



## Angioedema

### What is angioedema?

Angioedema is a skin reaction similar to hives or [urticaria](#). It is most often characterised by an abrupt and short-lived swelling of the skin and mucous membranes. All parts of the body may be affected but swelling most often occurs around the eyes and lips. In severe cases the internal lining of the upper respiratory tract and intestines may also be affected.

#### Angioedema



Image provided by Dr Janjua



### What's the difference between angioedema and urticaria?

Angioedema and urticaria are very similar in many ways and can co-exist and overlap. Urticaria occurs more commonly and is less severe than angioedema as it only affects the skin layers whereas angioedema affects the tissues beneath the skin (subcutaneous tissue). The main differences between urticaria and angioedema are shown in the following table.

Feature	Angioedema	Urticaria
Tissues involved	Subcutaneous and submucosal surfaces (beneath the dermis)	Epidermis (outer layer of skin) and dermis (inner layer of skin)
Organs affected	Skin and mucosa, particularly the eyelids and lips	Skin only

Duration	Transitory (usually lasts between 24–48 hours)	Transitory (usually lasts < 24 hours)
Physical signs	Red or skin coloured swellings occurring below the surface of the skin	Red patches and weals on the surface of skin
Symptoms	May or may not be itchy. Often accompanied by pain and tenderness.	Usually associated with an itch. Pain and tenderness uncommon.

## What causes angioedema?

The causes of angioedema depend on the type of angioedema a patient has. Angioedema can be classified into at least four types, acute allergic angioedema, non-allergic drug reactions, idiopathic angioedema and hereditary angioedema (HAE).

Angioedema type	Causes
<b>Acute allergic angioedema</b> (almost always occurs with urticaria within 1–2 hours of exposure to the allergen)	<ul style="list-style-type: none"> <li>• Foods, especially nuts, shellfish, milk, eggs</li> <li>• Drugs, e.g. penicillin, NSAIDs (aspirin), sulfa drugs</li> <li>• Radiocontrast media</li> <li>• <a href="#">Insect venoms</a></li> <li>• <a href="#">Natural rubber latex</a>, e.g. medicinal gloves, catheters, balloons, contraceptive devices</li> </ul>
<b>Non-allergic drug reaction</b> (onset may be days to months after first taking the medication)	<ul style="list-style-type: none"> <li>• Angiotensin-converting enzyme (ACE) inhibitors</li> <li>• Cascade of effects via kinin production, arachidonic acid metabolism and nitric oxide generation</li> </ul>
<b>Idiopathic angioedema</b> (frequently chronic and relapsing and usually occurs with urticaria)	<ul style="list-style-type: none"> <li>• In most cases the cause of angioedema is unknown</li> <li>• Recent research indicates that 30–50% of this type of angioedema may be associated with some types of autoimmune disorders including systemic <a href="#">lupus erythematosus</a> (SLE)</li> </ul>
<b>Hereditary angioedema</b> (very rare autosomal dominant inherited disease)	<ul style="list-style-type: none"> <li>• Inherited abnormal gene that causes a deficiency of a normal blood protein called C1 inhibitor which plays a role in regulating how the immune system functions</li> <li>• Some cases of C1 inhibitor deficiency may be acquired (i.e. acquired during life rather than inherited)</li> </ul>

Whatever the cause of angioedema, the actual mechanism behind the swelling is the same in all cases. Small blood vessels in the subcutaneous and/or submucosal tissues leak watery liquid through their walls and cause swelling. This same mechanism occurs in urticaria but just closer to the skin surface.

## What are the clinical features of angioedema?

Symptoms and signs of angioedema may vary slightly between the different types of angioedema but in general some or all of the following occur.

- Marked swelling, usually around the eyes and mouth
- Throat, tongue, hands, feet and/or genitals may be affected too
- Skin may appear normal, i.e. no hives or other rash
- Swellings may or may not be itchy
- Swellings may be painful, tender or burning

- In severe angioedema swelling of the throat and/or tongue may make it difficult to breath
- Swelling of the lining of the intestinal tracts may cause gastrointestinal pain and cramps

Some features specific to the different types of angioedema are listed below.

