

# HAE | TYPES OF ANGIOEDEMA

## Hereditary Angioedema TYPE I (HAE-I)

Represents approximately 80% to 85% of HAE cases. C1-Inhibitor levels are 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.

### COMMON SYMPTOMS

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.

### LABORATORY ANALYSIS

Low levels of C1-Inhibitor. C4 is almost always low. C1, C3, and C1q are normal. Low C1-Inhibitor levels and low C1-Inhibitor function.

## Hereditary Angioedema TYPE II (HAE-II)

Represents approximately 15% to 20% of HAE cases. Similar description to Type I, but caused by production of mutated dysfunctional C1-Inhibitor. Does not respond to antihistamines and corticosteroids.

### COMMON SYMPTOMS

Same as HAE-I

### LABORATORY ANALYSIS

C1-Inhibitor level is normal or elevated, but C1-Inhibitor function is low. C4 is almost always low. C1, C3, and C1q are normal.

## Hereditary Angioedema with NORMAL C1-INHIBITOR

Appears to be more rare than HAE Type I or II. People with HAE Normal C1-Inhibitor experience swelling similar to Types I and II, but have normal C1-Inhibitor levels and function by lab testing. To date, scientists have found mutations in 5 genes that may be associated with HAE Normal C1-Inhibitor: Factor XII, Plasminogen, Angiotensin-1, Kininogen-1, and Myoferlin. Currently, only Factor XII mutation analysis is readily available in commercial labs. Other genes may be sequenced in research laboratories or by special order from diagnostic labs. Scientists are continuing to look for other genetic mutations that cause HAE.

### COMMON SYMPTOMS

Similar to HAE-I and HAE-II. Much more common in women than men.

### LABORATORY ANALYSIS

C1-Inhibitor level and C1-Inhibitor function are normal. C4 level is normal.

## Acquired Angioedema (AAE-C1-INH)

AAE-C1-INH is caused by excessive consumption of C1-Inhibitor. AAE-C1-INH may be associated with an underlying B-cell lymphoproliferative disease or auto-immune anti-C1-Inhibitor autoantibodies.

### COMMON SYMPTOMS

Similar to HAE, however, 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.

### LABORATORY ANALYSIS

Low C1-Inhibitor level and C1-Inhibitor function and low C4. C1q is usually reduced, but not always. A lab test for autoantibodies may be appropriate.

## ACE-INHIBITOR (Angiotensin-Converting Enzyme Inhibitor)

Possible cause for 4% to 8% of people with angioedema.

Caused by ACE-Inhibitors, prescribed for high blood pressure (captopril, enalapril, genzapril, quinapril, ramipril). Angioedema symptoms may begin anywhere from a few hours to years after first starting medication.

### COMMON SYMPTOMS

Swelling may occur just about anywhere: throat, face, lips, tongue, hands, feet, genitals, intestines. If urticaria (hives) is present, it reduces the probability of a link to ACE-Inhibitors.

### LABORATORY ANALYSIS

Normal.

## ALLERGIC

This is the most common form of angioedema.

Angioedema and/or hives are a reaction to a specific external trigger such as food, insect sting, cold, heat, medication, or latex. The external trigger causes an allergic or mast-cell mediated reaction that leads to angioedema and/or hives.

### COMMON SYMPTOMS

Swelling occurs most often in the face and throat area. Urticaria (hives) may be present. If the angioedema and/or urticaria continue to recur beyond 6 weeks, this is considered chronic idiopathic (or spontaneous) and is very unlikely to be an allergic reaction.

### LABORATORY ANALYSIS

Normal.

## IDIOPATHIC HISTAMINERGIC

Idiopathic histaminergic angioedema involves recurrent angioedema episodes for greater than 6 weeks. Symptoms generally respond to high-dose antihistamines, corticosteroids, or other mast-cell targeted medications.

### COMMON SYMPTOMS

Swelling may occur just about anywhere and may be accompanied by urticaria (hives).

### LABORATORY ANALYSIS

Normal.

## IDIOPATHIC Non Histaminergic (INAE)

May occur in about 1 out of 20 cases of angioedema.

Recurrent angioedema episodes for greater than 6 weeks, however, there are no associated hives and symptoms are not responsive to high doses of antihistamines, corticosteroids, or other mast-cell targeted medications.

### COMMON SYMPTOMS

Swelling may occur anywhere: face, arms, legs, genitalia, throat, abdomen (but abdomen is less frequent than those with HAE).

### LABORATORY ANALYSIS

Normal.