CONDITION

Hereditary angioedema

Hereditary angioedema is an inherited condition that causes repeated swelling attacks in the skin, abdomen, or airway.

WHAT IT IS
Inherited condition causing repeated episodes of deep swelling

BODY SYSTEM
Skin, digestive system, and airway

MAIN SYMPTOMS
Skin swelling, abdominal pain, vomiting, throat swelling

WHAT CAUSES IT
Inherited changes affecting swelling-control proteins

HOW IT IS DIAGNOSED
C4 and C1-inhibitor blood tests; sometimes genetic testing

MAIN TREATMENT
Attack medicines and preventive medicines targeting bradykinin

CAN IT BE CURED?
No - the inherited tendency remains lifelong

IS IT AN EMERGENCY?
Sometimes - throat, tongue, or breathing symptoms

LONG-TERM OUTLOOK
Usually manageable with specialist care and effective medicines

Overview

Hereditary angioedema, usually shortened to HAE, is a rare inherited condition that causes sudden episodes of swelling. The swelling can affect the hands, feet, face, genitals, digestive tract, tongue, or throat.

HAE is different from the more common swelling caused by an allergy. Most HAE attacks result from too much activity of bradykinin , a natural chemical that makes blood vessels leak fluid into nearby tissue. Hives and itching are usually absent.

Many people with HAE have too little of a protein called C1 inhibitor , or they make C1 inhibitor that does not work properly. This protein helps control several chemical systems in the blood, including the pathway that produces bradykinin. Some less common forms of HAE occur even though C1-inhibitor levels and function are normal.

Abdominal attacks can be extremely painful. Swelling in the throat can block the airway and is a medical emergency. However, effective medicines can treat attacks and reduce how often they happen.

Symptoms

An HAE attack usually develops over several hours. Swelling often lasts for two to five days if it is not treated, although the timing can differ between attacks.

Common symptoms include:

Skin swelling may feel tight, painful, or uncomfortable rather than itchy. It usually does not leave a permanent mark.

Swelling in the bowel wall can cause intense pain and fluid loss. The abdomen may look swollen or feel tender. Because these symptoms can resemble appendicitis or another abdominal emergency, some people undergo investigations before HAE is recognised.

Attacks do not usually cause raised, itchy hives. Hives make an allergic cause more likely, although having hives does not completely exclude HAE or another condition.

Some people notice tiredness, tingling, mood changes, muscle aches, or a spreading ring-shaped rash before swelling begins. Others have no warning.

- Swelling of the hands, feet, arms, legs, face, or genitals
- Severe, cramping abdominal pain
- Nausea, vomiting, or diarrhoea during abdominal attacks
- Swelling of the tongue, mouth, or throat
- A tight throat, hoarse voice, or trouble swallowing
- A flat, non-itchy rash before or during some attacks

Causes and risk factors

Most HAE is caused by a change in the SERPING1 gene. This gene provides instructions for making C1 inhibitor.

In type 1 HAE, the body does not make enough working C1 inhibitor. In type 2 HAE, the amount may be normal or high, but the protein does not function properly.

HAE with normal C1 inhibitor is less common. It may be linked to changes in other genes involved in bradykinin production, but a specific genetic cause is not found in every family.

The common forms are inherited in an autosomal dominant pattern. This means a parent with HAE has a 1 in 2 chance of passing the altered gene to each child. HAE can also result from a new genetic change, so a person may have no known family history.

Attacks may occur without a clear cause. Possible triggers include:

A trigger does not always cause an attack, and triggers can change over time.

- Injury, pressure, surgery, or dental work
- Infection or illness
- Emotional stress
- Hormonal changes, including puberty, pregnancy, or menstruation
- Medicines containing oestrogen
- ACE inhibitors like lisinopril or ramipril, a group of medicines used for blood pressure and heart conditions

Diagnosis

Diagnosis usually starts with your symptoms, their pattern, and your family history. A family history supports the diagnosis, but its absence does not rule HAE out.

Blood tests measure:

Low C4 together with low C1-inhibitor amount or function supports HAE caused by C1-inhibitor deficiency. Tests are often repeated to confirm the result because treatment decisions and family screening may follow.

Genetic testing can identify some gene changes. It may be especially helpful when routine blood tests are normal, results are uncertain, or relatives need testing. A negative genetic test does not exclude every form of HAE.

Other causes of swelling may need to be considered. These include allergic angioedema, medicine-related swelling, and acquired C1-inhibitor deficiency. Acquired deficiency is not inherited and more often begins later in life. Additional testing, such as a C1q blood level, can help distinguish it from HAE.

- C4 , a protein in the complement immune system
- The amount of C1 inhibitor in the blood
- How well C1 inhibitor functions

Treatment and management

Treatment has three main aims: treating an attack, preventing attacks around high-risk events, and reducing attacks over the long term.

On-demand treatment is medicine taken when an attack begins. Options include C1-inhibitor replacement and medicines that block bradykinin production or action. The available products, age limits, and ways they are given differ by country.

Early treatment can shorten an attack and limit its severity. Anyone with suspected throat or tongue swelling still needs emergency assessment, even after using their usual attack medicine.

A specialist may arrange training so treatment can be stored and given at home. A written action plan should explain what to use, when to use it, and when to call emergency services.

Short-term preventive treatment may be considered before dental work, surgery, or procedures involving the mouth, throat, or airway. The plan depends on the procedure, previous attacks, and access to emergency treatment.

