**Hereditary Angioedema**

**Type**
- **Hereditary Type I (HAE-I)**
- **Hereditary Type II (HAE-II)**
- **Acquired Type I (AAE-I)**
- **Acquired Type II (AAE-II)**
- **Idiopathic**
- **Non-Histaminergic (NHA)**
- **Allergic**
- **ACE-Inhibitor**

**Description**
- Represents approximately 80 to 85% of HAE cases. C1-inhibitor is considerably below normal due to a defective gene on chromosome 11. There is no known family history of angioedema, but a number of cases are due to a spontaneous mutation of the gene.
- Represents approximately 15 to 20% of HAE cases. Similar description to Type I, but C1-inhibitor deficiency does not function properly.
- In children, swelling caused by A1-inhibitor deficiency is considered very rare; there are few reported cases.
- Autonomic nerves and present in HAE inhibitor function is an absence of underlying lym phangiography. Swelling and/or hives persist beyond 6 weeks.
- This is the most common form of angioedema.
- Angioedema without urticaria is also known as H1 antihistamine blockers. Paroxysmal, and autosomal dominant diseases are not present.
- This is the most common form of angioedema.
- Caused by ACE-inhibitors for high blood pressure and/or people with angioedema.

**Common Symptoms (1)**
- Swelling can occur on the extremities, abdomen, throat, and other organs. Swelling of the airway can be fatal.
- Swelling may occur just about anywhere: face, arms, abdomen, throat and other organs.
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- Avoid the substance or behavior that causes the allergic reaction.

**Complement System**
- Low levels of C1-inhibitor. C4 is almost always low. C1, C3 and C1q are normal. Abnormal complement (above) is the same whether the condition is hereditary or spontaneous. Abnormal steroids (also known as androgens) such as dexamethasone and methylprednisolone have been the most commonly prescribed HAE therapies. While experimental steroids have been shown to be useful, they are not well-tolerated by many women directly linked to liver toxicity and cause an increase in cholesterol levels. In addition, these drugs should not be used to treat children, some of whom, typically are severely affected and suffer frequent attacks. Research indicates that patients treated with aldosterone steroids can experience breakthrough laryngeal or abdominal attacks that require hospitalization.

**Possible Treatment**
- C1-inhibitor helps to regulate the complex biochemical interactions of blood-based systems involved in disease fighting, inflammatory response and coagulation. Because defective C1-inhibitor does not adequately perform its regulatory function, a biochemical imbalance can occur and produce unwanted peptides that induce the capillaries to release fluids into surrounding tissues, thereby causing edema. HAE is caused hereditary because the genetic defect is passed on in families. A child has a 50 percent chance of inheriting this disease if one of his or her parents has it. The absence of family history does not rule out the HAE diagnosis, however. Scientists report that as many as 20 percent of HAE cases result from patients who had a spontaneous mutation of the C1-inhibitor gene at conception. These patients can pass the defective gene to their offspring.

**What is Hereditary Angioedema?**

Hereditary Angioedema (HAE) is a very rare and potentially life-threatening genetic condition that occurs in about 1 in 10,000 to 1 in 50,000 people. HAE symptoms include episodes of edema (swelling) in various body parts including the hands, feet, face, and airway. In addition, patients often have bouts of exacerbating abdominal pain, nausea and vomiting that is caused by swelling in the intestinal wall. Airway swelling is particularly dangerous and can lead to death. People with HAE may have a defect in the gene that controls a blood protein called C1-inhibitor. The genetic defect results in production of either inadequate or non-functional C1-inhibitor protein. Normal C1-inhibitor helps to regulate the complex biochemical interactions of blood-based systems involved in disease fighting, inflammatory response and coagulation. Because defective C1-inhibitor does not adequately perform its regulatory function, a biochemical imbalance can occur and produce unwanted peptides that induce the capillaries to release fluids into surrounding tissues, thereby causing edema. HAE is caused hereditary because the genetic defect is passed on in families. A child has a 50 percent chance of inheriting this disease if one of his or her parents has it. The absence of family history does not rule out the HAE diagnosis, however. Scientists report that as many as 20 percent of HAE cases result from patients who had a spontaneous mutation of the C1-inhibitor gene at conception. These patients can pass the defective gene to their offspring.

Because the disease is very rare, it is not uncommon for patients to remain undiagnosed for many years. Many patients report that their frequent and severe abdominal pain was inappropriately diagnosed as psychosomatic, resulting in referral for psychiatric evaluation. Unnecessary exploratory surgery has been performed on patients experiencing gastrointestinal edema because abdominal HAE attacks mimic a surgical abdomen. Before therapy became available, the mortality rate from airway obstruction was reportedly as high as 30 percent.
blood tests that confirm HAE: an allergic reaction. Laboratory analysis of blood samples or genetic testing typically caused by something other than C1-inhibitor deficiency, usually from an inherited disorder.

Traditionally, HAE has been classified into two types. The most common form of the disease – Type I – is characterized by low quantitative levels of C1-inhibitor and affects about 85% of patients. Type II HAE affects the other 15% of patients who have normal or elevated levels of C1-inhibitor, but their C1-inhibitor does not function properly. Several investigators have noted a familial (and therefore inherited) angioedema, in patients with normal levels of C1 INH. Often grouped under the designation of “HAE Type III”, this form of angioedema is yet to be fully described or understood. In women, swellings have been correlated with pregnancy or the use of oral contraceptives; however, affected male family members have also been identified. Some scientists believe that a mutation in the gene for human coagulation Factor XII may be a potential cause for swelling in these patients.

What age do attacks of Hereditary Angioedema start? The age of HAE onset varies considerably, however, in one study, half of the patients reported onset of their symptoms by the age of seven, and over two thirds became symptomatic by the age of thirteen. There also seems to be an increased frequency of attacks during puberty or adolescence.

Characteristics of HAE Attacks Patients often report tingling or tightness in the area where edema will occur thirty minutes to several hours later. In some cases, this sensation can be present twelve to twenty-four hours before the onset of swelling. Approximately one fourth of HAE patients experience a red, non-itching red blood blub rash both before and during an attack. Unexplained, an average attack lasts for twenty-four to seventy-two hours, but some residual swelling may persist for up to four or more days. Attacks that involve the face or throat should be considered a medical emergency. Swelling of the extremities is uncomfortable and, according to some patients, can be painful and debilitating depending on the location of the edema. Attacks that involve the face and throat must be taken seriously and medical treatment should be sought without delay. Swelling of the throat can close the air passage and cause death by suffocation. The symptoms of an impending airway obstruction include difficulty swallowing and a change in voice pitch. Abdominal attacks cause severe pain, nausea, vomiting, dehydration and watery diarrhea. As noted above, abdominal attacks can mimic a surgical abdomen and some patients have been subjected to unnecessary exploratory surgery.

Newly-Approved Therapies Offer Additional Treatment Options New FDA-approved HAE treatments provide patients and their physicians with choices and an opportunity to develop an HAE treatment plan tailored to each patient’s unique needs. Cinryze™ brand of C1-inhibitor concentrate has been FDA-approved for preventing HAE attacks. Cinryze™ is delivered intravenously and is approved for home infusion. Berinert® brand of C1-inhibitor concentrate has been FDA-approved for treating acute facial and abdominal HAE attacks. Berinert® is delivered intravenously.

Kalbitor® brand of plasma kalikrein inhibitor has been FDA-approved to treat acute HAE attacks in patients 16 years of age and older. Kalbitor® is delivered through subcutaneous injections.

Contact your HAEA Regional Patient Services Representative (see list below) for more information about these products.