Angioedema type	Clinical features
Acute allergic	<ul style="list-style-type: none"> <li>• Almost always occurs with urticaria</li> <li>• Angioedema and urticaria both usually occur within 1–2 hours of exposure to allergen (exception is ACE inhibitor induced angioedema that usually occurs within the first week of treatment but can occur weeks to months later)</li> <li>• Reactions are usually self-limiting and subside within 1–3 days</li> <li>• Reactions will recur with repetitive exposures or exposure to cross-reactive substances</li> </ul>
Non-allergic drug reaction	<ul style="list-style-type: none"> <li>• ACE inhibitor induced angioedema occurs without urticaria</li> </ul>
Idiopathic/chronic	<ul style="list-style-type: none"> <li>• Similar to acute allergic but angioedema keeps on recurring and often no known cause is found</li> </ul>
Hereditary	<ul style="list-style-type: none"> <li>• Patients often experience no symptoms until they reach puberty</li> <li>• Swellings can occur without any provocation or induced by precipitating factors, including local trauma, vigorous exercise, emotional stress, alcohol, and hormonal factors</li> <li>• Some patients may get a transitory prodromal non-itchy rash</li> <li>• Face, hands, arms, legs, genitals, digestive tract and airway may be affected, swellings spread slowly and may last for 3–4 days</li> <li>• Abdominal cramps, nausea, vomiting and difficulty breathing from swelling of internal tracts</li> </ul>

### How is the diagnosis made?

A detailed medical history is invaluable in diagnosing angioedema.

- Keep a diary of exposure to possible irritants
- Tell your doctor about all medications you take, including over-the-counter (OTC) drugs and herbal remedies (even if taking them irregularly)
- Any family history of skin rash, allergies

[Skin prick testing](#) may be performed to try and identify any allergens. If hereditary angioedema is suspected, blood tests to check for levels and function of specific complement blood proteins may be done.

### What is the treatment for angioedema?

Treatment of angioedema depends on the severity of the condition. In cases where the respiratory tract is involved the first priority is to secure the airway. Patients may need emergency hospital care and require intubation (placement of a tube in the throat to keep the airway open).

Patients with mild acute angioedema can usually be treated the same way as those with an allergic reaction (see [urticaria](#)). In many cases the swelling is self-limiting and resolves spontaneously after a few hours or days. In more severe cases where there is persistent swelling, itchiness or pain the following medications may be used.

- Subcutaneous adrenaline (epinephrine)
- [Oral or intravenous corticosteroids](#)

- Oral or injected [antihistamines](#)

Chronic angioedema with chronic autoimmune or chronic idiopathic urticaria is often difficult to treat and response to medication variable. The following treatment steps are recommended. Each step is added to the previous one if inadequate response is obtained.

Step 1: non-sedating antihistamines, e.g. cetirizine

Step 2: sedating antihistamines, e.g. diphenhydramine

Step 3: a) oral corticosteroids, e.g. prednisone

b) immunosuppressants e.g. [ciclosporin](#) or [methotrexate](#)

The goal of treatment for chronic angioedema is to reduce itch, swelling, tenderness and pain to a tolerable level to maintain function (e.g. work, school, sleep).

Acute episodes of hereditary angioedema do not respond to adrenaline, antihistamine and corticosteroids. Fortunately most acute episodes are non life-threatening and the mainstay of emergency medical treatment is IV fresh frozen plasma or C1 inhibitor concentrate (special types of blood transfusion). Anabolic steroids, stanazolol and danazol, have also been used as they increase the circulating levels of normal functional C1 inhibitor.

#### [Related information](#)

##### References:

- Book: Textbook of Dermatology. Ed Rook A, Wilkinson DS, Ebling FJB, Champion RH, Burton JL. Fourth edition. Blackwell Scientific Publications.
- Kaplan AP, Greaves MW. Angioedema. J Am Acad Dermatol 2005;53:373-88. Medline.

##### On DermNet NZ:

- [Urticaria](#)
- [Contact urticaria](#)
- [Cholinergic urticaria](#)
- [Cold urticaria](#)
- [Dermographism](#)

##### Other websites:

- [Angioedema](#) - emedicine dermatology, the online textbook

##### Books about skin diseases:

See the [DermNet NZ bookstore](#)

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DermNet does not provide an on-line consultation service.

If you have any concerns with your skin or its treatment, see a [dermatologist](#) for advice.

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