Long-term preventive treatment can reduce the number of attacks. Options include C1-inhibitor replacement and medicines that reduce activity in the kallikrein-bradykinin pathway. Some are injected, while others are taken by mouth. The choice considers attack burden, age, pregnancy plans, other health conditions, and personal preferences.

Older treatments called attenuated androgens are now used less often in many settings because they can cause important long-term side effects.

Antihistamines and corticosteroids like prednisone or hydrocortisone , which are often used for allergic swelling, generally do not treat HAE attacks. Adrenaline is also not a specific HAE treatment. However, emergency teams may use allergy treatment when the cause of sudden swelling is uncertain or when an allergic reaction is also possible.

Medicines commonly used for this include icatibant . Which one suits you, if any, is a decision for you and your doctor.

Complications

The most serious complication is swelling of the tongue or throat. This can narrow or close the airway. It requires immediate treatment and emergency medical care.

Abdominal attacks can cause dehydration because of vomiting, diarrhoea, and fluid moving into the bowel wall. Severe pain may lead to emergency investigations or surgery if HAE has

not yet been identified.

Frequent or unpredictable attacks can disrupt school, work, travel, sleep, relationships, and mental wellbeing. Fear of airway swelling may remain even when attacks are uncommon. A reliable treatment plan and access to medicine can reduce this burden.

Medicines used for long-term prevention can also have side effects. Regular follow-up helps review whether treatment is effective and still suits your circumstances.

Prevention

HAE itself cannot currently be prevented because it is inherited. Genetic counselling can explain inheritance and reproductive options, but it does not remove the condition from someone who has it.

Not every attack can be prevented. You may be able to reduce risk by identifying personal triggers and planning ahead for dental work or surgery.

ACE inhibitors can trigger bradykinin-related swelling and are generally avoided in people with HAE. Oestrogen-containing contraception or hormone therapy can worsen symptoms in some people. Do not stop a prescribed medicine on your own; ask the prescriber about suitable alternatives.

Preventive medicine may be appropriate when attacks are frequent, severe, disruptive, or difficult to treat quickly. The need for prevention should be reviewed over time rather than based only on a fixed number of attacks.

Living with it and what to expect

HAE is lifelong, but its pattern is not fixed. Some people have attacks often, while others go months or years without one. A quiet period does not mean the condition has disappeared.

Attack frequency may change around puberty, pregnancy, menopause, illness, stress, or a change in medication. Symptoms may also differ within the same family.

Modern on-demand and preventive treatments allow many people with HAE to work, study, exercise, travel, and raise families. No treatment guarantees that all attacks will stop, so continued access to emergency medicine remains important.

It can help to carry:

Tell dentists and surgical teams about HAE before a procedure. Schools, workplaces, and regular caregivers may also need a simple plan explaining where medicine is kept and what to

do during an attack.

Routine specialist follow-up is used to review attacks, side effects, treatment access, pregnancy plans, and whether family members should be offered testing.

- Your prescribed attack medicine
- A medical identification card or bracelet
- A written emergency plan
- Contact details for your HAE specialist service
- Extra medicine and supporting documents when travelling

When to get medical help

Call emergency services immediately for swelling of the tongue, mouth, or throat; a hoarse or changing voice; noisy breathing; difficulty swallowing; shortness of breath; or a feeling that the throat is closing. Use your prescribed on-demand treatment promptly if your plan tells you to, but do not wait to see whether it works before seeking emergency help.

Severe weakness, fainting, confusion, or blue or grey lips also require emergency care.

Seek prompt medical advice for severe or persistent abdominal pain, repeated vomiting, inability to keep fluids down, or symptoms that are different from your usual attacks. HAE should not be assumed to explain every episode of abdominal pain.

Arrange routine follow-up if attacks are becoming more frequent, treatment is not controlling them, side effects are troubling you, or you are planning pregnancy, dental work, or surgery.

If you have repeated unexplained swelling without hives, especially with abdominal attacks or a family history, arrange a medical assessment. These symptoms have several possible causes, and blood tests are needed to identify HAE.

Common questions

Is hereditary angioedema an allergy?

No. HAE is usually caused by excess bradykinin, not the histamine pathway involved in most allergies. This is why HAE usually occurs without itchy hives and often does not improve with antihistamines or corticosteroids.

Can I pass HAE to my children?

For the common autosomal dominant forms, each child of an affected parent has a 1 in 2

chance of inheriting the altered gene. This chance is the same for each pregnancy. A genetics service can explain how this applies to your family.

Can HAE cause stomach pain without visible swelling?

Yes. Fluid can collect in the bowel wall even when there is no swelling of the face, hands, or feet. This can cause severe cramping, nausea, vomiting, diarrhoea, and abdominal swelling. New or unusual pain still needs assessment for other causes.

Can stress cause an HAE attack?

Stress can be a trigger for some people, but it is not the underlying cause of HAE. Attacks may also happen when you feel calm or when no trigger can be identified.

Can I exercise and travel with HAE?

Many people can. Pressure or injury may trigger attacks in some individuals, so activities may need personal planning rather than broad restriction. When travelling, keep medicine accessible, carry more than you expect to need, and bring your emergency plan and medical documentation.

Does HAE go away with age?

HAE does not usually go away. The frequency and severity of attacks may change over the years, including during hormonal changes. Effective treatment can greatly reduce its impact, but ongoing planning remains important.

Sources

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