CONDITION

Icelandic type amyloidosis

Icelandic type amyloidosis is an inherited condition that weakens brain arteries through abnormal cystatin C protein deposits.

WHAT IT IS
Inherited cystatin C amyloid buildup in brain arteries

BODY SYSTEM
Brain and blood vessels

MAIN SYMPTOMS
Sudden headache, one-sided weakness, speech difficulty, seizures

WHAT CAUSES IT
Inherited CST3 gene variant

HOW IT IS DIAGNOSED
CST3 genetic testing; tissue amyloid analysis when needed

MAIN TREATMENT
Emergency stroke care, rehabilitation, and complication management

CAN IT BE CURED?
No - no treatment removes cystatin C amyloid

IS IT AN EMERGENCY?
Sometimes - sudden stroke symptoms require emergency care

LONG-TERM OUTLOOK
Recurrent brain bleeds can cause disability and shorten life

Overview

Icelandic type amyloidosis is a very rare inherited condition affecting small and medium-sized arteries in the brain. It is also called hereditary cystatin C amyloid angiopathy, Iceland disease, or Type VI amyloidosis.

The condition causes an abnormal form of a protein called cystatin C to collect in artery walls. These protein deposits are called amyloid. Over time, the deposits can weaken the arteries and make them more likely to leak or rupture.

A ruptured artery causes bleeding within the brain, known as an intracerebral haemorrhage or haemorrhagic stroke. These bleeds can happen more than once. Their effects depend on the size and location of the bleeding.

This condition was first identified in several families in Iceland. It remains most closely associated with people from these families, although genetic testing rather than ancestry is needed to confirm it.

Icelandic type amyloidosis is different from the more common forms of amyloidosis that mainly affect the heart, kidneys, liver, or nerves. Its most important effects are on the brain and its blood vessels.

Symptoms

Some people have no clear symptoms before their first brain bleed. Symptoms often begin in early or middle adulthood, but the timing is not the same for everyone.

A brain bleed can cause:

These symptoms usually begin suddenly. A smaller bleed may cause less obvious problems, while a larger bleed can cause severe disability or be life-threatening.

Repeated bleeds can have cumulative effects. A person may develop increasing difficulty with walking, speech, memory, concentration, swallowing, or everyday tasks. Changes in mood, behaviour, or personality can also occur after brain injury.

Not every headache, memory lapse, or balance problem is caused by bleeding. New symptoms still need medical assessment, especially in someone known to carry the relevant genetic variant.

- A sudden, severe headache
- Weakness or numbness, often on one side
- Trouble speaking or understanding speech
- Loss of balance or coordination
- Changes in vision
- Confusion, unusual sleepiness, or loss of consciousness
- A seizure
- Nausea or vomiting with other neurological symptoms

Causes and risk factors

Icelandic type amyloidosis is caused by a harmful change in the CST3 gene. This gene provides

instructions for making cystatin C, a protein found throughout the body.

The Icelandic form is linked to a specific cystatin C change often called L68Q. The altered protein is more likely to form amyloid deposits. In the brain, these deposits build up in artery walls and reduce their strength.

The condition follows an autosomal dominant inheritance pattern. This means a person usually needs to inherit one altered copy of the gene to be at risk. Each child of a parent with the variant has a 1 in 2 chance of inheriting it. This chance is the same for every pregnancy.

Inheriting the variant does not show exactly when symptoms will start or how severe they will be. Members of the same family may have different experiences.

The main risk factor is having the familial CST3 variant. A close relative with genetically confirmed Icelandic type amyloidosis may therefore be important, particularly if the family has Icelandic ancestry or a history of brain bleeds at unusually young ages.

This condition is not caused by diet, stress, infection, or something a parent did during pregnancy.

Diagnosis

Diagnosis may begin after a brain bleed or because the condition is already known in the family.

A CT scan of the head can quickly identify fresh bleeding. MRI can give more detail and may show previous small bleeds, iron left behind from older bleeding, or other changes in brain tissue. Imaging shows what has happened, but it does not always identify the exact inherited cause.

A genetic blood or saliva test can look for the relevant CST3 variant. Finding a known harmful variant can confirm the inherited condition when it fits the person's medical and family history.

