A Comprehensive Table of Angeioedema Types

TYPE	DESCRIPTION	COMMOM SYMPTOMS (1)	COMPLEMENT SYSTEM	POSSIBLE TREATMENT*
Hereditary Angioedema Type I (HAE-I)	Represents approximately 80 to 85% of HAE cases. C1-inhibitor is considerably below normal due to a defective gene on chromosome 11. There is usually a family history of angioedema, but a number of cases are due to a spontaneous mutation of the gene. Does not respond to antihistamines and corticosteroids.	Swelling can occur in the extremities, abdomen, throat and other organs. Swelling of the airway can be fatal. Abdominal swelling usually involves pain, vomiting and diarrhea. Symptoms usually appear early in life, most often by age 13 and may increase in severity after puberty. Episodes may be spontaneous or triggered by physical trauma or emotional stress.	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.	Anabolic steroids (also known as androgens) such as danazol, oxandrolone and stanozolol have, historically, been the most commonly prescribed preventive HAE therapies. While anabolic steroids have been shown to be useful, they are not well-tolerated by many women, directly linked to liver toxicity and can cause an increase in cholesterol levels. In addition, these drugs should not be used to treat children, some of whom, tragically, are severely affected and suffer frequent attacks. Research indicates that patients treated with anabolic steroids can experience breakthrough laryngeal or abdominal attacks that require hospitalization. Five new treatments are now FDA-approved for treating HAE, including two C1-inhibitor products, a kallikrein inhibitor, and a bradykinin receptor antagonist. Patients and their physicians now have options for developing a non-steroidal HAE treatment plan tailored to meet each patient's unique needs. **Cinryze™** brand of C1-inhibitor has been FDA-approved for preventing HAE attacks. **Cinryze ™** is delivered intravenously and is approved for home infusion. **Berinert®** brand of C1-inhibitor has been FDA-approved for treating acute abdominal, facial or laryngeal HAE attacks. **Berinert®** is delivered intravenously and is approved for on-demand treatment through self-administration. **Kalbitor®** brand of plasma kallikrein inhibitor has been FDA-approved to treat acute HAE attacks in patients 12 years of age and older. **Kalbitor®** is delivered through subcutaneous injections. **Firazyr®** brand of bradykinin receptor antagonist has been FDA-approved for treating acute HAE attacks in patients 18 years and older. **Firazyr®** is delivered by subcutaneous injection and is approved for self-administration. **Ruconest®** brand of C1-inhibitor [recombinant] has been FDA-approved for treating acute HAE attacks in adults and adolescents. RUCONEST is delivered intravenously and is approved for self-administration.
Hereditary Angioedema Type II (HAE-II)	Represents approximately 15 to 20% of HAE cases. Similar description to Type I, but C1-inhibitor does not function properly. Does not respond to antihistamines and corticosteroids.	Same as HAE-I.	C1-inhibitor level may be normal or elevated, but it is dysfunctional. C1, C3 and C1q are normal, but C4 is almost always low.	Same as HAE-1
Hereditary Angioedema with Normal C1-Inhibitor	Number of cases unknown. Family history must be present. C1-inhibitor levels and function are normal. A minority of cases associated with mutations in the coagulation factor XII gene, however, this mutation has not been shown to be the cause of the condition. Predominantly reported in women, but affected male family members have also been identified. Swelling sometimes associated with pregnancy and the use of estrogen-containing oral contraceptives. Does not respond to antihistamines and corticosteroids.	Similar to HAE-I and HAE-II.	Normal.	Research continues. Published cases document response to FDA-approved HAE therapies.
Acquired Angioedema Type I (AAE-I) AAE-I & II are considered very rare; there are few reported cases.	Immune complexes that are usually linked to an underlying lymphoproliferative disorder destroy the function of C1-inhibitor. Angioedema can be an indicator that a lymphoproliferative disease is developing, so early detection needs to be emphasized.	Similar to HAE. The symptoms typically appear in the fourth decade of life or later. Because acquired angioedema is not related to a genetic defect there is an absence of a family history of symptoms.	Low level of C1-inhibitor and C4. C1q is usually reduced, but not always.	Diagnosis and treatment of underlying lymphoproliferative disease often eliminates the root cause. Antifibrinolytics such as tranexamic acid and epsilon-aminocaproic acid for possible prevention of episodes. Androgen therapy may help.
Acquired Angioedema Type II (AAE-II) AAE-I & II are considered very rare; there are few reported cases.	Autoantibodies are present and destroy C1-inhibitor function. There is no apparent underlying disorder.	Same as AAE-I.	Same as AAE-I. A lab test for autoantibodies may be appropriate.	Antifibrinolytics such as tranexamic acid and epsilon-aminocaproic acid for possible prevention. It is possible that immunosuppressive therapy might be successful.
Idiopathic	Swelling and/or hives persist beyond 6 weeks. Thyroid dysfunction should be considered.	Swelling may occur just about anywhere and may be accompanied by urticaria (hives).	Normal.	Primarily antihistamines. DHEA. 1-thyroxine for thyroid dysfunction.Prednisone therapy.
Nonhistaminergic (INAE) May occur in about 1 out of 20 cases of angioedema	Angioedema without urticaria (usually not responsive to H1 antihistamine blockers). Parasites, infections and autoimmune diseases are not present.	Swelling may occur anywhere: face, arms, legs, genitalia, throat, abdomen (but abdomen is less frequent than those with HAE). Symptoms do not change due to menstrual period or pregnancy.	Normal.	Antifibrinolytics such as tranexamic acid and epsilon-aminocaproic acid.
Allergic This is the most common form of angioedema.	Swelling and/or hives are a reaction to an outside influence such as food, bee sting, cold, heat, latex or drug. The outside influence provokes a histamine reaction, which leads to swelling and/or the hives.	Swelling occurs most often in the face and throat area. Urticaria (hives) may be present. If condition persists beyond 6 weeks it is considered chronic idiopathic and not an allergic reaction.	Normal.	Avoid the substance or behavior that causes the allergic reaction. Antihistamines. Adrenaline (epinephrine) possibly as autoinjectors (self-injecting pens) containing epinephrine for emergencies.
ACE-Inhibitor (Angiotensin-Converting Enzyme Inhibitor) Possible cause for 4 to 8% of people with angioedema.	Caused by ACE-Inhibitors for high blood pressure (captopril, enalapril, genzapril, quinapril, ramipril). Swelling may commence anywhere from a few hours to years after first starting medication.	Swelling may occur just about anywhere: throat, face, lips, tongue, hands, feet, genitals, intestines. If urticaria is present it reduces the probability of a link to ACE-Inhibitors.	Normal.	Suspension or change of medication

*Patients with the slightest hint of throat swelling should seek immediate treatment to ensure that their airway is not compromised. The medical literature and practitioner experience confirms that corticosteriods (Prednisone), antihistamines, and epinephrine are not effective in treating angioedema created by C1-inhibitor deficiency. However, a recent study noted success using inhaled epinephrine to prevent complete airway closure. NOTES: The presence of urticaria associated with angioedema usually suggests a diagnosis other than HAE or AAE.