

Urticaria

What is urticaria?

Urticaria, otherwise known as hives, is an itchy red blotchy rash resulting from swelling of the superficial part of the skin. It can be localised or more widespread. [Angio-oedema](#) occurs when the deeper tissues, the lower dermis and subcutaneous tissues, are involved and become swollen.

Appearance

The typical lesion is a central itchy white papule or plaque due to swelling of the surface of the skin (weal or wheal). This is surrounded by an erythematous flare. The lesions are variable in size and shape and may be associated with swelling of the soft tissues of the eyelids, lips and tongue (angio-oedema).

Individual lesions are typically transient. They come and go within a few minutes to hours and precise questioning may be needed to establish this. If there is uncertainty about how long each lesion lasts, a line drawn around one lesion will demonstrate any change when inspected the following day. Individual weals may join to form large patches.



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In terms of timescale, urticaria can be classified into: ^[1]

- Acute urticaria – where symptoms persist for less than six weeks.
- Chronic urticaria – where symptoms persist for more than six weeks.

How common is urticaria? (Epidemiology) ^[1]

Acute urticaria is much more common than chronic urticaria. The lifetime prevalence for all types of urticaria is 8-10%, compared to 20% for acute urticaria. The prevalence rate for chronic urticaria has been estimated as 2-3%. Acute urticaria is more common in children and adolescents than in adults, and is more common in women than in men, with a peak age range of 20-40. It is more common in individuals who have atopy.

Urticaria causes (Aetiology) ^[2]

Urticaria is due to activation of mast cells in the skin, resulting in the release of histamine and other mediators. These chemicals cause capillary leakage, which causes the swelling of the skin, and vasodilation causing the erythematous reaction. There may be a trigger identified which causes this release but often the cause is not identifiable, particularly in chronic urticaria. An autoimmune reaction is thought to be involved in many such cases.

Some of the triggers are listed below within the classification section.

Clinical classification ^[2]

There are some differences in terminology and classification internationally. ^[3]

British guidelines classify urticaria as follows:

Acute urticaria ^[1]

In acute urticaria, a cause is identified in only about half of cases. Possible triggers include:

- Allergies: foods, bites, stings, medication.
- Viral infections such as hepatitis.
- Bacterial infections such as *Helicobacter pylori*.
- Skin contact with chemicals, nettles, latex, etc.

- Physical stimuli: firm rubbing (dermatographism), pressure, cold, heat.

Chronic urticaria

Subtypes of chronic urticaria are:

- Chronic spontaneous urticaria. Triggers include medication, stress and infection. This was previously called idiopathic urticaria.
- Autoimmune urticaria (in the European guidelines this would come under the chronic spontaneous urticaria subtype above).^[4] This may account for half of all cases of chronic urticaria in adults and older children. There may be an association with other autoimmune conditions.
- Inducible urticaria. Triggers include:
 - Contact with hot or cold water (aquagenic).
 - Exercise or emotion (cholinergic).
 - Exposure to cold or heat.
 - Firm rubbing, minor trauma (dermatographism).
 - Pressure (delayed pressure).
 - Vibration.
 - Sun exposure (solar).

The British guideline refers to chronic urticaria/angio-oedema; it also lists angio-oedema without weals as a subtype and refers to urticarial vasculitis as a differential diagnosis. Urticarial vasculitis is vasculitis of the skin characterised by inflammation of the small blood vessels rather than urticaria.^[5] Causes include infection (hepatitis B/C, glandular fever or streptococcal infection), medication (penicillins, fluoxetine, thiazides, allopurinol, quinolones or carbamazepine), autoimmune disease, paraproteinaemia and malignancy.



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Differential diagnosis^[1]

- [Erythema multiforme](#).
- [Dermatitis herpetiformis](#).
- [Pemphigoid](#).
- [Erysipelas](#).
- [Eczema](#).
- [Urticaria pigmentosa](#).
- [Chronic pruritus](#).
- [Polymorphic eruption of pregnancy](#).
- [Urticarial vasculitis](#) (as above).

Investigation^[1] ^[2]

The diagnosis is usually made clinically and on history – particularly in acute ordinary urticaria – and no investigations are needed. It can be established once it has been shown that individual lesions only last a few hours. A detailed history may point to a trigger in some cases.

In chronic or recurring cases where investigations are needed, these will be guided by history.