Genetic counselling is recommended before predictive testing in someone without symptoms. Testing can affect emotional well-being, family relationships, reproductive choices, and sometimes insurance or employment issues, depending on local law. A counsellor can explain what the result can and cannot predict.

Amyloid can be identified by examining tissue under a microscope and testing which protein forms the deposits. However, taking tissue from the brain carries risk and is not usually needed when genetic testing is conclusive. Tissue testing may be considered if the diagnosis remains uncertain.

Other causes of brain bleeding must also be considered. These include high blood pressure, blood vessel abnormalities, head injury, medicines that affect clotting, and other inherited

forms of cerebral amyloid angiopathy.

Treatment and management

There is currently no treatment that removes cystatin C amyloid from brain arteries or corrects the genetic change. Care focuses on treating brain bleeds, reducing avoidable bleeding risks, supporting recovery, and managing long-term effects.

A suspected brain bleed requires emergency assessment. Hospital care may include brain imaging, monitoring of breathing and blood pressure, treatment of problems with blood clotting, and management of pressure inside the skull. Neurosurgery may be appropriate for some bleeds, depending on their location, size, and effects.

Rehabilitation can help after a stroke. It may involve:

Seizures may be treated with antiseizure medicine when they occur. Swallowing problems may require changes to food texture or another way of providing nutrition while recovery is assessed.

Blood pressure should be reviewed and managed because high blood pressure can place additional strain on brain arteries. There is limited treatment research specific to Icelandic type amyloidosis, so some care is based on evidence from brain haemorrhage and other forms of cerebral amyloid angiopathy.

Medicines that reduce blood clotting, including anticoagulants and antiplatelet medicines, can affect bleeding risk. They may still be needed for another serious condition. Do not stop a prescribed medicine without medical guidance; the risks of bleeding and unwanted blood clots must be weighed for each person.

Regular care may involve a neurologist or stroke specialist, a genetics service, rehabilitation professionals, and primary care. Follow-up should include a review of new symptoms, blood pressure, medicines, mobility, swallowing, cognition, and support needs.

- Physiotherapy for strength, balance, and movement
- Occupational therapy for everyday activities and independence
- Speech and language therapy for communication or swallowing
- Cognitive rehabilitation for memory, attention, and planning
- Psychological support for emotional and behavioural changes

Complications

The main complication is bleeding within the brain. A bleed can damage brain tissue and may cause lasting weakness, communication problems, impaired vision, seizures, or changes in thinking.

Further complications can include:

The outcome of one bleed does not reliably predict the next. Some people recover useful function after rehabilitation, while others are left with major disability.

- Repeated haemorrhagic strokes
- Falls and reduced mobility
- Swallowing problems and food or fluid entering the lungs
- Dependence on others for daily care
- Depression, anxiety, or changes in behaviour
- Life-threatening brain swelling or bleeding

Prevention

The inherited genetic variant cannot be prevented through lifestyle changes. Someone who carries it did not cause the condition through personal choices.

There is also no proven way to prevent all brain bleeds in a carrier. Managing blood pressure and reviewing medicines that affect clotting may reduce avoidable risks, although these steps cannot remove the amyloid already present.

When a familial variant is known, adult relatives can consider predictive genetic testing after counselling. Testing is a personal choice, particularly when a person has no symptoms and no treatment can prevent the underlying protein deposits.

People planning a family can discuss reproductive options with a genetics service. Depending on location and personal preferences, options may include natural conception, prenatal testing, or in vitro fertilisation with testing of embryos for the familial variant.

Living with it and what to expect

The course is often shaped by whether brain bleeds occur, where they happen, and how well a person recovers. Some people may feel well between events. Others have ongoing physical, communication, or cognitive difficulties after one or more strokes.

Historical reports from affected Icelandic families describe repeated brain haemorrhages, often beginning earlier in adult life than common forms of cerebral amyloid angiopathy. These events can cause increasing disability and may shorten life. Because the condition is exceptionally rare, there are no reliable modern estimates that predict an individual person's course.

