



What is Hereditary Angioedema (HAE)?

Hereditary Angioedema (HAE) is a very rare, potentially life-threatening genetic condition that causes episodes of swelling (edema) and fluid retention in various body parts, including the hands, feet, face, and airway. Only about 1 in 50,000 to 150,000 people has HAE. People suffering from HAE have a low level or decreased function of an important protein in their blood. The protein is called C1 esterase inhibitor (C1-INH). C1-INH regulates and "turns off" various reactions in the body.

What causes hereditary angioedema (HAE)?

HAE is usually inherited. The abnormality in the C1-INH gene is passed down from a parent to a child. However, 25% to 30% of HAE cases are caused by a new mutation, where there is no previous history of HAE in the family. If someone with HAE marries a healthy person, there is a 50% chance their child will have HAE. A person with HAE will have the disease for life because it is part of their genetic makeup. However, depending on the severity of the disease, some people will have many attacks each month, while others could go months or even years without a swelling attack.

Since HAE is hereditary, will I pass HAE to my children?

If you have HAE, each of your children has a 50/50 chance of having HAE.

Does the HAE inheritance skip generations?

No. If a parent has HAE but the child does not, the grandchildren do not have an increased chance of having HAE.

Are there different types of HAE?

There are 2 major types of HAE: Type I is caused by low levels of C1-INH; Type II is caused by a decreased function of some of the C1-INH protein; and Type III, which only recently has been identified, where patients usually have normal C1-INH levels.

What are the symptoms of HAE?

The primary symptoms of HAE are swelling or fluid retention in various body parts, including the hands, feet, face, and airway. Symptoms can mimic other types of medical conditions, such as allergic reactions or appendicitis, but there are clues that help distinguish HAE from other medical problems. Please see a physician to identify HAE.



How is HAE diagnosed?

A blood sample is taken to measure the level of C1-INH in the blood. C4 (another important blood protein) is often used in screening tests. A low level of C1-INH confirms a Type I HAE diagnosis. People with Type II HAE will have a normal C1-INH level, but an abnormal C1-INH functional level. No single test can diagnose Type III HAE.

Is there a cure for HAE?

Currently, there is not a cure for HAE. However, gene therapy offers hope for patients with many different types of diseases and could potentially provide a complete cure for people with HAE.

How serious is HAE?

The severity of HAE is determined by the frequency, location, and degree of swelling. Swelling in the throat can compromise the airway and be life-threatening. Swelling in the intestines and other organs may cause severe abdominal pain and discomfort. While the majority of attacks are not life-threatening, they can seriously affect the quality of life.

What causes HAE attacks?

Most attacks occur spontaneously with no apparent reason. However, anxiety, stress, minor trauma, surgery, and illnesses such as colds and flu can be triggers. Oral trauma caused by dental procedures make HAE patients particularly vulnerable to airway attacks. Patients have also reported swelling in extremities following typing, prolonged writing, pushing a lawn mower, hammering, shoveling, and other physical activities.

In women, menstruation and pregnancy seem to have a major effect on disease activity. Some women patients report a definite increase in the number of attacks during their menstrual periods. During pregnancy, some patients note an increase in the frequency of attacks, while others have reported a decrease. Use of oral contraceptives and hormone replacement therapy is associated with an increase in the frequency and severity of attacks.

How can I prevent HAE attacks?

There are 3 ways to prevent HAE attacks:

1. Avoid potential triggers
2. Short-term prevention therapy when you must be exposed to a known trigger
3. Long-term prevention therapy for people with frequent attacks



What should I do if I have an HAE attack?

People who experience symptoms of a laryngeal attack should get emergency help as soon as possible. A doctor who is an expert on HAE can help you determine what you should do, when you have an attack. The prescribed course of treatment may depend on the location of the attack, the frequency of attacks, and the type of medications available to you.

What is acquired angioedema?

A person can develop HAE-like symptoms (recurrent angioedema) later in life. It is usually caused by the development of antibodies to C1-INH. This condition may be associated with cancer in the lymphatic system or with an autoimmune disease, in which the body responds to normal body proteins as if they were dangerous bacteria or viruses.

How is HAE treated?

HAE treatment can be categorized into two methods: prophylaxis and treating acute attacks. Injection of purified C1-INH during HAE attacks has been used in many countries for almost 30 years, for treating acute attacks and for preventing attacks (“prophylaxis”). Two brands of C1-INH were approved for use in the United States in 2008 and 2009. Two additional drugs administered by subcutaneous injection were approved for HAE attacks in 2009 and 2011. You should contact your physician to learn more about these drugs.

An alternative treatment is fresh frozen plasma (FFP), containing many preserved blood protein products. FFP has been used to replace C1-INH in HAE patients during acute attacks and prophylaxis, especially when C1-INH is not available.

Prior to the availability of the 4 newly FDA- approved HAE therapies, androgen derivatives (also called “anabolic steroids”) such as danazol, oxandrin and stanozol, were commonly prescribed as a prophylactic treatment for HAE. While they have been shown to be useful, they are not well-tolerated by many women, have been directly linked to liver toxicity and cause an increase in cholesterol levels. In addition, these drugs should not be used to treat children.

What side effects might I have with treatment, and how do I manage them?

The type of side effects you experience will depend on the treatment option used, the dosage, and administration. It also depends on whether the treatment is for an acute attack or to prevent an attack.



If you have HAE, it is important for you to become your own advocate. Learn to recognize the symptoms of HAE and explore treatment options. You should monitor your symptoms and work with your doctor to choose the best treatment plan for you. The following information about disease treatment is important for you to know:

- **Acute Attacks:** There are now 3 FDA-approved treatments for acute HAE attacks, including replacement with C1 esterase inhibitor (C1-INH) and subcutaneous injections of ecallantide, an inhibitor of the protein kallikrein, or icatibant, an antagonist of bradykinin B2 receptors. Side effects vary with each of these medications and should be discussed with your doctor.

Because people who have abdominal attacks may release 1 to 2 liters of fluid into their abdomen and develop low blood pressure, they may require intravenous fluid replacement therapy.

- **Acute laryngeal edema:** Depending on the symptoms and sites of the angioedema, intensive support may be necessary, including intravenous fluids. This is often the case during a laryngeal edema (swelling) attack. This must be controlled to protect the person's airways. Sometimes, when the upper airway is blocked, a tracheotomy must be performed. An incision through the neck into the windpipe is made to allow oxygen to flow into the lungs.
- **Pregnancy:** Short-term use of androgens may be a treatment for HAE attacks in pregnant women during the third trimester of pregnancy. However, the risk of potentially masculinizing effects—particularly for a female fetus—are of concern, and many physicians view pregnancy as an absolute contraindication for the use of attenuated androgens. Some physicians view the judicious use of tranexamic acid as an option during pregnancy. In most countries, however, C1-INH is viewed as the treatment of choice during pregnancy.

Talk to your doctor about potential side effects based on your personal treatment and when you should call the doctor's office about a medical problem. Recording information about your symptoms and attacks will help you and your doctor track your progress and effectively manage your disease.