Tests may include:

- FBC.
- ESR or CRP.
- Liver function tests.
- Physical challenge. Cold provocation testing (ice cube), heat provocation test (warm water), pressure testing, UV light testing, exercise or hot bath provocation for cholinergic urticaria.
- Elicit dermatographism.
- Patch testing/prick testing for contact urticarias.
- IgE tests for specific allergens.
- Thyroid autoantibodies if autoimmune mechanism is suspected.
- Exclusion of suspected medication or food.
- Tests for infectious diseases such as hepatitis.
- Skin biopsy (urticarial vasculitis).
- *H. pylori* testing if there are gastrointestinal symptoms.
- Urine dipstick to look for haematuria and proteinuria.

Urticaria treatment and management^[1] ^[2]

Where possible, identify and treat the cause. Nonspecific aggravating factors should be minimised, such as overheating, stress, alcohol, caffeine and medication likely to cause urticaria (eg, non-steroidal anti-inflammatory drugs (NSAIDs) and angiotensin-converting enzyme (ACE) inhibitors). Topical anti-pruritic agents such as calamine lotion or topical menthol 1% in aqueous cream may help ease symptoms.

Non-sedating H₁ antihistamines are the mainstay of treatment. Cetirizine, loratadine and fexofenadine are usual choices. Studies comparing antihistamines are limited and so far no single antihistamine has shown itself to be superior for chronic spontaneous urticaria.^[6] Once symptom control has been achieved, the antihistamine should be continued for 3–6 months.

Where a standard dose of a non-sedating H₁ antihistamine is ineffective, doses of up to four times the standard dose may be used, or another antihistamine added. Evidence for up-titrating the dose varies.^[7] An additional sedating antihistamine such as chlorphenamine may be useful if itch is interfering with sleep. Avoid hydroxyzine if the person has a prolonged QT interval or risk factors for QT interval prolongation in line with recent guidance from the Medicines and Healthcare products Regulatory Agency (MHRA).^[8]

The issue of prescribing in pregnancy is always complex, as there is often a lack of good evidence. The website 'bumps' (best use of medicines in pregnancy) has useful information leaflets, which can be used by a healthcare professional or given to the patient. They have leaflets on all the commonly used antihistamines; as an example, the leaflet on cetirizine says that there is no evidence of the drug being associated with an increase in birth defects, increased risk of miscarriage, premature labour, low birth weight or stillbirth and that there have been no studies assessing longer-term impacts such as on learning and behaviour in older children.^[9] Antihistamines are usually not contra-indicated during breastfeeding.^[10]

Where symptoms are severe, a short course of oral steroids may be appropriate - for example, prednisolone 40 mg daily for seven days.

Second-line options which may be considered in secondary care for refractory chronic urticaria include:

- Antileukotrienes (eg, montelukast), which may provide additional benefit in some selected patients when combined with an H₁ antihistamine; there is little evidence that they are effective as monotherapy.
- Omalizumab, an anti-IgE antibody.^[11] It is effective in 80% but requires monthly injections and relapse is common when it is stopped. The National Institute for Health and Care Excellence (NICE) recommends omalizumab as an add-on treatment for refractory severe chronic spontaneous urticaria.^[12]
- Immunosuppressant drugs such as ciclosporin, mycophenolate mofetil or tacrolimus.

Evidence to help guide choice in second-line treatment is of variable quality.^[13]

When to refer^[1]

- If symptoms are not well controlled.
 - If antihistamines are needed continuously to control symptoms for more than six weeks.
 - If urticaria is painful and persistent, suspect vasculitic urticaria and refer for biopsy and histological diagnosis.
 - Urgent hospital admission is indicated if acute urticaria rapidly develops into angio-oedema or anaphylactic shock.
 - People with acute severe urticaria which is thought to be due to a food or latex allergy.
 - People with forms of chronic inducible urticaria that may be difficult to manage in primary care – for example, solar or cold urticaria.
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Prognosis^{[1] [2]}

This is variable. Most cases of idiopathic urticaria resolve over a period of six months but a minority can persist for many years. Some remit and then relapse. 50% of cases of chronic urticaria have resolved within 3–5 years. At least 20% of chronic urticaria patients requiring referral to secondary care are still symptomatic 10 years after first presentation. Factors associated with lasting duration include severe symptoms, associated angio-oedema and positive antithyroid antibodies.

Complications of chronic urticaria can include insomnia, depression and poorer quality of life. Anaphylaxis may occur in association with acute urticaria.

Further reading

- [Urticaria](#); DermNet NZ
- [Urticaria and angio-oedema: an overview](#); Primary Care Dermatology Society

- [Bernstein JA, Lang DM, Khan DA, et al](#); The diagnosis and management of acute and chronic urticaria: 2014 update. J Allergy Clin Immunol. 2014 May;133(5):1270-7. doi: 10.1016/j.jaci.2014.02.036.
- [Urticaria](#); NICE CKS, August 2021 (UK access only)

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