Life after a brain bleed may change over months as the brain heals and rehabilitation continues. Improvement can continue, but some changes may be permanent. Further bleeds can cause new problems or worsen existing ones.

Practical planning may include reviewing work or education, driving eligibility, home safety, communication needs, and help with finances or personal care. Driving rules after a stroke or seizure differ by location.

The emotional effects also matter. Living with an inherited risk can bring uncertainty, grief, or concern for relatives. Genetics services, stroke support organisations, counselling, and peer support may help. Care planning can be updated over time rather than decided all at once.

When to get medical help

Call emergency services immediately for symptoms that could be a stroke or brain bleed, including:

Do not drive yourself to hospital. Note when the symptoms started if you can. Emergency brain imaging is needed because symptoms alone cannot show whether a stroke is caused by bleeding or a blocked artery.

Arrange routine medical follow-up for gradually developing changes in memory, mood, balance, speech, swallowing, or daily function. These symptoms are not always an emergency, but they should not be ignored.

Non-urgent appointments are also appropriate before starting or stopping medicines that affect clotting, when planning pregnancy, or when considering genetic testing. A sudden change remains an emergency even if you already have a follow-up appointment booked.

- Sudden weakness, numbness, or facial drooping
- Sudden trouble speaking, understanding, seeing, or walking
- A sudden severe or unusual headache
- A first seizure, repeated seizures, or failure to recover normally
- Collapse, marked confusion, or loss of consciousness

- Repeated vomiting with a sudden headache or neurological symptoms

Common questions

Is Icelandic type amyloidosis the same as Alzheimer's disease?

No. Both involve amyloid, but the proteins and usual patterns of injury are different. Icelandic type amyloidosis involves altered cystatin C accumulating mainly in brain artery walls. Alzheimer's disease mainly involves other proteins and typically causes a gradually progressive loss of memory and thinking skills.

How rare is Icelandic type amyloidosis?

It is exceptionally rare and has mainly been described in related Icelandic families. Reliable population prevalence figures are not available. Having Icelandic ancestry alone does not mean that you have the condition.

If my parent has it, will I inherit it?

Each child of a person with the CST3 variant has a 1 in 2 chance of inheriting that variant. If you do not inherit it, you cannot pass that familial variant to your children. Genetic testing can clarify inheritance when the family's variant is known.

Can a genetic test tell me whether I will have a brain bleed?

It can show whether you carry the relevant CST3 variant, but it cannot give an exact age or date for a bleed. It also cannot precisely predict how severe a bleed would be. Genetic counselling can help you consider whether knowing the result would be useful to you.

Is there a cure?

There is no cure at present, and no established treatment removes cystatin C deposits from the brain's arteries. Emergency stroke treatment, rehabilitation, seizure care, blood pressure management, and support for disability can still make an important difference.

Will I definitely become disabled?

A genetic result cannot predict an exact outcome. Brain bleeds are a serious feature of the condition, and repeated bleeds can cause major disability. However, the effects differ according to the number, size, and location of the bleeds and the person's recovery.

Sources

- Jensson O, Gudmundsson G, Arnason A, and colleagues. "Hereditary cystatin C (gamma-trace) amyloid angiopathy of the central nervous system causing cerebral hemorrhage." Acta Neurologica Scandinavica . 1987;76(2):102-114.
- Palsdottir A, Abrahamson M, Thorsteinsson L, and colleagues. "Mutation in cystatin C gene causes hereditary brain haemorrhage." The Lancet . 1988;2(8611):603-604.
- Levy E, Lopez-Otin C, Ghiso J, Geltner D, Frangione B. "Stroke in Icelandic patients with hereditary amyloid angiopathy is related to a mutation in cystatin C, an inhibitor of cysteine proteases." Journal of Experimental Medicine . 1989;169(5):1771-1778.
- Revesz T, Holton JL, Lashley T, and colleagues. "Genetics and molecular pathogenesis of sporadic and hereditary cerebral amyloid angiopathies." Acta Neuropathologica . 2009;118(1):115-130.
- Charidimou A, Boulouis G, Gurol ME, and colleagues. "Emerging concepts in sporadic cerebral amyloid angiopathy." Brain . 2017;140(7):1829-1850.