyloid.

Most forms are inherited in an autosomal dominant pattern. This means a person with the gene change usually has a 1 in 2 chance of passing it to each child. Inheriting the change does not guarantee that the child will develop symptoms.

The exact gene change can influence the age at which symptoms begin and whether the nerves, heart, kidneys, or other organs are most affected. Family patterns can still be unpredictable. Someone may have no known family history because relatives were never diagnosed, developed different symptoms, or died before symptoms appeared.

Ancestry can make certain TTR changes more common in particular populations, but hereditary amyloidosis can affect people of any background. It is not caused by diet, exercise habits, stress, or anything a parent did during pregnancy.

Diagnosis

Diagnosis begins with your symptoms, medical history, family history, and a physical examination. Tests then look for organ involvement and identify the protein forming the amyloid.

Depending on your symptoms, testing may include:

Blood and urine tests are also used to look for abnormal antibodies called monoclonal proteins. This is important because AL amyloidosis requires different treatment and must not be confused with hereditary ATTR amyloidosis.

A biopsy removes a small tissue sample so it can be checked for amyloid. The sample may come from abdominal fat, a salivary gland, or an affected organ. A laboratory method such as mass spectrometry can identify the exact amyloid protein. A negative biopsy from one site does not always exclude the condition.

In some people with suspected ATTR affecting the heart, a specific nuclear scan can confirm cardiac ATTR without a heart biopsy. This approach is only reliable when testing has not found evidence of a monoclonal protein.

Genetic testing is needed to establish whether ATTR is hereditary rather than wild-type. It can also confirm other inherited forms. Genetic counselling can help you understand the result, its limits, and what it may mean for relatives.

A positive genetic test does not always mean that organ damage is present. Further

assessment is needed to separate being a gene carrier from having active amyloidosis.

- Blood and urine tests, including kidney and liver checks
- An electrocardiogram and heart ultrasound
- Cardiac MRI or nuclear imaging of the heart
- Nerve conduction studies
- Eye, nutrition, or digestive assessments

Treatment and management

Treatment depends on the amyloid protein, the organs affected, and how advanced the changes are. Care may involve specialists in neurology, cardiology, kidney medicine, genetics, eye care, and nutrition.

For hereditary ATTR amyloidosis, targeted medicines work in two main ways. TTR stabilisers help keep the transthyretin protein from breaking apart and forming amyloid. Gene-silencing medicines reduce the liver's production of transthyretin. The approved uses of these treatments differ by country and according to whether nerve or heart problems are present.

Treatment generally aims to slow further damage. Some symptoms or organ measurements may improve, but established nerve or heart damage may remain.

Supportive care is also important. It may include treatment for fluid buildup, abnormal heart rhythms, nerve pain, low blood pressure on standing, digestive problems, or poor nutrition. Physiotherapy, mobility aids, and foot care can help if sensation or strength is reduced.

Some standard heart medicines are poorly tolerated by people with cardiac amyloidosis because their blood pressure may already be low. Any changes should be guided by a clinician familiar with the condition.

Liver transplantation was historically used for selected forms of hereditary ATTR because the liver makes most transthyretin. It does not remove existing deposits, and heart problems can continue in some people. Heart, kidney, or combined transplantation may be considered in carefully selected situations. These are major procedures rather than routine treatment.

Research continues into treatments that remove amyloid or permanently reduce production of the abnormal protein.

Complications

Possible complications reflect the organs involved. They can include progressive weakness, difficulty walking, falls, unnoticed foot injuries, chronic digestive problems, and unintended weight loss.

Heart involvement may lead to heart failure, abnormal rhythms, electrical conduction block, blood clots, or stroke. Kidney involvement can progress to severe loss of kidney function.

Low blood pressure when standing can cause falls or fainting. Reduced sensation can allow burns, pressure sores, or infections to go unnoticed. Regular monitoring is intended to find these problems early and adjust support.

Prevention

The inherited gene change that causes hereditary amyloidosis cannot currently be prevented through lifestyle changes.

If a harmful gene change has been identified in a family, genetic counselling can explain testing options for adult relatives. Testing is a personal choice and may have emotional, family, employment, or insurance implications depending on local law.

Reproductive options may include testing during pregnancy or in vitro fertilisation with testing of embryos. These choices require specialist genetic and reproductive counselling.

For someone who carries a gene change but has no symptoms, planned monitoring may detect early organ or nerve changes. Monitoring does not prevent the inherited condition, but earlier recognition may allow treatment before extensive damage develops.

Living with it and what to expect

Hereditary amyloidosis is usually a long-term condition. Without effective treatment, amyloid can continue to build up over months and years. The rate of change is not the same for everyone.

Targeted treatment may slow progression or keep the condition stable for a period. It cannot reliably restore all lost nerve function or reverse advanced organ scarring. New symptoms can still develop, so follow-up remains important even when you feel well.

Monitoring may include heart tests, nerve assessments, blood and urine tests, walking or strength checks, weight and nutrition reviews, and questions about daily activities. The schedule is based on the gene change, existing symptoms, treatment, and organs at risk.

Daily life may require practical adjustments. These can include standing up slowly, checking

numb feet for injuries, planning rest around fatigue, adapting meals for digestive symptoms, or using mobility support. Work, travel, exercise, and family life often remain possible, although adjustments may be needed as symptoms change.

Living with an inherited condition can also bring worry about relatives or future children. Genetic counselling, psychological support, and patient organisations can help with decisions and uncertainty.

When to get medical help

Arrange routine follow-up if you have hereditary amyloidosis or a known family gene change, even if your symptoms appear stable. Contact your care team sooner if you develop increasing numbness, weakness, swelling, breathlessness, palpitations, weight loss, or repeated dizziness.

Seek urgent medical advice for a sudden decline in walking, repeated fainting, rapidly worsening swelling, persistent vomiting or diarrhoea, inability to keep fluids down, or a wound on a numb foot that looks infected.

Call emergency services for:

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

- Severe or sudden breathlessness
- Chest pain that does not settle
- Fainting with ongoing weakness, confusion, or palpitations
- Signs of a stroke, such as facial drooping, arm weakness, or speech difficulty
- Collapse, unresponsiveness, or severe difficulty breathing

Common questions

Is hereditary amyloidosis cancer?

No. Amyloidosis is caused by misfolded protein deposits, not cancer cells. AL amyloidosis can be linked to an abnormal group of bone marrow cells, but hereditary amyloidosis is caused by an inherited gene change.

Is hereditary amyloidosis the same as ATTR amyloidosis?

Not always. Hereditary ATTR is the most common inherited form, but other genes can produce different amyloid proteins. ATTR can also be wild-type, meaning it develops without an

inherited TTR change.

Will my children inherit it?

Most hereditary amyloidosis follows an autosomal dominant pattern. In that pattern, each child has a 1 in 2 chance of inheriting the gene change. A child who inherits it may never develop symptoms, or symptoms may begin at a different age. A genetics specialist can explain the pattern found in your family.

Does a positive genetic test mean I already have amyloidosis?

No. It shows that you carry a gene change associated with the condition. Tests of your nerves, heart, kidneys, or other organs are needed to look for active amyloid-related changes.

Can amyloid deposits go away?

Current treatments mainly reduce the formation of new amyloid. The body may clear some deposits slowly, and organ function can sometimes improve, but established damage may remain. Response differs according to the protein, organ, and stage of the condition.

Can hereditary amyloidosis be cured?

There is no established cure for most forms. Targeted medicines can slow the production or buildup of amyloid. Transplantation changes the source of the abnormal protein in selected situations, but it does not guarantee that existing organ damage will disappear.

Sources

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